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The Physiologist

A Publication for Physiologists and Physiology
Orr E. Reynolds, Editor

Volume 22, No. 4, August 1979

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PLEASE POST

ANNOUNCEMENT OF TRAVEL AWARDS

USA NATIONAL COMMITTEE FOR THE INTERNATIONAL UNION OF PHYSIOLOGICAL SCIENCES

The USA National Committee for the International Union of Physiological Sciences (IUPS) is sponsoring a travel grant program to benefit American scientists who could not attend the XXXVIII International Congress of Physiological Sciences in Budapest, HUNGARY, July 13-19, 1980, without such assistance. A limited number of grants will be available. Those eligible to apply for awards are qualified scientists who are citizens or permanent residents of any part of North America, and who plan to participate fully in the Congress. Each applicant will be judged on the merit of his contribution to the Congress in Budapest, considering his training, experience, and potential. Priority will be given to young scientists. Grants will be limited to transportation costs based on the lowest scheduled airline fare from airport of departure and return.

Requests for application forms should be addressed to:

USA National Committee for IUPS
Att: June S. Ewing, Staff Officer
Division of Medical Sciences
National Research Council
2101 Constitution Ave., NW
Washington, DC 20418

Deadline for receipt of completed applications is November 1, 1979. To the degree that it is possible, successful applicants will be notified by December 1, 1979.

APS FALL SCIENTIFIC MEETING

Guest Organizations: Commission on Gravitational Physiology - IUPS
Biosciences Section of the Gerontological Society

October 15-19, 1979
New Orleans Hilton Hotel
New Orleans, Louisiana

CALENDER OF EVENTS

Monday A.M. October 15

Refresher Course - Grand Ballroom C

MONDAY P.M. OCTOBER 15

Refresher Course - Grand Ballroom C
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Reception for new members - Grand Ballroom C—6:30
General Mixer - Grand Ballroom D—8:00

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Turtorial Lectures - Grand Ballroom C
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Endogenous Pyrogen Control
Substance P

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Aging

Miniseminar - Exhibit Area - Grand Salon B
Space Environment Workshop

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Regulation of Breathing: Reflex - Salon 11/14
Cardiac Dynamics - Salon 3/6
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Hypertension I
Immunophysiology

Teaching of Physiology - Learning Resource Center

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Teaching of Physiology - Learning Resource Center

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Local Control of Cerebral Blood Flow
Biotelemetry and Animal Models in the Study of Regulation of Ventilation

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Renal Transport and Metabolism

Teaching of Physiology - Learning Resource Center

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Teaching of Physiology - Learning Resource Center

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Teaching of Physiology - Learning Resource Center

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The Anomalous Osmotic Behavior of Human Red Cells

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Comparative Physiology of Temperature Adaptation - Cambridge

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Peripheral Circulation III

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Synaptic Transmission - Marlborough Suite A

THE EFFECTS OF TRACHEAL OCCLUSION AND VAGOTOMY UPON MEDULLARY RESPIRATORY NEURONS. E. Merrill Adams*, Alan D. Horres and Regina Frayser. Department of Physiology, Medical University of South Carolina, Charleston, South Carolina 29403.

Ventral respiratory group inspiratory neuron activity was recorded in ketamine anesthetized spontaneously breathing dogs. The pattern of neuron activity while breathing room air was typical of that reported previously: a rapid rise to peak frequency of firing, a short plateau, and a brief period of decreasing frequency prior to cessation of the burst. Following bilateral vagotomy, the inspiratory neuron exhibited a ramp-like pattern of almost linearly increasing frequency suddenly terminating at end inspiration. Tracheal occlusion prior to inspiration to prevent lung inflation and stretch receptor excitation resulted in a typical fast rise to peak frequency with a brief plateau and phase of decreasing frequency of firing but with a lengthening of the phase of decreased frequency of firing. Thus, the absence of stretch receptor excitation during occlusion increased the burst duration by lengthening the terminal phase of neuron activity without altering the early rapid rise to peak frequency, whereas vagotomy altered the pattern to a slower gradual linear rise to peak frequency and abrupt cessation of activity. These results suggest that afferent information in the vagus nerves is not only inspiratory inhibitory via stretch receptors but also inspiratory excitatory via other pulmonary receptors.

THE RELATIONSHIP OF EXERCISE PERFORMANCE TO VARIATIONS IN BLOOD ACID-BASE STATUS DUE TO CHANGES IN THE INSPIRED OXYGEN FRACTION. Richard P. Adams and Hugh G. Welch, University of Tennessee, Knoxville, TN 37916

To investigate the possibility that increased performance in hyperoxia might be due to factors other than increased use of O_2, we determined $[H^+]$, PCO_2, Lactic Acid (HLa), and $[HCO_3^-]$ of "arterialized" venous blood in six human subjects on three occasions. The test protocol varied only in inspired O_2 fraction (FIO_2): ($\bar{X}$ = .1682, .2093, .6003). O_2 uptake ($\dot{V}O_2$) and CO_2 output were also measured. Performance times were longer in hyperoxia than in normoxia or hypoxia. However, $\dot{V}O_2$ was not different at exhaustion in normoxia as compared to hypoxia ($p > .1$) or hyperoxia ($p = .09$). Performance, therefore, may not be related to increased O_2 use. Generally, higher FIO_2 values during exercise were associated with decreased HLa and increased $[H^+]$, PCO_2, and $[HCO_3^-]$. However, at exhaustion $[H^+]$ was not different under any FIO_2 ($p = .8$); during recovery the relative concentrations were reversed from exercise. We suggest that the effect of O_2 on performance is related to control of $[H^+]$.

(Supported in part by NSF Grant 5S07RR07088-11 and the East Tennessee Heart Association)

A METHOD TO MEASURE SHEAR STRESS AT THE WALL OF GLASS MODEL ARTERIAL BIFURCATIONS. S. Lee Adamson* (SPON: Dr. A. C. Burton). Univ. of Western Ontario, London, Ontario N6A 5C1

Hemodynamic stresses on arteries, particularly at branch sites, have been implicated in the etiology of arterial disease. A new technique for measuring shear stresses in glass models of arterial branching sites has been developed which allows any number of test sites to be chosen at the end of the experiment. The model is first filled with a viscous white pigment suspension which is subsequently washed out with a dark aqueous dye (Naphthol Blue Black). The light to dark transition of the model, recorded on videotape, occurs only when the pigment layer is thin (< 10% tube diameter). Since the decay rate of this transition is dependent on the shear exerted by the dye solution, video analysis (Videoanalyser 321, Colorado Video Inc.) at any point on the wall of the model can be used to assess shear during videotape playback. In straight cylindrical tubes shear stress can be measured to within 5% of that predicted for Poiseuille flow. In a model with a 90° side branch results of examination of the high shear stress region downstream from the branch are consistent with the limited results available from other studies in models.

(Supported by a grant from the Ontario Heart Foundation and a Studentship from the Medical Research Council).

RELEASE OF ACID HYDROLASES DURING EXTRACORPOREAL CIRCULATION. V.P. Addonizio, J.F. Strauss, L.K. Chang, R.W. Colman, L.H. Edmunds, Jr., Univ. of Penn., Phila., PA 19104

Contact with synthetic surfaces results in platelet release of granule contents. This study demonstrates that during extracorporeal circulation, release of lysosomal enzymes occurs concomitantly. When fresh, heparinized human blood (500 ml) was recirculated for 2 hrs. at 1000 ml/min at 37° C in silicone rubber circuits (N=16) containing a membrane oxygenator (0.95 m^2), plasma levels of the platelet specific protein LA-PF4 rose from < 0.5 to 14 ± 2 µg/ml plasma, indicating extensive release of platelet ∝ granule contents. Concurrently, plasma activity of the lysosomal hydrolytic enzymes, acid phosphatase and N-acetyl-B-glucosaminidase increased three and four fold respectively. Platelet inhibition with prostaglandins E_1 and I_2 and reducing surface affinity for platelets with albumin prevented release of LA-PF4 but failed to alter release of hydrolases. Lidocaine (10 µg/ml), however, effectively inhibited hydrolase release without altering secretion of LA-PF4. The failure of platelet inhibitors to block secretion of lysosomal enzymes and the efficacy of lidocaine without altering LA-PF4 secretion suggest that leucocytes, not platelets, are the source of released lysosomal enzymes. Release of hydrolytic enzymes during cardiopulmonary bypass may cause endothelial cell injury and thus contribute to the increased vascular permeability associated with extracorporeal circulation.

THE EFFECT OF VOLUME OVERLOAD ON LEFT VENTRICULAR WEIGHT AND CELL SIZE. Gerald E. Adomian*, Sheryl Osborne* and Michael M. Laks. Harbor_UCLA Medical Center, Torrance, CA 90509.

We have demonstrated that electronic pacing of the adult dog heart produced an increase in left ventricular (LV) weight (wt) but no increase in myocardial cell size. We hypothesized that myocardial hyperplasia was produced.

The aim of this study was to determine if myocardial hyperplasia can be produced in a LV volume overload model (femoral AV fistula (AVF)). AVFs were produced in six adult mongrel dogs. After 3-9 weeks, LV samples were removed from AVF and 7 normal dogs for microscopy.

	Lv Wt (gm)	Length (µ)	Width (µ)		CO (L/min)
Norm	66±3*	117±5	21±1	Pre AVF	4.9±0.3
AVF	78±3	121±8	22±1	Post AVF	7.3±0.5
P	0.025	0.5	0.2		0.005

After AVF, correlation coefficients between increase in cardiac output vs LV wt, cell length, and width were 0.95, 0.44, and 0.42 resp. In conclusion, muscle mass increased proportionally to volume overload suggestive of physiological hypertrophy. However, disparity between LV cell size and LV wt suggests that myocardial hyperplasia and/or fibrosis may have occurred concommitantly.

*X±SEM

METABOLIC EFFECTS OF ALANINE AND GLUCOSE ON INTESTINAL TRANSMURAL PD AND NET NA TRANSPORT IN FRESHWATER PRAWNS. Gregory A. Ahearn, James A. Wyban*, and Leigh A. Maginniss. Dept. of Zoology, Univ. of Hawaii, Honolulu, Hi. 96822

Mucosal addition of 1 mM L-alanine or D-glucose to the perfused intestine of the prawn, Macrobrachium rosenbergii, initiated an increase in transmural potential difference (PD) (serosa became more positive). Luminal perfusion with 1 mM D-alanine did not have an effect on the spontaneous PD across the tissue. Addition of 10 mM L-alanine to the serosal side of the tissue brought about a slow elevation of PD with the same polarity as with luminal alanine. The alanine-evoked PD was a hyperbolic function of luminal [alanine] and was abolished with serosal addition of 0.5 mM ouabain. Luminal 1 mM L-alanine stimulated net 22Na flux from mucosa to serosa from 1.29 ± 0.45 (control) to 2.83 ± 0.66 µmoles cm^{-2} hr^{-1}. Extensive metabolism of 1 mM 3H-L-alanine and 3H-D-glucose occurred during transmural movements of these solutes. Quantitatively insignificant amounts of Na were co-transported with 3H-alanine into the epithelium (approx. 52 nMoles cm^{-2} hr^{-1}) to account for increased net transmural Na flux in the presence of the amino acid. Electrogenic effects of luminal nutrients result from their catabolism to fuels for a baso-lateral Na-K-ATPase. Increased Na-pump activity increases organic solute-independent Na entry into cells and net transmural Na transport. This consequently elevates transmural PD. (Supported by NSF grant PCM 76-84105).

MECHANISMS OF PROPRANOLOL PROTECTION FROM ISCHEMIC ST RESPONSE TO EPINEPHRINE INFUSION. I. Ahmad*, M.F. Wilson and E. Schechter*. Veterans Administration Medical Center and Dept. of Medicine, OUHSC, Oklahoma City, Oklahoma 73104

While evaluating epinephrine infusion (Epi) as a stress test in 23 patients (Pt) with angiographically proven coronary artery disease we noted 12/12 Pt not receiving propranolol (NP) had a positive test, while 1/11 Pt on propranolol (P) had a positive test ($P < .001$). To investigate the reasons for this difference hemodynamic responses in the two groups were compared. Doses of Epi from .03 to .24 mcg/kg/min were infused. The ECG, BP, LVET and PEP were recorded at rest and during 5th min of each dose. In NP HR increased from 75±7 to 90±9/min and systolic BP from 124±25 to 138±34 mmHg, resulting in an increase of rate pressure product (RPP) from 94±26 to 123±34. In P HR decreased from 64±7 to 48±11 and systolic BP increased from 128±22 to 203±32 resulting in a small increase in RPP from 78±13 to 98±34. In NP PEP corrected for HR (PEPc) decreased from 149±22 to 123±13 and PEP/LVET ratio decreased from .45±.10 to .35±.06. In P similar decreases were noted for PEPc from 148±13 to 129±26 and PEP/LVET from .42±.07 to .33±.09, reflecting increased contractility in both groups. The endocardial viability ratio (EVR), an index of myocardial O_2 supply/demand, decreased in NP from 1.26±.31 to .84±.23 but increased in P from 1.38±.30 to 1.50±.49. The protective effect of P in blocking the ischemic ST change to Epi was due to increased O_2 supply from prolonged diastolic time and increased diastolic BP.

TEMPORAL RELATIONSHIP BETWEEN PHOSPHORYLATION OF THE 20,000 DALTON MYOSIN LIGHT CHAIN (LC) AND FORCE GENERATION IN ARTERIAL SMOOTH MUSCLE. M. O. Aksoy and R. A. Murphy. Dept. of Physiol., Univ. of Va., Charlottesville, VA 22908

Biochemical evidence suggests that Ca^{++} may regulate contraction in smooth muscle by stimulating a kinase which phosphorylates the LC, initiating the actin-myosin interaction. This study shows that LC phosphorylation occurs on activation of living tissues and that phosphorylation and dephosphorylation precede contraction and relaxation, respectively, in accordance with the proposed regulatory mechanism for Ca^{++} in smooth muscle. Strips of hog carotid media were quick-frozen at various times during contractions induced by high K^+ solutions. A 2-dimensional gel electrophoresis system was used to quantitatively estimate phosphorylated and non-phosphorylated LC in tissue homogenates. Unstimulated tissues with a low level of tone exhibited about 15% LC phosphorylation. On K^+ stimulation this rose rapidly to 60% within 1 min, preceding the development of force. On return to normal salt solutions, the LC phosphorylation returned to basal levels more rapidly than active force. However, during prolonged stimulation, force was maintained at plateau levels while the percent phosphorylated LC declined from the peak value to 35-40% after 2-4 min. This suggests that force can be maintained in arterial smooth muscle with decreased levels of LC phosphorylation. (Supported by NIH grants 1 P01 HL19242, 1 P60 AM22125, 5 S07 RR05431, and 1 F32 HL05796)

HOW DOES FUROSEMIDE REDUCE SHUNT IN LOW PRESSURE PULMONARY EDEMA? J. Ali*, C.J. Fisher*, K. Duke* and L.D.H. Wood*. (Spon: Arnold Naimark). University of Manitoba, Winnipeg.

Furosemide (F) reduces shunt in canine oleic acid (OA) pulmonary edema (E) without reducing E. To investigate the mechanism, we studied 20 dogs before (1) and 2 hours after (2) OA was injected into one lower lobe (LL), and again (3) 30 minutes after F (1 mg/kg) was given to 10 dogs (A) and saline (1 ml) to the other 10 (B). Lobar shunts (Q_{SL}/Qt) were calculated from O_2 contents sampled from LL venous catheters, and lobar blood flow (Q_L/Qt) was determined by radionuclide microspheres. Q_{SL}/Qt and Q_L/Qt of the uninjured LL (LLni) were normal in each condition, but the mean ± SD values of the injured LL (LLi) were (* denotes $P<.05$ by paired-t, 1 vs. 2, 2 vs. 3):

	Q_{SL}/Qt %		Q_L/Qt %	
	A	B	A	B
1	7.6 ± 2.3	4.5 ± 2.6	26.7 ± 6.6	29.4 ± 1.9
2	*40.1 ± 20.6	21.4 ± 14.0*	*18.2 ± 4.8	20.1 ± 3.5*
3	*28.6 ± 20.7	53.8 ± 26.9*	*21.6 ± 6.4	16.1 ± 4.4*

In B, Q_{SL}/Qt increased and Q_L/Qt decreased progressively. In A, F reduced Q_{SL}/Qt and increased Q_L/Qt. The wet weights (W) of LLi were not different between A and B, and were twice W of LLni. Pulmonary artery and alveolar pressure did not change with F. We conclude that F reduces shunt in canine OAE by pulmonary vasoactivity which increases blood flow to ventilated lung units adjacent injured flooded air spaces. (Supported by MRC of Canada).

EFFECTS OF NOREPINEPHRINE AND PHENOXYBENZAMINE ON CEREBRAL HEMODYNAMICS. John B. Allotey*, Denise Holder* and Bernell Coleman. Dept. of Physiology, Howard Univ. Coll. of Med., Washington, D. C. 20059.

The effects of intracarotid infusions of norepinephrine (NE), (0.04 μg/kg/min for 10 min), and phenoxybenzamine (PBZ), (0.1 mg/kg/min for 15 min) on total and regional cerebral blood flow (CBF and rCBF) were studied in anesthetized dogs using sequential left atrial injections of differently labelled 15 μm microspheres. Mean aortic pressure (MAP) and internal carotid artery pressure (ICAP) were measured simultaneously. The table below summarizes the results. Values are expressed as Mean ± SEM; differences compared to control significant at: $^*P<0.05$, $^{**}P<0.01$, $^{***}P<0.005$.

	Control	NE	PBZ	NE(after PBZ)
MAP	137±10	140±8	119±13*	102±16*
ICAP	112±13	118±14	97±14***	82±16***
CBF	22±2	25±4	27±4	28±2*
CVR (% of Control)	100%	94±14%	71±7%*	57±8%**

NE did not alter CBF, rCBF or cerebral vascular resistance (CVR) in any brain region. PBZ caused a fall in resistance in all regions but only the pons showed increased rCBF after 15 min of PBZ infusion. There were regional and time-dependent differences in flow response to PBZ. (Supported in part by NIH/BRS Grant RPG 470-P and NIH/NIGMS (MARC) Grant RPG 2046).

EFFECTS OF NEGATIVE END EXPIRATORY PRESSURE ON INTRACRANIAL PRESSURE. Frank D. Allman*, Barry Burns and Mark C. Rogers* Johns Hopkins Hospital, Baltimore, Maryland 21205

We evaluated the effect of Negative End Expiratory Pressure (NEEP) on intracranial pressure (ICP) in 6 anesthetized, paralyzed and ventilated dogs in the prone position at normal and artifically elevated ICP. ICP was measured with a catheter placed in the cisterna magna and referenced to the level of the auditory canel. Right atrial, esophageal, airway, and femoral artery pressures were also measured and cardiac output ($\dot{Q}$) was measured by thermodilution catheter. During inspiration (Harvard piston respirator), airway pressure was 8 torr during both NEEP and control ventilation; during expiration, NEEP airway pressure was -45 torr and control airway pressure was 0 torr. Despite the fact that $\dot{Q}$ was the same during control and NEEP ($P=.09$), the application of NEEP resulted in a prompt decrease in ICP from control value of 3.6 torr to 0.33 torr ($P=.018$, paired comparisons t-test). Three animals with low initial ICP developed negative ICP to -15 torr which persisted throughout NEEP. Even with elevated ICP produced by injection of 1-2cc mock CSF, ICP decreased faster with NEEP than with control ventilation. NEEP appears to lower ICP by either a reduction in cerebral venous blood volume or by alteration in volume of the CSF space produced by transmission of NEEP to the dura of the thoracic spinal cord. (Supported in part by N.I.H. Grant # 1R23 GM25790-01).

PREVENTION OF GALACTOSAMINE (GalN) INDUCED LIVER INJURY BY MACROPHAGE SUPPRESSION. A. Al-Tuwaijri*, K. Adkamar*, T. Godiwala* and N. Di Luzio. Depts. of Physiology and Medicine, Tulane University School of Medicine, New Orleans, LA 70112.

The Reticuloendothelial System (RES) has been implicated in GalN induced liver injury since, a correlation has been suggested between phagocytic function, endotoxemia and development of liver cell necrosis. In order to further evaluate this concept, the influence of GalN on liver function and histology was ascertained in control and methyl palmitate-treated rats. Methyl palmitate has been demonstrated to be a selective RES suppressant. Plasma concentration of glucose, bilirubin, cholesterol, albumin, lactic dehydrogenase, alkaline phosphatase and glutamic oxalacetic transaminase (SGOT) as well as the clearance of BSP was determined 24hours later ip administration of GalN (100mg/100g). Administration of GalN to control rats results in significant 7-fold elevation in SGOT, and 10% retention of BSP compared to control value of 0.7%. Hypoglycemia (49%↓) was also observed. Histological studies denoted hepatic necrosis and lymphocytic infiltration. Methyl palmitate administration did not induce any alteration in either the biochemical or histological parameters. However, pretreatment with methyl palmitate prevented GalN induced alterations in glucose, SGOT and BSP. Liver necrosis and lymphocyte infiltration were also reduced in methyl palmitate-treated GalN injected animals. The protective effect of methyl palmitate may be due to its unique ability to modify GalN-induced endotoxemia. (supported by NIH Grant AA-00309).

UTILITY OF PONY LEFT VENTRICLE IN STUDY OF NORMAL AND ISCHEMIC TRANSMURAL MYOCARDIAL PHENOMENA. J.F. Amend, J.E. Shapland,* D.M. Griggs, and H.E. Garner. Univ. of Nebraska-Lincoln, NE and Univ. of Missouri-Columbia, MO. 65211

Transmural heterogeneity in vascular, metabolic, or mechanical functions of left ventricular myocardium has been observed in several species. We considered that further resolution of such transmural phenomena might be supported by a model system in which greater mass of ventricle provided greater wall thickness, and therefore broader separation of subepicardial and subendocardial layers. Accordingly a series of pony hearts was examined, first in terms of specific anatomical criteria, and secondly in relation to regional mechanical, metabolic, and vascular phenomena. We noted that the pony heart, like the human heart, exhibits right coronary predominance. Further, one xeroradiograph of barium-gelatin injected pony coronary arterial distributions showed the presence of a subendocardial plexus of collateral vessels, again analogous to the human distribution.

It was possible to separate the pony ventricular wall into multiple layers from epicardium to endocardium, while retaining adequate sample mass for metabolic analysis. Size of surface coronary branches allowed dissection and occlusion with discretely localized rather than global effects of ischemia. The increased wall thickness also facilitates implantation of ultrasonic or other types of dimension gauges. The similarities in pony and human hearts, and the utility of the larger ventricular mass would appear to encourage its use.

AGE DEPENDENT CHANGES IN THE TEMPERATURE-ACTIVITY RELATIONSHIP FOR THE FREE LIVING NEMATODE CAENORHABDITIS ELEGANS. Gary L. Anderson and David B. Dusenbery*. School of Biology, Georgia Institute of Technology, Atlanta, GA. 30332

A variety of functional changes accompany aging in nematodes; among these is a reduction of neuromuscular function. Locomotor function is also temperature dependent in these, as in other, ectothermic species. The objective of this study was to determine if there are age related changes in the thermal dependence of locomotor activity in the free-living nematode, Caenorhabditis elegans. Synchronous populations of worms were grown monoxenically on petri plate cultures maintained at 15°C. Worms were collected for measurement of locomotor activity at 3 day intervals for a period of 15 days. Locomotor activity was accessed photographically at experimental temperatures within the range 6° to 30°C. The proportion of worms active at a given instant at growth temperature declines with age; activity at 15°C of worms 12 to 15 days old is more than 20% below that of worms 3 to 6 days old. There is also an effect of age upon the cold limit of locomotor function. The temperature at which 20% of the worms in a sample (50-150 worms) are active is approximately 3°C lower in 3 to 6 day old worms than in those 12 to 15 days old. We conclude that there are age dependent changes in the temperature-activity relationship in C. elegans, and that these are manifest not only at or near growth temperature but also as shifts in the cold limit for locomotor function.

DETERMINATION OF STRUCTURAL PROTEINS IN CELLS AND TISSUES. Peter J. Anderson, Dept. of Biochemistry, University of Ottawa, Ottawa, Canada.

Non-enzymatic proteins such as the microfilament forming protein actin and the microtubule forming protein tubulin have important roles in cell function. Fundemental to the understanding of structure-function relationships of such proteins is the accurate determination of their amount in cells and tissues. Since these proteins do not have any easily measured biological activities, methods to allow their quantitation in complex mixtures have been developed. Double radioisotope labelling and subsequent generation and isolation of peptides specific to a given protein provide an accurate, sensitive means of protein quantitation that is independent of the subcellular location, the state of aggregation and the solubility of the protein to be determined. Using such procedures the amounts of actin in cultured chicken and human fibroblasts and in skeletal muscle have been determined. The amounts of tubulin in brain and in 3T3 cells have also been measured. (Supported by MRC, Canada).

BENEFICIAL EFFECT OF $NaHCO_3$ ON RABBIT MYOCARDIUM:ENHANCEMENT OF ATP LEVELS AND MECHANICAL PERFORMANCE. D.A.Angello*E.E.Rau, and J.Tsai* Dept. Physiology, UCLA, Los Angeles, CA., 90024

The effect of solutions containing 12 mM or 28 mM $NaHCO_3$ on ATP and developed tension(DT) was studied in arterially perfused septa paced at 54/min at 37°C. Septa were perfused with a modified Ringer's solution also containing glucose; 5.6 mM, L-arginine; 1mM, pyruvate; 2mM and insulin 20 IU/l. A pH of 7.4 was maintained by equilibrating solutions with 98/2%-O_2/CO_2 or 95/5%-O_2/CO_2. Control DT was determined 30-40 min after cannulation when DT was stable. Septa were quick frozen after 2-4 hrs of perfusion and assayed for ATP. The following results were obtained (values are $\bar{x}$ ±SE, (n)):

	ATP	DT (% Control)	
	(μm/g dry tissue)	60 min	150 min
12mM HCO_3	14.9 ± 0.6 (27)	99 ± 1 (29)	83 ± 3 (19)
28mM HCO_3	18.2 ± 0.7*(12)	100 ± 2 (12)	103 ± 4*(11)

*p<.001 compared to 12 mM

These results indicate that septa perfused with 28 mM $NaHCO_3$ have significantly higher ATP levels and maintain DT better than septa perfused with 12mM $NaHCO_3$. The mechanism for these observations is unknown. It is possible that elevation of extracellular $NaHCO_3$, by improving intracellular buffering capacity, may stimulate anaerobic metabolism resulting in increased ATP levels and, therefore, enhanced mechanical performance. (Supported by American Heart Association, Greater Los Angeles Affiliate #570-C1 and NIH HL 21783-02).

PROTECTIVE ACTION OF APROTININ IN ACUTE TRAUMATIC SHOCK

Haruo Araki and Allan M. Lefer, Dept. of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA., 19107

The anti-shock actions of the protease inhibitor, aprotinin was examined in rats during traumatic shock. Trauma was induced by tumbling the pentobarbital-anesthetized rats in a Noble-Collip drum for 425 rotations at a speed of 45 rpm. In sham-operated control rats, intravenous administration of aprotinin (20,000 or 40,000 KIU/kg) showed no changes in mean arterial blood pressure and heart rate. In traumatized rats, aprotinin administration increased the arterial blood pressure gradually by 0.5 hr and then maintained this relatively higher pressure compared to rats given behicle. At a dose of 20,000 KIU/kg, aprotinin prolonged survival time of traumatized rats, to 2.1 ± 0.3 hr (mean ± SE, $p<0.05$) and at 40,000 KIU/kg survival was prolonged to a greater extent (3.1 ± 0.4 hr, $p<0.001$) compared to rats given only vehicle (1.1 ± 0.2). The improved survival in both aprotinin treated groups was accompanied by inhibition of the plasma accumulation of the cardiotoxic peptide, myocardial depressant factor (MDF). However, neither dose of aprotinin prevented the plasma accumulation of the lysosomal enzyme, cathepsin D. Aprotinin exerted a beneficial effect on Noble-Collip drum trauma shock in rats possibly by its potent inhibitory action on pancreatic proteases and the resultant prevention of MDF formation.

TISSUE DIFFUSION DISTANCE, MYOGLOBIN CONCENTRATION, P_{O_2} AND P_{CO_2} IN A COMPLETELY FOSSORIAL RODENT, THE MOLE RAT. R. Arieli* and A. Ar* (Spon: H.D. Van Liew). Dept. Zoology, Tel-Aviv Univ., Tel-Aviv, Israel.

The mole rat (*Spalax ehrenbergi*),which inhabits East Mediterranean soils, lives its entire life in sealed galleries and feeds by burrowing to plant roots. Energetic metabolism of the mole rat is unaffected by levels of hypoxia and hypercapnia that are deleterious to other mammals. Although it has normal resting metabolic rate, its ventilation and heart rates are low compared to other mammals of comparable size. Tissue characteristics were compared to the white rat. Mean diffusion distance in skeletal muscles was 21μ compared to 32μ for the white rat. Subcutaneous P_{O_2} and P_{CO_2} were 15 and 86 torr compared to 45 and 63 for the white rat. Masseter myoglobin was 3.3 times more concentrated in the mole rat than in the white rat. Assuming that capillary tensions approximate the tension of subcutaneous gas pockets, the muscle $\dot{M}_{O_2}$ can increase by 5 fold above the resting level for the mole rat compared to 4 for the rat. The small diffusion distance theoretically enables muscle $\dot{M}_{O_2}$ to increase by 10 fold when capillary-to-tissue P_{O_2} difference is 31 torr, whereas 117 torr difference is needed for rats. The tissue's capacity to utilize O_2 at low P_{O_2} and its resistance to high P_{CO_2} and low pH account for the high extraction of O_2 from the blood and the cardiopulmonary system's low output, low sensitivity to hypoxia and hypercapnia, and ability to increase function in extremes of low O_2 and high CO_2.

PRELIMINARY STUDIES UPON THE ANATOMY AND PHYSIOLOGY OF THE CORONARY VASCULATURE. J.A. Armour, G.A. Klassen and M. Rodger.* Department of Physiology and Biophysics, Dalhousie University, Halifax, Nova Scotia, B3H 4H7

The coronary vasculature is considered to have arterial, venous and capillary components. Using an open chest canine model we cannulated the small coronary epicardial veins and arteries, as well as the coronary sinus. We also measured left ventricular cavity and intramyocardial pressures, along with aortic pressure. During control states a minimal gradient was demonstrated from central to peripheral coronary arteries. However a peak systolic gradient of up to 30 mm Hg was present from small (1 mm diameter) to large veins (i.e., coronary sinus). The coronary venous pressure gradient was specifically responsive to neural, metabolic and pharmacologic interventions. Anatomic relationships of the coronary veins and arteries were displayed by injecting the vascular system with latex while the heart was beating. These casts demonstrated that the coronary vasculature has not only small branching vessels but also numerous large venous lakes lying between muscle bundles in the inner layers of the heart. Vascular control apparently is dependent upon alterations of coronary tone, particularly within the venous system.

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RELATIONSHIP BETWEEN MUSCLE AREA SHOWING GLYCOGEN LOSS AND MUSCULAR FORCE DURING LOCOMOTION. Robert B. Armstrong and C. Richard Taylor. Oral Roberts Univ., Tulsa, OK 74171 and MCZ, Harvard Univ., Cambridge, MA 02138

This experiment was designed to test the hypothesis that glycogen loss (GL) from fibers can be used to quantify active muscle cross-sectional area (MA) during locomotion. Muscular forces were increased by 24% during level running (30 m x min^{-1}) by pack-loading rats with a mass equal to 24% of their body mass. MA showing GL in the elbow and ankle extensor muscles of the loaded rats were compared with those in unloaded animals running at the same speed. MA displaying GL increased nearly proportionately to the added load in both the elbow (+17-33%) and ankle (+16-18%) extensor groups. However, the contributions by individual muscles within the groups to the increased total active MA varied. In the loaded rats, e.g., the MA of triceps brachii muscle, lateral head showing GL increased 67-72%, whereas in the medial and long heads it increased 21-33% and 0-26%, respectively. The increases in MA with GL in the loaded rats primarily resulted from loss in fast-twitch-glycolytic fibers. In conclusion, the approximate proportionality we observed between increased muscular force and increased MA with GL supports the validity of this technique for studying active MA during locomotion. The findings emphasize the importance of considering fiber recruitment within muscle groups rather than in individual muscles.
(Supported by NIH Grants AM25472 & AM18140)

CAPSAICIN INDUCED CARDIOVASCULAR CHANGES ELICITED FROM THE INFERIOR VENA CAVA OF THE CAT AND DOG. Juliet H. Ashton, Gary A. Iwamoto,* John C. Longhurst,* and Jere H. Mitchell. Univ. of Texas Health Science Center, Dallas, TX 75235

Even though there is some evidence for the existence of neuronal receptors in the great veins, the cardiovascular (CV) changes resulting from stimulation of these receptors have not been documented. To separate CV effects due to capsaicin (CAP) stimulated receptors located in the inferior vena cava (IVC) from those located in the cardiopulmonary region, the IVC was cannulated below the right atrium (RA) in 11 cats and 7 dogs. An equivalent dose of CAP (average 45µg/kg) was injected into the femoral vein (FV) of the cats and the dogs. CAP contaminated venous return blood was discarded and fresh equilibrated reservoir blood was returned to the RA through the external jugular vein during each injection period. RA and IVC pressures were maintained constant. CAP injected into the cats significantly increased systolic blood pressure (SBP) from 87±7 to 121±12 mmHg (mean±SEM) and peak dP/dt from 2886±243 to 4168±377 mmHg/sec (both $p<.002$). The beginning of the CV response after injection was 8.3±1.2 sec. Heart rate (HR) did not change. CAP injected into the FV of the dogs did not change SBP, peak dP/dt or HR. Thus, stimulation of receptors in the IVC by CAP significantly increases blood pressure and myocardial contractility in cats but not dogs. The physiological meaning of this response in cats and the reason for the species difference needs further investigation.

SARALASIN INHIBITS RENAL PROSTAGLANDIN E_2 BIOSYNTHESIS. A. Attallah* R. Stahl* D. Bloch* and J.B. Lee. SUNYAB, Buffalo, N.Y. 14215

Although there is much evidence implicating a close interrelationship between the renin-angiotensin and the prostaglandin systems, the precise interactions are yet unclear. We undertook this study to re-evaluate the influence of angiotensin II blockade with saralasin on renal PGE_2 biosynthesis utilizing a newly developed in vivo-in vitro approach. Saralasin was administered to conscious rabbits (270 µg/kg S.C.), the kidneys removed 90 min. later, and slices of cortex and inner medulla extracted for PGE_2 immediately and following 30 min. incubation in Krebs-Ringer HCO_3^-, 37°C. PGE_2 was analysed by specific radioimmunoassay. De novo biosynthesis was calculated as the difference between initial PGE_2 and that following incubation. Saralasin at doses which completely blocked the vasopressor action of 0.2 µg angiotensin II displayed no measurable effects by itself on blood pressure. However, saralasin significantly reduced cortical PGE_2 biosynthesis from 0.205 + 0.027 (n=12) to 0.028 ± 0.006 (n=12) µg/g/30 min ($p < 0.001$) and inner medullary synthesis from 45.0 + 7.55 (n=12) to 23.5 +0.96 (n=12) µg/g/30 min ($p < 0.01$). We conclude that renal PGE_2 biosynthesis may normally be modulated by angiotensin II.

HEPATIC SUBSTRATE BALANCE IN HYPERMETABOLIC, INJURED PATIENTS. L.H. Aulick, C.W. Goodwin,* S.L. Brahman,* R.A. Becker,* D.W. Wilmore.* USA Institute of Surgical Research, Brooke Army Medical Center, Fort Sam Houston, Texas 78234.

To determine the role of the splanchnic bed in substrate exchange in injured man, arterial (A) and hepatic venous (HV) catheters were placed in 10 resting, noninfected, post absorptive burn patients (mean burn size 48.5% TBS) 1-2 weeks post injury. Splanchnic blood flow, determined by ICG clearance, was elevated (2.811 ± 0.215 L/min, mean ± S.E.) and hepatic glucose production increased (1.14 ± 0.07 mM/min), 1½-2 times rates reported for post absorptive normals and fasting subjects. Splanchnic lactate and pyruvate uptakes were 0.95 ± 0.22 and 0.05 ± 0.01 mM/min. These precursors could contribute to as much as 45% of the glucose produced. HV plasma amino acid levels were less than A for 7 of the 25 measured (Thr, Asp, Gly, Ala, Meth, Tyr and His). With complete conversion to glucose, these 7 amino acids would account for 26% of the glucose; alanine alone providing approximately half. Normal hepatic extraction ratios and normal or depressed serum levels of glucose precursors persisted despite the previously reported increase in peripheral release of these substrates. Accelerated liver 3-carbon uptake and increased glucose production in injured man suggest that active changes in intrahepatic metabolism occur in concert with the rise in peripheral release of glucose precursors.

SYMPATHO-ADRENAL MEDULLARY ACTIVITY IN RESPONSE TO COLD EXPOSURE AND STARVATION. Edward V. Avakian* and Steven M. Horvath. University of California, Santa Barbara, CA 93106

The functional state of the sympathetic nervous system (SNS) and adrenal medulla was studied in young male rats after 2 days of starvation and/or 7 hours of cold exposure (4°C), imposed separately and simultaneously. Differential SNS activity to the heart (H) and spleen (S) was assessed by measuring endogenous organ norepinephrine (NE) content after blockage of NE synthesis with αMethyl-Tyrosine (αMT). Plasma and tissue catecholamines were radioenzymatically assayed. NE synthesis inhibition significantly decreased plasma NE levels up to 60% in control and all experimental groups, suggesting enhanced NE reuptake in response to increased impulse activity or αMT. Plasma epinephrine was highest in the Cold>Fast+Cold>Fast>control. Fasting markedly depressed SNS activity to both H and S compared to control values. Cold exposure was the greatest stimulus for SNS activity to both organs, but induced 25% more activity to H than S. Fasting+Cold elicited little SNS activity to S, substantial activity to H, but less than that by Cold alone. These results indicate that SNS impulse activity to different organs is selective and independently regulated, depending on the specific nature of the stressor.

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PHYSIOLOGICAL DIFFERENCES BETWEEN MEN AND WOMEN IN RESPONSE TO PROLONGED EXPOSURE TO DRY HEAT. B. A. Avellini*, Y. Shapiro*, and K. B. Pandolf (Spon: R. Francesconi). U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760

Heat acclimatized men (n=10) and women (n=9) were exposed to hot dry conditions (49°C, 20% rh) for 4 hrs to determine the effect of prolonged work in the heat on differences in physiological responses between the sexes. Each hr of exposure consisted of 10 min resting and 50 min walking at 1.34 m/s (metabolic rate = 195 and 170 W/m^2 for men and women, respectively). No significant difference in rectal temperature (T_{re}) was found between the sexes for each hr of exposure. Heart rate (HR) of women, however, averaged 10-15 b/min higher than that of men with the difference diminishing with time. Mean skin temperature ($\bar{T}_{sk}$) was also significantly higher in women throughout the exposure. For both men and women, the 4th hr T_{re}, HR and $\bar{T}_{sk}$ were significantly higher than the preceding 3 hrs. Metabolic rate did not change with time for either sex. The evaporation rate of men was 10% greater than that of women which corresponded to their 11% greater total heat load (M+R+C); heat conductance averaged 52% higher in women. No differences between men and women in total sweat rate (SR) or sweat sensitivity, as indicated by $SR/\Delta T_{re}$, were evident. It was concluded that: a) prolonged exposure to dry heat does not accentuate physiological differences between men and women; b) women are able to secrete sweat at rates comparable to men over a 4-hr period; c) women are under more cardiovascular stress in the heat when working at the same absolute work load as men.

MODULATION OF PHRENIC MOTONEURON TIMING BY OROPHARYNGEAL AND/OR PULMONARY PROPRIOCEPTORS IN MAN. Kenneth Axen* (SPON: F. Haas). Department of Rehabilitation Medicine, School of Medicine, New York University, New York, New York 10016.

Temporal alterations in phrenic motoneuron output during single-breath inspiratory loads in cervical cord-injured subjects were inferred from the difference between observed Ti and Te responses and those predicted assuming identical Pmus wave forms in the unloaded and loaded states. The ratio of the observed to predicted Ti response for the group did not differ significantly from control at any load studied, indicating that the average duration of the phrenic discharge remained constant under load conditions. The ratio of the observed to predicted Te response, however, monotonically decreased with elastic and increased with resistive loading, indicating that the silent period between successive phrenic bursts shortened with elastic loads and lengthened with resistive loads. The magnitude of this effect was proportional to the Ti response measured at the mouth ($P<.001$), but not to responses reflecting diaphragmatic force, movement or duration of contraction (i.e., peak Pmus, (V_T/Ti)/(predicted V_T/Ti), peak Paw, V_T, V_T/Ti or Ti/predicted Ti). These findings suggest that oropharyngeal and/or pulmonary proprioceptors able to detect the duration of the loaded inspiratory airflow and/or its accompanying subatmospheric airway pressure (rather than possible diaphragmatic length or tension proprioceptors) modulate the timing of the phrenic motor output in man.

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RELEASE OF GASTRIN IN RESPONSE TO AN INTESTINAL MEAL IN DOGS. A. Ayalon,* P. Devitt,* S. Guzman,* R.L. Suddith,* P.L. Rayford, and J.C. Thompson. Department of Surgery, The University of Texas Medical Branch, Galveston, Texas 77550.

The hypothesis that antral gastrin (G) is released in response to an intestinal meal is controversial. There is evidence for and against such an enterobombesin mechanism. We have measured the effect of duodenal instillation of liver extract on antral gastrin release. Methods: G levels were measured simultaneously in the antral vein (AV), duodenal vein (DV) and peripheral vein (PV). AV, DV and PV were cannulated in 6 anesthetized mongrel dogs prepared with innervated antral pouches. The duodenum and antrum were separated by complete division and suture. Liver extract (10%, pH 7) was infused intraduodenally for 1 hour. Results: Mean basal G values (pg/ml ± SE) were: AV, 236±74; DV, 40±5 and PV, 42±5. The results are expressed as percent of basal levels ± SE (* = significant increase above basal, p <0.05).

Time (min)	15	30	45	60	90	120
AV	162±29%	172±32	238±45*	240±22*	350±60*	287±52*
DV	110±12	120±17	118±13	142±34	162±40	157±25
PV	100±10	102±9	101±6	98±8	122±13	113±14

Conclusions: Antral gastrin is released in significant amounts in response to an intestinal meal. The fact that this rise is not seen in peripheral blood may be due to interference with gastrin dynamics because of antral vein cannulation.

A RAPID, ACCURATE METHOD FOR THE DETERMINATION OF RODENT BODY COMPOSITION. Ayres* J.J., Wilson* C.W., Kaman* R.L., & Raven, P.B., Dept. of Biochemistry and Institute for Human Fitness, Texas College of Osteopathic Medicine, Ft. Worth, TX 76107.

The current methodology for rodent body composition, while accurate and reproducible, involves several technically elaborate and time consuming techniques. (Kjeldahl protein analysis and either ether or methanol:water extraction of lipids) The present modifications (TCOM) resolve these problems without compromising accuracy or precision. Water analysis utilizes lyophilization of test tube samples. Ash determination follows standard techniques. Lipid analysis is accomplished by 30 minutes of inversion of dry homogenate in a butanol:diisopropyl ether (40:60) solvent followed by oven drying of the delipidated portion. Protein is measured as the weight lost during ashing, correcting for % fat. Comparisons with an outside laboratory (VPI) employing the Kjeldahl and ether extraction procedures showed no significant differences as outlined in Table.

	Protein	Fat	Ash
TCOM	20.4% ±0.2	11.23% ±0.27	3.38% ±0.22
VPI	20.58% ±0.2	11.32% ±0.29	3.11% ±0.27

The total recovery of the method was 99.97% ± 0.043. The results of these modifications provide a significant reduction in the time and cost necessary to complete the body composition analysis and the intricacy of the procedures involved.

ADRENAL MEDULLARY CATECHOLAMINE SECRETION SUPPORTS RENOVASCULAR RESISTANCE DURING CAROTID SINUS STIMULATION. E.M. Badder*, J.F. Seaton* and T.S. Harrison. Penn. State Univ., Depts. of Surg. & Physiol., Hershey Med. Ctr., Hershey, Penn. 17033 and Univ. of Md., Dept. of Surg., Baltimore, Md. 21202.

Are baro-stimulated regional neurovascular reflexes strengthened by adreno-medullary secretion raising endogenous plasma catecholamine content? Anesthetized (Na pentobarbital 70 mg/kg, 35 mg/kg prn, 98% O_2/2% CO_2, endotracheal volume ventilation) cervical vagotomized mongrel dogs were stimulated by a bilateral isolated carotid sinus perfusion system [Harvard pulsatile pump, fixed mean pressure at reactive (60 TORR) level, pulse amplitude varied (10,20,40 mmHg, 10 min. periods)]. Five normal controls (CON) and five adrenal medullary deprived (AMx) (right adrenalectomy, left splanchnic nerve section) dogs were studied. An aortic catheter and left renal-femoral, spleno-jugular and left adreno-femoral venous shunts were inserted to monitor simultaneously aortic and venous (renal, splenic) pressures (Statham transducers), organ blood flow (intraluminal electromagnetic flow probe, adrenal directly measured) and blood sampling. Renal and splenic vascular resistances and catecholamine (single isotope, radioenzymatic assay) fluxes were calculated and statistical comparisons made (Student's 't' test, Fisher's tables). In AMx, impaired renal, not splenic, resistance was noted at 20 mmHG, $p < .02$, and 40mmHg, $p < .02$, pulse amplitude. Baro-stimulated reflex adrenal medullary secretion appears to support vasomotor tone of selected (renal not splenic) vascular beds.

INCREASED TISSUE LIPOPROTEIN LIPASE ACTIVITY IN GUINEA PIG FOLLOWING BURN TRAUMA. G.J. Bagby, H.I. Miller, J.A. Spitzer and J.J. Spitzer. L.S.U. Med. Cntr., New Orleans, LA 70112.

Lipoprotein lipase activities (LPLA) are decreased in heart and skeletal muscle from endotoxin-treated rats while surgical trauma induced an increase in heart LPLA. The present investigation was initiated to ascertain if tissue LPLA were affected by burn trauma. LPLA were examined in guinea pigs subjected to a 30% body surface scald burn. Control and thermally injured animals were sacrificed 7 and 24h post treatment. Tissue LPLA were estimated using ^{3}H-labeled glycerol trioleate in a glycerol-based stable emulsion. Activities of selected tissues expressed in µmole FFA released x g^{-1} wet weight x h^{-1} were the following (x ± se, n=8):

	7h		24h	
	Control	Burn	Control	Burn
Heart	87.8±7.5	108.5±13.9	67.4±5.9	114.1±14.2
Diaphragm	27.6±4.0	37.8± 9.8	24.6±3.6	46.0± 4.8
Red vastus	4.4±0.9	11.8± 2.4	5.4±1.1	8.5± 1.6
Red tricep	22.7±3.8	29.6± 3.8	10.4±1.7	55.6±10.6
Adipose	11.8±3.2	19.1± 3.7	8.7±1.3	19.6± 4.6

Factorial analysis of variance demonstrated a significant burn effect in the tissues examined ($p<0.01$). These increases are comparable to previously described elevations in heart LPLA following surgical trauma but are at variance with decreases in heart and skeletal muscle activities observed during endotoxin shock. (Supported in part by NIH Grant HL 23329)

SIMULTANEOUS LOCALIZATION OF ALPHA-ACTININ AND MYOSIN IN CHICKEN GIZZARD SMOOTH MUSCLE CELLS. R.M.Bagby.Zool.Dept.U.Tenn.,Knoxville,TN 37916

Chicken gizzards were repeatedly blended in low-salt buffer with 0.5% Triton X-100(Eur.J.Biochem.55:49,1975);extracted with 0.5M KCl,0.05M KH_2PO_4,pH 6.6;and the residue washed with 0.15M KCl;1mM EDTA;and distilled H_2O.Alpha-actinin(aA) in the H_2O was precipitated with 30% saturated $(NH_4)_2SO_4$ and chromatographed on DEAE cellulose (0-.5M KCl gradient in pH 7.5 Tris-acetate).Antibodies were raised in rabbits.In Ouchterlony gels antisera gave a single line against aA.

Fluorescein-labelled IgG fraction of anti-aA (FAaA)stained only Z-line of skeletal myofibrils. FAaA and a previously described antimyosin(Histochem.58:219,1978)labelled with rhodamine(RAM)were used to double-stain isolated gizzard muscle cells.FAaA stained small patches of plasma and nuclear membranes and continuous or interrupted strips in the cytoplasm,while RAM stained only myofibrils.It appeared that much,if not all,of the cytoplasmic aA(dense bodies?)was within myofibrils.I thank Ute Gröschel-Stewart,Tech.Hochsch. Darmstadt,W.Ger.,for advice and facilities.(Supported by NIH Grant HL 18077 and by a Res.Investigatorship from Am.Heart Assoc.-Tenn.Affiliate.)

LUNG FUNCTION IN DOGS DURING HEMORRHAGE AND REINFUSION. E.M. Baile*, L.A. Brooks*, P.D. Paré* and J.C. Hogg (SPON: C.F. Cramer). UBC Pulmonary Research Laboratory, St. Paul's Hospital, Vancouver, Canada.

Recent studies have shown that subtle structural changes occur in the pulmonary capillary endothelium and the alveolar epithelium with hemorrhagic shock. To investigate the physiological consequences of this injury we studied 12 anesthetized, supine dogs. They were placed in a volume-sensitive body plethysmograph and ventilated with 100% O_2 throughout the 7-hr study. Six dogs served as controls (Gp 1) and 6 (Gp 2) were subjected to 2 hr of hypovolemic shock (BP $\sim$40 mm Hg) after control measurements and were studied for a further 2 hr after reinfusion of the shed blood. We measured subdivisions of lung volume, pressure-volume curves of the lung, pulmonary resistance, dynamic compliance, the slope of phase III of the single breath N_2 washout and pulmonary shunt (Qs/Qt). Pulmonary extravascular water (PEW) was measured from postmortem lung samples. We found that there were no significant changes in Gp 1. However, in Gp 2 shock produced an increase in FRC ($P<0.05$) that returned to control with reinfusion. There was no significant difference in PEW between Gps. We attribute the increased FRC to the decrease in pulmonary blood volume during shock and we conclude that hemorrhagic shock, reinfusion and 100% O_2 breathing are not associated with demonstrable alterations in lung mechanics or gas exchange.

CAPILLARY TRANSIT TIME OF RBC AND PLASMA BY INDICATOR DILUTION. Carleton H. Baker and Darrell L. Davis. Dept. of Physiology, Coll. of Med., Univ. of So. Fla., Tampa, Fla. 33612.

Techniques for obtaining time-concentration curves in parallel and series coupled microvessels subsequent to intra-arterial bolus injections (0.07 ml) of sulphemoglobin-RBC (SH-RBC) and FITC-Dextran (FID) in exposed mesentery of Dial-Urethane anesthetised cats (0.7 kg) have been previously reported. Control curves have been recorded in two groups of arterioles (35-40µm and 20-25µm) and two groups of venules (30-35µm and 45-50um) and again one-hour subsequent to a lethal-dose of endotoxin (3 mg/kg, i.v.). This latter is during a period of small arteriolar constriction (33%) and dilation of the larger arterioles (20%). Venular diameters are unchanged. For SH-RBC curves the appearance time (t_A) of the arterioles increased by one sec., but the venular t_A increased by 4.6 sec. The FID arteriolar t_A increased by about one sec, similar to the SH-RBC, but the venular t_A increased by only 1.5 sec. The curve width (t_A-t_E) of the venular curves increased by 3.5 sec for SH-RBC but increased by 12 sec for FID. These data would indicate that constriction of the small arterioles resulted in a reduced number of parallel pathways available to SH-RBC and of lower flow velocity in contrast to plasma (FID) pathways. (Supported by NIH grant HL-18866 and the American Heart Assn., Suncoast Chapter)

COUPLING OF AEROBIC METABOLISM TO Na-K-ATPase ACTIVITY IN THE KIDNEY. R.S. Balaban*, L.J. Mandel and S.P. Soltoff*. Dept. of Physiology, Duke Medical Center, Durham, N.C. 27710

The linear relationship between O_2 consumption (QO_2) and Na reabsorption (T_{Na}), as well as the inhibition of T_{Na} by aerobic metabolism inhibitors, indicate that a tight coupling exists between the aerobic conversion of energy and active ion transport in the kidney. However, the actual coupling mechanism between these energy converting and consuming processes within the renal cell has not been elucidated. Na-K-ATPase is believed to play a primary role in the utilization of aerobic energy for active T_{Na}. We report here the results of studies performed with an improved isolated rabbit cortical tubule suspension with open lumina and, thus, capable of transepithelial transport. Simultaneous measurements of the mitochondrial redox state (performed optically), the cellular ATP/ADP ratio and QO_2 were made under conditions known to alter the Na-K-ATPase turnover. Ouabain (10^{-5} M) inhibited QO_2 60%, reduced mitochondrial nicotinamide adenine dinucleotide (NAD) and increased the cellular ATP/ADP ratio. The effects of ouabain onQO_2 and NAD were completely inhibited by prior addition of 1799, a mitochondrial uncoupling agent. The addition of 5 mM K to tubules in K-free medium caused a 40% stimulation of QO_2 and an oxidation of NAD. These data indicate that the cellular ATP/ADP ratio may be part of the coupling mechanism linking Na-K-ATPase turnover and aerobic metabolic rate in the kidney. Supported by 1978-79-A10 N.C. Heart Assoc., GM-00929 and GM-07105 N.I.H.

Ca METABOLISM OF BULLFROG TADPOLES. Geraldine F. Baldwin* and P.J. Bentley. Dept. Pharmacol., Mt. Sinai School Med., New York, N.Y. 10029

The evolutionary transition from fish to tetrapods is associated with basic changes in Ca metabolism. The amphibians, especially their aquatic larvae, are in a unique phyletic position for the study of such changes. Tadpoles (Gosner stages 29-38) contained about 50 mmoles/kg Ca; 6% in the gut and 36% in the skin. The latter contains concentrations up to 200 mmoles/kg and is a major site of body Ca which is not however readily exchangeable at this stage (6% exchangeable with Ca-45 in 5 h in vitro, 2.3% in 3 days in vivo). In artificial pond water (0.2 mM Ca) tadpoles accumulated Ca-45 equivalent to about 5% body Ca/day. Accumulated Ca was 66% in skin and 34% in carcass (gut-free). Uptake increased by 60% after they had been kept in Ca-free pond water for 8 days indicating that regulation occurs. Ca accumulation in the gut then decreased by 57%. Loss of accumulated radioactivity indicates that Ca turnover is slow with 75% of the total counts remaining after 2 days. The gut appears to be an important site for Ca uptake; however the skin and gills may also contribute to Ca balance. (Supported by NSF grant #PCM78-21446).

LUNG DESATURASE: INHIBITION BY FATTY ACIDS. J.A. Balint, E.C. Kyriakides*, and D.A. Beeler*. Albany Medical College, Albany, New York, 12208.

Lung lecithins are more unsaturated when rats are fed essential fatty acid (EFA) deficient diets. Lung slices (300-500 mg/incubation) were prepared from rats fed fat free diets supplemented with 4% safflower oil (control) or 4% tripalmitin (EFAD) for 16-26 weeks, and incubated for 2 hours in buffers (O'Neil and Tierney, A.J.P. 226:867, 1974) containing either no added fatty acid, 1 mM oleate or 1 mM linoleate, before transfer to buffer containing 1-3 µC 1-^{14}C-stearate in tracer amounts. The methyl esters from phospholipids were separated by argentation TLC and radioactivity determined with the following results:

		^{14}C in monounsaturated fatty acids ($\bar{x}$ ± SEM)	"p" values	
a. Control	(17)	7.5 ± 0.4	a vs b	<.001
b. EFAD	(19)	12.5 ± 0.4	a vs c	<.025
c. EFAD + 18:1	(8)	9.6 ± 0.5	a vs d	NS
d. EFAD + 18:2	(9)	8.0 ± 0.4	b vs c	<.001
(n)= number of observations			c vs d	<.025

These results demonstrate that lung tissue is capable of fatty acid desaturation, that this activity is markedly increased in EFA deficiency, and that this may contribute to unsaturation of lecithins in this condition. Furthermore, in vitro addition of oleic or linoleic can directly inhibit the enhanced activity of this enzyme system in lung tissue from EFA deficient rats.

AN IMPROVED IMPULSE FLOWMETER. B.J. Barber and R.L. Hester. Dept. Physiol. & Biophy., Univ. Miss. Med. Cntr., Jackson MS 39216.

In circulatory studies it is frequently necessary to measure flows below the range of electromagnetic flowmeters (10 ml/min). We have developed an impulse flowmeter which eliminates many disadvantages of conventional drop counters. Drops trigger impulses from a photoelectric detector. The time interval between impulses is measured by a counting circuit driven by a precision clock generator. A voltage proportional to the reciprocal of this interval is generated by a multiplying D/A converter. This gives the fastest possible transient response for a drop detecting flowmeter. Given uniform drop size, this voltage will be proportional to flow on a drop to drop basis. Typical results using this device in an isolated dog gracilis muscle prepartion show, in response to a 35 mmHg decrease in perfusion pressure, a decrease in flow from 2.49 ml/min/100g to 1.42 ml/min/100g within 24 seconds followed by an autoregulatory return to 1.94 ml/min/100g within 50 seconds. We also found that a standard syringe infusion pump possessed periodic variations in flow between 0.3 and 0.64 ml/min with a period of 2 minutes at a setting of .5 ml/min. (Supported by NIH grant HL 11678.)

EFFECT OF TIME INTERVAL BETWEEN REPEATED CORONARY OCCLUSIONS ON BLOOD FLOW AND ELECTRICAL ACTIVITY. M. J. Barber, D. E. Euler, J. X. Thomas and W. C. Randall. Dept. of Physiology, Loyola Univ. of Chicago, Stritch Sch. Med.,Maywood, IL 60153

This study was performed to determine the effects of repeated short occlusions (5 min) of the LAD coronary artery on myocardial blood flow (MBF) and electrical properties of the myocardium. Bipolar and unipolar plaque electrodes sewn to the epicardium in the ischemic and non-ischemic zones allowed measurement of changes in local bipolar electrogram duration (BED) and ST-segment elevation (STE) with occlusion. MBF was measured 2 min after onset of each occlusion with 15μ microspheres. In each dog 4 occlusions of 5 min each were performed while pacing at 150 bpm. The first two occlusions and the final two occlusions were separated by a brief period of reperfusion (3-5 min) while the second and third occlusions were separated by longer periods of reperfusion (30-40 min). During successive occlusions MBF to the ischemic area was not significantly different from the flow observed during the initial occlusion. Initial occlusions resulted in increased BED and STE as well as marked arrhythmia. A short duration of reperfusion between two occlusions resulted in shorter BED, less STE, and less arrhythmia during the second occlusion. With longer periods of reperfusion, there was no difference in BED, STE or incidence of arrhythmia between two successive occlusions. Although electrical function improved with brief reperfusion, this improvement does not appear to be mediated by blood flow. (Supported by NIH Grant HL-08682.)

EFFECT OF SQ 14,225 (CAPTOPRIL) ON EXPERIMENTALLY-INDUCED THIRSTS IN RATS, C.C. Barney*, M.J. Katovich* and M.J. Fregly (Spon: G.A. Gerencser) Dept. of Physiology, University of Florida, Gainesville, FL 32610

The drinking response of female rats to either water deprivation for 24 hr or administration of hypertonic saline i.p. was studied following acute administration of the angiotensin converting enzyme inhibitor, SQ 14,225. Intraperitoneal administration of 50 mg SQ 14,225/kg at least 45 min prior to availability of water significantly attenuated the increased water intake observed in 24 hr water-deprived rats. Administration of 50 mg SQ 14,225/kg at intervals shorter than 45 min prior to availability of water had no significant effect on water intake. Administration of 1% b.w. of 0.25, 0.50, 0.75 or 1.00 M NaCl solution i.p. to rats resulted in graded increases in water intake, urine output, urinary sodium and potassium outputs and urinary Na/K ratio. Intraperitoneal administration of 35 mg SQ 14,225/kg 15 min prior to administration of NaCl solution had no significant effect on either the increased water intake or urine output and generally no effect on the urinary sodium and potassium outputs or urinary Na/K ratio at any dose of NaCl. These suggest that water deprivation-induced thirst involves an angiotensin II-sensitive component while cellular (hypertonic saline-induced) thirst does not. (Supported by contract N00014-75-C-0199 with the Office of Naval Research)

PHYSIOLOGICAL AND ANATOMICAL DETERMINATION OF LATERAL HYPOTHALAMIC AND LATERAL PREOPTIC AREA INTERCONNECTIONS. F. C. Barone*, M. J. Wayner, W. H. Tsai*, S. L. Scharoun*, W. W. Woodson, Jr.*, F. E. Barash* and J. E. Zrebiec*. Brain Research Lab, Syracuse University, Syracuse, NY 13210.

The effects of lateral hypothalamic (LH) stimulation on ipsalateral lateral preoptic area-medial forebrain bundle (LPA-MFB) single neural activity were determined in anesthetized rats. The effects of LPA stimulation on the activity of LH-MFB units were also determined. The results of 0.5 msec pulse stimulation (0 to 10 volts) and trains of pulses (0 to 20 Hz) indicated that both excitatory and inhibitory mono and polysynaptic interconnections between the LPA and LH exist. In another series of experiments horseradish peroxidase (HRP) was applied microiontophoretically in the LPA and LH of rats. Labeled axons and cell bodies were found along the stria hypothalamic tract, the LPA and LH, and along the MFB into the mesencephalon. These results, based on the retrograde movement of HRP and on the electrical stimulation data, unequivocally demonstrate considerable interconnections along the extent of the LPA-LH-MFB neuropil. (Supported by NIH Grant NINCDS USPHS No. 13543)

THE EFFECTS OF SCOPOLAMINE ON SHOCK AVOIDANCE LEARNING AND RETENTION IN THE COCKROACH, P. AMERICANA. D. A. BARRACO,* E. M. EISENSTEIN, and J. M. DEAN.* Department of Physiology and Biophysics, Michigan State University, E. Lansing, MI 48824.

Scopolamine is known to block the muscarinic receptors in the brains of vertebrates. It also is known to produce retention deficits; the latter is one factor in implicating the cholinergic system in memory processes.

Adult male cockroaches were injected with either saline (20 μl) or scopolamine (500μg/20μl) 1 hour before shock avoidance training in a T-maze and then tested for retention 5 hours later. The results showed that the scopolamine treated animals learned and retained the training as well as controls. Evidence that the drug was acting centrally was indicated by the faster runway times for the experimental group. Since there are no known peripheral cholinergic synapses in the cockroach this effect had to be central.

Our past work utilizing the same paradigm indicated that retention but not aquisition was affected by pre-training injections of puromycin.

The puromycin and scopolamine data suggest the possibility that puromycin may not be interfering with cholinergic synapses in the CNS of the cockroach to produce its amnesic effect.

(Supported in part by the Biomedical Research Support Grant to the College of Natural Science, Michigan State Univ)

RENAL FUNCTION AND PROTEINURIA IN EXPERIMENTAL DIABETES. J.W. Bauman, Jr., G. Schubert* and J. Schnermann. Physiologisches Institut Der Universitat Munchen, Munchen, West Germany.

Micropuncture and whole kidney measurements were carried out in Munich-Wistar rats with streptozotocin-induced diabetes of 4 to more than 120 days duration. Glomerular filtration rates (GFR), as determined by single kidney ^{14}C inulin clearances, were not significantly different at 4,10, 30 or 90-127 days after induction of diabetes. SNGFR in 4-5 day diabetic rats was 27.2 ± 6.1 nl/min and in 10-14 day rats was 28.2 + nl/min. Although feedback reduction of SNGFR was demonstrable by loop perfusion in 3 of 4 rats with diabetes of more than 100 days duration, early distal sodium and chlorides were low (63 ± 23.9 and 50.6 ± 19.3 mEg/l, respectively), and are thus consistent with the GFR and SNGFR values observed. Protein excretion rates were significantly increased by day 4 after streptozotocin treatment (24.9 ± 9.3 μg/min) and further increased to maximum rates by day 30 (63.9 ± 22.1 μg/min). From day 30 through day 127, protein excretion rates declined somewhat to a value of 42 ± 13.3 μg/min on day 127. The electrophoretic patterns of proteins in urine samples concentrated so as to approximate plasma concentrations were not different from those of non-diabetic rats or from S-D rats made proteinuric with angiotensin or aminonucleoside. The studies indicate that the mechanism of diabetic proteinuria is not dependent on decreased GFR and may be independent of changes in Kf.

A MODIFIED METHOD FOR ISOLATING RAT LIVER PLASMA MEMBRANE AND MODIFICATIONS FOR MEASURING PROSTAGLANDINS OF THE E-SERIES USING A PLASMA MEMBRANE RADIO-RECEPTOR ASSAY (MRRA). S. Bauman*, D. Toft*, J. Kim*, T. Dousa, J. Strand and J. C. Romero. Departments of Physiology and Molecular Medicine, Mayo Clinic, Rochester, MN 55901.

This study was undertaken with the purpose of modifying the membrane isolation method of Frölich et al (Biochimica et Biophysica Acta, 348:241, 1974), in order to use standard laboratory equipment and conventional isolation techniques (Fitzpatrick, et al., J. Biol. Chem., 244:3561, 1969). The protein binding assay was adapted in order to count labelled PGE directly, after trapping the bound fraction on glass microfibre discs, with construction of a standard curve comparable to that used in radioimmunoassay. The sensitivity of this adapted method permits measurement of prostaglandins of the E-series in the low picogram range (150-1000 pg). MRRA selectively binds PGE_1 and PGE_2 equally, but shows negligible cross reactivity for $PGF_{1\alpha}$ (<0.24%), $PGF_{2\alpha}$ (0.45%), PGA_2 (5.7%), arachidic acid (0.12%), arachidonic acid (<0.12%), endoperoxide I and II analogs (0.11% and 0.022% respectively), 6-keto $F_{1\alpha}$ (0.10%), and thromboxane B_2 (0.07%). Schatchard analysis reveals high and low affinity components. The high affinity sites show a dissociation constant ($Kd = 6.7 \times 10^{-9}M$) and a binding capacity (3.8×10^{-1} picomoles/mg protein) similar to that reported by Frölich et al. (Supported by grants HL 16496 and AM 16105).

THE EFFECTS OF AGE AND FITNESS LEVEL ON THE RESPONSE TO LOCAL COLD PRESSOR TEST. W.B. BAUN* and P.B. Raven. Dept. of Physiology, NTSU/TCOM, Ft. Worth, TX 76107.

Recently LeBlanc (J.A.P. 44:813,1978) and others have shown that many individual factors influence the human's autonomic response to the local cold pressor test. In this study the effects of age (18-55) and differing levels of fitness (VO_2 max ranging from 35.3 ml.kg.$^{-1}$min.$^{-1}$ to 68.8 ml.kg.$^{-1}$ min.$^{-1}$) on the heart rate (HR) response to the cold hand (CH) pressor test and the cold face (CF) test were investigated. Forty-one male subjects were evaluated with CH and CF on separate days following a treadmill test for VO_2 max. HR was measured at 6 s intervals for 5 min. prior to stress, 2 min. of stress and 3 min. of recovery. The group was divided into 2 age groups (18-30 and 35-55) which were further subdivided into trained (Tng) and untrained (Utng) categories using the VO_2 max value. No significant differences in heart rate response were found between the young and old or the Tng and Utng populations for both the CF and CH tests. With the removal of 2 extreme cases from the data set a significant difference between old and young response to the CH test was revealed. Correlation analysis revealed that the minimum recovery HR after the CH test was directly related to the response during stress of the CF test for the total population (R=.60). It also revealed that the CH response was significantly correlated to the CF test (R=54). The results suggest that the heart rate response to hand and face tests are related, and that age effects the local cooling response.

ENVIRONMENTAL HOMEOTHERMY IN AN ANTARCTIC INSECT.

J.G. Baust[1], J. Edwards[2]*and R. Brown[1]*, Dept. of Biology, U. of Houston, Houston, TX 77004[1] and Dept. of Zoology, U. of Washington, Seattle, Wash. 98195[2]

Belgica antarctica, a wingless fly and only free-living holometabolous insect of the Antarctic continent, is uniquely adapted for survival under perennial "winter conditions". Larvae are freezing tolerant throughout the year and elaborate a complex of cryoprotectants including erythritol, glucose, sucrose and trehalose. Maintenance on artificial diets indicates that "antifreeze" profiles have food-source and temperature dependent components. Direct utilization of dietary cryoprotectants is suggested. The terresterial microhabitat of the mid Antarctic Peninsula provides a novel thermostable environment. The annual range of habitat temperatures did not exceed -7 to 11°C during the two year study. Accordingly, this species lacks adaptative plasticity common to arctic insects. The following indicators of chill tolerance did not vary seasonally or during acclimation attempts. Supercooling points remained constant at -5.7° ± 0.5. Lower lethal temperatures were also constant at -10°(LT 50), and prolonged exposure to ≥ 10° = resulted in impaired carbohydrate metabolism. The thermostability of the environment of this species has resulted in the evolution of an obligate insect homeotherm. (Supported by NSF Grant DPP76-24205).

THE EFFECT OF FEED RESTRICTION ON BODY COMPOSITION AND LONGEVITY OF RATS. Roy E. Beauchene, Connie W. Bales, Charlotte A. Smith*, Sarah M. Tucker and Rossie L. Mason. Department of Food Science, Nutrition, and Food Systems Administration, College of Home Economics and Agricultural Experiment Station, Univ. of Tennessee, Knoxville, TN 37916

Two groups of Wistar male rats were fed Wayne Lab Blox on an ad libitum (A) or on an every other night basis (R). Some animals from each group were transferred from 1 dietary regimen to the other at 1 year of age, e.g., from ad libitum to restricted (AR) or from restricted to ad libitum (RA). Mean lifespan of rats restricted-fed throughout life was 163.4±3.9 weeks (Mean±SEM) and was significantly greater than those of other groups (A=133.1± 4.1; AR=150.0±4.6; and RA=149.2±3.6). Mean lifespans of transferred groups (AR and RA) were not significantly different from each other but were greater than that of group A. At 2 years of age ad libitum-fed rats (A) had significantly greater body weights and absolute amounts of body protein, moisture, ash, and fat and a substantially higher relative fat content than restricted-fed rats (R). Relative mean body fat content of group AR was similar to that of group R, while that of RA was similar to that of A. Two-year old animals restricted-fed during the second year of life (R,AR) had relative body compositions similar to that of 1-year old rats. Relationships among growth, body composition, and longevity will be discussed.

CYCLIC ADENOSINE MONOPHOSPHATE SENSITIVITY OF SKELETAL MUSCLE MYOFIBRILLAR ADENOSINE TRIPHOSPHATASE IN YOUNG AND MATURE RATS. A.N. Belcastro*, G.N. Pierce*, M. Sopper*, M. Low*, A. Bonen*, (SPON: Bela Issekutz Jr.) School of Physical Education, Dalhousie University, Halifax, Nova Scotia, Canada.

Myofibrillar ATPase activity increased from young to adult and decreased from adult to old animals ($p \leq 0.05$). The addition of cAMP (1uM) did not alter the development pattern. At 3 days the cAMP sensitive ATPase activity (0.242 ± 0.021 umoles Pi/mg/min) was higher than control ATPase levels (0.200 ± 0.015 umoles Pi/mg/min)($p \leq 0.05$), No effect occurred for adult or old animals ($p \geq 0.05$). Increasing the calcium content (100 uM) did not alter any of the control or cAMP stimulated ATPase activities ($p \geq 0.05$). Increasing ionic strength depressed the ATPase activities for all age groups ($p \leq 0.05$). With cAMP the ATPase activities for 3 day animals were 21% greater than control valves ($p \leq 0.05$) at similar ionic strengths. The EGTA sensitive ATPase changes at 10 day, 6 week and 18 months were unaltered with cAMP. The 3 day levels were 6% lower than control EGTA sensitive ATPase activities. The results suggest that cAMP may be capable of altering the requirement of the contractile enzyme for calcium with advancing age in skeletal muscle. (Support by NSERC grants A-6629 and A-6449).

TUBULO-GLOMERULAR FEEDBACK RESPONSES AND DISTAL TUBULAR FLUID COMPOSITION DURING PERFUSION WITH NON-ELECTROLYTE SOLUTIONS IN THE RAT. P.D. Bell, C.B. McLean* and L.G. Navar. Univ. of Alabama Medical Center, Birmingham, AL 35294.

Previous studies have demonstrated that decreases in stop flow pressure (SFP) can occur during perfusion with both non-electrolyte and electrolyte solutions. The present study was conducted to assess the changes in distal fluid chloride concentration (Cl^-) and osmolality (Osm) that occur during perfusion with solutions of urea and mannitol as compared to an artificial tubular fluid solution (ATF). For the micropuncture procedure, a proximal tubule segment was blocked with wax and perfused distally at a low rate of 10 nl/min and a high rate of 35 nl/min; either SFP feedback responses or distal fluid samples were obtained. At the high perfusion rate, SFP was reduced by 11±0.8 mmHg (ATF, n=28), 11.8±1.1 mmHg (mannitol solution, n=29) and 12±1.1 mmHg (urea solution, n=22). During perfusion with ATF (n=11), Cl^- increased from 90±6 to 131±8 mEq/l and Osm rose from 202±8 to 256±10 mOsm/kg. Using the urea solution (n=11), Cl^- did not change significantly (66±4 to 73±6 mEq/l) but Osm increased from 200± 9 to 268±11 mOsm/kg. With the mannitol solution (n=16), Cl^- decreased from 85±4 to 66±4 mEq/l; however, Osm increased from 291±8 to 322±11 mOsm/kg. Thus, non-electrolyte solutions elicited feedback mediated decreases in SFP without increases in Cl^-. In contrast, increases in perfusion rate led to increases in distal fluid osmolality during perfusion with all three solutions.

PRESSURE-FLOW RELATIONS IN THE CANINE RIGHT CORONARY CIRCULATION. R.F.Bellamy* and H.S.Lowensohn. Walter Reed Army Institute of Research, Washington, D.C. 20012.

The relationship between right coronary artery flow (Q) and aortic pressure (P) was studied in nine conscious chronically instrumented dogs with right ventricular pressures (RVP) of 14 to 154 mmHg. Dogs with elevated RVP had congenital pulmonic stenosis. P—Q relations were constructed from phasic recordings of diastoles > 1 second in length and systolic data were measured during the terminal 0.1 second of systole. Two levels of Q were studied: resting (RQ) and peak flow reactive hyperemia (RH). Diastolic P and Q were well correlated by a linear model ($r = 0.92$). Both the diastolic regression slope and pressure axis intercept (P_c) were affected by vasodilation: slope RH/ slope RQ = 2.5 ± 0.5, $RQP_c - RHP_c = 20 \pm 10$ mmHg ($\bar{x} \pm 1SD$). Systolic P and Q were less well fitted by a linear model ($r = 0.78$). At RQ and when RVP was $< \frac{1}{2}$ P, ventricular systole translated the diastolic P—Q relation to a higher P_c without change in slope. Systole increased the diastolic P_c by an average of 76% of RVP. The data support Downey and Kirk's hypothesis that systole inhibits coronary Q by a vascular waterfall mechanism. During RH and when RVP was $> \frac{1}{2}$ P, systole both increased P_c and decreased the slope of the diastolic P—Q relation. During RH, the average systolic P_c was only 49% of the RQ value. Thus the magnitude of the systolic waterfall effect appears to depend upon vasomotor tone as well as the extravascular compression of ventricular systole.

THE EFFECT OF DORSOMEDIAL HYPOTHALAMIC LESIONS (DMNL) ON BRAIN NOREPINEPHRINE (NE) AND DOPAMINE (DA) AND THE CONSUMATORY RESPONSES TO PHENFORMIN. L.L. Bellinger, L.L. Bernardis*, R.E. Dill*. Baylor College of Dentistry, Dallas, TX 75246 and V.A. Medical Center, Buffalo, NY 14215.

DMNL rats are hypophagic and hypodipsic compared to shams (S) and show regulatory deficits in glucose monitoring (Bellinger et al AJP 235 R 168.1978). We first investigated the effects of DMNL on hypothalamic (HYP) and forebrain (FB) NE and DA levels. Secondly we investigated the effect of phenformin, a drug that produces anorexia possibly through changes in brain catecholamines or glucose utilization on DMNL rats. Exp 1, Rats were DMNL or S operated, at sacrifice the body weight (BW) and nasoanal length (NAL) of the DMNL was less ($P < 0.001$) than S (262.2 ± 13.8g vs 344.2 ± 10.1g; 214.8 ± 2.2mm vs 236 ± 1.0mm). FB NE, DA and HYP DA did not differ, however HYP NE was less ($P < 0.02$) in DMNL ($n=6$, 1.09 ± 0.8ug/g vs $n=7$, 1.38 ± 0.7 ug/g). Exp 2, Rats were DMNL ($n=17$) or S ($n=8$) operated. All the rats were fed for 6 hr/day beginning at the start of the dark period. In a counter balance design the rats were injected 30 min. before feeding with saline or 10 or 15mg/kg of Phenformin and then FI and WI were recorded hourly for 6 hrs. Both the 10 and 15mg/kg dose depressed FI and WI during the first hr and all subsequent hours ($P < 0.01$), but WI was normal compared to saline controls by the sixth hr. The percentage depression of FI and WI were similar in DMNL and S. At sacrifice the BW and NAL of DMNL were less ($P < 0.01$) than S (320.2 ± 7.6 vs 414.0 ± 7.1g; 223.9 ± 1.6mm vs 238.4 ± 2.3mm $P < 0.01$).

INCREASED VASCULAR REACTIVITY AS A PRIMARY MECHANISM IN SPONTANEOUS AND DEOXYCORTICOSTERONE HYPERTENSION IN RATS K.H. Berecek, R.D. Murray and F. Gross*. Univ. Heidelberg, Dept. Pharmacology, Fed. Rep. Germany.

Changes in vascular reactivity were studied in isolated, constant flow perfused kidneys from stroke-prone spontaneously hypertensive rats (spSHR) as compared to Wistar-Kyoto rats (WKY) and in Sprague-Dawley (SD) rats treated with deoxycorticosterone acetate (DOCA) as compared to control SD rats. Rats were studied at pre-hypertensive and chronic stages of hypertension. At both stages, kidneys from spSHR demonstrated enhanced reactivity to norepinephrine, vasopressin and angiotensin. Dose-response curves showed leftward shifts, steeper slopes and ↑ maximal responses (indicating a structural thickening of the vascular wall) as well as decreased thresholds (indicating an ↑ in vascular smooth muscle sensitivity). With increasing severity of hypertension response curve slopes were steeper and maximal responses greater. DOCA rats also showed enhanced reactivity in both stages. In the pre-hypertensive stage response curves showed parallel leftward shifts and ↓ thresholds. In the chronic stage curve slopes became steeper and maximal responses greater. Thus in two different models of hypertension increased vascular reactivity occurs in the pre-hypertensive stage and may be a primary mechanism underlying the rise in arterial pressure.
(Deutsche Forschungsgemeineschaft, SFB 90)

LOBAR PRESSURE-VOLUME CHARACTERISTICS OF EXCISED HUMAN LUNGS. N. Berend*, C. Skoog*, D.W. Galaugher*, and W.M. Thurlbeck* (SPON: N.R. Anthonisen). Department of Pathology, University of Manitoba, Winnipeg, Manitoba R3E 0Z3, Canada.

It is important for the interpretation of the distribution of ventilation and nitrogen washout curves to know whether the pressure-volume (p-v) characteristics of individual lobes of the lung differ. This study documents the p-v curves of 12 whole (left) lungs and their individual lobes obtained at autopsy and selected for the presence of a complete interlobar fissure. P-v curves were obtained in a volume displacement plethysmograph, transpulmonary pressure (P_L) being measured with a pressure transducer. The p-v curves of the lungs and subsequently the isolated lobes were recorded from P_L 30 to P_L 0 cmH_2O. The p-v curves, with the volume axis expressed as % volume at P_L 30 cmH_2O (Vmax), of upper and lower lobes, were virtually superimposable and there were no significant differences in the P_L at 50, 60, 70, 80, and 90% Vmax. We conclude that the p-v characteristics of upper and lower lobes of excised human lungs are identical.

EFFECTS OF PARATHYROID HORMONE AND CALCITONIN: COMPARISON OF RABBIT AND RAT. T. Berndt* and F. Knox, Depts. of Physiol. & Med., Mayo Clinic, Rochester, MN 55901 SPON: J. C. Strand

The effects of parathyroid hormone (PTH) have been evaluated in the rabbit both in vitro and in vivo; however, the characteristic PTH-mediated changes in phosphate transport were not observed. To further evaluate this unique PTH response, to correlate the electrolyte changes with data from the isolated tubule, and to allow more direct comparison of hormone responsiveness between species, parallel dose response studies with PTH and calcitonin (CT) were performed in normocapnic rabbits and rats. Following thyroparathyroidectomy, progressively increasing doses (.03, 0.1, 0.3, 1 U/kg/min) of PTH or CT were infused. In 5 rats, PTH increased FE_p from control $.13 \pm .02$ to $36 \pm 3\%$* at the highest dose. Corresponding values in 6 rabbits were $18 \pm 4\%$ to $28 \pm 4\%$*. FE_{Ca} decreased in the rat from $2 \pm .6$ to $.7 \pm .2\%$* and from $23 \pm 7\%$ to $7 \pm 1\%$* in the rabbit. In 5 rats, CT increased FE_p from $.4 \pm .1\%$ to $12 \pm 5\%$*, but CT decreased FE_p from $22 \pm 5\%$ to $14 \pm 8\%$* in the rabbit. CT increased FE_{Na} in the rat from $.2 \pm .1\%$ to $1.6 \pm .5\%$* and from $4 \pm .5\%$ to $18 \pm 3\%$* in the rabbit with a parallel increase in FE_{Cl} $6 \pm .6\%$ to $23 \pm 4\%$*. In summary, PTH affected phosphate and calcium reabsorption in both species; however, the magnitude of the response varied between species. CT, on the other hand, predominantly increased phosphate excretion in the rat and NaCl excretion in the rabbit. (Supported by AM 19715) *Significance $p < .05$

FOOD RESTRICTION PREVENTS THE LOSS OF CATECHOLAMINE-STIMULATED LIPOLYSIS. H.A. Bertrand, E.J. Masoro and B.P. Yu. Univ. of Texas Health Sci. Ctr., San Antonio, Texas, 78284.

Male SPF Fischer 344 rats were fed ad libitum (Group A) or 60% ad libitum food intake (Group R) from 6 weeks of age. At 6 months of age and at 6 month intervals thereafter, the epididymal and perirenal adipocytes from 10 rats of both groups were analyzed for cell size, cell number and lipolytic responsiveness to epinephrine and norepinephrine between 0 and 1 mM. Although the adipocytes from 6 month-old Group A rats were larger than those from Group R rats of the same age, their epinephrine-stimulated lipolysis was not different. Beyond 6 months of age, the lipolytic response to catecholamines of Group A adipocytes fell markedly. However, the catecholamine-stimulated lipolysis of adipocytes from Group R rats was fully maintained until 18 months of age and never declined to the extent that was seen with adipocytes from old Group A rats. Indeed, very late in life when there was little or no difference in the adipocyte dimensions of Group A and Group R rats, the lipolytic response to catecholamines was markedly greater in Group R than in Group A rat adipocytes. We conclude that it is the life-long nutritional history of a rat population which determines the changes in responsiveness of adipocytes to the catecholamines with age and that this rarely examined parameter is the reason why a loss of catecholamine-stimulated lipolysis with age is not a universal observation.
(Supported by NIH Grant AG0166)

OSCILLATING ACCELERATION FOR THE PREVENTION OF CARDIOVASCULAR DECONDITIONING. A. Bhattacharya*, C. F. Knapp*, E. P. McCutcheon, and A. Cornish*, Wenner-Gren Res. Lab., Univ. of Ky., Lexington, KY 40506, & Univ. S.C., Columbia, SC 29208

Because of the loss of the dynamic force environment in O-G, whole body oscillating acceleration (WBOA) was evaluated as a countermeasure (CM) to cardiovascular deconditioning (CVD) induced by 6 hrs of neck level water-immersion (WI). The WBOA technique employs an oscillating bed programmed to simulate force profiles of adults performing repetitive jumping. The bed was programmed to produce half sine displacement, at a repetition rate of 1 Hz and peak acceleration of 1.5 G_z (subject restrained horizontally; G along the spine). Six subjects (mean age 22.8 ± 2.4 SD yrs) were exposed to a protocol of 1) control, orthostatic tolerance test (OT) of 70° head up tilt for 20 min; 2) OT after WI; and 3) OT after WI + 18 min WBOA exposure. Based on the OT time and heart rate (HR) response, WBOA caused complete or partial recovery from CVD in all subjects, although in one subject the improvement was slight. With WI, plasma volume (PV) changes were negative (range -5% to -20%), hematocrit changes were positive (range +2% to +15%) and fluid balance was variable (range -1421 ml to +760 ml). However, there were no consistent correlations between these changes and improvements in OT time and HR with the WBOA exposure. Hence, improvement in OT with WBOA could be attributed to other mechanisms regulating pressure and volume distribution. Supported by NASA, Grant NSG-2318.

UPTAKE AND ESTERIFICATION OF PLANT STEROLS BY THE SMALL INTESTINE OF RAT. Ashim K. Bhattacharyya, Depts. of Pathology and Physiology, LSU Medical Center, New Orleans, La., 70112.

Plant sterols (PS) structurally differ little from cholesterol but are absorbed in small amounts. Since mucosal cell uptake and esterification are important steps in absorption, these were studied for PS, β-sitosterol (sito), campesterol (campes) and stigmasterol (stig) in rats in vitro using everted sacs. In in vivo studies, each sterol was fed dissolved in oil (8 mg/g), 4 hrs later intestines were dissected, washed and dried. Sterols were quantitated by GLC. In everted sacs % uptake of sterols (mean ± SEM of 4 rats) in different segments were as follows:

Sterols	Proximal	Middle	Distal
Sito	0.32±0.03	0.25±0.02	0.27±0.03
Campes	0.51±0.02*	0.33±0.01*	0.40±0.04*
Stig	0.06±0.01	0.05±0.02	0.06±0.03

*Significantly higher than those for sito

On feeding PS, campes was found in significantly larger amounts (2.22 mg/g dry wt) than sito (1.5 mg/g) in proximal and middle segments. Stig was found in very small amounts (0.39 mg/g). Total intestinal contents of sito, campes and stig were 14.7, 27.8 and 5.5% of dose fed. 10-20% campes and 7-11% sito were esterified whereas only 2% stig was esterified. The results indicate that in rats campes uptake and esterification are greater than sito whereas those for stig is negligible. These differences are probably related to structural differences in side chain of the sterol molecule. (Supported by Emery Goff Research Award, AHA-La., Inc.)

TRANSITION FROM Na TRANSPORT TO Cl TRANSPORT AFTER EXPOSURE OF EXTERNAL SURFACE OF FROG SKIN to $FeCl_3$. Thomas U.L. Biber and Terry L. Mullen*, Med. Coll. of Va., Richmond, Va. 23298

The effect of addition of 10^{-3} M $FeCl_3$ to media bathing the skin of Rana pipiens was studied under short-circuit conditions by measuring current, Na influx (J_{13}^{Na}), Na efflux, Cl influx (J_{13}^{Cl}) and Cl efflux (J_{31}^{Cl}) across the epithelium. With normal NaCl Ringer's on both sides of the skin, addition of $FeCl_3$ to the external medium caused in 8 skins (a) nearly complete inhibition of active Na transport as J_{13}^{Na} decreased from 1.30 ± 0.14 to 0.10 ± 0.04 μeq/cm²h and (b) a reversal of net Cl movement ($J_{31}^{Cl}-J_{13}^{Cl}$) from -0.17 ± 0.04 to 0.38 ± 0.05 μeq/cm²h. Net outward Cl movement was also induced by addition of $FeCl_3$ to an external medium which contained either Na free choline Cl Ringer's or a low ionic strength solution. In the latter case net Na movement was virtually eliminated by $FeCl_3$. Addition of $FeCl_3$ to the serosal medium caused a delayed inhibition of J_{13}^{Na} but no changes in Cl fluxes. Immediate and profound changes in Na and Cl transport after external application of $FeCl_3$ indicate a change in ion selectivity of the apical cell membrane thus strongly suggesting charge effects on the surface of the membrane close to or in ion channels. As net Na transfer is equal to net charge transfer, the observation of net inward Cl movement under control conditions suggests electroneutral net Cl movement across the apical cell membrane which does not involve NaCl transfer but possibly $Cl^- - HCO_3$ exchange. However, net outward Cl movement seen after $FeCl_3$ is accompanied by net charge transfer.

ANALYSIS OF CO_2 ELIMINATION IN THE LUNG: EFFECTS OF RED CELL CHLORIDE SHIFT KINETICS. A. Bidani* and E.D. Crandall. U. of Texas, Galveston, TX 77550 and UCLA, Los Angeles, CA 90024

A mathematical model describing the events that occur in blood during and after gas exchange has been used to study the influence of erythrocyte membrane HCO_3^-/Cl^- exchange kinetics on CO_2 elimination in the lung. In addition to the chloride shift, the model includes: 1) CO_2-H_2CO_3 hydration-dehydration reactions in plasma and erythrocytes; 2) CO_2 reactions with hemoglobin; 3) O_2 binding to hemoglobin; 4) buffering of H^+ intra- and extracellularly; 5) diffusion of gases between alveolar gas and blood; and 6) red cell volume changes. Ion and water fluxes are assumed to occur passively down their electrochemical and osmotic gradients respectively. The analysis was performed assuming variable amounts of carbonic anhydrase activity are present in plasma, with acceleration of the extracellular reactions ranging from 0 to 1000. Phenomenological permeability coefficients for HCO_3^- and Cl^- ranged from 10^{-9}-10^{-1} cm/sec. The results show that reduction of red cell membrane permeability leads to a decrease in pulmonary CO_2 elimination of up to 30%, whether or not carbonic anhydrase activity is present in plasma. Characteristic downstream pH and pCO_2 changes are predicted for each case. We conclude that red cell membrane HCO_3^-/Cl^- exchange partially limits CO_2 elimination from blood in the lung, and may have a major influence on gas exchange when the permeability of the membrane to HCO_3^- and Cl^- is abnormally low. (Supported by HL 19737, AHA 75-992, and RCDA HL 00134.)

CORONARY VASCULAR RESPONSE TO BEHAVIORAL STRESS IN DOG. G.E. Billman & D.C. Randall. Univ. KY Col. Med., Lexington, KY 40536

Left circumflex coronary blood flow (CBF) was measured in 5 dogs during classical aversive conditioning (30 sec. tone followed by 1 sec. shock) using continuous wave doppler flow transducers. The conditional response (CR) consisted of a mean increase in: a) aortic pressure of 14.6 ± 2.8 mm Hg (12% ↑); b) d(LVP)/dt of 1,405 ± 226 mm Hg/sec (45.3% ↑); and, c) heart rate of 46.1 ± 6.0/min (46.6% ↑). To assess the contributions of metabolic and direct neural factors in controlling CBF the dogs received: a) pacing at 180/min, b) cardioselective β-blockade (CBB) [metoprolol, 1.5 mg/kg], and c) CBB + pacing. Late diastolic (LD) and mean CBF, and coronary vascular resistance (CVR) changed as follows (Paired t test: * P < .05, † P < .01):

Test	#	LD CBF ml/min	CBF ml/min	LD CVR mmHg/ml/min	CVR mmHg/ml/min
control	5	32.9 ± 2.6*	21.5 ± 2.2†	-0.7 ± .1*	-1.3 ± .1†
pace	4	8.4 ± 4.7*	7.8 ± 3.0*	-0.2 ± .1†	-0.4 ± .2*
CBB	4	3.6 ± 2.1	3.8 ± 2.0	-0.2 ± .2	-0.8 ± .5
CBB + pace	4	3.4 ± 3.3	3.9 ± 2.6	0.1 ± .1	-0.2 ± .1

These data show that the CR is primarily mediated by metabolic factors, though preliminary experiments (α-blockade) indicate a small neurally mediated coronary vasoconstriction may also occur. (Sponsored by NIH grant HL 19343)

DIFFERENCES IN PLACENTAL DIFFUSION PERMEABILITIES AND VOLUMES OF DISTRIBUTION FOR $^{22}Na^+$ IN NEPHRECTOMIZED AND NORMAL SHEEP FETUSES. Nancy D. Binder,* Kent L. Thornburg, and J. Job Faber, Dept. of Physiology, School of Medicine, University of Oregon Health Sciences Center, Portland, OR 97201

We measured the placental diffusion permeability and the fetal volume of distribution for $^{22}Na^+$ in 9 nephrectomized and 7 control fetuses. All fetuses had chronic indwelling catheters. Experiments were performed 2 to 21 days (mean 6) days after surgery. The mean volume of distribution per kilogram fetal weight was 554 ml/kg (range 329 - 695) for control fetuses and 1004 ml/kg (range 572 - 1902) for nephrectomized fetuses, ($p<0.005$ by the Mann-Whitney U test). The mean permeability per kilogram fetal weight was 5.30 10^{-3} ml/(min kg) (range 4.02 10^{-3} - 6.07 10^{-3} for control fetuses versus 13.84 10^{-3} (range 6.58 10^{-3} - 3.21 10^{-2}) for the nephrectomized fetuses, ($p<<0.005$). There was no significant correlation between the volume of distribution or the permeability (per kilogram) and the fetal weight for either the control or the experimental fetuses. There was also no significant correlation between either measurement and the interval between surgery and experiment.

Supported by NIH HD12017.

RECRUDESCENT PERIPHERAL CHEMORECEPTOR SENSITIVITY FOLLOWING DENERVATION. Gerald E. Bisgard, Hubert V. Forster and John P. Klein*. Univ. of Wisconsin, Madison, WI 53706

We previously demonstrated progressive recovery of peripheral chemoreceptor (PC) activity after carotid body (CB) denervation (D) in 7 ponies (JAP 40:184, 1976). Data from that study suggested aortic bodies may have been responsible for the recovery of function. We have subsequently studied 6 ponies over a period of 4 years following total PCD. Return of PC activity was slower than after CBD alone and was characterized by variable return of resting $\dot{V}_E$ toward normal. Responses to acute hypoxia and to NaCN (50 µg/kg IV) recovered variably but remained depressed (Table).

		Period after PCD					
	Contr	3 wk	12 wk	10.5 mo	17 mo	22 mo	48 mo
$PaCO_2$	40.2	48.9	46.6	44.4	45.3	42.8	42.0
$\Delta PaCO_2$ Hypoxia*	-7.5	+2.5	-0.4	-2.3	-3.7	-4.2	-1.63
VR+ Hypoxia	2.2	1.19	1.22	1.26	1.70	1.51	1.24
VR+ NaCN	8.47	1.13	1.24	1.45	1.55	2.04	1.65

*Change in $PaCO_2$ from normoxia to PaO_2 ~40 torr;
+VR = Test $\dot{V}_E$/Control $\dot{V}_E$

Ventilatory acclimization to chronic hypobaric hypoxia was not sustained 4 wk (JAP 41:878, 1976) and 48 mo after PCD. We conclude that only partial recovery of PC function is possible after PCD. (Supported by USPHS, NIH Grant HL 15473)

RENAL VASODILATION AND $U_{Na}V$ DURING CONSCIOUSNESS AND ANESTHESIA IN SHEEP. Edward H. Blaine, Mary C. Dunlay* and Mark B. Zimmerman*. Merck Institute for Therapeutic Research, West Point, PA 19486.

We previously reported (PSEBM 158:250, 1978) that renal vasodilation by papaverine in conscious sheep did not augment $U_{Na}V$ but did so in chloralose-anesthetized animals. In this previous experiment, two separate groups of animals were studied. We have extended these findings by studying the effects of 3 doses of papaverine (5, 7 and 10 mg/min infused into the renal artery) in the same sheep during a period of consciousness followed by barbiturate anesthesia. Papaverine increased renal blood flow during both consciousness and anesthesia. $U_{Na}V$ did not change during consciousness (-4±4, -5±5, -1±6 µEq/min) but increased (54±39, 108±52, 172±73 µEq/min) in a dose-related manner after induction of anesthesia. Likewise, papaverine had no significant effect on FE_{Na} while the sheep were conscious but increased FE_{Na} during anesthesia (0.9±0.4, 1.8±0.6, 3.0±1.0%). Anesthesia increased arterial BP (90±2 vs. 105±4 mm Hg) and GFR (44±5 vs. 59±5 ml/min) and decreased RBF (427±26 vs. 396±37 ml/min). BP was not significantly altered by the papaverine infusion and GFR tended to decrease slightly. It was concluded that renal vasodilation per se does not increase $U_{Na}V$ in sheep and that anesthesia can significantly alter the renal response to vasodilators.

REFLEX CHANGE IN FELINE CARDIAC REFRACTORY PERIOD. R.W. Blair* and V.S. Bishop. Univ. of Tx. Hlth. Sci. Ctr. at San Antonio, Tx. 78284

We have previously reported that afferent stimulation of the caudovagal nerve (CVS) reflexly increases the refractory period (RP) of the left ventricle. The present study extends the initial work to further define the reflex pathways involved. The caudovagal nerve was cut distally and the central end was stimulated with pulses of 35-50 Hz, 0.2-1.0 msec duration, and 2-4 V. During the determination of RP, hearts were paced at intervals of 224-315 msec. Control CVS increased RP 8 msec. Left cardiac sympathectomy (symx) had no effect on the response, but right symx limited it to 6 msec. Bilateral symx was similar to right symx alone. Subsequent atropine administration (0.2 mg/kg) blocked 4 msec of the remaining response. Atropine given before symx limited the increase in RP due to CVS to 4 msec. After subsequent right symx the increase in RP was only 1 msec. Left symx after atropine decreased the response only 1 msec. Total symx after atropine abolished the response. We conclude that: (1) the dominant efferent reflex path lies in the vagi; (2) the sympathetics have a significant role only when the vagi are blocked; and (3) when active, the efferent sympathetic paths course mostly through the right side. (Supported by NIH grant HL-12415 and AFOSR #73-2525)

THERMAL PROTECTION IN NEONATE MUSKOX. A. S. Blix, R. G. White and H. J. Gray, Inst. of Arctic Biology, University of Alaska, Fairbanks, Alaska 99701

Neonate muskox (Ovibos moschatus) are well protected against cold stress through fur insulation of both trunk and legs. In newborn calves exposed to -25°C subcutaneous temperatures were about 34°C and no evidence was found for counter current heat exchange in the legs. The fasting metabolism of 1 and 7 d old calves at thermoneutrality was, respectively, 5 and 3.6 $W \cdot kg^{-1}$ (i.e. 2.5 and 1.9 times standard fasting metabolism). In the 7 day old calf the lower critical temperature was about -8°C and at a temperature of -30°C a 50% increase in metabolic rate was recorded. The upper critical temperature was 20°C. Electron microscopic studies and in vitro studies of isolated mitochondria from the brownish fat deposits (in the abdominal cavity) revealed that this tissue might contribute heavily to nonshivering thermogenesis (NST) by virtue of loosely coupled mitochondria. No evidence for NST was obtained in skeletal muscle. Field studies indicate that newborn muskox shiver only during initial drying. (Supported by NSF grant no. DPP 7718384 and A/S Norsk Moskus.)

EARLY CARDIOVASCULAR ADAPTATION TO ZERO GRAVITY SIMULATED BY HEAD-DOWN TILT. C. Gunnar Blomqvist*, J.V. Nixon*, Robert L. Johnson, Jr., and Jere H. Mitchell. Southwestern Med Sch, Univ of Tx Health Sci Ctr, Dallas, TX 75235.

Early adaptive responses to 0g, simulated by a 24 h period of head-down tilt at 5°, were studied in 10 normal young men. Tilt produced a central fluid shift, documented by a decrease in leg volume from 15.1 to 14.2 L ($p<0.01$). Orthostatic tolerance and upright exercise capacity were reduced post-tilt. Heart rate during lower body negative pressure at -40 mmHg was 24 bpm higher ($p<0.05$) and maximal O2 uptake 22% lower ($p<0.05$). These changes were similar to those observed during and after space flight. CVP increased from 4.9 to 7.4cm H_2O after 30 min ($p<0.02$) but returned to baseline within 60 min. Echocardiographic left ventricular end-diastolic diameter showed a delayed transient increase from 4.09cm to 4.56 at 90 min ($p<0.01$). Cardiac output (C_2H_2 rebreathing), blood pressure, and left ventricular contractile state did not change. Stroke volume was 6.2% above baseline at 90 min and 6.7% below at 24 h ($p<0.02$). Urine flow was 1.98 ml/min during the initial 8 h and 1.36 during the final 16 h ($p<0.05$). Blood volume decreased by 0.36 L ($p<0.001$). Plasma renin activity, aldosterone, and ADH were depressed initially but returned to baseline within 24 h. Venous compliance and arterial vasoconstrictor responses were unchanged. The data indicate that head-down tilt is a valid model of 0g. Hemodynamic adaptation occurs rapidly and includes a diuresis and reduction in blood volume.

LACTATE UTILIZATION BY RAT LUNG. H. J. Blytt* and R. A. Rhoades. Department of Physiology, Indiana University School of Medicine, Indianapolis, Indiana 46223

The lung produces and utilizes lactate. The present investigation examined the regulation of lactate oxidation and incorporation into biosynthetic products by rat lung slices. Lung slices incubated in the presence of 5 mM glucose, 5 mM [1-^{14}C]lactate produced 92.4 ± 4.2 nmole $^{14}CO_2$/min/g wet wt (mean ± SE). Omission of glucose increased the rate by 21%. With lactate as a variable substrate, the apparent Km was 3.9 ± 0.7 mM and V_{max} was 166 ± 14 nmol $^{14}CO_2$/min/g. Omission of glucose reduced the Km to 1.6 ± 0.3 mM with no effect on V_{max}. These data indicate that lactate produced from glycolysis competes with exogenous lactate. The active form of pyruvate dehydrogenase (PDH) was 50.2 ± 3.8 nmol/min/g. Streptozotocin induced diabetes decreased the active PDH by 89%. Dichloroacetate (DCA) injection (2 mM/kg, IP) also increased the active PDH by 117%. Lung slices from diabetic rats produced 34% less $^{14}CO_2$. Addition of 1.6 mM DCA to the incubation did not increase $^{14}CO_2$ production by lung slices. These data suggest that the active form of PDH is higher in vitro than in vivo. The utilization of [3-^{14}C] versus [1-^{14}C]lactate in vitro showed that 40% of the acetyl CoA derived from lactate is oxidized to CO_2 and 20% is incorporated into lung lipids. (Supported by NIH HL 20566 and Research Career Development Award K04 HL 317).

FACTORS LIMITING PERFORMANCE IN SCLEUS AND GRACILIS MUSCLES OF CATS. Emma L. Bockman. Dept. of Physiology, LSU Med. Ctr., 1542 Tulane Ave., New Orleans, LA 70112.

Force development (F), O_2 consumption (VO_2) and blood flow were compared in slow twitch, oxidative (soleus; N=8) and fast twitch, low oxidative (gracilis; N=8) muscles. Venous outflow was measured with a drop counter. Muscles were stimulated to contract isometrically via the nerve. Maximum F was similar in both muscles (104±16 and 88±12 g force/g muscle for soleus and gracilis, respectively). The energy cost for twitch contractions was less for soleus than for gracilis as indicated by $VO_2/(F \times Hz)$: 3.4±0.5 and 11.6±1.5 µl O_2/kg F for soleus and gracilis, respectively. In soleus, the energy cost for tetanic (0.8 µl O_2/kg F) was less than for twitch contractions. Soleus showed little tendency to fatigue while F in gracilis decreased to less than 40% of maximum at 1 Hz. Although maximum blood flow and VO_2 were less in gracilis (28 ml/min/100g and 3 ml O_2/min/100g) than in soleus (37 ml/min/100g and 5.5 ml O_2/min/100g), limitation of O_2 delivery did not seem to be the cause of fatigue. As VO_2 increased towards maximum in gracilis, O_2 extraction decreased from a high of 15 vol% to 10 vol%. Thus, more O_2 was delivered than was consumed. These results indicate that performance of gracilis muscle is limited by its oxidative capacity. Performance of soleus muscles was not limited as the result of greater maximum blood flow (O_2 delivery) and oxidative capacity as well as lower energy cost for contraction and lower fusion frequency. Supported by HL 17932.

GRACILIS ARTERY (GA) NOREPINEPHRINE (NE) SENSITIVITY DURING HYPO AND NORMOVOLEMIC SHOCK. R. F. Bond, L. C. Peissner, E. S. Manning* and C. H. Bond*. Kirksville College of Osteopathic Medicine, Kirksville, MO 63501

Previous reports have provided evidence for a significant loss of GA tone during late hemorrhagic shock. The objective of the present investigation was to determine: 1) if an α-receptor desensitization plays a role in this loss of tone, and 2) does α-receptor function remain viable throughout normovolemic shock. To accomplish these objectives the NE responsiveness of GAs removed from dogs during various stages of hypo- and normovolemic shock was evaluated. The GAs were placed in 34 ml tissue chambers where they were perfused and bathed with Krebs-Henseleit (37°C) bubbled with 95% O_2 and 5% CO_2 (pH 7.3). NE dose response curves were obtained using 9 NE bath concentrations between 0.1 µm and 1 mM. The ED_{50}s indicated no significant differences between control (3.69 ± .86 µm, n=10) and compensatory hypovolemic shock (6.29 ± 2.18 µm, n=9); however, significant reductions were noted during decompensatory hypovolemia (1.42 ± .27 µm, n=9), normovolemic normotension (1.30 ± 23 µm, n=8) and normovolemic hypotension (1.13 ± .18 µm, n=7). These data suggest that the α-receptors in GAs become more sensitive to NE as the animal progresses into irreversible hemorrhagic shock and that the loss of vascular tone is more likely the result of an adrenergic transmission failure than α-receptor desensitization.
(Supported by AOA Grant 75-98 and NIH grant RR09130.)

CARDIOVASCULAR RESPONSES TO ISOMETRIC EXERCISE DURING SIMULATED ZERO GRAVITY. F. Bonde-Petersen Y. Suzuki and Tomoko Sadamoto. August Krogh Institute, Universitetsparken 13, DK 2100 Copenhagen University, Copenhagen, Denmark.

Exercise during space flights is rather static than dynamic. Six subjects performed isometric exercise during 2 min of knee extension, plantar flexion and handgrip at 40% maximum strength in both sitting (1 G) and supine (zero G) position. Forearm blood flow (FBF)(air plethysmograph) heart rate (HR)(ECG) and arterial blood pressures (BP) (arm cuff) were followed. During knee extension, sitting, mean BP (MAP) increased 39%, forearm vascular resistance (FVR) by 19%, HR 16% and FBF by 33%. Supine resting HR, MBP, FBF and FVR decreased (vagal effect). During supine knee extension all parameters recorded showed lower values than during sitting. During handgrip and plantar flexion similar patterns were observed. The variation in cardiovascular parameters between muscle groups did not correlate to muscle mass but more closely followed the rated perceived exertion (Borg scale). We conclude that baroreceptors are more successful in attempt to autoregulate during zero gravity than in 1 G due to the increased sympathetic tone in the latter condition.

ELECTRICAL STIMULATION OF CHOLINERGIC NERVES TO SUBMUCOSAL GLANDS IN FERRET TRACHEA IN VITRO. B. Borson,* R. Chinn,* B. Davis and J. Nadel. C.V.R.I., UCSF, San Francisco,CA 94143

We excised tracheas from ferrets, mounted pieces (0.79 cm^2) as flat sheets in a chamber and perfused the submucosal side with oxygenated (95% O_2, 5% CO_2) Krebs-Henseleit solution at 37°C to maintain viability. We sprayed powdered tantalum on the luminal surface which was open to the air. After electrical stimulation (100 V, 30 cps, 0.5 msec) via metal pins through the edge of the trachea or after adding a drug to the submucosal bath, secretions from the gland duct openings formed elevations in the tantalum layer (hillocks). We photographed and counted hillocks at the end of timed periods before and after the stimulus. Electrical stimulation increased the rate of hillock formation from 23 to 152/cm^2·min. This effect was blocked by tetrodotoxin (10^{-5} M), a specific toxin for nerves. After tetrodotoxin, acetylcholine (10^{-3} M) increased rate of hillock formation. Atropine (10^{-5} M) decreased the response to electrical stimulation of the nerves. These studies used a new method to show that the tracheal mucus glands are innervated by cholinergic efferent nerves in ferrets. The new method is suitable for studies of regulation of airway submucosal gland secretion. (Supported in part by NHLBI Grants HL-06285, HL-21150 and the Cystic Fibrosis Foundation)

ORIGIN OF LOCAL CIRCUIT CURRENT FOR PROPAGATION OF INTESTINAL SLOW WAVES. Alex Bortoff, Upstate Med. Ctr., SUNY, Syracuse, N.Y. 13210.

The purpose of these experiments was to test the hypothesis that circular muscle (CM) plays an active role in the propagation of intestinal slow waves (SW's) (J. Physiol. 273: 665, 1977). The following results are incompatible with this hypothesis: (1) SW's propagated without decrement along segments of cat intestine devoid of a ring of CM up to 3 mm wide, i.e., across a LM bridge more than 4 space constants long (9/11), but did not propagate across a circumferential cut through the LM layer (14/14); (2) the membrane current associated with the SW had a pronounced inward component in the LM bridge, but was entirely outward in adjacent CM; (3) the differences in propagation velocities between duodenum and mid-jejunum could be correlated with differences in the longitudinal internal resistance of LM, as predicted by core conductor theory. In some preparations in which SW's did not traverse the lesion small deflections occurred which corresponded to potential deflections associated with propagated SW's on the opposite side of the lesion, indicating that electrotonic current flows between both muscle layers. Finally, notches appearing in records obtained in volume from CM corresponded to the negative deflection recorded from LM, suggesting that the large initial depolarization and notch sometimes recorded intracellularly from LM may be due to superposition of field potentials on the transmembrane potential change. (Supported by USPHS, NIH Grant AM 06958)

THE EFFECT OF NITROGLYCERIN ON EXCITATION OF UNMYELINATED AFFERENT CARDIAC SYMPATHETIC NERVES DURING MYOCARDIAL ISCHEMIA. Z.J. Bosnjak*, J.L. Seagard, and J.P. Kampine. Med. College of Wisconsin and Wood VA Ctr., Milwaukee, WI 53193

Acute left anterior descending or left circumflex coronary artery occlusion produced excitation of cardiac sympathetic afferent unmyelinated fibers originating from receptors located within the ischemic myocardium. The present study was designed to determine the affect of direct action of nitroglycerin on these cardiac receptors. Six mongrel dogs were anesthetized with sodium pentobarbital (30-40 mg/kg). Left ventricular and systemic blood pressure, ECG, myocardial length and afferent nerve activity were measured before, during and after (30 sec) snare occlusion of the coronary arteries. Sympathetic afferent nerve activity was recorded in single and small multifiber preparations dissected from the slips of the left T_3 white rami communicantes. Only nerve activity recorded from the left ventricular receptors was selected for this study. Local intracoronary injection of nitroglycerin (100 µg) had no effect on excitation of the unmyelinated fibers during coronary occlusion. When systemic blood pressure was lowered with nitroglycerin (100 µg/kg) excitation of afferent nerve fibers was greatly reduced. It appears that nitroglycerin has no direct effect on the afferent sympathetic C fibers which are excited during coronary occlusion, but inhibits the same due to a decrease in myocardial oxygen requirements or by elimination of the systolic bulge. (Supported by NIH Grant HL 16511 and the VA).

REGIONAL BIOELECTRIC PROPERTIES AND ION FLUXES IN CANINE AIRWAYS. R.C. Boucher* and J.T. Gatzy* (SPON: J.C. Parker). University of North Carolina, Chapel Hill, N.C., 27514.

Our in vivo measurements of transmural bioelectric potential differences (PD) and analyses of surface liquid have suggested regional differences in electrolyte permeability and transport in canine airways. These possibilities were explored in vitro. Paired preparations of epithelia from canine trachea (T), main stem bronchi (MS) and ~7 mm (4-6th generation) bronchi (B) were mounted in Ussing chambers with an aperture of .53 cm^2. PD and short circuit current (I_{SC}) were recorded, conductance (G) calculated, and ^{22}Na, ^{42}K and ^{36}Cl fluxes (J) were measured under short circuit conditions. The means for tissues from 11 dogs were:

	PD (mV)	I_{SC} ($\mu amp/cm^2$)	G (mS/cm^2)	J_{net} lumen (M)≠serosa (S) ($\mu eq/cm^2hr$) Na^+	Cl^-	K^+
T	35.3	76	2.07	1.04 M→S	1.70 S→M	.016 M→S
MS	13.4	74	5.78	.87 M→S	1.25 S→M	.004 S→M
B	8.9	60	7.15	1.64 M→S	.09 S→M	.028 S→M

The sum of the partial ionic conductances ($J_{passive}$) for Na^+ and Cl^- approximated G in all preparations. The net flow of NaCl equalled I_{SC} of T and MS but accounted for 75% of I_{SC} of B, suggesting active translocation of an unidentified ion(s). We conclude that whereas the trachea may be described as a low G epithelia with a small net ion secretion, canine bronchi are characterized by greater G, K^+ secretion and, probably, active NaCl reabsorption. (Support: HL16674 and HL22924.)

EFFECT OF TOTAL LUNG TIME CONSTANT ON SCALING PULMONARY VARIABLES. R. L. Boyd*, M. J. Fisher, M. J. Jaeger, and C. Tu*. Departments of Pediatrics, Physiology, and Pharmacology and Therapeutics, University Of Florida, Gainesville, FL 32601

In a lung model of two parallel compartments, differences in the compartmental compliances ($C_1 \neq C_2$) and resistances ($R_1 \neq R_2$) lead to frequency dependence of compliance and frequency dependence of phase difference (PD) between mean alveolar pressure and flow rate at the mouth (Otis et al., J. Appl. Physiol. 8: 427-443, 1956 and Jaeger, Klin. Wsch. 46: 1156-1162, 1968). We used equations for effective compliance (Ce) and PD to determine the effect of the total lung time constant [$T_L = (C_1 + C_2)/(1/R_1 + 1/R_2)$] on these pulmonary variables. For a given set of C_1/C_2 and R_1/R_2 ratios we conclude the following: 1) the frequency (f) at which a particular Ce [expressed as a ratio of Ce at f = 0 (Ce/C_o)] or PD occurs is inversely proportional to T_L; 2) the minimal value of Ce/C_o is the same for all values of T_L; 3) the maximal value of PD is the same for all values of T_L; and 4) the product of T_L and f at a particular Ce/C_o or PD is constant. These conclusions suggest that both frequency dependence of Ce/C_o and frequency dependence of PD become comparable between lungs with different T_L values if the frequencies are multiplied by T_L and thus provide a basis for comparison of animals of different sizes. (Supported by NIH TR 05979 and the Parker B. Francis Foundation.)

COMPARISON OF SUBCUTANEOUS TRANSCAPILLARY STARLING FORCES IN GUINEA-PIG FETUS AND MOTHER. Robert A. Brace Depts. of Physiology and Perinatal Biology, Loma Linda University, Loma Linda, CA 92350

This study was designed to determine each of the 4 transcapillary Starling forces in subcutaneous tissue of the near-term guinea-pig fetus and to compare these forces with those in the mother. Plasma colloid osmotic pressure (πp) was measured by placing a plasma sample on an osmometer fitted with a membrane which restricted protein movement (Amicon UM-10). Interstitial fluid pressure (Pif) was measured by placing a subcutaneous tissue sample on an osmometer fitted with a membrane which did not restrict protein movement. Interstitial fluid colloid osmotic pressure (πif) was determined from the difference in absorption pressures of the subcutaneous tissue recorded on the above two osmometers. The average effective capillary pressure (Pc) was then calculated from the other 3 measured Starling forces by assuming the net pressure drop across the capillary membrane was negligible. The results (in mmHg) are as follows:

	πc	Pc	πif	Pif
fetus	14.0	7.0	5.2	-1.8
mother	12.6	8.1	2.5	-2.1

when comparing the fetus and mother, only the difference in πp and πif are significant. The near term guinea-pig fetus appears different from other mammals because πp is normally higher in the mother than fetus.

EARLY CARDIOVASCULAR RESPONSES CHARACTERISTIC OF SURVIVAL IN ENDOTOXIN SHOCK. D.J. Brackett*, M.F. Wilson, G.L. White*, and L.B. Hinshaw. Veterans Administration Medical Center and Depts. of Medicine and Physiology, OUHSC, Oklahoma City, Oklahoma 73104

Cardiovascular responses were examined in early stages of shock from slow endotoxin infusion into 11 closed chest, anesthetized dogs to search for distinguishing characteristics relating to survival. Methylprednisolone was used to increase survival. No differences existed between 6 survivors (S) and 5 non-survivors (NS) during the six hour observation period in hematocrit, leukocyte count, and blood glucose. Cardiac output, blood pressure, minute work, stroke work, stroke volume, (+) and (-) dP/dt decreased abruptly in NS, remained depressed for two hours, then rose to a plateau. Each parameter was lower in NS than S after one hour. The response in S was a gentle decline in the first two hours to near the plateau levels observed for the remaining four hours. Heart rate did not change for either group in the first two hours, but did increase in NS in the remainder of the observation period. Positive dP/dt in S remained at the plateau level, while it returned to control level in NS despite decreased preload and afterload. Respiration rate did not change in S but increased after 30 minutes and climbed during the entire 6 hours in NS. The attenuated cardiovascular response in S compared to NS indicates less initial withdrawal of circulating blood volume and/or greater early cardiac compensation to maintain tissue perfusion.

HIGH PRESSURE INHIBITION OF ADH RESPONSE IN TOAD BLADDER. Robert J. Brady*, Daniel H. Pope* and Robert H. Parsons, Department of Biology, Rensselaer Polytechnic Institute, Troy, N.Y. 12181

There have been numerous studies done in an attempt to elucidate the molecular events which are responsible for the biological effects of vasopressin (ADH). What physical or chemical changes in the membrane ultimately result in an increase in water permeability are not well understood. One possibility that has been studied recently, using pharmacological agents, is that vasopressin induces changes in microfilaments or microtubules which in turn cause a change in the membrane osmotic permeability. This study makes use of a technique, high hydrostatic pressure, which has been very useful in studying the role of microtubules in other cellular processes (mitolic spindle, ameboid movement, etc.). Pressure, 8,000 psi., causes a rapid inhibition (80-100%), when applied for 10 minutes simultaneously with the addition of ADH (20 mU/ml), of the hydroosmotic response in toad bladder. Upon release of the pressure there is a recovery to 50% inhibition at 30 min. after ADH stimulation. Pressure applied for 10 min. just prior to ADH stimulation results in a 25% inhibition at 30 min. Pressure applied for 10 min. 20 minutes before ADH stimulation (10 min. recovery) has no effect. Thus, the response of toad bladder to ADH shows a rapid inhibition and a rapid recovery when exposed to hydrostatic pressure.

LACTATE ABSORPTION IN PROXIMAL TUBULE. Paul H. Brand and R. Stansbury*, Medical College of Ohio, Toledo, Ohio, 43699.

Lactate is absorbed in the proximal tubule. A proposed mechanism involves passive luminal entry of lactate into the cell, conversion to glucose, and exit of glucose at the antiluminal border. To test this hypothesis, and to develop a system for study of proximal tubular lactate transport, we perfused individual proximal tubules from Thamnophis (Garter snake) kidney in vitro. In the same tubule, the undirectional fluxes of lactate from lumen to bath (J1b lact) and from bath to lumen (Jb1 lact) were measured at 25° and 5° C using $U^{14}C$-L(+) lactate, [lactate] = 1 mM. In both proximal proximal (PP) and distal proximal (DP) segments, J1b lact > Jb1 lact, with $\bar{X}$ flux ratios in DP = 3.11 ± 1.89, n = 7, and in PP = 3.06 ± 0.661, n = 5. Net flux was similar in DP and PP and was ~ 1.60×10^{-12} $M \cdot min^{-1} \cdot mm^{-1}$. Both J1b lact and Jb1 lact were markedly decreased at 5°. To test for metabolic conversion of lactate during absorption, J1b lact was measured in 10 DP and the amount of ^{14}C lost from the lumen was compared to the amount found in the bath. Also, aliquots of bath were assayed for lactate by thin layer chromatography (TLC). The amount of ^{14}C found in the bath was 93.1 ± 14.3% of the amount lost from the lumen, and by TLC was 93 ± 2.43% lactate. We conclude that during absorption in Thamnophis proximal tubule, lactate moves against an electrochemical gradient, and does not undergo significant metabolic conversion.

Morphology and blood flow patterns of the avian renal portal system (RPS) Eldon J. Braun, Gary L. Anderson*, and Robert F. Wideman*. Dept. of Physiol, Coll Med, U of Ariz, Tucson, AZ 85724

The peritubular surfaces of the nephrons within the avian kidney are perfused by blood from two sources: 1) efferent glomerular blood, and 2) afferent venous blood (RPS). However several points remain unclear concerning the nature of this dual perfusion. To clarify these perfusion patterns, gelatin casts were made of the efferent venous, afferent venous (RPS) and tubular systems of domestic fowl kidneys. The following pattern became apparent. The small nephrons (reptilian type; RT) near the surface of the kidney are arranged in a radiating pattern about a central core, the central vein (CV). The periphery of these cylinders are marked by the interlobular renal portal vessels (IRPV). These vessels give off right angle branches which run parallel to the renal tubules and eventually empty into the CV. These branches are sinus like in nature. An individual RT nephron spans the space between the CV and IRPV. Intralobular arteries (IA) run parallel to the CV and IRPV at a point equidistant between the CV and IRPV. Afferent arterioles branch at right angles from the IA. The efferent arterioles (EA), without branching, course toward the IRPV and enter the RP capillaries. In this arrangement only the early portion of the PT is bathed by EA blood. The remainder of the nephron is bathed by a mixture of EA and RP blood as this blood flows from the periphery of the cylinder to the CV. NIH AM 16290 NSF 77-04958

QUANTITATIVE ANALYSIS OF AGE CHANGES IN SHORT-TERM MEMORY, NEURON POPULATIONS, SYNAPTIC JUNCTIONS AND ASTROGLIAL PROCESSES IN THE HIPPOCAMPUS OF THE RHESUS MONKEY. K.R. Brizzee, C. A. Knox*, S. K. Jirge*, R. T. Bartus*, and J. M. Ordy, Delta Regional Primate Center and Departments of Anatomy and Neurosurgery, Tulane University, Covington and N.O., La.

Five young adult and 5 old rhesus monkeys were compared on short-term memory in a delayed response task. The aged monkeys were significantly inferior in short-term memory in delayed response performance at 15 and 30 second delay intervals. In another group of 3 young adult and 3 old rhesus monkeys the mediolateral width of the CA-1 zone (Sommer's sector), as observed in toluidine blue-stained transverse sections of Epon-imbedded hippocampal tissues was smaller in old than in young adult animals, but the difference was not statistically significant. However, the mean depth of the lamina pyramidale in the CA-1 zone was significantly less ($p<.05$) in old than in the young adult specimens. The mean number of pyramidale neurons per 55μm segment of the lamina pyramidale in the CA-1 zone was significantly less ($p<.01$) while the number of glial cells was significantly greater ($p<.05$) in the old than in the young adult animals. The numerical density of synaptic junctions in the stratum radiatum decreased by 25% and the volume density of astroglial processes increased by 567% in 3 old as compared with 2 young adult subjects. (Supported in part by NIH RR-00164-16 and by a grant from the Lederle American Cyanamid Corp.)

EFFECT OF PHYSICAL TRAINING IN COOL AND HOT ENVIRONMENTS ON $+G_z$ ACCELERATION TOLERANCE IN WOMEN. P. J. Brock*, D. Sciaraffa*, and J. E. Greenleaf. NASA, Ames Research Center, Moffett Field, CA 94035.

To investigate the hypothesis that isotonic exercise training may decrease acceleration tolerance, 15 women (21-41 yr) were divided into 3 groups; a group (EH) who exercised in the heat (40.6°C, 42% rh) for 2 hr/d for 8 consecutive days at 52% of their maximal O_2 uptake ($\dot{V}O_2$ max), and 2 groups in a cool environment (18.7°C, 48% rh); one (EC) exercised for 2 hr/d for 8 days at 55% $\dot{V}O_2$ max, and the third was a sedentary, control group (CC). During the training periods the $\bar{X}$ (±SE) $\dot{V}O_2$ max increased from 3.01 ± 0.16 to 3.25 ± 0.14 (+8%, NS) and terminal heart rate decreased from 167 ± 8 to 140 ± 7 b/min (-16%, $P<0.05$) in the EH group; in the EC group $\dot{V}O_2$ max decreased from 2.58 ± 0.19 to 2.33 ± 0.12 L/min (-10%, $P<0.05$) and heart rate decreased from 145 ± 8 to 128 ± 6 b/min (-12%, $P<0.05$). In spite of these training effects, acceleration tolerance (seconds at 0.5 G/min to greyout) was unchanged in all 3 groups: EH was 392 to 381 sec (NS), EC was 376 to 398 sec (NS), and CC was 410 to 373 sec (NS). It is concluded that 8 days of moderately hard isotonic exercise training in cool or hot environments has no significant effect upon tolerance to $+G_z$ acceleration at 0.5 G/min.

EFFECT OF ATROPINE ON RESPIRATORY HEAT LOSS (RHL) IN ASTHMATICS. Frank J. Breslin*, E.R. McFadden, Jr., R.H. Ingram, Jr., E. Chandler Deal, Jr.* Peter Bent Brigham Hospital and Harvard Medical School, Boston, MA 02115.

Recent evidence demonstrates that the stimulus for post-exertional airway obstruction in asthmatics is airway cooling. Previously, we have observed that although atropine does not alter the magnitude of the response to exercise while breathing cold air, it does cause the predominant site of obstruction to move into the lung periphery. These observations have led us to speculate that this drug might, through mucosal drying, impair the heat exchanging capacity of large airways thus allowing deeper penetration of poorly conditioned air. As a first step in testing this hypothesis we measured RHL and retrotracheal and retrocardiac esophageal temperatures in 8 asthmatic subjects while they performed eucapnic hyperventilation with cold air both before and after the inhalation of 6 mg of atropine. We also recorded multiple aspects of pulmonary mechanics before and 5 minutes after each challenge. Significant and equivalent airway obstruction developed with and whthout atropine (control ΔFEV_1=1.0±0.2 L SEM; post atropine=0.9±0.3 L). Despite similar obstruction, RHL was 17.1% greater and retrotracheal temperature fell 16% more after atropine. These data show that atropine increases RHL and both the rate and magnitude of airway cooling. Further they suggest to us that this agent shifts the overall airway response to RHL in addition to changing the distribution of bronchial obstruction.

PULMONARY EDEMA IN DOGS AFTER METHOXYFLURANE ANESTHESIA & RAPID INTRAVENOUS MANNITOL INFUSION. K. A. Brock* and J. C. Thurmon*, Dept: Veterinary Clinical Medicine, University of Illinois, Urbana, IL 61801. (SPON: W. C. Wagner)

Mannitol 20% was infused into 8 healthy Methoxyflurane-anesthetized dogs (5 with IPPB, 3 spontaneously breathing) @ 2.2 gm/kg. Previous clinical experience of pulmonary edema after this combination suggested the possibility of decreased left ventricular (LV) performance, compared with the increased intravascular volume from the osmotic effect of Mannitol. The parameters measured in this study were:

	Pulmonary Artery (PA) Pressure (torr)	PA Wedge Pressure (torr)	Central Venous Pressure (torr)	Aortic Pressure (torr)	Cardiac Index (litres/min/kg)
Control	14.0/7.5	6.75/4.5	3.0/-1.0	112/79	0.13
End Infusion	15.6/8.2	6.85/4.5	4.7/1.4	121/74	0.19
90 minutes post infusion	14.3/5.5	5.9/4.25	2.96/-0.5	95/60	0.08

Six dogs had pulmonary edema of varying degrees, evident on histopathological examination; the edema fluid had low or no protein content. The LV dP/dt_{max} values did not alter significantly during this study, suggesting that inotropic state of the myocardium probably did not change. These observations suggest that under these conditions, pulmonary edema may occur despite unaltered or enhanced LV function, thus indicating it to be noncardiogenic edema associated with minimal or no change in pulmonary microvascular permeability.

ELEVATED PLASMA VASOPRESSIN AFTER CHRONIC INTRACEREBROVENTRICULAR (ICV) INFUSION OF ANGIOTENSIN II. T. A. Brock*, P.C. Jobe* and J.N. Diana, Depts. of Physiology and Pharmacology, L.S.U. Medical Center, Shreveport, LA 71130.

The increase in blood pressure (BP) in rats in response to ICV injections of angiotensin II (A-II) is known to be partially mediated by the release of vasopressin (ADH). In the present experiments we have studied the possibility that chronic ICV infusion of A-II may elevate plasma ADH levels and increase BP. Rats were implanted with chronic ICV cannulae attached to an Alzet osmotic minipump and infused with 6μg/hr of A-II for a period of 2 weeks. Water consumption in the A-II infused rats increased to a peak within the first 24-72 hrs in all rats and then declined but remained significantly elevated throughout the 2 week period. Urine output rose and fell concommitantly with water intake. After 2 weeks of ICV A-II infusion, rats exhibited a significant increase in BP (126±4, 174±7mmHg) whereas ICV saline infused rats showed no increase in BP (125±3, 127±3mmHg). Plasma ADH levels were increased approximately 5 fold in the A-II infused group (8.6±1.4 pg/ml) when compared to the saline infused group (1.8±0.5 pg/ml). Plasma Na^+ and K^+ levels remained unchanged between groups. The data suggest that an increase in plasma ADH levels may play an important role in elevating blood pressure in this form of hypertension.

IN VIVO MEASUREMENTS OF TRACHEAL BIOELECTRIC POTENTIAL DIFFERENCES IN NORMAL HUMAN SUBJECTS. P. Bromberg, W. Buntin,* J. Gatzy,* R. Boucher.* The University of North Carolina School of Medicine, Chapel Hill, NC 27514.

Transmural bioelectric potential differences (PD) reflect active and passive ion permeabilities of respiratory epithelia. In vitro tracheal PD values reported for animal species range from 6 mV (rat) to 30 mV (dog), lumen negative, and in vivo PD measurements in intubated, anesthetized dogs were similar to the in vitro results. No human studies have been reported. Healthy subjects, mean age 28 years, who required anesthesia and endotracheal intubation for diagnostic or therapeutic procedures were studied. The subjects denied symptoms of respiratory disease, cigarette smoking or medication use. To measure tracheal PD, a fluid-filled polyethylene bridge catheter, continuously perfused (0.4 ml/min) with Ringers was placed on the tracheal surface via the endotracheal tube. A reference electrode (19 gauge butterfly needle filled with Ringer-4% agar) was inserted subcutaneously. Each bridge was connected via paired calomel half cells to a voltmeter and PD recorded on a strip chart. Mean tracheal PD in 18 subjects was 32 mV ±4.4 S.D., lumen negative. No significant differences in PD were observed between male (-31 mV) and female (-32 mV) subjects. We conclude that human tracheal PD can be readily measured with a fluid-filled bridge and within the spectrum of reported mammalian values, tracheal PD's in normal adults are comparatively high.

RENIN SECRETION DURING CAROTID SINUS NERVE STIMULATION AND HEMORRHAGE IN DOGS. K. Bridget Brosnihan, Cleveland Clinic Research Division, Cleveland, Ohio 44106.

To clarify the role of the sympathetic nervous system in reflex regulation of renin release, a combination of stimuli which alternately reduce and increase reflex sympathetic tone was assessed in relation to renin release. Electrical stimulation of the carotid sinus nerve (CSN) and hemorrhage (H) were applied to α-chloralose-anesthetized dogs which had been previously sodium depleted. Under the two conditions mean arterial pressure (MAP) was reduced similarly (59 ± 7 mm Hg vs 61 ± 8 mm Hg, CSN vs H) to insure that the intrarenal baroreceptor would be stimulated in comparable fashion. CSN stimulation alone did not influence renal blood flow (RBF), reflecting the small contribution of tonic renal vasomotor tone. Therefore the elevated renal vein plasma renin activity (PRA)(33.13 ± 5.37 to 55.23 ± 10.35 ng/ml, $p < 0.05$) during CSN stimulation must reflect stimulation of the intrarenal baroreceptor. For the same decrease in MAP, H significantly reduced RBF (167.5 ± 20.2 ml/min to 101 ± 24.8 ml/min), and renal vein PRA was more markedly increased (45.8 ± 9.1 to 93.7 ± 13.3 ng/ml, $p < 0.05$). The 32% increase in PRA in H over that found with CSN stimulation reflects the contribution of the sympathetic nervous system, whereas 68% of PRA can be attributed to intrarenal baroreceptor stimulation. (Supported in part by a grant from American Heart Association, Northeast Ohio affiliate).

THE EFFECT OF BOVINE SERUM ALBUMIN ON THE RELEASE OF RENIN IN THE ISOLATED PERFUSED RAT KIDNEY. Mamie E. Brown* and Joseph B. Myers. Department of Biology, Atlanta University, Atlanta, GA 30314.

Plasma renin activity (PRA) was measured in rats in which the perfusate contained all of the components found in Krebs-Henseleit solution except bovine serum albumin (BSA). The purpose, therefore, of this experiment was to determine the influence of BSA on the isolated perfused rat kidney system at a relatively high perfusion pressure. Rats were anesthetized with sodium pentobarbital (Nembutal, 30mg/kg) and the abdominal aorta was cannulated at the iliac bifurcation. All secondary arteries were ligated distal to the renal artery after which the right kidney was removed. At a constant perfusion pressure of 150 mmHg perfusate samples were collected at 15, 30, 60 and 90 min. intervals. PRA values averaged 11.3, 17.2, 20.4 and 2.6 ng/ml/hr respectively. Kidneys from normotensive rats in which the BSA concentration in the perfusate was 7g/100ml and the perfusion pressure at 110mmHg, PRA values plateaued at 43.3 ng/ml/hr. Our preliminary results suggest that BSA in perfused kidneys removed from normotensive rats plays a major role in renin release. In as much as when BSA is absent from the perfusion medium renin activity is significantly reduced. These findings indicate that plasma protein concentration at the glomerular level by some mechanism affects the translocation of important ions, most likely Ca^{++}. (Supported by the NIH-MBS Project, Grant No. RR 8006-4).

TIME COURSE OF PERIPHERAL HETEROTHERMY IN A HOMEOTHERM.

R. Brown* and J.G. Baust. Dept. of Biology, U. of Houston, Houston, TX. 77004.

The intensity of the peripheral heterothermic response was monitored in adult Sprague-Dawley rats during cold acclimation. Subcutaneous temperature gradients were simultaneously recorded in a chilled hind limb and the contralateral control limb after acclimation to 5° ± 1°C for periods up to 28 days. Control animals responded to the cooling regimen (25 to 0°C at 0.5°C/min) in a "poikilothermic" manner indicating local cold induced vasoconstriction (CIVC). Civc was released when tissue temperatures reached 21.7° ± 3.8°C whereupon non-patterned limb temperature fluctuations occured. Limb temperature fluctuations occurred synchronously in the contralateral control limb despite its elevated temperature. After 21 days of 5°C exposure, limb exposure to 0°C resulted in a 2-5°C drop in tissue temperature. The results indicate a decrease in the intensity of heterothermy indicative of an earlier onset of cold induced vasodilation (CIVD) and increased resistence to tissue cooling with increasing acclimation time. Evidence for a central component of the hunting response is also provided. Cold acclimation is accomplished in 19-21 days for this species according to these criteria. (Supported by NR 207-116).

EFFECTS OF APOMORPHINE AND PIMOZIDE INJECTED INTO THE SUBSTANTIA NIGRA OF RATS. S.J. Brown*, F. Mora and C.V. Gisolfi. Univ. of Iowa, Iowa City, Iowa 52242.

Eleven male Sprague-Dawley rats (275-325 g) were stereotaxically implanted above the substantia nigra (SN) with 23-gauge stainless steel guide tubes. Injections of apomorphine (APO), pimozide, or 0.9% saline were made bilaterally in 1.0μl volumes using a Harvard infusion pump. Colonic (Tc) and tail-skin (Ts) temperatures were monitored every 5 min. A dose-dependent decline in Tc was observed within 14±1.71 (M±S.E.) min after injecting APO. Maximal changes in Tc were (M±S.E.):

APO Dose	2.5μg	5.0μg	10.0μg	20.0μg
ΔTc	-0.34±.02*	-0.53±.05*	-1.21±.12*	-1.04±.04*

*Significantly ($p<.50$) different from saline controls.

Tc responses to all doses differed from each other ($p<.05$) except between 10 and 20μg. Although a dose-dependent change in Ts was not observed, in 7 of 11 animals Ts rose 1.54±.24°C within the first 10 min after injecting APO (10μg). Corresponding changes in Tc and Ts after injecting saline were +0.33±.08 and +0.27±.34°C, respectively. Systemic pretreatment with pimozide (0.5 mg/kg, i.p.) 2-hrs prior to the central injection of APO (10μg) blocked the hypothermia. Tc fell only 0.18±.11°C. Pimozide (0.5μg) injected into the SN also blocked the effects of APO (10μg) injected 20-min later. Tc fell only 0.28±.13°C. These results suggest that dopamine receptors are located in the SN and may play a role in thermoregulation.

(Supported by ONR Contract N00014-74-C-0597).

CENTRAL CHEMICAL DRIVE AND REFLEX INFLUENCES ON PHRENIC ACTIVITY AFTER HIGH IPSILATERAL CERVICAL HEMISECTION. E. Bruce*, C.V. Euler*, and S. Yamashiro, Karolinska Instit., Stockholm, Sweden (Spon: M. Goldman)

Central respiratory drive related excitation reaches each phrenic motor nucleus by two pathways: 1) by monosynaptic, ipsilateral descending tracts; 2) by unidentified contralateral tracts which are said to contribute to diaphragm excitation only at high respiratory drive ("crossed phrenic" phenomenon). We have studied the characteristics of the latter pathway under a variety of chemical and reflex drives. Eight chloralase anesthetized and paralyzed cats were ventilated by a phrenic-driven respirator. The spinal cord was hemisected transversely at C_2 or C_3. Ipsilateral to the hemisection phrenic C_5 activity showed two phases, a slow rate of increase early in inspiration and a much greater rate of increase later in inspiration. As PCO_2 increased, the onset of the second phase came earlier in inspiration. At resting end-tidal PCO_2 some phrenic units were active early in inspiration. At high PCO_2 ipsilateral phrenic activity at end-inspiration was about 25% of that before hemisection. Two observations suggest that transmission in the crossing pathway is frequency-dependent: 1) the 70-110 Hz oscillations in phrenic nerve discharge disappear ipsilaterally after cervical hemisection; 2) rapid transient excitations due to vagal stimulation or augmented breaths are more attenuated ipsilaterally, relative to contralateral responses, than is the slow rhythmic respiratory activity.

COMPARISON OF THE RESPONSE OF THYROTROPIN-RELEASING HORMONE (TRH) AND A DEAMIDATED METABOLITE (TRA) ON ANTRAL MOTILITY *IN VITRO*. Larry A. Bruce, Faiz M. Behsudi and C.P. Fawcett*. Department of Physiology, Univ. Texas Hlth. Sci. Ctr., Southwestern Med. Sch., Dallas, Texas 75235

TRH has been shown to influence gastrointestinal (GI) function *in vitro* and *in vivo*. The detection of TRH in GI tissue suggests a possible physiological role in GI function (Morley *et al.*, Biochem. Biophy. Res. Commun. 79: 314, 1977). A recent report from our laboratory indicates that TRH stimulates antral tissue *in vitro* through a histaminergic pathway (Gastroenterology 76: 908, 1979). In support of a TRH-histaminergic interaction, we report here that the response of antral tissue *in vitro* challenged with the deamidated free acid of TRH (pyro-Glu-His-Pro-OH) (TRA) is not significantly different from antral tissue response *in vitro* challenged with TRH over a concentration range of 10^{-8} to 10^{-5} M (P>.05). These data suggest that the active site on the TRH molecule is common to both TRH and TRA. This excludes the TRH amide group which is required for TRH activity on the pituitary. (Supported in part by NIH Grants AM 21657 and AM 21163).

DIETHYL MALEATE AND/OR OZONE (10 ppm) REDUCE VENTILATION BY 60-80% IN AWAKE MICE. M.C. Bruce, E.N. Bruce, D.E. Leith, and S.D. Murphy. Harvard Sch. of Publ. Health, Boston, MA 02115.

Diethyl maleate (DEM, 0.5-1.0 g/kg i.p. in propylene glycol) protects mice against lethal concentrations of ozone (Bruce, M.C., and S.D. Murphy, Toxicol. and Appl. Pharmacol. 41: 184, 1977). By itself, DEM also reduces rectal temperature by as much as 10°C, oxygen consumption by 50-60%, and lung ventilation ($\dot{V}_E$) by 60-70%. Thus one possible mechanism for its protective effect is a decrease in the inhaled dose of ozone. We tested this possibility by measuring $\dot{V}_E$ during air breathing and during ozone exposure (10 ppm) in awake mice pretreated with DEM in propylene glycol or with propylene glycol alone. $\dot{V}_E$ was reduced to 20% of control during ozone exposure in both groups. We conclude that the protective effect of DEM against pulmonary edema and death is not due to a decrease in the inhaled dose of ozone. The mechanism(s) for the profound decreases in metabolism are unknown. (Supported in part by: NIEHS Center Grant ES 00002.)

CEREBRAL METABOLIC STATE DURING SEVERE HYPOGLYCEMIA AND RECOVERY. R.M. Bryan and F.F. Jobsis. Dept. of Physiology Duke Medical Center, Durham, N.C. 27710.

The cerebral metabolic state was studied during insulin induced hypoglycemia and recovery in cats anesthetized with nitrous oxide. Changes in the redox states of nicotinamide adenine dinucleotide (NAD) and cytochrome a,a_3 (cyt a,a_3) were monitored separately in the exposed left cortex using microflourometry and reflectance spectrophotometry respectively. In other experiments changes in cyt a,a_3 were monitored directly through the skull by infrared spectrophotometry. EEG was simultaneously recorded from the right hemisphere. After insulin injections blood glucose fell from 3.82 μmoles/ml ± 0.16 SEM (n=6) to 0.44 μmoles/ml ± 0.10 SEM (n=6) in 4 hours and was accompanied by an oxidation of NADH. EEG became isoelectric when blood glucose fell below 0.35 μmoles/ml ± 0.01 SEM (n=5). Upon intravenous glucose infusion a re-reduction of the NAD occured within 10-20 seconds and showed saturation kinetics. When blood glucose reached 1.74 moles/ml ± 0.09 SEM (n=5) the re-reduction was complete. The redox state of cyt a,a_3 did not change during either the onset of severe hypoglycemia or the recovery after glucose infusion. We conclude that glucose deprivation in the cerebral cortex can be detected at the substrate end of the respiratory chain (NAD) when blood glucose falls below a critical level but not at the terminal oxidase (cyt a,a_3) step of the respiratory chain.

THE EFFECTS OF SHORT VS LONG TERM PSYCHOLOGICAL STRESS ON THE BLOOD PRESSURE OF RATS. R.A. Buchholz,* J.E. Lawler,* and G.F. Barker,* (SPON: K.J. Kant) University of Tennessee Knoxville, TN 37916.)

Twenty-four rats were assigned to 3 groups of 8 rats each: experimental, or E (animal required to make a response to avoid electric shock); yoked, or Y (animal receives same shock as given to E); and non-shock restraint control, or C. Animals were studied 3½ hrs/day for 3 wks. Weekly measurements of SBP via tail cuff, taken a minimum of 2 hrs following stress, revealed no significant differences between groups. Another group of 24 animals was studied exactly as those above, except that they were studied an additional 8 wks with modified stress contingencies. SBP increased in all groups across study, but rose significantly more in E and Y groups than in C. In addition, a chi-square analysis ($p<.05$) revealed that significantly more SBP readings in E and Y animals (34% and 38%, respectively) were greater than 150 than in C animals (13%). Direct monitoring of arterial blood pressure via indwelling catheters revealed significant increases in SBP during and immediately following stress sessions in both E and Y, but not C, subjects. It appears that reducing the opportunity to cope effectively with stress elevates SBP not only during the stress itself, but at least for a 2 hr period afterward. The stress procedure produces a significant increase in the incidence of SBP readings in the "hypertensive" range. (Supported by Am Heart Assn and NIH HL 19680.)

EFFECTS OF AUTONOMIC BLOCKADE ON RESTING AND EXERCISING HEART RATE IN HIGH-ALTITUDE AND SEA-LEVEL RESIDENTS. R. L. Burse, J. T. Maher, L. H. Hartley, J. C. Cruz and R. F. Grover. U.S. Army Res. Inst. of Envir. Med., Natick, MA, 01760; Harvard Med. Sch., Boston, MA 02215; and Univ. of Colo. Med. Ctr., Denver, CO 80220.

HR was measured at rest and during 2 levels of bicycle exercise [light (LE) ≃ 40% $\dot{V}O_2$ max; moderate (ME) ≃ 60% $\dot{V}O_2$ max] in 7 sea-level residents (SLR) at SL (150 m) and in 6 high-altitude residents (HAR) at HA (4350 m) before and after i.v. atropine blockade (AB, 0.03 mg·kg^{-1}), propranolol blockade (PB, 0.15 mg·kg^{-1}) or combined blockade (CB, atropine 0.04 mg·kg^{-1} plus propranolol 0.20 mg·kg^{-1}) on separate days in a counterbalanced design. With AB, HR rose in both groups ($p<0.001$), significantly more so (32%) in HAR than SLR during rest but not exercise. Extent of rise diminished with exercise intensity: rate ≃ 0.4 beat·min^{-1} per % $\dot{V}O_2$ max. With PB, HR was significantly below control values for both groups during rest ($p<0.01$), LE and ME ($p<0.001$). Extent of decrement increased with exercise intensity: rate ≃ 0.3 beat·min^{-1} per % $\dot{V}O_2$ max. With CB, resting HR rose equally in both groups; control HR averaged 27% less than "intrinsic" HR. Resting sympathetic tone averaged 7% of intrinsic HR in HAR and 10% in SLR; parasympathetic tone was 57% and 39%, respectively. With CB, HR fell nearly to control values during LE and 6-10% below control during ME for HAR and SLR. We conclude that previously reported lower resting and exercise HR in HAR result from their greater parasympathetic tone, which is maximal at rest.

DIFFERENTIAL REGULATION OF ADRENERGIC RECEPTORS IN SUBMAXILLARY GLANDS FROM CHRONICALLY RESERPINIZED RATS, David B. Bylund* and J. Ricardo Martinez, Depts. Pharmacology and Child Health, Univ. Missouri, Columbia, MO 65212.

The chronically reserpinized rat appears to be a useful animal model for diseases such as cystic fibrosis which may involve abnormalities in the autonomic regulation of exocrine gland secretions. Using the radioligand receptor binding technique, we studied β-adrenergic (^{3}H-dihydroalprenolol), α_1-adrenergic (^{3}H-WB4101), α_2-adrenergic (^{3}H-clonidine) and muscarinic cholinergic (^{3}H-quinuclidinyl benzilate) receptor binding in submaxillary gland membranes. The β-adrenergic receptors in submaxillary gland are all of the β_1-subtype, while both subtypes of α-adrenergic receptors are present, although α_1-receptor binding predominates. After 7 daily doses of reserpine (0.5 mg/kg, i.p.) β_1-adrenergic and α_2-adrenergic receptor binding increased markedly, α_1-binding increased moderately, and muscarinic binding was unchanged. The increased binding is due to an increase in the apparent number of receptors (B_{max})(β_1,211±10% of control; α_1,156±6% of control) with no change in affinity of the receptor for various ligands. These increases in adrenergic receptor levels may play an important role in the altered responsiveness of these exocrine glands to secretagogues and in the secretion of abnormal saliva both in the proposed animal model and in the human disease. Supported by NIH Grant AM18150 and NSF Grant BNS 7824715.

SPROUTING OF ACTIVE NERVE TERMINALS IN PARTIALLY INACTIVE MUSCLE. J.H. Caldwell* and R.R. Ribchester* (Spon.W.J.Betz) Univ. of Colorado Med. Sch., Denver, CO 80262, U.S.A.

Experiments were done to investigate the role of muscle fiber inactivity in stimulating motor nerve sprouting. The medial and lateral plantar nerves in the hind foot of rats were blocked with tetrodotoxin. Certain specific muscles remained partially active due to additional innervation by the sural nerve. Other muscles in the same foot received their entire innervation from the plantar nerves and thus were totally inactive. In partially inactive muscles, the active terminals were stained selectively. Sprouting of blocked and active terminals took place (about 35% of the terminals had sprouts) and the sprouts were of comparable length (12μm) in both cases. In other experiments these muscles were partially denervated in order to compare effects of nerve block and nerve section; about 65% of these terminals had sprouts and the sprouts averaged 24μm in length. Physiological and histological observations suggested that sprouts in paralyzed muscles, unlike those in partially denervated muscles, seldom, if ever, made new synapses on neighboring muscle fibers, even after 12-13 d of nerve block. These results indicate that inactive muscle fibers can cause terminals on neighboring fibers to sprout perhaps by releasing a diffusible factor and this is part of the stimulus for motor nerve sprouting in partially denervated muscle.

CHANGES IN CORTICOSTERONE-BINDING ACTIVITY DURING PREGNANCY, LACTATION AND WEANING IN INDIVIDUAL RATS. Steve Calvano* and Robert W. Reynolds. University of California, Santa Barbara, Santa Barbara, California 93106

Adult Sprague-Dawley rats were bled daily by tail vein puncture beginning at mid-gestation and continuing until 14 days post-weaning. Following removal of endogenous steroids plasma samples so obtained were assayed for corticosterone-binding activity (CBA) by a binding site saturation assay. According to other investigators, CBA decreases approximately 50% at parturition and remains at this level until weaning, at which time it increases, reaching normal levels by 4 days post-weaning. Our data reveal that CBA drops slowly during the last 5-6 days of gestation to 55%-60% of normal at parturition. These levels are maintained until days 14-20 of lactation at which time CBA decreases another 10%-20%. At weaning, there is a precipitous increase in CBA which by days 4-5 post-weaning is actually 10%-15% above normal levels. These supranormal levels are followed by a drop to values 10%-20% below normal before CBA returns to control levels on days 12-14 following weaning. The results are consistant with the hypothesis (Gala and Westphal, Endocrinology, 1965, 76, 1079.) that changes in CBA and free levels of adrenal glucocorticoids may play a role in the initiation and maintenance of lactation. (Supported by University of California Faculty Research Grant 144 and NIMH Training Grant MH-11342.)

THE RELATIONSHIP OF NEONATAL GONADAL STATUS, BODY WEIGHT, AND BLOOD PRESSURE IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). L.J. Cambotti,* F.E. Cole,* E.D. Frohlich, and A.A. MacPhee,* Ochsner Medical Institutions and Tulane Univ., New Orleans, 70121.

Hypertension develops earlier in male than in female SHR. This research evaluated whether steroid hormones circulating during critical developmental periods, which direct differentiation of male and female morphology and behavior, influence sex-dependent essential hypertension. The following 4 groups were established: males sham-operated or castrated on the day of birth, females injected with oil or 1.25 mg testosterone propionate (TP) on the day after birth. Beginning at 4 weeks of age, systolic blood pressure (BP) determined by tail plethysmography and body weight (BW) were recorded weekly. Mean values for the 8 weeks are shown below.

Treatment	Mean Weekly BW(g)	Mean Weekly BP(mm Hg)
Sham-operated males	133	166
Neonatally castrated males	108	144
TP injected females	107	154
Oil injected females	96	131

Analyses of variance for BP and BW showed that the differences among the 4 groups and age periods were significant ($p<.001$). The interaction between treatment groups and age was significant ($p<.001$), reflecting a higher rate of increase of blood pressure in control than in neonatally castrated males and females and in TP-injected females than in control females. The results demonstrate that perinatal gonadal hormones can influence the development of hypertension and BW in the SHR.

AGE-RELATED ALTERATIONS IN THE HEAT-STABILITY OF MOUSE HEART PHOSPHORYLASE. Joseph M. Capasso and Jay A. Zimmerman. St. John's Univ., Jamaica, N.Y. 11439.

The progressive loss of adaptability of the aged myocardium during stress is well documented. Cardiac glycogen, the reserve store of energy utilized during stress, is mobilized soley by the enzyme phosphorylase. Myocardial phosphorylase from 6-month (young) and 24-month (old) C57Bl/6J male mice was subjected to inactivation by incubation at 47.5° C for 0 - 30 minutes. Phosphorylase from the hearts of old mice displayed an increased resistance to inactivation by heat during the initial 10 minutes at 47.5° C. Linear regression analysis revealed that 25% of the phosphorylase molecules in the old heart were not only more resistant to heat than the remainder of the population but also 95% of the phosphorylase molecules from their younger counterparts. Sucrose density gradient studies further revealed that phosphorylase from old hearts contained approximately 40% of its total activity in a less active tetrameric species. Young animals contained only 10 - 15% activity in the tetrameric form. The tetramer in both age groups is converted to the more active dimer upon initial heating and then to the non-active monomer upon prolonged incubation at 47.5° C. These results suggest that the increased heat stability of old phosphorylase is due to an increase in a less active tetrameric species. This increase in the tetrameric phosphorylase may contribute to age-related decreases in myocardial response to stress.

ATHLETIC TRAINING AND BODY COMPOSITION AS FACTORS IN SECONDARY AMENORRHEA. K.A. Carlberg* and M.L. Riedesel.

Questionnaires were given to 363 university students, including 81 varsity athletes, 72 dance students, and 210 biology students. Amenorrhea was present in 12% of the athletes, 3% of the dancers, and 2% of the biology students ($p<.002$). Five of the 8 amenorrheic athletes were among the top 25% performers ($p<.01$). Interviews with 34 amenorrheic or irregularly menstruating athletes revealed that 74% considered exercise to be a contributing factor in their menstrual irregularities, 68% thought psychological stress was involved, and 26% believed low body weight was important. Analysis of exercise habits suggested that the amenorrheic athletes may spend more time in aerobic activity than regularly or irregularly menstruating athletes, but not in anaerobic, power, or total activity; exercise intensity did not appear influential. Hydrostatic weighing of 6 athletes with 4 or fewer periods/year and 9 regularly menstruating athletes and dancers demonstrated that the amenorrheic/oligomenorrheic women were lower in percent body fat (11.8 vs 16.3%, N.S.), fat weight (5.8 vs 9.3 kg, $p<.025$), lean body weight (43.2 vs 46.9 kg, $p<.05$), total body weight (49.0 vs 56.2 kg, $p<.01$), and percent ideal body weight (91 vs 102%, $p<.01$); mean heights were identical (165.6 vs 165.1 cm). It is concluded that amenorrhea is more common in athletes than in nonathletes, and is most common in the best athletes. Amenorrheic/oligomenorrheic athletes are lower in both body fat and lean body mass.

ORGANIZATION OF THE LATERAL HYPOTHALAMUS(LH) FOR CONTROL OF ACTH IN THE CAT. Drew E. Carlson, Anne Dornhorst*, Helen Santana*, and Donald S. Gann. The Johns Hopkins University School of Medicine, Baltimore, Md. 21205

Regions in the ventral midbrain that project to the LH have been implicated in the control of ACTH. To define further those areas in the LH through which afferent signals might pass, we stimulated electrically 188 sites in the LH of 20 cats anesthetized with chloralose-urethane. Stimulations were monophasic pulses of DC(200μA,0.2msec,100Hz,20sec). Venous samples were drawn over 30sec at 0.5min prior to and 1.5 min post stimulation. ACTH was assayed by RIA. Areas were defined in which stimulation led to increased, decreased, or unchanged ACTH. At the level of the mammillary bodies(MMB), a facilitatory area occupied the ventral portion of the medial forebrain bundle(MFB). This area extended rostrally and medially to join the medial aspect of the MFB. Continuity with the mediobasal hypothalamus(MBH) was seen only anteriorly in the area of the supraoptic decussations(SOD). An inhibitory area occupied the dorsal extent of the MFB at the level of the MMB. It extended rostrally and laterally around the caudal pole of the supraoptic nucleus and then medially at the level of the optic chiasm(OC). Previously, ACTH-facilitatory and inhibitory areas were defined in the ventral midbrain. The present data indicate that these areas join the MFB to traverse the LH. Only at the level of the SOD and the OC do these areas appear to project medially to enter the MBH. Supported by Grants AM14952 and GM07031 from the NIH.

CEREBRAL BLOOD FLOW AND OXIDATIVE METABOLISM IN THE HYPOXIC NEWBORN DOG. M.S. Casciotti,* M.J. Hernández, R.C. Vannucci, G.S. Bowman* and R.W. Brennan.* Hershey Medical Center, Hershey, PA 17033

Hypoxia is frequently associated with neurological deficits in early life; however, its effects on neonatal cerebral blood flow (CBF) and oxidative metabolism are unclear. In this study we determined the effects of hypoxia on CBF and cerebral metabolic rate for oxygen ($CMRO_2$) in the newborn dog. CBF was measured in mongrel dogs 1-7 days of age by means of a modification of the Kety and Schmidt technique employing ^{133}Xenon as indicator. The control dogs were paralyzed and passively ventilated with a gas mixture of 70% N_2O and 30% O_2. Another group of dogs was made hypoxic by ventilation with a gas mixture of 70% N_2O, 8% O_2, and balance N_2. $CMRO_2$ was calculated as the product of the $[A-V]O_2$ and CBF. The results are summarized as follows:

	pO_2(mmHg)	MABP(mmHg)	CBF (ml/min/100g)	$CMRO_2$ (ml O_2/min/100g)
Control	126±20	60±9	26±8	1.06±0.27
Hypoxia	26±4*	53±14	37±11*	0.84±0.34

The present findings indicate that the degree of hypoxia induced in this study increases CBF significantly (*P<0.02) in the newborn dog. In addition, it appears that these increments in CBF are sufficient to maintain $CMRO_2$ constant. In this fashion, the newborn brain appears to be at least partially protected against hypoxic brain injury.

PRESSURE-VOLUME (P-V) CHARACTERISTICS OF THE REFLEX CARDIOVASCULAR (CV) RESPONSE TO LUNG INFLATION IN DOGS. Sharon S. Cassidy and Robert L. Johnson, Jr. University of Texas Southwestern Medical School, Dallas, TX 75235

Hyperinflation of the lung has been shown previously to reflexly decrease heart rate (HR) and blood pressure (BP). The purpose of this study was to determine the relationship between the magnitude of this response to lung inflation and the inflation pressure and volume. The mechanical effects of left lung inflation on the heart and circulation were eliminated by diverting all pulmonary artery blood flow and all ventilation to the right lung in open-chest dogs. The level of inflation pressure was increased step-wise to 50cmH_2O and was then decreased step-wise to 5cmH_2O before and after section of the left vagus nerve. (Lung volume = LV)

	Lung Inflation Pressure (cmH_2O)							
	10	20	30	40	30	20	10	30*
% fall BP	3	11	23	30	25	17	2	6
% fall HR	1	15	35	42	39	22	0	-3
LV (ml)	19	171	310	589	671	473	71	554

* post left vagotomy

The threshold response was between 5 and 15cmH_2O. Above this threshold the fall in BP and HR during lung inflation is proportional to the volume of inflation. Hysteresis is evident in the inflation P-V relationship. Left vagotomy eliminates the BP and HR response.

POSTURAL CHANGES IN THE CONFIGURATION OF MAXIMAL EXPIRATORY FLOW-VOLUME CURVES (MEFVC's) IN NORMAL MAN. R. Castile,* J. Mead, A. Jackson, M. Wohl, and D. Stokes*. Harvard School of Public Health and Children's Hospital Medical Center, Boston, MA. 02115

Tien et al. (J.A.P. 46:565, 1979) found reproducible details ("bumps") in the configuration of averaged MEFVC's. They suggested that these "bumps" represented sudden relocations of airway choke points. The occurrence of choke points depends on factors affecting local airway pressure-diameter behavior. We postulated that changes in posture as they affect the distribution of lung recoil on airways might change the locations of choke points and thereby alter flow-volume configuration. Twenty normal adults performed 5 MEFVC's in each of 4 postures (standing, supine, right and left lateral). Volume was measured with a Krogh spirometer and airflow with a #4 Fleisch pneumotachometer. Curves were digitally filtered and plotted relative to upright TLC. Five curves in each posture were averaged at 0.1 L/S increments of flow and average volumes at given flows were compared using the Student T-test. Significant differences ($p<0.01$) in mean volumes at given flows occurred in all subjects from standing to supine and/or right to left lateral postures. Large changes in configuration were apparent in one of the two postural pairs in 8 subjects. We conclude that changes in posture result in significant changes in flow-volume configuration in most normal adults. (Supported in part by NIH Grant # HL 14580-06).

CENTRAL AND PERIPHERAL BLOOD FLOW ADJUSTMENTS TO EXERCISE IN DOGS.

Cerretelli P., D.R. Pendergast*, J. Krasney, J. Plewes* and D.W. Rennie. Dept. of Physiology, S.U.N.Y. at Buffalo, BUFFALO, N.Y. 14214 and Dept. of Physiology (III) University of Milano, MILANO, Italy.

The role of cardiac output ($\dot{Q}$) and muscular blood flow (MBF) in O_2 transport of dogs was evaluated at various exercise levels as well as during the transient between rest and square waves of work or vice-versa. Three dogs (18-20 kg) were exercised on a treadmill at five increasing speeds up to 13 km.h^{-1}. $\dot{V}_{O_2}$ was measured on a breath by breath basis, $\dot{Q}$ by thermodilution, the rate of adjustment of MBF in the gastrocnemius, vastus lateralis, and long head of the triceps by ^{133}Xe clearance, absolute MBF in the same muscles by microsphere trapping and blood lactate concentration, $[La_b]$, enzymatically. $\dot{V}_{O_2}$ increased linearly from .1 at rest to .9 l.min^{-1} without attaining a plateau; $\dot{Q}$ from 2.5 to a maximum of 7.8 l.min^{-1} which was attained at 12 km.h^{-1}; MBF from .1 to a maximum plateau of .85 ml.g^{-1}.min^{-1} reached at 9.5 km.h; no La_b increase was found. The half times (t 1/2, s) of both the on -and off- responses were 15-24 s for $\dot{V}_{O_2}$, 18-22 s for $\dot{Q}$, 3-12 s for MBF. For given work loads average MBF were the same in the investigated muscles while regional flow distribution within each muscle was grossly uneven. It is concluded that: 1) the t 1/2 of $\dot{V}_{O_2}$ on -and off- responses is not imposed by the rate of adjustment of $\dot{Q}$ or MBF since these are faster than that of $\dot{V}_{O_2}$; 2) the limit to $\dot{V}_{O_2}$max appears to be peripheral since maximum MBF is attained at 70% $\dot{V}_{O_2}$max when $\dot{Q}$ is still increasing.

* Supported by NHLB Grant HL 14414-06 and by a Grant from the University of Milano.

EFFECT OF POSTURAL CHANGES ON MINUTE VENTILATION, FUNCTIONAL RESIDUAL CAPACITY AND PULMONARY N_2 CLEARANCE. E Up Chae and Sung Ho Bae.* Department of Physiology Kyungpook Nat. Univ. School of Med. Taegu, Korea.

An attempt was made to study respiratory responses to the passive tilt. Anesthetized dogs were tilted from horizontal to upright (+90°) and head down (-90°) position. Minute ventilation was decreased in the upright position and increased in the head down position comparing to that in the horizontal position. The Functional Residual Capacity(FRC) was increased in the upright position while decreased in the head down position. The nitrogen clearance time was significantly prolonged in the upright position, and was approximately equal in the head down position to that in the horizontal position. Oxygen saturation percentage of arterial blood decreased in the both upright and head down position, and that of the mixed venous blood also decreased in the both positions. In conclusion, the decreased FRC was compensated by the increased minute ventilation and that an adequate per cent oxygen saturation of arterial blood was maintained in the head down position. On the contrary despite of the increased FRC, minute ventiration was diminished and lung clearance time was prolonged and that the per cent oxygen saturation of arterial blood was decreased in the upright position.

BLOOD FLOW AND OXYGEN UPTAKE IN SCIATIC DENERVATED CANINE SKELETAL MUSCLE DURING ACUTE ANEMIA. C.K. Chapler and S.M. Cain. Depts of Physiology, Queen's University, Kingston, Ont. K7L 3N6 and University of Alabama in Birmingham, Al. 35294.

We have previously reported that oxygen uptake in canine skeletal muscle increased during acute anemia. This response was abolished by β-blockade. The purpose of the present study was to determine if partial denervation of muscle would alter this response. In 8 anesthetized dogs, venous outflow from the gastrocnemius-plantaris muscle group was isolated and the sciatic nerve sectioned. Values from cardiac output ($\dot{Q}$) and total body oxygen uptake ($\dot{V}_{O_2}$), muscle blood flow and muscle oxygen uptake were obtained during a control period and at 30 min of anemia (Hct = 14%) produced by dextran-for-blood exchange. These results were compared to data from a control series (8 animals) with intact muscle innervation. In both groups the $\dot{Q}$ at 30 min of anemia increased about 80% ($p < 0.01$) while $\dot{V}_{O_2}$ remained constant. Prior to anemia there were no differences in either muscle oxygen uptake or blood flow between the two groups. At 30 min of anemia in the nerve sectioned group neither of these parameters changed; both were increased significantly in the control series. The results suggest that sympathetic fibers in the sciatic contribute to the increase in muscle oxygen consumption observed in the intact animals during anemia. (Supported by the MRC of Canada and NHLBI 14693).

THE REFLECTION COEFFICIENT OF UREA IN THE HUMAN RED CELL: EFFECT OF PCMBS. Bernard Chasan* and A. K. Solomon. Biophysical Laboratory, Harvard Medical School, Boston, Mass. 02115

Red cells subjected to an osmotic gradient of an impermeable solute, $\Delta\pi(i)$, exhibit a zero time rate of volume change $(dv(i)/dt) = CL_p \Delta\pi(i)$ where C is a constant and L_p is the hydraulic conductivity. If the gradient is entirely due to a permeable solute, then $(dv(p)/dt) = C\sigma L_p \Delta\pi(p)$ in which σ is the reflection coefficient for the permeating molecule. We have determined σ for urea from the ratio of these zero time rates of volume flow, using the stop-flow light scattering method to measure the time course of cell volumes. Both (dv(i)/dt) and (dv(urea)/dt) were found to depend linearly on the initial concentration gradient, indicating that L_p and σ are essentially constant up to gradients of several hundred milliosmoles. In preliminary experiments using blood from two donors, we find that σ = 0.7 ± 0.1. When cells are treated with 1 mM p-chloromercuriphenyl sulfonic acid (PCMBS) for 40 minutes, σ rises to 1.0, demonstrably larger than the value for untreated cells. The present value for σ is consistent with the values of 0.5 - 0.6 obtained earlier in this laboratory (Sha'afi et al., (1970) J. Gen. Physiol. 55, 427) but differs significantly from the value of σ = 1.0 computed by Macey and Wadzinski ((1974) Fed. Proc. 33, 2323) and advanced by them as an argument to favor carrier transport of urea. (Supported in part by USPHS grants GM00782 and HL14820)

FIBRINOGEN AND FIBRINOID IN EARLY AND LATE STAGES OF EXPERIMENTAL MALIGNANT AND BENIGN HYPERTENSION. Ricardo E. Chatelain,* Beatriz N. Dardik,* Carlos M. Ferrario and John R. Shainoff.* Cleveland Clinic, Cleveland, Ohio 44106.

Aortic ligation between the renal arteries in Sprague-Dawley rats resulted in the prompt development of hypertension which after 3 days averaged 160 ± 2 mm Hg (Sham 120 ± 3 mm Hg). Plasma fibrinogen levels rose from 228 ± 22 to 333 ± 24 mg/100 ml and microscopic examination revealed foci of acute fibrinoid deposition into the medial arterial layer of all rats. Twelve days after aortic ligation fibrinoid deposits disappeared while moderately increased levels of plasma fibrinogen (275 ± 21 mg/100 ml) occurred in rats developing benign hypertension (203 ± 2 mm Hg). In contrast, rats with malignant hypertension (201 ± 5 mm Hg) showed a marked increase in plasma fibrinogen (549 ± 85 mg/100 ml), widespread necrotizing arteritis and massive fibrinoid deposition. Malignant hypertension was further characterized by high renin levels, hemolysis, fragmented erythrocytes and the presence of fibrin degradation products in the serum. These experiments indicate that, in malignant hypertension, an initial period of vascular damage is followed by a persistent elevation of fibrinogen and fibrin degradation products. This, coupled with the damaging effect of increased humoral factors and elevated blood pressure, suggests the existence of a chronic hypercoagulability state which may contribute to enhance fibrin deposition. (Supported in part by NHLBI grants #HL-6835 and #HL-16361).

THE EFFECT OF CORONARY HYPOTENSION AND ENDOTOXIN ON LEFT VENTRICULAR FUNCTION. James E. Cheatham, Jr.*, Marvin D. Peyton* and Ronald C. Elkins. VA Medical Center, Okla. City, Ok 73125.

Coronary hypotension and endotoxin shock have been incriminated in the pathogenesis of left ventricular failure. To evaluate their respective roles, adult dogs were instrumented for cardiopulmonary bypass and independent coronary perfusion with a left intraventricular balloon used for isovolumetric pressure measurements and divided into 5 groups.Group I-LD_{100} endotoxin, 1 hr low coronary perfusion (LCP)(40 mmHg), 5 hrs normal coronary perfusion (NCP)(100 mmHg), Group II-LD_{100} endotoxin, 2 hrs LCP, 5 hrs NCP, Group III-LD_{100} endotoxin, 7 hrs LCP, Group IV, 7 hrs LCP, Group V, 7 hrs NCP. Groups III and IV showed evidence of left ventricular failure at hr 5 with significantly elevated levels of left ventricular end-diastolic pressure (LVEDP) {(Group III-49.7 mmHg ($p<.01$), Group IV-75.8 mmHg ($p<.005$)} and diastolic force (DF){(Group I-24.88 gm wt/cm^2($p<.01$), Group IV-28.4 gm wt/cm^2 ($p<.01$)} with no significant change demonstrated within the other groups. There was no difference between Groups I and II and the control group (Group V). Groups III and IV demonstrated a significantly elevated LVEDP, DF and left ventricular systolic pressure when compared to the other groups. There were no significant differences between Groups III and IV. The findings in this study suggest that coronary hypotension plays a primary role in left ventricular failure but that its effect is reversible within the first 2 hrs. Endotoxin does not appear to play a direct role in myocardial failure.

ATROPINE AND EXERCISE-INDUCED ASTHMA. W.Y. Chen*, A.M. Brenner*, P.C. Weiser, and H. Chai*. National Asthma Center, Denver, CO. 80204.

Six asthmatic children were studied to determine whether supplemental, parenteral atropine would increase the effects of bronchodilation and protection against exercise-induced asthma (EIA) after maximal effects had been achieved by inhalation. First, we determined the amount of inhaled (Inh) atropine sulfate (AS) which would give maximal bronchodilation for each patient at rest. This quantity of AS was designated as "A". Then, all subjects walked for 10 min. on a treadmill for 5 sessions with the following pre-treatments: (a) Inh distilled water + intramuscular (IM) saline, (b) Inh "A" AS + IM saline, (c) Inh distilled water + 0.35 mg IM AS, (d) Inh "A" AS + 0.35 mg IM AS, (e) Inh 2x"A" AS + IM saline. The results show that the combination of Inh and IM atropine has the greatest bronchodilation effect and the greatest protective effect against EIA. AS inhalation alone ("A" dose) or IM injection (0.35 mg) was not as effective in bronchodilation nor in alleviation of EIA. Doubling the dose of inhalation (2A) did not increase the effects of "A" dose. These results support others' observations that Inh atropine does not reach all the airways where cholinergic receptors are present. When the receptors can only be partially blocked by atropine by inhalation and/or with the limited quantity of parenteral injection that can be used in human subjects, it may not be possible to use atropine data to assess the extent of the vagal reflex involvement in EIA. (Supported by NIH Grant HL 21126)

LIPOPROTEIN BINDING TO RAT LUTEAL TISSUE. M.H. Christie*, L.A. Schuler*, and J.F. Strauss, III; Depts. of OB/GYN and Physiology, Univ. of Pennsylvania School of Medicine, Philadelphia, PA 19104.

Lipoprotein carried cholesterol is a primary substrate for steroidogenesis by ovaries of rats (Schuler, Scavo, Kirsch, Flickinger and Strauss, J. Biol. Chem., in press, 1979). Lowering blood cholesterol levels from 51 mg/dl to 11 mg/dl by 4-aminopyrazolopyrimidine (APP) treatment diminished blood progestin levels by 80% and decreased ovarian sterol ester storage by 90%. Increasing cholesterol levels to 275 mg/dl with dietary sterol supplements had no effect upon blood progestin concentrations or ovarian sterol metabolism. These observations suggested the ovarian lipoprotein uptake mechanism is saturated at normal cholesterol levels. We next looked for binding of high density lipoproteins (HDL), the primary lipoprotein of rats, to plasma membrane-enriched (microsomal) subcellular fractions of superovulated ovaries. Rats were pretreated with APP to reduce occupancy of binding sites by endogenous lipoproteins. Saturable, high affinity binding at 4°C of rat HDL, labeled with ^{3}H-cholesterol, was observed with an apparent Kd of 2.4 x 10^{-7}M. Low affinity, non-saturable binding was also observed. High affinity binding was complete after 60 min of incubation. Unlabeled rat and human HDL inhibited ^{3}H-HDL binding. The role of the high affinity HDL binding in regulation of luteal lipoprotein utilization remains to be determined. (Supported by the Rockefeller Foundation and USPHS HD-12314).

SODIUM (Na) RETENTION AND THE ROLE OF ALDOSTERONE (Aldo) IN THE PREGNANT RAT. S.E. Churchill, H.H. Bengele and E.A. Alexander. Thorndike Mem. Lab., Boston City Hosp.; Depts. Med. & Physiol., Boston Univ. Sch. Med., Boston, Ma. 02118.

Na retention occurs during normal pregnancy, but the regulatory mechanisms are poorly understood. To define the temporal relationship and distribution of this retained Na we have measured daily Na balance in 7 control (C) and 6 pregnant (P) Charles River rats for the 21 day gestation period. During the first 14 days P were in slight but not significant positive Na balance. During the last 7 days, however, P retained 9.5 ± 0.6 mEq Na, while C retained only 1.1 ± 0.2 mEq ($p<0.01$). At term plasma Na (P_{Na}), hematocrit (HCT) and total protein (TP) all decreased significantly in P. Extracellular fluid space at term (26 ± 1% nonconceptus BW) was significantly greater than C (20 ± 1% BW) or P at 14 days (23 ± 1% nonconceptus BW). 60% of the net Na retained by P was found in the conceptus products. Since the importance of aldo in the Na retention of pregnancy remains unclear, we also measured Na balance in 10 P rats injected with 10 mg/Kg BW spironolactone twice daily for the last two weeks of gestation (P-Sp). Comparing P-Sp and P, no statistically significant differences were found in Na retention during the second or third week of pregnancy or in P_{Na}, HCT or TP. We conclude that Na retention in rat gestation occurs primarily in the third trimester and that the retained Na is shared by the dam and conceptus products. This Na retention does not appear to be mediated by aldosterone.

GOBLET CELL DIMORPHISM AND POTASSIUM TRANSPORT IN THE MIDGUT OF THE TOBACCO HORNWORM LARVA, MANDUCA SEXTA. Moira Cioffi* (SPON: A.R. Freeman). Temple Univ., Philadelphia, PA 19122

In isolated midguts of M. sexta, potassium is actively transported from blood side to lumen side, biophysical evidence suggesting that this occurs via the goblet cells. Goblet cells contain a cavity formed by invagination of the apical membrane, which is folded to form projections into the cavity. The cytoplasmic side of the membrane is studded with particles implicated in potassium transport. This study showed that the midgut can be divided into anterior, middle and posterior regions on the basis of the pattern of folding of the epithelium and variations in goblet and columnar cell structure. Two distinct types of goblet cell are found. In the anterior and middle regions, the goblet cavity is large, basally located, and mitochondria are present in the apical membrane projections as a potential energy source for active transport. In the posterior region, the cavity occupies only the apical half of the goblet cell, and mitochondria are not associated with the transport particles. Measurement of the short circuit current (I_{sc}) and ion fluxes showed that while all three midgut regions can actively transport potassium, they do not have the same I_{sc} decay profile or net flux. Therefore the transport mechanism, the cellular pathway or the energy source may be different for each type of goblet cell. Thus, comparison of the three regions can provide a useful tool for studying transport by the midgut and testing hypotheses. (Supported in part by NIH grant # AI-09503)

The INTERRELATION BETWEEN HEAD AND BODY SWAY AND THE MOVEMENT OF THE GRAVITATIONAL CENTER OF THE HUMAN BODY DURING STEPPING! Claus-F. Claussen, University Head Center, 87 Würzburg, West-Germany.

Head and body movements can easily be recorded by light tracings with a superimposed polar coordinate reference system through the technique of craniocorpo-graphy (Claussen). The movement pattern is taken on polaroid films which can be measured out for number of steps, length of way,deviation,spin and body sway. For the clinical diagnostics of equilibrium disorders the deviation and the sway during 100 steps on the spot are significant.Calculating the movements of the center of gravity and comparing it with the sway distances of the head shows corresponding values in normals, when linearly connecting foot and head through the center of gravity. (Supported by grant InSan I-0776-V-063,Fraunhofer Ges.)

EFFECT OF EXTRACELLULAR ATP ON THE CALCIUM PARADOX IN ISOLATED WORKING RAT HEART. Mark Clemens and Thomas Forrester. St. Louis University Medical School, St. Louis, MO 63104

Restoration of normal extracellular Ca to mammalian heart after a period of Ca free perfusion results in loss of contractility and efflux of intracellular molecules into the coronary effluent (Ca paradox). These experiments were performed to investigate the effect of exogenously applied ATP on the Ca paradox in isolated working rat heart during 30 sec Ca-free perfusion. Absorbance of the coronary effluent at 260 nm (A260) and aortic pulse pressure were used as indices of myocyte damage. A260·ml/min·g dry wt^{-1} increased linearly as a function of the log of exogenous ATP concentration from 10^{-6} to 10^{-4} M ATP. The release of A260 material showed an apparent maximum rate at 10^{-4} M exogenous ATP, but this level is only about one-fifth of that seen during irreversible Ca paradox (10 min Ca free perfusion). A decline in recovery of aortic pulse pressure also occurred with increased ATP concentration. The apparent saturation (i.e. maximum rate of A260 release) along with the presence of Mg in the perfusate make it unlikely that this is a direct chelation effect. The exacerbation of the Ca paradox seen in these experiments may be the result of mobilization of a membrane bound Ca pool in response to ATP binding.
(Supported by BRSG #368).

NEUROTENSIN STIMULATES HISTAMINE RELEASE FROM RAT MAST CELLS. D.E.Cochrane*, J.B.Lansman*, B.Paterson, Tufts Univ., Medford, MA 02155 and R. Carraway*a,' S.E.Leeman, Harvard Medical School, Boston, MA 02115.

Neurotensin (NT), a peptide from brain and gut, has been shown to specifically bind to receptor sites on the rat mast cell with a K_D=154nM (J.Bio.Chem 252:7174,1977). We report here that this peptide also elicits the release of histamine from rat mast cells bathed in Ca-Locke (mM:150 NaCl,5 KCl, 2 $CaCl_2$,10 HEPES pH 7.2). Histamine release was detectable at 10^{-9}M NT and increased as the concentration of NT was raised, showing a plateau value of 20% from 10^{-7}-10^{-5}M NT. With further increases in NT, histamine release increased sharply with no apparent saturation. This may reflect a non-specific stimulatory effect of basic peptides (PSEBM 142: 1252,1973). The amidated form of NT was much less effective. Seen by phase contrast microscopy, mast cells stimulated by NT extrude granules and undergo the classical degranulation response. This response has been shown by electron microscopy to be the result of exocytosis (J.Cell Biol 51:465, 1971). Prior incubation of mast cells in Ca-free Locke containing EGTA(2mM) or glucose deprivation and treatment with antimycin A abolished histamine release in response to NT. Replacement of Na and K ions with sucrose significantly reduced the amount of histamine released in response to NT. We show that NT can stimulate histamine release from mast cells that depends on Ca and energy. Part of NT's physiological effects may be indirect via histamine release.

THE PINEAL GLAND: A PROMINENT LYMPHOID TISSUE IN YOUNG CHICKENS. Larry A. Cogburn* and Bruce Glick. Mississippi State University, Box 5188, Mississippi State, MS 39762

No lymphoblasts--except those contained within venules--were found in serial sagittal sections of 2-day-old pineals. At 1 wk, lymphoblasts were present in the interlobular spaces and in venous sinuses along the border and choroid plexus. Numerous germinal centers (GC), surrounded by diffuse lymphatic tissue, were evident in 2 wk pineals. Maximum lymphoid accumulation was observed by 1 mo. While 50% of 2-mo-old birds had lymphoid tissue in central areas (CA) of the gland, no lymphocytes were found in CA of 3 and 4 mo pineals. However, a small nodule was observed within pineal capsular tissue. Bursectomy (BSX) at hatch suppressed the formation of GC while BSX + thymectomy + irradiation reduced the total lymphocyte pool of the pineal. A cytotoxic assay, using appropriate anti-lymphocyte sera, indicated that single cell suspensions of pineal lymphocytes from 6-wk-old birds were composed of B-cells (42%) and T-cells (51%). Numerous pyronin-positive cells were produced in pineals four days following a carotid artery injection of soluble antigen (bovine serum albumen) while particulate antigens (sheep erythocytes and B. abortus) failed to stimulate pyroninophilia. These findings indicate that pineal lymphocytes are (1) blood-borne presumably from bursa and thymus elements, (2) age-dependent in distribution and mass, and (3) readily stimulated by soluble--rather than by particulate--antigens.

HUMAN LYMPHOCYTE ACTIVATION IS DEPRESSED AT LOW-g AND ENHANCED AT HIGH-g. A. Cogoli*, M. Valluchi*, M. Müller* and W. Briegleb*, Laboratorium für Biochemie, ETH-Zürich, CH-8092, Switzerland.

Lymphocytes from crew members of spaceships showed depressed reactivity toward mitogens after flight. We will study the effect of a space environment on lymphocytes in-vitro during the Spacelab-1 Mission. Here we present an investigation on lymphocytes exposed to mitogens and grown in a centrifuge at 4 and 16g or in a clinostat at 0.02g. Activation was determined by incorporation of tritiated thymidine into DNA, ultrastructure by electron microscopy, and cell movements in the clinostat were recorded by a cinecamera. At high-g cells show maximum activation on day 2 of culture instead of day 3 as 1g controls. Cell swelling and high number of vacuols indicate that cell aging is more rapid at high than at low-g. At low-g: 1) Activation is depressed by 50%, 2) Cells are distributed in two populations, one with ultrastructure similar to that of activated 1g controls, the other characterized by unusual high amount of mitochondria and lack of vacuols, 3) Amoebial movements are more frequent than at 1g, 4) Organelles stream in the cytoplasm at a speed of 0.72 μm/min.
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EFFECTS OF A LOW SODIUM DIET ON HEMODYNAMICS IN DOCA HYPERTENSIVE PIGS. D.M.Cohen, R.J.Grekin*, J.Mitchell*, W.H.Rice* and D.F.Bohr. Univ. Mich. Med. Sch., Ann Arbor, MI 48109

A 3 wk. reduction in Na^+ intake from 200 to 15 mEq/24 hrs. produced the following changes in DOCA hypertensive(D) & control(C) pigs:

		MEAN ARTERIAL PRESSURE (mmHg)			CARDIAC OUTPUT (% of PRE)			TOTAL PERIPHERAL RESISTANCE (% of PRE)		
PIG TYPE	NO.	PRE	$POST_1$	$POST_2$	PRE	$POST_1$	$POST_2$	PRE	$POST_1$	$POST_2$
CONTROL	3	90	97	93	100	110	111	100	98	93
DOCA RESPONDERS	5	134	104	104*	100	100	102*	100	80	74*
DOCA NON-RESPONDERS	3	153	145	137	100	93	95	100	101	94

PRE = Average values for three days preceeding low Na^+ intervention
$POST_1$ = Average values for days 8, 9 and 10 on low Na^+
$POST_2$ = Average values for days 15, 16 and 17 on low Na^+ *N = 4

Decreased Na^+ intake lowered blood pressure(BP) to normal in some D pigs[responders(R)] but not in others[non-responders (NR)]. Cardiac output(CO) decreased or did not change in all D pigs. Since continued growth should lead to increased CO (see C pigs), no change in CO is equivalent to a functional decrease. Hence, the reason for maintained high BP in NR pigs was their inability to decrease total peripheral resistance. NR pigs had a higher PRE BP than that of R pigs. Since similar D pigs have already developed structural vascular changes, it is possible that NR pigs have developed irreversible changes in vessel wall geometry more rapidly than R pigs. Supported by NHLBI grant #HL-18575.

MITOCHONDRIAL FUNCTION IN THE PRESENCE OF MYOGLOBIN. R.P. Cole, * J.B. Wittenberg, and B.A. Wittenberg. College of Physicians and Surgeons, New York, NY 10032, and Albert Einstein College of Medicine, Bronx, NY 10461.

The effect of myoglobin (Mb) on respiration and ATP production by skeletal muscle mitochondria was studied under steady state conditions of O_2 supply. The O_2 partial pressure in stirred suspensions of mitochondria from rat hind limb muscle was measured with an O_2 electrode. The gas phase O_2 content was maintained constant. Oxygen consumption was determined from the first order response time of the system and the difference in steady state gas and liquid phase [O_2]. ATP production was determined from the rate of production of glucose-6-P in the presence of hexokinase. Determinations of O_2 consumption and ATP production were made only after steady states of liquid phase [O_2] were achieved. ATP production was linear with time up to 30 minutes. Oxygen consumption determined with this system correlated well with the standard closed chamber polarographic technique ($r = 0.96$). Measurements were made at [O_2] from 150μM to levels where ATP production was [O_2] dependent. ATP production in the presence of functional or ferric Mb (60-180μM) was unchanged from controls with no Mb present. The steady state liquid phase [O_2] was increased in the presence of functional Mb, suggesting enhanced transport of O_2 across the gas-liquid interface. (Supported by NIH HL-17813, Parker B. Francis Foundation).

TUBULOGLOMERULAR FEEDBACK DOES NOT EXPLAIN AUTOREGULATION OF RENAL BLOOD FLOW AND GLOMERULAR FILTRATION RATE. Thomas G. Coleman and John E. Hall. University of Mississippi Medical Center, Jackson, Mississippi, 39216.

A mathematical model of hemodynamics, filtration, and reabsorption in a single canine nephron was used to study feedback-autoregulation relationships in the kidney. It was assumed that tubuloglomerular feedback is proportional to early distal tubular flow and that only afferent resistance is affected. The feedback response was quantitated using micropuncture data from Bell et al. (Am. J. Physiol. 234:F154, 1978). The model predicted that renal blood flow and glomerular filtration rate would fall to 68% and 53% of control values as renal perfusion pressure is reduced from 120 mm Hg to 80 mm Hg. This response is not appreciably different than the predicted response for no tubuloglomerular feedback at all. Data from whole kidneys, on the other hand, typically show that blood flow falls about 5% and filtration remains unchanged with comparable pressure changes (Hall et al., Am. J. Physiol. 233:F366, 1977). In order to simulate the autoregulation seen in the intact kidney, tubuloglomerular feedback gain had to be increased in the model to 70 times the original value. We conclude that tubuloglomerular feedback, as it is presently understood, does not have the potency to explain renal blood flow and filtration autoregulation. (Supported by HL 11678 and HL 23502.)

CHANGES IN EXCITATORY END PLATE POTENTIAL AMPLITUDE DURING OXYGEN AT HIGH PRESSURE, Carol A. Colton and Joel S. Colton, Department of Physiology, University of Nevada Medical School Reno, Nevada, 89557

The effect of oxygen at high pressure (OHP) on excitatory end plate potentials was studied on the lobster neuromuscular junction. End plate potential (EPP) amplitude was seen to increase slightly (less than 10%) in 100% oxygen at ambient pressure. When compressed to 150 PSIG (100% oxygen) the EPP amplitude decreased to 20% of control within 30 minutes of continual stimulation at a frequency of 3/sec. With intermittent stimulation (3/sec. for 1 minute every 10 minutes) EPP amplitude decreased to 60% of control. After 50 minutes of pressurization with 100% oxygen at 150 PSIG, 2×10^{-4}M glutamate was perfused onto the postsynaptic membrane and the response compared to control (ambient oxygen and ambient pressure). In each case the postsynaptic response was equal to or greater than control. Examination of EPP amplitude during pressure controls (i.e. 640 mmHg ambient air plus 150 PSIG Helium) revealed a similar decrease in EPP amplitude over time. However, no increased EPP amplitude was seen. The postsynaptic response to 2×10^{-4}M glutamate was also similar to that in 100% oxygen at 150 PSIG in that the response was equal to or greater than ambient controls. In both 100% oxygen at 150 PSIG and Helium at 150 PSIG, quantal content per fiber was decreased at 30 minutes. This, coupled with the normal postsynaptic glutamate response, indicates a presynaptic site of action for OHP and pressure.

FSH PROFILES IN THE OVARIECTOMIZED ESTROGEN-IMPLANTED RAT: EFFECTS OF PORCINE FOLLICULAR FLUID ON THE AFTERNOON FSH SURGE AND PRELIMINARY EVIDENCE FOR A CNS SITE OF ACTION. Timothy P. Condon*, Robert E. Leipheimer* and John J. Curry. Dept. of Physiology, The Ohio State Univ., Columbus, OH 43210

Plasma FSH levels were determined by radioimmunoassay over a 24 hr period in ovariectomized rats bearing 5mm, 3mm and 1 mm silastic implants containing 17ß-estradiol. Although FSH levels were high at all times, clearly recognizable primary and secondary surges were seen at 1700 hrs and 2100 hrs respectively in the 5mm implanted rats. No recognizable surges were seen in either the 3mm or 1mm implanted rats. The primary FSH surge seen in the 5mm implanted animals could be attenuated by systemic injection of either porcine follicular fluid (PFF), ether extracted to remove steroids or a PFF extract (PFFX) limited to molecular weights between 10,000 and 30,000 daltons by membrane ultrafiltration. The primary FSH surge also appeared to be suppressed by application of PFFX directly to the region of the dorsal anterior hypothalamic area (DAHA) by means of stereotaxically implanted cannulae, but not by application to the medial preoptic area (MPOA). The elevated FSH levels seen during the 24 hr profiles along with the attenuation of the primary surge by systemic or CNS administration of PFF and/or PFFX support the existance of a non-steriodal ovarian factor, ie., inhibin, capable of suppressing FSH secretion and provide the first preliminary evidence for a CNS site of action. (Supported by a grant from the Graduate School of The Ohio State University)

ELEVATED THROMBOXANE LEVELS IN ENDOTOXIC SHOCK. J.A. Cook,* W.C. Wise, and P.V. Halushka*. (Spon: D.D. Wheeler). Depts. of Physiology, Pharmacology, and Medicine, Medical Univ. of South Carolina, Charleston, S.C. 29403

The potential deleterious role of the proaggregatory-vasoconstrictor, thromboxane A_2(TxA_2) in endotoxic shock has not been delineated. Studies from our laboratory have demonstrated, however, that treatment of rats with imidazole (Im), a Tx synthetase inhibitor, (i.p., 30mg/kg) one hour prior to endotoxin reduces mortality 60% from lethal endotoxic shock ($P<.01$). Likewise, essential fatty acid(EFA)-deficient rats which are depleted of TxA_2 precursors, are also refractory to endotoxic shock ($P<.01$). Therefore, studies were initiated to measure TxA_2 levels, via radioimmunoassay of its stable metabolite TxB_2, in rats following iv S. enteritidis endotoxin (20mg/kg). Within 30 mins. after iv endotoxin in control rats, plasma TxB_2 levels increased from nondetectable levels (<375pg/ml) in normal control rats to 2054±524 pg/ml (N=8). After 60 and 120 min. post-endotoxic shock, plasma levels still remained elevated at 2701±429 pg/ml and 1,119± 319 pg/ml respectively. In contrast to high TxB_2 levels and mortality in shocked controls, the enhanced survival of Im treated and EFA-deficient rats was associated with minimal or nondetectable levels of TxB_2 at 30 and 60 min. ($P<.001$) after endotoxin injection. This data demonstrates that endotoxin induces elevated TxB_2 and suggests that TxA_2 contributes to the pathogenesis of endotoxic shock. (Supported in part by the AHA #77731 and NIH, GM 20387).

tRNA AND AMINOACYL-tRNA SYNTHETASES IN ADULT AND SENESCENT RAT LIVER. J.R. Cook* and D.E. Buetow. Department of Physiology and Biophysics, University of Illinois, Urbana, IL 61801

Senescent (24-30 mo.) female Wistar rat liver aminoacyl-tRNA synthetases were on the average 21% less active than adult (10-13 mo.) liver synthetases in in vitro protein synthesis experiments (N=5). Senescent tRNA was on the average 11% less active than adult tRNA (N=5). In in vitro aminoacylation reactions with 17 amino acids, no decrease was observed in the total activity of senescent synthetases or in the total charging of senescent tRNA. With individual amino acids, only $tRNA^{met}$ charged less ($p < .05$) in homologous senescent (senescent synthetase plus senescent tRNA) compared to homologous adult assays. Senescent synthetases were less active than adult synthetases when charging adult $tRNA^{met}$, $tRNA^{ile}$, $tRNA^{phe}$, $tRNA^{pro}$, and when charging senescent $tRNA^{met}$ and $tRNA^{glu}$. Two-dimensional gel electrophoresis of adult and senescent tRNA detected no decreases with aging in either the number (50) or the relative quantities of isoaccepting species. Gel electrophoresis of tRNAs containing the hypermodified nucleoside Q, however, showed that the proportion of one isoacceptor increased by 75% in senescent liver. Reduced protein synthetic activity of synthetases and tRNA with age can be explained, at least in part, by reduced charging activities of certain synthetases and by changes in tRNA modifications, respectively. (Supported by NIH grants GM 19641 and GM 07143.)

SYSTEMIC ARTERIAL pH SERVOCONTROLLED VENTILATOR SIMULATION OF THE RESPIRATORY CONTROL SYSTEM. R.L. Coon, E.J. Zuperku, and J.P. Kampine. Wood VA Med. Center and Med. Col. of Wisconsin, Milwaukee, WI 53193

Ponies and humans have been shown to have the ability to increase ventilation sufficiently to clear low levels of inspired CO_2 (1.0-2.0%) without a measurable change in systemic arterial pH or PCO_2. The terminology "infinite sensitivity" has been used to describe this ability of respiratory control system to increase ventilation without an apparent change in the error signal. Recently a control system for the systemic arterial pH servocontrol of mechanical ventilation has been developed. The control loop consists of an anesthetized dog, dual-function pH/PCO_2 intra-arterial sensor, sensor amplifier servoventilator and controller. The controller has both proportional and integral gain. The combination of proportional and integral control used produces a system by which the desired set point is maintained with virtually a zero steady state error. The purpose of this series of experiments was to demonstrate the ability of this artificial system to clear low levels of CO_2 with little or no change in the controlled parameter. In 8 runs in five dogs, 2.0 to 2.5% CO_2 in the inspired gas produced an increase of ventilation of 3.1 L/min with a mean error signal of less than .005 pH units. Whether such a control system has any relevance to the physiological control system is open to discussion. However, it does allow a unique way of investigating in an artificial system the possibilities by which the physiological system may work.

INSULIN AND GLUCOSE TOLERANCE IN RATS WITH REGENERATING LIVERS. Robert P. Cornell. NE Missouri State Univ., Kirksville, MO 63501

Insulin and glucose are important during liver regeneration as a hepatotrophic factor and an energy substrate for enhanced mitochondrial oxidative phosphorylation, respectively. In the present study, male Holtzman rats were fasted and subjected to partial (67%) hepatectomy or a surgical sham control procedure under ether anesthesia. Then immediately after (0 hr) and at 8, 24, and 48 hr post-surgery rats were injected with 133 mg D-glucose/100g body wt iv, and the glucose clearance half-time in min was determined. In addition, peripheral plasma insulin was evaluated by RIA at 15 and 40 min post-glucose. It is not surprising that at 0 hr the experimental group had an insulin level elevated by 50% over control but a normal glucose clearance half-time. These findings may be due to decreased hepatic extraction of both insulin and glucose immediately after a 67% reduction in liver mass. What is surprising is that at 24 hr the experimental group had an insulin level elevated by 250% over control and a more rapid glucose clearance half-time. These data suggest increased glucose uptake by the hepatic cells prior to accelerated DNA synthesis as well as enhanced pancreatic insulin secretion in response to glucose possibly due to a factor released from the compromised liver. This pancreatic stimulatory factor could be endogenous pyrogen secreted by hepatic Kupffer cells after phagocytosis of necrotic liver tissue. Thus, the regenerating liver may be responsible for recruiting its own hepatotrophic factor-insulin. (Supported by DCWA of St. Louis, MO and NIH Grant AM 22102).

TRANSPORT CHARACTERISTICS OF JEJUNAL MUCOSA IN THE PIEBALD MOUSE MODEL FOR HIRSCHSPRUNG'S DISEASE. Helen J. Cooke and J. D. Wood. Dept. of Physiology, Univ. of Kansas Medical Center, Kansas City, KS.

Growth of piebald-lethal mice with congenital megacolon is stunted and could be due to small intestinal malabsorption. Unidirectional transmural fluxes of alanine (Ala), methionine (Met) and Na were measured under short circuit-conditions on paired, isolated flat sheets of jejunum from 3-4 week old normal and piebald mice (P) or normal mice with megacolon induced by anal cautery (I). Segments from both P and I mice exhibited a greater transmural electrical potential difference and corresponding short circuit current than normal mice. In 14 animals tissue conductance averaged 39.4 ± 0.6 mS/cm^2 in P mice and was approximately twice that found in normal mice. Net Na absorption was 1.2 ± 0.9 and increased to 4.5 ± 1.9 μEq/cm^{2}hr in normal mice when 6mM Ala was added; whereas in P mice, net Na absorption initially was 4.4 ± 1.3 and increased to 8.6 ± 2.9 μEq/cm^{2}hr upon addition of Ala. Ala and Met were actively absorbed and the net fluxes were 2-3 times greater in P or I mice than in normals. These results suggest that the jejunum of piebald mice with congenital megacolon or of normal mice with induced megacolon absorb amino acids at a greater rate than normals and this observation is consistant with a greater rate of Na absorption. The enhanced absorptive rates, however, cannot account for the retarded growth of mice with megacolon.

STRESS-INDUCED MYOCARDIAL CALCIUM CHANGES IN SQUIRREL MONKEY. K.C. Corley, T.W. Coffey*, F.O'M. Shiel* and J.L. Poland. Va. Commonwealth Univ., Richmond, VA 23298.

Total myocardial calcium (Ca) and Ca uptake of sarcoplasmic reticulum (SR) associated with shock stress sufficient to induce myocardial degeneration were studied in squirrel monkeys. Total myocardial Ca was compared among six avoidance (control of shock), five yoked (no control of shock) and two control (no shock) monkeys. Ca of the left ventricle of the avoidance but not the yoked monkeys (.154 and 167 μg Ca/mg) was significantly lower than that of the controls (.231 μg Ca/mg). Also, Ca of the left compared to the right ventricle was consistently lower in only the avoidance monkeys. Thus, the effect of shock stress was more evident in the avoidance than the yoked monkeys. Total Ca and SR Ca uptake were also measured in five avoidance monkeys which had sympathetic effects on the myocardium enhanced by atropine. Ca of the left ventricle was always lower than the right ventricle (.195 vs .226 μg Ca/mg) but not different from the control ventricles. Comparison of SR Ca uptake velocity and capacity between subendo- and subepicardium of the left ventricle revealed a significant difference of velocity (5.08 vs. 6.71 μmole Ca/gm/min) but not capacity. Since these velocities were elevated relative to those of subendo- and subepicardium of two controls (4.99 and 5.18 μmole Ca/gm/min), impaired SR function was not indicated. Thus, stress induced Ca changes of the left ventricle, but no dysfunction of the SR was observed. (Supported in part by NIH HL 13454).

KINETIC ANALYSIS OF THE ELIMINATION OF AN I.V. 10% FAT EMULSION FROM THE BLOOD STREAM OF CYNOMOLGUS MONKEYS R. Cotter, L. Martis*, F. Cosmes*, S. Young*, D. Dalgard*, H. Sargent*, E. Woods

There is little available data on the elimination of I.V. fat emulsions from the blood stream of nonhuman primates. This study was undertaken to elucidate the nature of the kinetics of the elimination process of such an emulsion. Four cynomolgus monkeys, 2 males and 2 females (1.9-2.3 kg), were administered a 2 g/kg dose of 10% soybean fat emulsion, at a rate of 0.17 ml/min. During the infusion, the emulsion levels in the plasma were monitored as plasma triglyceride (Tg) concentrations and by nephelometry. The plasma concentration time data so obtained were analyzed using nonlinear regression analysis. These analyses indicated an elimination process that is exponential in nature. Kinetic parameters that describe this process are as follows: Tg analysis indicated a fractional removal rate of 11.1 ± 8.1%/hr, a clearance rate of 4.9 ± 2.8 μ moles/ml/hr.kg and a half life of 722 ± 708 min. The maximal plasma Tg concentration during infusion was 46.39 ± 7.0 μ moles/ml. Nephelometry indicated a fractional removal rate of 34.5 ± 17.4%/hr, a clearance rate of 26.1 ± 11.1 μ moles/ml/hr.kg, and a half life of 143 ± 65 min. Maximal plasma emulsion concentration during infusion was 21.1 ± 8.0 μ moles/ml. These data would indicate the elimination of fat emulsion from our test system was by an exponential process.

OXYGEN DEBT IN REPTILES: RELATIONSHIP BETWEEN TIME NEEDED FOR REPAYMENT AND METABOLIC RATE. R. A. Coulson and T. Hernandez. La. State Univ. Med. Ctr., New Orleans, LA 70112

It has been postulated that the amount of energy required for protein synthesis or for the resynthesis of glycogen from lactate would be the same in all animals and that it would be independent of metabolic rate (M.R.). The theory was tested by measuring oxygen consumption after exhaustive work and after feeding a high protein meal to alligators (A. mississippiensis) and to chameleons (Anolis carolinensis). The 5g chameleon has about 6X the metabolic rate of a kilogram alligator. Although feeding produced a 300% increase in M.R. in the alligator, and only 40% in the lizard, the more prolonged increase in the alligator was responsible for the fact that the extra O_2 consumed was the same in both. After hard work, both animals increased blood lactate to the same degree and both increased M.R. 300%. Once again, the total increase in O_2 used was the same in both (on a wt. basis). In keeping with the differences in M.R., it took the alligator 6X as long to dispose of the lactic acid. It was concluded that any action leading to the production of an oxygen debt renders an animal of low M.R. almost incapable of aerobic work for a considerable time whereas those with high M.R. are only incapacitated for a brief period. (Supported in part by the La. Dept. of Wildlife and Fisheries).

MYOTHERMIC ANALYSIS OF LENGTH-DEPENDENT ACTIVATION IN CARDIAC MUSCLE USING OVERDRIVE SUPPRESSION AS A STIMULUS. Richard L. Coulson, S. R. Houser and E. A. Breisch. Southern Illinois University School of Medicine, Carbondale, IL 62901 and The Cardiology Section, Temple University Medical School.

The energy of activation (A) in cardiac muscle corresponds to the net metabolic energy expenditure associated with the movement of Ca^{++} out from cellular storage sites and back from the contractile proteins to the sarcoplasmic reticulum at the hands of an active calcium pump which hydrolyses 1M ATP/2M Ca^{++} pumped. It is difficult to measure A in cardiac muscle because actin-myosin interaction (AM) cannot be eliminated by stretching sarcomeres to lengths > Lmax where filament overlap is diminished or eliminated. Reducing AM by preshortening muscle is confounded by both non force-producing AM and effects of length dependent A. Overdrive suppression (OS) (Fed. Proc. 38:974, 1979) provides a mechanism for varying the strength of contraction without alteration of muscle length. Using a cardiac calorimeter (J. Physiol. 260:45-53, 1976) a force-heat diagram (FH) can be constructed with OS used to vary the magnitude of contractions at a single muscle length < Lmax. Extrapolation of the FH to the heat axis is then indicative of contraction threshold A. Using the same OS stimulus at different muscle lengths < Lmax permits recognition of variation in A with muscle length. Using this technique a contraction threshold value of about 30nM Ca^{++} pumped per gram heart was established at a muscle length of 85% of Lmax. This increased to about 50nM Ca^{++} pumped at Lmax.

MULTIPLE INDICATOR DILUTION STUDIES OF THE UPTAKE OF NOREPINEPHRINE BY THE MYOCARDIUM OF THE DOG IN VIVO. D. Cousineau,* C.P. Rose* and C.A. Goresky. McGill University Medical Clinic, Montreal General Hospital, Montreal, Canada H3G 1A4

The kinetics underlying the steady balance of norepinephrine (NE) across dog heart at rest were studied in a working preparation with the multiple indicator dilution technique. The circumflex coronary artery was perfused with blood from the femoral artery, with a pressure-dependent system. A small bolus containing labeled albumin (a tracer confined to the vascular space), labeled sucrose (which penetrates into the extracellular space in a barrier-limited fashion), and labeled NE was injected into the artery and outflow dilution curves were obtained from the coronary sinus. Endogenous levels of NE were measured simultaneously in aortic and coronary sinus blood with a radioenzymic assay. Net extraction of a major proportion of the labeled NE was evident while the arteriovenous concentrations of endogenous NE showed no difference, indicating a simultaneous equivalent release of NE by the myocardium. Analysis of data enabled us to assess separately the myocardial capillary permeability for NE, the unidirectional flux at the neuronal membrane (equivalent to neuronal uptake) and the proportional uptake of NE. Infusion of desmethylimipramine selectively diminished the apparently unidirectional flux of labeled NE into the neuronal terminals. The findings indicate that the tracer approach is needed to appraise the uptake and release of NE by the heart.

PRODUCTION OF ENDOGENOUS PYROGEN (EP) BY HUMAN LEUKEMIA CELL LINES AND MURINE MACROPHAGES. Patrick S. Cox* and Clark M. Blatteis. University of Tennessee Center for the Health Sciences, Memphis, TN 38163

Spontaneous and endotoxin (LPS, S. enteritidis)-stimulated production of EP by selected in vitro human leukemia cell lines (NALM-1, NALM-16, K-562, RAJI, BALM, RPMI-8402, and MOLT) and murine macrophage cell lines (P388-D1 and IC-21) were assessed by bioassay of culture supernatants in rabbits. The culture supernatants were injected into a marginal ear vein; colonic temperature was monitored continuously for 3 h. To assess spontaneous EP production, 5 ml of culture medium (RPMI-1640 with 10% fetal calf serum) was incubated with the tumor cells (final density 1 x 10^7 cells/ml) for 48 h (37°C), and tested. Supernatants from the following cell lines induced fever ($\Delta T > 0.5$°C): K-562, NALM-1, and P388-D1. The spontaneous production of EP by leukemia cells may provide an explanation for fevers of unknown origin in leukemia patients. Fresh culture medium, injected as control, caused no fever. To assess LPS-stimulated EP production, 25 x 10^6 cells were incubated (37°C) with 8 µg LPS for 1 h, centrifuged and resuspended in saline for 4 h (37°C). The supernatant was then tested, using saline as a control. Supernatants from the following cell lines induced fever: NALM-1, NALM-16, K-562, RAJI, P388-D1 and IC-21. These results indicate that certain in vitro tumor cells are capable of producing EP. (Supported in part by ACS Grant IN8M17.)

PHYSIOLOGICAL CHARACTERISTICS OF PSYCHOLOGICALLY REACTIVE AND NON-REACTIVE INDIVIDUALS. R.H. Cox,* E.T. Howley,* J.E. Lawler,* and K.A. Lawler,* (SPON: H.G. Welch) University of Tennessee, Knoxville, TN. 37916.

The purpose of this study was to investigate the cardiovascular (CV) and metabolic responses during graded treadmill walking in two groups of individuals suspected of showing differences in vulnerability to hypertension. Five individuals who responded with a heart rate (HR) increase of 30 or more beats per minute to a shock avoidance task were compared to 5 individuals who manifested an HR response of less than 10 beats per minute. While higher HR and blood pressure (BP) responses were evoked in the reactive group when challenged by mental arithmetic and a reaction time task for monetary reward, CV adjustments to the exercise stress were similar for both groups. Maximum O_2 uptake and maximum HR did not distinguish the two groups, though significant individual variation was observed. We concluded that the exaggerated CV response to psychological stress was not due to differences in CV capacities. The regression of HR and BP against O_2 consumption at approximately 30, 50, 70 and 90% of maximum O_2 uptake for each individual provided a means for quantifying psychological stress responses. The reactive individuals displayed HR and BP responses during psychological stress comparable to responses seen during work requiring 30 to 50% of the O_2 uptake capacity.

ALTERATIONS IN THE MECHANICS, COMPOSITION AND MORPHOLOGY OF CANINE ARTERIAL SMOOTH MUSCLE BY COLLAGENASE TREATMENT. Robert H. Cox, Bockus Institute, Graduate Hospital and Dept. of Physiol., Univ. of Penna, Philadelphia, PA 19146.

The role of collagen fibers in the mechanics of carotid artery was assessed by incubation in purified collagenase (30 units/ml, Worthington CLSPA). Pressure-diameter data were obtained with passive smooth muscle (SM) in 0-mM Ca^{+2} and 2-mM EGTA. Isometric responses to 145-mM K^+ were performed at a muscle length equivalent to 100 mmHg (ie, $\approx L_{max}$). Enzyme treatment removed collagen at a rate of about 10%/hr incubation. Small decreases in passive stiffness were found with incubation. Isometric force development to K^+ decreased by about 8%/hr. A small increase in muscle length (L) of about 1.2%/hr was found. Series elastic element stiffness measured during the isometric contraction was unchanged despite the increase in L. K^+ and Mg^{+2} contents increased slightly with treatment (about 8%/hr) suggesting that cell permeability was only minimally affected. Enzyme treatment was associated with adventitia reduction (0-2 hr), the appearance of rounded nuclear profiles (2-4 hr), and the ultimate loss of cells (20 hr). Intracellular and membrane ultrastructure appeared normal in enzyme treated segments. Alterations were found in regions where cell-to-cell and cell-to-matrix continuity was often interrupted. These results are consistent with the hypothesis that collagen may be involved as a link in the intercellular coupling of cellular force development in arterial smooth muscle. (Supported by HL-17840 from NHLBI).

PARATHYROID HORMONE-A POTENT CORONARY VASODILATOR. M. F. Crass, III, D. J. Paulson and P. K. T. Pang. Texas Tech Univ. School of Medicine, Lubbock, TX 79430.

The ability of the amino-terminal region 1-34 of bovine parathyroid hormone, PTH-(1-34), to decrease coronary vascular resistance was assessed in open-chest mongrel dogs. The dogs were anesthetized with Na pentobarbital (30 mg/kg) and ventilated with room air using a Harvard respirator. A left thoracotomy was performed and a Carolina electromagnetic flow probe placed on the left circumflex coronary artery. A 23-gauge butterfly needle tip was inserted into the artery and left indwelling for injection of isotonic saline (control) or PTH-(1-34) (10,000 U/mg). Peripheral venous injections were performed via the right femoral vein. The coronary vasodilator response induced by PTH-(1-34) was observed by both modes of injection. The response to intracoronary injection was dose-dependent over the range of 0.01-20 U/kg and that to peripheral injection over the range of 1-10 U/kg. The maximal response was obtained by intracoronary administration of 1.0 U/kg, resulting in >200% increase in flow rate; onset occuring within 30 sec with an overall duration of 8-9 min. When administered intravenously (10 U/kg), PTH-(1-34) produced a 10-15% increase in coronary blood flow. These new findings suggest that parathyroid hormone, in addition to its other well-known biologic activities, may serve an important role in the regulation of coronary vascular resistance.

SYMPATHETIC NEURAL INFLUENCE ON SURFACE ACTIVE MATERIAL (SAM) IN CATS. Daniel J. Crittenden* and David L. Beckman, School of Medicine, East Carolina Univ., Greenville, N.C. 27834

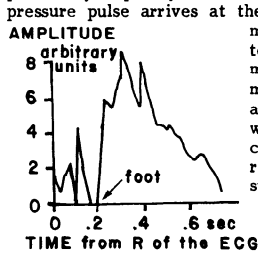
Recent evidence suggests that hyperventilation leads to release of SAM via beta adrenergic and cholinergic mechanisms (JAP 43:39,1977), whereas subsequent inactivation of SAM may occur via alpha adrenergic activity (JAP 44:327,1978). The present study determined the effects of sympathetic stimulation via stellate ganglion stimulation (SGS) in spontaneously breathing cats on release of disaturated phosphatidyl choline (DSPC) and total phospholipids (TPL) in lung lavage fluid (10 ml saline/g lung). In 8 sham-operated controls DSPC=1.545 ±.131 (SE) mg/g and TPL=3.258±.123; in 8 SGS cats (7V, 10cps, 1 min) DSPC increased by 26% to 1.949±.155 (P<0.05) and TPL by 28% to 4.155±.292 (P<0.01). In 6 cats, DSPC after 6 min SGS was 1.591±.109 mg/g. Compliance measured by intrapleural catheter in 7 intact cats decreased 15% (P<0.01) during SGS. FRC increased 8-10 ml initially but returned to normal after 4-6 breaths. Mean pulmonary arterial pressure in 5 cats increased slightly from 13.4±3.1 mm Hg to 15.0±3.6. Normal respiratory rates and blood gases were unchanged by SGS. Evidence from histological and functional studies discounted any contribution of airway constriction to the compliance decrease. While SGS leads to inactivation of SAM as indicated by high surface tension and decreased compliance (JAP 30:394, 1971), these results show that direct sympathetic neural stimulation induces release of SAM.
(Supported in part by N.C. United Way)

PRESSOR RESPONSIVENESS TO VASOPRESSIN IN THE RAT WITH DOC-SALT HYPERTENSION. J.T. Crofton*, L. Share, B.C. Wang and R.E. Shade. University of Tennessee Center for the Health Sciences, Memphis, TN 38163

Vasopressin is elevated in DOC-salt hypertension. Since the plasma concentration of vasopressin appears to be too low to alone account for the elevated, sustained blood pressure seen in this model, one must postulate an increased pressor responsiveness to vasopressin. Experiments were undertaken to study this question. Rats were unilaterally nephrectomized; one group was treated with desoxycorticosterone pivalate (30 mg/kg sc, weekly) and given 1% saline to drink (DOC); drinking fluid for the other groups was 1% saline (NaCl) or water (H_2O). When the DOC animals showed a marked increase in systolic blood pressure accompanied by a decrease in body weight, femoral catheters were implanted, the animals were allowed to recover, and pressor responsiveness to vasopressin and angiotensin II were tested in the conscious rat. A NaCl and H_2O rat were also tested on the same day. The pressor response to vasopressin in the DOC rats was approximately twice ($p < 0.05$) that in either the NaCl or H_2O rats. Pressor responsiveness to angiotensin II was similarly enhanced. These studies further support a role for vasopressin in the later stages of DOC-salt hypertension. (Supported by USPHS Grants HL-19209 and HL-129910.)

INCREASED GAS FLOW INTO THE MOUTH DURING BREATH HOLDING DUE TO N_2O UPTAKE. Julio C. Cruz and John T. Reeves. Cardiovasc. Pulm. Res. Lab., Univ. of Colo. Med. Cntr., Denver, CO 80262.

Alveolar-pulmonary capillary gas transfer (O_2 & CO_2) may be observed during a breath holding maneuver using a body plethysmograph-pneumatic flow meter. If N_2O is inhaled and the breath held with an open glottis, the large uptake signal has been used to time the arrival of pulmonary capillary pulse wave. However, the plethysmograph should not be necessary if the gas uptake results in bulk inflow at the mouth. Using a pneumotachograph, the flow signal obtained during breath holding after a breath of room air was substracted from one obtained after a N_2O breath. The result (Figure) shows the increased flow at the mouth caused by the N_2O uptake at the pulmonary capillary level. This uptake occurs when the vascular pressure pulse arrives at the pulmonary capillaries. Arrival time measured from the R wave of the ECG to the foot of this pulse, was 248 ± 12 msec sitting and shortened to 159 ± 7 msec supine (n=6, $p < 0.005$). This arrival time (velocity) may correlate with pulmonary arterial pressure, according to Reuben. If so, our data may reflect a rise in pulmonary artery pressure from sitting to supine position.



PRESSURE-FLOW AUTOREGULATION IN NORMAL AND REPERFUSED CORONARY CIRCULATIONS. George J. Crystal*, H. Fred Downey, and Fouad A. Bashour. Dept. of Physiol., Univ. TX Hlth. Sci. Ctr. and Cardiovasc. Res. Ctr., Dallas, TX 75235

Pressure-flow autoregulation was compared in normal and reperfused left anterior descending coronary beds (LAD) in 7 anesthetized, open-chest dogs. LAD was perfused at controlled perfusion pressure (PP) with flow measured by electromagnetic flow transducer. At base-line PP, flow was 24.5 ml/min in normal LAD and 19.9 ml/min after 2 hours of occlusion and 2 hours of reperfusion. A 50 mmHg elevation in PP resulted in initial increases in flow of 107 and 173% in normal and reperfused LAD, respectively. From this maximum, flow decreased by 27% in normal LAD and 15% in reperfused LAD to reach steady state values of 37.2 ml/min and 46.2 ml/min, respectively. A 50 mmHg reduction in PP resulted in initial decreases in flow of 42 and 61% in normal and reperfused LAD, respectively. From this minimum, flow increased by 31% in normal LAD and by 19% in reperfused LAD to reach steady state values of 18.6 ml/min and 9.3 ml/min, respectively. Results indicate that occlusion and reperfusion of coronary circulation accentuates passive dimensional changes and attenuates autoregulation following changes in PP.

ENDURANCE TRAINING IN THE LEOPARD FROG, RANA PIPIENS. John W. Cummings* (SPON: S.S. Easter). The University of Michigan, Ann Arbor, MI 48109.

The exercise endurance of Rana pipiens increased 35% after 6½ weeks of treadmill training. Despite considerable reliance on anaerobic metabolism for support of activity, the leopard frog demonstrated no increase in its anaerobic capacity during training. Lactate production during exhaustive exercise was not significantly different in either the trained or untrained frogs. At fatigue, muscle lactate concentration had increased 3.5-fold to 2.77 ± .21 mg/g in the trained and 2.82 ± .13 mg/g in the untrained animals, while whole body lactate levels were elevated threefold to 1.32 ± .10 and 1.47 ± .06 mg/g, respectively. The magnitude of muscle glycogen depletion was also similar for both groups. The primary adaptation to training was an augmentation of the aerobic capacity of the muscle as assessed by a 38% increase in the maximum activity of citrate synthase, a TCA cycle enzyme. The maximum activity of this enzyme was positively correlated with both the level of maximum performance of all animals ($r=.61$, $p<0.01$) and with the degree of improvement in the trained frogs ($r=.72$, $p<0.05$).

EFFECTS OF HIGH DOSES OF AN H_1-RECEPTOR AGONIST ON FORELIMB VASCULAR PRESSURES AND SKIN LYMPH IN THE ANESTHETIZED DOG. Joe M. Dabney, Carol A. Creed* and David E. Dobbins. Dept. Physiol., Uniformed Services University, Bethesda, Md. 20014

We have previously reported that the intraarterial infusion of H_1 and H_2 histamine-receptor agonists, singly or in combination, in a dose range of 8-40 µg base/min., failed to mimic histamine's effects on lymph flow, lymph total protein concentration and lymph total protein transport. We now report the effects of the infusion of high doses of the H_1 histamine-receptor agonist 2(2-pyridyl) ethylamine (PEA) on vascular pressures and skin lymph in the canine forelimb perfused at constant flow. The intraarterial infusion of PEA at 80,160,200 and 400 µg base/min. for twenty minute periods each resulted in a significant increase in forelimb perfusion pressure from minute 50 onward and a transiently significant increase in skin small artery pressure. Skin small vein pressure was significantly elevated only at the highest infusion rate while systemic pressure and heart rate were not significantly different from control values at any time during the infusion of PEA. Lymph flow, lymph total protein transport and lymph total protein concentration were significantly increased above control by minutes 10,20 and 30 of the infusion period respectively. There were no significant changes in arterial plasma protein concentrations during PEA infusion. These data lend further support to the role of the H_1-receptor in the mediation of histamine-induced increases in capillary permeability.

TEACHING NEUROPHYSIOLOGY USING STUDENT EVALUATED LEARNING OBJECTIVES. Nancy Ann Dahl. Univ. Kansas. Lawrence, KS 66045

J.B. Gilmore's method of self evaluated learning objectives (J. Col. Sci. Teach. 2:53, 1973) has been applied to a neurophysiology class for medically oriented students (e.g. occupational therapists). The method defines the course content, motivates the student to examine all aspects of the course and allows each aspect to be analyzed. The student is given 200 learning objectives and evaluates her own level of knowledge on each objective, 50 at a time. (Expert-3 points; learned-2; non learned-0). The average objective score determines the estimated grade(2.2 or more-A; less than 1-F). Exams are then given on 20% of the objectives to determine the students reliability and a correction is made if exam performance on a given objective differs from the student's estimate on that objective. E.g. failing an objective does not change the grade if it has been estimated "not learned." The average correction factor is used to adjust the estimated grade and give an "unbiased estimate" of the student's knowledge. The self evaluation and exam are graded and compared on a computer. This allows rapid and accurate feedback as well as detailed analysis of the course. This analysis reveals items the students cannot or will not learn and highlights items that need revision. The method has improved student satisfaction and grades. The A's have doubled although 13% still fail (D, F and drop). The few students who do not understand the method tend to distrust the system.

ULTRASTRUCTURAL CHANGES IN NON-MYELINATED NEURONS DURING ENERGY DEPRIVATION. Nancy Ann Dahl, Greg A. Looney* and William H. Black*. Univ. Kansas, Lawrence, KS 66045

The neuropathology of oxygen-glucose deprivation uncomplicated by stagnant conditions was examined. Rabbit vagus nerves were pulled into a multicompartment perfusion chamber, stimulated 5/sec and deprived of energy by substituting N_2 and deoxyglucose for O_2 and glucose in the Locke's perfursate. At 0, 0.5, 1, 2 and 4 hours nerves were prepared for EM. Cross sectional areas of 100 randomly selected C fiber axons per nerve were measured. Control neurons had a mean area of .84μ^2(S.D.+.46). 0.5 and 1 hour of energy deprivation did not significantly affect the appearance of the C fibers. At 2 hours the axons were smaller and flattened (mean area .62μ^2) and the number of axons smaller than .4μ^2 increased from 10 to 30%. By 4 hours 50% of the axons were less than .4μ^2 and 30% were less than .1μ^2. These tiny axons seldom had microtubules or mitochondria but were packed with neurofilaments. The 4 hour nerves also showed a few huge axons, up to 13μ^2. 8% of all axons were over 2.6μ^2 (.8% in controls). These large axons contained flocculant material and membrane fragments. Both tiny and huge axons were embedded in normal looking Schwann cells. Thus shrinking is the most prominent result of low energy and only later do a few axons swell, though they comprise 50% of the volume. It appears the early swelling reported in brain anoxia or ischemia may not be due to lack of energy, per se. (Supported by a Grant-in-Aid from the Am. Heart Association)

EFFECTS OF DESOXYCORTICOSTERONE ACETATE ON SALT APPETITE IN ADRENALECTOMIZED RATS. A.D. Dalhouse*, H.G. Langford, B. Folk*, and L. F. Jefcoat*. Univ. Miss. Med. Cntr., Jackson, MS 39216.

Twenty-four Sprague-Dawley albino rats(250-450 gms) were adrenalectomized and tested in a two-choice situation for 3% NaCl and H_2O ingestion after 100, 200, 400, 800, 1000 µg/kg/i.m. desoxycorticosterone acetate(DOCA). The experimental animals showed significant differences from the control animals in the % change of their food, water, saline uptake ($p<.05$) after DOCA treatment. DOCA up to 400 µg/kg were accompanied by decreasing NaCl intake and increasing H_2O intake. The % changes in intake from control levels were not nearly as dramatic as those reported by Fregly and Walters, however, the within-group variance was great. In an attempt to reduce this within-group variance a second experiment was conducted using 30 rats in a within-group(all animals received all levels of the treatment in a randomized order). This experiment yielded similar results. The experimental animals showed significant differences from their control counterparts in the % change of water and saline intake($p<.05$) after DOCA treatment. Increasing doses of DOCA up to 800 µg/kg produced decreasing NaCl and increased H_2O intake. Intra-animal variability was not as great as in experiment I, but still large enough to be of concern. Plasma levels of renin were measured and found to be compatible with renin control of salt appetite at low DOCA doses, and DOCA control at high doses. Supported by Grants T32-HL07392-01 and R01-HL18891-02.

THE EFFECTS OF PULMONARY IMPAIRMENT ON DEPOSITION AND RETENTION OF AN INSOLUBLE AEROSOL IN FISCHER-344 RATS. Edward G. Damon and Brian V. Mokler*. Lovelace Biomedical and Environmental Research Institute, Albuquerque, NM 87115

Most of the deposition and retention studies which have been conducted in the past have utilized healthy, young adult animals as test subjects. The human population which may be exposed to environmental pollutants includes not only healthy individuals but also people with lung impairment as a result of emphysema, bronchitis and other respriatory diseases. The purpose of this study was to assess the effects of elastase-induced emphysema or inhalation of an irritant aerosol (Triton X-100, a nonionic surfactant similar to those used in a number of pressurized consumer products) on the deposition and retention of an insoluble test aerosol (Fe_2O_3 labeled with ^{59}Fe). Animals were exposed to aerosolized $^{59}Fe_2O_3$ 2 to 3 weeks after intratracheal instillation of 1 IU of elastase per g body weight or either 18 hours or 7 days after exposure to aerosolized Triton X-100. Animals exposed to elastase exhibited significant reduction in ^{59}Fe lung burden compared to untreated controls at times ranging from 1 to 31 days post exposure ($P < 0.01$). Triton X-100 resulted in dose-related increases in ^{59}Fe whole body burden when administered 18 hours prior to exposure to $^{59}Fe_2O_3$. (Research performed under an Interagency Agreement between the Consumer Product Safety Commission and DOE Contract EY-76-C-04-1013 in facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care).

MODES OF INSULIN DELIVERY AND THEIR EFFECTIVENESS ON GLUCOSE UPTAKE BY RAT SKELETAL MUSCLE. **E.L. Daniels*S.B. Lewis and T.A. Schultz*. Naval Regional Medical Ctr. Oakland, Ca. 94627**

In these studies we compared the effectiveness of continuous infusion and bolus injections of insulin on glucose uptake in the noncyclically perfused rat hindlimb. Ten mM glucose was infused at 3ml/min, venous glucose monitored at 2 min intervals, & glucose uptake calculated as µMoles/min/100 g rat. Insulin boluses were given every 10 min at doses equal to the amount of insulin continuously infused for 10 min & glucose uptake compared. At all doses tested (50, 100, 200, & 2000 µU/min) there was no significant difference between the two modes of insulin delivery. At the low doses (50 µU/min) neither delivery was significantly higher than the control (1.85 µM/min/100 g rat). When doses of 200 to 2000 µU/min were compared, a dose response was obtained. Glucose uptakes shown below are for continuous insulin infusion experiments.

Insulin	Glucose Uptake µM/min/100 g rat + S.E.		
µU/min	10 min	20 min	30 min
0	1.60 + 0.04	1.76 + 0.10	1.96 + 0.08
200	1.75 + 0.12	2.47 + 0.15	2.91 + 0.10
1000	2.38 + 0.23	3.74 + 0.14	4.47 + 0.06
2000	2.76 + 0.12	4.34 + 0.17	5.22 + 0.35

From these results we conclude that insulin given as a bolus is equal to continuous insulin infusion in stimulating glucose uptake by rat skeletal muscle.

EFFECTS OF SANDFLY FEVER ON SUBMAXIMAL WORK PERFORMANCE. W.L. Daniels*, J.E. Wright*, J.A. Vogel, D.S. Sharp*, G. Friman*, & W.R. Beisel*. U.S. Army Rsch Inst of Env Med, Natick, MA 01760 and U.S. Army Med Rsch Inst of Inf Dis, Ft. Detrick, MD 21701.

Acute viral infections commonly result in myalgia and negative nitrogen balance. To investigate the affect of acute infection on work performance, 9 male volunteers (7 experimentals, 2 placebos) were evaluated before, during and after an experimentally induced episode of sandfly fever. Subjects performed a continuous walking test at 3 mph with a 3% increase in grade every 3 minutes up to 15% grade. Resting rectal temperatures were elevated in the experimental group during infection ($\bar{x}$ = 38.6°C, $p < 0.05$). The rate of increase in rectal temperature with exercise was not altered by infection. Resting heart rate was increased ($p < 0.01$) during fever. Heart rate and RPE were increased with exercise during fever, however, the increases were only significant ($p < 0.05$) at lower workloads (<6% grade): During fever, 3 subjects were unable to complete the walk. $\dot{V}O_2$ and $\dot{V}CO_2$ were unchanged at each absolute workload throughout the study. $\dot{V}_E$BTPS, VEQ and R were increased in both experimental and control subjects. Our results indicate that the physiological response to submaximal exercise was only minimally affected by viral infection. However, the fact that 3 out of 7 experimental subjects were unable to complete the walking test during the fever episode demonstrates a marked effect upon their ability and/or willingness to perform work.

A STUDY OF THE PLASTICITY OF REPOSITIONED FAST AND SLOW SKELETAL MUSCLE. Kurt A. Dasse*, Dorothy Chase*, and William C. Ullrick. Boston Univ. Sch. Med., Boston, MA 02118

It has been suggested that the basic structural, metabolic, and contractile properties of fast and slow skeletal muscles are dependent upon their innervation, and that these two types of muscle coexist to perform different functions. Furthermore, an alteration in the afferent activity arising from a muscle has been reported to result in a change in its intrinsic properties. Experiments have been performed to test these suggestions. The origins of the slow soleus and fast plantaris muscles in the rat have been surgically reversed leaving the nerves and vessels intact, so that the slow muscle performed the action of the fast muscle, and vice versa. The histochemical and contractile characteristics were then examined 2 to 12 weeks following the surgery. Although there was an increase in the Tetanic:Twitch ratio of the slow muscle, no changes were observed in the time characteristics or the histochemical properties of either of these muscles. These results suggest that the action, and perhaps the function a muscle serves, may not markedly influence its intrinsic properties. (Supported by USPHS NIH Grant 1-R01-NS14033 and 1-T32-07224)

"THE RELATIONSHIP BETWEEN TRANSPULMONARY PRESSURE (P_{TP}) AND SLOWLY ADAPTING PULMONARY STRETCH RECEPTORS (PSR) DURING RESISTIVE LOADING". P.W. Davenport, D.T. Frazier, & F.W. Zechman. Dept. of Physiol., Univ. of Ky., Lexington, Ky. 40536.

These experiments were performed on supine, anesthetized, spontaneously breathing cats. The trachea was cannulated and connected to a pneumotach to measure flow ($\dot{V}$) and volume (V) by integration. The pneumotach was connected to a resistive loading manifold for the selective loading of insp. or exp. Tracheal press. (P_T) was measured at the tracheal cannula. Esophageal press. (P_{ES}) was measured by a microtransducer in the esophagus. The difference between P_T and P_{ES} was taken as P_{TP}. Single unit PSR activity was recorded from the peripheral end of the right vagus. PSR frequency (f_{PSR}, from a rate meter), P_{TP} and V were sampled every 100 msec for control and loaded breaths. f_{PSR} was plotted against both P_{TP} and V by computer. The f_{PSR}-V curves for control breaths showed clockwise hysteresis, peak f_{PSR} occuring prior to max. V. There were hysteresis loops with both insp. and exp. loads, the curves were not identical to the control curves. Control f_{PSR}-P_{TP} curves were linear and had little hysteresis within the tidal volume range of breathing. Loading of either insp. or exp. resulted in f_{PSR}-P_{TP} curves that were superimposable on the control curves. Results indicate that in intact animals the P_{TP} is a more adequate reflection of the stimulus seen by PSR's than V. (Supported by NIH Grant #HL-16878).

EFFECT OF AGE AND ULTRAVIOLET EXPOSURE ON THE MECHANICAL AND BIOCHEMICAL PROPERTIES OF ALBINO GUINEA PIG SKIN. Douglas J. Darr*, Thomas H. Cook* and Robert B. Mitchell. Pennsylvania State University, University Park, PA 16802

A major objective of this study was to test the sensitivity of the Cook strip-biaxial mechanical testing device for in vivo, noninvasive measuring of the physical stress-strain properties of skin.

Abdominal skin of four groups of seven month old animals was irradiated with varying known doses of UV light over a five month period. Baseline mechanical tests were performed on all animals before irradiation and again after each group received its total dosage. Biochemical tests were done on skin samples to assess soluble and insoluble collagen, type I and type III collagen ratios, and total glycosaminoglans.

Mechanical stress-strain analyses showed an increased "stiffness" of animal skin for the control group with age. With increasing doses of radiation, mechanical tests again revealed a progressive increase in "stiffness", but this was followed by a dramatic loss in "stiffness" in those animals which received the highest UV dose. Biochemical changes in dermal collagen composition correlate with and partly account for mechanical property changes. Both with age and UV exposure, dermal collagen became increasingly insoluble, and with high doses of radiation the type I to type III ratio of collagen decreased. No significant changes were detected in dermal glycosaminoglycan content.

CHANGES IN GASTRIC VASCULAR PERMEABILITY TO PLASMA PROTEINS DURING A MODEL PROTEIN-LOSING STATE. Horace W. Davenport and John G. Wood.* Univ. of Michigan, Ann Arbor MI 48109

When the mucosa of a dog's stomach is covered with 10 mM dithiothreitol (DTT) in buffer, pH 7, vascular resistance falls to 70% of control in 15 min, and copious plasma shedding occurs (Gastroenterology 60:870, 1971). Filtration and PS products for albumin and fibrinogen were measured as described in accompanying abstract in control states and after exposure of the mucosa to DTT. In addition, the reflection coefficient (σ) for each protein was calculated.

	Control	DTT
Filtration, ml min^{-1} 100 gm dry wt^{-1}	2.7±0.6	7.5±0.8
PS, Albumin, cm^3 sec^{-1} gm dry wt^{-1} x 10^4	6.5±1.0	14.2±2.2
PS, Fibrinogen, same units	2.3±1.2	4.7±0.9
σ,	0.7	0.4
σ,	0.9	0.7

(Supported by USPHS NIH Grant AM 08716)

PAPAVERINE ENHANCES α-ADRENERGIC STIMULATION OF MUCUS GLANDS IN CANINE TRACHEA IN VIVO. B. Davis, R. Chinn*, P. Graf*, D. Popovac*, and J. Nadel (SPON: H. Coleridge). CVRI and Depts. of Medicine and Physiol, UCSF, San Francisco, CA 94143

In anesthetized dogs, ventilated via the lower trachea, we cut both superior laryngeal nerves and cannulated both cranial thyroid arteries for local drug injection. We exposed the upper tracheal mucosa and sprayed it with powdered tantalum. Secretions from the mucus glands caused elevations in the tantalum layer (hillocks). We examined an area (1.2 cm^2) of tantalum coated epithelium at the end of 1 min periods before and after drug injection, counted the number of hillocks, and measured the diameters of 6 round hillocks. Phenylephrine (40 µg in 2 ml) constricted the tracheal vessels seen on an angiogram but increased the number of hillocks from 10 ± 3 to 22 ± 5 hillocks/cm^2 (mean ± SE; n=6, $p<0.01$) and increased the mean hillock diameter from 0.2 ± 0.1 to 0.4 ± 0.1 mm (n=6, $p<0.01$). After papaverine (60 mg in 2 ml) a peripheral vasodilator, phenylephrine increased the number of hillocks from 17 ± 6 to 47 ± 10 hillocks/cm^2 (n=6, $p<0.01$) and increased the mean hillock diameter from 0.1 ± 0.1 to 0.4 ± 0.0 mm (n=6, $p<0.01$). The effects of phenylephrine were prevented by phentolamine (1 mg in 2 ml). These studies show that papaverine increases the number of canine tracheal mucus glands affected by local injection of an α-adrenergic agonist. This effect may be caused by increased blood flow to the glands. (Supported in part by NHLBI Grants HL-06285 and HL-21150 and the Cystic Fibrosis Foundation)

CATABOLISM OF VERY LOW DENSITY LIPOPROTEINS BY DIFFERENTIATED 3T3-L1 CELLS. Roger A. Davis and Arthur D. Hartman. Louisiana State Univeristy Medical Center, New Orleans, LA.

3T3-L1 swiss fibroblasts are a cloned heterogenous cell population that differentiate into "adipocytes" as defined by a morphology which includes multilocular lipid inclusions. Several other investigators have shown that upon differentiation, 3T3-L1 cells express specific enzymes which are characteristic of adipocytes and are not expressed in the undifferentiated fibroblast state, including lipoprotein lipase (LPL). A major function of LPL is to hydrolyze VLDL triglyceride, a process which is essential for peripheral fat utilization. In vivo LPL in adipose tissue is highly sensitive to insulin. We investigated the ability of 3T3-L1 cells to metabolize VLDL in culture. ^{14}C-Triglyceride labelled VLDL was prepared in vivo by injecting rats with ^{14}C-oleic acid bound to albumin. Addition of VLDL to differentiated 3T3-L1 cells resulted in a linear decrease in medium triglyceride and a reciprocal linear increase in medium free fatty acids. After 2 hrs 50% of the initial VLDL (100 µg/ml) was metabolized. Additional studies show that triglyceride lipolysis by 3T3-L1 cells is inhibited by salt (90%), requires serum for maximal activity and is stimulated by prior treatment of cells with insulin. These data support the use of 3T3-L1 cells as an in vitro model of membrane bound LPL which is sensitive to hormones.

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ETHANOL-INDUCED BICARBONATE PRODUCTION BY CANINE GASTRIC MUCOSA. Merril T. Dayton*, Jerry F. Schlegel, Joseph Steinbach*, Jean Deregnaucourt*, and Charles F. Code. CURE, VA Wadsworth Hospital, UCLA, Los Angeles, California 90073

This study was undertaken to determine gastric mucosal HCO_3^- production directly using the Natelson microgasometer, under basal conditions and after challenge by ethanol. Four fasted dogs, two with Pavlov pouches and two with Heidenhain pouches, were used; cimetidine given at 5 mg/kg/hr prevented HCl secretion. Prior to testing, the pouches were rinsed with 150 mM NaCl until the pH of the solution remained at 6.1 or greater. 50 ml of test solution was placed in the pouches, mixed, and a zero time sample taken. At 30 minutes the pouches were emptied and a final sample taken. Potential difference was monitored, and pH and HCO_3^-, K^+, Na^+, and Cl^- concentrations determined. ^{14}C-PEG provided a residual volume marker. Two periods using 150 mM NaCl were followed by one using 20% or 40% ethanol in 150 mM NaCl.

Net HCO_3^- Production, uEq/30 minutes (Means of 4 dogs)

Test Solution	Mean	Test Solution	Mean
NaCl	10.5	NaCl	9.5
NaCl	15.3	NaCl	3.8
20% Ethanol	210.3	40% Ethanol	248.8

Significant reduction in potential difference and increased fluxes of Cl^- and K^+ during the ethanol periods indicated mucosal damage. We conclude that exposure of the gastric mucosa to 20% or 40% ethanol in neutral solution greatly increases the production of HCO_3^- by the mucosa.

ENHANCED ENDOCYTOSIS OF EXOGENOUS ANTIGENS IN SKELETAL MUSCLE CONNECTIVE TISSUE CELLS FOLLOWING IN VITRO ANAPHYLAXIS. F. Alonso-deFlorida, A. Gutiérrez-López* and H. Merchant-Larios*. Instituto de Investigaciones Biomédicas, U.N.A.M. México

Guinea pigs were actively allergized by Al-adsorbed antigen (Ag=ferritin or horseradish peroxidase). Their left hemidiaphragmatic muscle was chronically denervated. Thereafter, two strips (Ss) of muscle symmetrically cut from each hemidiaphragm were suspended in O_2-CO_2 equilibrated warm (38°) saline medium. Repeated histamine doses and medium washings preceded and followed a period (45 min) of exposure to the antigen (800 µg P/ml). The Ss were then transferred to fixative for EM study. The micrographs showed primitive reticular cells (PRCs) exhibiting cytoplasmic processes appearing to be in close contact with one another, forming a meshwork in the perimysium of the muscle fibers. Ag was detected in many PRCs in both denervated and innervated specifically sensitized Ss. Conversely, small amounts of the exogenous protein appeared in only a few PRCs in the non-sensitized Ss which were run in parallel experiments. These results suggest that the Ag-Ab interaction drives some PRCs to produce endocytosis directed to the Ag itself. This does not imply any Ag-induced muscle contraction mechanism.

THE PROSTAGLANDINS, RENIN RELEASE AND RENAL FUNCTION: EVALUATION IN 3 HIGH RENIN CONSCIOUS DOG MODELS. J.M. DeForrest, J.O. Davis, R.H. Freeman, A.A. Seymour*, G.M. Williams* and B.P. Rowe*.

Indomethacin was given to dogs with either 1) 2 kidney hypertension (2 KHT), 2) 1 kidney hypertension (1 KHT), or 3) low output heart failure with ascites. All dogs had indwelling femoral artery and vein catheters, and were conscious during all studies. The dogs used in the 2 KHT and 1 KHT series were fed a diet containing 60 mEq Na+ daily, bilaterally renal denervated and placed on propranolol (25 mg/kg/day t.i.d.) for 7 days to insure complete blockade of B-receptor mediated renin release. In 2 KHT, indomethacin (5 mg/kg) caused an 80% fall in PRA while not causing any change in arterial pressure (AP). In 1 KHT dogs, indomethacin reduced PRA by 68% and AP fell from 137 to 117 mm Hg; no change was observed in renal function or salt and water excretion. The dogs used in the low output heart failure study were maintained on a diet containing 35 mEq Na daily. In these animals indomethacin lowered PRA by 43%, GFR by 64%, ERPF by 54%, and urine volume, sodium excretion and potassium excretion by 72%, 41% and 86%, respectively. AP was not changed by indomethacin. The present findings suggest an important role of the prostaglandins as regulators of renin release in all three "high renin" models, and an important role for the prostaglandins as homeostatic agents which maintain renal function in dogs with low output heart failure and ascites.

DIFFERENTIATION OF CHOLESTEROL-FEEDING AND HYPOTHYROIDISM ON PLASMA LIPIDS AND APOLIPOPROTEINS IN THE RAT. John G. Delamatre* and Paul S. Roheim. L.S.U. Medical Center, New Orleans, LA 70119.

Models of hypercholesterolemia generally studied are induced by feeding animals high fat, high cholesterol diets that include propylthiouracil (PTU). Using these models it is not possible to differentiate between the effect of cholesterol-feeding and thyroid supression. In order to discern these different influences, three experiments were performed: 1: rats were fed a high cholesterol-high fat diet (CF); 2: rats were fed 3 doses of PTU; 3: rats were fed high fat-high cholesterol-PTU diets (CFPTU). 1 week and 4 week samples were taken. In exp. 1, CF rats had an increased chol. conc. of 50-80%. Apo B conc. were doubled. This increase resulted from an accumulation of apo B in the d<1.006 g/ml and 1.006-1.03 g/ml densities. Apo E conc. were decreased 33% at 1 wk and 50% at 4 wks. In exp. 2 chol. conc. were increased 60-100% due to PTU treatment. Apo B increased 85-150% as a result of a large accumulation of apo B in the 1.03-1.063 g/ml density. Apo E increased from 40% to 100% in the PTU-treated rats. In exp. 3 chol. increased 240% and apo B increased by 375% in the CFPTU group. Apo E was unchanged in the CFPTU group after 1 wk. It is concluded that in order to interpret the hypercholesterolemia induced by cholesterol-PTU feeding, the separate effects of cholesterol and PTU need to be considered.

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ON THE DECOUPLING ACTION OF OUABAIN IN CARDIAC FIBERS. W.C. De Mello. Dept. of Pharmacol., Medical Sciences Campus, G.P.O. Box 5067, San Juan, P. R. 00936.

When canine Purkinje fibers were exposed to ouabain (2×10^{-6} M) the intracellular longitudinal resistance (r_i) increased and cell decoupling occurred in about 60 min. Cell-to-cell diffusion of Lucifer Yellow (mol. wt. 443) studied with the cut-end method, was also suppressed by ouabain. The action of the glycoside was dependent on the increase in Ca uptake since Mn (4 mM) abolished the effect of the compound. The intracellular injection of EDTA restablished the electrical coupling. Since the intracellular injection of H^+ was found to cause electrical uncoupling in normal Purkinje fibers, the decoupling action of ouabain might be also related to a fall in pH_i. In fibers previously exposed to NH_4Cl (20 mM) for 60 min. to cause an intracellular alkalosis, ouabain had a neglegible effect on cell communication. These results indicate: 1) that an increase in free $(Ca)_i$ is essential for the decoupling action of ouabain; 2) that a fall in intracellular pH, probably elicited by a rise in free $(Ca)_i$ may be also involved in the action of the glycoside. Supported by a grant from NIH and from P.R. Heart Association.

RELAXATION OF THE ISOLATED CANINE FEMORAL ARTERY CAUSED BY ACETYLCHOLINE AND BY POTASSIUM IONS.

Jozef G. De Mey and Paul M. Vanhoutte. Department of Medicine, University of Antwerp, 2610 Wilrijk, Belgium.

Experiments were performed to compare the direct inhibitory effect of acetylcholine and potassium on vascular smooth muscle cells. Rings of isolated canine femoral arteries were mounted for isometric tension recording in organ chambers filled with Krebs-Ringer solution. During contractile responses to norepinephrine, acetylcholine caused dose-dependent relaxations which were inhibited by atropine. Preparations incubated in low-K^+ solution and made to contract with norepinephrine responded to an increase in K^+-concentration with transient relaxations. Ouabain, removal of sodium and cooling (to 22°C) inhibited the relaxations caused by acetylcholine and K^+. Incubation in K^+-free solution depressed the relaxant effect of acetylcholine and augmented that of K^+. Anoxia abolished the relaxatory effect of acetylcholine, and inhibited that of K^+. Iproveratril reduced the K^+-relaxation but not that caused by acetylcholine. The relaxant effect of acetylcholine, but not that of K^+, was less when higher concentrations of norepinephrine were used to induce contraction of greater amplitude. These experiments suggest that Na^+, K^+-ATPase is involved in an indirect way in the inhibitory effect of acetylcholine on vascular smooth muscle cells.

ACTH IS THE PRINCIPLE REGULATOR OF CORTISOL SECRETION IN RESPONSE TO HEMORRHAGE

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Earlier experiments in dogs with sporadic sampling of plasma ACTH(A) and cortisol secretion rate($\dot{F}$) following modest hemorrhage suggested that the small rise observed in A might not be sufficient to account for the large rise in F. We explored this further in 7 awake dogs with chronic adrenal vein cannulas, hemorrhaged at 10ml/kg/3min. A was measured by RIA in continuous samples. A rose abruptly at 4 min, peaked(Δ35±12pg/ml) at 6min, and remained elevated until 26min. The increase in $\dot{F}$, measured by RIA($\Delta\dot{F}$-H,table) was similar to that observed previously. To test the ability of A to account for $\Delta\dot{F}$-H, we infused ACTH in 5 experiments at rates calculated to produce a step rise in A of 30pg/ml. The resulting increase in $\dot{F}$($\Delta\dot{F}$-I,table) was measured as before. No significant difference between the two groups was seen(ANOVA). The results indicate that the rise in A following hemorrhage can entirely account for the increase in $\dot{F}$.

time(min)	0	6	9	12	21	24
$\Delta\dot{F}$-H ug/min	0.5	2.6	4.4	5.1	2.9	2.9
M±SE	±0.2	±1.6	±2.1	±2.3	±2.0	±1.6
$\Delta\dot{F}$-I ug/min	0.0	5.8	7.7	6.4	2.6	2.7
M±SE	±0.2	±1.2	±0.9	±1.7	±0.4	±0.8

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THE EFFECT OF PLACENTAL EXTRACT ON LH AND FSH RELEASE BY THE RAT ANTERIOR PITUITARY GLAND IN VITRO.

Louis DePalatis* and Robert P. Fiorindo. Dept. of Physiology, The Ohio State Univ., Columbus, OH 43210.

We have previously reported that the 19 day rat placenta contains Luteinizing Hormone-Releasing Hormone (LHRH) - like material as demonstrated by immunohistochemical staining (Physiologist 21:7, 1978). The following experiments were performed to determine whether or not the identified substance is physiologically active. Anterior pituitary (AP) glands from adult male rats were excised and incubated in: a) medium 199 alone (controls), b) medium + LHRH, or c) medium + placental extract (PE). After a 4 hour incubation period, Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) released into the medium were measured by radioimmunoassay and expressed as µg/10mg AP wet weight. The concentrations of LH and FSH released into the medium by control AP's were 14.0 µg ± 3.0 µg and 7.8 µg ± 1.0 µg, respectively. AP's incubated with LHRH and PE released significantly greater amounts of LH (28.4 µg ± 6.5 µg and 41.7 µg ± 10.3 µg, respectively; P<.01) as well as FSH (14.6 µg ± 2.2 µg and 18.1 µg ± 2.0 µg, respectively; P<.001) into the incubation medium. These data suggest that the rat placental LHRH-immunoreactive substance is physiologically active. (Supported in part by OSU-GRS grant no. 7426).

AFLATOXIN B1 ACUTE EFFECTS UPON THREE HEPATIC UREA CYCLE ENZYMES AS A MODEL FOR REYE'S SYNDROME.

Robert Desai* Peter Thurlow* Paul Newberne* and Henry Brown. M.I.T. and Harvard Medical School, Cambridge, MA 02138 and SUNY Medical School, Stony Brook, N.Y., 11790.

Etiology of Reye's Syndrome characterized by coma and fulminant hepatic failure with urea cycle enzyme changes is unknown, but aflatoxin B1 has been suggested as a contributing factor. A laboratory model with Fischer rats (120-150 gm) receiving an acute toxic dose of aflatoxin B1, 3 mg/kg was used to study this hypothesis. Activities of urea cycle enzymes carbamyl phosphate synthetase (CPS) ornithine transcarbamylase (OTC) and arginase (ARG) may be determined through colorimetric analysis of intermediates in the urea cycle, urea and citrulline. A new semi-automatic method was used for these measurements with liver samples from animals 24 hours after aflatoxin administration. CPS and OTC values were 61 and 67% respectively of control values. ARG activity was within the normal range. Urea cycle enzyme activity from biopsy specimens from children with Reye's Syndrome has been reported to be similar to this pattern. (Supported in part by USPHS NIH Grant POIES 00597).

VASCULAR REACTIVITY: THE ALGEBRAIC SUM OF VASCULAR CONTRACTILITY AND HYPERPOLARIZING ELECTROGENESIS.

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Vascular reactivity observed while studying isolated vascular smooth muscle under physiological conditions may not reflect the maximum potential of this muscle to contract especially if certain of the many concurrent cellular processes operating under these conditions may exert a dominating negative influence on contraction. The vascular reactivity which reflects the maximum potential to contract in response to a given stimulus (i.e., to a given molar concentration of a particular agonist) may be defined as "vascular contractility". Using small artery samples taken from rabbit skeletal muscle, it is shown that vascular reactivity obtained while briefly inactivating Na-K ATPase with G-strophanthin, 10^{-6}M, reflects a property of vascular smooth muscle which satisfies this definition of vascular contractility. Accordingly, vascular reactivity is defined as the algebraic sum of two distinct properties of vascular smooth muscle; contractility (a relatively constant property) representing the potential to contract, and hyperpolarizing electrogenesis (a relatively variable property) representing a negative electrical feedback that modulates contractile responsiveness by opposing contractility. It is suggested that changes in vascular reactivity can be produced by changes in either vascular contractility or hyperpolarizing electrogenesis. (Supported by THE EDUCATIONAL FOUNDATION OF AMERICA.)

EFFECT OF SUBMAXIMAL NEUROMUSCULAR BLOCKADE (SMNB) ON RESPIRATORY MECHANICS IN CONSCIOUS MAN.

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To explore the influence of respiratory muscle weakness on respiratory mechanics, we measured lung volume and static pressure-volume(PV) curves of the lung and relaxed chest wall in 6 sitting, awake, trained volunteers, before and after small doses of pancuronium had reduced the static recoil pressures of the lung(Pel) at TLC to 60 ± 10% of control. VC decreased 10%, but RV was not increased. Although deflation lung PV curves showed a slight increase in Pel, there was no change in PV relationship during inflation, indicating that the changes observed during deflation were only due to the hysteresis characteristics of the lung. In all subjects SMNB decreased both FRC and Pel at FRC, and transposed the deflation chest wall PV curve to lower volumes at a given trans chest wall pressure. We conclude that SMNA 1) does not affect the elastic properties of the lung, and 2) decreases the tendency of the chest wall to recoil outward. This indicates that a tonic respiratory muscle activity influences the elastic behaviour of the relaxed chest wall and that suppression of this activity results in a fall in FRC.

AGE RELATED LOSS OF NEURONS IN THE MACULAR PROJECTION AREA OF THE HUMAN VISUAL CORTEX. K. Devaney and H.A. Johnson. Department of Pathology, Tulane University School of Medicine, New Orleans, LA 70112.

The decline of visual acuity with increasing age is a result of loss of function both in the eye and in the central sensory system. We have investigated the latter by measuring the change in concentration, or packing density, of neurons in the human visual cortex with increasing age. Formalin fixed cortex from the macular projection area was weighed and transformed into a cellular suspension by ultrasound. Stained cells were then counted with a hemacytometer and classified as neurons or glia. The rate of cell destruction by ultrasound was not significant in either young or old brains. In 23 brains of individuals with no known neurological disease, the number of neurons per gram of visual cortex decreased from over 4×10^7 in the third decade to about 2×10^7 in the eighth decade of life. The concentrations of glial cells increased slightly over this interval. This decrease in neuron packing density together with the decrease in overall brain mass indicates an absolute loss of visual cortical neurons in the range of 50% or more in old age.

CHARACTERIZATION OF THE HISTAMINE RESPONSE OF ISOLATED RAT PARIETAL CELLS USING ^{14}C-AMINOPYRINE. E. J. Dial, W.J. Thompson and G.C. Rosenfeld* (SPON: G.A. Castro). Univ. Tex. Med. Sch., Houston, Tx. 77030

Gastric acid secretion in isolated rat parietal cells was indirectly estimated by measuring the uptake of ^{14}C-aminopyrine (AP) in response to various stimuli. Isolated cells were incubated with drugs for 60 min. at 37° under 95% O_2:5% CO_2. Histamine(H) stimulated the cells with an ED50 of 38µM. Other H agonists which stimulated AP uptake (ED50 between 40 and 80µM) were N-methylhistamine, N,N-dimethylhistamine, dimaprit and 4-methylhistamine. Little or no stimulation was seen with 2-methylhistamine, 3-methylhistamine, 2-pyridylethylamine, 3-(2-aminoethyl)-1,2,4-triazole, and 2-thiazolylamine. The response to H (10^{-3}M) was completely blocked by 10^{-4}M cimetidine or metiamide, concentrations which did not inhibit AP uptake in response to carbachol (C) or dibutyryl cyclic AMP (DbcAMP). Mepyramine and promethazine blocked H stimulated AP accumulation at 10^{-5} and 10^{-6}M, respectively. However they were also found to block AP accumulation in response to C and DbcAMP. Atropine, scopolamine, hexamethonium and phentolamine were inactive at 10^{-4}M on H stimulated accumulation of AP. These results are consistent with the interaction of H with H_2-receptors of isolated rat parietal cells and the subsequent stimulation of acid secretion. (Supported in part by USPHS. NIH Grant AM 20431)

STATIC VS. DYNAMIC INDICATORS OF SMOOTH MUSCLE ACTIVATION. Patrick F. Dillon and R. A. Murphy. Dept. of Physiology, Univ. of Virginia Sch. of Med., Charlottesville, VA 22908

Developed force is often used as an index of muscle activation. Strips of swine carotid media stimulated with K^+, norepinephrine (NE), or histamine (H) develop force over a period of two minutes to a plateau which is maintained. At various times following stimulation, the tissues were subjected to a quick-release and allowed to shorten isotonically. The load was approximately 13% of the isometric plateau. Shortening velocities increased to a maximum within the first minute of stimulation, and then declined exponentially to values at 8 min of 49 ± 12% SD (K^+), 46 ± 8% (NE), and 67 ± 7% (H) of peak velocities. Complete force-velocity curves obtained with the Hill Equation after 1 or 10 min of K^+ stimulation showed significant differences for the maximal shortening velocities, V_o, (0.078 ± 0.012 vs. 0.045 ± 0.011), and the velocity parameter, b, (0.0073 ± 0.0019 vs. 0.0037 ± 0.0004) in muscle lengths/sec. The value of a/P_o was not significantly different (0.094 ± 0.014 vs. 0.082 ± 0.023) at 1 min and 10 min respectively. In summary, when developed force indicates no change in the number of functioning cross-bridges, there is a temporal decline in parameters (V_o and b) reflecting cross-bridge cycling rates. Developed force is an incomplete index of activation in vascular smooth muscle. (Supported by NIH grants 1 PO1 HL19242 and HL07284)

PANCREATIC POLYPEPTIDE RELEASE IN RESPONSE TO INTESTINAL FAT. P Devitt,* A Ayalon,* J Lonovics,* K Hejtmancik,* PL Rayford, JC Thompson. Department of Surgery, The University of Texas Medical Branch, Galveston, Texas 77550.

The mechanism of pancreatic polypeptide (PP) release after a meal is unclear. The specific roles for neural and humoral mechanisms have not been delineated. Direct release of PP is unlikely: 1) there are few PP cells in the gut and 2) iv amino acids do not release PP. We have shown release of PP by exogenous CCK in physiologic doses. In this study we have evaluated the role of humoral mechanisms in PP release. Methods: Six dogs with gastric and duodenal fistulas were given an oleate infusion (10 mmol/hr) through a duodenal cannula. Blood samples for radioimmunoassay of CCK and PP were taken every 15 minutes. Results:

	Basal	15 min	30	45	60	75
PP	291±60	717±254	789±123*	636±108*	560±135	440±100
CCK	27±12	50±15	70±27	51±9*	56±9*	34±7

* = significant elevation above basal (p <0.05).

Conclusions: Oleate caused a simultaneous release of both CCK and PP. Since exogenous CCK, when given in physiologic doses, releases PP, there is most likely a humoral factor in the release of PP after a meal and CCK appears to fit that role.

CHANGES IN BLOOD VOLUME AND RESPONSE TO VASO-ACTIVE DRUGS IN HORIZONTALLY CASTED PRIMATES. D.T.Dickey*, K.K.Teoh*, H. Sandler, H.L. Stone, Dept. of Physiology, Univ.of Oklahoma, Health Science Center, Oklahoma City, Oklahoma 73190.

Six rhesus monkeys were horizontally casted for 14 days. Aortic diastolic pressure (DP), pulse pressure (PP), and heart rate (HR) responses to norepinephrine (NE), phenylephrine (PE) and nitroprusside (NP) were measured. The blood volume was determined using Cr^{51} and I^{125}. Resting HR increased significantly (P<0.05) after casting from 147±24 to 161±16 (mean ±S.D.), but DP (73±21 to 78±9) and PP (36±14 to 38±11) were unchanged. The change in DP (39±5 to 22±12), PP (30±12 to 10±11) and HR (-21±22 to -6±11) response to NE were decreased, as was the change in DP (32±10 to 22±9) and HR (-28±25 to -8±9) response to PE; PP difference (11±9 to 5±2) response to PE was unchanged. The response to NP remained unaltered. The average blood volume was reduced by 14.2±7.3% after 14 days of horizontal casting. These data indicate that the constrictor response to vasopressor drugs of the peripheral system was impaired, whereas the dilator response remained unchanged. The reflex heart rate changes were similarly affected; i.e. attenuation of the bradycardia to an increase in arterial pressure and no change with decreasing arterial pressure. The reduction in blood volume is similar to that observed in human subjects during space flight and in a simulated zero-G environment. The results indicate an alteration in peripheral and central neural regulations of blood pressure. (Supported by Grant #NSG 2282.)

INSTRUCTIONAL PROGRAM IN LIVER PHYSIOLOGY, N.R. Di Luzio, Dept. Physiology, Tulane University School of Medicine, New Orleans, LA 70112.

In spite of the fact that the liver is the largest organ of the body and marked advances have been made in appreciating the multifaceted and extensive role of the liver in health and disease, the physiology of the liver is grossly neglected in medical physiology programs. Only four Physiology Departments of U.S. medical schools provide a fundamental consideration of hepatic physiology. Likewise, a survey of textbooks of medical physiology denote an equivalent absence of coherent coverage of hepatic physiology. It is the goal of the Tulane program to provide medical and graduate students a basic foundation in hepatic physiology in order that they can appreciate the highly diverse contributions of the liver. An innovative method of teaching hepatic physiology in medical physiology has been developed. The "hepatic block" format involves a series of 11 lectures, a 4 hour presentation and discussion of selected clinical cases and 2 clinical correlations in liver and Reticuloendothelial physiology. On occasinn, laboratory endeavors involving "Liver Unknowns" are utilized. These composite endeavors transmit relevant information and concepts regarding the unique role the liver plays in regulating the internal environment both from the concept of homeostasis as well as regulating the purity and sterility of the internal environment through the contribution of hepatic Kupffer cells, the major functional component of the reticuloendothelial system.

MULTIPLE FORMS OF MYOSIN LIGHT CHAIN KINASE IN MAMMALIAN MUSCLE. J. Di Salvo, J.T. Stull* and D. Blumenthal*. Univ. of Cin., Col. of Med., Cin. OH 45267 & UTHSCD, Dal. TX

Myosin light chain kinase (MLCK) may influence contractile phenomena through phosphorylation of the 15,000-20,000 dalton myoson light chains. We suspected that multiple forms of MLCKS might exist in mammalian muscle because of known functional differences between different types of muscle. To test this hypothesis MLCK was detected in extracts of bovine skeletal, ventricular, and aortic vascular smooth muscle by a new technique involving isoelectric focusing on polyacrylamide gels and autoradiography. Multiple bands showing incorporation of ^{32}p from ATP γ ^{32}P (MLCK activity) were always found in either skeletal or aortic smooth muscle. However, the 3-4 bands found in skeletal muscle focused at pH values (pH 5.2, 6.4, 6.6 & 7.0) distinctly different from the 2-4 bands found in aorta (pH 5.5, 5.8, 6.4 & 6.7). Furthermore, the greatest activity of MLCK in skeletal muscle was usually in the most acidic band, whereas the greatest activity in aorta was usually at pH 6.4-6.7. In contrast, only a single band of MLCK activity was found in cardiac muscle (pH 5.2), but such activity was relatively low in magnitude and seen in only 3 of 7 hearts studied. In all muscles studied MLCK activity was dependent on Ca^{++} and calmodulin. These findings suggest that multiple forms of MLCK probably exist in a single type of mammalian muscle, and that different forms of the enzyme may exist in different types of muscles of the same species. (Supp. NIH/HL 20196)

BLOCKADE OF HISTAMINE-INDUCED INCREASES IN MICROVASCULAR PERMEABILITY BY A LOW DOSE OF AN H_1-RECEPTOR ANTAGONIST. David E. Dobbins, Carol A. Creed* and Joe M. Dabney. Dept. Physiol., Uniformed Services University, Bethesda, Md. 20014

The local intraarterial infusion of high doses of an H_1-receptor antagonist blocks the ability of simultaneously infused histamine to increase microvascular permeability. We now report the effects of infusion of 10µg base/min tripelennamine on the ability of simultaneously infused histamine (1.4µg base/min) to alter microvascular permeability. Intra-arterial infusion of histamine in the canine forelimb significantly decreases forelimb perfusion pressure and skin small artery pressure while skin small vein pressure is increased. There are no significant changes in either systemic pressure or heart rate. Lymph flow and lymph total protein transport are significantly increased from minute 10 of the infusion period onward. Lymph total protein concentration is significantly increased from minute 30 of the infusion period onward. Infusion of histamine during infusion of tripelennamine results in changes in vascular pressures which are directionally similar to those seen during the infusion of histamine alone. In contrast, infusion of histamine during tripelennamine infusion failed to significantly alter lymph parameters. These data indicate that infusion of a markedly lower dose of an H_1-receptor antagonist than has been previously reported is capable of effectively blocking histamine-mediated increases in microvascular permeability.

THE PYRAMIDAL TRACT OF THE WOODCHUCK, RACCOON AND SLOW LORIS. G.S. Doetsch*, R.H. Ray, A.M. Kelahan* and A.L. Towe. Med. Coll. Ga., Augusta, GA 30912 & Univ. Wash., Seattle, WA 98195.

Several organizational features of the pyramidal tract (PT) were studied in representatives of 3 mammalian lines. The cerebral origins of the PT were mapped by recording the early antidromic response (a wave) to electrical stimulation of the ipsilateral medullary pyramid. In all species, widespread regions contribute axons to the PT, including a major focus in sensorimotor cortex. With unilateral lesions of this cerebral tissue, the Nauta-Gygax method was used to trace the spinal course of the PT. The corticospinal tract (CST) of the woodchuck occupies the ventral part of the dorsal funiculus and extends to sacral levels; dense axonal degeneration was found in the dorsal horn, less in the intermediate grey and little in the ventral horn. The CST of the raccoon and slow loris is located in the lateral funiculus, and more axonal debris is present in the ventral horn. Using light microscopy, the mean cross-sectional areas A (mm^2), fiber numbers N and fiber diameters D (µm) of the pyramids were estimated; their relationships to mean body weights P(kg) and brain weights E(g) are:

	A	N	D	P	E	N/A	N/P	N/E
Woodchuck	1.1	98K	1.4	3.4	12.8	89K	28.8K	7.7K
Raccoon	3.1	273K	2.0	6.1	46.1	88K	44.8K	5.9K
Slow Loris	0.9	197K	1.2	1.4	10.8	219K	140.7K	18.2K

These results support the view (Towe, Brain Behav. Evol. 7:1, 1973) that the size of the mammalian PT is primarily related to body and brain size, with $N=kP^{0.4}$, $N=kE^{0.5}$ and $N/E=kP^{-0.4}$

CO_2 vs H^+ RESPONSE OF THE CAROTID BODY. D. F. Donnelly*, E. J. Smith* and R. E. Dutton. Department of Physiology, Albany Medical College, Albany, NY 12208

Biscoe (J. Physiol. 208:121, 1971) indicates that the carotid body responds to isohydric hypercapnia while other investigators claim that the CO_2 response is solely mediated by its concomitant acidosis. To help resolve this controversy, we compared CO_2 and H ion responses in 5 pentobarbital anesthetised, paralyzed cats. After placement on a respirator, single carotid body nerve fibers were dissected free and were placed on unipolar platinum wire electrodes. Then the fiber responses to room air and the last two min of 6 min inhalations of 3%, 6% and 9% inspired CO_2 in air were recorded, and blood samples were drawn for gas tension measurements. Following return to room air activity, 1N NaH_2PO_4 (2ml/kg) was infused over a three minute period and the respirator frequency was adjusted to hold end tidal CO_2 constant. The room air activity was recorded, and blood samples were drawn before and at 5,10,20,30,40 and 50 min following the start of acid infusion. The results from all 5 cats showed a marked displacement to the right of the CO_2 response line at 5 min, but a return to the CO_2 response line from 10-30 min. These results suggest that CO_2 and H ion are transduced by the same mechanism; however, there is a slow equilibration time for H ion in the range of 10-30 minutes. (Supported by NIH Grants HL-12564 and HL-07194)

EFFECT OF ISOMETRIC DIAPHRAGMATIC CONTRACTION ON CARDIAC OUTPUT AND MUSCLE BLOOD FLOW. E. Donovan*, T. Trippenbach*, A. Grassino*, P.T. Macklem, and C. Roussos*. Meakins Christie Labs., McGill Univ. Clinic, Royal Victoria Hosp., Montreal, Quebec

We measured diaphragmatic, $\dot{Q}di$, and quadriceps, $\dot{Q}q$, blood flow and cardiac output, $\dot{Q}c$, as a function of transdiaphragmatic pressure, Pdi, during quasi-isometric diaphragmatic contraction in 10 supine anesthetized dogs, with the abdomen strapped. We produced sustained diaphragmatic contractions with Pdi from 2 to 100 cmH_2O by bilateral phrenic nerve stimulation. $\dot{Q}di$, $\dot{Q}q$ and $\dot{Q}c$ were measured using radionuclide labelled microspheres during quiet breathing and at various Pdi's. $\dot{Q}c$ decreased ($1.56 \pm .29$ to $1.12 \pm .16$ L/min, mean $\pm$ SE, $p < 0.025$), $\dot{Q}q$ fell proportionately (3.5 ± 6 to 1.4 ± 4 ml/100 g/min; $p < .01$) whereas $\dot{Q}di$ increased (9.5 ± 2.0 to 43.4 ± 4.5 ml/100 g/min; $p < .001$) during phrenic stimulation. Peak $\dot{Q}di$ was 767% of $\dot{Q}di$ during quiet breathing but mean $\dot{Q}di$ decreased at maximum Pdi from a peak of 56.3 ± 5.4 to 37.5 ± 7.6 ml/100 g/min; $p \leq 0.025$). We conclude that quasi-isometric diaphragmatic contraction leads to an increase in $\dot{Q}di$, in spite of a fall in $\dot{Q}c$ due to in part to a redistribution of $\dot{Q}c$ away from non-working skeletal muscles. Supported by the Medical Research Council of Canada.

EFFECT OF TEMPERATURE ON THERMOREGULATION IN DEHYDRATED CATS. P.A. Doris*, M.A. Baker and H.F. Blair*. Dept. Biol. and Div. Biomed. Sci., U.C. Riverside, Riverside, CA 92521.

We measured metabolic rate (MR), evaporative water loss (EWL), body (peritoneal cavity) temperature (T_b) and respiratory rate (RR) in nine cats (mean hydrated weight 3.83kg) living in daily temperature cycles (18:6hr) of 25C:35C, 25C:38C and 25C:40C. Measurements were made at the high ambient temperature (T_A) on animals hydrated ad lib and once daily after removal of drinking water. Dehydration was continued 92hr at 25C:35C and at 25C:38C and 70hr at 25C:40C. Mean hydrated EWL was 6.66 ± 0.43 W (n=19) at 40C, 4.26 ± 0.49W (n=9) at 38C and 3.05 ± 0.26W (n=16) at 35C. At 35C, EWL fell to 63% of hydrated levels after one day of dehydration and was sustained ca 53% for 3 more days. At 38C, EWL fell progressively over 4 days of dehydration, reaching 50% of hydrated EWL on the final day. At 40C, EWL did not drop until day 2 of dehydration, the maximum reduction at 40C being 80% of hydrated EWL. RR correlated highly (r=0.95) with EWL at all T_A's. Body temperature rose progressively during dehydration at all T_A's. At 40C, T_b rose from 39.3C in hydrated cats to 40.5C on day 3 of dehydration. At 38C, T_b rose from 39.1C to 39.7C on day 4. At 35C, T_b rose from 38.8C to 39.0C on day 4. MR was 7.37W at 40C, 5.84W at 38C and 7.92W at 35C. No trend in MR was apparent during dehydration. Plots of EWL against T_b showed a rightward shift as dehydration progressed at 40C and 38C, dehydrated animals evaporating less at a given T_b. (Supported by NSF Grant BNS76-81839 and PHS BRDG Grant RR09070).

INTERACTION BETWEEN OSCILLATORY RESISTANCE AND BIAS FLOW IN TUBES AND IN A HUMAN AIRWAY CAST. H.L. Dorkin*, A.C. Jackson, S.V. Dawson and D.J. Strieder. Children's Hospital Med. Ctr, Harvard Med. School and Harvard School of Public Health, Boston, MA 02115.

Because the frequency response of pneumotachometers is accurate only at low frequencies, a new method of measuring oscillatory flow generated by a loudspeaker was developed (Jackson and Vinegar, JAP in press). The speaker is mounted between a test chamber delivering the usual pressure and flow signals, and an airtight reference chamber undergoing pressure changes, from which oscillatory flow is calculated (speaker plethysmograph). The device was tested by measuring oscillatory resistance (real part of impedance), R_{OS}, at 2-64 Hz in straight tubes. Plotted as a universal function of $\alpha = r\sqrt{\omega/\nu}$ (r: tube radius, $\omega=2\pi$.frequency, ν: kinematic viscosity), R_{OS} without bias flow closely matched the theory (Crandall: Theory of Vibrating Systems, 1926). With steady state bias flow superimposed, R_{OS} increased with increasing bias flow particularly at low frequencies. In a human central airway cast R_{OS} increased with increasing frequency for all values of bias flow. We conclude that the airway cast may follow Rohrer's equation at very low frequencies but at the frequencies tested its oscillatory resistance is frequency- as well as bias flow-dependent. (Supported by a P.B. Francis Foundation Fellowship (HLD) and by NIH grants HL #22178, 14580 and 10346).

THE INTERRELATIONSHIP OF TEMPERATURE AND HYDROSTATIC PRESSURE ON PURKINJE ACTION POTENTIALS. T. J. Doubt and P. M. Hogan. Dept. Physiology, State Univ. of N.Y. at Buffalo, Buffalo, NY 14214

The combined effect of hydrostatic pressure and temperature on cardiac electrogenesis was studied in canine Purkinje fibers. Action potential duration (APD) increased both as a function of lower temperature and higher pressure.

% Change APD from 1 ATA/37°C

	37°C	32°C	27°C
1 ATA	--	44 ± 2	83 ± 8
150 ATA	16 ± 6	63 ± 7	92 ± 7

At 27°C pressure had no significant effect on APD. Resting membrane potential decreased 4.1 mV/10° decrease in temperature at 1 ATA, and 9.1 mV/10°C at 150 ATA. Conduction time increased progressively from 37°C to 27°C at 1 ATA. For each increase in CT there was a corresponding decrease in maximum upstroke velocity ($\dot{V}_{max}$), indicating that the slowing of conduction was, in part, due to a decrease in $\dot{V}_{max}$. The results indicate that decreases in temperature and increases in hydrostatic pressure have a combined effect to prolong the action potential and slow conduction. The resultant deficits are potentially arrhythmogenic in humans exposed to cold hyperbaric environments. (Supported by Grants: USPHS HL-16135 and POI HL-14414.)

PLASMA RENIN RESPONSE TO ACUTE HYPOXIA IN THE EWE AND FETAL LAMB. W.H. Drummond*, C.A. Lindheimer*, (SPON: D.V. Eitzman). U. of FL, Gainesville, FL 32610.

Eleven pregnant ewes and fetuses were catheterized between 106 and 121 days gestation and studied at least 4 days after surgery. Paired fetal and maternal blood gases and plasma renin samples were drawn onto ice at time 0, 60 min., 120 min., and 180 min. Ventilatory hypoxia was induced in the experimental group (n=6) by administering 0.5-0.6 Atm. O_2 to the ewe from time 0 to 120 minutes. The control group (n=5) was studied with identical sampling technique and ventilatory apparatus, using room air. Plasma renin activity was assayed using a commercial radioimmunoassay kit. PaO_2 decreased in both fetuses (17.8 vs. 9.1 torr $p<.001$) and ewes (83 vs. 34 torr $p<.001$). Mean arterial blood pressure increased by 120 minutes in the fetuses (39 vs. 45 torr $p<.05$) but not in the ewes. Heart rate increased in both fetuses (170 vs. 202 beats/min. $p<.02$), and ewes (103 vs. 123 beats/ min. $p<.05$). pH increased in the ewes by 60 minutes (7.52 vs. 7.63 $p<.05$), but decreased in the fetuses by 120 minutes (7.41 vs 7.31 $p<.05$). Fetal plasma renin activity increased ($p<.05$*):

	T=0	T=60	T=120	T=180
Control (ng/ml/hr)	1.14±.86	1.22±6.7	1.43±.72	.60±.2
Hypoxia (ng/ml/hr)	.48±.18	6.6±3.0*	11.6±6.3*	3.18±2.7

Ewe plasma renin activity did not change during hypoxia. Thus, we conclude that fetal plasma renin increases during acute hypoxemia, but that a similar increase does not occur in the adult pregnant ewe.

THE EFFECT OF RADIOTHYROIDECTOMY ON APOLIPOPROTEIN PROFILE OF RATS. Ladislav Dory* and Paul S. Roheim. L.S.U. Medical Center, New Orleans, LA 70119.

The effect of hypothyroidism on plasma apolipoprotein concentration and distribution was studied. Hypothyroidism was induced in male Sprague-Dawley rats by an i.p. injection of 1 mC ^{131}I/rat. This treatment resulted in a 90% decrease in plasma T_4 values (from 25 to 2.5 g/ml) in 23 days. Decrease in T_4 values was accompanied by a 50% increase in plasma cholesterol (from 48 to 73 mg%) and little change in plasma triglyceride concentrations. Total protein content of the isolated individual lipoprotein fractions isolated by ultracentrifugation indicated a 2-4 fold increase in the LDL fraction and a moderate rise in HDL fraction of the hypothyroid rats. The various apolipoprotein plasma concentrations were determined by electroimmunoassay and the findings were consistent with lipoprotein changes described above. Total plasma apo B increased by 120%, all of which was recovered in the IDL and LDL density range. Similarly plasma apo E increased by 50% and most of the increment was recovered in the LDL fraction. These results indicate that the thyroid hormones play an important role in apolipoprotein metabolism. The underlying mechanism for these changes is presently being investigated.
This work is supported by NIH Grant HL 20954.

HEMODYNAMIC RESPONSES TO PROGRESSIVE AFTERLOAD INCREASES IN EXERCISE CONDITIONED AND AORTIC CONSTRICTED RATS. Russell T. Dowell, Eileen M. Hasser*, and Judith L. Haithcoat*. Dept. of Physiology & Biophysics, Univ. of Oklahoma Health Sciences Center, Oklahoma City, OK 73190.

Hemodynamic responses to progressive afterload increases were determined in rats conditioned by a moderate treadmill exercise program (EC) and in rats subjected to 5 weeks of abdominal aortic constriction (AC). Rats of comparable age served as controls (C). Initial in situ hemodynamic values for C rats (n=19) were as follows: left ventricular pressure (LVP)=124±4 mm Hg, mean arterial pressure = 99±4 mm Hg, max. dP/dt = 6520±290 mm Hg/sec, and cardiac index (CI) = 145±8 ml/min/kg. Although minor variations were noted, initial hemodynamic values for EC rats (n=10) were within the normal range and no LV hypertrophy was present. AC rats (n=7) exhibited a 48% increase in LV weight as well as significant differences in LVP (173±9 mm Hg) and CI (117±10 ml/min/kg. Sequentially increasing doses of methoxamine (0.04-3.62 ml/kg/min.) were infused iv to elevate myocardial afterload. When compared to C rats, EC animals were better able to maintain CI at comparable degrees of afterload increase. This CI response was mediated by enhanced employment of both the Frank-Starling mechanism and positive inotropic effects. In contrast, AC rats demonstrated profound reductions in hemodynamic compensation to increased afterload challenge. (Supported by NIH Grants HL 23025 and HL 23206).

INCREASED CARDIAC OUTPUT DOES NOT REDISTRIBUTE TOWARD EDEMATOUS LUNG LOBES. Krika Duke*, J. Ali*, C.J. Fisher*, and L.D.H. Wood*. (Spon: N.R. Anthonisen). University of Manitoba, Winnipeg, Canada.

Pulmonary shunt (Qs/Qt) varies directly with cardiac output (CO) in canine oleic acid (OA) pulmonary edema. To confirm that a greater proportion of increased CO goes to edematous regions and to relate the change in CO distribution to Qs/Qt, we studied 5 supine anaesthetized dogs 2 hours after OA was injected into one lower lobe (LL) (1), and again 10 minutes after a systemic arteriovenous shunt was opened (2) to increase mean (±SD) CO from 1.3 ± 0.2 to 2.0 ± 0.5 lpm ($P<.05$). Lobar shunts (QsL/Qt) were calculated from O_2 contents sampled from LL venous catheters, and lobar blood flow (Q_L/Qt) was determined by radionuclide microspheres. Injured LL (LLi) weighed twice as much as non-injured LL (LLni). The mean (±SD) results were:

	LLi QsL/Qt%	LLni	Qs/Qt%	LLi Q_L/Qt%	LLni
1	48.3±26.5	6.5±4.9	14.2±4.5	17.0±1.9	28.8±2.8
2	68.1±32.0	6.0±1.3	19.7±5.3	16.6±1.6	27.6±5.2

Increased cardiac output did not distribute preferentially to the edematous lobe, but Qs/Qt increased with cardiac output because lobar shunt in LLi increased considerably. We conclude that increased pulmonary blood flow reduces vascular resistance (R) to edematous regions and increases R in the adjacent lung units of the same lobe. (Supported by MRC of Canada).

FREEZE TOLERANCE IN LARVAE OF THE PYROCHROID BEETLE, DENDROIDES CANADENSIS. John G. Duman. Biology Department, University of Notre Dame, Notre Dame, Indiana 46556.

Overwintering larvae of the beetle, Dendroides canadensis, collected in northern Indiana are able to survive freezing at temperatures down to -30°C. During a mid-winter thaw or upon warm acclimation the larvae become freeze susceptible. However, cold acclimation or acclimatization renders them freeze tolerant again. Concentrations of polyols (glycerol and sorbitol), ice nucleating agents and thermal hysteresis producing proteins increase in the autumn, peak in mid-winter and decline in spring. These and other, as yet unknown, factors are responsible for the capacity of Dendroides to survive subzero temperatures. Because of the proliferation of ice nucleating agents in winter the larvae supercool only slightly (generally a few tenths of a degree) below the hemolymph freezing point. Therefore, the freezing point depression provided by the thermal hysteresis proteins and polyols becomes essential to survival of the larvae during periods, such as winter thaws, when the larvae are freeze susceptible. (Supported by USNSF Grant PCM77-03475).

EFFECTS OF ACUTE HEMORRHAGIC PANCREATITIS ON PULMONARY CAPILLARY PERMEABILITY. Frazier Eales* and Edward W. Humphrey. Univ. of Minn, Mpls., Minn. 55455

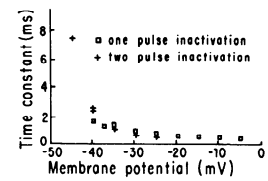
To investigate the relationship of acute hemorrhagic pancreatitis (AHP) to the adult respiratory distress syndrome, AHP was produced in 8 sheep by injection of autologous bile and trypsin directly into the pancreatic duct via an implanted catheter after two hours of baseline (BL) measurements. Severe AHP was produced in all animals. Pulmonary lymph from the efferent duct of the caudal mediastinal lymph node was collected in awake sheep according to the method of Staub. Cardiac output (CO), aortic (A) and pulmonary artery (PA) pressures (P), arterial blood gases, lymph flow (J_v) and albumin concentrations in lymph (C_L) and plasma (C_P) were measured. Determinations of serum amylase (AMY), lipase (LIP) and phospholipase (PhLIP) were obtained. Fibrin split products (FSP) and fibrinogen (FGN) were also measured. AMY and LIP increased seven to ten-fold at one and 24 hours. PhLIP, normally not detectable in serum, averaged 44 IU/L at one and 24 hours. J_v increased 100% at one hour and 200% at 24 hours. There was no change in C_L/C_P for ALB. CO, AP, PAP, FGN andFSP were unchanged. From the significant increase in J_v with no change in hemodynamics or in the C_L/C_P for ALB, we conclude that AHP is associated with increased pulmonary capillary permeability. This may be the result of increased circulating PhLIP. (USPHS grant HL 18762)

MECHANISMS OF BAROREFLEX CONTROL OF HEART RATE IN RENAL HYPERTENSION. C.L. Eastham*, M.D. Thames, & M.L. Marcus. Dept of Med & CV Center, U of I and VA Hosp, Iowa City, IA 52242.

Recent evidence suggests that in renal hypertension(RH) baroreceptors with nonmedullated afferents(NB)are reset less than are those with medullated afferents(MB). NB mediate changes in heart rate(HR)mainly via parasympathetic(P)mechanisms while MB mediate HR changes via both sympathetic(S)and P mechanisms. We determined if the differential resetting of NB and MB alters the role of S and P mechanisms in the baroreflex control of HR in RH. Changes in HR in response to nitroglycerin(NTG)induced decreases in arterial pressure(AP)and phenylephrine(PE)induced increases in AP were determined in 9 normotensive(mean AP 92±4(SE)mmHg)and 9 RH conscious dogs before and after beta adrenergic receptor blockade with propranolol and before and after P blockade with atropine. The RH dogs had raised mean AP(139±10mmHg)for 6-10 weeks. Control HR for the normotensive and HT groups were not different(91± 4 and 93±7 beats/min, respectively). Atropine reduced but did not abolish the tachycardia in response to NTG and the bradycardia in response to PE and propranolol reduced but did not abolish the HR responses to PE and NTG. There were no significant differences between the responses of normotensive dogs and those with RH. These data show that baroreceptor induced changes in HR are mediated by reciprocal alterations in P and S influences. The reported differential resetting of MB and NB does not alter the autonomic mechanisms of baroreflex control of HR in conscious dogs with RH.

SODIUM CURRENTS IN CULTURED EMBRYONIC HEART CELLS L. Ebihara,* N. Shigeto,* M. Lieberman and E.A. Johnson. Dept. Physiology, Duke Univ. Med. Ctr., Durham, N.C. 27710

The two microelectrode voltage clamp technique was used to study the rapid inward current in spherical clusters of 11-day embryonic chick heart cells. The preparations, ranging in size between 60-90μm diameter were maintained at 37°C in a HCO_3/CO_2 buffered tissue culture medium. Using these preparations, it was possible to achieve adequate voltage control of the membrane in less than 150 μs. The rapid inward current exhibited a voltage- and time dependence similar to that observed in other excitable tissues. The measured reversal potential was close to that predicted by the Nernst equation for sodium ions. A single and double voltage-step protocol was used to study the time constant of inactivation of the current; no significant difference between the two time constants was found. Furthermore, the time constant of inactivation and reactivation at the same potential were similar. This, together with the magnitude and voltage dependence of the time constants show the current to have H-H kinetics with speeds comparable to that of the squid axon. Supported in part by NIH Grant HL 12157 and 5-T32 GM 07184-04.



THE RELATIONSHIP BETWEEN THE FIRING PATTERN OF PURKINJE CELLS, THEIR RESPONSIVENESS TO NATURAL STIMULI, AND THE ACTION OF CLIMBING FIBERS. Timothy J. Ebner* and James R. Bloedel. Dept. of Neurosurgery & Physiology, Univ. of Mn., Mpls., Mn. 55455.

The autocorrelation of the simple spike activity recorded from Purkinje cells was examined in the anterior lobe of decerebrate, unanesthetized cats. During spontaneous activity two types of autocorrelations were observed. Type I exhibits a large positive correlation about time 0 which decays slowly (50-300 msec) to a constant baseline. Type II characteristically also possesses a strong positive correlation, but this rapidly (<10 msec) returns to a constant level. Using a generalized autocorrelation function for non-stationary stochastic processes which allows referencing of the autocorrelation to absolute time, structure in type I correlations was demonstrated to occur following the climbing fiber response of the Purkinje cell. When the cells were studied for their responsiveness to muscle stretch or cutaneous stimuli, those cells whose simple spike activity were modulated had predominantly type I autocorrelations (>85%). These results suggest that a specific Purkinje cell firing pattern (Type I) is present if the cell is modulated by peripheral inputs and that the structure of this autocorrelation appears tightly coupled to the action of the climbing fibers on cerebellar cortical neurons. (Supported by NIH Grants # 2R01-NS09447 and 1R01-NS-13002, Dr. Ebner by Ins. Med. Scientist Sch. Fund).

GRAVITY, METABOLIC RATE AND SIZE OF MAMMALS. A.C.Economos, Biolog. Sciences, San Jose State University, San Jose, CA95192

Galileo's concept of geometric dissimilarity of animal build from gravitational loading, was extended to animal function. Across the mammalian class, as body size increases, the maximal gravitational field to which an animal can adapt (Gravitational Tolerance or GT) decreases and the degree of depression of growth increases. A hypothesis, that a limit to the metabolic cost of gravity that can be tolerated underlies this phenomenon, was found in good quantitative agreement with the observations. By extrapolation, the size of the largest possible mammal (one with a GT equal to normal gravity or 1G) was deduced to be about 20,000 kg, which agrees with the estimated weight of the largest known mammal, the extinct Baluchitherium. From the hypergravity data, the metabolic cost of gravity was found to be proportional to $m_b^{0.89}$ (m_b= body mass), and basal metabolic rate was expressed as the sum of a gravitational component ($\propto m_b^{0.89}$) and a geometric component ($\propto m_b^{0.67}$), i.e., $BMR = 12m_b^{0.89} + 58m_b^{0.67}$. Goodness of fit of data from 22 mammals (57 values) by this equation (standard error = 544.2) compares well with Kleiber's equation, $BMR = 70m_b^{0.75}$ (standard error = 592.7). The present gravitational model agrees with the finding of a change in Kleiber's exponent from 0.67 in the Arctic to 0.90 in the Tropics. The theory also explains observed deviations of mammalian body dimensions from those obtained based on purely structural-mechanical analyses by Galileo (17th century) and more recently by McMahon(Science, 129: 1201, 1973).

EFFECT OF PROPRANOLOL ON HIGH ENERGY PHOSPHATE TURNOVER IN ISCHEMIC MYOCARDIUM. L.J. Eddy, M.D. Goodlett*, and J.M. Downey. Depts. Pharmacology and Physiology, Univ. So. Al., Mobile, AL 36688.

It is not known whether propranolol (Pro) reduces infarct size through decreased metabolic demand or through enhanced collateral blood flow. To answer this question we used a canine model in which we perfused two coronary arteries on the same heart at identical but reduced rates. Into one region we also infused 40 µg/min Pro while the other region received an equal volume of saline. Microsphere measurements revealed that flow in both segments were the same with the subendocardiums receiving 43% and the subepicardiums receiving 57% of normal flow. After one hour of perfusion at reduced flow, biopsies were taken from a normal region and the two ischemic regions, quick frozen, and analyzed for ATP and creatine phosphate (CP) content. In the nonischemic area ATP and CP were 5.6±0.20 and 11.3±0.3 µmoles/g tissue, respectively with no transmural differences. ATP and CP levels fell in the saline perfused area to 60% and 59% of normal values, respectively. Although ATP and CP levels fell to similar values in the subendocardium of the Pro treated segment, high energy phosphate titers were clearly preserved in the less ischemic subepicardium of the Pro treated segment. These results indicate that a direct protective effect can be realized with Pro if the level of ischemia is not too great.

EFFECTS OF ELECTROACUPUNCTURAL STIMULATION ON EVOKED POTENTIALS IN THE THALAMUS AND CORTEX OF CAT. A.E.U. Edisen and Y.K. Liu*, Tulane University Medical Center, New Orleans, Louisiana.

Electrical stimulation of the sciatic nerve, 1/10 sec., and of sufficient intensity and duration to excite the totality of Group A fibers, elicited responses in the homo- and contralateral postcruciate cortex and the nuclei centrum medianum and ventralis posterolateralis (VPL) of the thalamus of cats anesthetized with chloralose. Decamethonium was used to minimize movement. Histological examination was done to confirm electrode placement. Electroacupuncture stimulation was applied to acupuncture points GB 30 (region of the greater trochanter of femur) and St 36 (motor point of the tibialis anterior) bilaterally. Frequencies close to 3-5/sec., used clinically, were most effective in reducing amplitudes of the evoked potentials. The electroacupuctural stimulation used did not, by itself, evoke potentials in the cortex or thalamus. Current strength was increased, as in clinical practice, until the evoked potentials were depressed and/or obliterated. This suppression increased with time and was maintained throughout the duration of applied stimulation, 30-60 min. or longer. Evoked potentials were restored immediately to full control height upon cessation of the electroacupunctural stimulation. (The support of the Edward G. Schlieder Foundation of New Orleans is gratefully acknowledged.)

VASOPRESSIN-SENSITIVE ADENYLATE CYCLASE (AdC) IN ASCENDING LIMB OF HENLE'S LOOP AND IN COLLECTING TUBULES OF MICE WITH HEREDITARY NEPHROGENIC DIABETES INSIPIDUS (HNDI). R.M. Edwards*, B.A. Jackson* and T.P. Dousa. Mayo Clinic & Foundation, Rochester, MN 55901.

Previous studies have shown that AdC in membrane fractions from renal medulla of HNDI mice is stimulated by vasopressin to a lesser degree than in controls. Basal activity of AdC and the activity stimulated by 10^{-6}M [8-Arg]-vasopressin (AVP), was assayed in the medullary collecting tubule (MCT) and medullary thick ascending limb of Henle's loop (MAL) microdissected from kidneys of control mice with normal concentrating ability and in mice with HNDI. In control mice, the AVP-stimulated activity (in fmol cyclic AMP/mm/30 min ± SEM) in MAL (386 ± 30) was significantly ($P < 0.02$) higher than in MCT (236 ± 5). In the MCT basal AdC activity or the activity stimulated by AVP was not significantly different between control and NHDI mice. On the other hand, AVP-stimulated AdC activity in MAL (199 ± 5) was significantly ($P < 0.005$) lower in HNDI mice than in MAL of control mice. These results indicate, that the lower rate of cyclic AMP formation in response to AVP in mice with HNDI is localized specifically in MAL and that the response of AdC in MCT to AVP is intact. These observations suggest that the impaired cAMP-mediated response to AVP in MAL may be a basis of the urinary concentrating defect in HNDI mice. (Supported by AM-16105, AHA-74182, Mayo Foundation and the National Kidney Foundation.)

LUNG INFLATION, ALVEOLAR EPITHELIAL ALBUMIN PERMEABILITY, AND ALVEOLAR FLOODING. Edmund A. Egan & Bruce McIntyre, SUNYAB & CHILDREN'S HOSPITAL BUFFALO, NY 14222.

Experiments were conducted in anesthetized rabbits to determine if hyperinflation with O2 produced alveolar flooding from changes in alveolar solute permeability. Inflation was at 40 cm H2O through a tracheostomy to the whole lung or through a cannula wedged into a bronchus when only a sub-segment was hyperinflated. Permeability was calculated from measured efflux of radiolabeled solutes from alveolar saline; total lung water from wet/dry lung weight; and presence of alveolar water from dilution of solutes in lung lavage saline. Hyperinflation increased lung volumes 340% when applied to the whole lung, but much more, 600%, if restricted to a single sub-segment. The difference in inflation volumes was reflected in permeability results: whole lung hyperinflation did not induce an albumin permeability in the epithelium, isolated sub-segment hyperinflation did. However, neither hyperinflation experiment produced alveolar liquid, solute dilutions in lung lavages averaged less than 1%. Wet/dry lung weight was 4.2±0.5 in hyperinflated animals and 3.9±0.3 in controls. It appears that 40 cm H2O inflation pressure to the whole lung in vivo is insufficient to produce an albumin permeant epithelium. Sub-segment hyperinflation produces an albumin permeant epithelium, but without alveolar flooding, which supports the concept that alveolar lumen hydrostatic pressure exceeds interstitial.

THE EFFECT OF ENHANCED SYMPATHETIC NERVOUS FUNCTION AND OF ALPHA-ADRENERGIC BLOCKADE ON INSTANTANEOUS RENAL ARTERY PRESSURE-FLOW RELATIONS IN ANESTHETIZED DOGS. W. Ehrlich and R. W. Baer*, The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205.

Instantaneous renal artery pressure flow (inst. r.a. $P/\dot{Q}$) investigations produce straight lines whose zero flow intercepts indicate an effective downstream pressure (Ped) of about 20 mm Hg. Their slopes indicate an arterial resistance (Ra) of about 7 mm Hg.(1) In this study the sympathetic nervous activity is enhanced by bilateral carotid artery occlusion. The results from 65 inst. r.a. $P/\dot{Q}$ investigations in 6 anesthetized dogs during carotid artery occlusion compared with 80 control investigations show that carotid artery occlusion elevates aortic pressure and lowers r.a. flow. It elevates Ped and Ra to r.a. flow. The results from 37 investigations in 4 dogs after 5 mg/kg dibenzyline with 42 control investigations show that alpha-adrenergic blockade lowers aortic pressure and r.a. flow. It lowers Ped and Ra to r.a. flow. (Supported by NIH Grant HL 10342)

(1) Ehrlich W. et al., Fed. Proc. 38:1036, 1979.

RESPIRATORY EFFECT OF CENTRALLY INJECTED SEROTONIN. F. L. Eldridge, D. E. Millhorn* and T. G. Waldrop*. University of North Carolina, Chapel Hill, N.C. 27514

Since the neurotransmitter, serotonin, does not cross the blood-brain barrier, its direct central action on respiration was assessed by injection into the 3rd ventricle or onto the ventral medulla. Two groups of cats anesthetized with chloralose and urethan were studied. In 4 cats with intact carotid bodies and vagi, breathing was spontaneous. Ventilation was measured by pneumotachography; arterial pressure and end-tidal P_{CO_2} were continuously recorded. After obtaining stable control levels, first saline (200 µl) and then serotonin (1 µg in 200 µl saline) were injected into the 3rd ventricle through a needle passed through the nose and cribriform plate. Saline caused a 25 ml/min rise in $\dot{V}_E$; $P_{ET_{CO_2}}$ decreased 1.5 Torr. Serotonin caused a significantly larger rise in $\dot{V}_E$ (170 ml/min); $P_{ET_{CO_2}}$ fell 5 Torr. Another five cats, with cut carotid sinus nerves and vagi, were paralyzed and kept isocapnic with a servoventilator; phrenic nerve activity was used to quantify respiratory output (RO). Saline again led to only small rises in RO, whereas serotonin had significantly greater increases lasting > 20 min. Injecting serotonin onto the ventral surface of the medulla (2 cats) led to similar increases of RO; saline did not. In no case did injection of serotonin cause a depression of respiration. We conclude that one of the actions of serotonin in the brain is to stimulate respiration. (Supported by USPHS Grants HL-17689, NS-11132 and Pulmonary Training Grant HL-07106)

EFFECTS OF LOCAL HYPOXIA AND HYPOCAPNIA ON THE RESPONSE OF THE RIGHT CORONARY CIRCULATION TO SYMPATHETIC STIMULATION. Stephen Ely*, Ronald Korthuis*, Donald Sawyer*, Jerry B. Scott. Depts. of Physiology, and Small Animal Surgery and Medicine, Michigan State University, East Lansing, MI 48824

This study was undertaken to determine the effects of local hypoxia (HX) and/or hypocapnia (HC) on right coronary and right ventricular (RV) hemodynamics, and to what extent these changes modulate the response to baroreflex sympathetic stimulation (SS). A sternotomy was performed on six anesthetized, ventilated, vagotomized dogs, and the right coronary was perfused at constant flow. A lung was interposed in the perfusion line to alter blood gas tensions. Control SS resulted in an increased heart rate (HR), arterial pressure (PA), RV systolic pressure (RVSP), DP/DT, and coronary resistance (CVR) by 20%,42%,24%,35% and 8%, respectively. Local HC (pCO_2=7mmHg) increased CVR by 36%. Subsequent SS resulted in an increased HR, PA, RVSP, DP/DT and CVR of 15%,35%,13%, 20% and 4%, respectively. Local HX (pO_2=13mmHg) resulted in a 50% decrease in CVR. With subsequent SS, PA increased by 31%. Combination of HC and HX resulted in a 50% decreased CVR. Subsequent SS resulted in an increased PA, RVSP, DP/DT and CVR by 33%,15%,19% and 6%, respectively. These studies demonstrate that 1) local HC produces significant coronary constriction, 2) local HX and HC + HX produces significant coronary dilation. Consequently, changes in local blood gas tensions greatly alter right CVR, and local HX may modulate the response to SS.

INITIATION OF THE LEFT VENTRICULAR (LV) MECHANORECEPTOR REFLEX BY RATE-INDUCED CHANGES IN CONTRACTILITY. R.W. Emery*, J.A. Estrin*, G.M. Wahler*, C.R. Swayze* and I.J. Fox. University of Minnesota, Minneapolis, MN 55455

We have reported that the LV mechanoreceptor reflex (reflex systemic hypotension), which is considered to play an important role in the control of the systemic arterial blood pressure (peripheral resistance), is initiated by increasing LV myocardial contractility as by intracoronary catecholamines, etc. To further support this claim, experiments in which the hearts with total heart block were electrically paced were performed in 2 pneumonectomized dogs (chloralose-Flaxedil) on total cardiac bypass with the systemic and coronary circulations isolated and perfused separately, the systemic circulation being perfused at a constant rate so that changes in pressure reflected changes in resistance. Increasing the heart rate from 75 to 150/min (N = 20), which was associated with an increase in LV contractility (LV peak dP/dt) of 70 ± 8% (SEM) produced a fall in the systemic pressure averaging 11 ± 1% ($P < 0.001$) of the control value of 74 ± 2 mm Hg. Contrariwise, decreasing the heart rate from 150 to 75/min (N = 18), which was associated with a decrease in LV peak dP/dt of 38 ± 3%, produced a rise in the systemic pressure averaging 9 ± 1% ($P < 0.001$) above the control value of 69 ± 2 mm Hg. It is concluded that rate-induced changes in myocardial contractility are a physiological means of producing directionally opposite changes in systemic resistance such as occur during exercise.

EXPERIMENTAL HEMATOLOGIC CHANGES INDUCED BY HYPERGRAVITY. Georgeta Enachescu and Alexandru Vrabiescu. National Institute of Gerontology, Bucharest, 78178, Romania.

Hematologic changes were studied in 145 white rats subjected to 4,5 and 6,5g by centrifugation. In non-treated animals, sacrificed immediately after return to 1g, the study showed: a significant decrease of erythrocytes and Hb-values, the inversion of the leukocytic formula, in the sense that neutrophyl granulocytes increased and relative leukocyties decreased. There was a total decrease of elements in the medullary erythropoietic system, maturation inhibition of erythropoietic series, a decrease of medullary mitotic index and leftward deviation to the prophase of the medullary mitotic curves. Decrease of hematopoietic activity with its effects on peripheral blood were in proportion to the hypergravitation at values 4.5 and 6.5g, compared to 1g. These changes though showing a tendency to recover towaed normal ranges two months after return to an environment of 1g. The favourable effect of vitamin B_{12} and folic acid were demonstrated in the treated groups of animals by the prevention of premature hematologic lesions and by resistance against late effects of exces gravity.

CIRCADIAN CHANGES IN ADRENAL SENSITIVITY TO ACTH IN AWAKE DOGS AND ITS MODIFICATION BY HEMORRHAGE (HEM) W.C. Engeland, G.J. Byrnes*, K. Presnell*, P. Bonitz*, and D.S. Gann. Johns Hopkins university School of Medicine, Baltimore, MD 21205

In the awake dog increased adrenal sensitivity to ACTH may contribute to increased cortisol secretion(F) after hem(Endocrin.104:627A,1979). To determine if adrenal sensitivity to ACTH changes in the resting animal, F was measured in 9 awake dogs with chronic adrenal venous cannula in the AM(0700-0900) and in the PM (1500-1700h) before and 7.5 min after iv ACTH (2.5, 5 and 10 mU). The PM response was also measured after an AM 10 ml/kg hem. Plasma ACTH and F were assayed by RIA;data were analysed by ANOVA and regression. Resting ACTH was not different in the AM and PM (36+5 vs 39+4 pg/ml;$p>0.1$) but AM resting F was greater than PM resting F (1.49±0.2 vs 0.87± 0.1 ug/min;$p<0.01$). The AM response to ACTH was greater than the PM ($p<0.05$) in the absence of AM hem, but not after AM hem($p>0.1$). The AM sensitivity to ACTH was greater than the PM (estimated by slope(m) of log-dose response curves) in the absence of AM hem (7.97 vs 3.43;$p<0.05$), but not after AM hem (7.97 vs 10.23;$p>0.1$). Thus, adrenal sensitivity varies as a function of the time of observation in the absence of an AM-PM difference in resting plasma ACTH. Also, despite a meager ACTH response to AM hem, adrenal sensitivity is increased as long as 6-8h after stimulation. These data suggest that in awake dogs both circadian cues and stimulation by hem alter adrenal sensitivity to ACTH by one or more extra-ACTH mechanisms. Supported by grant AM14952 and Fshp. AM05731 from NIH.

CHANGES OF PULMONARY LAVAGE PHOSPHOLIPID AND SURFACE TENSION PRODUCED BY ETHANOL INGESTION IN THE CANINE. R. L. Engen, Iowa State University, Ames, IA 50010

This study was conducted to determine the influence of orally ingested alcohol on the phospholipid and surface tension characteristics of the alveolar lining material. Control lobar pulmonary lavage was completed on seven mongrel dogs 2-3 weeks prior to ethanol treatment. The dogs were given ethanol four times each day at 1 ml/kg, 1 ml/kg, 1.5 ml and 2.0 ml/kg for two consecutive days. On the third day, each animal was given one dose of ethanol (2 ml/kg). After 1 1/2-2 hrs, the second lobar pulmonary lavage was performed. The lavage samples were lyophilized and lipid extracts (LEX) prepared. Phospholipids were determined by thin layer chromotography and surface tension measurements were conducted on lipid extracts and on bulk alveolar lining material. Ethanol caused no significant changes in the sphingomyelin (Sp) or phosphatidyl lecithin (PL) (Sp pre 10.3-post 8.03%; PL pre 71.7-post 70.42%). Ethanol caused a significant increase in Phosphatidyl serine (pre 7.20-post 13.6%) and a significant decrease in phosphatidylethanolamine (pre 20.9-post 9.0%). No significant changes were determined in the surface tension of ALM or the low surface tension of LEX.

HEMODYNAMICS OF LOBAR ATELECTASIS. S. Enjeti*, P.B. Terry*, H.A. Menkes, R.J. Traystman. The Johns Hopkins Medical Insts., Baltimore, Maryland 21205.

Atelectasis of a sublobar portion of pig lung reduces sublobar blood flow and vascular conductance to 12% of control. (Am.Rev.Resp.Dis.117(4):332). In this study we evaluated the effect of lobar atelectasis on pulmonary blood flow ($\dot{Q}$) in 6 anesthetized, paralyzed, ventilated pigs using the radiolabeled microsphere technique. Under control conditions $\dot{Q}$ to the left (control-LLL) and right (experimental-RLL) lower lobes was similar (81.7 ± 15.5 SE and 75.1 ± 10.6 ml/min/g dry lung). One hour after bronchial obstruction of the denitrogenated RLL, $\dot{Q}$ and vascular conductance (G) of RLL decreased by 52.7% and 51.4%. $\dot{Q}$ to LLL increased by 63% due to redistribution of cardiac output ($\dot{Q}_t$), which was unchanged by the obstruction. Inflation of the non-obstructed lung to a transpulmonary pressure of 14.5 ± 2.5 cmH_2O above functional residual capacity, while RLL remained obstructed, reduced $\dot{Q}$ and G of LLL by 39.4% and 46.6% and decreased $\dot{Q}_t$ by 38.5%. $\dot{Q}$ and G of RLL remained unchanged; however, the shunt fraction ($\dot{Q}_{RLL}/\dot{Q}_t$) doubled (16.0 ± 2.5% to 32.5 ± 5.8%), since G in the atelectatic lung increased relative to the surrounding lung. Since oxygen tension of mixed venous blood perfusing atelectatic regions is similar in lobar and sublobar atelectasis, mechanical factors related to interlinkage of the sublobar region to the surrounding lung appear to be responsible for the greater reduction in $\dot{Q}$ and G in the sublobar region with atelectasis. (Supported by NIH HL-14153 and HL-07137.)

MODULATION OF LEFT VENTRICULAR (LV) MECHANORECEPTOR THRESHOLD BY ENDOGENOUS CATECHOLAMINES. J.A. Estrin*, R.W. Emery*, G.M. Wahler*, C.R. Swayze* and I.J. Fox. University of Minnesota, Minneapolis, MN 55455

Sympathetic amines have been shown to have a facilitatory action on mechanoreceptive sense organs, e.g., Pacinian corpuscles, frog skin mechanoreceptors, etc., by lowering their threshold to mechanical stimulation and decreasing their adaptation rate (W.R. Loewenstein, J. Physiol. 132:40, 1956). Four pneumonectomized dogs (chloralose-Flaxedil) were studied on total cardiac bypass with the systemic and coronary circulations isolated and perfused separately, the systemic circulation being perfused at constant rate so that changes in pressure reflected changes in resistance. Aortic (mean and instantaneous) and LV pressures, LV dP/dt and an ECG were continuously recorded. To study the effect of removal of the sympathetic input on the LV mechanoreceptors, successive injections of propranolol (0.5-1.0 mg) were made at one minute intervals to produce β blockade. At 10 minutes there was a rise in the systemic arterial pressure, which was not a progressive one, averaging 15.0 ± 3.1 mm Hg (13 ± 3.5%) above a control value of 115 ± 10 mm Hg and which was not accompanied by a change in LV myocardial contractility (LV peak dP/dt). This rise in systemic pressure without apparent change in contractility is felt to be due to raising of the LV mechanoreceptors' threshold to activation by basal LV contraction as a result of progressive withdrawal of adrenergic input by propranolol.

AGE-RELATED INFLUENCE OF EXTRACELLULAR POTASSIUM AND TETRAETHYLAMMONIUM UPON RABBIT PURKINJE FIBERS. Alan M. Ezrin*, Marion S. Gaide*, Robert J. Myerburg*, Arthur L. Bassett and Henry Gelband. Univ. of Miami School of Medicine, Miami, Florida 33101

Neonatal rabbit Purkinje fibers (PF) have shorter action potential duration at 90% repolarization (APD_{90}) compared to adult PF. In a group of 10 neonatal fibers, mean APD_{90} was 170 ± 20 msec while in 6 adult PF, APD_{90} was 316 ± 18 msec. The ionic mechanisms for the shorter APD_{90} in neonates is unknown. To determine if shorter neonatal APD_{90} involves enhanced K^+ efflux during repolarization, or abbreviated slow inward current, neonatal and adult PF were exposed to either graded $[K^+]_o$ (4-33 mM) or tetraethylammonium (TEA). Exposure of neonatal PF to 12 mM $[K^+]_o$ (15 min) decreased APD_{90} 23% and reduced resting potential (Em) 31% (control = 85 ± 2 mV). Higher $[K^+]_o$ (16-33 mM) were required to induce slow responses, which were blocked by verapamil (1 µg/ml). In contrast to neonatal PF, slow responses occurred in adult PF at lower $[K^+]_o$ (12 mM). TEA (20 mM) increased APD_{90} ∿ 30% in adult and neonatal PF. Threshold [TEA] for initial APD_{90} prolongation was lower in adult PF (5 mM). Age-related differences in the relationship of high $[K^+]_o$, initiation of slow responses, and differential TEA sensitivity suggest enhanced K^+ efflux may underlie the shorter APD_{90} observed in neonatal PF. (Supported in part by NIH grants HL 19044, HL 21735, HL T32 07188, and Miami Heart Association.)

IN UTERO VENTILATION OF THE UNANESTHETIZED NEAR TERM LAMB. J. Job Faber, John M. Bissonnette, and Kent L. Thornburg, Departments of Physiology and Obstetrics and Gynecology, School of Medicine, Univ. of Oregon Health Sciences Center, Portland, OR 97201

Two to seven days after surgery (mean 5) we obtained control data on 12 lambs, 8 of whom were subsequently ventilated with intermittent positive pressure ventilation in utero. The preparations had indwelling vascular and tracheal catheters and a flow sensor either on the pulmonary artery or on the ascending aorta. The postventilatory increase in femoral artery P_{O_2} did not correlate with pulmonary blood flow but did correlate with fetal weight ($P<0.001$). The pressure gradients between carotid artery and pulmonary artery ($P<0.02$) and between the left and right atria ($P<0.05$) increased. The ratio of left to right ventricular outputs (control=0.82) increased with increasing pulmonary blood flow ($P<0.001$) and flows in the aortic arch ($P<0.001$) and in the ductus arteriosus ($P<0.02$) showed strong positive and negative correlations respectively with pulmonary blood flow. We conclude that slight right ventricular dominance before birth changed to left ventricular dominance upon the onset of ventilation.

Supported by the Oregon Heart Association and NIH HD10034.

CHANGES IN VENTILATION AND THE ELECTRICAL ACTIVITY OF THE DIAPHRAGM AND EXTERNAL OBLIQUE MUSCLES IN THE AWAKE GOAT DURING CO_2 REBREATHING. M.J. Evanich, E. Jones*, M. Levitzky, R. Lowe, M. Wegmann* and R. Menendez*. Depts. of Physiology, Tulane Univ. and L.S.U., New Orleans, LA 70112.

We have characterized the change in ventilation($\dot{V}_E$), tidal volume (V_T) and frequency of breathing (F) in 10 awake goats during the course of CO_2 rebreathing. In three of these goats, we implanted stainless steel wire electrodes to monitor changes in the electrical activity of both the diaphragm (EMG_{di}) and external oblique (EMG_{ob}) muscles. Both signals were quantified as peak moving time average. Changes in $\dot{V}_E$, V_T and F were linearly and significantly correlated to changes in end-tidal PCO_2 when studied either several times on the same day or on different days. For a given animal, these responses were reproducible approximately 85% of the time. Both EMG_{di} and EMG_{ob} were linearly related to changes in end-tidal PCO_2 and were reproducible in 12 out of 15 trials over a three day period. EMG_{ob} was also linearly correlated to changes in EMG_{di} during rebreathing. In two of the three goats studied, EMG_{ob} was present during the early phase of inspiration while the diaphragm was still active. These data suggest that the goat may prove to be a useful model for the study of the neural, muscular and mechanical events involved in the control of respiration and that the expiratory muscles may assist in inspiratory muscle pressure generation. (Supported in part by NIH Grant HL21743 and The E.G. Schlieder Foundation)

PROSTAGLANDIN SYNTHESIS BLOCKADE IN A NEW PREPARATION FOR STUDY OF THE SKELETAL MUSCLE MICROCIRCULATION IN UNANESTHETIZED RATS. J.E. Faber*, P.D. Harris, D.L. Wiegman*, F.N. Miller* and I.G. Joshua*. Microcirculatory Systems Res. Grp. Dalton Res. Ctr., Univ. of Missouri, Columbia, Mo. 65211.

The cremaster muscles (with intact circulation and innervation) of 10 unanesthetized, decerebrate, Sprague-Dawley rats were suspended in a Krebs bath (pO_2=25-40mmHg, pCO_2=40-50 mmHg, pH=7.4). Diameters of 2nd (A2), 3rd (A3), and 4th (A4) order arterioles with (V) or without (NV) vasomotion during the control period were measured via television microscopy. Results before (Control) and after Indomethacin (2.5×10^{-5}M) are given as the maximum (MAX), minimum (MIN), and mean (MEAN) diameters (µm) and as the frequency (FREQ in cycles/min.) of vasomotion. (*$p<.05$ for paired comparison to control).

Group	N	Control (x±SEM)				Indomethacin (x±SEM)			
		MAX	MIN	MEAN	FREQ	MAX	MIN	MEAN	FREQ
A2-NV	8			75±3	0			42±8*	0
A3-NV	4			29±4	0	10±2*	6±1*	8±2*	50±1*
A3-V	6	24±3	19±3	22±3	35±2	10±1*	7±1*	9±1*	49±2*
A4-V	3	6±2	3±2	4±2	39±1	3±2*	1±1	2±1*	57±2*

These animals, in contrast to urethane-chloralose anesthetized rats, exhibited marked arteriolar vasomotion during control periods. We observed that blockade of prostaglandin synthesis resulted in vasoconstriction and augmentation of vasomotion. These data suggest that prostaglandins participate in the moment-to-moment regulation of tissue blood flow in skeletal muscle. (Supported by USPHS HL 12614 and HL 07094)

PULMONARY MICROVASCULAR PERMEABILITY CHARACTERISTICS WITH ETHCHLORVYNOL INJECTION. P. Fairman, F. Glauser, R. Falls, J.E. Millen. Department of Medicine, Medical College of Virginia-V.A. Hospitals, Richmond, Virginia 23298

The I.V. injection of ethchlorvynol (ECV) produces a high permeability pulmonary edema. Employing the saline filled dog lung model, alveolar epithelial permeability increases for substances up to 500,000 MW dextran. The effect of ECV on pulmonary microvascular permeability has not been studied. We, therefore, established in 10 dogs the right lymph duct cannulation technique and measured total lymph flow/hour, lymph albumin and 500,000 MW dextran concentration, lymph/plasma albumin and dextran ratios before and after 15-25mg/kg I.V. ECV.

	Control	Ethchlorvynol	P
Lymph flow/hr	.7 ± .3	3.1 ± .5	<0.01
Lymph/plasma			
albumin	.8 ± .1	.8 ± .2	NS
dextran	.3 ± .05	.18 ± .02	<0.05
Lymph concentration			
albumin, gm%	1.8 ± .03	1.7 ± .04	NS
dextran, mg%	3.0 ± 1.0	1.8 ± .2	<0.05

Following ECV injection, there is an increase in microvascular permeability to albumin and 500,000 MW dextrans. However, dextran flux is less than albumin. This is compatible with a membrane model consisting of two "pores" - the larger of which is relatively unaffected by ECV.

INVESTIGATION OF RED BLOOD CELL HEMOLYSIS IN LONG DISTANCE RUNNERS. H.L. Falsetti, G. Klee, C. Huss, and H. Hamilton. Depts of Int Med and Pathology, CV Div, CV Ctr, Univ of Iowa, Iowa City, IA 52242.

Haematological investigations were done in 7 marathon runners to measure effects of long distance running on red blood cells. The average number of miles run per week was 75 (range 55-110 miles). Laboratory evidence of hemolysis was monitored by measuring red counts, hemoglobin concentration, plasma and urine hemoglobin, haptoglobin, and serum enzymes (LDH,CPK) before and after a 15 mile run. The mechanism of hemolysis was investigated by measuring pH, serum complement levels, red cell fragility, Coombs' test, and coagulation functions (platelets, PT, PTT, FDP, and fibrin monomer). The primary evidence for hemolysis is a significant drop in haptoglobin ($p<.05$). There were significant elevations in CPK and LDH, but most of these changes are probably due to muscle enzymes. The amount of hemolysis was small, since plasma hemoglobin did not increase and no hemoglobin was found in the urine. The hemoglobin concentration generally increased due to dehydration. There were no significant changes in pH, complement levels, or coagulation functions. The cells from runners had increased mechanical fragility prior to running when compared to 5 non-running controls. Mechanical fragility changed after running indicating the fragile cells were destroyed during running. In summary, these results indicate that there is low grade hemolysis in marathon runners. The cause of this hemolysis is not determined.

RESPIRATORY AND BEHAVIORAL EFFECTS OF NALOXONE AND MORPHINE IN THE DEVELOPING OPOSSUM. J. P. Farber and M. A. Maltby*. Dept. of Physiology & Biophysics, Univ. of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73190.

To evaluate possible effects of endogenous opiates on respiration and behavior in the developing opossum, the opiate antagonist, naloxone (.8 mg/kg), or control solutions were injected subcutaneously in animals between 15 and 50 days of age. In the youngest animals naloxone uniformly evoked behavioral arousal (assessed using electromyography) with increases in ventilation (assessed using pressure plethysmography). The behavioral effect became inconsistent with increasing age. In the absence of behavioral arousal after naloxone, increases in ventilation were not typically observed. Subcutaneous administration of the opiate, morphine (20 mg/kg), resulted in fatal respiratory depression in the youngest animals; but in animals older than 25-30 days of age, morphine produced only moderate depression of ventilation (to 65% of control values, $\pm$ 20% S.D.). The youngest animals could not uniformly tolerate doses of morphine as low as 1 mg/kg. These data suggest that endogenous opiates exert an inhibitory effect on behavioral arousal in young opossums and the effect is paralleled by high respiratory sensitivity to an exogenous opiate. Depression of breathing caused by endogenous opiates, independent of behavioral influences, was not demonstrated. (Supported by NIH Grant HL 23601).

EVIDENCE THAT THE ADRENAL MEDULLA IS ONLY OF MINIMAL IMPORTANCE IN CERTAIN CARDIOVASCULAR REFLEXES. D.C. Fater*, W.D. Sundet*, B.C. Wang, and K.L. Goetz. St. Luke's Hospital and Foundation, Kansas City, Missouri 64111

The degree of participation of the adrenal medulla in the reflex regulation of the circulation is somewhat controversial. During studies performed on dogs with denervated hearts, we noticed that heart rate remained constant or increased only slightly in response to serial hemorrhages. After a loss of 24% of total blood volume, the average heart rate of seven chloralose-anesthetized dogs had increased by less than two beats per minute; there was no significant change in mean arterial pressure. In other studies, heart rate remained constant or increased only by a few beats per min in response to the i.v. injection of nitroglycerin (24 µg/kg) even though mean arterial pressure decreased by 40-50 mm Hg. Finally, insulin shock, which is known to cause release of catecholamines from the adrenal medulla, was produced in dogs with denervated hearts to ensure that the denervated heart was responsive to an increase in circulating catecholamines. The insulin-induced decrease in blood glucose levels was accompanied by a substantial increase in heart rate. Since hemorrhage and nitroglycerin produced either no change or only a negligible increase in heart rate in dogs with denervated hearts and an intact adrenal medulla, we conclude that the adrenal medulla is only of minor importance in the reflex regulation of the circulation. (Supported by NIH grant HL13623).

PHYSIOLOGICAL-HISTOCHEMICAL CORRELATIONS FOR LIMB AND MASTICATORY MUSCLES OF MONKEYS. J.A. Faulkner, K.K. McCully*, L.C. Maxwell, T.P. White, and J.A. McNamara*. Departments of Physiology, Anatomy, and Physical Education, University of Michigan, Ann Arbor, MI. 48109. Small bundles of skeletal muscle fibers, approximately 25 mm long and 15 to 20 mm^2 in cross-sectional area, were dissected from the extensor digitorum longus (EDL), soleus (SOL), masseter (MST), and temporalis (TMP) muscles of Rhesus monkeys. The small bundles were cleared of damaged fibers, tied at each end, and then mounted in a muscle bath. The range for the time to peak twitch tension (TPT) and the half relaxation time (1/2 RT) was from 20 to 40 msec and for the maximum velocity of shortening for a single sarcomere (Vo) was from 6 to 20 µm/sec. As observed in other species, the relationship between Vo and 1/TPT was linear. After measurement of contractile properties, the bundles were quick frozen and sections were incubated for myofibrillar ATPase activity. The area of the small bundles composed of Type II (fast) muscle fibers ranged from 5% in the SOL to 95% in the EDL and the values for the MST and TMP ranged from 7 to 50%. For SOL, EDL, and TMP muscles, the Vo and 1/TPT were highly correlated with the percentage area of Type II fibers, but for the MST muscle the relationship was significantly different. Myofibrillar ATPase is highly correlated with calcium activated myosin ATPase. Consequently, the slow myosin ATPase of the MST muscle is modulated to produce a relatively fast TPT and 1/2 RT. (Supported by Muscular Dystrophy Association, Inc., USPH grant #DE 04227, & Contract #DE 52478.

RESPONSE TO INHALATION OF LOW CO_2 PARTIAL PRESSURES IN THE CHICKEN. M. R. Fedde and W. D. Kuhlmann*. Dept. Anatomy and Physiology, Kansas State Univ., Manhattan, KS 66506.

The ventilatory and arterial blood gas responses produced by small changes in the partial pressure of CO_2 in the inspiratory gas (P_ICO_2) were studied using a 4 x 4 Latin square design in 10 decerebrate, adult, male White Leghorn-type chickens (av. body wt., 1.8 kg). The birds were placed upright in a body plethysmograph and a plastic chamber, through which test gas flowed at 6 $L \cdot min^{-1}$, was placed over the head. Each bird was exposed to four levels of P_ICO_2 (.02 torr $\pm$ .07SD; 5.6 torr $\pm$ 1.2; 9.1 torr $\pm$ 0.9; 12.5 torr $\pm$ 1.0). Inhaling these CO_2 partial pressures produced progressive and significant ($P < .01$) increases in $PaCO_2$, tidal volume and minute ventilation ($\dot{V}$) and a decrease in pHa but no differences in respiratory frequency or partial pressure of CO_2 in end-expired gas. $PaCO_2$ increased from a mean of 33.3 torr at P_ICO_2 of .02 torr to a mean of 34.4 torr at P_ICO_2 of 12.5 torr; $\dot{V}$ increased from a mean of 566 $ml \cdot min^{-1}$ at P_ICO_2 of .02 torr to a mean of 746 $ml \cdot min^{-1}$ at P_ICO_2 of 12.5 torr. The sensitivity of the respiratory system to CO_2, if expressed in terms of $PaCO_2$ was 90 $ml \cdot min^{-1} \cdot kg^{-1} \cdot torr^{-1}$. The increase in ventilation was not sufficient to prevent a rise in $PaCO_2$ when low P_ICO_2 was inhaled and the ventilatory sensitivity was comparable to that in awake dogs. (Supported in part by a grant-in-aid from the American Heart Association Kansas Affiliate, Inc.).

NOREPINEPHRINE TURNOVER IN BROWN FAT, SKELETAL MUSCLE AND SPLEEN OF COLD EXPOSED AND COLD ACCLIMATED ALASKAN RED-BACKED VOLES. Dale D. Feist. Institute of Arctic Biology, Univ. of Alaska, Fairbanks, Alaska 99701.

After subcutaneous injection of L-norepinephrine-^3H (^3H-NE) into Alaskan red-backed voles (*Clethrionomys rutilus dawsoni*), the NE turnover rate (µg NE/g·h), an index of the sympathetic nerve activity, was estimated in interscapular brown fat, skeletal muscle and spleen. In 20°C acclimated voles at 20°C, NE turnover in brown fat and spleen was similar (0.125 µg NE/g·h) and 6 times higher than that in muscle. In 20°C acclimated voles at 0°C, NE turnover was increased 1.4x in brown fat, 1.8x in muscle and 1.3x in spleen. After acclimation to 5°C for 2 mo, NE turnover was increased in muscle and spleen but not in brown fat (compared to 20°C acclimated voles at 20°C). In 5°C acclimated voles at 0°C, NE turnover in brown fat was increased to the same level as in 20°C acclimated voles at 0°C. Endogenous NE (µg NE/g) remained unchanged in tissues of all groups exposed to cold. The results indicate that red-backed voles show increased sympathetic activity in certain tissues during cold exposure which resembles that of rats and hamsters. However, the capacity of warm acclimated red-backed voles to maintain a steady state level of NE in these tissues during acute cold exposure suggests an adaptation to colder latitudes which may not be shared by temperate small mammals. (Supported in part by USPHS NIH Grants ES00689 and GM10402)

THE INFLUENCE OF PHOTOPERIOD AND THERMAL ACCLIMATION UPON COLD SURVIVAL IN MICE. J. Homer Ferguson. University of Idaho, Moscow, ID. 83843.

Male albino mice (Swiss-Webster) were raised at 5C under short (8L:16D) and long (16L:8D) light periods and at 42 days of age were exposed to -40C to determine resistance time (RT) or time until loss of righting response occurred (CTmin). Under the short photoperiod RT was 49.3 ± 4.4 minutes and under long photoperiods RT was 38.7 ± 1.9 minutes ($P < 0.05$). A second group of mice was raised at room temperature (22C) either under constant darkness or short day lengths (4L:20D) and at 42 days of age were exposed to -20C to determine RT. RT for animals maintained in constant dark was 80 minutes and 61 minutes for animals raised in 4L:20D ($P < 0.01$). After 30 minutes mean rectal temperatures were 32.07 ± 0.47C for constant darkness animals and 30.46 ± 0.43C for short day animals ($P < 0.02$) and after 60 minutes the mean rectal temperatures were 23.7 ± 1.6C and 17.3 ± 1.5 respectively ($P < 0.01$). All mice were housed in groups of 3 to 5 in plastic mouse cages (16x12x28 cm) with food and water ad lib. All cold exposure was carried out between 10:00 a.m. and 4:00 p.m. From these data, it is obvious that photoperiod influences cold resistance at both cold and thermoneutral acclimation temperatures although ambient temperature is the predominant environmental factor.

A COMPARISON OF ANGIOTENSIN II (AII) AND ANGIOTENSIN III (AIII) AS MESENTERIC VASCULATURE VASOCONSTRICTORS. M. J. Fiksen-Olsen*, S. L. Britton, J. M. Sexton*, P. G. Werness*, and J. C. Romero, Department of Physiology, Mayo Clinic, Rochester, Minnesota 55901.

AII is more potent as a vasopressor than AIII when given intravenously. We tested the hypothesis that differential changes in mesenteric blood flow contribute to this potency difference. The effects of AII and AIII on mesenteric blood flow were compared in 31 pentobarbital anesthetized dogs. These agonists were administered as either bolus injections or as constant infusions directly into the superior mesenteric artery. Approximately equipressor doses of AII and AIII were also given intravenously. On the basis of duration and graphical integration, but not on the basis of absolute change in amplitude of the blood flow response, AII was more potent than AIII as a mesenteric vasoconstrictor. Intra-arterial and intravenous AII and AIII constant infusion doses were repeated after the administration of meclofenamate. Meclofenamate did not alter the responses to AII or AIII. We conclude that the differential constrictor properties of these compounds in the mesenteric vasculature contribute to the greater potency of intravenously administered AII upon arterial pressure. No evidence was found for a modulatory role of prostaglandins on vasoconstrictor responses to AII and AIII in the mesenteric vasculature of the dog. Supported by Grant HL 16496.

ENDOTOXIN INCREASES PRODUCTION OF MACROPHAGE INSULIN-LIKE ACTIVITY (MILA). James P. Filkins. Dept. of Physiology, Loyola Univ. of Chgo., Stritch Sch. Med., Maywood, IL 60153

Peritoneal macrophages (M) release a mediator with insulin-like activity (ILA) as assessed by glucose oxidation increments in rat epididymal fat pads (J. of the RE Society 25: June, 1979). The present study evaluated the effects of endotoxin on the release of macrophage insulin-like activity (MILA). Rat peritoneal M obtained from 96 hr caseinate exudates were co-incubated in Krebs-Ringer bicarbonate media with epididymal fat pads (EFP) and adipose tissue oxidation of U-D-^{14}C-glucose was quantitated as an index of ILA. Co-incubations of EFP with M (5×10^6/ml) increased EFP glucose oxidation from 48,652 ± 4251 to 79,321 ± 5656 DPM of $^{14}CO_2$/gram EFP/hr (N=12). Addition of S. enteriditis endotoxin at 100ng/ml to the EFP plus M incubations further increased glucose oxidation to 121,152 ± 8491 units (N=12). Supernatants obtained from 18 hr cultures of M increased EFP glucose oxidation from 51,667 ± 4897 to 86,118 ± 6256 units (N=12). Addition of endotoxin during the 18 hr M culture period resulted in a supernatant which further increased EFP glucose oxidation to 164,887 ± 12,112 units (N=12). The data indicate (i) that peritoneal M elaborate a monokine with insulin-like activity (MILA) and (ii) that endotoxin increases production of MILA. It is suggested that MILA may be involved in the functional hyperinsulinism and resultant hypoglycemia which are hallmarks of fatal endotoxin shock. (Supported by NIH Grant HL-08682.)

THE EFFECT OF ANTIORTHOSTATIC BED REST ON CARDIOVASCULAR AND EXERCISE RESPONSE. Stan Fink*, Technology Incorporated and W.C.Alexander, NASA Johnson Space Center, Houston, Texas 77058

The effectiveness of head-down tilt as a model for weightlessness was studied in eight male subjects exposed to exercise stress and to lower body negative pressure (LBNP) both before and after 7 days of bed rest. Two groups of four subjects were placed in either the horizontal (G-I) or 6° head-down position (G-II). The subjects were tested during a 7-day control period and a 6-day recovery period (R+0 to R+6). Maximal and submaximal exercise and LBNP tolerances were recorded. Neither group showed significant changes in maximal working capacity. The transient response in attaining 75% of maximum aerobic capacity showed significant changes on R+0. G-I showed a 10.7% ($p<0.05$) increase in heart rate (HR) and a 6.2% (n.s.) decrease in oxygen pulse, as compared to pre bed rest. G-II showed a 10.2% ($p<0.05$) increase in HR and a -9.8% ($p<0.005$) decrease in oxygen pulse. On R+2, G-II exhibited significant changes from pre bed rest exercise response. HR was increased 6.9% ($p<0.05$) and oxygen consumption 7.8% ($p<0.02$). G-II showed significant HR elevations to LBNP stress. At -40mmHg, the increase in HR was 34.2% ($p<0.02$) on R+0, 11.5% (n.s.) on R+2, and 14.6% ($p<0.01$) on R+6. At -50mmHg, HR increases were 33.2% ($p<0.05$) on R+0, 16.7% (n.s.) on R+2, and 17.7% (n.s.) on R+6. These data and those recorded in Skylab support the conclusion that 6° head-down tilt simulates the effects of weightlessness more effectively than supine bed rest.

UBIQUITOUS SIGNALS IN SINGLE NEURON RECORDING -- FACT OR ARTIFACT? Edward P. Finnerty* and Samuel H.H. Chan. Department of Life Sciences, Indiana State Univ., Terre Haute, IN 47809

In the course of an electrophysiological study involving extracellular microelectrode recording of potentials from single neurons in the caudate nucleus and substantia nigra of rats, an intriguing phenomenon was observed. Signals that displayed a pattern similar to electrocardiogram (EKG) and possessed an audio quality similar to phonocardiogram were consistently recorded, independent of the neuronal activities. The present study is our attempt to delineate the origin of these ubiquitous signals, based on established responses of the heart to pharmacological treatments. While intravenous injection of saline produced no appreciable effect, pentobarbital sodium (15 mg/kg, i.v.) was found to depress these potentials without affecting the nervous impulses. Saturated magnesium sulfate, used as a lethal agent, induced changes in these signals that resembled the pattern of fibrillation as seen in EKG tracings. When conventional EKG was monitored simultaneously on the oscilloscope, it was interesting to note that the R-wave coincided with the occurrence of the signals. Further, both potentials exhibited parallel responses to pentobarbital. It is concluded that the observed signals are manifestations of electrical activities from the heart, recorded by the microelectrode via the principle of volume conduction.

EFFECT OF ESTRADIOL AND CONTRACEPTIVE STEROIDS ON CHOLESTEROL IN PLASMA AND AORTA OF RATS FED A NORMAL OR AN ATHEROGENIC DIET. Grace M. Fischer and Margaret L. Swain*. Univ. of Pennsylvania, Philadelphia, PA 19104

The following studies were done to ascertain whether estradiol (E) or mestranol-norethynodrel (MN) has the same effect on plasma and aortic cholesterol (C) in rats fed an atherogenic diet as in rats fed a normal diet. Female ovariectomized and intact rats were divided into four groups and treated as follows. Ovariectomized: I oil, II E; Intact: III oil, IV MN. One half of the rats in each group were fed a normal diet and the other half a 4% C-4% coconut oil supplemented diet (A). After 4½ months plasma and aortic C was determined. The plasma levels of total C (mg/dl ± S.E.) were as follows. I 112 ± 9; IA 219 ± 16; II 137 ± 19; IIA 330 ± 32; III 134 ± 14; IIIA 298 ± 24; IV 114 ± 9; IVA 384 ± 64. Aortic concentrations followed the same general pattern except that MN did not reduce concentration. Conclusions: (1) The hypercholesterolemic effect of E is accentuated in rats fed an atherogenic diet; (2) In intact rats MN lowered plasma C but this effect was lost when excess C was present in the diet; (3) There was no protective effect by E or MN against deposition of C in vascular tissue. The results suggest that the "protective" effect of estrogen against vascular disease is not mediated through its effect on C accumulation and that the effect of MN on plasma C is dependent upon the amount of C in the diet. (Supported by USPHS Grant HL 17721)

PROSTACYCLIN AS ANTICOAGULANT FOR EXTRACORPOREAL CIRCULATION (ECC). C. Fisher*, R.W. Colman, L.H. Edmunds, Jr., V.P. Addonizio, Univ. of Penn., Philadelphia, PA 19104

Systemic heparinization contributes to excessive bleeding following ECC. We, therefore, attempted to identify the pathways of coagulation operative during ECC. Recirculating 500 ml of fresh, heparinized, human blood at 37° C in a silicone rubber perfusion circuit containing a membrane oxygenator (0.95 m^2), resulted in an 83 ± 5 S.E.M.% decline in the circulating platelet count and extensive release of platelet α granule contents with plasma levels of the platelet specific protein LA-PF4 rising to 15 ± 3 μg/ml. In contrast, no detectable activation of Hageman factor occurred as evidenced by stability of plasma concentrations of prekallikrein (with either heparin or citrate as anticoagulant). Furthermore, circulating monocytes failed to demonstrate procoagulant properties. Thus, the circuit provides, at most, a weak stimulus for intrinsic and monocyte-mediated extrinsic pathways of coagulation. We then tested the hypothesis that temporary inhibition of platelet function with prostacyclin (PGI_2) would provide effective anticoagulation. PGI_2 (≥ 25 ηM) prevented platelet loss (95% of initial levels at 2 hrs.) and platelet secretion (plasma LA-PF4 < 0.5 μg/ml at 2 hrs.) but failed to prevent immediate coagulation when heparin was reversed. Coagulation in the presence of platelet inhibition suggests that alternative pathways exist. During simulated ECC, prostacyclin prevents contact initiated platelet activation but cannot serve by itself as an anticoagulant.

EFFECT OF POSITIVE END EXPIRATORY PRESSURE (PEEP) ON INTRAPULMONARY SHUNT AND REGIONAL PULMONARY PERFUSION IN PULMONARY EDEMA. C.J. Fisher*, and L.D.H. Wood*. (Spon: J.F. Green). Sec. of Resp. Dis., University of Manitoba, Winnipeg, Man.

We measured lobar perfusion ($\dot{Q}L/\dot{Q}t$) with differentially labelled microspheres and lobar ($\dot{Q}sL/\dot{Q}t$) and total $\dot{Q}s/\dot{Q}t$ intrapulmonary shunt using blood samples from the aorta, pulmonary artery and right (RLL) and left (LLL) lower lobe veins in six open chest dogs at FRC (4 cm H_2O PEEP). Measurements were made before (C), two hrs after oleic acid (OA) was injected into the LLL pulmonary artery, and again 10 mins after PEEP was increased to 10 cm H_2O. Mean (± SE) results were:

	LEFT		TOTAL
	$\dot{Q}L/\dot{Q}t$	$\dot{Q}s/\dot{Q}t$	
C	23.5±1.3	13.0±2.3	10.7±1.6
OA	16.0±1.9*	51.5±7.2*	11.1±2.3
10 PEEP	21.6±1.7*	9.8±1.3*	9.9±2.6

*P <.05

$\dot{Q}sL/\dot{Q}t$ in LLL increased again to 41.0±9 10 mins after PEEP was removed. These results indicated that the large $\dot{Q}sL/\dot{Q}t$ of the edematous region had little effect on total $\dot{Q}s/\dot{Q}t$ because $\dot{Q}L/\dot{Q}t$ decreased by 32%. We conclude that PEEP reduces $\dot{Q}sL/\dot{Q}t$ by restoring ventilation of perfused lung units possibly by redistributing the excess lung liquid such that it no longer impairs O_2 exchange. This was associated with increased perfusion of the edematous region due to blocking of hypoxic vasoconstriction or to removing extravascular mechanical obstruction. (Supported by MRC of Canada)

ROLE OF THE VAGUS IN VENTILATORY COMPENSATION TO INSPIRATORY ELASTIC LOADS IN NEWBORN RABBITS. John T. Fisher and Jacopo P. Mortola. McGill University, Montreal, Canada, H3G 1Y6.

We have studied the immediate ventilatory stability (first loaded breath) of anesthetized newborn rabbits (2-10 days) during inspiratory elastic loading. The addition of loads of 2, 10, or 20 times the magnitude of the passive elastance of the respiratory system (E_{rs}) reduced tidal volume (V_T) to 60, 28, and 17% respectively of the control value. Ventilation exhibited a response similar to that of V_T since loading had no effect on respiratory frequency (f). Vagotomy resulted in a decrease in "effective" elastance (E'rs) to 65% of the pre vagotomy value. Application of the same loads as in the pre vagotomy condition decreased V_T to 49, 22, and 12% of the post vagotomy control values. Once again $\dot{V}_E$ showed a similar response to V_T since f did not change with loading. By comparing the pre and post vagotomy condition it was calculated that the mean vagal contribution accounted for 23% of the immediate compensation of V_T and $\dot{V}_E$ to inspiratory elastic loads.
(Supported by the Canadian MRC).

INTRACELLULAR VOLTAGE OF "SPLIT" FROG SKINS DETERMINED BY IMPALEMENTS ACROSS THE INNER BARRIER. R. Fisher*, D. Erlij, and S. Helman. Univ. of Illinois, Urbana, Ill. 61801

Previous investigations of isolated frog skin with microelectrode impalements across the outer barrier indicated that for tissues short-circuited, the intracellular voltage, V_o^{sc}, is markedly negative averaging near -90 to -100 mV. The present studies were done to investigate isolated "split skins" after removal of the corium that permitted impalement of the epithelium from the inner solution across the basolateral barriers of the cells. Skins were split after using 0.4 mg/ml collagenase (inner solution) in Cl-HCO_3 Ringer for 3 hours and the procedure modified so that hydrostatic pressure was not required. Repeated impalements gave similar intracellular voltages. For Na transporting skins (I_{sc} = 27.3±8.6 μA/cm^2, n=5) the V_o^{sc}, fR_o and E_1' were -91.6±3.0 mV, .874±.031, and 104.9±2.6 mV, respectively, where fR_o is the fractional transcellular resistance at the outer barrier, and E_1 is the transepithelial voltage when V_o is 0 mV. With 10^{-5} M amiloride in the outer solution (I_{sc} = 2.1±0.8 μA/cm^2, n=6), the V_o^{sc}, fR_o, and E_1' were -101.8±3.1 mV, .986±.011, and 112.1±2.2 mV, respectively. These data are similar to those obtained with punctures across the outer barrier, and thus rule out artifacts that might exist with impalements at the outer barrier. Moreover, the epithelial layers of frog skin appear to be electrically coupled into a functional syncitium. (Supported by HEW PHS AM 16663.)

THE EFFECT OF PROLONGED ACTIVITY ON THE SARCOPLASMIC RETICULUM AND MYOFIBRILS OF FAST AND SLOW SKELETAL MUSCLE. R.H. Fitts*, D.H. Kim*, and F.A. Witzmann* (SPON: B.E. Piacsek). Biology Dept., Marquette Univ., Milwaukee, WI 53233.

Following 7 hrs. of swimming the myofibrils (MF) and sarcoplasmic reticulum (SR) were isolated by differential centrifugation from the slow, type I, soleus(SOL), the fast, type IIB, superficial vastus lateralis (SVL),the fast, type IIA, deep vastus lateralis(DVL), and the mixed fast, type IIA and IIB, extensor digitorum longus(EDL). Following partial purification the ATPase activity of the MF and SR, as well as the Ca^{2+} uptake of the SR were measured in fatigued and control samples. The MF Ca^{2+} stimulated ATPase(μMoles P_i/mg/min) of the fast muscles was unaltered (range 0.250 to 0.300), while the fatigued SOL MF showed a depressed activity of 0.074±0.011 compared to 0.099±0.009 for controls.The SR yield from fatigued SOL (0.57±0.17 mg/g) was lower than control (0.81±0.17 mg/g), while the SR yield of the fast muscles was unaltered (1.5-2.0 mg/g). None of the muscles exhibited any change in the SR Ca^{2+} stimulated ATPase activity, however all vesicles showed a depressed rate and extent of Ca^{2+} uptake. The control and fatigued values for SR Ca^{2+} uptake (μMoles Ca^{2+}/mg SR) were 0.955±0.064 and 0.630±0.120 for SOL; and 2.607±0.157 and 1.537±0.170 for DVL. In conclusion, prolonged endurance activity primarily affects type I and IIA fibers with the function of the SR being particularly susceptible to fatigue. (Supported by Marquette Faculty Research Grant.)

HYPERCAPNIA AND THE ISOLATED VASCULARLY PERFUSED RAT HEMIDIAPHRAGM (HD). R. Fitzgerald, G. Bierkamper* and C. Hauer*. The Johns Hopkins U. Med. Inst., Baltimore, MD 21205.

A possible role for CO_2 in respiratory muscle fatigue and failure was studied in the HD preparation. The HD was excised from Sprague-Dawley rats (250 gm) and after cannulation of the phrenic vein, was mounted in a chamber ventilated with humidified 95%O_2/5%CO_2 or with 80%O_2/20%CO_2 at 25°C. Krebs Ringer bicarbonate solution (PO_2=408torr; PCO_2=35.8torr; pH= 7.455)was perfused retrogradely through the HD. The phrenic nerve was stimulated (0.8V, 0.5 Hz, 0.2 msec duration) and the force of the isometric twitch contraction measured (FC). The HD was then perfused with a new solution for 20 min (PO_2= 310torr; PCO_2=98.9torr; pH=6.972).

n=5 runs in 3 HD's	CONTROL	4'	10'	20'
mean FC (grams)	44.8	46.5*	41.5*	37.9*
± S.E.	1.1	1.2	1.2	0.6

* = significantly different from control at 0.005 level

All muscles recovered when perfusion of control medium was restored, or when isoprel (10^{-5}M) was added to the hypercapnic perfusate. The effect of isoprel was reversed by propanolol. These data corroborate data previously reported for another preparation (The Physiologist 20:29, 1977). We conclude: (1) the vascularly perfused HD responds to these agents like the more classical HD preparation; (2) hypercapnia may well play a role in respiratory muscle fatigue and failure. (Supported by HL 10342).

PRESERVATION OF BLOOD FLOW TO KIDNEY AND GUT BY INTRAVENOUS NITROGLYCERIN DURING EXERCISE IN RATS WITH HEART FAILURE. Stephen F.Flaim, Richard Weitzel*, & Robert Zelis.Cardiology, Penn. State Univ. School of Medicine, Hershey, Pa. 17033

The effects of intravenous nitroglycerin(NTG)(8μgm/kg)on the cardiac and peripheral circulatory(radioactive microspheres)response to exercise(EX)were evaluated in heart failure(HF)(chronic volume overload)and control(C)sham rats.Data were collected at rest and after 5 min of minimal treadmill EX(30% maximum)during infusion of saline(S)(30μl/min)and NTG. Data obtained during EX are as follows:

	RESPONSE TO EXERCISE			
	C-S	C-NTG	HF-S	HF-NTG
CO(ml/min/kg)	371	373	270	377
RENAL BF	792	580	204	511*
GUT BF	268	204	91	194*
SK. MUSCLE BF	48	40	45	44
SKIN BF	16	9	4	10
LV BF	970	975	1043	1379

CO=cardiac output (exclusive of shunt BF in HF), BF=blood flow(ml/min/100gms), GUT=ileum, SK. MUSCLE=quadriceps femoris, LV=left ventricle, *=p<.05 compared to HF-S.

These data indicate that intravenous NTG tends to improve the CO response to minimal exercise in HF. The improvement in CO is reflected primarily in a normalization of the EX hyperemia response of the gut and renal circulatory beds. (Supported in part by USPHS.NIH Grant HL05434 & HL17853).

A23187 EFFECTS ON ^{42}K EFFLUX IN CARDIAC PACEMAKER TISSUE B.P. Fleming* and W.R. Giles* (Spons. W.G. Guntheroth) University of Washington, Seattle, Washington 98195

The fractional escape rate of ^{42}K (^{42}K FER) from isolated turtle sinus venosus preparations was measured, and the ionophore A23187 was utilized to study whether raising intracellular Ca++ increases ^{42}K efflux. Addition of 2.5mM Ca++ to A23187-containing (10μg/ml), but Ca++ depleted (2.0mM EGTA), Ringers solution produced a rapid and large increase in ^{42}K FER (90 ± 14%, n = 17). However, when hemicholinium (10^{-5}M) was added to the loading solution, and field stimulation (10 volts, 0.5msec, 50 Hz) was applied during the loading period (3.5 hours), the A23187-induced increase in ^{42}K FER was reduced to 31 ± 5%, (n = 17). Since acetylcholine (ACh) is known to increase ^{42}K FER in cardiac pacemaker tissue, we conclude that a significant part of this A23187 response is produced by release of ACh from nerve endings within the preparation. (Supported by A.H.A. Grant 77691 and USPHS NIH Grant HL 22426).

INCREASED LUNG VASCULAR PERMEABILITY AFTER MICROEMBOLI IN UNANESTHETIZED SHEEP REQUIRES CIRCULATING LEUCOCYTES. M.R. Flick*, A. Perel* and N.C. Staub. Cardiovasc Res Inst and Dept Physiology, Univ of California, San Francisco, CA 94143

In 3 unanesthetized sheep we measured lung lymph flow ($\dot{Q}$lym), pulmonary arterial (Ppa) and left atrial (Pla) pressures, cardiac output ($\dot{Q}$b) and lymph and plasma protein concentrations. We calculated pulmonary vascular resistance (PVR) and protein flow ($\dot{Q}$prt) in lung lymph. After a 2h baseline we infused air emboli i.v. at a constant rate to increase PVR 2-3 fold. We depleted circulating leucocytes by 93% with nitrogen mustard (0.8mg/kg i.a.) over 6d (2 doses), then repeated the experiment. The table shows mean values for baseline and post-embolic steady states for the 2 conditions.

Condition	Ppa (cm H_2O)	Pla (cm H_2O)	$\dot{Q}$b (l/min)	PVR (units)	$\dot{Q}$lym (ml/h)	$\dot{Q}$prt (mg/h)
Normal						
baseline	20.3	6.7	7.4	1.9	5.8	224
post-emboli	33.8	1.0	6.4	5.3	15.5	596
Leucopenic						
baseline	15.9	-0.9	4.7	3.7	5.5	155
post-emboli	28.4	-1.3	3.9	7.9	8.1	216

When leucopenic, the sheep had significantly lesser increases in $\dot{Q}$lym and $\dot{Q}$prt even though the degree of obstruction (PVR) caused by air emboli was greater. Most of the increased lung microvascular permeability that occurs after air emboli is caused by circulating leucocytes. [Supported in part by HL19155 (Pulmonary SCOR) and HL06285 (Program Project)].

VENTILATORY ACCLIMATIZATION DURING CHRONIC HYPOXIA IN GOATS: ROLE OF CAROTID CHEMORECEPTORS. H.V. Forster, G.E. Bisgard and J.P. Klein. Dept. Vet. Sci., Univ. of Wisconsin-Madison, Dept. of Physiology, Med. Col. of Wisconsin and Wood VA Med. Ctr., Milwaukee, WI 53193.

Seven normal (N) goats and 7 goats (D) whose carotid chemoreceptors had been surgically excised were studied under control conditions (P_B = 740 mmHg) and repeatedly during 4-5 days of hypobaria which reduced Pa_{O_2} to ~45 mmHg in the first hour. Prior to and during chronic hypoxia, $\dot{V}_E$ increased 97 and 141% in N goats in response to 4 breaths of N_2 and i.v. injection of NaCN, respectively, but these stimuli only increased $\dot{V}_E$ 25 and 22%, respectively, in the D goats. The N goats did not hyperventilate during the first hour of hypoxia; hence, carotid chemoreceptor stimulation of $\dot{V}_E$ must be countered by a depressant action of hypoxia in the CNS. By 4 hours of hypoxia, hyperventilation was sufficient in the N goats to decrease Pa_{CO_2} by 4 mmHg below control. Subsequently, hyperventilation increased gradually so that by 60 hours Pa_{CO_2} reached its nadir 7-8 mmHg below control. The D goats did not hyperventilate at any point during chronic hypoxia; thus, ventilatory acclimatization during chronic hypoxia in goats is dependent upon intact carotid chemoreceptors. During 15 min of normoxia after 80 hours of hypoxia, $\dot{V}_E$ in N goats decreased slightly (ΔPa_{CO_2} = +2.7 mmHg), but in the D goats it increased slightly (ΔPa_{CO_2} = -2.0 mmHg). This hyperventilation in the D goats may suggest that chronic hypoxia causes changes in suprapontine modulation of $\dot{V}_E$. (Supported by USPHS NIH Grant 15473).

ALTERATIONS IN BLOOD VOLUME AND EXERCISE PERFORMANCE. S.M. Fortney*, E.R. Nadel, C.B. Wenger, J.R. Bove*. J.B. Pierce Fndn. Lab., and Yale Univ. Sch. Med., New Haven, CT. 06519

Blood volume expansion is one result of physical training believed to help improve exercise performance. The present study examined the effects of acute changes in blood volume upon cardiovascular responses during cycle ergometer exercise Six subjects were tested under control conditions, after withdrawal (WD) of 10% of each subjects blood volume and 2 weeks later after reinfusion (RI) of his blood. Subjects exercised at 60% $\dot{V}O_2$ max for 30 min in the heat (35°C). Esophageal and mean skin temperatures (T_{es} and $\bar{T}_{sk}$) were monitored continuously, forearm blood flow (BF) was measured twice per min and cardiac output ($\dot{Q}$) and heart rate (HR) were estimated at intervals. After WD, $\dot{Q}$ and stroke volume (SV) were significantly lower (12.4 and 6.1% respectively) during the first 10 min of exercise, with no significant differences in HR. After RI, $\dot{Q}$ was increased slightly, HR was 12-14/bpm lower and SV was 20% greater during the last 10 min of exercise. WD shifted the vasodilatory threshold to a higher T_{es} and decreased the slope of the BF:T_{es} relationship. In contrast, after RI, the vasodilatory threshold was lowered and the slope increased. In conclusion, volume depletion significantly decreased cardiac performance during the first 10 min of exercise, after which peripheral vasoconstriction helped maintain $\dot{Q}$ and SV. Hypervolemia significantly raised SV, lowered HR and allowed increased skin perfusion at a given T_{es}.

ASSESSMENT OF DL_{O_2} BY COMPARISON OF SIMULTANEOUS O_2 AND INERT GAS EXCHANGE. J.B.Fortune* and P.D.Wagner.Dept.of Med.Univ. of Calif. San Diego, La Jolla, Ca.92093.

Determination of pulmonary diffusing capacity for O_2(DL_{O_2}) requires assumption of the degree of ventilation-perfusion $\dot{V}_A/\dot{Q}$ inequality. This prevents the accurate determination of that part of the alveolar-arterial O_2 difference ((A-aD_{O_2})) solely due to diffusion limitation.Because diffusion equilibration is much more rapid for inert gases than O_2, the multiple inert gas elimination technique can be used to separate the components of the (A-a)D_{O_2}.Ten anesthetized dogs were hyperventilated with 6% and ~8% O_2 and $\dot{V}_A/\dot{Q}$ distributions were measured. Five of the dogs were additionally ventilated with 10% and 12% O_2. Mixed expired and arterial P_{O_2} were simultaneously measured under each condition and the difference ((E-a)D_{O_2}) calculated. From the measured $\dot{V}_A/\dot{Q}$ distributions, (E-a)D_{O_2} was predicted assuming no diffusion limitation. For F_{IO_2}=0.06 and 0.08, 93% of the measured (E-a)D_{O_2} values (n= 41) were greater than those predicted. For F_{IO_2}=0.10 and 0.12, there was no detectable difference between measured and predicted (E-a)D_{O_2}. Bohr integration was then used to predict (E-a)D_{O_2} from each $\dot{V}_A/\dot{Q}$ distribution assuming a finite DL_{O_2} distributed uniformly in proportion to $\dot{Q}$. Measured (E-a)D_{O_2} could best be predicted for all dogs when $D_{L_{O_2}}$=22 ml/min/mmHg. This is consistent with previously reported values and suggests the absence of measurable diffusion limitation in all but severe hypoxic conditions. Supported by NIH grants HL 17731, HL 07212, HL 00111 and the Francis North Foundation.

INTERPRETATION OF URINARY ESTRIOL LEVELS BASED UPON URINARY CREATININE EXCRETION. William C. Foster and Robert A. Donato.* Lab.Clin.Chem., Jeanes Hosp., Philadelphia, PA 19111

The relationship between urinary estriol and viability has been established.[1] Variation in urinary output has created questionable results. Urinary creatinine is accepted as being remarkably constant. It was conceived that urinary estriol be expressed as mg.estriol per gm.creatinine. However, the latter is dependent on renal function. It was thought important to study the relationship between urinary estriol per 24 hr.urine and urinary creatinine. In 330 pregnant subjects the urinary output ranged from 240-4200 ml/24 hrs. Only 8% of the subjects were in the 1300 ml.range, but 36% were below. Creatinine in 28% of the subjects was below 0.6-1.5 gm/24 hrs., and 10% above, leaving 62% within normal range. In comparing estriol in urinary output, vs. creatinine, 29% of subjects were found to have estriols below 12 mg. in the latter, and 9% in the former. Therefore, urinary creatinine was 300% higher in subjects in the danger zone.

1. Greene, J.W., Jr. and Touchstone, J.C., Amer.J. Obstet.Gynec. 85:1-9 (1963)

HYPOTENSION ASSOCIATED WITH PLASMA PROTEIN FRACTION (PPF): EFFECTS OF ACETATE ION. Michael A. Fournel*, Ruben J. Guzman* and John Hidalgo* (SPON: N. Goldstein). Research Division, Cutter Laboratories, Inc., Berkeley, California 94710

Transient hypotension has been an infrequent but potential complication associated with the clinical use of Plasma Protein Fraction (PPF) even when the absence of kinin-system components has been demonstrated. Monitoring both the systemic arterial blood pressure and coronary arterial flow in anesthetized dogs, a dialyzable component of PPF has been shown to be a vasodilator and hypotensive agent. Further analysis revealed this agent to be acetate ion which alone produces a dose-dependent transient decrease in mean arterial pressure and increase in coronary artery flow when infused intra-venously at rapid rates. Subsequent studies in dogs subjected to deep hemorrhagic shock demonstrated a significant improvement in pressor response to volume expansion with acetate-ion-poor PPF as compared to PPF containing acetate.

EFFECTS OF HYPOTHERMIA INDUCED BY 5-THIO-D-GLUCOSE ON TREADMILL PERFORMANCE IN THE HEAT. R. P. Francesconi and M. Mager. US Army Res. Inst. Environ. Med., Natick, MA 01760.

To assess the effects of 5-thio-D-glucose (5-TG) induced hypothermia on treadmill performance in the heat, male rats (270-330 g) were administered 5-TG (10 mg) intravenously and placed under restraint in a cold room (4°C) until a rectal temperature (Tre) of 30°C was achieved. A 1.0 ml blood sample was taken at this time; the animals were then placed in a hot environment (35°C) where they exercised on a treadmill (9.14 m/min) to hyperthermic exhaustion (42.5 - 43°C), and a second blood sample was obtained. Preinduced hypothermia had no effects on K^+ levels, but did cause a significant ($p<.02$) increment in lactate levels. Hypothermia significantly ($p<.001$) increased their endurance capacity when compared with normothermic controls. Because of the initially reduced Tre among the hypothermic animals, increments (°C/min) in Tre during exercise were significantly greater ($p<.005$). Initial hypothermia did not prevent the occurrence after exercise of significant increases in circulating lactate ($p<.001$) and potassium (K^+) ($p<.05$). Treatment with 5-TG induced significant ($p<.001$) increases in circulating glucose levels which were reduced ($p<.001$) at termination of the run. These results indicated that while preinduced hypothermia increased endurance capacity, no additional effects on thermoregulation or the clinical chemical indices of heat injury were observed.

EFFECTS OF DANTROLENE SODIUM ON ADRENAL CORTICAL FUNCTION K. T. Francis and M.E. Hamrick.* Univ. of Ala.in B'ham. Birmingham, Alabama 35294.

Dantrolene, a hydantoin derivative that became commercially available in 1974, has been used to decrease skeletal muscle spasticity in patients with various disorders. Adverse effects of dantrolene include abnormal liver function test, hepatic injury and alteration of the hepatic MFO cytochrome P450 system. The effective dose of dantrolene that has been shown to decrease hepatic cytochrome P450 also causes adrenal enlargement with a marked reduction in serum glucocorticoids. The ratio os adrenal wet wt./body wt. was significantly ($P<0.05$) increased following 5 days injection with a minimum dose of 25mg dantrolene/kg body wt. The minimum effective dose of dantrolene that significantly ($P<0.05$) lowered serum glucocorticoids was 50mg/kg body wt. Serum glucocorticoids were reduced in half following 5 days treatment with 100mg dantrolene/kg body wt. The level of serum glucocorticoids were 80% of control serum levels and the adrenal wet wt./body wt. ratio was 85% of control values following 3 days of recovery after 5 days pretreatment with 100mg/kg of dantrolene. It appears that dantrolene acts in a similar manner as phenytoin to reduce adrenal glucocorticoid secretion with a possible alteration or reduction in the negative feedback response to the pituitary with resultant enlargment of the adrenals. (Supported by Rehab. Res. & Training Center Grant No. R68)

UPTAKE AND OXIDATION OF GLUTAMATE BY THE HEART. C.J.Frangakis*, M.Yeh*, S.Makhija* and H.McDaniel.UAB and VAMC,Birmingham,Ala.

Myocardial glutamate metabolism is of interest because it is one of the few amino acids taken up by the heart in man. It has been reported to have a protective effect on the heart during ischemia. Using isolated heart cells and tissue slices we have studied the uptake and oxidation of glutamate. In both preparations there is rapid uptake of glutamate with a peak at 10 min. of incubation followed by rapid oxidation over a period of 30 min. to carbon dioxide. The K_m and V_{max} for glutamate uptake was determined in isolated rat heart cells prepared by the procedure of Frangakis and McDaniel so that they are not damaged by physiological concentrations of calcium. The uptake of glutamate was temperature sensitive and substrate specific, with a K_m of 6 mM and a V_{max} 4 nmoles/mg of protein. The oxidation of glutamate to carbon dioxide was 2 fold greater than the rate of uptake under these conditions. Addition of glucose to the incubation medium stimulated glutamate uptake. Determination of the enzymes involved in glutamate metabolism in rat heart homogenates revealed that the glutamate-oxaloacetate transaminase was 4 fold more active than glutamate-pyruvate transaminase.Glutamate dehydrogenase was also present in the cell sap. Our conclusions are: Plasma glutamate levels are rate limiting in the metabolism of glutamate by the heart, It is readily oxidized to carbon dioxide, and GDH is present in the soluble fraction and plays a role in the metabolism of glutamate.

A MODEL OF STATIC LUNG HYSTERESIS. D.G. Frazer* and G.N. Franz. ALOSH, NIOSH, CDC, DHEW, and Dept. of Physiology and Biophysics, WVU, Morgantown, West Virginia 26506.

A model of the lung representing the mechanical events described by a static pressure (PL) - volume (VL) curve assumes that VL is the composite of many small volume elements, i.e., $VL=\Sigma Vu$, where Vu represents the volume of an elementary open lung "unit". If all such units are similar in size, and if No equals the number of open units, then $VL=[No]Vu$. Differentiation with respect to PL gives $dVL/dPL=[No]dVu/dPL + [Vu]dNo/dPL$. Here, dVL/dPL represents the compliance of the static P-V curve and dVu/dPL that of a single open unit, while dNo/dPL reflects the recruitment-derecruitment process. During lung deflation dNo/dPL is zero when PL > 4cm H_2O and, therefore, in that region $dVL/dPL=[No]dVu/dPL$. We assume that open elementary units display negligible hysteresis and thus have a compliance proportional to whole lung compliance during deflation. Hence, dNo/dPL can be determined for inflation, and deflation below 4cm H_2O, from the compliance equation. We have applied this model to interpret the difference between the quasi-static compliance of a rat lung, ventilated at 3.82cc/min, and that observed during small sinusoidal perturbations (0.5cc, 0.5Hz) superimposed on the quasi-static expansion. From this we conclude that elementary lung units (1) are recruited continuously throughout inflation, and (2) close during deflation between +3 and +0.5cm H_2O, as found previously (Respir. Physiol. 36:121-129, 1979). Supported in part by DOE Contract #EY-77-C-21-8087.

EFFECT OF SQ 14,225 (CAPTOPRIL) ON DEVELOPMENT OF RENAL HYPERTENSION IN RATS. M.J. Fregly and O.E. Lockley*, Dept. Physiol. Univ. Florida, Gainesville, Florida 32610.

Forty-two female rats (230-260 g) made hypertensive by renal encapsulation with latex envelopes were divided into 3 equal groups. Two groups were administered the angiotensin converting enzyme inhibitor, SQ 14,225, in drinking water at 25 and 50 mg/kg/day respectively. The third group was untreated. A fourth group (14 rats) served as normotensive control group. Systolic blood pressures (BP) and body weights were measured weekly during a 4 week control and 8 week experimental period. Both doses protected against elevation of BP to that of hypertensive controls but failed to maintain BP at normotensive levels. Mean body weights of all renal encapsulated rats were less than that of normotensive controls. SQ 14,225 had no additional effect on body weight. To test completeness of blockade, angiotensin I (1.25, 6.25, 12.5 and 25 µg/kg) was administered i.v. to anesthetized rats following carotid artery cannulation. Although neither dose of SQ 14,225 prevented a rise of BP to administered angiotensin I, the lower dose was the more effective. At autopsy heart and kidneys of treated groups were reduced from that of hypertensive controls but were significantly greater than that of normotensive controls. These results suggest that SQ 14,225 provided significant protection against elevation of BP in renal hypertensive rats. (Supported by grant HL 14526-7 from NHLBI).

CARDIOVASCULAR RESPONSES TO A MENTAL TASK: EFFECTS OF SEX, AGE, AND RESTING BLOOD PRESSURE. M.A.B.Frey and R.M.Siervogel* Wright State University School of Medicine, Dayton, OH 45431

Cardiovascular variables were noninvasively monitored in 56 male and female subjects, 8 to 78 years, supine, at rest and during a visually presented mental task. Data were analyzed for correlations between cardiovascular variables and subject sex, age, and resting systolic (SP) and diastolic (DP) pressures and for responses to the stress, ie differences from resting values (T test). Male subjects had lower resting HR and longer heart-to-carotid pulse transmission time (PTT) than females. At rest, pre-ejection period (PEP), PEP/left ventricular ejection time (LVET), respiratory interval, and DP were correlated (+) and PTT and amplitude of the carotid dD/dt correlated (-) with age; and dD/dt correlated (-) with resting blood pressure (BP). The mental task elicited a significant rise in SP (+9 mmHg), DP (+7 mmHg), and HR (+6 bpm), with a corresponding decrease in LVET (-6 msec). SP response was correlated (+) with age; HR change was correlated (+) with resting SP for males only. PEP was unchanged by the stress; however, PEP/LVET was significantly increased, and dD/dt depressed. The changes in dD/dt were correlated (-) with resting BP and age, ie older subjects and those with higher resting BP had greater depression of dD/dt during the task. This study provides evidence that even a simple, nonthreatening mental task elicits cardiovascular responses which are influenced by age and resting BP. (Supported in part by NHLBI grant # RO1-HL19931-01.)

THE EFFECTS OF HEPARIN PRETREATMENT ON THE DEVELOPMENT OF PULMONARY EDEMA FOLLOWING MICROEMBOLIZATION. Mitchell Friedman and Gilbert C. White, II.* (SPON: A.L. Finn). Univ. of N.C., Chapel Hill, N.C., 27514.

Glass bead microembolism has previously been shown to result in non-cardiogenic pulmonary edema in dogs (JAP 43:51, 1977) and increased capillary permeability in sheep (Fed. Proc. 37:636, 1978). Pretreatment with heparin appeared to prevent the edema in dogs but not prevent lung capillary permeability changes in sheep. We have reinvestigated this problem in anesthetized dogs who were embolized with 0.01 g/kg of hollow glass beads (<130 µm in diameter) injected into the right atrium to produce a 3-fold increase in pulmonary artery pressure. All animals were serially studied for one hour after microembolization. 7 animals were pretreated with 500 units/kg beef heparin (Group I). 4 dogs received no heparin pretreatment (Group II). Post-embolization changes in vascular pressures and gas exchange were similar in the 2 groups. The wet/dry lung weight ratio was 4.63±.27 (SD) in Group I which is similar to normal dogs in our laboratory. This ratio was significantly increased ($p<.001$) in Group II to 5.52±.16 (SD). In addition, a progressive decrease in clotting factors V, VIII, X, XI, XII and fibrinogen were noted in pulmonary arterial blood samples in Group II after microembolization. Thus, glass bead microembolism-induced pulmonary edema in dogs is associated with an intravascular coagulopathy and is prevented by anticoagulation. (Supported by N.C. Lung Association and N.C. United Way.)

SOUND CYCLES EXERT CIRCADIAN PHASE CONTROL AFTER PARTIAL SUPRACHIASMATIC NUCLEUS LESIONS IN THE SQUIRREL MONKEY. C.A. Fuller, F.M. Sulzman and M.C. Moore-Ede. Dept. of Physiology, Harvard Medical School, Boston, MA 02115.

The circadian system of intact squirrel monkeys (Saimiri sciureus) can be entrained to a 24 hr period by light-dark and food availability cycles but not by cycles of sound intensity, social cues, environmental temperature or drinking. In isolation chambers with constant light and food ad lib., the monkeys' circadian rhythms free-run with periods of ~25 hrs. However after lesioning the suprachiasmatic nuclei (SCN) of 3 animals, we observed phase control of the circadian rhythm of drinking to a 24 hr period even in constant light and food ad lib. Another animal after SCN lesions showed relative coordination with a modulation of the circadian period at the same phase of the cycle at which entrainment occurred in the other animals. The temporal cue perceived by the SCN-lesioned monkeys was a 24 hr cycle of sound intensity since when all sound cues entering the chamber were obscured by continuous white noise, the circadian rhythm of drinking free-ran. Preliminary histology demonstrates that this occurs after subtotal destruction of the SCN. Thus when the integrity of the SCN is damaged, the circadian timing system of the squirrel monkey becomes sensitive to sound cycles. (Supported by NIH Grant NS 13921.)

EFFECT OF AMRINONE ON CONTRACTION AND POTASSIUM-INDUCED CONTRACTURE OF CAT VENTRICULAR MUSCLE. M.S. Gaide*, A.M. Ezrin*, R.F. Palmer*, H. Gelband and A.L. Bassett. University of Miami School of Medicine, Miami, Fl. 33101

Amrinone, a bipyridine derivative (MW = 187.2), increases cardiac contractile force in vitro and in vivo. To further evaluate its inotropic activity, isolated cat ventricular muscles were exposed to amrinone (18.7, 50 and 100 µg/ml) in the presence or absence of beta-adrenergic blockade (nadolol) at 32-36°C during: 1) isometric contractions (0.5 Hz) in Tyrode's solution (4 mM K^+, 150.8 mM Na^+, 2.7 mM Ca^{2+}) and 2) maintained depolarization and contracture induced by high K^+ Tyrode's (133 mM K^+, 21.8 mM Na^+, 2.7 mM Ca^{2+}). Amrinone increased peak contractile force (P_o) in a concentration-dependent manner while reducing K^+-induced contracture force (P_c). In nadolol (10^{-5} M), amrinone (100 µg/ml) increased $P_o \sim 40\%$, although in 5 min P_o declined and stabilized at $\sim 25\%$ above control; amrinone decreased both initial and secondary phases of high K^+ contracture in nadolol-treated muscles. Results suggest that amrinone may affect P_o and P_c Ca^{2+} differentially and/or disparate Ca^{2+} pools may initiate and maintain phasic cardiac contraction and K^+-contracture. (Supported in part by NIH grants HL 19044, HL 07188, HL 05849 and Florida Heart Association--Suncoast Chapter.)

EFFECTS OF ISOPROTERENOL ON REGIONAL BLOOD FLOW AND SEGMENTAL SHORTENING IN CONSCIOUS DOGS WITH MILD CORONARY STENOSIS. Kim P. Gallagher*, Toshiaki Kumada*, Alex Battler*, Dan McKown*, W. Scott Kemper*, John Ross, Jr., M.D. University of California School of Medicine, La Jolla, California 92093

Seven dogs were studied 2-3 weeks after implantation of ultrasonic dimension gauges in the subendocardium (ENDO) and, subepicardium (EPI) supplied by the circumflex artery. To create a steady level of increased cardiac work, we infused isoproterenol (ISO, 0.2 µg/kg/min IV) and measured regional myocardial blood flow (MBF) with 7-10 µm microspheres before and after mild coronary stenosis (CS), which caused no dysfunction at rest, was produced by a hydraulic cuff. Without CS, regional MBF and segmental shortening (%ΔL) in ENDO and EPI increased comparably during ISO. With CS, as expected, ENDO MBF was reduced more than EPI MBF; however, %ΔL in EPI decreased much more than %ΔL in ENDO. To examine this phenomenon more closely, linear regression analysis of regional %ΔL vs. regional MBF was performed: ENDO, $y=0.92x - 0.21$, and EPI, $y=1.56x - 1.24$, where y = %ΔL ISO/%ΔL REST and x = MBF. The ENDO x-intercept (0.13±0.14 ml/min/g) which represents the regional MBF at which active %ΔL ceased was significantly less than the EPI x-intercept (0.77±0.11/ml/min/g) ($p<.02$). Thus, EPI function was more sensitive to ischemia than ENDO function during ISO stress, EPI flow being well preserved when EPI shortening ceased. We conclude that ISO can produce severe ENDO ischemia in the presence of mild CS, and that severe EPI dysfunction can occur without EPI ischemia.

INTERACTION OF 2.45 GHz MICROWAVE RADIATION WITH EMBRYONIC QUAIL HEARTS. M.J. Galvin, M. Lieberman and D.I. McRee*. NIEHS, Res. Triangle Park, N.C. 27709 and Dept. Physiology, Duke, Univ. Med. Center, Durham, N.C. 27710

Exposure to nonionizing radiation has been reported to induce a variety of systemic alterations during embryonic development. This study was designed to examine effects of microwave radiation on cardiogenesis. Japanese quail embryos were exposed during the first 8 days of development to 2.45 GHz microwaves at an incident power density of 5 mW/cm^2 or 20 mW/cm^2. The specific absorption rate was 4.03 and 16.2 mW/g, respectively. The ambient temperature for each exposure was set to maintain the embryonated eggs at 37.5°C. This did not preclude thermal gradients in the irradiated embryos since microwaves may not be uniformly absorbed. The results show neither exposure level was capable of inducing changes in either the morphology of the embryonic heart, or the ultrastructure of the myocardial cells. Lactate dehydrogenase and glutamic-oxaloacetic transaminase activities were not different from the control. The values for these two enzymes for all groups were approximately 350 Sigma Units, and 40 Karmen Units per 100 µg protein. Although creatine phosphokinase (CPK) activity in the 5 mW/cm^2 exposure group was similar to the control value, the CPK level was lower (255 vs 131 IU/100 mg protein, $P < 0.01$) in the 20 mW/cm^2 group. Although the data indicate that 2.45 GHz microwave irradiation at 5 mW/cm^2 has no effect on the developing myocardium, there appears to be an effect at 20 mW/cm^2 on the cytoplasmic enzyme content.

Na-DEPENDENT CHLORIDE ACCUMULATION IN NECTURUS GALLBLADDER. J.F. García-Díaz*and W. McD. Armstrong. Department of Physiology, Indiana University School of Medicine, Indianapolis, IN 46223.

Membrane potentials, Ψ_{mc}, and intracellular chloride activities, a^i_{Cl}, were measured in epithelial cells of Necturus gallbladder with conventional open tip and Cl-selective (Corning 477315) microelectrodes at various external Na concentrations, $[Na]_o$. Gallbladders were mounted in a divided chamber that exposed their mucosal surface, and perfused with HCO_3-free phosphate Ringer's solution containing, in mEq/l, 100 Cl, 5.4 K and 0,10,20,60 and 100 Na. Tris was substituted for Na. Ψ_{mc} did not change significantly when $[Na]_o$ was changed from 100 mEq/l (-53.4 ± 0.4 mV, 130 impalements, 9 animals) to 0 mEq/l (-52.0 ± 1.0 mV, 53 impalements, 4 animals). a^i_{Cl} increased in a saturable fashion from 10.3 ± 0.4 mEq/l (0 mEqNa/l, 29 impalements, 4 animals) to 17.3 ± 0.3 mEq/l (100 mEqNa/l 105 impalements, 9 animals), i.e. a^i_{Cl} increased from 1.03 to 1.82 times its equilibrium value. These results provide further evidence for electroneutral NaCl co-transport in gallbladder. The saturable behavior of Cl accumulation may reflect either a kinetic or an energetic limitation of the co-transport mechanism. (Supported by USPHS grants 12715; HL 23332. J.F.G-D. partially supported by the Ministerio de Educación y Ciencia, Spain.)

AEROSOL PENETRATION AS AN INDEX OF AIRWAY FUNCTION IN HEALTHY SUBJECTS. C.S. Garrard, T.R. Gerrity, R.V. Lourenço, and D.B. Yeates. Section of Environmental Medicine, Department of Medicine, University of Illinois at Medical Center, Chicago, IL

Ten healthy nonsmoking subjects inhaled a 7.9 µm aerodynamic aerosol labelled with Tc-99m using a standard inhalation pattern (V_T = 700 ml, mean $\dot{V}$ = 500 ml/sec). Each subject was studied twice. The deposition of aerosol and the retention at 24 hours was measured (PA) with a gamma camera. Tests of forced expiratory pulmonary function were performed prior to each study (FEV_1, FVC, MMFR, EF_{50} and EF_{75}). A deposition profile across a horizontal band in the mid lung region was divided anatomically into central (I), mid (II) and peripheral (III) regions. The ratio of gradients (III/II) of initial deposited activity across these regions for the first and second studies were correlated with the 24 hour retention ($r = 0.91$, $DF = 8$, $P < 0.001$ and $r = 0.88$, $DF = 7$, $P < 0.001$). Deposition patterns were reproducible within subjects. However intra-subjects changes in III/II ratios were associated with commensurate changes in the 24 hour retention which fell on the group data regression ($r = 0.84$, $DF = 17$, $P < 0.001$). In contrast no correlation was found between the indices derived from the forced expiratory maneuver and deposition gradient analysis. These data suggest that the ratio of the deposition gradients (III/II) is a reliable index of aerosol penetration and that this test may be a more discriminating measurement of airway function during resting ventilation than a forced expiratory maneuver.

IN VITRO VENTRICULAR FUNCTION OF HEARTS REMOVED FROM ALLOXAN-DIABETIC RATS. David W. Garber, Deborah A. Berkich* and James R. Neely. Dept. of Physiology, Hershey Med. Cent., The Penn. State Univ., Hershey, PA 17033

Ventricular function was determined under high work conditions by perfusing isolated hearts with buffer containing various substrates. When perfused with buffer containing 11 mM glucose, hearts from 48-hour alloxan-diabetic animals (60 mg/kg) performed less mechanical work under maximal work conditions and utilized glucose at a slower rate. Glucose utilization was not stimulated by increased cardiac work. Insulin improved ventricular function and glucose utilization, but glycolytic rate remained depressed. Hearts from 37.5 mg/kg alloxan-diabetic animals (removed 7 days following alloxan injection) performed less maximum work, but submaximal work loads were maintained at normal levels. Glucose utilization was stimulated to normal rates by increased mechanical work. Addition of pyruvate, β-hydroxybutyrate or palmitate to the perfusate along with glucose restored normal mechanical function of hearts from 60 mg/kg alloxan diabetic animals. Rates of palmitate oxidation were normal at both high and low levels of cardiac work. These data indicate that much of the depressed mechanical activity of diabetic hearts perfused in vitro is related to the inability of these hearts to stimulate glucose utilization with increased mechanical activity. (This work was supported by grant #HL-20484).

CIRCADIAN INFLUENCE ON RAT MUSCLE GLYCOGEN METABOLISM DURING AND AFTER HIGH-INTENSITY EXERCISE. Lawrence P. Garetto* and Robert B. Armstrong. Boston Univ., Boston, MA 02215

Marked diurnal fluctuations in resting rat skeletal muscle glycogen contents are known to occur but the functional consequences of these rhythmic changes are unknown. We tested the hypothesis that circadian rhythms significantly alter muscle glycogen metabolism during and/or after high-intensity exercise. Randomly assigned day (D) and night (N) groups of rats performed 5 1-min runs at 75 m x min^{-1} with 1-3 min rests at 0800 and 2000 hr, respectively. Glycogen contents of soleus (S) and red (R) and white (W) gastrocnemius muscles and liver (L) were determined 0, 0.5, 1, 2, and 4 hr following running in rested control and exercised animals. Resting 0 hr glycogen concentrations were lower in S (-26%), R (-23%), W (-18%), and L (-40%) in N as compared with D, but the rate of glycogen loss for each tissue during exercise was similar for D and N. This suggests N would have been unable to exercise as long as D. Rates of glycogen restoration after exercise were significantly higher (about 2-fold) in D in R, W, and L, although restoration rates in S were similar at the two times. We conclude that circadian fluctuations primarily affect glycogen metabolism during recovery from high-intensity exercise, although the different initial glycogen levels would be expected to influence performance time. (Supported by NIH Grant AM18123)

THE EFFECT OF PILOCARPINE NITRATE ON THE GOBLET CELLS OF THE RABBIT TRACHEA. Louis A. Gatto and Robert F. Amberger*. Biological Sciences, SUNY at Cortland. Cortland, N.Y. 13045.

The trachea of the albino rabbit was studied histochemically for mucus-secreting structures and their morphological changes following the subcutaneous administration of a cholinergic agent, pilocarpine nitrate, for a period of 12 consecutive days. Alcian blue (AB) at pH 2.6 was used to stain acidic mucus, while periodic acid-Schiff (PAS) with amylase pretreatment were used to stain neutral mucus. Routine hematoxylin and eosin preparations served as reference. Submucosal mucous glands were absent in the upper airways below the level of the cricoid cartilage. Only those epithelial cells that reached the tracheal lumen were counted, and their specific secretory types were expressed as percents of the total of cells counted. Thus, goblet cells (AB+ and PAS+) were 32% in the control animals, and they increased by a 69% following pilocarpine stimulation. Point-counts were not entered here since the average width of the cells that reached the lumen increased following pilocarpine treatment ($t=9.84$; $P<0.001$). The acidic goblet cell population (AB+) increased from 27% in the controls to 49% in the pilocarpine-treated group. The neutral (PAS+) goblet cells showed no significant differences between the two groups ($t=0.395$; $P>0.60$). Systemic pilocarpine stimulation was therefore followed by a significant increase in the number of AB+ goblet cells which appeared independent from changes in the number of PAS+ goblets in an experimental model where submucosal glands are not present.

AMPHOTERICIN B AND ION FLOW ACROSS CANINE TRACHEA. J.T. Gatzy* and R.C. Boucher* (SPON: M. Friedman). Depts. of Pharmacol. and Med., Univ. of N.C., Chapel Hill, N.C., 27514.

Exposure of the luminal surface of many epithelia to amphotericin B (AmB) induces changes in paracellular ion permselectivity and active transcellular cation flow. Our study evaluated the effects of AmB on ^{22}Na, ^{42}K and ^{36}Cl unidirectional fluxes across excised, short-circuited canine trachea. 10^{-5}M AmB raised short-circuit current (I_{SC}) from 65 to 87 $\mu a/cm^2$ and conductance (G) from 2 to 8.2 mS/cm^2. All unidirectional ion flows increased. Net Na^+ reabsorption (lumen → serosa) increased from 1.1 to 2.9 $\mu eq/cm^2hr$, Cl^- secretion fell from 1.6 to .3 $\mu eq/cm^2hr$, and a K^+ secretion of .86 $\mu eq/cm^2hr$ was induced. These changes persisted for at least 60 min. The effects of 3 x 10^{-6}M were qualitatively similar. 10^{-6}M AmB induced a K^+ secretion of .18 $\mu eq/cm^2hr$ without increasing any other ion flux, G, or I_{SC} by more than 25%. We suggest that AmB increases the cation permeability of the luminal membrane of the tracheal mucosa. Actively accumulated cell K^+ leaks into the lumen whereas an increased entry of luminal Na^+ into the cells of the epithelium raises active Na^+ extrusion across the basal lateral membrane. The decrease in Cl^- secretion could result from a fall in the electric PD across the luminal membrane (cell becomes less negative) and/or an increase in cell Na^+ that reduces coupled Cl^-—Na^+ entry across the basal lateral barrier.
(Supported by HL-16674 and HL-22924.)

STATIC MAXIMAL PRESSURES IN CHILDREN. Cl. Gaultier* and R. Zinman* (SPON. L.A. Engel). Dept. of Physiology and Meakins-Christie Laboratory, McGill University, Montreal, Canada.

Static maximal pressures were studied in 118 school children 7 to 12 years of age. Lung volumes were measured in a volume-displacement body plethysmograph. Both inspiratory and expiratory maximal static pressures ($P_I max$, $P_E max$), measured with a pressure transducer, were generated at functional residual capacity (FRC), and near total lung capacity (TLC) and residual volume (RV). As in adults, with increasing lung volume $P_I max$ decreased and $P_E max$ increased. Both $P_I max$ and $P_E max$ increased with age and were greater in males than in females.

			$P_I max$			$P_E max$		
AGE	SEX	NO.	RV	FRC	TLC	TLC	FRC	RV
7-8	M	11	77(24)*	70(24)	28(23)	99(23)	83(16)	57(17)
	F	15	70(29)	59(21)	18(14)	74(25)	65(18)	47(20)
9-10	M	26	102(23)	97(22)	41(26)	123(27)	101(33)	63(22)
	F	16	86(25)	77(27)	31(19)	108(40)	88(32)	52(23)
11-12	M	23	115(27)	105(23)	48(27)	161(37)	133(33)	85(25)
	F	27	108(29)	98(25)	34(20)	126(32)	101(26)	62(27)

*mean value ± 1 standard deviation.

The increase in pressure with age may underestimate that which occurs in muscle force, since pressure is equal to force divided by surface area and the latter also increases with age. Furthermore the ability of a young child to generate large pressures may relate to a small surface area.

THE LONG UTERINE ACTION OF DEAMINO-OXYTOCIN IN RATS, by Diana Gazis*, J. Roy* and I. L. Schwartz. Dept. of Physiol. & Biophysics, Mt. Sinai Med. School, N.Y., NY 10029

Single injections of deamino-oxytocin produced uterine responses in rats which lasted up to 3 hours. The increments in response length as the injected dose of oxytocin was doubled were 3.7 ± 0.5, 3.0 ± 0.4, and 3.5 ± 0.4 min for pressor, milk ejection, and uterine responses (values which are similar to its plasma half-life). For deamino-oxytocin, these increments were 3.0 ± 0.6 (pressor), 3.4 ± 0.4 (milk ejection) and 26 ± 4 (uterus in vivo). The plasma half-life of deamino-oxytocin is thus probably similar to that of oxytocin and is therefore not responsible for its long uterine action.

The uterine response to deamino-oxytocin could be inhibited at any point in its time course by injections of the competitive inhibitor, N-acetyl-O-methyltyrosine-oxytocin; therefore, the long uterine action (which persists after deamino-oxytocin has been cleared from the plasma) is maintained by specifically-bound deamino-oxytocin and is not merely triggered by bound peptide.

N-acetyl-O-methyltyrosine-oxytocin inhibited similar doses of deamino-oxytocin and oxytocin to a similar degree. By this test, deamino-oxytocin and oxytocin bind to the rat uterus with similar affinities, and therefore strong binding is not the reason that specifically-bound deamino-oxytocin remains in the uterus after the plasma has been cleared of peptide.

LOCALIZATION OF AN ASCENDING INOTROPIC PATHWAY. G. Steven Geis and Robert D. Wurster. Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153

Cardiac parameters were monitored in cats during peripheral nerve stimulation before and after making spinal lesions. Cats were paralyzed, β-blocked and the right carotid sinus (CSN) and right peroneal nerves (PN) were isolated. After thoracotomy, a strain gauge arch was sutured to the right ventricle and a left ventricular catheter was inserted. Strain gauge output and dP/dt served as indices of ventricular contractility (VC). Hearts were paced by electrodes inserted into the ventricle and a laminectomy was performed to expose spinal cord segment L4.

CSN stimulation produced VC decreases which were attenuated by simultaneous PN stimulation. After making a lesion in the right dorsolateral sulcus (DLS) at L4, the VC decrease during stimulation of both nerves was greater than before the lesion but less than that produced by CSN stimulation. After making bilateral DLS lesions, the response to stimulation of both nerves was not different from the response to CSN stimulation.

The data suggest an ascending pathway located bilaterally in the DLS inhibits CSN induced vagal inhibition of ventricular contractility. (Supported by NIH Grant HL08682)

SUPPRESSION OF VOLUNTARY ALCOHOL INTAKE IN MICE IS STEREO-SPECIFIC FOR (-)NALOXONE BUT THE RESPONSE IS NOT SPECIFIC FOR ALCOHOL. R. Thomas Gentry*, Ann Ho*, and Vincent P. Dole. Rockefeller Univ., New York, N.Y. 10021.

The effect of the opiate antagonist Naloxone on voluntary alcohol consumption (VAC) was tested in 24 NCS mice heterogeneous in alcohol preference. After ad lib choice between a 10% alcohol solution and water for 5 months, and following a 14-hour deprivation of both fluids, VAC was measured by automatic recording of licks in a 2-bottle, 10% ethanol-water choice test. Immediately before testing, each mouse was injected i.p. with (-)Naloxone, with (+)Naloxone or with the saline vehicle in a repeated-measures design, counterbalanced for order of treatment.

Two doses of the active isomer, (-)Naloxone, significantly decreased VAC: -34% at 1 mg/kg and -58% at 2 mg/kg. There was no decrease in water consumption. The stereospecificty of the drug was shown by a lack of effect on VAC of (+)Naloxone at either dose.

The response specificity for alcohol was tested in similar experiments offering a 5% sucrose-water choice. Both the 1 mg/kg and 2 mg/kg doses of (-)Naloxone decreased sucrose but not water consumption.

Thus, the suppression of VAC was shown to be stereo-specific for the opiate antagonist (-)Naloxone, but not specific for alcohol. It is suggested therefore, that this effect of Naloxone is part of a general anorexia rather than a specific effect on alcohol consumption.

ISOLATED RAT LUNGS RELEASE PROSTAGLANDIN I_2 (PGI_2) DURING HYPOXIC VASOCONSTRICTION. J. G. Gerber*, N. F. Voelkel*, A. S. Nies*, L F. McMurtry, and J. T. Reeves. Univ. Colo. Hlth. Sci. Cntr., Denver, CO 80262

Inhibitors of prostaglandin synthesis potentiate the pulmonary pressor response to airway hypoxia in both intact animals and isolated lungs. This finding suggests that a vasodilator prostaglandin is generated during hypoxic vasoconstriction. To test this idea, we infused 2-4 μCi of 14C sodium arachidonate into the arterial line of six isolated rat lungs perfused with physiological salt solution. 96% of the sodium arachidonate was taken up by the lung in a single pass. Nonspecifically bound sodium arachidonate was washed out of the lung by 15 min of perfusion with salt solution containing 0.1% albumin. Ten min before ventilation with hypoxic gas (0% O_2-5% CO_2-95% N_2), the perfusate was switched to salt solution containing washed rat erythrocytes. Radioactivity of the effluent perfusate was then measured before and during hypoxia. Acute hypoxia lowered the PO_2 of the effluent perfusate to 31±3 mmHg and increased perfusion pressure by 10±2 mmHg. Effluent radioactivity increased from 164±29 dpm/ml before hypoxia to 232±39 dpm/ml during hypoxia ($P<.05$). Thin layer chromatography of the effluent sampled during hypoxic vasoconstriction showed that 6 keto $PGF_{1\alpha}$, the hydrolysis product of PGI_2, and arachidonic acid were the major products. These results indicate that the synthesis and release of PGI_2, a pulmonary vasodilator, by the rat lung is increased during hypoxic vasoconstriction. Blockade of PGI_2 production probably accounts for potentiation of the hypoxic pressor response by prostaglandin synthetase inhibitors (USPHS NIH Grant HL-14985, HL-21308).

STIMULATION OF CHLORIDE TRANSPORT BY EXOGENOUS AMINO ACIDS IN APLYSIA CALIFORNICA INTESTINE. G. A. Gerencser. Dept. of Physiology, University of Florida, College of Medicine, Gainesville, Florida 32610.

Isolated Aplysia californica intestine mounted in a conventional Ussing chamber maintains a stable transmural p.d. (serosa side negative). This has been shown to be due to a net active chloride transfer from mucosa to serosa. Mucosal glycine elicited rapid, sustained increases in transmural p.d. and short-circuit current. Serosal glycine had no significant effect on the measured electrical characteristics. The change in short-circuit current increased curvilinearly with increasing concentrations of mucosal glycine. Mucosal glycine enhanced transmural p.d. and short-circuit current after serosal ouabain had abolished the electrical characteristics. Determination of unidirectional chloride fluxes using ^{36}Cl in paired preparations when their short-circuit currents matched revealed a marked asymmetry between the M → S and S → M fluxes of this ion after mucosal glycine addition, the M → S flux being significantly greater ($P < 0.05$). The average net mucosal to serosal chloride flux was significantly greater than the corresponding mean short-circuit current ($P < 0.05$). These results suggest that a coupling mechanism exists between the actively transported amino acid and chloride. (Supported by Whitehall Foundation, Grant #78-156 ck-1).

MATHEMATICAL MODEL PREDICTIONS OF THE ROLE OF INHALED PARTICLES IN AIRWAYS DISEASE. T. Gerrity, P. Lee and R. Lourenço. Section of Environmental Medicine, Department of Medicine, University of Illinois at the Medical Center, Chicago, IL.

To assess the airway dose of an inhaled aerosol a mathematical model of aerosol deposition and mucociliary clearance was developed. The deposition pattern was calculated as a function of airway generation in the Weibel A lung model and took into account inertial impaction, gravitational sedimentation and Brownian diffusion. The mucociliary clearance phase of the model was constructed by applying the equation of flow continuity to the particle density in each airway generation. The number of particles in each generation was calculated as a function of time and leads to mucus transport rates and clearance curves which are in good agreement with experimental data. Based on these calculations, 8 micron aerodynamic diameter particles, inhaled during resting breathing, produce a surface concentration which rises nearly two orders of magnitude between the trachea and the segmental bronchi, and then falls nearly three orders of magnitude toward the terminal bronchioles. However, the residence half-times of deposited particles increases from 2 minutes at the segmental bronchi to 300 minutes at the terminal bronchioles. These results suggest that particle concentration may play an important role in the pathogenesis of large airways disease whereas particle residence time may play a more important role in the pathogenesis of small airways disease.

DIFFERENT SENSITIVITY OF CANINE ENDOCARDIUM AND EPICARDIUM TO HYPOXIA, HYPERKALEMIA AND ACIDOSIS. Robert F. Gilmour, Jr.* and Douglas P. Zipes. Krannert Inst. of Cardiology, Indiana University School of Medicine, Indianapolis, In. 46202

Why ventricular endocardium (EN) develops less conduction delay than epicardium (EP) during acute myocardial ischemia (MI) following coronary artery occlusion is not clear. To determine if EN and EP have intrinsically different sensitivities to metabolic alterations that occur during MI (↓pO_2, ↓pH, ↑$[K^+]_o$), mongrel dogs (n=15) were anesthetized with secobarbital and a 2 x 2 cm square of right ventricle was excised. A cut through the midwall divided EN from EP. Both pieces, now separated, were pinned to the floor of the same chamber with EN and EP surfaces up, superfused with Tyrode's solution (pO_2>400, pH-7.35 $[K^+]_o$-4.0) or altered Tyrode's (AT, pO_2<70, pH-6.9 $[K^+]_o$-8.0) at 37°C and stimulated at 2 Hz. Action potentials (AP) from EP muscle (EPM) and EN muscle (ENM) or Purkinje fibers (ENP) were recorded simultaneously using standard microelectrode techniques. During AT superfusion, all cells showed progressive decreases in AP duration, amplitude, dV/dt, and resting potential and increases in conduction time. The magnitude of these changes were EPM>ENM>EP. Refractoriness outlasting repolarization and spontaneous repetitive responses were more common in EP than EN. EPM was unresponsive after 15 min. AT but ENM and ENP were still responsive. These data indicate that EP is more severely affected by ↓pO_2, ↓pH, and ↑$[K^+]_o$ than EN *in vitro* and may partially explain differential effects observed during MI *in vivo*.

REFLEX STIMULATION OF SUBMUCOSAL GLAND SECRETION BY MECHANICAL IRRITATION OF THE LARYNX IN CATS. Victor German*, Iris Ueki*, and Jay Nadel, CVRI, UCSF, San Francisco, CA 94143

We studied the effects of mechanical irritation of the larynx on tracheal gland secretion using our microcollection technique for sampling of individual submucosal glands. Cats were anesthetized with chloralose and urethane, paralyzed with gallamine, and ventilated mechanically. We stimulated the larynx gently with a soft cotton pledget for 30 sec and collected 1 min samples from single mucous glands over a 10 min period. The secretory rate increased from 18.6 ± 2.0 to 47.8 ± 4.1 nl/min (mean ± SE; $p<0.05$; n=8) during stimulation and returned to control values within 4 min. Cooling both vagi (0°C to -3°C) or cutting both superior laryngeal nerves abolished the effect of laryngeal stimulation on mucous gland secretion. Electrical stimulation of the central end of a cut superior laryngeal nerve (5 V, 20 Hz, 15 sec) increased the secretory rate 200 ± 50% (mean ± SE; $p<0.05$; n=6) within 1 min of the stimulus and established the afferent pathway of this pulmonary reflex. Thus, mechanical stimulation of the larynx reflexly stimulates submucosal gland secretion; the response may be an integral part of the normal cough reflex. (Supported in part by USPHS NIH Grant HL-06285)

INFLUENCE OF ENDOGENOUS PITUITARY HORMONES ON GASTRIN (G) LEVELS OF PAIR FED RATS. Robert M. Ghrist* and Lenard M. Lichtenberger. U. of Texas Med. Sch., Houston, TX 77030.

Previous studies have shown that gastrin levels are decreased by hypophysectomy (H). Since these changes can be indirectly caused by alterations in food intake, we used pair-fed rats to study the influence of prolactin (PRL) and growth hormone (GH) on antral (A) and serum G levels. Ectopic pituitary transplants (PT) can be used to increase PRL levels in H rats; however, the effect of PT on GH has not been adequately studied. In this experiment, female normal (N), H, and H rats with PT were pair-fed, 11 gms./day, for a 10 day period, after which they were sacrificed. Serum G, GH, and PRL levels and AG conc. were determined by radioimmunoassay. The results are shown below, X ± SEM, ( ) = no. rats/group, * and ∇ represent statistical difference ($P < 0.05$) in comparison to N and H values, respectively.

Group	PRL(ng/ml)	GH(ng/ml)	G(fmol/ml)	AG(nmol/g)
N	479±219(5)	10.9±2.3(13)∇	25.4±3.2(13)	4.44±0.44(13)∇
H	38±164(5)	3.5±0.5(5)*	24.5±2.5(9)	8.13±0.71(12)*
H+PT	639±126(9)∇	11.9±1.9(15)∇	16.9±3.6(15)	7.53±0.58(15)*

Conclusion: The increase seen in AG levels after H in pair-fed rats is not due to changes in either PRL or GH levels, and other pituitary factors may be involved. (This work was supported by NIH grant AM 20686).

WHEELCHAIR VS ARM CRANK ERGOMETRY: CARDIORESPIRATORY RESPONSES. R.M. Glaser, M.N. Sawka*, S.W. Wilde*, A.G. Suryaprasad* and T.C. von Luhrte*, Wright State Univ. Sch. of Med., Dayton, OH 45435 and VA Med. Ctr., Dayton, OH 45428

The purpose of this study was to compare cardiorespiratory responses to wheelchair ergometer (WERG) and arm crank ergometer (ACE) exercise at power output (PO) levels of 30, 90, 150 and 210 kpm·min^{-1}. Wheelchair-dependent (N=2) and able-bodied (N=7) subjects performed WERG and ACE exercise on a combination ergometer. Exercise at each PO was 6 min in duration followed by 5 min of rest. Steady state values for oxygen uptake ($\dot{V}O_2$), pulmonary ventilation ($\dot{V}E$), cardiac output (CO), heart rate (HR), stroke volume (SV), arteriovenous O_2 difference ($a-\bar{v}\ O_2$) and systolic blood pressure (SBP) were determined at each PO. With the exception of $a-\bar{v}\ O_2$, each variable tended to increase with PO. Generally, $\dot{V}O_2$, $\dot{V}E$, CO, HR and SBP responses were consistently higher for WERG than ACE exercise at each PO level. No consistent differences, however, were found for SV and $a-\bar{v}\ O_2$. For a given $\dot{V}O_2$, similar response magnitudes were found for each variable between the two exercise modes. These results suggest that energy wasteful propulsive biomechanics are responsible for the greater cardiorespiratory stresses of WERG exercise. Therefore, wheelchair designs utilizing arm crank propulsion should be studied as a possible means to reduce stresses of locomotion. (Supported in part by the Medical Research Service of the VA).

INHIBITION OF PORCINE PULMONARY VASCULAR NEUROTRANSMISSION BY ENDOTHELIAL STRIPPING AND SUPERIOR MESENTERIC ARTERIAL OCCLUSION (SMAO) SHOCK. Thomas M. Glenn*, Lynne Eddy and Stan Greenberg, Univ. S. Ala., Coll. Med., Mobile, AL 36688

The role of the vascular endothelium on sympathetic neuroeffector transmission was examined in porcine, intralobar pulmonary arteries (PA), and veins (PV). Small (1-2mm O.D.) rings of PA and PV were subjected to transmural nerve stimulation (TNS; 10V, 2msec duration and delay, 0.5-32 Hz, for 30 sec). The responses of PA and PV to TNS were contraction sensitive to inhibition by blockade of alpha receptors. Destruction of the vascular endothelium by mechanical stripping decreased the responses of PA and PV to TNS. This procedure did not effect the responses to potassium ion or norepinephrine. Depression of endothelial prostacyclin (PGI) synthesis with tranylcypromine also inhibited the responses of PA and PV to TNS. Histology of PA and PV revealed destruction of the endothelium with no damage to the media. The responses of PA and PV to TNS obtained from SMAO shocked swine were depressed similar to that observed with endothelial stripping and tranylcypromine when compared with PA and PV obtained from sham shocked swine. These data suggest that TNS in porcine PA and PV is modulated by the vascular endothelium, possibly by the actions of PGI. The data also suggest that SMAO shock may, in part, depress TNS secondary to degenerative changes in the vascular endothelium.
(Supported in part by RCDA HL 00438-03, HL 22216 and HL 22177)

REGIONAL MYOCARDIAL BLOOD FLOW DURING ACUTE RIGHT VENTRICULAR FAILURE. Frank L. Gold and Robert J. Bache. University of Minnesota, Minneapolis, Minnesota 55455.

Previous data have shown that right ventricular (RV) failure (F) during acute systolic hypertension (SH) can be reversed by augmenting perfusion pressure in the right coronary artery. Thus, RVF has been attributed to ischemia which occurs when maximal coronary vasodilation is achieved so that further increase in myocardial blood flow (MBF) cannot occur. This study examined RV and left ventricular (LV) endocardial (endo) and epicardial (epi) MBF (ml/min·g) with 15μ microspheres in 7 awake dogs. RVSH with and without F was produced by a hydraulic occluder on the main pulmonary artery; RVF was defined by a rise in RV end-diastolic pressure and a fall in arterial pressure (AP). Finally, MBF was measured after AP was restored by constriction (C) of the descending aorta. Heart rate was held constant by pacing.

	CONTROL	RVSH	RVSH + F	RVSH + F (C)
RVP(mmHg)	39/5±2/1	81/8±9/2*	70/14±6/1	89/10±6/2*
AP(mmHg)	85±4	88±6	58±7*†	88±6
RVMBF	0.81±.10	1.74±.33*	0.91±.22	1.40±.18*
RV endo/epi	1.16±.05	1.40±.18	0.79±.09†	1.36±.23*
LVMBF	0.96±.14	1.10±.10	0.80±.11†	1.17±.17

Values are mean±SE. *P<0.05 vs. control †P<0.05 vs RVSH

These data show that significant RV subendocardial underperfusion occurred during RVF. Restoration of AP reversed this perfusion deficit and corrected RVF without altering mean RVMBF. LV endo/epi remained uniform throughout.

DOPAMINE (D) AND PHENTOLAMINE (Phe) EFFECTS ON LUNG VESSELS. H. Goldberg*, W. Macedo*, R. Graham*, J. Rabson*, and L. Oppenheimer*. (Spon: N.R. Anthonisen). U. of Man., Winnipeg.

Two groups of blood perfused Zone II canine lobes were studied. Alveolar pressure was kept constant at 5 cmH_2O with 100% O_2. Artery pressure was varied by incremental lowering of an inflow reservoir. In group 1, D was given as a bolus into the circulating blood at 4-7 microgm/ml. D in 4/4 lobes decreased vascular compliance (Civ) 25+19 SD % (control =1.73+.75 ml/cmH_2O, D=1.22+.42). In one lobe pulmonary edema prevented accurate determination of Civ. In group 2 Phe (1 microgm/ml) increased Civ in 5/5 lobes 12+9% (control = .98+.2, Phe=1.1+.23). D plus an additional dose of Phe was associated with a further increase in Civ 5+9%. Part-Palv was determined at 50% maximal control flow (P_{50}). With D P_{50} increased in 5/5 lobes. With Phe P_{50} decreased in 5/5 lobes. When D was added with an additional dose of Phe no consistent change in P_{50} was observed. The slopes of pressure-flow curves from maximal to 25% of maximal flow were determined. With D the slope decreased in 5/5 lobes (mean control=37.2 ml/min/cmH_2O + 30.2 S.D., mean D=23.9+10.9). With Phe the slope increased in 5/5 lobes (mean control=30.5+12.6, mean Phe=35.4+15.7). Adding an additional dose of Phe plus D there was no consistent change in this value. We conclude that D causes an increase in flow resistance and a decrease in vascular compliance. Phe causes a decrease in resistance and an increase in compliance. Phe ameliorates the effects of D. (Supported by the Manitoba Heart Association).

CANINE P WAVE MORPHOLOGY AND NON-SA NODAL SUPRAVENTRICULAR PACEMAKER LOCALIZATION. J. M. Goldberg, M. H. J. Lynn,* and B. Neely.* Univ. Calif. Davis, CA. 95616

P wave morphology recorded in limb leads I, II and III was correlated with atrial activation observed with non-SA nodal supraventricular pacemaker localization in anesthetized, open chest dogs. Bipolar electrograms were recorded from six sites along the sulcus terminalis and nine sites on the interatrial septum. In addition, two electrograms were recorded from the left atrium. Pacemaker localization was neurally shifted to multiple non-SA nodal, supraventricular sites in the interatrial septum, along the sulcus terminalis, and to the left atrium. Non-SA nodal, supraventricular pacemaker localization produced upright P waves in the three leads. However, the amplitude was less than with SA nodal activation and they exhibited more notching. The small positive component at the initial inscription of the P wave which has been observed with SA nodal pacemaker localization was either absent or lower in amplitude and in many instances biphasic. Activation originating from the posterior left atrium produced low amplitude oscillations in lead I and a prominent negative P wave in lead II and III. These results demonstrate that atrial activation can originate from multiple atrial sites. The P waves observed with these pacemakers have distinct morphological characteristics which enable differentiation between nodal and non-SA nodal supraventricular, pacemaker localization. (Supported by Golden Empire Heart Association Grant 78-N116.)

A MECHANISM FOR THE ENDOTOXIN SHOCK ACCELERATING ACTION OF LEUCINE. R.D. Goldfarb, P. Weber, J. Eisenman, D.J. Loegering Depts. of Physiol., Biochem., Albany Med. Col., Albany, N.Y.

We have previously documented the ability of exogenous leucine (leu) to accelerate the endotoxin shock syndrome. In further experiments we tested the hypothesis that the mechanism for this action of leu was via an induction of pancreatic insulin hypersecretion. Pentobarbital anesthetized rats were injected with 1 mg/100g S enteritidis endotoxin (E) (LD90) or vehicle and infused with either Krebs Henseleit (KH) or 0.153 M leu in KH with a dose of 7.6 mMoles/kg. The leu administered E shocked rats expired sooner than the KH controls (185±10[8] vs 274±24[9] min, (x±SE[N]). Plasma leu of KH infused group was elevated in E shocked rats at expiration. Plasma leu levels of leu infused E shocked rats were significantly higher than the leu infused sham rats at 30 min after infusion of leu. Insulin levels dropped significantly 30 min after infusion in the KH infused E shocked rats but at 2 hr insulin concentration approached preshock levels. In the leu infused E shocked rats, insulin levels were markedly higher 2 hr after leu infusion. In the sham shocked rats infused with either KH or leu, no significant changes of insulin levels were noted at 30 min or 2 hrs post-infusion. Therefore, the shock accelerating action of leu may be due to a direct stimulation of insulin secretion inducing a prolonged hyperinsulinemia.
(Supported by NIH HL-19977 and HL-00947)

NEURAL COUPLING BETWEEN DIAPHRAGM AND PARASTERNAL INTERCOSTAL (PS) MUSCLES. M.D. Goldman, P. Kosch*, E.N. Bruce*, J. Mead, M. Altose, and N.S. Cherniack. Case Western Reserve Univ., Cleveland, Oh. 44106 and Harvard School Pub. Hlth., Boston, Mass. 02115

In normal man, Taylor (J.Physiol., 1960) showed that PS muscles are active in quiet inspiration (bipolar needle electrodes), in contrast to inspiratory intercostal (ICI) muscles in other areas of the thorax. We have observed activity in PS surface EMG recordings during attempts to produce "pure" diaphragmatic contractions against a closed airway, and questioned whether such activity represented contraction of PS or other more distant muscles. We therefore compared activity measured from surface and fine bipolar wire electrodes in PS and other intercostal muscles with surface recordings of diaphragm EMG (Edi) during a variety of respiratory maneuvers. We found PS, but not other ICI, EMG activity during spontaneous quiet breathing. In addition, whenever Edi was detectable there was associated PS activity, and increases in Edi were accompanied by increases in PS EMG. In contrast, during both inspiratory and expiratory maneuvers in which the diaphragm was voluntarily inhibited, PS EMG was diminished or absent in the face of large signals from other ICI muscles. During CO_2 rebreathing PS EMG paralleled Edi rather than other ICI EMG. We conclude that PS muscles are driven primarily by neural activation coupled to that of the diaphragm, while receiving in addition, inputs in common with those to other ICI muscles.

METABOLIC VERSUS VASOCONSTRICTIVE RESPONSE TO COLD WATER IMMERSION. R. F. Goldman, H. Friedman*, G. Gee*, G. Bynum*, J. Bogart*, C. Levell* and L. H. Strong*. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760.

Predicting water immersion heat loss requires factors for four types of insulation: 1) internal vasoconstriction 2) subcutaneous body fat 3) external clothing 4) surface still water film. The still surface film provides ~ 0.05 clo (~ 111 $W \cdot m^{-2} \cdot {}^{\circ}C$), dropping to ~ 0.02 clo (~ 278 $W \cdot m^{-2} \cdot {}^{\circ}C$) with water/body motion. Wet suits providing 2 to 3.5 clo in air (3 to 1.8 $W \cdot m^{-2} \cdot {}^{\circ}C$), when immersed provide ~ 0.3 clo (21 $W \cdot m^{-2} \cdot {}^{\circ}C$); insulation values vary by ± 10 to 20% when worn by individuals of varying body conformation. Subcutaneous fat provides, on average, 0.08 clo per cm of skinfold thickness ($\bar{x}$ of double fat fold at 4 sites). The insulation range from vasodilation to vasoconstriction covers the range 0.2 to 0.8 clo (32 to 8 $W \cdot m^{-2} \cdot {}^{\circ}C$) including modest fat. Data on 26 Ss (26 nude and 10 wearing 3 types of wet suits, 0.4 to 0.75 clo) with body fat of 11 to 22% have been fitted, some by empiric and some by rationally derived modelling techniques. Calculated heat input from core to skin ranged from 16 W/m^2 nude in 28°C water, to 90 W/m^2 nude in 20°C water. Whether a given individual adopts a metabolic response (i.e. shivering to increase heat production) or an insulative response (i.e. vasoconstricting to reduce heat loss) appears to depend on the ratios % body mass and fat/m^2 surface area. Shivering may not be of benefit unless there is substantial subcutaneous and/or external insulation, presumably because shivering degrades both the internal (vasoconstrictive) and surface (still water film) insulation.

BIPOLAR ELECTRICAL IMPEDANCE CARDIOGRAPHY FOR SYSTOLIC TIME INTERVAL MEASUREMENTS. Frank Gollan and Joanne McDermott*. Miami VA Medical Center and University of Miami, FL. 33125.

Tetrapolar electrodes have been used for electrical impedance cardiography (Nyboer, 1940: Kubicek, 1964) because they create a more uniform current density, reduce the capacitive component and eliminate electrode polarization errors. These are of importance in attempts to calculate stroke volume from the first derivative of the impedance wave (DZ/DT). However if DZ/DT is used as a time marker to measure the velocity of cardiac mechanics, two electrodes may be sufficient. This was accomplished by automatic analysis of 64 cycles for ECG and DZ/DT features in a healthy volunteer for each of 3 positions: vertical, supine and 10° head-down tilt. Analysis showed a high correlation between the signals derived from both electrode systems. For the pre-ejection period the r value was 0.803, the slope 0.66, the intercept 35.3 and difference of means <0.001. The corresponding values for the left ventricular ejection time were 0.989, 1.03, -6.5 and <0.001. Thus, if DZ/DT is used for the definition of systolic time intervals, the bipolar electrode system has the advantage of simplicity. (Supported by the VA Res. Service, the Deborah Heart and Lung Center and the American Heart Association.)

ACTH 4-10 AND ELECTROPHYSIOLOGICAL AND CONTRACTILE PARAMETERS OF RAT SKELETAL MUSCLE. Eulogio Gonzalez and Fleur L. Strand. Biol. Dept., N.Y.U., New York 10003.

The effects of hypophysectomy and replacement therapy with ACTH 4-10 (0.01 ug; 0.05 ug and 1.0 ug/kg) were studied in situ in the rat. The extensor digitorum longus (EDL) muscle was stimulated directly or indirectly through its nerve (supermax. stimulation; 10/sec; 0.01 msec duration for indirect and 0.1 msec for direct stimulation) for 30 min and isometric muscle contractions and muscle action potentials (APs) recorded.

ACTH 4-10 has a biphasic effect, facilitatory at low dosages (0.01 ug/kg) and inhibitory at high dosages (1.0 ug/kg) on contraction amplitudes of hypx rats. In addition, APs recorded from EDL of ACTH 4-10 treated rats (0.01 and 0.05 ug/kg) were higher only during the early phase of continuous stimulation. The peptide had no effect on either mechanical or electrophysiological characteristics of EDL following direct stimulation, or after stimulation of the peripheral stump of the cut motor nerve. Miniature endplate potentials (mepps) were recorded from the extensor digitorum brevis (EDB) to test the effect of intra-arterial administration of this peptide on neuromuscular transmission. An increase in mepp frequency, with no change in mepp amplitude or of the resting membrane potential, was observed. These results suggest that ACTH 4-10 is a neurotropic hormone acting centrally on motoneurons to modulate neuronal activity.

EFFECT OF AGE, SEX AND PHYSICAL FITNESS ON THERMOREGULATORY COMPETENCE TO THERMAL TRANSIENTS. R. R. Gonzalez, L. Berglund*, C. C. Haselgrave*, and L. A. I. Stolwijk. J. B. Pierce Foundation, Yale University, New Haven, CT. 06519

A standard thermal transient protocol was used to study the activity of the thermoregulatory system. $\dot{V}O_2max$ ($ml \cdot min^{-1} \cdot kg^{-1}$) on each person was obtained prior to experiments. 35 unacclimated males and females (age 8 to 67 yr) were each exposed (0-clo) for 1 h at T_a 29° C with a 20° C T_{dp} followed by increases in T_a ($1.5\ C \cdot min^{-1}$) up to 50 C. Responses at T_a 50 C/20 C T_{dp} were observed for 30 min at which time T_{dp} was increased to 30 C at the same T_a for 30 min. T_a and T_{dp} were decreased to 10 C and maintained for 1 h. Continuous measurements were made of T_{es}, $\bar{T}_{sk}$, heart rate, metabolic rate (M), weight loss by evaporation (E_{sk}), chest sweating and thermal discomfort. Analysis of transients to heat showed that: (1) better fit persons had earlier $\dot{m}_s$ onset; $\Delta E_{sk}/\Delta \bar{T}_b$ composed of $.1\ \bar{T}_{sk} + .9\ T_{es}$ was linearly related to $\dot{V}O_2$ max ($r = .76$). In response to cold transients: (1) females, regardless of age group, had a $> \Delta M/\Delta \bar{T}_b$ than males; in both, a significant decline in the $\Delta M/\Delta \bar{T}_b$ occurred with age > 40 yrs.
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SELECTIVITY AND DEVELOPMENTAL PERMEABILITY CHANGES FOR THE ALVEOLAR EPITHELIUM. Barbara Goodman and Douglas Wangensteen. Dept. Physiol., Univ. of Minn., Minneapolis, Minn. 55455

To investigate developmental changes in alveolar epithelial permeability, we studied isolated Ringer-perfused lungs from mature and immature rabbits. Test molecules in Ringers solution were instilled into the trachea and monitored in the recirculated perfusate. The (permeability)(area)/(diffusion coefficient) ratios for small molecules compared to sucrose in 4-week-old rabbits are listed below (± SEM).

	D-Glucose	L-Glucose	Mannitol	Erythritol	Urea
$\frac{(PA/D)_x}{(PA/D)_s}$	4.36±.4	1.06±.03	.75±.055	.87±.03	1.50±.16

This indicates that in 4-week-old rabbits the alveolar epithelium is not selective for small molecules. The D-glucose data probably indicate a special transport process. The urea data can be accounted for by transport through the epithelial cell membranes. Preliminary data for albumin, ovalbumin, and sucrose show a similar lack of selectivity in adults. A comparison of the urea and sucrose permeabilities in adult and immature rabbits is shown below.

$(cm/sec) \times 10^8 \pm SEM$	Adult	4-week-old	1-week-old
$P_{sucrose}$	.31±.04	.81±.08	1.93±.17
P_{urea}	2.45±.35	5.00±.58	5.22±1.05

All these data are suggestive of an epithelial transport process such as bulk flow or pinocytosis, with decreasing "permeabilities" during development. (Supported by NIH Grants HD08981 and HL21376.)

EFFECT OF INTRAVENTRICULAR NOREPINEPHRINE AND SEROTONIN ON THE CHANGE IN FIRING RATE AND THERMAL SENSITIVITY OF NEURONS IN THE PREOPTIC/ANTERIOR HYPOTHALAMUS OF UNANESTHETIZED RABBITS. C.J. Gordon* and J.E. Heath. Univ. of Illinois, Urbana.

Rabbits were stereotaxically implanted with a guide tube to direct a microelectrode into the preoptic/anterior hypothalamus (POAH), a thermode and thermocouple reentrant tube to change and measure POAH temperature, respectively, and a cannula in the lateral ventricle (LV) to inject norepinephrine (NE) and serotonin (5-HT). Firing rate of single units was recorded while the temperature of the POAH was clamped near 41°C and 34°C. Thermally studied neurons were treated with an LV injection of NE or 5-HT (30-100 µg/animal). Occasionally the single units were thermally stimulated before and after the application of a neurotransmitter. Fifty-five units were studied for both thermal responsiveness and sensitivity to NE or 5-HT. 34% of the cells were classified as warm-sensitive (WS), 24% as cold-sensitive (CS), and 42% as thermal insensitive (IS). 5/5 CS cells were facilitated by NE and 3/4 CS cells were inhibited by 5-HT. 6/14 WS cells were facilitated by 5-HT and 2/5 WS cells were inhibited by NE. NE inhibited 10/17 IS cells while 5-HT inhibited 4/7. 5-HT converted 7/13 WS into IS units. NE converted 3 IS units into CS units, increased the cold sensitivity of 1 CS unit, and converted 2 CS units into WS units. The effect of NE and 5-HT on neuron firing rate and thermal sensitivity provides evidence for the role of these neurotransmitters in thermoregulation. Supported by NIH training grant HEW PHS GM7143.

EFFECT OF HEAT STRESS ON THE BARORECEPTOR CONTROL OF HEART RATE. A.J. Gorman* and D.W. Proppe*. (SPON: J.M. Johnson) Univ. of Texas Health Sci. Ctr., San Antonio, Texas, 78284.

The objective of this study was to investigate the effect of heat stress on the baroreceptor reflex control of heart rate (HR) in the unanesthetized, chronically instrumented baboon. To enable manipulation of arterial blood pressure (AP), perivascular balloon occluders were placed around the thoracic descending aorta and inferior vena cava (IVC). AP and blood temperature (T_{bl}) were measured from axillary artery catheters. Following determination of HR responses to graded changes in AP (± 5 to ± 25 mmHg) in the normothermic baboon (T_{bl} < 37.6°C), the animal was subjected to environmental heating (T_a = 40-45°C) which was maintained until T_{bl} rose to 39.6-39.9°C. HR responses to graded aortic and IVC occlusions were again determined at peak T_{bl} and these HR responses were compared to those obtained in normothermic state. Accompanying the rise in T_{bl} was a 50-70 bpm increase in HR, but AP showed no significant change. The results of this study are: 1) the HR increases to the hypotensive stimulus was much larger than the HR fall to a hypertensive stimulus of the same magnitude in both states; 2) at peak T_{bl}, the overall HR-AP response curve shifted upward; 3) at peak T_{bl}, the HR sensitivity ($\Delta HR/\Delta AP$) to AP changes was diminished for reductions in AP, but enhanced for increases in AP. These results suggest that the thermoregulatory and baroreceptor reflex systems interact in the control of HR. (Supported by NIH grant #HL-21451)

AUTOREGULATION OF RENAL BLOOD FLOW (RBF) IN THE NONFILTERING KIDNEY. Robert Gotshall, Thomas Hess* and Timothy Mills.* Wright State University, Dayton, Ohio. 45435

The present investigation examined the role of the renal tubular system in the autoregulation of RBF. To examine the possibility of macula densa feedback regulation of RBF, the nonfiltering kidney model was used. In this model, glomerular filtration and tubular flow are stopped thus eliminating the possibility of macula densa feedback regulation of RBF. Seven dogs were prepared with a single nonfiltering kidney. To establish that the nonfiltering kidney was indeed nonfiltering, Sodium Ferrocyanide was infused at the end of the experiment. Sodium Ferrocyanide was precipitated as Prussian Blue and the kidney slices observed microscopically. Compared to normal filtering kidneys, the nonfiltering kidneys demonstrated a lack of Prussian Blue in the tubules. Therefore, there was an absence of glomerular filtration throughout all populations of nephrons in these nonfiltering kidneys. Changes in RBF in response to successive progressive reductions in renal perfusion pressure in 20 mm Hg steps were monitored using an electromagnetic flowmeter. RBF did not change significantly from Control (136 ± 21 ml/min) until blood pressure was reduced from 139 ± 6 to 74 ± 7 mm Hg. Thus, RBF was effectively autoregulated in the absence of tubular flow passed the macula densa. This indicates that changes in tubular flow or composition are not necessary for autoregulation of RBF. (Supported by NIH-HL 21382.)

THE EFFECT OF ELEVATED P_{CO_2} ON LACTATE METABOLISM DURING STEADY-STATE WORK. T. GRAHAM*, B.A.WILSON* and M.SAMPLE* (SPON.: J. K. Barclay). Human Kinetics, University of Guelph, Guelph, Ontario Canada N1G 2W1

Studies on isolated muscle and resting man have demonstrated that altering CO_2 stores influences lactate metabolism and/or tissue release. Subjects (n=6) performed steady-state work for 30 min. while inspiring 0,2,4 or 6% CO_2 and 21% O_2. They were tested on 8 occasions, 4 at 50% and 4 at 65% $\dot{V}_{O_2}$ max. Arterialized-venous blood P_{CO_2} increased in proportion to F_I CO_2 ($p<0.05$); the mean P_{CO_2} was 34.8 mm. with 0% CO_2 and 51.7 mm. with 6% CO_2. Blood pH had a similar but inverse relationship, decreasing from 7.371 to 7.233 ($p<0.05$). $\dot{V}_I$ increased directly with P_{CO_2} ($p<0.05$), but no differences were found for $\dot{V}_{O_2}$ or $\dot{V}_{CO_2}$. The R decreased in proportion to P_{CO_2} ($p<0.05$) at both work loads. Blood lactate was reduced ($p<0.05$) with CO_2; at 65% $\dot{V}_{O_2}$ max. lactate had an inverse, linear relationship with blood P_{CO_2} ($p<0.05$) (the mean lactate decreased 43% from 3.88 $mM \cdot \ell^{-1}$ with 0% CO_2 to 2.22 $mM \cdot \ell^{-1}$ with 6% CO_2). The O_2 cost of the work was unaltered implying the supression in blood lactate was not due to changes in anaerobic metabolism. The R shift suggests that carbohydrate metabolism was inhibited and lipid metabolism enhanced. (Supported in part by NSERC (A6466) and R.A.B. (University of Guelph)).

EFFECTS OF VOLUME ABSORPTION ON TISSUE EXCLUSION OF ALBUMIN IN THE SMALL BOWEL. D. N. Granger, N. A. Mortillaro, P. R. Kvietys, and J. C. Parker, Dept. of Physiology, Univ. of South Alabama, Mobile, Alabama 36688.

The excluded volume fraction for interstitial albumin (F_E) was estimated in the small bowel of 10 cats under control conditions and during net volume absorption. ^{51}Cr red cells, $^{99}T_C$ - DTPA, and ^{125}I - albumin activities in blood, lymph and tissue were used to estimate tissue blood volume, interstitial volume (V_I) and albumin space, respectively. Net transmucosal volume flow ($J_{v,m}$) was determined using a volume recovery method. Assuming lymph is representative of interstitial fluid we estimate a control F_E and V_I of 0.40 ± .02, and 27 ml/100g, respectively. V_I and lymph flow (Jv) increased as $J_{v,m}$ increased such that $V_I = 1.05\ (J_{v,m}) + 23.7$ ($r=.86$, $P<.01$) and $J_v = .23\ (V_I) - .58$ ($r=.80$, $P<.01$). A significant inverse correlation was observed between F_E and V_I, i.e., $F_E = -1.8\ (V_I) + .87$ ($r=-.88$, $P<.01$). The results of this study indicate that the exclusion of macromolecules from the interstitium is significantly reduced during net volume absorption. The significant interstitial expansion during absorption should serve to greatly increase the hydraulic conductance of the interstitial matrix thereby facilitating the removal of newly absorbed volume by the intestinal capillaries and lymphatics. Supported by HL 22569 and 22392

RELATIONSHIP OF EXTRAVASCULAR LUNG THERMAL VOLUME (Ve) TO EXTRAVASCULAR LUNG MASS (Me). B.A. Gray, R.C. Allison*, R.M. Smith*, B.E. Pennock, and J.T. Myers*. Pulmonary Disease Section, V.A. Medical Center and Department of Medicine, University of Oklahoma, Oklahoma City, OK 73104

To measure Ve we have used thermal (T) and dye (D) dilution curves recorded in the aorta after sequential injections of 1.5 mg indocyanine green dissolved in 5 ml 5% dextrose at 0°C into the right atrium (RAT and RAD) and left atrium (LAT and LAD) in closed-chest dogs. Curves were corrected for recirculation using a mono-exponential extrapolation corresponding to at least 50% of the downslope ($r \geq 0.99$). Mean transit time ($\bar{t}$) from each curve and the flow (F) from the RAT curve were used to calculate Ve:

$$Ve = F\left[(\bar{t}_{RAT} - \bar{t}_{LAT}) - (\bar{t}_{RAD} - \bar{t}_{LAD})\right].$$

Me was determined as lung mass minus blood mass, based on hemoglobin in lung homogenate (LH) and blood (B). Samples of LH and B were also used to measure blood density ($\rho b = 1.05$) and the specific heats for Me (Se = 0.91) and B(Sb = 0.88) by calorimetry. In theory, $Ve/Me = Se/Sb \cdot \rho b$ or $Ve/Me = 0.985$. In 23 dogs with Me 5.9-17.8 g/kg, Ve/Me = 1.072 ± 0.16 S.D. ($r = 0.870$). In 11 dogs given alloxan, 75-150 mg/kg (Me 8.12-37.4 g/kg) Ve/Me = 0.994 ± 0.12 S.D. ($r = 0.968$). We conclude that Ve accurately measures Me, even in alloxan edema. (Supported by the Veterans Administration and by USPHS NIH grants HL 7155 and HL 7210.)

COLLATERAL BLOOD SUPPLY OF THE CANINE HIND LIMB. J. Grayson, S. Simha and M. Leveson, Department of Physiology, University of Toronto.

In seven nembutal anaesthetized dogs a polyethylene loop was established in the left femoral artery and used to occlude the artery and measure pressure distal to the occlusion. A loop in the femoral vein was used for direct outflow measurement and venous blood sampling. The opposite femoral artery was used for arterial blood sampling. Mean arterial pressure was 155 mm Hg, venous flow was 57 ml/min. Mean a-v O_2 difference was 4.2 ml/100 ml; OER was 21%. After occlusion mean pressure distal was 83 mm Hg rising in 10 mins to 99 mm Hg. Venous outflow fell by 21%, then remained steady; a-v O_2 rose but not significantly. In the territory of drainage of the femoral vein, it may be concluded that despite obliteration of the anatomically dominant arterial input to the leg the arterio-arterial anastomoses are adequate to prevent more than a 21% fall in blood flow and to maintain an adequate oxygen supply. Work supported by Ontario Heart Foundation Grant # 1-35.

INTRAVASCULAR REDISTRIBUTION OF BLOOD VOLUME (BV) INDUCED BY HYPOXIC HYPOXIA (HH). Jerry Franklin Green and Alan P. Jackman*. University of California, Davis, CA 95616.

This study was undertaken to investigate the vascular mechanism responsible for HH induced increases in venous return (VR). A right heart bypass in 10 anesthetized dogs separated VR into splanchnic and nonsplanchnic flows. Each channel drained into a reservoir. Blood was then returned to the pulmonary artery (PA) at constant flow (80 $ml \cdot kg^{-1} \cdot min^{-1}$). Venous resistances and compliances of both channels were calculated from transient and steady-state BV shifts which occurred following rapid drops in venous pressure. Arterial pressure and resistances were also measured. HH to a PaO_2 of 35 mm Hg produced a significant decrease in only arterial resistances ($P<.001$). In another preparation, 8 lungs were isolated by total cardiac bypass. VR drained into a right side reservoir and was pumped into the PA. Pulmonary VR drained into a left side reservoir and was pumped into the femoral arteries. The heart was fibrillated and pump flows matched at 80 $ml \cdot kg^{-1} \cdot min^{-1}$. Left atrial pressure was maintained high enough to keep the lung in zone III. HH produced an average increase in BV in the left reservoir of 190±30 ml as PPA rose from 16±0.8 to 21±0.9 mm Hg (average dog = 25 kg). BV in the right reservoir did not change. These experiments suggest that HH induces an intravascular redistribution of BV from the pulmonary to systemic circulations sufficient to increase mean systemic pressure 34%. (Supported by NHLBI Grant HL 20371)

RUNNING IN CIRCLES. Peter R. Greene* and Thomas A. McMahon. Biomechanics Laboratory, Harvard University, 40 Oxford St., Cambridge, Massachusetts 02138

One technique for simulating the effects of enhanced gravitational acceleration on locomotion is to cause an animal to run along a circular trajectory. In a series of trials, 5 male subjects 20-22 yrs. of age ran at maximum speed along a straight track and then along ruled circular arcs 80, 60, 30, 20 and 12 ft. in radius. A ciné camera operating at 120 frames/sec. recorded the run between markers placed at 10 ft. intervals. The runners were instructed only to run as fast as possible. Results showed that stride frequency was unchanged by running in circles, but the stance phase was substantially increased and the aerial phase decreased, so that running speed was decreased to as little as half the straight-track value. A simple theory may be suggested which assumes that the mean vertical force produced by the anti-gravity muscles has reached a physiological maximum and is therefore independent of running conditions. This theory was found to account for the observations in a satisfactory way. (Supported in part by USPHS, NIH Grants AM 25829 and AM 19638)

LUNG VASCULAR PERMEABILITY CHANGES FOLLOWING ACID ASPIRATION: EFFECT OF ALTERING PLASMA PROTEIN CONCENTRATION. F. A. Crimbert*, J. C. Parker, D. N. Granger, and A. E. Taylor. Dept. of Physiology, Univ. of South Alabama, Mobile, AL 36688

Small lymphatic vessels were cannulated in the open-chested dog and lymph flow (J_L) and lymphatic total protein concentration (C_L) were continuously measured following baseline measurements. The capillary pressure was then increased to 17.5 mmHg ± 1.3 (S.E.M.): J_L increased to 4 ± .85 times control while C_L decreased from 4.6 ± 0.25 to 3.6 ± .3 gm%. Following the tracheal administration of 2 ml/kg of 0.1 N HCl capillary pressure was again elevated to 17.5 ± 1.3 mmHg. J_L and C_L attained new steady state values of 8.5 ± 1.5 times control and 3.75 ± .2 gm%, respectively. In another series of animals the same procedure was followed with the exception that 25 gms of albumin was infused 10 min after the acid insult and furosemide was also administered to the animals (1 mg/kg). In this treatment group, J_L increased to 4.9 ± .9 times control while C_L increased to 5 gm% ± .4 which resulted in part, from an increase in plasma proteins from 6.4 to 7.15 gm%. Thus, acid damage increases vascular permeability as estimated by lymph protein clearance. When plasma protein concentration was increased, lymph protein clearance also significantly increased above normal controls. This would indicate that albumin does not reverse the acid damage, but the lymph protein clearance does appear to be lower than that observed in the presence of acid alone and may reflect changes in Starling forces in non-damaged areas of the lung. Supported by NIH grant No. 22549

VENOUS HYPERTROPHY IN ONE KIDNEY AND TWO KIDNEY GOLDBLATT HYPERTENSIVE RATS. Stan Greenberg, Univ. South Alabama, Medical School, Mobile, AL 36688

Recent studies demonstrated venous hypertrophy in spontaneously hypertensive rats. The possibility existed that this was a genetically linked defect of the vasculature in this model of hypertension. The present study examined portal vein (PV), femoral vein (FV), and pulmonary artery (PA) function and structure in one kidney Goldblatt (1-KGH), and two kidney Goldblatt (2-KGH) hypertensive Wistar-Kyoto rats. Three weeks after induction of 1-KGH or 2-KGH, mean arterial pressure was elevated compared to nephrectomized (NEPHREX) or sham controls. PV, PA, and FV pressures were normal. PV, PA, and FV obtained from both 1-KGH and 2-KGH demonstrated the following compared with PV, PA, and FV obtained from NEPHREX and sham animals: 1) enhanced contractility, 2) decreased extensibility, 3) increased protein content, 4) increased wet weight, 5) increased incorporation of precursors of membrane glycoproteins, 6) increased incorporation of leucine and lyscine, and 7) increased synthesis of prostaglandins. These data demonstrate that venous changes and hypertrophy occur in 1-KGH and 2-KGH models of hypertension. These changes are linked to the hypertensive process and are not merely unrelated genetic changes. The mechanism of the hypertrophy is currently under investigation and remains to be defined. (Supported in part by RCDA HL 00438-03, HL 22216, and HL 22177)

FLUID SHIFTS AND ENDOCRINE RESPONSES DURING CHAIR-REST AND WATER IMMERSION IN MAN. J.E. Greenleaf, E. Shvartz‡ S. Kravik‡ and L.C. Keil. NASA, Ames Res. Ctr., Moffett Field, CA 94035

To determine the effect of external water pressure per se on intercompartmental fluid volume shifts, plasma and urine electrolyte, osmotic and endocrine responses were compared in 4 men (21-22 yr) during 8 hr of water immersion (T_{H2O} = 34°C) and during 8 hr of chair-rest (T_a = 22.5°C) followed by 16 hr of bed rest in both regimens. Water intake was 1,800 ml during both 8-hr exposures. Urine vol. during immersion was 2,954 ml/8 hr and 1,538 ml/8 hr ($P< 0.01$) during chair-rest; the respective decreases in extracellular vol. (ECV) were 2,980 ml/8 hr and 1,890 ml/8 hr. Losses from the interstitial vol. (2.55 vs 1.67 L) and plasma vol. (0.42 vs 0.23 L) during immersion and rest, respectively, were proportional to their normal ratios. With a negative (H_2O balance during immersion (-1,234 ml) and a positive (+190 ml) balance during chair-rest, there was a shift of ECV to the intracellular compartment in both regimens. There was suppression of both plasma vasopressin (AVP) and renin-activity (PRA) during chair-rest and immersion. The increased central blood vol. appears to be the primary stimulus for AVP secretion, while plasma osmolality regulates PRA secretion. In hyperhydrated subjects, about half (6.7%) of the immersion plasma vol. loss of 12.6% could be attributed to orthostatic responses associated with the upright body position during chair-rest, and the remaining half to the external water pressure.

ISOMETRIC CONTRACTILE CHARACTERISTICS IN ALLOXAN DIABETIC SKELETAL MUSCLE. J. Grossie, Dept. of Physiology, OSU Coll. of Med., Columbus, Ohio 43210.

Rats were given alloxan (45-50 mg/kg) IV and 48 hrs later given Na-insulin for 6 days. Control rats were administered saline instead of alloxan or insulin. Extensor digitorum longus muscles were analyzed in vitro at 20°C before and 2 and 4 days after cessation of insulin treatment in alloxan diabetic (Ad) rats. All Ad rats used in this study were glycosuric and hyperglycemic. After insulin withdrawal Ad rats with mild diabetes (Md) lost less than 10 gms/day whereas severe diabetic (Sd) lost more than 10 gms/day. During saline treatment in control rats, indirect (Ind) elicited twitch (Tw) tetanic (Tet) (100/s) forces were 2279 ± 85 and 5516 ± 127 gms/cm^2, respectively. During insulin treatment in Ad rats, Ind Tw and Tet forces were 88 and 89% of controls, respectively; the differences insignificant. In Md rats two days after insulin withdrawal, Ind Tw and Tet forces were not significantly different from similar controls. In Sd rats, Ind Tw and Tet forces were significantly reduced to 75 and 83% of controls respectively. Four days after saline withdrawal, control muscles showed Tw and Tet forces of 2318 ± 81 and 5445 ± 259 gms/cm^2 respectively. Md contractile forces were uneffected but Sd Tw and Tet forces were 47 and 51% of controls. Direct stimulation produced similar results. Configuration of the twitch was uneffected in Ad rats. Additional data show that fibers of muscle from Sd rats were significantly depolarized. (Supported-NIH AM23019)

DOPAMINE AND EPINEPHRINE ELEVATE PLASMA PROLACTIN LEVELS WHEN INFUSED INTRAVENOUSLY INTO FEMALE RATS. C.E. Grosvenor. University of Tennessee Center for the Health Sciences, Memphis, TN 38163

Equilibrium plasma prolactin (Prl) levels were determined in young adult female rats during continuous infusion of 200 ng rat Prl (NIAMDD B-1 or B-2)/min both before and during the simultaneous infusion of either dopamine (DA) or epinephrine (Epi). DA infused either at 0.25 µg or 0.5 µg/min for 20 min rapidly (within 10 min) increased the equilibrium plasma Prl concentration from 150 to 400 ng/ml. The infusion of either 0.5 or 1.0 µg Epi/min for 20 min similarly increased plasma Prl concentration from 151 to 424 ng/ml within 10 min. The infusion of 50 ng DA/min or a bolus injection of 1 µg of DA did not alter plasma Prl levels. Since the infusion of DA (0.25 µg/min) or Epi (1.0 µg/min) for 30 min did not alter Prl levels in non-Prl infused rats, it is concluded that DA and Epi elevate plasma Prl levels in the rat via interference with peripheral degradative and/or excretory mechanisms. Computation of metabolic clearance rates for Prl before and after DA infusion averaged 1.35 and 0.5 ml/min; those before and after Epi averaged 1.35 and 0.47 ml/min. (Supported by USPHS Grant HD-04358)

THE ACTION OF SIMULATED AND TRUE WEIGHTLESSNESS ON DIGESTIVE TRACT OF RATS. **P.Groza, A.Bordeianu, A.Boca, S.Cananău, Institute of Physiology, Bucharest, Romania**

By restraining rats in special cages 15, 30 and 60 days, mimicing this way weightlessness,we found in the submaxillary and gastric glands, stomach surface and intestine epithelium decreased mucopolysaccharide (MPZ) and increased of some enzymes activity, activated state of gastrin secreting G cells, hypersecretion of gastric acid and pepsin secretion. These modifications were maximal after 15-30 days of hypokinetical state and correspond with a glucocorticoid hypersecretion. We found very similar histochemical changes in rats submitted to a true 18½ days space flight. These reactions were due to a nonspecific stress reaction. The weightlessness as such has a reduced effect on digestive tract, as may be concluded from a partially restored MPZ secretion of rats centrifugated in flight.

EFFECTS OF A WEIGHTLESSNESS SIMULATION ON THE VELOCITY CURVES MEASURED BY DOPPLER SONOGRAPHY AT THE LEVEL OF THE CAROTID SYSTEM. A. Guell, A. Bes, L. Braak, M. Barrere. Department of Neurology C.H.U. Rangueil 31054 Toulouse Cedex France.

A simulation of weightlessness (7 days of prolonged bedrest in antiorthostatic position - 4°) was performed with the help of 4 healthy volunteer subjects. Quantitatively, 4 parameters were studied the systolic time which varies in the same sense as the L.V.E.T., the index of arterial resistance, the surface ratios and the average velocity index which varie in the same sense as the cerebral blood flow. All the index were correlated, in preliminar studies with the invasive methods. The results shown a significant increase in the systolic time (from the 10th hour to the 4th day). The index of arterial resistance was increased during the 4 first days. This is consistent and logical, in as much as there exists a "pooling" of blood in the cerebral vascular bed. The surface ratios and the average velocity index diminishe significantly after the second hour and return to the basal state after 48 hours : Oualitatively, we noted a decrease in the second positive wave of the sonogram (winkessel effect) : this corresponds with a decrea se in the arterial tonus.

PULMONARY MICROCIRCULATION: SHEET-AND-POST VS TUBES Warren Guntheroth, Isamu Kawabori* and Daniel Luchtel* University of Washington, Seattle, Washington 98195

From the time of Malpighi, capillaries for both the systemic and pulmonary circulation were universally regarded as tubular structures. In the past 10 years, Fung and Sobin have proposed that the pulmonary microcirculation consists of sheets-and-posts, in contrast to Weibel's hexagon of intersecting cylinders. We studied corrosion casts of the pulmonary microcirculation. The pulmonary artery in rats was cannulated, washed out with lactated Ringer's solution and filled with a mixture of Geon latexes. Tissue was digested away with 6% Na hypochlorite. Specimens were coated with gold-palladium and the replicas examined with a JEOL scanning electron microscope. Two distinct patterns of pulmonary microcirculation were found. Non-alveolar, long tubular capillaries comprise the thin sub-pleural layer and appear as "filler" in the peribronchial spaces. The alveolar microcirculation is composed of matted, confluent tubules in spherical arrays, appearing superficially as sheets; however, the morphology is not consistent with the post-and-sheet model, nor with hexagons, nor any regular geometry. Measurement at 1680 magnification revealed that non-alveolar capillary diameters averaged 5.47 µ and the "interpost" dimension for alveolar vessels was 5.75 µ. We conclude that the pulmonary microcirculation is not different from other capillary beds: the basic structure is tubular, and not sheet-and-post.

SPECIFIC OPIATE RECEPTOR BLOCKADE IMPROVES CARDIAC PERFORMANCE AND SURVIVAL IN CANINE HYPOVOLEMIC SHOCK. N. Curll, R. Lechner,* D. Reynolds, and T. Vargish.* Dept. of Surgery, University of Iowa, College of Medicine, Iowa City, IA 52242.

Naloxone improves left ventricular contractility (LV dp/dt) and survival in lethal canine hypovolemic shock. Since naloxone also blocks γ-aminobutyric acid (GABA), a hypotensive agent, we used naltrexone which is devoid of anti-GABA activity. Mongrel dogs were bled to a mean arterial pressure (MAP) of 45 mm Hg at t = 0. A reservoir maintained MAP until t = 1 hr when it was clamped. Either naltrexone (N, n = 5) 5 mg/kg or saline (C, n = 5) was given at t = 1 and 3 hr. MAP, cardiac output (CO, L/min), stroke volume (SV, ml) and LV dp/dt (mm Hg x 10^3/sec) were determined during baseline (B), hypovolemia (H), and after treatment (T):

	MAP			LV dp/dt		
	B	H	T	B	H	T
C	151±6	44±1	34±4	2.7±0.1	1.0±0.1	1.2±0.2
N	244±4	45±0	83±5*	2.5±0.2	1.0±0.1	2.3±0.2*
	SV			CO		
C	17±3	2±1	2±1	2.5±0.2	0.5±0.1	0.5±0.1
N	19±3	3±1	5±1*	2.7±0.2	0.5±0.1	1.0±0.1*

*p<.05 vs C

Despite reinfusion of shed blood at t = 2 hr none of the C dogs survived; 4/5 of the N dogs survived to sacrifice at t = 3 da. Improved survival and cardiac function with specific opiate receptor blockade suggests involvement of endorphins and not GABA in the pathophysiology of hypovolemic shock.

EFFECT OF INTRACORONARY INJECTION OF NOREPINEPHRINE IN CONSCIOUS DOGS. P.A. Gwirtz and H.L.Stone. Univ. of Oklahoma, Health Sciences Ctr.,Dept.of Physiology, Okla.City,OK.73190

The direct action of norepinephrine (NE) on coronary vessels were examined in conscious dogs. Eight dogs were surgically instrumented to measure left circumflex artery flow velocity (LCV) using a Doppler flow probe. A silastic catheter was positioned in the left circumflex artery to permit direct injections of NE and to measure coronary blood pressure(BP). The ECG was used to obtain heart rate(HR). With the dogs lying quietly NE (0.3µg) was injected through the coronary catheter under control, α, β1, a nd total adrenergic receptor blockade using 1 mg of phentolamine, practocol, and propranolol, respectively. In 2 additional dogs, the response to NE was compared before and after left stellate ganglionectomy (LSGχ). Intracoronary injections of NE had no effect on BP. (96 ± 4mm Hg). CFV initially increased (26±2 to 45± 2 cm/sec) and then decreased to (21±2, P<0.05). The late vasoconstriction was eliminated by α blockade, while the early vasodilation was removed with β1-blockade, NE caused an immediate increase in HR(116± 9 to 144±10 bpm.) β1-blockade eliminated the increase in HR. LSGχ eliminated the increase in HR, indicating a reflex effect of NE. α-blockade attenuated the effect of NE on HR but the mechanism for this is unknown. A reflex increase in heart rate resulted from small intracoronary injections of NE which was blocked by both α and β-blockade. (Supported by HL 22154 & HL05835)

ISOPROTERENOL INDUCTION OF ORNITHINE DECARBOXYLASE DURING ONTOGENY OF THE MURINE HEART.
Mari K. Haddox*, William R. Roeske* and Diane Haddock Russell. Arizona Health Sciences Center, University of Arizona, Tucson, Arizona 85724.

Ornithine decarboxylase (ODC) activity has been demonstrated as a universal marker of hypertrophy. During embryogenesis, the level of activity relates directly to the rate of increased RNA and protein synthesis. ODC induction appears to be transcriptionally regulated by a cyclic AMP-mediated event in response to polypeptide and amine trophic hormones. Therefore, we studied the induction of ODC during normal cardiac ontogenesis and in response to isoproterenol administration. ODC activity was maximal (27 pmol/min/mg protein) at the earliest time that hearts could be dissected, 13 days of embryogenesis, and declined by 17 days to a level which was maintained in the heart until birth (9 pmol/min/mg protein). However, the ability of an optimal dose of isoproterenol (10 mg/kg IP into mother) to induce ODC was maximal at 15 days of development, elevating the enzyme activity to 55 pmol/min/mg protein. Later injections resulted in induction of ODC to a level ca. 30 pmol/min/mg protein. The trophic responsiveness of the fetal heart to isoproterenol precedes the time of β-receptor coupling to the chronotropic response. Therefore, the β-receptors present in 13-15 day murine hearts appear to be coupled only to macromolecular synthesis as measured by the extent of ODC induction.

EFFECTS OF CLONIDINE UPON THE THORACIC SYMPATHETIC EFFERENT DISCHARGES OF A CARDIOGENIC HYPERTENSIVE CHEMOREFLEX.
G. R. Hageman, F. Urthaler*, T. N. James* and R. H. Swatzell, Jr.*. Cardiovascular Research and Training Center, University of Alabama School of Medicine, Birmingham, Alabama 35294.

Clonidine is a powerful antihypertensive agent with a primary action thought to be mediated by alpha adrenergic stimulation in the CNS, thus inhibiting sympathetic efferent outflow. Serotonin activates a cardiogenic hypertensive chemoreflex (Circ 52:179, 1975) which induces discharges of sympathetic efferent neurons. The purpose of this study was to determine the effects of clonidine (100-300 µg/kg, I.V.) upon the thoracic sympathetic efferent discharges in 9 chloralose anesthetized dogs. Their autonomic receptors were blocked by pretreatment with intravenous atropine, propranolol and phentolamine. Efferent nerve traffic was quantified using a Schmitt trigger and Digital PDP8e computer. Control spontaneous activity (tone) following autonomic blockade was normalized at 100%. Serotonin (100 µg/ml, 2 ml, left atrium) caused an increase in the efferent sympathetic activity to 192 (± 16 SEM)% (p<.001). There were no significant changes in blood pressure. Following clonidine, the tone was decreased to 63 ± 6% of control. The reflex sympathetic discharge elicited by serotonin following clonidine was reduced from 192% to 116 ± 9% of control (p<.001). The attenuation of the reflexly elicited discharge was significantly (p<.05) greater than the attenuation of the tone.

ESTRADIOL " INCREASES HUMAN FIBROBLAST GROWTH-PROMOTING FACTOR" BINDING TO NORMAL AND NEOPLASTIC HUMAN EPITHELIAL CELL MEMBRANE. Anwar A. Hakim. Univ. of Illinois at the Medical Center. Chicago. Illinois 60680.

Human Fibroblast Growth-Promoting Factor "HFGPF is a protein from condition culture media of human skin fibroblasts (HSF)(Hakim, Experientia 34,1515,1978). It is essential for in vitro proliferation of human normal mammary(HNMEC) and mammary carcinoma (HMCC) cells. The recent observations that human melanoma cells (HMMC) have both nerve growth factor (NGF) and NGF-membrane receptors sugest that HFGPF may play an important role in the growth-promoting effect of estradiol(E).The present studies examined the responses to E of HNMEC,HMCC,USF and HMMC cell lines. The responses were monitored by thymidine incorporation and by HFGPF-binding capacity.Estradiol evoked a dose-dependent and two-phase dose dependent thymidine incorporation and HFGPF-binding to HNMEC and HMCC cells, respectively. The magnitude of the response was E-concentration dependent. Depending on HMMC cell line E evoked a dose-dependent, a two-phase dose-dependent and no response as revealed by thymidine incorporation and NGF-binding capacity. HFGPF causes a concentration-dependent thymidine incorporation in HNMEC and HMCC cells. Treatment of HNMEC cells with neuraminidase (VCN) increases,whereas treatment of HMCC and HMMC with VCN decreases E and HFGPF binding capacity. It is suggested that E promotes the formation of HFGPF membrane receptors.

PLASMA VOLUME CHANGES RELATED TO POSTURE AND EXERCISE.
R.D. Hagan,* F.J. Diaz,* R.G. McMurray,* and S.M. Horvath Inst. of Environ. Stress, UCSB, Santa Barbara, CA 93106

Plasma volume shifts were investigated in four male subjects who remained in either the upright or low-sit posture on a bicycle ergometer during 60 min of rest, 45 min of exercise, and 45 min of recovery. Rest in the upright and low-sit posture induced plasma volume decreases of 14 and 6.9%, respectively. When postural effects were partialed out exercise in the upright posture resulted in minimal alterations in plasma volume. Work in the low-sit posture was characterized by hemoconcentration during the early phases of pedalling followed by a slight increase in plasma volume which remained stable for the duration of the exercise period. During recovery plasma volumes returned rapidly to the pre-exercise magnitude associated with each seated posture. It is evident that when analyzing fluid shifts, posture and time should be rigorously controlled so as to differentiate between the effects of posture and exercise. (Supported in part by NIH Grant AG00021, Air Force Office of Sci. Res. Grant AFOSR 78-3534, and Amer. Heart Assoc.).

HEART CYCLIC AMP AND CYCLIC GMP RESPONSES TO SUSTAINED AORTIC CONSTRICTION IN NEONATAL AND ADULT RATS. Judith L. Haithcoat* and Russell T. Dowell. Dept. of Physiology & Biophysics, Univ. of Okla. Health Sci. Ctr., Oklahoma City, OK 73190.

Heart cyclic AMP (cAMP) and cyclic GMP (cGMP) levels (pm/gm) were measured in neonatal (neo) and adult male rats. Animals were studied 3,5,7, and 10 days after sham operation (S) or abdominal aortic constriction (AC). All neo and adult AC rats had a 30-50 mm Hg increase in LVP. At 3 days post surgery, AC neo rat cAMP levels were elevated (2380±680) vs neo S(880±60), but returned to control values at 7 and 10 days post surgery. Similar cAMP elevations were not observed in adult AC rats. Heart cGMP levels in adult S rats (approx. 15-20) were lower than neo S rats (approx. 35). With the exception of a rise in cGMP levels (51±6) in AC neo rats at 5 days post surgery, no remarkable alterations in cGMP levels were noted in any AC group. A consistent cAMP/cGMP ratio was observed in S rats at all time points studied and this ratio was higher in S adult (74±6) than in S neo rats (32±3). Due to the large increase in cAMP, the cAMP/cGMP ratio in AC neo rats attained adult levels at 3 and 5 days post surgery. The cAMP/cGMP ratio then declined to or below control levels at 7 and 10 days post surgery. No systematic alteration in cAMP/cGMP ratio was noted in adult AC rats. These results indicate that large increases in cAMP levels occur in AC neo rat hearts during the early phases (3-5 days) of pressure overload. The relationship between this cyclic nucleotide response and heart cellular activity remains to be determined. (Supported by NIH Grants HL 23025 and HL 23206).

THE EFFECTS OF PROPRANOLOL ON LUNG FLUID BALANCE. T.S. Hakim*, H. van der Zee*, P. Neumann*, N. Gertzberg* and A.B. Malik, Dept. of Physiol., Albany Medical College, Albany, N.Y. 12208

We studied the role of basal α-adrenergic activity on lung fluid balance in anesthetized sheep by blocking β-receptors with propranolol(P). Lung lymph flow($\dot{Q}_l$), lymph-to-plasma protein conc. ratio(L/P), protein clearance(C), pulmonary arterial pressure($\bar{P}_{pa}$), and vascular resistance(PVR) during baseline and at 15, 60 and 120 min after P injection(2mg/kg) are listed ($\bar{x}$ ±SE).

	Baseline	15'	60'	120'
$\dot{Q}_l$,ml/hr	5.8 ±1.3	6.8 ±1.6*	8.2 ±1.6*	10.8 ±1.5*
L/P ratio	0.74±0.07	0.70±0.06*	0.64±0.05*	0.69±0.07
C,ml/hr	4.1 ±0.8	4.6 ±1.1	5.3 ±1.2*	7.4 ±1.3*
$\bar{P}_{pa}$,mmHg	19.1 ±1.6	23.0 ±0.8*	20.3 ±1.9	20.5 ±1.4
PVR (mmHg/l/min)	7.9 ±1.2	9.5 ±0.9	9.2 ±2.1	8.8 ±2.0

*different from baseline ($p<0.05$)

The increase in $\dot{Q}_l$ and decrease in L/P ratio in the first hr suggest ultrafiltration of protein-poor plasma due to increased microvascular pressure; the progressive increase in $\dot{Q}_l$ and steady L/P ratio in the second hr suggest increase in lung vascular permeability to proteins. The early increase in ultrafiltration and delayed increase in vascular permeability may be due to unmasking of α-adrenergic receptors. Therefore, β-adrenergic mechanisms play a role in regulating transcapillary exchange in the lung.
(Supported by HL-17355, GM-07033 and HL-00363)

CONTROL OF GLOMERULAR FILTRATION RATE (GFR) BY RENIN-ANGIOTENSIN SYSTEM (RAS): ROLE OF CIRCULATING ANGIOTENSIN II (AII). J.E. Hall, T.G. Coleman, A.C. Guyton, P.R. Kastner*, and H.C. Salgado*. Univ. Miss. Med. Cntr., Jackson MS 39216

Previous studies from our laboratory have provided evidence that the RAS controls GFR through an efferent arteriolar vasoconstrictor mechanism; however, the relative importance of circulating versus intrarenally formed AII in this control has not been determined. In the present study, the role of circulating AII in regulating GFR during reduced renal artery pressure(RAP) was examined in 7 sodium-depleted dogs anesthetized with sodium pentobarbital. After 90 mins of infusion of the angiotensin converting enzyme inhibitor SQ-14225, which presumably inhibited formation of both circulating and intrarenal AII, reduction of RAP to 80±2 mm Hg resulted in marked decreases in GFR, filtration fraction(FF), and calculated efferent arteriolar resistance(ER), while renal blood flow (RBF) was maintained approximately 35% above control levels. Replacement of circulating AII, by i.v. infusion at rates which decreased RBF to control levels, caused marked increases in GFR(40%), FF(114%), and ER (132%) to levels not substantially different from control even though RAP was maintained constant by aortic constriction. These observations suggest that circulating AII may play an important role in regulating efferent arteriolar resistance and GFR during reductions in RAP. The importance of intrarenally formed AII in controlling GFR remains to be determined.(Supp. by NIH HL 23502, HL 11678; Miss.HeartAssn)

DIFFERENTIAL EFFECTS OF ANESTHETICS ON THE CARDIOVASCULAR RESPONSE TO HYPOTHALAMIC OR VISCERAL AND SOMATIC AFFERENT STIMULATION IN THE CAT. Richard E. Hall, Richard W. Patterson, Eduardo H. Rubinstein, UCLA, Los Angeles, Cal., 90024.

Cardiovascular changes were elicited in awake instrumented cats during injection of 0.2 mEq KCl into the inferior mesenteric (VISC) or deep circumflex iliac (SOMA) arteries respectively. Comparable responses were evoked by hypothalamic stimulation via stereotaxically implanted electrodes. Peak responses are represented as the mean ± S.E. of aortic pressure (MAP) and heart rate (HR) during control (C), hypothalamic (HYP), visceral (VISC) and somatic (SOMA) afferent stimulation in 3 cats tested awake (W) and during halothane (HAL), enflurane (ENF), and ketamine (KET) anesthesia.

		C	HYP	VISC	SOMA
	W	103±5	143±8	147±7	136±9
MAP	HAL	77±4	98±3	103±4	94±5
torr	ENF	89±5	114±4	132±5	126±4
	KET	98±5	139±5	142±8	140±6
	W	183±7	110±4	242±8	223±6
HR	HAL	155±4	128±5	172±6	162±4
b/min	ENF	179±5	156±6	221±6	214±5
	KET	211±4	152±6	243±7	230±6

The results indicate that inhalation anesthetics blocked selectively centrally mediated cardiovascular responses with less effect on peripherally evoked reflexes while ketamine had no effect. Supported by grants from NIH GMS 22974 and AHA-GLA 437IG.

LOW MOLECULAR WEIGHT MACROPHAGE MIGRATION INHIBITION FACTOR (MIF) FROM A HUMAN B LYMPHOID CELL LINE. H. B. Halsall* and D. E. Coyle* (SPON: M. K. Halsall), Univ. of Cincinnati, Dept of Chemistry, Cincinnati, Ohio 45221

The B lymphoid cell line RPMI 1788 produces macromolecules with MIF activity in the molecular weight range 13,000 to 25,000. The supernatant from 50 liters of cells, which contained this activity was purified by Sephadex G-75 and, after dividing the activity into high (25,000) and low (13,000) mol. wt. fractions, by DEAE-A50 chromatography. All assays were by the MASS microassay (Fed. Proc. 37, 452 (1978)). The high mol. wt. fraction showed the physicochemical properties of "classic" MIF except for heat stability at 80°C. The low mol. wt. fraction corresponded to "classic" MIF except for mol. wt. Neither fraction was cytotoxic. MIF activity in both fractions was abolished when they were treated under mild reducing conditions with dithiothreitol, and alkylated with iodoacetic acid. This indicates a requirement of disulfide bridges to maintain structural integrity in the MIF molecule. The existence of a monomer-dimer equilibrium is not likely since the high mol. wt. MIF would not pass through a 14,000 dalton cut-off dialysis membrane, but the low mol. wt. did this freely. As with guinea pig MIF, human MIF appears to exist in multiple molecular forms.

ESTRADIOL AFFECTS NOREPINEPHRINE RELEASE AND METABOLISM AT ADRENERGIC NERVE ENDINGS IN VASCULAR SMOOTH MUSCLE. Martha A. Hamlet*, Duane K. Rorie* and Gertrude M. Tyce* (SPON: Charles A. Owen, Jr.). Mayo Fdn., Rochester, MN 55901.

Studies have been made of the direct in vitro effects of 17β-estradiol (E_2) on vascular reactivity and on the release of norepinephrine (NE) and its metabolites from dog saphenous vein. Helical strips of vein were incubated with ^{3}H(-)-NE ($1x10^{-6}$M) and suspended for superfusion with Krebs-Ringer bicarbonate glucose buffer containing E_2 (0.1, 1 and 10 μg/ml) or vehicle (controls, C). Electric stimulation (ES;10 V, 2 ms, 2 Hz) was then applied for 18 min. Total ^{3}H, ^{3}H-NE and its ^{3}H-metabolites were measured in superfusate and in vein extracts (AJP 234:H235,1978). E_2 at 10 μg/ml increased spontaneous overflow of total ^{3}H, ^{3}H-NE (111%) and ^{3}H-dihydroxyphenylglycol (^{3}H-DOPEG)(32%). Basal ^{3}H-NE output was also elevated (143%) by 1 μg/ml E_2. While ES-induced tension responses were not clearly different, ^{3}H-NE overflow exceeded C levels during ES at the highest dose of E_2. ^{3}H-DOPEG overflow failed to increase during ES at this dose, suggesting blockade of neuronal uptake. The expected increase in non-neuronal metabolites during ES was less at the higher doses suggesting that extraneuronal uptake was also blocked. E_2 at 10 μg/ml increased ^{3}H-dihydroxymandelic acid which suggests an inhibition of catechol-O-methyltransferase. Thus E_2 appears to (1) increase basal NE release and (2) inhibit neuronal and extraneuronal uptake or metabolism of NE. Supported by Grants AM 07147 and NS 9143.

TOTAL METABOLISM OF MARINE BIVALVE MOLLUSKS DURING TRANSITION TO ANOXIA. C. S. Hammen. Univ. Rhode Island, Kingston, R. I. 02881

Bivalve mollusks are exceptionally tolerant of anoxia, and chemical evidence suggests that they reduce their metabolic rates markedly during anoxia. In order to determine the exact quantitative relations between aerobic and anaerobic metabolism in the same animals, a microcalorimeter-respirometer was devised to measure heat production (Q_H) and oxygen consumption (Q_O) simultaneously. Bivalves were placed in a measured volume of aerated sea water of known salinity in a stoppered Dewar flask equipped with polarographic oxygen sensor and electronic thermometer probe. Experiments with one or a few specimens of Mytilus edulis showed maximum Q_O at 10 minutes, followed by a rapid decline, then a more gradual stepwise decline to zero at about 2 hours. Q_H at the start was greater than Q_O calculated from the caloric equivalent of glucose oxidation; Q_O (max) did not exceed 73% of Q_H (aerobic), indicating a large fraction of anaerobic heat production during the aerobic phase. Q_H reached a maximum of double the initial value about 20 minutes after Q_O (max). Then heat production also declined as the water was depleted of oxygen, and after 2 hours anoxia it was 45% of the initial rate.

HYPOXIA DEPRESSES THE PULMONARY VASCULAR RESPONSE TO PROSTAGLANDIN $F_{2\alpha}$. A.L. Harabin, J.T. Sylvester and R.S. Frank*. The Johns Hopkins Medical Institutions, Balto., Md. 21205.

When alveolar P_{O_2} (P_{AO_2}) is lowered from 670 mmHg in isolated pig lungs, steady state pulmonary vasomotor tone increases, reaching a maximum at P_{AO_2}=50; further decreases in P_{AO_2}, however, cause vasodilation (Am.Rev.Respir.Dis.119: 390,1979). If this vasodilation were due to diminished availability of high energy phosphates, the vascular response to vasoconstrictor agents such as prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) should also be inhibited at P_{AO_2}<50. We tested this possibility in isolated pig lungs, perfused in situ with autologous blood, by measuring the changes in pulmonary artery pressure-flow relationships induced by 10 min. infusions of $PGF_{2\alpha}$ (10 and 20 μg/min) at P_{AO_2}'s of 100 and 10 mmHg. These P_{AO_2}'s were chosen because the steady state pressure-flow relationships were the same, permitting comparison of the responses to $PGF_{2\alpha}$ from the same baseline tone. In 6 animals the increases in pulmonary vasomotor tone induced by $PGF_{2\alpha}$ were significantly depressed when P_{AO_2} was 10. Additional studies of complete $PGF_{2\alpha}$ dose-response relationships in 2 animals show that the maximal response to $PGF_{2\alpha}$ is also decreased. Thus, our results are consistent with the possibility that diminished availability of high energy phosphates is responsible for hypoxic pulmonary vasodilation observed at P_{AO_2}<50. (Supported by NIH HL-10342 and HL-07199)

EFFECT OF MANNITOL ON PROXIMAL TUBULAR FUNCTION OF NEWBORN DOGS. Aviad Haramati* and Leonard I. Kleinman. University of Cincinnati College of Medicine, Cincinnati, Ohio 45267

We have previously demonstrated (FED. PROC. 38:1122, '79) a dependence of proximal tubule (PT) Cl reabsorption upon HCO_3 reabsorption using Acetazolamide (ACZ) during distal blockade (DB) in puppies. ACZ increased NaCl and H_2O excretion and simultaneously decreased the U/P Cl ratio from 1.34 ±.01 to 1.19 ± .01 ($p < .01$). To test whether the effects on Cl were secondary to the osmotic effect of unreabsorbed HCO_3 and not specifically related to inhibition of HCO_3 transport, we studied the effect of 15% Mannitol (M) infusion on PT reabsorption of NaCl and H_2O in 6 puppies, 4-24 days of age undergoing DB. During DB, achieved with ethacrynic acid (2.0 mg/kg) and amiloride (2.4 mg/kg), U/P OSM and U/P Na were not different from 1.0 Fractional excretion (FE) of H_2O = 32.3 ± 3.0%, FE_{Na} = 32.4 ± 3.0%, FE_{Cl} = 41.6 ± 3.5%. After M, H_2O and electrolyte excretion rose significantly ($p < .01$) (FE_{H_2O} = 41.6 ± 3.9%, FE_{Na} = 40.5 ± 3.9%, FE_{Cl} = 51.9 ±4.3%) the change being similar to that for ACZ. However, M had no effect on FE_{HCO_3} (5.4 ± 1.8 to 5.6 ± 2.8) or the U/P Cl ratio (1.29 ± .03 to 1.25 ± .02). Thus, the results of the ACZ studies which demonstrated a relationship between PT Cl gradient and HCO_3 reabsorption were not due to the osmotic effect of non-reabsorbed HCO_3 but rather to a partial dependence of PT Cl reabsorption upon HCO_3 reabsorption.

MEMBRANE ELECTRICAL EFFECTS OF HISTAMINE ON VASCULAR SMOOTH MUSCLE OF CANINE CORONARY ARTERY. David R. Harder, East Tennessee State University College of Medicine, Johnson City, TN.

This study was undertaken to determine some of the electrophysiological effects of histamine on the coronary arterial vascular smooth muscle of the dog. Transmembrane potentials were recorded from isolated canine coronary arteries with glass microelectrodes filled with 3M KCl. Histamine (10 exp-6M) increased the resting membrane potential (Rm) from -55 to -62 mv and reduced input resistence from 9.8 to 4.0 megohms. These effects of histamine were abolished when added in the presence of Mn++ (1mM) to block calcium influx. In the presence of histamine the amplitude, maximal rate of rise, and frequency of the TEA-induced calcium-dependent action potential increased in a dose dependent manner (10 exp-7 to 10 exp -5M). The effect of histamine on the action potential was inhibited by the H1 antagonist pyrilamine maleate (10 exp-7M). High doses (10 exp-5M) of pyrilamine maleate blocked the TEA-induced action potential suggesting that it has local anesthetic effects at this dose. These data suggest that histamine increases calcium inward current in coronary arterial smooth muscle. The histamine induced hyperpolarization may be due to an increased potassium conductance mediated by an increased calcium influx since inhibition of calcium influx prevented the hyperpolarization.

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FLUID BALANCE IN THE GREEN TURTLE. Alan R. Hargens, Dept. of Surgery, V.A. Medical Center and University of California, San Diego, CA 92161

The green turtle, *Chelonia mydas*, is exposed to periods of dehydration during extended migration in deep ocean waters with food deprivation. Fluid balance in 12 turtles was studied during a 3 week period of dehydration on board the R/V ALPHA HELIX near Puerto Limon, Costa Rica. Measurements of colloid osmotic pressure (COP), using an osmometer with a molecular-weight retention of 30,000 daltons, indicated significant shifts of fluid from the peritoneal and pericardial cavities into blood, lymph, and interstitial spaces. During 3 weeks of dehydration, COP rose from 9.6±3.2 to 21±4.5 cm H_2O in peritoneal fluid and 8.0 to 23±4.2 in pericardial fluid. No significant change occurred in COP of blood, lymph, lung interstitial fluid or subcutaneous interstitial fluid. Analyses of total osmotic pressure indicated that salt concentration rose significantly in all fluid compartments sampled. Measurements of hydrostatic pressure by the wick catheter demonstrated that lung and subcutaneous interstitial-fluid pressures remained constant in a normal, negative range (-6 to -2 cm H_2O) during the 3 week period of dehydration. These studies suggest that the peritoneal and pericardial fluid cavities are important reservoirs of water which the green turtle mobilizes to maintain interstitial fluidity during periods of dehydration. (Supported by NSF grant 77-24919, the Veterans Administration, and USPHS/NIH grants GM-24901 and AM-18824.)

DEVELOPMENT AND USE OF ASSAYS FOR PHYSIOLOGIAL AGE IN MICE. David E. Harrison Jackson Laboratory, Bar Harbor, ME 04609

Physiological changes that occur with age may be useful in estimating the physiological ages of certain tissues. The following changes with age in healthy mice have been significant, and are being evaluated as assays of physiological age: collagen denaturation rates, immune responses to the phytohemagglutinin mitogen and to sheep erythrocytes, minimal and maximal oxygen consumption per g metabolically active tissue, and urine concentrating ability. By far the most direct correlations with chronological ages were found in collagen denaturation rates. The following treatments are being tested that may alter aging rates: food restriction, hypophysectomy, immunologic rejuvenation using irradiation followed by grafts of young marrow cells and an infant thymus, parabiosis and voluntary exercise. In initial results, only the first two treatments retarded physiological changes with age in several different tissues, and no treatment affected all assays of physiological age equally. The degrees of similarity in the same individuals between different physiological age assays, and the possible relationships of these assays to subsequent life expectancies are being evaluated.

LIPOPROTEIN LIPASE ACTIVITIES IN ADIPOSE TISSUES AND MUSCLE IN LEAN AND OBESE ZUCKER RATS. Arthur D. Hartman, Dept. Physiology, LSU Medical Center, New Orleans, La. 70119

The aim of the present research was to examine in both sexes whether the obesity observed in the genetically obese Zucker rat could be explained by an altered adipose tissue distribution of lipoprotein lipase (LPL). In addition, LPL activity was measured in the left ventricle and gastrocnemius muscle in rats of different ages;7-9 weeks and 15-20 weeks. In both age ranges obese animals of both sexes were significantly heavier and had significantly larger adipocytes in three depots examined as compared to lean controls. In small animals of both sexes there were no consistent differences in LPL between depots nor were there any differences in adipose tissue LPL between lean and obese animals; the same conclusions are true of the older animals. In addition, no differences in distribution of LPL within individual depots could be found to explain the increased adipocity at either age. In marked contrast, in young, but not in older rats, heart LPL of both sexes was 50% higher in lean animals whereas there was a significant 25% increase in striated muscle of lean rats compared to obese. These data suggest that in obese rats plasma triglyceride fatty acids are shunted away from heart and skeletal muscles toward adipose tissue. In addition, since LPL of adipose tissue is not saturated at physiologic triglyceride concentrations and because obese rats are hypertriglyceridemic, the apparent in vivo LPL activity in the obese animal would be higher than in lean.

RECEPTORS SIGNALING GRAVITY ORIENTATION INFORMATION IN AN INSECT. H. Bernard Hartman. Texas Tech Univ., Lubbock, TX 79409.

It is generally believed that insects lack specialized gravity receptors analogous to statocysts or otoliths. However, we have found on the ventral surface of each cercus of burrowing cockroaches (Arenivaga sp.) are two rows of singly innervated pendulous receptors that signal the equilibrium parameter of spatial position (Hartman et al, 1979). Electrophysiological recordings indicate that input from each row drives a specific giant interneuron. Receptors in the lateral row drive an interneuron in a contralateral connective while those in the medial row provide input to an interneuron in an ipsilateral connective.

Displacement in any direction from primary orientation evokes tonic activity from at least one of the four interneurons; the receptive field for each interneuron occupies slightly more than a quadrant; the receptive field of each interneuron is the same as that of the row of receptors providing the input; displacements about the least stable axis (0-180°) or roll and the most stable axis (90-270°) or pitch are unambiguously signaled by pairs of interneurons.

Because there are only thirty gravity receptors, and they are accessible and manipulable, this preparation provides a unique opportunity to study the short and long term affects of receptor immobilization on sensory neurons and interneurons.

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INTRATUBULAR PRESSURE CHANGES DURING MEASUREMENT OF SINGLE NEPHRON FILTRATION RATE (SNGFR) IN THE DOG. D. A. Hartupee, A.H.B. Gillies* and F. G. Knox, Dept. of Physiology & Biophysics, Mayo Clinic, Rochester, MN 55901

The validity of SNGFR measurement depends on the maintenance of normal effective filtration pressure during collection of tubular fluid. Any fall of intratubular hydrostatic pressure should, if transmitted back to the glomerulus, increase SNGFR. Pressure changes during collection of proximal tubular fluid are reported not to be transmitted back to Bowman's space in the rat. The properties of dog proximal tubule are unknown. Early proximal tubular pressure (Ppt) was measured continuously with a servo null device during introduction of a late proximal oil block and complete collection of tubule fluid for measurement of SNGFR.

	HYDROPENIC (n=17)	VOLUME EXPANDED (n=10)
Ppt (free flow) mmHg	19.9±1.9	19.7±1.2
Ppt (collection) mmHg	12.8±2.3	9.6±1.7
ΔPpt mmHg	7.0±1.2	10.0±1.5
SNGFR, nl/min	66.7±4.6	113±13

$p<0.001$ compared to zero

Early Ppt declined during complete collection of proximal tubular fluid irrespective of freeflow pressure or nephron flow rate. This suggests that usual collection procedures for SNGFR decrease pressure in Bowman's space and therefore reported values for SNGFR in the dog may be overestimates.

VENTRICULAR PERFORMANCE IN HEARTS OF ADULT AND NEONATAL RATS SUBJECTED TO AORTIC CONSTRICTION. Eileen M. Hasser* and Russell T. Dowell, Univ. of Okla.HSC, Oklahoma City, OK 73190.

In neonatal (NEO) and adult rats aortic constricted (AC) for 5 wks, NEO AC rats exhibit normal LV pump and muscle function, while adult AC have depressed pump and muscle reserve capacity. To evaluate the early response to pressure overload, NEO and adult rats were subjected to AC for 5 days with sham operated (S) rats as controls. At control, LVP is elevated in AC animals, both adult (179±6 vs 142±8 mm Hg) and NEO (122±11 vs 89±6). Control cardiac index (CI) of AC and S is equal in both the adult (78±21 vs 74±17 ml/min) and NEO (140±27 vs 176±43), as is a load-dependent index of contractility, dP/dt max. Compared to NEO, adults exhibit elevated LVP and dP/dt, with similar HR and lower CI. Isoproterenol was infused IV to evaluate muscle reserve capacity. In S adults, dP/dt increased 19%, to 8762±730 mm Hg/sec, while AC increased by 10%, to 7003±765. Both S and AC NEO exhibited a 34% increase in dP/dt, to 5152±600 and 5351±562. To evaluate pump reserve capacity, saline was infused. In the adult group, CI increased in S from 45±6 ml/min to 89±8 (96%) and from 53±17 to 99±30 (87%) in AC. In NEO, CI increased from 158±34 to 248±9 (57%) in S, and from 168±106 to 255±116 (52%) in AC. These results suggest that at 5 days post AC, control function and pump reserve capacity is normal in both NEO and adults. Muscle reserve capacity is normal in NEO AC but appears to be depressed in adult AC. (Supported by NIH Grants HL 23025 and HL 23206).

THE HYPOTENSIVE AND NATRIURETIC ACTION OF CAPTOPRIL IS DUE TO INHIBITION OF ANGIOTENSIN II FORMATION. S.F.Hathcock*, J.E. Bass* and R.E. McCaa. Dept. Physiol. and Biophys., Univ. of Miss. Sch. of Med., Jackson, Mississippi 39216.

Competitive inhibition of angiotensin I converting enzyme (kininase II) with Captopril results in decreased circulating and renal levels of angiotensin II and increased circulating and renal levels of kinins. The present study was designed to determine whether the hypotensive and natriuretic action of Captopril is due to inhibition of angiotensin formation or to the accumulation of vasodepressor peptides. Sodium deficient dogs were maintained on Captopril infusion for 14 days (400 mg/day) to inhibit angiotensin II formation and to increase circulating and renal concentration of kinins. In response to Captopril infusion arterial pressure (AP) decreased from 100 ± 3 to 68 ± 2 mm Hg, urinary sodium excretion ($U_{Na}V$) increased from 0.68 ± 0.23 to 6.7 ± 1.2 mEq/day, and plasma aldosterone concentration (PAC) decreased from 39.7 ± 6.5 to 18.4 ± 3.7 ng/dl. Continuous angiotensin II infusion at the rate of 5 ng/kg/min was begun in five sodium deficient dogs maintained on Captopril infusion. In response to angiotensin II $U_{Na}V$ decreased from 6.7 ± 1.2 to 0.52 ± 0.16 mEq/day within 24 hrs, AP increased from 67 ± 2 to 95 ± 3 mm Hg within 48 hrs. and PAC increased from 18.4 ± 3.7 to 34.7 ± 8.9 ng/dl. These data demonstrate that the hypotensive and natriuretic action of Captopril is due to the inhibition of angiotensin II formation and not accumulation of kinins. (Supported by USPHS, NIH Grant HL 09921.)

POSITIVE END-EXPIRATORY PRESSURE (PEEP) SHIFTS LEFT VENTRICULAR DIASTOLIC PRESSURE-AREA CURVES. J.B. Haynes*, S.D. Carson*, T.M. Hyers* and Peter Steele*. (SPON: Robert F. Grover). Denver VA Med. Ctr., Denver, CO 80262.

PEEP ventilation is frequently associated with reduction in cardiac output despite unchanged transmural left ventricular end-diastolic pressure(LVEDPtm). These observations have been interpreted to represent decreased LV contractility but could be explained by altered diastolic pressure-volume characteristics. To study this latter possibility, radiopaque markers were inserted into a plane of the LV in 9 dogs. Transmural pressure(LV-pericardial)was synchronized with area under four conditions: 1) zero end-expiratory pressure(ZEEP), 2) 15cm H_2O PEEP, 3) PEEP after 10ml/kg dextran load and 4) ZEEP after 15ml/kg phlebotomy. PEEP caused a 20% decrease in end-diastolic area(EDA), a 47% decrease in stroke area(SA) and a decrease in LVEDPtm from 4.0 to 2.0mm Hg ($p<.05$). Volume expansion normalized EDA and SA but LVEDPtm rose above ZEEP levels to 5.7mm Hg ($p<.05$). At equivalent EDA (ZEEP vs. PEEP/dextran), SA work was equal, suggesting PEEP does not decrease contractility. Statistical analysis of mean polynomial curves fit to the diastolic pressure-area data demonstrate PEEP and PEEP/dextran curves are shifted upward relative to ZEEP and ZEEP/phlebotomy ($p<.0001$). We conclude PEEP alters left ventricular diastolic pressure-area characteristics which may explain previous observations suggesting PEEP decreases left ventricular contractility.

EFFECTS OF GRADED HYPOXIA ON BRAINSTEM AUDITORY EVOKED RESPONSES. James E. Heavner* and Robert D. Guthrie* (Spon: T.F. Hornbein) University of Washington, Seattle, WA 98195.

The brainstem auditory evoked response (BAER) is assumed to be an electrical measure of the viability of the brainstem. In 6 adult rabbits paralyzed with gallamine, anesthetized with 1.13% halothane, and mechanically ventilated, the BAER was less affected by hypoxia, and was more resilient following hypoxic-induced depression than was the electroencephalogram (EEG). Under control conditions, the power spectrum of the EEG typically consisted of activity extending from 0.5Hz to 14Hz. This pattern did not change significantly when FIO_2=0.1. However, when FIO_2=0.06, peak power frequencies of 0.5Hz and 4Hz became evident; when FIO_2=0.04, total EEG power was markedly diminished with small power peaks at 0.5 and 4Hz as long as cardiovascular collapse did not occur. The largest positive wave (wave 3 or 4-5) and the largest negative wave (following wave 5) of the BAER increased slightly in amplitude when FIO_2=0.1, were unchanged when FIO_2=0.06 and decreased to 0-80% of control when FIO_2=0.04. When severe cardiovascular depression occurred, the EEG became isoelectric before all traces of the BAER disappeared, and successful resuscitation was followed by return of the BAER to near normal with continued isoelectric EEG. These results are consistent with the conclusion that the brainstem is less sensitive to hypoxia-induced depression and can recover more effectively from hypoxic insults than can the cerebral cortex. (Supported by NIH Grants 15991 and 19187.)

THE PHASIC RELATIONSHIP BETWEEN THE AORTIC/INTRAMYOCARDIAL PRESSURE GRADIENT AND CORONARY BLOOD FLOW. F.W. Heineman*, J. Grayson and C.E. Bayliss(*SPON: H. Sonnenberg). University of Toronto, Toronto, Canada, M5S 1A8

The vascular waterfall model predicts that the effective pressure for coronary perfusion is the difference between the aortic (AP) and intramyocardial (IMP) pressures. This was studied using 10 open-chested, anesthetized dogs in which IMP was measured from micropipettes in the left ventricular free wall using a servo-nulling transducer. The AP was recorded from a catheter tip transducer and IMP electrically subtracted from it to give the AP/IMP gradient (GP). The anterior descending coronary arterial blood flow (CF) was measured with an electromagnetic flow probe. Values for GP and CF were taken at 0.01 second intervals and used to determine the correlation coefficients and the Fourier components. Predicted flows (PF) were calculated from the Fourier analysis of GP and correlated with CF. There was a high degree of correlation for GP vs. CF and CF vs. PF ($p<.001$). The results indicate that the functional perfusion pressure in the coronary circulation is the AP/IMP gradient. (Supported by the Ontario Heart Foundation).

EFFECT OF ADENOSINE AND DIPYRIDAMOLE ON CEREBRAL BLOOD FLOW. D.D. Heistad and M.L. Marcus. CV Center and Dept of Med, Univ of Iowa Col of Med and VA Hosp, Iowa City, IA 52242.

Infusion of adenosine into the carotid artery produces little or no effect on cerebral blood flow (CBF) in dogs. Recently we found that other drugs produce much greater cerebral vasodilatation in rabbits than in dogs, apparently because the amount of vasodilator drug that is delivered to cerebral vessels during infusion into the carotid artery is minimal in dogs. The large size of the internal carotid artery in rabbits, and ability to ligate the external carotid without creating a "steal", probably accounts for the greater responsiveness of rabbits than dogs. In this study we measured CBF (microspheres) in anesthetized rabbits during infusion of adenosine (n=7) or dipyridamole (n=5) into one carotid artery. Infusion of adenosine 1 and 10 μM/min increased ipsilateral CBF from 47±8 (mean±SE) to 75±15 and 90±9 ml/min per 100 gm ($p<0.05$), respectively. Flow to the contralateral cerebrum did not change significantly during infusion of adenosine. Flow to grey matter increased three-fold and flow to white matter increased two-fold. Infusion of dipyridamole 2 and 20 μM/min increased ipsilateral flow to the cerebrum from 61±9 to 83±21 and 158±33 ml/min per 100 gm ($p<0.05$), respectively. Flow to grey matter increased 2.5 fold and flow to white matter increased three-fold. We conclude that increases in adenosine, either exogenous (infusion of adenosine) or endogenous (dipyridamole), produce pronounced cerebral vasodilatation in rabbits.

INDOMETHACIN INDUCED INCREASE IN COLLATERAL BLOOD FLOW AFTER AORTIC THROMBOSIS. Cecilia Helinski*, Robert Schaub, and Royce Roberts*. University of Tennessee, Knoxville, TN 37901

Permanent ligation of the feline aorta at the iliac bifurcation is followed by rapid opening of pre-existing collateral blood vessels. However, if ligation is combined with thrombus formation collateral development is inhibited. Drugs which alter serotonin function reverse this inhibition. Serotonin will aggregate platelets. Therefore, this study assessed the effect of platelet inhibition by indomethacin on thrombus induced collateral inhibition. Twelve adult mixed breed cats were used. Control cats (3) were ligated. Thrombosed cats were untreated (4) or were treated one hour prior to surgery with indomethacin (5) at a dose of 20 mg/kg. Collateral circulation was assessed from aortograms taken 3 hours after occlusion. Aortograms of control cats indicated substantial collateral development. Untreated thrombosed cats exhibited almost no flow to the hindlimbs. Four of the treated cats had aortograms similar to controls. These results suggest: (1) The clinical consequences of arterial thrombosis cannot be entirely attributed to mechanical occlusion, but may relate to humoral inhibition of collateral blood flow. (2) This inhibition may be related to platelet activation and release of serotonin, thromboxane A_2, and other vasoconstrictive substances. (3) The inhibition can be reversed by indomethacin. This study was supported by NIH Grant #RR09012 and East Tennessee Heart Association Grant #18173301.

REGULATION OF BODY TEMPERATURE AS A FUNCTION OF SLEEP/WAKEFULNESS AND CIRCADIAN TIME IN PIGEONS. H.C. Heller, R. Graff* and W. Rautenberg*. Stanford Univ., Stanford, CA 94305.

Pigeons were chronically prepared with cortical EEG, EOG, and neck muscle EMG electrodes, and with water perfused thermodes in the vertebral canal. Metabolic rate and respiratory rate were recorded as a function of spinal cord temperature, arousal state, and circadian time. The threshold spinal cord temperature for the metabolic heat production (MHP) response in awake pigeons was 1 to 2°C lower during the inactive phase than during the active phase of the animals' circadian rhythms. During the inactive phase there was an additional 1 to 2°C decrease in this threshold during episodes of slow wave sleep (SWS). The threshold spinal cord temperature for thermal polypnea in awake birds also was lower during the inactive than during the active phase and showed an additional decrease during SWS. Shivering and thermal polypnea stopped during brief episodes of REM sleep. The daily rhythm of body temperature in pigeons is due to both circadian and arousal state related changes in the central nervous thermoregulatory system. (Supported by grants from NIH and DFG.)

VITAMIN B-12 ABSORPTION AND INTESTINAL TRANSIT IN CECECTOMIZED GNOTOBIOTIC RATS. James B. Heneghan, Myra Y. Mittelbronn*, Patrick A. Hattier*. Departments of Physiology and Surgery, LSU School of Medicine, New Orleans, LA. 70112

Previous studies have shown increased Vitamin B-12 absorption in conventional (CV) rats compared to germfree (GF). To determine the effects of the enlarged cecum and its ability to retain intestinal contents, a test meal of ^{57}Co-labeled Vitamin B-12 (0.36 uCi,2,000 pg) and the non-absorbable marker, polyethylene glycol (PEG,275 mg) was fed to 23 conventional and 21 germfree Sprague-Dawley rats (males, avg.wt. 490 gms). Rats were placed in metabolism cages and urine and feces were separated, collected, and analyzed daily for 1 week. The results were: a) Vitamin B-12 absorption was increased in normal rats, CV 61% compared to GF 49%, whereas cecectomy abolished these differences, CV 55% compared to GF 53%; b) cecectomy reduced the time required to recover 100% of the PEG in the feces of CV rats from 74 to 45 hrs and in GF from 96 to 34 hrs; and c) cecectomy also increased the radioactivity recovered in the feces after all PEG had been recovered, from 3 to 6% in CV rats and from 7 to 10% in GF rats, representing B-12 absorbed, metabolized, and label secreted. Thus, microbial status and/or cecectomy had minimal effects on Vitamin B-12 absorption, but significant effects on intestinal transit time and intestinal secretion of radioactivity. The use of PEG has allowed a more precise interpretation of fecal radioactivity in Vitamin B-12 balance studies. (Supported by U.S.P.H.S. Grant AM-18886)

INSECT HEMOLYMPH IS IN DYNAMIC CONSTANCY AND HAS FEW SINK FUNCTIONS. J. Michael Henry* and Arthur M. Jungreis. Dept. of Zoology, Univ. of Tenn., Knoxville, TN 37916

Blood in non-vertebrates has traditionally been viewed as a sink wherein components are merely stored until needed for synthetic or metabolic purposes. We have measured the conc. of 8 amino acids, determined their flux through the blood pool, and examined the fate of the labeled amino acids in the tobacco hornworm, *Manduca sexta*, during the larval-pupal transformation. The amino acids: Lys, Arg, Ala, Leu, His, Val, Pro and Gln were found to exhibit half lives in the range 0.5 to 100 hrs. Concentrations of individual amino acids varied by as much as 12X, but the maximal 6 fold difference in fluxes appeared independent of the changes in concentration. The bulk of the labeled amino acids was incorporated into protein and released back into hemolymph. The pattern of protein incorporation was one wherein rates of blood protein synthesis declined during the period between feeding and apolysis, increasing to half of feeding levels immediately before the larval-pupal ecdysis. We conclude that the concentrations of blood amino acids are dynamically maintained, and that the "sink" concept of non-vertebrate blood is incorrect. Supported by USPHS NIH Grant AI-12779.

NITROGEN EXCRETION IN ALLIGATORS FED DAILY *AD LIB*. Jack D. Herbert* (SPON: R.A. Coulson). La. State Univ. Med. Ctr., New Orleans, LA 70112.

Fasting or occasionally-fed alligators (*A. Mississipiensis*) excrete nitrogen in the form of uric acid and NH_4HCO_3 in about equal quantities. Since alligators fed daily *ad lib.* for long periods tend to develop gout, plasma uric acid and amino acid levels and nitrogen excretion patterns were examined in such "maximally-fed" (Max-Fed) animals. Sample results:

	Urine		Plasma	
	Uric Acid (mmoles N/kg/day)	Ammonia	Uric Acid (mM)	Amino Acids (mM)
Fasting	0.5	0.5	0.26	1.77
Single-meal (peak)	4.0	6.3	0.54	7.41
Max-Fed (peak)	4.1	40.7	0.22	6.16

The ammonia excretion mechanism seemed to have been stimulated greatly in Max-Fed animals, with the following results: 1) less nitrogen diverted into uric acid formation, 2) increased urine volume due to osmotic diuresis and thus increased uric acid clearance, resulting in 3) a consistently low plasma uric acid level. The modest ammonia output (and coincident rise in plasma uric acid) in animals fed a single meal after a long fast suggests that development of gout could be linked to changes in renal ammonia excretion. (Supported in part by the La. Dept. of Wildlife & Fisheries).

EFFECT OF ELECTRICAL STIMULATION ON ACETYLCHOLINE SENSITIVITY AND FIBRILLATION POTENTIALS IN SKELETAL MUSCLES OF THE RAT. Gerald J. Herbison, M. Mazher Jaweed* and John F. Ditunno, Jr.* Thomas Jefferson University, Philadelphia, PA 19107

Thirty-six adult (BW between 200 and 225 grams) female Wistar rats were implanted unilaterally with intramuscular electrodes to stimulate the soleus muscles. In half of the animals (D), the sciatic nerve was crushed bilaterally at the sciatic notch; while the remaining animals were designated as normal controls (N). Three groups in each of the N and D (n=6) lots were stimulated at 10 Hz by a 2-4 milliamp current for a duration of 4 msec for 8 hours each day for 5, 10, or 15 days. At the end of each period the actively contracting soleus (S) and passively stretched Extensor Digitorum Longus (EDL) were evaluated for the muscle weights, Acetylcholine (ACh) - sensitivity and Fibillation Potentials (FPs). The data showed no change in any parameter in the N groups. However, only the D groups soleus muscles showed a 17-40% decrease in Ach sensitivity and 25-50% fewer FPs after 10-15 days of electrical stimulation. These data suggest a significant role of active tension, and not the passive stretch, in suppression of the Ach-sensitivity and FPs. (Supported in part by a MDA Grant)

GEOMETRICAL CONSTRAINTS ASSOCIATED WITH THE USE OF HELICALLY-CUT VASCULAR STRIPS. Jeremiah T. Herlihy, Department of Physiology, University of Texas Health Science Center, San Antonio, Texas 78284.

The smooth muscle strip preparation cut helically from the vascular wall has been used in the past to compare the tension developed by smooth muscle from vessels of different sizes. The present study considers constraints associated with the use of such strips obtained from rat aorta. The angle (ϕ) at which a strip is cut, i.e. the angle formed by the intersection of the cut and a line drawn parallel to the long axis of the vessel can be defined as follows:

$$\cos \phi = \text{strip width/vessel circumference}$$

Therefore, if strips of the same width are to be obtained from vessels of different diameters, then the angles at which the strips are cut must differ. The tension (kg-wt/cm^2) developed by vascular strips was found to be a function of ϕ. Strips cut transverse to the long axis of the vascular segment developed 0.58 ± 0.05 kg-wt/cm^2; whereas those cut parallel to the long axis developed 0.03 ± 0.01 kg-wt/cm^2. Strips cut at other angles develop intermediate tensions. The present study demonstrates that when helically-cut strips are employed to measure the force generation of vascular smooth muscle the geometrical considerations of strip width, vessel diameter and the pitch of the helix must be taken into account. (Supported in part by Grant #HL19082 from the NIH).

PURIFICATION OF MB CREATINE KINASE FROM HUMAN MYOCARDIUM. Ceil A. Herman* and Robert Roberts. Washington University, St. Louis, Missouri 63110

Elevated plasma MB creatine kinase (CK) is considered the most sensitive and specific diagnostic indicator of myocardial infarction. We developed a radioimmunoassay (RIA) for MB CK based on an antibody to the B subunit using BB CK as the labeled ligand, which is competitively displaced by unlabeled human MB CK. It is preferable to use MB CK as the labeled ligand, but it has not been possible to purify MB CK free of albumin. Accordingly, we have developed a method to purify human myocardial MB CK. The tissue was homogenized in 50 mM Tris-HCl (pH 7.4), 2 mM BME. The CK was recovered from the supernatant (31,000 xg) by ethanol extractions (50 and 70%). The resuspended pellet was fractionated on DEAE-A50 Sephadex with a salt gradient (50-500 mM, pH 8.0). The MB fraction (specific activity 21.3 IU/mg) contained 90% albumin. The preparation was bound to an Affigel Blue column and contaminating proteins other than albumin were eluted with 50 mM Tris-HCl (pH 8.0), 2 mM BME. MB CK was eluted with 250 mM NaCl, but the albumin remained bound. The MB fraction (specific activity 453 IU/mg) represented a 500 fold increase in purity and exhibited a single protein band on polyacrylamide gels, with no albumin (bromcresyl green test). Purified MB CK competetively displaced MB in the RIA system, and exhibited a sensitivity for detection of plasma MB CK at the nanogram level.

FACTORS AFFECTING OXYGEN CONSUMPTION IN THE ALLIGATOR. T. Hernandez and R. A. Coulson. La. State Univ. Med. Ctr., New Orleans, LA 70112

Under basal conditions a one kilogram alligator consumes 800 ml/kg/day of oxygen at 28°C. An increase in temperature produces a sharp rise in metabolic rate. In recent studies (J. Nutrit. 109, 538-500, 1979) protein synthesis was found to have a high energy requirement as evidenced by an increased O_2 consumption after feeding, whereas protein digestion and amino acid absorption and transport were low energy processes. In the present studies maximum effort (work) caused a sharp rise in O_2 consumption which appeared to parallel the energy required to repay the O_2 debt from anaerobic glycolysis. An increase in O_2 consumption was also demonstrated following the administration of lactate and pyruvate which reflected the moles of ATP required for glycogen synthesis. The administration of glucose had no effect. A number of sympathomimetic drugs increased O_2 consumption, especially those catecholamines that stimulated glycolysis and increased lactate production. Some adrenergic blocking agents blocked the glycolysis and thereby prevented any increases in O_2 consumption. Results using non-catecholamines were less impressive. The magnitude of anaerobic glycolysis (lactate produced) appear to dictate the amount of increase in the O_2 consumed. (Supported in part by La. Dept. of Wildlife and Fisheries)

TESTOSTERONE LEVELS DURING SEXUAL BEHAVIOR OF RHESUS MONKEYS AS MEASURED IN SAMPLES COLLECTED BY AN ANIMAL-WORN BLOOD SAMPLING DEVICE. James G. Herndon*, Adrian A. Perachio*, Delwood C. Collins and Jane J. Turner*. Yerkes Reg. Primate Res. Ctr., Emory Univ., Atlanta, GA 30322.

Sexual activity has been associated with short-term increases in blood levels of testosterone in males of a number of species. However, copulatory behavior in macaques has been reported to have no short-term influence on testosterone secretion. We examined more closely the effect of copulatory activity on testosterone by obtaining blood samples from rhesus monkeys at various time-points during bouts of sexual activity. The experiment was conducted using an animal-worn, radio-activated blood sampling device which was developed in our laboratory. This device permits collection of eight separate samples through a permanently implanted catheter without interrupting the sexual behavior of the animals. Blood samples were collected from four males during 11 test periods with a receptive female in which one or more ejaculations occurred. The mean increase in testosterone during these sessions was 105%. In sessions without sexual behavior, the increase was 15%. One animal showed a distinctly smaller increase in testosterone than the other three, suggesting individual differences in the testicular response to sexual activity. (Supported by NIH Grants NS 09688 and RR 00165, NSF Grant BNS76-84314 and NASA Grant NGR 11-001-045.)

ENERGETICS OF RUNNING COCKROACHES. Clyde F. Herreid II, David A. Prawel* and Robert J. Full*. SUNY/Buffalo, N.Y. 14260

Cockroaches (Gromphadorhina portentosa) were run at varying speeds on a minature treadmill enclosed in a plexiglass chamber. The average weight of 10 animals was 5.2 g. Oxygen consumption ($\dot{V}_{O_2}$) was monitored with a S3A Applied Electrochemistry unit prior to exercise, during exercise bouts of 20 min., and during a one hour recovery period. $\dot{V}_{O_2}$ varied as a linear function of velocity, $\dot{V}_{O_2}$ = .38 + (4.1) (velocity). The estimated cost of transport 4.1 ml O_2/g x km for the roaches is remarkably similar to the value predicted for quadraped vertebrates (4.4 ml O_2/g x km) of a similar weight. The $\dot{V}_{O_2}$ predicted for resting roaches based upon the above equation is 2.4 times higher than the actual resting rate of .16 ml O_2/g x hr. Such an elevated rate during exercise has been recorded for vertebrates also. Brief O_2 debts were measured; their magnitude was a direct function of the running velocity.

EFFECT OF CALCIUM ANTAGONISTS ON A MUSCLE WHICH HAS LITTLE OR NO SARCOPLASMIC RETICULUM. Robert B. Hill. Bermuda Biological Station, St. George's West, Bermuda.

The longitudinal retractors of the body wall of Isostichopus badionotus have little or no sarcoplasmic reticulum and yet they have cellular stores of calcium which suffice for EC coupling for up to ten hours of incubation in calcium-free solutions of chelating agents. It has been hypothesized that the major calcium stores are in the sarcoplasmic reticulum and its extraordinary extensions. In this study calcium antagonists have been used in order to identify the site of calcium stores for EC coupling in ACh contracture, in caffeine contracture, and in tetanus. Closely reproducible contractions can be elicited over a very long period of time by 10^{-8}M ACh in eserinized muscle, by 10 mM caffeine in muscle pretreated with ionophore, and by subfusion tetanus. All are reversibly blocked by Mn, nearly irreversibly blocked by La, and not blocked at all by Danotrolene. This supports the hypothesis that calcium stores for EC coupling are located in the membrane and not in intracellular sites.

CARDIOVASCULAR RESPONSE OF RATS EXPOSED TO 60-HZ ELECTRIC FIELDS. David I. Hilton* and Richard D. Phillips. Battelle Pacific Northwest Laboratory, Richland, WA 99352.

Recent studies have shown that exposure to high-strength electric fields can influence electrocardiogram (ECG) patterns, heart rates and blood pressures in various species of animals. Our studies were designed to evaluate these reported effects and to help clarify some of the conflicting reports in the literature. Various cardiovascular parameters were measured in Sprague Dawley rats exposed (or sham exposed) to 60-Hz, 80- or 100-kV/m fields for periods through 4 mo. No significant differences in heart rates, ECG patterns, blood pressures or vascular reactivity measurements were found between exposed and sham-exposed rats after 8 h, 40 h, 1 mo or 4 mo of exposure. Blood pressure and heart rate measurements, also taken during exposure to a 100 kV/m field for 1 h, revealed no significant differences between exposed and sham-exposed groups. In addition, physiological reserve capabilities, measured in rats exposed to 100 kV/m for 1 mo and then subjected to cold stress, showed that electric field exposure had no significant effect on the animals' physiological response to the cold stress. Our studies cannot be directly compared to the work of other investigators because of differences in animal species and electric field characteristics. Our failure to detect any cardiovascular changes may have been the result of eliminating secondary field effects such as microcurrent shocks, corona and ozone.

AUTOANTICOAGULATION DURING ARTERIOVENOUS PERFUSION IN DOGS: INTRA- AND EXTRACORPOREAL REQUIREMENTS. L. B. Hinshaw, B. Beller-Todd*, L. Archer*, B. Benjamin*, T. Murphy*, S. Sofer*, and F. B. Taylor, Jr.*. VA Medical Center and Univ. Oklahoma Health Sci. Ctr., Oklahoma City, OK 73104.

Our laboratory has developed an arteriovenous extracorporeal perfusion system in dogs which results in autoanticoagulation and "infinite" Lee-White whole blood clotting time (>24 hr)(Circ. Shock, in press). To extend and refine this system, we studied intra- and extracorporeal requirements for the "autoanticoagulation" phenomenon. The intracorporeal system was tested using intact and eviscerated dog preparations. The extracorporeal system was studied by varying the individual components, including tubing, pump, reservoir, and the introduction of exogenous heparinization. We found that the liver must be present in the intracorporeal system to achieve infinite clotting time. The non-occlusive roller-type pump was required in the extracorporeal system to attain infinite clotting time, while the reservoir was optional and either plastic or rubber tubing was equally effective. Furthermore, early minimal exogenous heparinization (1.0 mg/kg) did not interfere with, nor accelerate, "infinite clotting time". Termination of perfusion resulted in restoration of normal clotting time within 3 hr, and infusion of 1 mg/kg of protamine rapidly restored normal clotting time during perfusion. (Supported by VA Med. Ctr., US Navy Project N00014-76-C-0229, and NIH Program-Project HL17812.)

VAGAL REFLEX ACTIONS OF PROSTAGLANDINS IN THE CAT. T.H. Hintze*, M.J. Panzenbeck* and Gabor Kaley. Dept. of Physiology, New York Medical College, Valhalla, N.Y. 10595.

The purpose of this study was to examine the role of the vagus nerve in the heart rate and blood pressure responses to injections of arachidonic acid (AA), prostaglandins (PG) and nitroprusside (NP). Anesthetized male cats with carotid arteries tied (in order to blunt baroreflex function) received intravenous AA (1,2,3 mgs), PGI_2 (5,20,40 µg), PGE_1 (5,10 µg), PGE_2 (5,10 µg), $PGF_{2\alpha}$ (10,20,30 µg) or NP (25,50, 100 µg) before and after bilateral vagal section (N=6), atropine (N=6) and indomethacin (N=15). The increase in heart rate and the decrease in blood pressure to PGE_2, PGE_1 and NP were unchanged by vagotomy, atropine, or indomethacin. In contrast $PGF_{2\alpha}$, PGI_2 and AA caused bradycardia and a decrease in pressure. The fall in heart rate was significantly attenuated or reversed by atropine or vagotomy indicating vagal participation in the response. In addition, tying the carotid arteries potentiated the bradycardia to AA and PGI_2. Indomethacin inhibited the reduction in heart rate and blood pressure to AA and $PGF_{2\alpha}$ but had no effect on the PGI_2 induced changes. These results suggest that release of PGI_2 is responsible for the heart rate and blood pressure lowering effects of both AA and $PGF_{2\alpha}$. In summary, the injection into the cat of $PGF_{2\alpha}$ or PGI_2 as well as the in vivo synthesis of PGs cause the activation of a vagal reflex, most probably within the heart, resulting in cardiac slowing and hypotension (Supported by the Whitehall Foundation).

EVOLUTION OF SENESCENCE: INFLUENCE OF SURVIVORSHIP PATTERNS ON THE RATE OF INCREASE OF POPULATION. Henry R. Hirsch. Dept. of Physiology and Biophysics, U. of Kentucky, Lexington, Ky. 40536

A model population is proposed in which senescence is identified with an increase in death rate with age and in which selective advantage is measured by the Malthusian parameter, i. e. by the rate of population growth when the age distribution is stable. It is assumed that the birth rate is constant or changes exponentially with age and that the time derivatives of the survivorship curves are gamma density functions of integral order n. The survivorship curves are normalized such that the mean longevity is independent of n, but, with increasing n, the death rate is reduced at early ages and is augmented in old age.

The Volterra equation is derived from a general renewal equation, applied to the model population, and solved for the Malthusian parameter. An example is given in which the Volterra equation has more than one real root. In general, higher values of n, which favor greater survival in youth at the expense of lesser survival in old age, lead to increases in the Malthusian parameter that reflect greater selective advantage. The results illustrate and support Medawar's conclusion (1) that senescence would evolve even in the absence of need for a post-reproductive period of parental care.

(1) Medawar, P. B. An Unsolved Problem of Biology. London: H. K. Lewis, 1952.

CEREBROSPINAL FLUID ACID-BASE HOMEOSTASIS DURING ASPHYXIC DIVING, HYPERCAPNIA, AND ANOXIA IN TURTLES. B.M. Hitzig* and E.E. Nattie, Dartmouth Med. Sch., Hanover, NH 03755.

Turtles can maintain prolonged apneic dives and emerge in good condition. To study the CSF changes associated with diving and assess the contribution of the components of asphyxia (hypercapnia and anoxia), unanesthetized turtles (Pseudemys scripta elegans, 1-2 Kg) were subjected to 2h simulated anoxic dives (n=6), 2h of hypercapnia (8% CO_2 in air) (n=5), or 2h of N_2 breathing with normocapnia (n=4). Measurements were made of arterial pH, and arterial and CSF TCO_2, $[Na^+]$, $[K^+]$, and $[Cl^-]$. Comparisons with suitable controls revealed a significant ionic change in the CSF following each stress. Hypercapnia resulted in a marked increase in both CSF $[Na^+]$ and TCO_2, whereas anoxia resulted in a large decrease in TCO_2. The decrease in CSF TCO_2 during diving was much less than in the anoxic state, indicating that hypercapnia acted in a manner which helped stabilize CSF acid-base status. The CSF $[Cl^-]$ was lower than control during diving, but was slightly higher than control in anoxia. Changes in $[Na^+]$ increased the CSF strong ion difference resulting in maintenance of acid-base balance by effecting suitable changes in the $[HCO_3]$.

CSF	Control	Dive	Hypercap	Anoxia
$[Na^+]$	130 mEq/L	146	144	148
$[K^+]$	2.7	3.5	3.6	3.5
$[Cl^-]$	100	93	99	104
TCO_2	32.5	30.5	44.6	21.1

Supported by Parker B. Francis Found., HL10351, RCDA HL 00364.

MOUSE MODELS OF NARCOTIC ADDICTION: BEHAVIORAL TOLERANCE AFTER CHRONIC ORAL SELF-ADMINISTRATION OF MORPHINE. Ann Ho* & Vincent P. Dole. Rockefeller Univ., New York, N.Y. 10021

C57 mice had been drinking morphine sulphate in a sucrose solution (or the sucrose vehicle) for ≥ 4 months when they were studied in a series of behavioral tests.

Behavioral tolerance was shown in two tests. Learning of a water-escape task was as rapid in mice maintained on morphine sucrose as it was in sucrose controls. Further, tolerance to a 10 mg/kg dose of morphine injected i.p. was shown by the disruption of the well-learned escape task in the sucrose control mice with no impairment of the performance in morphine-drinking mice.

Persistent effects of the self-administered morphine-sucrose solution (mean ≥ 300 mg/kg daily) were found in two behavioral indeces. A chronic activating effect was suggested by the significantly higher levels of running-wheel activity found in the morphine group compared to controls. Also, although both groups showed a clear circadian rhythm over the 12-12 hour light-dark cycle, the morphine-drinking mice distributed their fluid intake more evenly throughout the 24-hour day than did the control mice.

(Supported in part by NY State ODAS Grant #C 113340)

EFFECTS OF ALPHA BLOCKADE AND ANGIOTENSIN ANTAGONIST ON INTRARENAL BLOOD FLOW DISTRIBUTION DURING HEMORRHAGE IN DOGS. Carl E. Hock*, John C. Passmore, Jay I. Levin* and Richard E. Neiberger*. Dept. Physiology, Univ. of Louisville, Louisville, Kentucky 40232.

Alpha receptor blockade and angiotensin antagonist were used to study renal cortical vasoconstrictor mechanisms during hemorrhage to 70 mm Hg. Radioactive microspheres (M) and a freeze-dissection ^{133}Xe disappearance technique (F-D) were utilized to assess renal flow patterns. Hemorrhage alone caused a 30% decrease in total renal blood flow (TRBF) and a 40-50% decrease on outer cortical blood flow (M & F-D). Inner cortical flow decreased approximately 30%. Outer medullary blood flow decreased 25% (F-D). Renal arterial infusion of phentolamine (25 µg/Kg/min for 12 min) beginning 20 min posthemorrhage (PH) produced no alteration in PH TRBF or its distribution (M, F-D). Plasma renin activity increased 6-7 fold in the hemorrhage group as well as in the hemorrhage plus phentolamine group. Saralasin treatment (2 µg/Kg/min for 12 min) beginning 20 min PH produced a pattern in which TRBF decreased only slightly and cortical blood flow was unaffected by the hemorrhage (M). Alpha blockade blocks neither renin secretion nor TRBF and distribution changes during hemorrhage. It is likely that angiotensin II is the strong renal cortical vasoconstrictor during hemorrhage. (Supported by Ky. Heart Assoc. and Heart Assoc. of Louisville and Jefferson County and Louisville Medical Research Foundation. Saralasin provided by Norwich-Eaton.)

HEMODYNAMIC CHANGES IN DOGS WITH AN OLEIC ACID INDUCED PULMONARY EDEMA. W.F. Hofman, I.C. Ehrhart, D.A. Miller and W. Granger*. Dept. of Physiology, Medical College of Georgia Augusta, GA 30912.

Oleic acid has been shown to produce a severe pulmonary edema in dogs. In this study, 5 mechanically ventilated, anesthetized dogs were administered 0.18 ml/Kg oleic acid into the right heart while hemodynamic changes were monitored. Following a control period, measurements of aortic and pulmonary artery pressure (P_{pa}), pulmonary wedge pressure (P_{wp}) cardiac output (Q), heart rate (HR), blood hematocrit (Hct), hemoglobin concentration [Hb], pH, PCO_2 and PO_2 were made at half hour intervals. Total pulmonary compliance (C), pulmonary vascular resistance (PVR) and shunt fractions ($\dot{Q}s/\dot{Q}t$) were calculated for each measurement period. Both HR and Q showed a decrease following oleic acid administration whereas the Hct and [Hb] progressively increased indicative of decreased plasma volume. Lung wet to dry weight ratios were significantly higher in oleic acid dogs (6.5±0.2) than in non-treated dogs (4.7±0.1). P_{pa} and PVR progressively increased after oleic acid without a significant change in P_{wp}. Both venous and arterial PO_2 and pH declined along with an elevation in PCO_2. The relationship between C and $\dot{Q}s/\dot{Q}t$ suggests two stages of edema formation. The initial stage is marked by a large decrease in C without a significant change in $\dot{Q}s/\dot{Q}t$. The second stage shows a large increase in $\dot{Q}s/\dot{Q}t$ with a further reduction in C suggesting the onset of alveolar flooding. (Supported by Biomed. Res. Gr. 5S07-RR5365-17)

THE ANTAGONISM OF BICARBONATE-RELATED CHANGES IN ACTION POTENTIAL DURATION BY THE ANION SELECTIVE BLOCKING AGENT SITS. Perry M. Hogan, Physiology Dept., State University of New York at Buffalo, Buffalo, NY 14214.

Studies were performed on canine cardiac Purkinje fibers to evaluate the role of bicarbonate in action potential repolarization. We have demonstrated previously (Spitzer and Hogan, *J. Gen. Physiol.*, 1979) that reductions in extracellular bicarbonate $[HCO_3^-]_e$ lengthen action potential duration (APD). To test the possibility that a HCO_3^- current *per se* is responsible for this effect the anion selective blocking agent, SITS, (4-acetamido-4'-isothiocyano-2,2'-disulfonic stilbene) was used to antagonize the APD response to changes in $[HCO_3^-]_e$. Under control conditions a reduction in $[HCO_3^-]_e$ from 24 to 6 mM caused a 33 msec increase in APD. In the presence of SITS (0.5 mM) APD increased by about 32 msec under control conditions (24 mM HCO_3^-) and the response to lowered $[HCO_3^-]_e$ was completely blocked. Probenecid, a competitive inhibitor of organic anion transport in the kidney, had no effect on bicarbonate induced changes in APD but did cause a marked decrease in APD of 46 msec. These results are consistent with our suggestion that a bicarbonate current may participate in repolarization. (Supported by grants: USPHS HL-16135, POI HL-14414 and POI HL-15194.)

HYPOPHYSECTOMY INHIBITS THE THERAPEUTIC EFFECTS OF NALOXONE IN ENDOTOXIC AND HYPOVOLEMIC SHOCK. John W. Holaday* and Alan I. Faden* (SPON: R. WYLIE). Walter Reed Army Institute of Research, Washington, D.C. 20012.

We have previously shown that the pure narcotic antagonist naloxone significantly improves the cardiovascular pathophysiology associated with endotoxic and hypovolemic shock in rats (Nature 275, 450; Science, in press). The purpose of the present studies was to determine if this effect of naloxone was mediated through a specific antagonism of pituitary endorphins. Hypophysectomized and sham-operated adult male Sprague Dawley rats (225-250g) were purchased from Zivic Miller Labs. and maintained on isotonic salt solution and rat chow ad libitum for 1 week at an ambient temperature of 27°C. One day following implantation of tail artery and external jugular cannulae, conscious hypophysectomized and sham-control rats were injected with endotoxin (60 mg/Kg, Difco #649448) or bled through the implanted cannulae (see above reports for details). When rats had attained pre-established shock criteria, either naloxone HCl (10 mg/Kg) or saline were administered intravenously. Preliminary results indicate that naloxone was without effect in improving blood pressure or pulse pressure in hypophysectomized rats subjected to either shock model, whereas in sham-operated control rats, this dose of naloxone produced the expected improvement in these parameters. These initial results suggest that the release of pituitary endorphins plays a causative role in the cardiovascular pathophysiology of endotoxic and hypovolemic shock.

SEASONAL ENERGY AND WATER METABOLISM IN FREE-LIVING ALASKAN VOLES. D. F. Holleman,* R. G. White* and D. D. Feist. Inst. of Arctic Biology, Univ. of Alaska, Fairbanks, Alaska 99701

Using the doubly labeled water method, energy metabolism and body water turnover were determined during various seasons in free-living Alaskan red-backed voles, Clethrionomys rutilus. Energy metabolism was similar in summer, fall and winter (7.30 ± 0.40 ml CO_2/g FFBW-h) and lowest in spring (5.71 ± 0.55 ml CO_2/g FFBW-h). The average daily metabolic rate (ADMR) of free-living voles was 3.7 (spring) to 4.8 (summer, fall and winter) times the calculated standard metabolic rate (3.8 $W^{-0.27}$ ml O_2/g BW-h). Body water turnover was lowest in winter and spring (0.277 ± 0.010 ml H_2O/g FFBW-d) and highest in summer (0.373 ± 0.022 ml H_2O/g FFBW-d). Body water turnover was correlated with energy metabolism in all seasons except winter. In winter energy metabolism increased while body water turnover decreased. Although this suggests that body water conservation is an acclimatization feature for survival in this extreme cold environment, the caloric saving resulting from a winter decrease in body water turnover (14.1 cal/g FFBW-d or 1.4% of the ADMR) does not seem to support this suggestion. (Supported by grant NIH GM10402.)

EFFECT OF INCREASED WORK ON FLOW AND ADENOSINE RELEASE IN ISOLATED GUINEA PIG HEARTS. G. Holmes* and V.T. Wiedmeier, Dept. of Physiology, Med. Coll. of Ga., Augusta, GA 30912.

Myocardial oxygen consumption ($M\dot{V}O_2$), a determinant of tissue oxygen balance, and coronary blood flow (CBF) have been shown to increase when external cardiac work is increased. Using a system in which external cardiac work could be varied while diastolic coronary inflow pressure remained constant, either the volume or the pressure work of the left heart was increased to known values from initial conditions of no external work. In one group of hearts two levels of volume work were done while in another group two levels of pressure work were done. In all cases of increased work from initial "non-working" conditions, flow levels and adenosine release increased. In the working preparation, doubling the volume work by doubling the venous return at a constant afterload produced a 35% increase in coronary flow but no measureable increase in adenosine release. Doubling the afterload however, produced a 65% increase in coronary flow and an 88% increase in adenosine release, although external work did not double because of decreased cardiac output. Flow levels and adenosine release were higher at the highest level of pressure work than at the highest level of volume work even though the external work was greater in the later. These findings are in concert with the known relationships between cardiac work, $M\dot{V}O_2$ and CBF and support the concept that adenosine may play a key role in the metabolic regulation of CBF. Supported by Biomed. Res. Grant 5S07-RR05365-17.

THE ROLE OF TISSUE DIFFUSION IN THE WASHOUT OF INERT GASES. L. D. Homer and P. K. Weathersby.* Naval Medical Research Institute, NNMC, Bethesda, Maryland 20014

The role of tissue diffusion in the exchange of inert gases is analyzed by considering the joint effects of convective flow, radial diffusion, and axial diffusion on the variance of the distribution of capillary transit times. We conclude for individual capillaries: (a) for small tissue diffusion coefficients (D), radial capillary diffusion is the principal source of variation, and the variance is inversely proportional to D; (b) if D is about 0.5 x 10^{-6} cm^2/sec, the variance depends on both axial and radial diffusion and is nearly independent of D; (c) if D is large enough so that radial diffusion is nearly complete, then axial diffusion alone is important, and the variance is proportional to D. By treating whole body washout as a renewal process we further conclude: If diffusion is a principal source of variation, no simple monotonic relation exists between exchange rates and D. In the washout of N_2 and Ar, N_2 is lost more rapidly at first, but Ar approaches equilibrium sooner. If heterogeneity of capillary perfusion is a major source of variation in the distribution of transit times, the stated conclusions may still be correct.

ACCLIMATION TO EXERCISE IN DRY HEAT: ACTIVE MEN VS ACTIVE WOMEN. D. Horstman, E. Christensen* and T. Downs*. U.S. Army Rsch.Inst.Environ.Med., Natick, MA 01760

Performance of and physiological responses to exercise at 45°C DB/22°C WB (HOT) were compared between 6 active men (M) and 4 active women (W) on the 1st, 6th, and 11th days of heat acclimation. $\dot{V}O_2$ max for M and W were 52.4±1.9 and 47.0±1.0 ml/kg•min. To acclimate, subjects cycled a maximum of 2 hours at 40% $\dot{V}O_2$ max under HOT conditions; performance time (PT), sweat rate (SR), heart rate (HR) and rectal temperature (Tr) were measured. On day 1, there were no differences between M and W for PT, 74.2±9.7 vs 82.5±8.5 min; rate of increase of Tr (dTr/hr), 1.51±0.20 vs 1.41±0.20°C; or SR per °C rise of Tr (SR/°C), 376±51 vs 341±40 mg/cm^2• SR was greater for M (569±37 mg/cm • hr) than for W (461±38 mg/cm^2• hr). HR for W was 15 to 20 bpm higher than for W. By day 6, W had better PT than M, 120±0 vs 98.3±9.7 min. Although M had greater SR than W, 635±56 vs 490±52 mg/cm^2• hr, dTr/hr for W (0.68±0.10°C) was much less than for M (1.19±0.16°C) and SR/°C for W (722±45 mg/cm^2) was higher than for M (567±58 mg/cm^2); HR was not different. On day 11, W had better PT than M, 120±0 vs 100±6.5 min. Again, M had greater SR than W, 694±76 vs 517±47 mg/cm^2• hr, but dTr/hr for W (0.53±0.03°C) was less than for M (0.83±0.12°C) and SR/°C_2 for W (956±79 mg/cm^2 was higher than for M (839±69 mg/cm^2); HR was not different. Thus, for the conditions of exercise of equal relative intensity in dry heat, unacclimated active men and women performed equally. Moreover, the women acclimated to this condition at a faster rate or to a greater extent than did the men.

HIPPOCAMPAL-INDUCED EVOKED POTENTIALS IN THE MEDIAL PREOPTIC AREA OF THE HYPOTHALAMUS FOLLOWING BILATERAL FORNICOTOMY. Thomas M. Holt*, John G. Blackburn, and Richard M. Dom*. Departments of Anatomy and Physiology, Medical University of South Carolina, Charleston, South Carolina 29403.

Bilateral transection of the fornix abolishes the modulating influence which the hippocampus exerts over the electrical and humoral activity of the hypothalamus. The possibility of re-establishment of functional connections between the hippocampus and hypothalamus was investigated in urethane anesthetized, female Sprague-Dawley rats using electrophysiological techniques. Evoked potentials were recorded from the medial preoptic area following electrical stimulation of the ventral hippocampus. These well-defined potentials were lost immediately after bilateral surgical transection of the fornix. However, the responses reappeared at varying time intervals following the fornicotomy. Evoked potentials, similar to control responses, were recorded in lesioned animals after two months. The results of this study indicate that the hippocampus may re-establish functional connections with the hypothalamus following lesions to the fornical pathways. (Supported in part by 1978-79 South Carolina Biomedical Research Support Grant).

CENTRIFUGE HIGH-g EFFECTS ON TEMPERATURE REGULATION IN UNANESTHETIZED RATS. J. M. Horowitz, E. Schertel*, and B. A. Horwitz. University of California, Davis, CA 95616.

In previous studies, rats that were centrifuged at 2g and concurrently exposed to cold, were found to exhibit an impaired ability to maintain colonic temperature during the one hour drop in ambient temperature (T_a) (Fuller, et al., J. Appl. Physiol. 42:74, 1977). The magnitude of this impairment was proportional to the hypergravitational field over a range of 1.5 to 4g (Horowitz & Horwitz, COSPAR: Life Science and Space Research XVI, 1978); and the impairment was alleviated upon return to 1g. That is, rats exposed to cold immediately after exposure to hypergravic fields were able to maintain core temperature (Giacchino, et al., J. Appl. Physiol., in press). In the present study we have examined the effects of the duration of the exposure to 3g prior to the onset of cold ($T_a \cong 12°C$), applied concurrently with the 3g field. Rats were implanted with thermsitors near the carotid artery, in the brain and in the interscapular brown fat pad. They were allowed to recover from surgery for 5 days and were then exposed to a 3g field using a 1.37 m centrifuge. Preliminary results indicate that even after 36 hours at 3g, the rat's ability to maintain core temperature during the one hour of cold was still impaired. (The technical assistance provided by the Chronic Acceleration Lab at UCD is gratefully acknowledged. This research was supported in part by research grants from the National Aeronautics and Space Agency.)

EFFECTS OF ALTITUDE ON RESPIRATION AND METABOLISM IN WOMEN DURING PROLONGED WORK. S.M. Horvath, J.A. Wagner, and D.S. Miles*. Inst. Environ. Stress, UCSB, Santa Barbara, CA 93106.

Five women (23-32 yrs) bicycled for 2 h at 41% of their altitude maximal oxygen uptakes ($\dot{V}O_2$) at simulated altitudes of 2030, 3050, and 4270 m and their responses were compared to comparable work at sea level (SL). Steady-state $\dot{V}O_2$ was achieved within 5 min at all altitudes. Although mean ± SE pulmonary ventilations ($\dot{V}_E$ BTPS = 29.2 ± 1.9 L/min) and respiratory rates (f_R = 22 ± 2 breaths/min) were similar at all altitudes, these variables increased with time at 3050 and 4270 m. Respiratory exchange ratios (R) increased at altitude and decreased with duration of work regardless of altitude. Ventilatory equivalents ($\dot{V}E/O_2$) were inversely related to absolute $\dot{V}O_2$. $\dot{V}E/O_2$'s were constant for 2 h at SL, 2030, and 3050 m but increased with time at 4270 m. $\dot{V}E/CO_2$ increased with time during all exposures and was similar at SL, 2030, and 3050 m but elevated at 4270 m. Blood lactates (HLa) did not change with work duration and were similar at SL and 2030 m but progressively increased at 3050 and 4270 m. $\dot{V}E/O_2$ changes indicated hypoxia rather than CO_2 as the stimulus for $\dot{V}_E$ BTPS during prolonged work. The constancy of $\dot{V}O_2$ and HLa for 2 h at these altitudes was different from the increases in $\dot{V}O_2$ and decreases in HLa frequently reported for men. Increased HLa at altitude at the same relative workload as SL also differed from the male response of similar HLa at the same relative workload. (Supported in part by AFOSR 78-3534)

BILATERAL RENAL FUNCTION RESPONSES TO CONVERTING ENZYME INHIBITOR (SQ 20881) IN ONE CLIP, TWO KIDNEY RENAL HYPERTENSIVE RATS. W.C. Huang*, P.D. Bell, D.W. Ploth, and L.G. Navar. Univ. of Alabama Medical Center, Birmingham, Alabama 35294.

To study the possible influence of the renin-angiotensin system in individual kidney function of one clip, two kidney Goldblatt hypertensive (GH) rats, converting enzyme inhibitor (CEI, SQ 20881) was infused intravenously, and sequential bilateral renal responses were examined. CEI was administered intravenously to 10 GH and 11 normal rats at a rate of 3 mg/kg·hr for 3 hours. In GH rats, arterial blood pressure (BP) fell significantly from 148±8 to 132±6 mmHg at 90 min. Despite the decrease in BP, significant increases in GFR (69%), urine flow (115%), sodium excretion (697%) and fractional sodium excretion (258%) were observed in the unclipped contralateral kidney. In the clipped kidney, GFR decreased significantly, whereas sodium excretion, urine flow and fractional sodium excretion were not altered greatly from control values. In normal rats, CEI infusion did not cause significant changes in BP, although bilateral diuresis, natriuresis and GFR elevation were observed. However, the increases in GFR, urine flow and sodium excretion were substantially less than that observed in the unclipped kidney of GH rats. These observations suggest that hemodynamics and sodium excretion in the renin depleted unclipped contralateral kidneys of GH rats are influenced by circulating angiotensin II, which, in turn, may contribute to the pathophysiology of hypertension.

A REDUCTION IN THE INCIDENCE OF RAT HEATSTROKE MORTALITY FOLLOWING PRIOR EXPOSURE TO SHORT, DAILY BOUTS OF SUB-LETHAL HYPERTHERMIA. R. Hubbard, C. Kelly, D. Watkins and M. Mager. U.S. Army Research Institute Environmental Medicine, Natick, MA 01760.

On each of five successive days, experimental animals (~ 500 g; n=54) were removed from their cages (26C), were fitted with rectal thermocouples (6.5 cm) and were restrained in an environmental chamber at 41.5C until a T core of 40.4C was achieved. Controls (n=42) were treated similarly, but restrained at 26C without resultant hyperthermia. Following a 48 h rest plus a 24 h fast (72 h total), all rats were restrained at 41.5C until a hyperthermic exposure calculated to produce an LD 90 within 24 h was achieved (> 60 deg·min above a T core of 40.4C). After removal from the heat, rats were monitored at 26C and were allowed water but no food. All rats alive after 24 h were counted as survivors. Since the heating rate of the experimental group was significantly lower than the controls (0.06 ± 0.02 vs 0.09 ± 0.03°C/min), these rats were exposed to the heat for a significantly longer time (84 ± 50 vs 55 ± 15 min) and lost more body weight (18 ± 7 vs 13 ± 5 g). Despite this, the experimental group maintained significant reductions in both hematocrit (48 ± 4 vs 51 ± 3) and core temperature (42.1 ± 0.4 vs 42.4 ± 0.4C). The resultant mortality rate of these rats (24%) was less than could be predicted from the hyperthermic exposure (61 ± 15 deg·min > 40.C; LD 93.4). These results suggest that short, daily bouts of sub-lethal hyperthermia can produce an increased resistance to subsequent lethal heat exposures.

DIFFERENTIAL EFFECTS OF VANADATE ON AORTIC AND INTESTINAL SMOOTH MUSCLE. Patricia M. Hudgins* and Guy H. Bond. Kirksville Col. Osteopathic Med., Kirksville, MO 63501

We examined the influence of vanadate (Vi) on isolated segments of rabbit aorta and ileum. Tissues were exposed to 250 μM Vi for various times before contractile responses were elicited. K^+-induced contractile responses were altered by Vi in ileum, but not in aorta. After a 10-min exposure to 250 μM Vi, the ileum was more sensitive to K^+; however, responses to 10^{-7}M acetylcholine were not altered. The increased sensitivity to K^+ was found to be dependent upon Vi concentration and exposure time. Concentrations below 50 μM were not effective.

Inhibition of NaK-ATPase by Vi is facilitated by K^+. Vi has been shown to inhibit from inside, and K^+ from outside the cell. NaK-ATPase serves as the Na-pump in all cells. The response to an increase in extracellular K^+ appears to be a dose-related reduction in membrane potential (depolarization). In addition, K^+ also facilitates inhibition of the Na-pump by Vi. Thus more depolarization would result if the pump is electrogenic. Our observations of a differential effect on vascular and intestinal smooth muscle can be explained if ileum is more permeable to Vi, or if the pump is more electrogenic as compared to aorta. (Supported by a grant from the American Heart Association, Missouri Affiliate, Inc.)

EFFECTS OF VASOACTIVE INTESTINAL POLYPEPTIDE ON POTENTIAL AND SHORT-CIRCUIT CURRENT IN ISOLATED DOG TRACHEAL EPITHELIAL SHEETS. R. Hutto*, D. N. Granger, and A. E. Taylor. Dept. of Physiology, Univ. of South Alabama, Mobile, AL 36688.

Tracheal mucosal strips were mounted between two lucite chambers in an Ussing apparatus. Potential difference (PD) and short-circuit current (SCC) were then continuously measured. Following the attainment of a steady state, vasoactive intestinal polypeptide (VIP) was placed into either the serosal or mucosal bathing fluids in doses ranging between 0.17-0.68 μg/ml. The maximal change in SCC and PD were observed at a VIP concentration of 0.51 μg/ml when applied to the serosal side and no changes in PD or SCC were observed when VIP was added to the mucosal solution at these doses. Using the maximal response dosage SCC and PD were measured in 5 additional mucosal strips following the addition of VIP to the serosal solutions. PD increased by 5.4 ± 1.5 mv (mucosal negative with respect to serosa) and SCC increased by 16 ± 6 μA/cm. The resistance following VIP, averaged 337 Ωcm^2 which was not statistically different from the control averages or published values for the resistance of isolated mucosal strips. Since VIP is known to increase adenyl cyclase activity in lung tissue, then these experiments indicate that VIP most likely increased the Cl^- transport across the mucosa by increasing cAMP levels. To further examine the hypothesis theophylline (10^{-3}M) also increased PD and SCC by 2.9 ± .9, and 12.8 ± 3.7, respectively. (We would like to thank Drs. S. Said & Mutt for providing the VIP) Supported by HL 22549.

POSSIBLE EFFECTS OF AN UNSTIRRED LAYER ON O2 UPTAKE BY RED CELLS. A THEORETICAL STUDY. V.H.Huxley, C.Delson* and H. Kutchai Depts. of Physiol. and Bio. Med. Eng., Univ. of Va., Charlottesville, VA 22908

Red cells (RBC) in the rapid reaction apparatus take up O2 more slowly than is predicted by calculations for layers of hemoglobin (Hb) solution. This discrepancy has traditionally been attributed to the diffusion resistance of the RBC membrane. We employed numerical solutions to the set of partial differential equations describing O2 uptake by layers of Hb, Hb with a 100 Å membrane and an unstirred layer at the membrane surface. Assuming an O2 diffusion coefficient of 7.5 x 10-6 cm^2/sec (Fischkoff and Vanderkooi,1975) and an O2 solubility of 6.2 x10-9 moles/cm^3mmHg (Battino,et al.,1968) in the membrane, we found that the membrane does not significantly influence the kinetics of O2 uptake. The addition of a relatively small unstirred layer (0.88 um) caused a 2-fold increase in the time required to reach 50% RBC O2 saturation. These results support more recent evidence that an effective unstirred layer may play a significant role in the retardation of O2 uptake by red cells in the rapid reaction apparatus. Unstirred layers influencing O2 uptake are likely to be present under physiological circumstances.
(Supported by HL 17967 from the NIH)

Free Mg^{++} Affects Phosphorylation of Na^+K^+ATPase. Edward S. Hyman. Touro Research Institute, New Orleans, La. 70115

Failure of .01 M EDTA to arrest phosphorylation of rabbit kidney Na^+K^+ATPase (E) in the presence of .001 M Mg^{++} led to the finding that traces of Mg^{++} (< 1 x 10^{-8} M) in C.P. reagents will support phosphorylation (Biophys. J. 25, 105a, 1979). Mg^{++} binds to about 3 times as many sites on E as does ATP, with a K_a of 4 x 10^{-4} M^{-1} (less with Na^+) (Fed. Proc. 38, 1041, 1979). This suggests that Mg^{++} may have some other function. Phosphorylation of E at 37°C was measured at 0.3 second, at a series of concentrations of Mg^{++} from 1 x 10^{-7} to 1 x 10^{-2} M, using 0.14 M Na^+, 0.01 M imidazole buffer at pH 7.5, and a series of concentrations of ATP with ATP^{32}. Because of contamination of C.P reagents, lower concentrations of Mg^{++} were fixed with Mg EDTA buffers. The concentrations of chelates were calculated using Ka = 1.68 x 10^4 for MgATP and 2.25 x 10^6 for Mg EDTA. A plot of $E{\cdot}P^{32}$ vs log Mg ATP at each concentration of Mg^{++} resulted in a family of sigmoid curves with half phosphorylation at log MgATP = -7.1 for 1 x 10^{-7} M Mg^{++} and at log MgATP = -6.3 for 1 x 10^{-2} M Mg^{++}. Almost the entire 6 fold shift occurred between 2 x 10^{-4} and 2 x 10^{-5} M. Although total intracellular Mg^{++} is in the millimolar range, the intracellular phosphates may reduce free Mg^{++} to the 10^{-5} range reported for Ca^{++} (Fed. Proc. 38, 963,1979) in which range intracellular Mg^{++} could have a regulatory effect on phosphorylation of E in vivo.
(NIH No. AM 12718)

THE EFFECT OF METHIMAZOLE (MMI) ON THE BLOOD PRESSURE AND PLASMA CATECHOLAMINE LEVELS IN THE SPONTANEOUSLY HYPERTENSIVE RAT (SHR). S.G. Iams* and S.J. Blumenthal* (SPON:R.T. Thurber) East Carolina University, Greenville, NC 27834

The thyroid has been reported to play a role in the genesis of hypertension in the SHR. Surgical thyroidectomy (Cir. Res. 40:306,76) will greatly reduce the hypertension in the SHR. The hypothalamic-pituitary-thyroid axis develops during the neonatal period of the rat. Treatment of neonates with MMI or propylthiouracil to produce hypothyroidism is reported to have long term physiological effects. In this study SHR and WKY males were treated with MMI at the time of parturition for 10 days via drinking water of the mother. Heart to body weight ratios were significantly lower ($P<.05$) in the treated animals of both strains at 5 and 10 days of age, only; blood pressure and body weight showed no long term effect of treatment. However, in 90 day old SHRs treated continuously from birth, body weights, heart rates (HR) and mean arterial pressures (MAP) were significantly lower ($P<.01$) than the controls; plasma epinephrine (EPI) and norepinephrine (NE) levels were significantly higher.

	n	Body Wt	HR	MAP	NE pg/ml	EPI pg/ml
Control	(6)	232±18†	415± 9	171±9	377± 75	277±94
MMI	(7)	120± 2	330±11	119±5	1025±159	880±80

† (SEM)

These results suggest that short term suppression of the thyroid in the neonate has no effect on the genesis of hypertension in the SHR, while continuous suppression will completely inhibit its development. (Supported in part by NC Heart Assoc)

EFFECTS OF MUCOSAL ACID ON RABBIT URINARY BLADDER. Mark S. Ifshin and D.C. Eaton. Univ. of Texas Med. Br., Galveston, TX 77550

The mammalian urinary bladder may be exposed to fairly acid urine. To better understand how the bladder handles this increased acid content, we studied the effects of mucosal acid loads on transepithelial transport in the rabbit urinary bladder. Using a modified Ussing chamber and conventional microelectrodes, the short-circuit current (SSC), the transepithelial conductance (G_T), and the voltage divider ratio (R_a/R_b) were measured. A pH electrode was placed directly in the mucosal chamber so that pH of the mucosal solution could be monitored directly. The pH was lowered using several different acids in either normal Ringer or Ringer containing HEPES and acetic acid for extra buffering capacity. It was observed that increased acidity markedly and reversably increased G_T and SSC and decreased the voltage divider ratio. These effects would begin to take place in seconds or minutes after application of the acid load but may have taken up to several hours to reach steady state. A step change in pH would usually be accompanied by an early change in G_T and SSC that would be larger than the steady state values. (Supported in part by grant DHEW 5R01-AM-20068)

GRAVITATIONAL PHYSIOLOGY STUDIES ABOARD BIOSATELLITES COSMOS AND MANNED SPACECRAFT. E.A.Ilyin* (SPON: O.G. Gazenko). Institute of Biomedical Problems, Moscow, USSR

Weightlessness is the most unique and hardly reproducible on the Earth space flight factor. The USSR has carried out a large number of experiments to study its physiological effects on crewmembers of manned spacecraft and on various biological objects - unicellular organisms, plant and animal tissues, seeds and plants, insects, turtles, fish, small laboratory animals, and dogs. The scope of the pertinent investigations was significantly enlarged due to the launch of the long-term orbital stations Salyut and biosatellites of the series Cosmos. The development of specially designed flight hardware also contributed to the success of gravitational physiology studies.

BASE SECRETION BY AMPHIUMA SMALL INTESTINE: EFFECT OF ACETAZOLAMIDE. Michael A. Imon* and John F. White, Dept. Physiol. Emory Univ. Atlanta, GA 30322.

Amphiuma small intestine absorbs Cl^- by a process which requires HCO_3^- and is inhibited with low concentrations of acetazolamide (White, J.F. Fed. Proc. Abst. 38: 1061, 1979). This study sought to determine if HCO_3^- secretion occurs simultaneously and if so, whether it is sensitive to acetazolamide. Stripped proximal segments of Amphiuma small intestine (10.7 cm^2) when mounted in a lucite chamber and bathed with unbuffered media alkalinized the mucosal media and acidified the serosal media. Gradients of H^+ exceeding 2 pH units were observed. With media containing 25 mM HCO_3^- (gassed with 95% O_2, 5% CO_2) on the serosal side and unbuffered media on the mucosal side statted at pH 7.8 by addition of HCl the base secretory rate declined from 1.7 to 1.0 μeq/hr cm^2 over 5 hrs under short-circuited conditions. After 5 hrs of anoxia (95% N_2, 5% CO_2) the base secretory rate was 0.35 μeq/hr cm^2. Mucosal lactate secretion under anoxia was estimated to be about 0.05 μeq/hr cm^2. Base secretion was completely inhibited in the absence of serosal CO_2 and O_2 (i.e. 100% N_2). Acetazolamide (10^{-4}M) rapidly reduced I_{sc} and base-secretion by 20-78%. These results indicate that base secretion occurs under conditions in which the intestine is absorbing Cl^- and suggest that acetazolamide inhibition of Cl^- absorption follows inhibition of carbonic anhydrase. (Supported by the Cystic Fibrosis Foundation and NIH grant AM 17361)

EFFECTS OF CIGAR SMOKING ON CORONARY VASCULAR RESISTANCE AND BLOOD FLOW IN THE DOG HEART. D.J. Inciarte*, B.T. Swindall*, J.T. O'Neill, J. Johnston*, and F.J. Haddy. Dept. of Physiol. Uniformed Services University, Bethesda, MD. 20014

Coronary sinus outflow (F) was measured in 19 pentobarbitalized open chest dogs. Other measurements included aortic pressure (AP), coronary sinus pressure, left ventricular contractile force (CF), left ventricular dP/dt max, and heart rate (HR). A lit cigar was inserted into one leg of a Y tube attached to the input port of the ventilator. Smoking was adjusted to 3 rates with a resistance on the 3rd leg of the Y tube. F increased at the intermediate and particularly at the high rates of smoking, resulting mainly from decreases in coronary vascular resistance (R). CF and dP/dt also increased but HR was unaffected. When 5 animals underwent a second smoking series at the same rates, the responses were essentially the same. Propranolol (1 mg/Kg iv), after the initial series of smokes (N=7), increased R and decreased F, CF, and dP/dt. Phentolamine (.7 mg/min iv), after the first series of smokes (N=7), decreased R and AP. However, the responses to smoking were similar to those before propranolol or phentolamine. Arterial blood obtained during the high smoking rate, in the absence of drugs, revealed a reduced O_2 Cont, PO_2, and pH. Calculations indicated a rise in COHb%. Coronary sinus PO_2 did not change but pH fell. Thus, rapid cigar smoking decreased coronary resistance and increased coronary flow and these changes were not blocked by propranolol or phentolamine.

TEMPERATURE EFFECTS ON LUNG MECHANICS. C. Inoue*, H. Inoue*, and J. Hildebrandt, Virginia Mason Res. Ctr., Seattle,WA 98101

Effect of temp (T) on lung PV curves and on reversibility was studied in the range 21° to 52°C in 25 freshly excised rabbit lungs. Two air PV curves were obtained after degassing at a control T of 21°C, then the collapsed lungs were equilibrated at one of 5 test T for 60 m where PV was repeated, and finally returned to control T in the same fashion. Test T's were 32° (n=4), 37° (n=5), 42° (n=5), 47° (n=6) and 52°C (n=5). Peak infl V (100% TLC) was always the V at Ptp = 30 cm W on the sec infl cycle at 21°C. Elastic recoil (Pel) at 10 fixed % TLC (eg, at 10% TLC, etc, up to 100% TLC) were obtained from each infl and defl. First cycles resembled data shown by Clements for rats (ARRD 115:67, 1977) except that our transition occurred about 5° higher (42° to 47°) and was 2/3 as large. In sec cycles, the transition on the defl curve was further reduced, but a new transition (also at 42°) appeared on infl curves below 70% TLC. Upon return to 21°C, defl curves were reversible except above 47°C in the range 80-95% TLC, and infl curves below 70% TLC were shifted to higher Pel compared to controls. In additional fluid filled lungs, Pel was much less sensitive to T, suggesting that the results obtained with air mainly represented surface alterations. Our transition zone on defl curves was just above that of pure DPL (41°). Our data confirm the general trends shown by Clements, with some differences: the range of stability is extended from 37°C to above 42°, and the magnitude of the transition is less marked. (Supported by NIH grant HL 14854).

EFFECT OF MUSCLE TONE IN DOG LOBAR BRONCHI AND ARTERIES ON PERIBRONCHIAL FLUID PRESSURE (Px(f)). H. Inoue*, C. Inoue*, and J. Hildebrandt, Virginia Mason Res. Ctr.,Seattle,WA 98101.

Px(f) was measured in 5 fresh lower lobes, using modified wick catheters inserted between bronchus and artery to a depth of 1.7 ± 0.3 cm from the hilum. Lobes were inflated by pos pressure at zero vascular pressure, expressing Px(f) relative to Ppl. Pharmacological reagents were applied locally by pledget in either arteries or bronchi to depths of 2.5-3.5 cm from the hilum. Px(f) was measured on at least 5 points of each 3 min infl-defl cycle to 30 cm W, and repeated 4-6 times for each reagent. Drugs used were: saline, carbachol (bronchoconstrictor), isoproterenol (bronchodilator), L-norepinephrine (vasoconst), and papaverine (vasodil). At resting lobe volume Px(f) was slightly neg (around-6 cm W) in all groups, and became significantly more neg with infl. At max infl pressure, no difference was detected between control (Px(f) = -30.0 ± 3.0) and saline application (Px(f) = -30.4 ± 5.7 cm W). Peak neg Px(f) after constrictors were -36.8 ± 4.5 (carb.) and -34.9 ± 10.2 (norepi.); Px(f) became more positive after dilators, eg, -28.4 ± 3.3 (isoprot.) and -21.9 ± 1.3 (pap.). These changes were almost reversible. The data suggest that although Px(f) is primarily influenced by bronchovascular to parenchymal interdependence, smooth muscle tone can significantly modify interstitial fluid pressure of the lung. Muscle tone could thus affect fluid leakage from the microvessels and influence fluid pooling in the peribronchial/perivascular spaces. (Supported by NIH HL 20773).

NONCHOLINERGIC,NONADRENERGIC BRONCHODILATATION:ROLE OF ATP AND AMINOPHYLLINE, C.G. Irvin*, R.Boileau*, J. Tremblay*,R.R. Martin and P.T. Macklem (SPON: M. King). Meakins Christie Labs., Royal Victoria Hosp. Montreal, Quebec.

We stimulated the sympathetic (S) and parasympathetic (P) branches of the vagus nerve in anesthetized cats during i.v. infusion of 5-hydroxytryptamine (20-100 ug/kg/min). Propranolol (3mg/kg) and phentolamine (2mg/kg) abolished the fall in pulmonary resistance R_L, produced by stimulation of S, whereas following atropine (2mg/kg) stimulation of P produced bronchodilatation which was slower in onset and longer in action than that following stimulation of the unblocked S. Reserpine pretreatment (4mg/kg) failed to alter the results. ATP caused variable changes in R_L and when dilatation occurred it required doses in excess of 10mg/kg. Aminophylline (1mg/kg/min) blocked the fall in R_L during stimulation of P when the accumulated dose exceeded 50 mg/kg in spite of persistent bronchoconstriction. We conclude that although aminophylline blocks nonadrenergic bronchodilatation, ATP is unlikely to be the neurotransmitter as suggested by Burnstock for the gut (Pharmacol.Rev. 24:509, 1972) because of the variable response and high dosage required for bronchodilatation. Supported by NIH Fellowship #H10578401 and the MRC of Canada.

HEMODYNAMIC RESPONSES TO EXOGENOUS ANGIOTENSIN II IN THE LAMB FETUS. Harriet S. Iwamoto* and Abraham M. Rudolph. UCSF. San Francisco, CA. 94143.

Although it is known that angiotensin II (AII) is a potent vasoconstrictor and that AII administration to fetal lambs increases blood pressure, the effect of AII on cardiac output (CO) and its regional distribution are unknown. We investigated the effects of exogenous AII on arterial blood pressure (BP), CO and its distribution, and organ blood flow in 9 fetal lambs at 120-131 days of gestation. AII was measured by radioimmunoassay and CO and organ blood flow by injecting 15μm diameter radionuclide-labeled microspheres while withdrawing reference blood samples. AII (Hypertensin,CIBA) was infused at a rate of 169 ± 52 ng/min per kg fetal weight (mean ± SEM). Fetal plasma AII increased from a control value of 87 ± 16 to 341 ± 129pg/ml. Mean BP increased from 46 ± 2 to 56 ± 3 mmHg ($p<0.01$) and CO increased from 514 ± 33 to 601 ± 22 ml/min per kg ($p<0.02$) The proportion of blood flow to the umbilical-placental circulationdecreased from 41 ± 2 to 34 ± 2% of CO. Renal blood flow decreased from 200 ± 15 to 118 ± 15 ml/min per 100gm. Blood flow to the gut and thyroid also decreased significantly. Pulmonary blood flow markedly increased from 95 ± 19 to 340 ± 18 ml/min per 100gm. This represents an increase from 5 to 15% of CO. Blood flow to the heart also increased significantly. Infusion of AII into fetal lambs increased BP and CO and altered the regional distribution of blood flow.

GLUTAMINE, GLN, TOLERANCE IN NONACIDOTIC, NA, AND CHRONICALLY ACIDOTIC, A, RATS. Anne Jackson* and T.C. Welbourne. LSU Medical Center, Shreveport, La. 71130

As an index of Gln utilization in NH_4Cl induced metabolic acidosis, fasted male Sprague-Dawley rats were given an oral Gln load, 10mmoles Kg^{-1}, under light ether anesthesia. Serial blood samples were drawn via cardiac puncture at timed intervals and analyzed for total CO_2, Gln and urea. NH_4Cl administration reduced total CO_2, 19.8±2.1 vs 26.8± 1.3mM while plasma Gln, 0.63±0.04 NA, vs 0.66±0.05mM A, was unchanged. With the Gln load, plasma Gln levels rose with a maximum at 15 minutes and then declined to the preload levels over a 90 min. time course in both groups. At the maximum, however, NA Gln levels were three times the pre-load levels and significantly ($P<.05$) higher than the A maximum which rose only 2 fold suggesting a greater rate of Gln utilization in A. During this time, plasma urea levels rose at a significantly greater rate in A than NA consistent with a greater rate of hepatic uptake and conversion to urea. Slices from liver and kidney cortex were incubated in 1.67 mM Gln and the rates of NH_3 and urea production determined. For both tissues, A slices produced significantly more NH_3 while A liver slices also produced 3 fold more urea than NA. These results are consonant with a greater Gln utilization rate, at least at elevated Gln levels, in A.

DIFFERENTIAL EFFECT OF IBUPROFEN ON VASOPRESSIN-SENSITIVE ADENYLATE CYCLASE (AdC) IN MEDULLARY COLLECTING TUBULES (MCT) AND IN MEDULLARY ASCENDING LIMB OF HENLE'S LOOP (MAL). B.A. Jackson*, R.M. Edwards* and T.P. Dousa. Mayo Clinic and Foundation, Rochester, MN 55901.

Renal effects of [8-Arg]-vasopressin (AVP) are likely modulated by prostaglandins (PG). Administration of PG synthetase inhibitors in vivo was reported to potentiate the antidiuretic effect of AVP. It is now known that AVP acts both on MCT and on MAL to stimulate cyclic AMP formation. In the present study we examined the effects of Ibuprofen, a potent inhibitor of PG synthetase, on AVP-stimulated AdC activity in MCT and MAL isolated from the rat kidney. MCT and MAL were dissected from the rat medulla and preincubated for 20 min in the presence or absence of 10^{-6}M Ibuprofen. Segments were then assayed for AdC activity both in the presence and absence of 5×10^{-9}M AVP. Preincubation with Ibuprofen did not influence basal AdC activity in MCT. However, preincubation with Ibuprofen increased (Δ + 30%; $P < 0.01$) stimulation of AdC by AVP in this segment. In contrast preincubation with Ibuprofen decreased (Δ - 30%; $P < 0.05$) stimulation of AdC by AVP in MAL. These observations suggest that Ibuprofen potentiates the stimulation of AdC by AVP specifically in MCT (compared to MAL), probably by inhibiting endogenous PG synthesis. (Supported by AM-16105, AHA-74182, by Mayo Foundation and by National Kidney Foundation.)

VENTILATION AND ACID-BASE STATUS IN GREEN SEA TURTLES AT VARIOUS TEMPERATURES. Donald C. Jackson and David R. Kraus*. Brown Univ., Providence, RI 02912.

Lung ventilation, metabolic rate and blood acid-base status were measured on two groups of green sea turtles, Chelonia mydas, at temperatures between 15 and 35 C. The first group (I) were immature yearling turtles (N=8) weighing 0.48-1.24 kg; the second group (A) were adult animals (N=6) weighing 54-127 kg. Both groups exhibited typical temperature dependence of metabolic rate with the Q_{10} for groups I and A being 2.8 and 3.0, respectively. Ventilation also increased with temperature, but the Q_{10} was smaller; in group I, Q_{10} from 15-25 C was 1.72 and from 25-35 C was 1.55. In group A, the Q_{10} between 17 and 26 C was 1.40. Consequently, the ratio between ventilation and O_2 consumption fell with temperature in both groups, in group I over the entire range tested, but in group A only between 17 and 26 C. Only 3 adult animals were tested at 30 C or above and these had ratios similar to the 25 C animals. Arterial blood pH was unchanged in group I from 15-25 C, but fell significantly (7.50 to 7.36) from 25-35 C. We conclude that the green turtles in both age groups adhere to the temperature-acid-base pattern characteristic of most ectothermic vertebrates, but within a narrower temperature range than the freshwater turtles. (Supported by NSF Grants PCM 76-24443 and PCM 77-24919.

BOUNDARY LAYERS AND DIFFUSION ACROSS TROUT (Salmo gairdneri) GILLS. W.F. Jackson and P.O. Fromm. Dept. of Physiology, Michigan State University, East Lansing, MI 48824

Boundary ("unstirred") layers are known to increase the apparent permeability of biological systems. We were interested in determining if boundary layers played a significant role in limiting the rate of diffusion of tritiated water (^3HOH) across trout gills, in vitro. Second gill arches were perfused at 0.25 ml/(s.g dry filaments) with Cortland saline containing 30 g/L bovine albumin with (Epi) or without (No-Epi) 10 µmol epinephrine. Gills were suspended in a 300 ml bath of 1% Ringer containing ^3HOH (8.3 kBq/ml). The rate of revolution of a stirring bar, located in the bath, was varied between 0 and 18.8 Hz. An estimate of the permeability-surface area product (PdA) was calculated at each rate. PdA increased asymptotically with the stirring rate for both Epi and No-Epi gills, the asymptotes being 18 and 8 µl/(s.g dry filaments) respectively. These asymptotic values of PdA were 2.5 and 2.9 times greater, respectively, than the values of PdA estimated with no stirring. The PdA response curves for Epi and No-Epi gills were parallel. These results suggest that boundary layers are present at the surface of gills and that they may provide a significant barrier to diffusion of molecules, especially highly diffusible substances such as oxygen. The data confirm the calculations of Hills and Hughes (Resp. Physiol. 9:126, 1970). (Supported by NSF ENV 77-12300.)

HOMOGENEITY OF REGIONAL SPINAL CORD BLOOD FLOW UNDER PROFOUND HYPOTENSION. H. Kurt Jacobs, Jonas V. Lieponis*, Michael J. Barber, Wilton H. Bunch and M. Ramez Salem.* Res. & RER & D, Hines VA Hosp., Hines, Il. & Depts. Surg., Phys., Orthpedic Surg., & Anes., Loyola Univ. of Chicago, Maywood, Il. 60153.

Concerns are frequently expressed that a hypotensive episode or a period of deliberate hypotension contributes to a diminished spinal cord blood flow (SCBF) particularly in the T_5-T_{11} area of the cord. Such a diminished flow could lead to neurological dysfunction on a temporary or prolonged basis. To test this hypothesis SCBF was measured by microspheres (15±3µ) in twelve halothane anesthetized mongrel dogs under four conditions. These conditions were at control mean arterial blood pressure (MAP), 60 torr MAP using sodium nitroprusside (NPS), 50 torr MAP using NPS and following re-establishment of normotension. Specific levels of the cord examined were: cervical, T_1-T_4, T_5-T_{11}, T_{12}-T_{13}, and lumbo-sacral. Although there was a trend for a diminished flow in the upper levels of the cord under 60 torr MAP (Wilcoxon signed rank test) an analysis of variance of the data showed that there were no changes in flow to any area of the cord under either hypotensive condition. Venous blood drawn from a catheter inserted via a T_6-T_7 intercostal vein and advanced deep toward the spinal column did not exhibit any significant drop in oxygen content even though the arterial-venous oxygen content difference assumed to be across the cord did increase to 7.93±1.11 vol% under 50 torr MAP. Thus canine SCBF is homogeneously maintained under NPS hypotension.

METABOLIC VS OSMOTIC HYPEREMIA OF THE GUT. Eugene D. Jacobson, Wieslaw W. Pawlik*, and Joseph D. Fondacaro*. College of Medicine, Univ. Cincinnati, Cincinnati, OH 45267

Intestinal instillation of 5% glucose in isotonic saline causes hyperemia, presumably mediated through metabolites from enhanced active co-transport of glucose and sodium. 5% glucose is also hypertonic. Osmotic and metabolic contributions to intestinal vasodilation were studied in 14 anesthetized laporatomized dogs where we measured superior mesenteric artery blood flow, the arteriovenous oxygen difference (A-V O_2), and the gut wall distribution of radiolabeled microspheres. During 30-min periods of control and of instillation of different solutions of actively and passively transported sugars dissolved in saline results were:

SOLUTION	% CHANGE COMPARED WITH CONTROL (ISOTONIC SALINE)			
	BLOOD FLOW	A-V O_2	OXYGEN UPTAKE	
0.1% GLUCOSE	8 ± 2*	14 ± 2*	26 ± 4*	*p .05
5% GLUCOSE	22 ± 2*	25 ± 3*	52 ± 4*	
5% MANNITOL	17 ± 3*	-9 ± 3*	10 ± 3*	

Mucosal microsphere distribution was unchanged by 0.1% glucose and significantly increased by 5% glucose and 5% mannitol. Thus: 1) metabolic hyperemia shows a small increase in blood flow and A-V O_2 and no change in mucosal blood flow distribution; and 2) osmotic hyperemia shows a larger increase in blood flow, a decrease in A-V O_2, and an increase in mucosal blood flow distribution (supported by a grant from the John A. Hartford Foundation, Inc.)

The Closing Volume and the Volume Closed. Marc Jaeger Dept. Physiology, college of Medicine, University of Fla, Gainesville, Fal., 32610.

In subjects with an increased closed volume some airways appear to be closed when the subject breaths normally at FRC. The alveolar pressure in the open compartments of the lung varies in phase with the flow at the mouth. The alveolar pressure in the closed compartment varies in phase with pleural pressure and has the same amplitude. As a result mean alveolar pressure is out of phase with flow during normal breathing at the mouth. We found the mean phase difference in 29 smokers to be 9.5°. When breathing at increased lung volume (above closing volume) the phase difference disappeared in 21 subjects; presumably because of the opening of the airways a fact which supports our assumptions. Knowing pleural pressure, compression and expansion of gas in the closed area and flow rate one can determine the "volume closed" i.e., the volume of gas trapped behind the closing airways. We found it to be in the average of 196 ml.

GEOTROPIC MODULATION OF BEANS BY RESPONSE TO MECHANICAL STIMULATION. Mordecai J. Jaffe. Laboratory of Sensory Physiology, Botany Dept., Ohio University, Athens, Ohio, 4 5701, U.S.A.

When the stems of bean plants are mechanically perturbed by wind or rubbing, negative geotropic curvature is inhibited. The initial transient positive curvature also is eliminated, but when the mechanical stimulus is given several hours before the gravitic stimulus, the positive curvature is enhanced but the negative which follows is no longer effected. These observations are interpreted as adaptive advantage to a plageotropically growing vining stem.

If bean plants are placed horizontally, either on or off a clinostat, there are prolonged effects on the pulvinar movements. The action of the horizontal clinostat itself, induces a specific effect on the pulvini. The changes in pulvinar (and therefore leaf) movements are accentuated by mechanical stimulation. (Supported by NASA grant No. NSG 7352.

CENTRAL PROTECTION AGAINST ENDOTOXIN INDUCED HYPOTENSION WITH VENTRICULO-CISTERNAL (V-C) PERFUSION OF NALOXONE. H. F. Janssen* and L. O. Lutherer. Dept. of Physiology, Texas Tech Sch. of Med., Lubbock, Texas, 79430.

The typical fall in mean blood pressure ($\overline{BP}$) seen in the dog following an IV injection of E. coli endotoxin (.5 mg/kg) was truncated with naloxone (3.75 mg/dl) administered via a V-C perfusion (.5 ml/min) of artificial CSF. The experimental group of respired anesthetized mongrel dogs underwent a stabilization period and 30 minutes of V-C naloxone perfusion prior to endotoxin injection. The control group received endotoxin only.

	Control	At Injection	1 hr	2 hr	3 hr
naloxone ($\overline{BP}$)	138 ±6.0	158 ±9.4	121 ±18.5	127 ±15.6	124 ±15.3
control ($\overline{BP}$) (mm Hg) (±SEM)	129 ±2.3	123 ±8.2	73 ±14.7	72 ±12.4	78 ±17.9

Centrally administered naloxone produces an elevation in both $\overline{BP}$ and pulse pressure. Further, the naloxone prevented a significant decrease in $\overline{BP}$ following endotoxin administration. These results suggest that (1) the effects of naloxone are centrally mediated, (2) an endorphin/enkephalin system normally depresses $\overline{BP}$ and (3) this depression is exaggerated during endotoxin shock.

ACETATE AND LACTATE-INDUCED CONTRACTION AND RELAXATION OF THE ISOLATED MESENTERIC ARTERY. J.R. Jauchem*, F.N. Miller*, D.L. Wiegman*, I.G. Joshua*, and P.D. Harris. Microcirculatory Systems Research Group, Dalton Research Center, University of Missouri, Columbia, MO 65211.

Previous studies in our laboratory have shown that peritoneal dialysis solutions produce dilation of arterioles in vivo. Our present experiments investigated the in vitro effects of the major buffer anions of these solutions, acetate and lactate, on tension of rat mesenteric arteries. Arterial rings were contracted by an ED50 concentration of norepinphrine, and either Na lactate or Na acetate was added. Normal osmolality was maintained. These anions produced a biphasic response, contraction followed by relaxation. These responses (n=6, $\bar{x}$+SEM) are expressed as a percentage of the norepinephrine-induced increase in tension.

	Acetate		Lactate		
	30 mM		30 mM	45 mM	60 mM
contraction (%)	22+3	NS	24+3	35+8	29+4
relaxation (%)	55+6	p<.05	23+9	24+8	26+9

Increasing the concentration of lactate to 45 or 60 mM did not increase the magnitude of either the contraction or relaxation phases of the response. This indicates that lactate is less efficacious for relaxation, but that these anions may involve similar mechanisms for alteration of vascular smooth muscle function. (Supported in part by NIH NO1 AM7 2217, HL 12614, and HL 21901).

CSF [NH_3] AND [LACTATE] IN RELATION TO CSF ACID-BASE BALANCE DURING ACUTE AND CHRONIC RESPIRATORY ACIDOSIS (5% CO_2) IN AWAKE DOGS. Donald B. Jennings and John S.D. Davidson*. Queen's University, Dept of Physiology, Kingston, Ontario, Canada K7L 3N6.

NH_3 and lactate in the central nervous system have been implicated in the adaptation to respiratory acid-base disturbances. We have sampled cisternal cerebrospinal fluid (CSF) from 7 awake dogs during air control and for up to 26 days of exposure to a hypercapnic environment of 5% CO_2. NH_3 was measured using an ion specific electrode and lactate was measured by an enzymatic technique. CSF [NH_3] tended to decrease at 1 hour of hypercapnia, but subsequently increased two-fold to reach a peak concentration in the CSF at 1.5 days of respiratory acidosis. CSF [HCO_3-] increased rapidly during hypercapnia and between 1 hour and 1.5 days the increase in CSF [HCO_3-] was correlated with CSF [NH_3] ($r = 0.76$). Therefore, in this early period of respiratory acidosis NH_3 probably contributed to the generation of CSF HCO_3-. Subsequently, CSF [HCO_3-] plateaued and CSF [NH_3] decreased toward control levels. Despite the increase in [HCO_3-], CSF [H+] remained elevated (about 46 nM/ℓ) throughout 26 days of hypercapnia compared to air control (42.5 nM/ℓ). The sustained acidosis of the CSF during chronic hypercapnia was not accounted for by changes in lactate which decreased slightly at 1 hour of hypercapnia and then returned to air control levels. (Supported by the Medical Research Council, the Ontario Thoracic Society and the Ontario Ministry of Health Lottery Fund).

EFFECT OF GRANULOCYTOPENIA ON EXTRAVASCULAR LUNG WATER CONTENT AFTER PULMONARY MICROEMBOLISM IN DOGS. A.Johnson*, A.S. Weiser*, P.H.Neumann*, N.Gertzberg* and A.B.Malik. Dept. of Physiology, Albany Medical College, Albany, NY 12208

Pulmonary microembolism was induced in anesthetized, controlled ventilated dogs by injecting (within 5 min) 0.7 to 1.5g/kg 100μm diameter non-siliconized glass beads into the right atrium. Selective granulocytopenia was induced by hydroxyurea (180mg/kg) given for 3 days. Pre-embolization arterial granulocyte count of 242±96 per μl in treated group was less than 3569±1240 per μl in controls. Baseline and post-embolization (PE) pulmonary perfusion pressures ($P_{\overline{\Delta P}}$) and vascular resistances (PVR), and final extravascular lung water content/bloodless dry lung weight (W/D) ($\bar{x}$±SE) were:

	Control(n=8)		Granulocytopenia(n=4)	
	Baseline	PE	Baseline	PE
$P_{\overline{\Delta P}}$, mm Hg	10.3±1.1	31.3± 2.5	12.1±1.5	34.9±3.2
PVR, mm Hg/l/min/kg	59.7±8.2	207.9±14.1	73.0±12.2	216.0±34.5
W/D, ml/g		4.53± .24		4.35±0.40

W/D values in the two groups were both greater ($p<0.05$) than our normal value of 2.84±0.22. The pulmonary hemodynamic changes in the two groups were not different. Therefore, granulocytopenia in dogs did not protect against pulmonary edema after pulmonary microembolization. (Supported by HL-17355 and HL-00363)

SITE OF GUT ACTIVATION OF PANCREATIC POLYPEPTILE (APP) REFEEDING RESPONSE IN CHICKENS. Elizabeth M. Johnson* and Robert L. Hazelwood. University of Houston, Houston, Texas 77004.

A striking increase in plasma APP levels is observed immediately after refeeding previously fasted (24 hr) chickens (650-950 gm). Refeeding elevated plasma APP levels from 4.93 to 23.49 ng/ml within 10 min., then declining gradually to 60% above normal at 90 min. The 10-min. APP peak corresponded with food passage to approx. midway between the initial ileum and yolk stalk loci. Refeeding responses were observed also in birds when loose ligatures were placed at various sites in the G-I tract 48 hrs before and tied immediately prior to refeeding. Significant increases in APP were observed with ligatures below the crop and midway in the duodenum (both 80-100% above control) 60 min. later. Control birds (ligatures in place, not tied, refed) responded with a 6-fold increase in APP levels. Yolk stalk ligatured chickens responded almost to same extent (4-fold above fasted) as did untied control birds. We conclude that the major component of the APP-refeeding response is initiated by a gut site in the early ileum region. Precise localization of the "trigger" site is now underway.

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THE ROLE OF LUMINAL OSMOLALITY AND pH ON PASSIVE DUODENAL MUCOSAL PERMEABILITY. GM Johnson* and RSK Chung. VA Medical Center and University of Iowa College of Medicine, Iowa City, Iowa, 52240.

Passive duodenal permeability to erythritol was measured at luminal osmolalities simulating interdigestive (isosmotic) and post-prandial (450 mOsm/Kg H_2O) phases. Under Innovar anesthesia the duodenum of Sprague-Dawley rats was cannulated and perfused at 37°C. Perfusates contained (mM) 138 Na^+, 106 Cl^-, at a pH of either 6, 3, 2.3, 2, or 1.7, maintained constant by a pH stat. Osmolality was adjusted with mannitol, tritiated polyethylene glycol was used as volume marker and ^{14}C erythritol as a passive permeability marker. The mean net erythritol effluxes, expressed as η moles/30 min/mg dry weight are as follows:

Luminal pH	6.0	3.0	2.3	2.0	1.7
Isosmotic	42.0	15.0	59.7	134.9	167.4
450 mOsm/Kg H_2O	30.4	2.8	24.8	68.2	119.9

Passive mucosal permeability, as determined by net erythritol efflux, was significantly increased at low pH. However, hyperosmolality decreased mucosal permeability, partially annulling the effect of low pH. We conclude that the acid chyme, usually hyperosmotic with respect to plasma, increases duodenal mucosal permeability much less than predicted by acid perfusion alone.

(Supported by VA Research Funds)

ACTION OF ISOPROTERENOL ON CYCLIC AMP IN THE MUSCLE AND EPITHELIUM OF THE GUINEA PIG SEMINAL VESICLE. **Jane H. Johnson* and John W. Lloyd. Department of Physiology, Howard Univ., Washington, D.C. 20059**

In vitro isoproterenol can elevate endogenous levels of cyclic AMP in male sex accessory tissues of the rat (Lloyd et al, Pharmacologist 15:423, 1973). The present study was designed to assess the relative effects of isoproterenol upon the levels of cyclic AMP in the muscle and epithelial components of the guinea pig seminal vesicle. Seminal vesicles from intact or castrate animals were excised and separated into its muscle and epithelial layers as described by Levey and Szego (American Journal of Physiology 182:507, 1955). The tissue was sectioned in half. Half of the tissue served to establish control levels, the other half was incubated with varying concentrations of isoproterenol. Threshold response for both the epithelium and muscle was obtained with 1×10^{-6}M isoproterenol. At 1×10^{-4}M isoproterenol the amount of cyclic AMP generated by the epitheluim (73 ± 4 pmol/mg protein) was almost twice that found in the muscle (40 ± 3 pmol/mg protein). Castration resulted in a diminished cyclic AMP response in both the epitheluim and muscle. The attenuation was greater ($p \leq 0.05$) in the epithelial component. The data suggest that the in vitro increase in the level of cyclic AMP of the guinea pig seminal vesicle following isoproterenol treatment is confined primarily to the epithelial component.

ALDOSTERONE INDUCED HYPERTENSION IN RATS. Allan Jones, Ellen Garwitz*, Marsha Shellhart Mertens* and Linda Foster.* Dept. of Physiology, University of Missouri, Columbia, MO 65212.

Although hypertension has often been induced in rats by the implantation or injection of deoxycorticosterone acetate (DOC) few studies have attempted to mimic the effects of an aldosterone secreting tumor. Aldosterone (Aldo) was infused at 2 µg/hr via osmotic minipumps (Alza Corp). The uninephrectomized rats were given saline supplemented with K as needed to maintain weight. Control rats (150 gram) were uninephrectomized and placed on saline. Saline consumption was elevated in Aldo rats after one week's infusion. Systolic blood pressure was significantly elevated at two weeks and reached 215±4 versus 123±7 mm Hg by 4 weeks. Plasma Aldo levels were also elevated at term.[42] K turnover in aortic smooth muscle was increased by Aldo (0.0169±0.0018 vs 0.0072±0.0003 min^{-1}). These preliminary results indicate infusion of Aldo increases blood pressure and ion turnover in vascular smooth muscle. These results are similar to chronic DOC, but occur at much lower doses (Supported in part by HL 15852 and the American Heart Association).

THE ROLE OF INTRAPULMONARY, SYSTEMIC AND CENTRAL CHEMORECEPTORS IN THE VENTILATORY RESPONSE TO CO_2 IN THE DUCK. David R. Jones, William K. Milsom and Geoffrey R.J. Gabbott*. Dept. of Zoology, Univ. of British Columbia, Vancouver, B.C., Canada V6T 1W5.

Using cross-perfusion between pairs of animals we examined the effects of static changes in arterial CO_2 tension (Pa_{CO_2}) at pulmonary, carotid body and central chemoreceptors on minute ventilation ($\dot{V}_E$), tidal volume (V_T) and respiratory frequency (f) in unanaesthetized, spontaneously breathing, White Pekin ducks. By adjusting the level of inspired CO_2 (PI_{CO_2}) of either the experimental (R) or donor (D) animals it was possible to manipulate Pa_{CO_2} at any one or combination of the receptor groups. All experimental animals (R) had one intact lung and one lung denervated by vagotomy. Increasing Pa_{CO_2} from 3.3 to 6.0 kPa caused a 250% increase in $\dot{V}_E$ resulting from a 200% increase in f and only a 20% increase in V_T. Stimulation of central chemosensitive areas alone was 3 to 4 times more effective in increasing both f and $\dot{V}_E$ than stimulation of the carotid bodies alone. Increases in V_T were small in both instances. Stimulation of pulmonary receptors alone by increasing Pa_{CO_2}, obtained by raising PI_{CO_2} to the denervated lung, had no effect on $\dot{V}_E$. When CO_2 was present in the air presented to the intact lung breathing was abnormal becoming more so at higher levels of PI_{CO_2}. We conclude that central chemoreceptors play the major role in the response of awake ducks to CO_2.

WATER BALANCE IN NORMAL AND DIABETES INSIPIDUS RATS AT HIGH ALTITUDE. R. Jones,* K. Johnson,* J. Flynn* and S.M. Tenney. Dept. of Physiology, Dartmouth Med. School, Hanover, NH 03755

Acute decreases of water intake and urine output at high altitude likely contribute to the syndromes of acute mountain sickness and possibly of high altitude pulmonary edema (HAPE). In a study of both Normal (N) and Diabetes Insipidus (DI) rats water intake decreased (to 29% of SL in N; 49% in DI) promptly upon exposure to hypobaric hypoxia (P_B=380), and decreased urine output (to 67% of SL in N; 50% in DI) was observed by the end of HA day 1. Drinking responses to controlled extra- and intracellular thirst stimuli at different inspired O_2 levels (P_{O_2}=57; 70; 85; 150 torr) indicated that hypoxia shifted the threshold to higher osmotic stimulus intensity without changing the sensitivity of response. The hypoxic effect appeared to be graded. DI rats recovered normal drinking and urine output by HA day 4, while urine output in N rats remained depressed and did not track input. Since urinary vasopressin (AVP) excretion was significantly reduced in N rats for 4 days at P_B=380, the low urine output at HA was likely due to reduced intake. Urine osmolality of N rats did not change significantly during this period. Plasma Na and osmotic concentrations increased significantly in DI rats but not in N rats after 3 days of HA. Plasma volume and hematocrit measurements after 3 days of HA suggested that DI rats were better able to maintain plasma volume at altitude. Lung H_2O/dry lung wt. increased significantly by HA day 3 in N rats but remained unchanged in DI rats. (Supported by PHS Grant NHLBI 02888-23.)

NALOXONE REVERSAL OF RESPIRATORY CHANGES AFTER DIAZEPAM. C.Jordan*, J.R.Lehane* and J.G.Jones*.(SPON: C. G. Caro) Clinical Research Centre, Harrow, England.

In a double blind cross-over trial in 6 subjects, we have compared the effects of naloxone and saline on the respiratory changes produced by diazepam. At 60 and 95 mins after 15mg diazepam i.v. each subject received either a 15mg dose of naloxone i.v. or the equivalent volume of saline. After 50 mins, diazepam produced significant depression of the slope of the rebreathing ventilatory response to CO_2 ($\Delta\dot{V}_I/\Delta PCO_2$) to 53% of control ($P<0.05$), reducing to 50% of control after the 1st dose of saline but recovering to 61% of control after the 1st dose of naloxone. Following the 2nd dose of naloxone, $\Delta\dot{V}_I/\Delta PCO_2$ recovered to 76% of control compared to 61% after saline. 120 mins after the 2nd dose of naloxone, $\Delta\dot{V}_I/\Delta PCO_2$ returned to control values but remained depressed following saline (68% of control, $P<0.05$). The paired t-test showed that $\Delta\dot{V}_I/\Delta PCO_2$ was significantly greater after naloxone than after saline ($P<0.05$) for 180 mins following the 1st dose. The mouth occlusion pressure response to CO_2 showed similar changes which were not statistically significant. End-tidal CO_2 during quiet breathing, and inspiratory resistive loaded breathing (8 kPa l^{-1} s) showed small increases after diazepam which were not significantly reduced by naloxone. The results of this study suggest that a large dose of naloxone may be effective in relieving respiratory depression following diazepam by reducing depression of CO_2 sensitivity.

EFFECT OF SIMULATED WEIGHTLESSNESS ON ENERGY METABOLISM IN THE RAT. J.P. Jordan, H.A. Sykes*, J.C. Crownover*, C.L. Schatte, J.B. Simmons, II* and D.P. Jordan*. Colorado State University, Ft. Collins, CO 80523

To identify the bioenergetic responses to chronic exposure to weightlessness, 24 pairs of male rats were used each consisting of a control and an experimental animal. 12 pairs were fed ad libitum and 12 were in a pair-fed experiment. Weightlessness was simulated by suspending the experimental animal in a harness so that the anti-gravity muscles were not supporting the body. During a 14 day treatment period the experimental rats were harnessed and suspended from day 1 through day 7 inclusively while the control animal of each pair wore an identical harness for the treatment period but was never suspended. On days 0, 1, 7, 8, and 14 of the treatment period both rats in each pair were injected intraperitoneally with 100 µCi per kilogram of metabolic weight ($W_{Kg}^{3/4}$) of D-glucose-UL^{14}C; monitored for 2½ hours for rate of expiration of ^{14}C-carbon dioxide, total carbon dioxide and oxygen consumption. Food intake and body weights were recorded daily. Parameters were computed in terms of units per $W_{Kg}^{3/4}$. Metabolic rate was decreased in experimental rats through 7 days of continuous simulated weightlessness. Parameters returned to the pretreatment level when hypokinesia was discontinued. Only part of the decreased metabolic rate could be explained on the basis of energy intake; simulated weightlessness itself accounts for a significant reduction in metabolic rate. (Supported by NASA Grant NSG-2232)

REVERSIBLE CHANGES OF FREE ENERGY IN MUSCULAR CONTRACTION Norman R. Joseph, University of Illinois at the Medical Center, Chicago, Il. 60612

Intracellular sodium in relaxed adult skeletal muscle is characterized by high free energy of about 80 g. cal. per kg. intrafibrillar water. This yields the same value for the maximal work of reversible contraction. For an adult the total free energy of sodium ions is about 2000 g. cal. for the entire system of contractile myofibrils. As compared with the level of basal metabolism the ratio is about 1 part muscular free energy to 1000 parts nutrient calories, More than 99 percent of the nutrient energy is converted irreversibly to heat. The remainder is available to the organism as reversible internal work or changes of tension. This implies reversible cyclic processes in skeletal muscle and other tissues. Production of external heat or enthalpy (ΔH) is equal quantitatively to the irreversible conversion of free energy (ΔG). This is Carnot's condition for invariance (second law of thermodynamics). All internal processes depend on reversible changes of the free energy of sodium. The other ions occur in non-reactive forms in the sarcoplasm. Sodium occurs in inaccessible central regions. This applies to all systems of reversible irritability: cardiovascular, digestive, respiratory, and to smooth muscle in general.

GABA APPEARING IN BLOOD OF TOBACCO HORNWORMS ORIGINATES IN NEURAL AND NOT EPITHELIAL TISSUES. Arthur M. Jungreis and Kristine K. Whitnable*. Zoology Department, University of Tennessee, Knoxville, TN 37916

The presence of GABA at the mM level has recently been reported in blood of *Manduca sexta* [Jungreis & Omilianowski, Physiologist 21,61 (1978)]. This observation contrasts with that in vertebrates, where GABA is unable to pass across the blood-brain barrier. We now report that the source of blood GABA in insects is neuronal, but not epithelial. When incubated with exogenous GABA, the 3 major tissues: gut, fat body and integument are collectively able to degrade GABA *in vitro* at rates comparable to those observed *in vivo*. Release of GABA in excess of that present initially in neural tissues is noted when abdominal ganglia, thoracic ganglia or brain are incubated *in vitro*. Using insects ligated at different times in larval-pupal development, GABA release by the abdominal ganglia is influenced by neurosecretory activity in the brain as evidenced by a) failure of exogenous ß-ecdysone to cause an increase in blood GABA when animals are ligated before ecdysiotropin (brain hormone) release, and b) programmed increases in blood GABA occur in insects ligated after ecdysiotropin release. We conclude that GABA appearing in blood originates in neural and not epithelial tissues, and that by inference, it does so by passing across a so-called "blood-brain" barrier. (Supported by USPHS NIH Grant AI-12779)

NEURAL STRUCTURAL BASIS FOR THE PRODUCTION OF REFLEX PULMONARY VASOCONSTRICTION. C.E. Juratsch, C.A. Lemmi*, W.F. Walby*, M.M. Laks. Harbor-UCLA Med. Ctr., Torrance, CA.

Distention of the main pulmonary artery (DMPA) induces reflex pulmonary vasoconstriction. 6-hydroxydopamine (6-OHDA) can abolish this reflex and destroy adrenergic nerve endings. Therefore, the purpose of this study was to relate the nerve network density (ND) in the pulmonary arteries and veins (0.5 - 1.5 mm diameter) to this reflex before and after 6-OHDA. In dogs, after the reflex responses to DMPA were obtained, small lung vessels were excised, stretched on microscope slides, and treated fresh with glyoxylic acid to produce catecholamine histofluorescence. The ND was determined by overlaying a measuring grating on photomicrographs. Before 6-OHDA, DMPA increased the pulmonary vascular resistance (PVR) from 3.56 ± 0.41** to 7.10 ± 0.65 ($P<0.05$). Associated with this increase in PVR was an ND of 12.2 ± 0.93 for small pulmonary arteries which was greater than the 7.6 ± 0.66 ND obtained for small pulmonary veins ($P<0.05$). After 6-OHDA, the reflex response to DMPA was abolished or markedly reduced along with a disappearance of the catecholamine histofluorescence in both the pulmonary arteries and veins. We conclude, therefore, that (1) adrenergic innervation of pulmonary arteries and veins is necessary for DMPA induced pulmonary vasoconstriction and (2) small pulmonary arteries have 61% more adrenergic innervation than correspondingly sized pulmonary veins.
**Mean ± SEM

BODY TEMPERATURE VARIATIONS RELATED TO OVIPOSITION IN THE LAYING HEN. H. Kadono* and E. L. Besch. Department of Metabolism, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610.

Deep body temperature of the unrestrained laying hen was measured continuously by telemetry with simultaneous recording of the exact time of oviposition. Photoperiod regime was LD (14L:10D) and LL (continuous light). The fluctuation in body temperature under LD coincided with the photoperiod; elevated during light (L) and lowered dark (D). The oscillation of body temperature under LL appeared to be a free-running, circadian type and this rhythm coincided approximately with the egg-laying cycle. From periodic analysis, the length of body temperature period under LL condition averaged 25.2 hr. Typically, body temperature increased during oviposition. This body temperature rise lasts about 1.5 hr.; the increase being 0.5 to 0.7C. Usually the egg is oviposited 15-20 min before peak temperature. In many cases, a small deflection on the down slope of this temperature curve was observed; this appears to represent the time of ovulation. Occasionally, oviposition did not occur concomitant with an increase in body temperature. In these instances, although the animal displayed characteristic prelaying behavior and temperature rise in the predicted oviposition time, actual oviposition preceded (premature oviposition) or followed (delayed oviposition) the temperature rise. When premature oviposition was induced experimentally (intravenous vasopressin), the increase in body temperature appeared at the predicted time.

EFFECTS OF HALOTHANE ON VENTILATORY CONTROL IN CATS: Enid R. Kafer University of North Carolina, Chapel Hill, N.C. 27514.

The effects of halothane (1.6% end tidal) on the ventilatory and neural responses to isocapnic hypoxemia ($Pa0_2 55$) and to inspiratory elastic loads were examined, and compared with the responses in cats anesthetized with chloralose-urethan (C/U). The phrenic neurogram and external intercostal myogram were recorded and integrated (time constant of decay 100 ms) (IPN and IEIM) to give peak heights and slopes (peak height/inspiratory time). Halothane anesthesia was associated with a high respiratory frequency (64.85 ± SEM 6.94 $minute^{-1}$) (freq.) and small tidal volumes (19.6 ± SEM 1.6 ml) (V_T) and there was no change in these variables during hypoxemia. In comparison during normoxia in the cats anesthetized with C/U the V_T was 37.4 ± SEM 2.2 ml and freq. was 20.43 ± 1.36 minute and hypoxemia resulted in a 64% increase in V_T and 20% decrease respiratory frequency. The V_T and inspiratory time (T_I) responses to inspiratory elastic loads expressed as the ratio of loaded/control in the halothane series were similar to the C/U series and were not altered by hypoxemia. However, in the cats anesthetized with halothane the peak heights and slopes of the IPN and IEIM were reduced during the loaded breath. Halothane anesthesia has an overriding effect on respiratory timing and prevents any shortening in response to hypoxemia. In addition during halothane anesthesia recruitment of larger motor neurons is inhibited during the loaded breath.

BRAIN STEM PROJECTIONS OF THE EXTRATHORACIC TRACHEA IN THE CAT. M. Kalia, Dept. Physiol., Hahnemann Med. Col., Philadelphia, PA 19102

The tetramethyl benzidine (TMB) reaction for horseradish peroxidase (HRP) histochemistry was used to trace the sensory and motor connections of the extrathoracic (ET) trachea in the cat. In anesthetized adult cats, a 33% soln. of HRP was injected into the submucosal layer of the ET trachea as well as in the trachealis muscle over a length of 5 cm. Following a 48 hr survival time, the brains were perfused and the tissue reacted for HRP histochemistry using TMB as the substrate. HRP label was visualized in the following regions: Sensory projections - HRP-labeled sensory terminals were found extending from 2.5 mm rostral to 0.5 mm caudal to obex. These terminals were localized in the ventrolateral and ventromedial subnuclei of the nucleus of the tractus solitarius (NTS) as well as in the commissural nucleus. The densest sensory projection was found to the ventrolateral NTS (vlNTS). Motor projections - HRP-labeled cell bodies were found in the brain stem from 5.5mm rostral to 7mm caudal to the obex, numerous HRP-labeled neurons were found in the nucleus ambiguus (NA) from 5.5mm rostral to 1mm caudal to obex. More caudally HRP label was found in neurons of the nucleus retroambigualis (NRA) and in the nucleus of the XIth nerve, these projections extended from 2mm to 7mm caudal to the obex. This study demonstrates anatomical connections between the extrathoracic trachea, vlNTS, vmNTS, NA and NRA. (Supported by USPHS grant HL-17800 and RCDA HL-00103.)

THE EFFECT OF THEOPHYLLINE ON GLUCACON AND SECRETIN STIMULATED BILE FLOW. Donald L. Kaminski and Y.G. Deshpande.* St. Louis University, St. Louis, MO 63104.

Current concepts suggest that theophylline and glucagon act at the canalicular level and secretin at the ductular level to stimulate bile flow. This study compares the effect of a canalicular stimulant (theophylline) on canalicular (glucagon) and ductular (secretin) stimulated bile flow. Dogs with chronic biliary and gastric fistulas were used. The dose response curve of synthetic secretin indicated that the calculated maximal response (CMR) for bile flow was 475 µl/min while the D_{50} was 0.11 $nmol/kg^{-1}hr^{-1}$. The CMR for glucagon was 488 µl/min while the D_{50} was twice as great (0.27 $nmol/kg^{-1}hr^{-1}$) as that of secretin. Maximal bile flow rates produced by secretin were significantly increased by theophylline with evidence of a summation of effects suggesting that theophylline and secretin utilize different receptors to stimulate bile flow. The CMR of glucagon plus theophylline was unchanged (465 µl/min) from values produced by glucagon alone while the D_{50} was decreased suggesting that theophylline is a competitive agonist of glucagon and utilizes the same mechanism to stimulate bile flow. The results of this study are compatible with the concept that secretin acts at one locus in the biliary tree and theophylline and glucagon at another. Two diverse agents such as theophylline and glucagon having the same mechanism suggests that their activity may be mediated by cyclic AMP. (Supported by USPHSAM 17084)

CARDIOPULMONARY EFFECTS OF POSITIVE END-EXPIRATORY PRESSURE IN CONSCIOUS, SPONTANEOUSLY BREATHING DOGS. J.T. Kanusky*, W.B. Strawn*, S.M. Hall*, and M.G. Levitzky. Dept. of Physiology, LSU Medical Center, New Orleans, LA. 70112.

Chronic dogs with electromagnetic flow probes implanted on their pulmonary arteries, catheters in their left atria and external jugular veins, and chronic tracheostomies breathed 100% O_2 through endotracheal tubes, pneumotachographs, and one-way valves. Swan-Ganz catheters were placed in their pulmonary arteries via the jugular vein catheters. Following a 20 min control period the expiratory tubes were submerged for 10 min each under 5, 10, 15 and 20 cm H_2O. At the end of each period, mean pulmonary artery pressure and mean left atrial pressure, cardiac output, arterial and mixed venous blood gases and ventilation were determined. Mean pulmonary artery pressure and pulmonary vascular resistance increased significantly as PEEP was increased. Cardiac output, right ventricular stroke volume, and heart rate did not change. Arterial and mixed venous CO_2 rose significantly and arterial and mixed venous pH fell significantly as PEEP was increased. There was no change in minute ventilation, tidal volume or ventilatory frequency. These results indicate that the stress of moderate levels of PEEP can be met by the conscious, spontaneously breathing dog. (Supported by NHLBI Grant HL 22641.)

THE EFFECTS OF INSULIN ON PROTEIN TURNOVER IN ISOLATED ADULT RAT MYOCARDIAL CELLS. Race L. Kao, Sinnan L. Luh*, Linda E. Metzger*, Edward H. Williams*, and G. Frank O. Tyers*, Dept. of Surg., Univ. of Tx. Med. Br., Galveston, Tx. 77550

Isolated heart cells have distinct advantages over other preparations for the study of myocardial metabolism. Heart cells from the adult rat were isolated by perfusion and incubation with buffer containing collagenase and hyaluronidase. This method gives a high yield of viable cells with normal morphology and metabolic properties. The isolated cells have physiologic levels of ATP (20.4±1.7μmole/g protein), creatine phosphate (24.1±3.6μmole/g protein) and lactate (34.0±4.4μmole /g protein). For studies of protein synthesis and degradation, the cells were washed free of digesting enzymes and incubated in Krebs-Henseleit bicarbonate buffer containing 15mM glucose, normal plasma levels of calcium (10mg%) and all 20 amino acids except phenylalanine (phe). Insulin (25mU/ml) was added to the treated groups at the beginning of incubation. Protein synthesis was determined by the incorporation of ^{14}C-phe and degradation by both the net release of phe and the release of phe in the presence of 2 x 10^{-5}M cycloheximide. The addition of insulin resulted in a significantly higher rate of protein synthesis during the second and third hours of incubation. A significant decrease in proteolysis occurred in both the presence and absence of cycloheximide. These results confirm our earlier studies in the isolated perfused rat heart, which demonstrated that insulin acted to preserve levels of myocardial protein by stimulating protein synthesis and inhibiting protein degradation.

THE ROLE OF THE VAGUS NERVE IN THE RESPONSE OF COLLATERAL CHANNELS TO HISTAMINE. J. Kaplan*, G. Smaldone*, P.B. Terry*, H.A. Menkes, R.J. Traystman and D. Swift*. Johns Hopkins Medical Institutions, Baltimore, Md. 21205.

We studied the role of the vagus nerve in the response of collateral channels to exogenous histamine in 5 anesthetized, paralyzed dogs. A fiberoptic bronchoscope (OD 5.5mm) was wedged into a peripheral airway. With a constant flow of air ($\dot{V}_{Coll}$) delivered through the bronchoscope, resistance to collateral flow (Rcoll)=(Ps-Palv)/$\dot{V}$coll where Ps=pressure in the obstructed segment of lung and Palv=pressure in the surrounding lung. When $\dot{V}$coll was stopped, Ps decayed toward Palv. The compliance of the collaterally ventilated unit (Cs') was calculated as Tcoll/Rcoll where Tcoll=time for Ps to fall 63% after stop $\dot{V}$coll. A solution of 6.4mM histamine was aerosolized in a DeVilbiss nebulizer. The histamine nuclei passed through a Sinclair-LaMer condensation generator to yield a monodispersed aerosol with an aerodynamic mass median diameter ranging from 0.6 to 1.0 microns. The aerosol was delivered through the bronchoscope for periods of 5 minutes. Before vagotomy, histamine increased Rcoll by 78 ± SE 26% and decreased Cs' by 9 ± 10%. After vagotomy, histamine increased Rcoll by 73 ± 20% and decreased Cs' by 14 ± 5%. Changes in Rcoll and Cs' following histamine before vagotomy were not significantly different from those seen after vagotomy. We conclude that responses of collateral channels to histamine result from direct action of the drug and are not mediated by vagal reflex pathways. (Supp. by NIH HL-14153)

RELATIONSHIP OF PLASMINOLYSIS TO RETICULOENDOTHELIAL FUNCTION DURING INTRAVASCULAR COAGULATION. John E. Kaplan, Frank A. Blumenstock*, and Thomas M. Saba. Dept. of Physiology, Albany Medical College, Albany, New York 12208.

Recent studies demonstrated depressed reticuloendothelial system (RES) phagocytic clearance during intravascular coagulation (IVC). The present study addressed the hypothesis that this results from plasminolysis of plasma fibronectin (α_2SB opsonic glycoprotein, cold-insoluble globulin) an important regulator of RES function. Degradation might result in non-opsonic fibronectin and/or phagocytic inhibitory fragments. RES function was assessed in rats by clearance and organ localization of a gelatinized ^{131}I-lipid emulsion. IVC was initiated by IP bovine thrombin(500U/100g). Plasmin activity was inhibited by IV transexamic acid(50mg/100g). IVC resulted in RES depression with delayed blood clearance ($p<0.001$); reduced hepatic colloid uptake($p<0.001$); and elevated extrahepatic (lung, spleen, bone marrow) colloid localization($p<0.001$). Transexamic acid had no effect on RES function. When transexamic acid was injected prior to IVC there was amelioration($p<0.05$) of the depressed clearance and hepatic uptake. In further studies gelatin adherent fibronectin was isolated from normal rats and rats during IVC. Injection of this material resulted in reduction($p<0.05$) in hepatic colloid uptake compared with that isolated from normal rats. It is suggested that plasmin degradation of circulating fibronectin during IVC contributes to reticuloendothelial phagocytic impairment. (NIH GM-25946, GM-21447)

NATRIURESIS AND DIURESIS INDUCED BY CEPHALAD FLUID SHIFTS IN A CONSCIOUS PRIMATE: NOCTURNAL SUPPRESSION OF THE RESPONSE. D.A. Kass*, F.M. Sulzman, C.A. Fuller and M.C. Moore-Ede. Dept. Physiology, Harvard Medical School, Boston, MA 02115.

Renal and hemodynamic responses to central vascular volume expansion induced by 4 hrs of continuous lower body positive air pressure (LBPP) were examined in conscious, chair-restrained squirrel monkeys in an isolation chamber with a light-dark (LD12:12) cycle. LBPP during both day (12^{00}-16^{00}) and night (00^{00}-04^{00}) induced the same 4 cmH_2O increase in CVP ($P<.001$), rise in heart rate of 28/min ($P<.02$), and minimal changes in mean arterial blood pressure. However, while daytime LBPP induced a significant increase in urine flow ($\dot{V}$) from 2.12±.31 to 3.6±.45 ml/hr ($P<.02$) and sodium excretion ($U_{Na}\dot{V}$) from 71.1±14 to 279.56±41.7 μEq/hr ($P<.001$), as well as a reduction in urine osmolality (U_{Osm}) from 1426±197 to 635±156 mOsm/kg ($P<.05$), nighttime LBPP produced no significant increases in $\dot{V}$ or $U_{Na}\dot{V}$. The reduction in U_{Osm} was nearly identical to that observed during the day. $U_K\dot{V}$ was not significantly affected by either exposure. The results demonstrate a marked nocturnal inhibition of increases in $\dot{V}$ and $U_{Na}\dot{V}$ in response to cephalad fluid shifts in conscious primates. Comparisons of the time course and diurnal regulation of the responses suggest several separate efferent pathways are involved. (Supported by NASA Grant NSG9054.)

LSD CAN ENHANCE LATERAL INHIBITION IN LIMULUS: IS IT AN ACTIVE UPTAKE BLOCKER? Leonard Kass*, Peter H. Hartline* and Alan R. Adolph. Eye Research Institute, Boston, MA 02114.

Lateral inhibition in the lateral eye of Limulus appears to be mediated by a 5-HT synapse. Experiments with 5-HT analogs, precursors and blockers suggest that LSD may obstruct 5-HT active uptake (Adolph and Kass, JGP, in press). LSD has previously been shown to block 5-HT inhibition (Adolph, '76). We now report that LSD in low concentrations can enhance lateral inhibition. We record optic nerve spikes from isolated photoreceptor cells and apply an adjacent spot of light to elicit the inhibition. The inhibitory light is sinusoidally modulated at different frequencies to obtain the inhibitory transfer functions. Low LSD enhances this inhibition at all frequencies, but the enhancement is greatest at the lower frequencies of inhibitory light modulation. Inhibition evoked by a step of light is also enhanced by LSD. Inhibition fatigues or desensitizes more rapidly in LSD than in the normal eye. The LSD effects are concentration dependent; higher LSD effectively blocks the inhibition. Hypothesis: In low LSD, partial blockage of 5-HT presynaptic uptake recognition sites prolongs 5-HT lifetime and enhances inhibition; in higher LSD more sites are blocked, leading to very high levels of synaptic 5-HT and postsynaptic desensitization. Our model may also account for incongruent LSD effects reported in mammalian CNS literature: (i) LSD agonistic/antagonistic effects within the same tissue, (ii) concentration dependence on LSD action, and (iii) the effect of LSD on 5-HT turn-over rate.

EFFECT OF PROPRANOLOL ON EXPERIMENTALLY INDUCED THIRSTS. M.J. Katovich*, C.C. Barney*, and M.J. Fregly. Dept. of Physiol., University of Florida, Gainesville, FL 32610

The effect of acute administration of d,l propranolol, a B-adrenergic antagonist, on the drinking response of female rats to both extracellular and intracellular thirst stimuli was investigated. As examples of extracellular thirst stimuli, administration of either isoproterenol (25 ug/kg) or angiotensin II (200 ug/kg) and removal from cold (thermogenic drinking) were studied. As an example of cellular thirst, a 1M NaCl solution was administered (1% B.W.) Water deprivation (20 hr), which has both extracellular and cellular components, was also examined as a dipsogenic stimulus. All of the aforementioned stimuli resulted in a significant increase in water intake over corresponding controls. All dipsogenic stimuli, except cellular thirst (1M NaCl load), were attenuated significantly when the animals were pretreated with d,l propranolol (1-6 mg/kg) 1 hr prior to measurement of water intake. Since propranolol is known to possess anesthetic-like properties, d-propranolol was also used. This isomer has little B-blocking activity but possesses anesthetic-like activity. Administration of the same doses as d,l propranolol, did not result in any alteration in water intake when any of the above dipsogenic stimuli were studied. These results suggest that a B-adrenergic receptor is necessary for the total dipsogenic response to occur in the extracellular, but not the cellular, type of thirst stimulus. (Supported by American Heart Association, Florida Affiliate.)

BONE GROWTH AND COMPOSITION IN WEANLING AND MATURE RATS EXPOSED TO CHRONIC CENTRIFUGATION. Lanny C. Keil and J. Warren Evans. NASA-Ames Res. Ctr., Moffett Field, CA 94035 and The University of California, Davis, CA 95616.

Femur growth and mineral composition was studied in weanling (80-90g) male rats exposed to either -2.7 or $4.1G_x$ for periods of 2, 4, 8 and 18 weeks, and sexually mature male rats (200-400g) exposed to $-4.1G_x$ for 2 or 4 weeks. A number of rats of the same age from each group were maintained as noncentrifuged controls. Centrifugation at either 2.7 or 4.1G reduced femur fat-free dry weight in weanlings by 16 to 31% ($P<0.005$) and 17 to 20% ($P<0.005$) in mature animals when compared to controls. Femur length and width was also reduced by 7 to 12% ($P<0.005$) in weanlings and 4 to 12% ($P<0.005$) in mature rats. Exposure to hypergravity for 2 or 4 weeks produced a small but significant decrease in plasma calcium and phosphorus levels in both age groups. Bone calcium and phosphorus content was lower ($P<0.05$) in weanling rats after 2 weeks at either 2.7 or 4.1G. No alterations in bone composition was noted in mature animals. Results of this investigation indicates that chronic exposure of young rats to hypergravity retards bone development dispite the increased gravitational loads imposed upon the skeletal system.

GLUCOSE METABOLISM FOLLOWING ENDOTOXIN ADMINISTRATION IN DIABETIC RATS. D.L. Kelleher*, G.J. Bagby and J.J. Spitzer. Dept. of Physiology, LSU Medical Center, New Orleans, LA 70112.

The effect of streptozotocin-induced diabetes on glucose turnover (GT) following E.coli endotoxin (ET) administration was investigated by primed-constant infusion tracer techniques. Fasted euglycemic-saline treated, euglycemic-ET treated, diabetic-saline treated, and diabetic-ET treated rats were anesthetized with pentobarbital and catheterized for blood pressure (BP), heart rate (HR), ^{3}H-glucose infusion and urinary glucose excretion (UG). Blood pH, plasma glucose (PG), lactate (PL) and glucose specific activity were determined prior to and 120 min after i.v. injection of 0.1 mg ET/100g or saline. BP fell following ET (30%), and a compensatory rise of HR (15%) occurred in both euglycemic and diabetic rats. ET elevated PG (45%) and PL (250%) in diabetic rats and increased PL (135%) in euglycemic rats. Arterial pH remained unchanged. Control GT was elevated in diabetic vs euglycemic rats (88 vs 35 μmoles/kg min) while ET increased turnover in both groups. Metabolic clearance of glucose [(GT - UG)/PG] was reduced in diabetics but not affected by ET in either group. While basic differences in glucose metabolism exist between diabetic and euglycemic rats, they do appear to respond similarly to ET at the dose and time period studied. (Supported by NIH Grants HL 22101 and GM 07029 and the E.G. Schlieder Educational Foundation)

THE ROLE OF PINOCYTOSIS IN LEAD ABSORPTION IN SUCKLING MICE. Charles A. Keller* and Richard A. Doherty* (Spon:P. Horowicz) Univ. of Rochester School of Medicine, Rochester, NY 14642

Young animals absorb a greater fraction of an oral dose of lead than do adults. The role of pinocytosis in lead absorption was studied following an oral dose of radiolabeled lead (5 mg/kg) and polyvinylpyrrolidone (PVP, 50 mg/kg) to 12 day old and adult mice. After 24 hr. small intestines were removed, flushed clear of contents, and divided into 24 equal length segments for analysis of lead and PVP content. In young mice the distal jejunum and ileum exhibited the greatest pinocytotic activity (PVP uptake) and also retained the greatest amount of lead. Lead and PVP uptake into adult intestine was much less than uptake in young mice, and was uniform along the length of the intestine. Pretreatment of young mice with 35 mg/kg cortisone acetate (s.c.) 6 days before the lead and PVP dose resulted in a 37% decrease in pinocytotic uptake of PVP and in a 54% decrease in lead absorption. Pretreatment of young mice with 370 mg/kg cortisone resulted in an 86% decrease in lead absorption relative to controls. Cortisone pretreatment of young mice reduced lead concentrations in blood, kidney, liver and brain. Cortisone pretreatment of adult mice had no effect on lead absorption. It is concluded that pinocytosis is the major mechanism involved in intestinal lead absorption in suckling mice, and accounts for most of the difference in lead absorption between suckling and adult mice. (Supported by NIEHS Grant ES01247 and 01248, and US/DOE contract UR-3490-1663.)

BLOOD FLOW TO THE EXTRA-OCULAR MUSCLES. E.M. Keough*, L.M. Wilcox*, R.J. Connolly*, and C.E. Hotte* (SPON: E. Bloomquist) Tufts NEMCH Boston, MA 02111.

Although skeletal muscle blood flow has been extensively studied, little attention has been given to blood flow to the extra-ocular muscles (EOM). This study determined blood flow in primate and canine EOM by the reference blood flow technique using Ru^{103} labeled microspheres (15±3u). Six mongrel dogs, four assamese macaques and two baboons were placed under continuous cardiovascular monitoring, including Swan-Ganz catheterization, for the duration of the experiment. Microspheres (1.12×10^6/kgbwt primate; 0.5×10^6/kgbwt canine) were injected into the left ventricle and a 1 min. reference blood sample was taken from the femoral artery. At 5 min. post-injection the animal was sacrificed, eyes enucleated, and recti muscles dissected back to their orbital apex. Muscles were fixed, weighed, counted in a single-channel well type detector and blood flow values (BFV) determined. Mean BFV for primate (0.48± 0.21 ml/min/g) and canine (0.33±0.06 ml/min/g) recti are the first reported for these animals and the first determined for any EOM using gamma labeled microspheres. BFV for the recti are 4-5 times higher than those for other skeletal muscle, probably due to their unique electrical and metabolic activities.

GLUCOSE TRANSPORT IS RATE-LIMITING FOR GLYCOLYSIS IN RAT LUNG. J.S. Kerr, A. Kleinzeller and A.B. Fisher. Dept. Physiol. Univ. Penna. Sch. of Med., Phila., PA 19104

The role of glucose transport in the perfused rat lung was investigated by measuring glucose utilization, intracellular glucose and glucose-6-phosphate under normal conditions and in the presence of phlorizin. Isolated rat lungs were ventilated with 5% CO_2 in air and perfused with bicarbonate buffer containing 3% albumin and 5.6 mM [5-^{3}H]-D-glucose. Lungs were perfused for 100 mins. and did not develop significant edema. Glucose utilization was determined from the rate of ^3H_2O production. Tissue glucose was measured enzymatically before and after precipitation of phosphorylated glucose with $Ba(OH)_2$ and $ZnSO_4$. Extracellular space was measured by distribution of [^{14}C]-polyethylene glycol (MW 4000). Glucose utilization was 55.9 ± 8.1 μmol/hr/g dry wt (mean ±SE; n=4). Tissue glucose corrected for extracellular space, i.e. intracellular glucose, was zero under all experimental conditions. Tissue glucose-6-P was 5.32 ± 0.24 μmol/ml intracellular H_2O (n=6). Increasing phlorizin concentrations (0.5-5mM) progressively depressed glucose utilization by 39% and glucose-6-P content by 55%. The effect of phlorizin was probably not on mitochondrial respiration, since anoxia has been shown to increase lung glucose utilization. The zero level of intracellular glucose and the effect of phlorizin on glucose utilization and glucose-6-P content suggest that the rate of glucose transport by lung cells may be rate-limiting for its metabolism.

EFFECTS OF DOPAMINE ON THE DISTRIBUTION OF SMALL INTESTINAL BLOOD FLOW IN SUBHUMAN PRIMATES. John C. Kerr and Kenneth G. Swan. Department of Surgery, New Jersey Medical School, Newark, New Jersey 07103

This study presents the effects of dopamine (DP) on the distribution of blood flow within the small intestines (SI) of anesthetized Rhesus monkeys. Blood flow to the mucosal (M) and submucosal-muscularis (SM) layers of the SI was determined using an intracardiac injection of radioactive microspheres (RMS), 15±3μ and reference sample technique. The M was separated from the SM layers of the SI by scrapping and radioactivity determined in a well-type gamma scintillation counter. Mean arterial (AP) and portal venous (PP) pressures were recorded. Cardiac output (CO) was determined by thermodilution. RMS were injected during a control period and, at the ninth minute of a ten-minute intra-superior mesenteric arterial infusion of DP at a concentration of 10^2 μg kg/min. Control AP and PP were 119±7 and 6.5±0.4 mmHg, respectively; CO 1.19±0.12 L/min; SI blood flow was 68±18 ml/min (64% M and 36% SM). Infusions of DP did not significantly change CO or AP but significantly ($P < .01$) increased PP to 11.0±0.4 mmHg. SI Q was significantly increased to 120±25 ml/min ($p < .05$) which represented a redistribution of 77% M and 23% SM. These data suggest that dopamine selectively increases blood flow to the mucosal wall of the small intestines.

GRAVITY SENSING, POLAR TRANSPORT AND CYTOPLASMIC STREAMING IN PLANT CELLS. John O. Kessler. Physics Department, University of Arizona, Tucson AZ 85721.

It is generally believed that the response of plant cells to gravity is mediated by intracellular organelle sedimentation. A hypothesis presented here suggests that some aspects of polar transport are gravity-related, resulting in the perception and transduction of gravitational stimuli. A transcellular density gradient component perpendicular to the normal direction of gravity is required, in conjunction with a peripherally-driven cytoplasmic stream. The internodal cells of Nitella provide an extreme example. The symmetric bilateral viscous sag of the cytoplasm, due to the density gradient, must be added vectorially to the antisymmetric cyclosis, resulting in a net difference between the up and down streaming velocities. Conservation of mass requires a proportional difference in thickness of the up and down streams. Kamiya has reported (1) observation of the velocity effect, without explanation. It amounted to 3 to 9 %. If the convective transport is significant (Péclet number ≥ 1) in the translocation of molecular species controlling plant metabolism and attitude, the gravitationally-determined streaming velocity differences provide for differential polar transport which lends itself to the regulation of cell size in extended neighborhoods.

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CHANGES IN CARDIAC LYMPH COMPOSITION AFTER ACUTE MYOCARDIAL ISCHEMIA IN DOGS. M. Jack Keyl, Russell T. Dowell and Andy A. Yunice. Dept. of Physiology and Biophysics, University of Oklahoma Health Sciences Center and Veterans Administration Hospital, Oklahoma City, OK 73190.

The composition of cardiac lymph, arterial and coronary sinus plasma was determined in 14 anesthetized dogs with acute ligation of the left circumflex artery and with sham ligation. There was no change in glucose, pyruvate, total protein or lactic dehydrogenase. Lactate concentration increased in lymph with time, there being no difference between sham and ligated animals. Creatine phosphokinase increased in both arterial and coronary sinus blood with ligation but did not change in lymph. In six additional animals electrolytes were determined before and after ligation. There was no change in magnesium, calcium, zinc or copper. It is concluded that none of the components of lymph determined can be used as a measure of acute cardiac ischemia in the dog. (Supported in part by Oklahoma Affiliate of American Heart Association Grant #0-78-G-59).

IMPROVED NONINVASIVE ESTIMATION OF PULMONARY BLOOD FLOW USING NONUNIFORM BREATHING PATTERNS. M.C.K. Khoo and R.E. Kronauer, Div. Appl. Sci. Harvard Univ., Cambridge, MA 02138 (SPON: H. Hechtman).

All of the parameters necessary to describe a single-alveolar-compartment gas exchange model (with dead space) can be deduced by fitting expired CO_2 and O_2 data if ventilation is measured and zero alveolar-arterial (A-a) gradient is assumed. These parameters include blood flow ($\dot{Q}$), venous tensions (P_vCO_2 and P_vO_2), FRC and equivalent lung tissue CO_2 storage volume (V_{LT}). Deductions based on almost-uniform breath sequences are extremely susceptible to measurement error. Use of strongly nonuniform breath sequences greatly reduces measurement error effects. Gas analyzer response and sampling delay are modelled in detail. From a 60 second record of a supine healthy adult at 4300 m altitude (which includes 3 spontaneous apneas) the following mean estimates are found: $\dot{Q}$ = 6.6 L/min, P_vCO_2 = 42.3 torr, P_vO_2 = 19.0 torr, FRC = 1.71 L, V_{LT} = 1.1 L. Use of only 40 sec of data gives estimates within 3% of these. Estimates of $\dot{Q}$ can be made separately from CO_2 or O_2 data. Those deduced from O_2 are 5% lower indicating a small A-a O_2 gradient initially unaccounted for.

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ELECTROLYTES, AMINO ACIDS AND INTERSTITIAL FLUID PRESSURES DURING IMMERSION DIURESIS IN MAN. Savita S. Khosla* and Arthur B. DuBois. John B. Pierce Fndn. and Yale Univ., New Haven, CT. 06519

Five healthy male subjects were studied lying in air 1 1/2 hr, sitting in 34°C water up to the neck 1 hr, and again lying in air 1 1/2 hr in 2 sets of experiments. For the first set, vasopressin (0.75 i.u., s.c.) was injected before immersion. Blood and urine samples were drawn every 1/2 hr in air and every 20 min in water. Urinary Na, K, and osmolal clearences were significantly increased during immersion. For the mean of 5 subjects, Hct ↓ 1.1 units, plasma concentrations of Na ↓ 3.9 mEq/L, Cl↓ 3.5 mEq/L, K↓ 0.2mEq/L, osmolality ↓ 7.9 mOsm/kg H_2O, and proteins ↓ 0.25gm %, while bicarbonate ↑ 1.33 mM/L, threonine ↑ 11.6%, proline ↑ 9.0%, methionine ↑ 14.0%, and alanine ↑ 29% during immersion. Plasma volume ↑ 6.1% and RBC volume ↑ 3.5% calculated from Hct and Hb. In the second set of experiments interstitial fluid pressures (IFP) were measured with a cotton wick in PE 50 tubing inserted subcutaneously. A mean IFP of + 1.3cm H_2O was observed lying in air. It had started to decrease by 20 min of immersion with a maximum decrease during immersion averaging 2.4cm H_2O. We conclude that hypoosmotic fluid is mobilized into the blood from interstitial and other extravascular spaces during immersion. (NIH HL-17407).

TIME COURSE OF NOREPINEPHRINE-INDUCED CHANGES IN ARTERIAL TENSION DEVELOPMENT AND CALCIUM FLUXES. D.C. Kikta* and D.L. Davis. Dept. of Physiology, Coll. of Medicine, Univ. of South Florida, Tampa, FL 33612.

The time course of tension development, intracellular ^{45}Calcium concentration ([Ca]i), ^{45}Ca-influx, and ^{45}Ca-efflux were studied in 4mm, adventitia-free, canine anterior tibial artery rings during a 2 min exposure to norepinephrine (NE). Rings were equilibrated 1-2 hrs at constant resting tension in HEPES-buffered PSS (pH 7.4) at 37°C. Tension development to 10^{-4} and 10^{-3}M NE followed essentially the same time course, continuously rising during the 2 mins. Responses to 10-5 and 10^{-6}M NE showed dose dependently less tension development and began to relax during the 2 min; 10^{-5}M at 90 sec and 10^{-6}M at 35 sec. Net changes in [Ca]i showed dose dependent initial and secondary increases. The initial increase occurred earlier (10^{-4} and 10^{-3}M, 20 sec; 10^{-5}M, 30 sec; 10^{-6}M, 45 sec) and the secondary rate of rise was steeper the higher the [NE]. After 20 sec, ^{45}Ca-influx dose dependently increased while ^{45}Ca-efflux appeared to dose dependently decrease during the 2 min; 10^{-4} and 10^{-3}M NE again acting similarly in both cases. These data indicate that there may be an extracellular source of Ca important in the early part of the NE response and that the tension may be maintained, at least during the first 2 min, by both an increased influx and a decreased efflux of Ca.

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CATION TRANSPORT AND THE EFFECT OF ANTI-L IN YOUNG RED CELLS OF MASSIVELY BLED LOW POTASSIUM (LK) SHEEP. H.D. Kim, B.E. Theg*,and P.K. Lauf. Depts. Physiol. Univ. of Arizona Med. Center, Tuscon, Az.,and Duke Univ.Med.Center, Durham, N.C.

LK sheep produce after massive anemic stress transiently red cells of high potassium(HK) content attributed to temporary retention of HK membrane transport properties(Lee et al. J.Gen.Physiol. 50:379,1966).The LK status is genetically associated with the L-antigen, an inhibitor of the Na/K pump.We studied cation transport and the action of anti-L during the LK-HK-LK transition in young red cells separated by density. In 2 animals, at day(d) 7 after bleeding, the lightest cells were nearly 100% reticulocytes with a cell volume,V_c,of 60-80 μ^3, hemoglobin (MCH) of $1.6x10^{-11}$g,and cell K,$(K)_c$,and Na, $(Na)_c$,concentrations of ca 80 and 30 mM/L cells, resp. At ds 9,17 & 23, these parameters declined in the young cells except for $(Na)_c$ which rose.Simultaneously, V_c,MCH and $(K)_c$ increased in the denser cell fractions while $(Na)_c$ fell. On d7, K-pump flux ($^iM_K^p$) increased by 3-4fold in unseparated cells with small changes in k_K^L, the leak rate coefficient,while in young cells $^iM_K^p$ and k_K^L were ca. 26 and 10 fold greater at d7 than at ds 0 or 23. Anti-L stimulated $^iM_K^p$ at all times.Young cells kept in vitro at 37°C for 22h showed a sharp drop of $^iM_K^p$ and k_K^L within 18h although $(K)_c$ remained relatively unchanged. Hence the newly produced cells maintain their large volume and HK content as they assume higher densities while pump and leak assume LK character. Supp.in part by AM 17723 & AM-00316 (H.D.K.) and NIH 2PO1-12.157 (P.K.L.).

VENTILATORY RESPONSE CURVES AND DONNAN'S r. Neal B. Kindig* and Giles F. Filley. Webb-Waring Lung Institute, Denver, CO 80262

To explain striking resemblances between $\dot{V}_E$-P_{CO_2}, $\dot{V}_E$-P_{O_2} and the corresponding r-P_{CO_2}, r-P_{O_2} curves of L.J. Henderson, an analysis of extra and intracellular buffering, ion exchange and Donnan's r as functions of P_{CO_2} and P_{O_2} were undertaken. It is shown that the r increase with P_{CO_2} is affected by bicarbonate loading in the same way as $\dot{V}_E$ in ventriculocisternal perfusion experiments (Berkenbosch et al, 1978), i.e., the curves shift to the right with high external $NaHCO_3$ because of added Na^+ and not added HCO_3^-. In contrast the r-P_{CO_2} curve shifts to the left with increased buffering in red cells as (HbO_2) decreases just as the $\dot{V}_E$ curve shifts to the left as P_{O_2} falls. The analysis uses a log q-pH plot, where q is charge concentration, to establish the charge neutral point where the negative bicarbonate charge HCO_3^- dictated by the P_{CO_2} equals the net positive charge of nonvolatile ions such as Na^+, Cl^-, Hb^- and HPO_4^-. HCO_3^- and H^+ are dependent variables. When plasma is in contact with cells the requirement for $rCl^- = rH^+$ forces chloride ion exchange. The analysis quantitates the effect of a small compartment volume, e.g., ECF between brain cells, on shared buffering. (Supported by NIH 07085 and RTCG (6-P-56815))

VARIATION OF THE TEMPERATURE OF CHOICE WITH VARYING HYDROSTATIC PRESSURE IN A MARINE GAMMARID CRUSTACEAN. Michael Kinney*, Rocky Royal*, William Jones* and Ralph W. Brauer. Institute of Marine Biomedical Research, 7205 Wrightsville Avenue, Wilmington, North Carolina 28403

A temperature gradient tube has been devised which provides a 10° temperature gradient over a 11 cm distance, orthogonal to the flow of water which establishes the gradient. The entire device is compatible with the Mark III High Pressure Aquarium System and permits studies of the effects of change in hydrostatic pressure from 1 to 300 atm upon temperature of choice in aquatic animals up to 10 mm in length. This assembly has been applied to the measurement of temperature of choice in the marine gammarid Hyale sp., acclimatized to various temperatures. The basic phenomenon observed is that an increase in chamber pressure from 1 atm to 100 atm, well below convulsion pressure for this gammarid, results in an increase of the temperature preferendum by approximately 7°C. Data will be reported concerning the relation between the magnitude of this temperature shift and the hydrostatic pressure applied, as well as concerning the relation between acclimatization temperature, temperature preferendum, and pressure for this species. The data will be discussed from the point of view of their probable bearing upon the nature of the effect of pressure on temperature preferenda and from the point of view of their bearing on the evolution of deep sea fauna.
(Supported by Griffis Foundation & National Science Foundation)

HEMODYNAMIC RESPONSES TO BILATERAL LESIONS OF NUCLEUS TRACTUS SOLITARII IN SPONTANEOUSLY HYPERTENSIVE AND WISTAR-KYOTO RATS. Yoshio Kitamura,* Shozo Ishise,* Barbara L. Pegram,* and Edward D. Frohlich. Ochsner Med. Fdn., New Orleans 70121.

To compare the hemodynamic responses to bilateral lesions of nucleus tractus solitarii (NTS) of spontaneously hypertensive rats (SHR)(9 female 33±1 wk) and Wistar-Kyoto rats (WKY)(13 female 32±1 wk), cardiac output (CO) and blood flow (BF) to various organs were determined with the microsphere method under chloralose-urethane anesthesia. Six of the 13 WKY studied had systemic arteriovenous shunts (AVS)(WKY-S), as evidenced by 52±6% of the microspheres trapped in the lungs. Percent changes (mean±SE) in mean arterial pressure (MAP), CO, total peripheral resistance (TPR), and BF to the brain (B), heart (H), small intestine (I), and kidney (K) 10 min post lesion are listed below:

	MAP	CO	TPR	B	H	I	K
SHR	123± 4[c]	99± 6	129± 9[b]	154±18	103± 8[c]	66± 3[a]	67±7
WKY-N	149± 5	88± 7	178±16	127±17	165±18	96±11	67±8
WKY-S	142±12	129±14[a]	114± 8[c]	102± 9	160±39	66± 8	61±7

where WKY-N is WKY without AVS. a=p<0.05; b=p<0.02; c=p<0.01 when compared with WKY-N.

The contribution of the splanchnic organs, liver and K vasculatures to the change in systemic conductance was 34.4 and 77.3%, respectively, in WKY-N and SHR. The data indicate a greater effect of the visceral vasculature on hemodynamics in SHR following the NTS lesions. Further, the presence of AVS significantly modifies the hemodynamic responses in rats.

CIGARETTE SMOKE INCREASES RAT LUNG CYCLIC GMP IN VIVO. D.J. Klass*and E. Lesperance* (Spon: A. Naimark). Dept. of Med., University of Manitoba, Winnipeg, Canada.

The enzyme guanylate cyclase (G.C.) is stimulated in vitro by a variety of oxidant gases. In particular, cigarette smoke (C.S.) has been shown to stimulate G.C., and to produce increased steady state levels of cyclic GMP in lung tissue in vitro. We tested for increases in lung tissue cyclic nucleotides in animals exposed in vivo to C.S. Male, Sprague -Dawley rats, 4-500 gm are anaesthetized (pentobarbital 50 mg/kg) and ventilated via a tracheostomy with controlled rate (72 cycles/min) and inspiratory pressure (10 cm H_2O). In one group, a reservoir filled with smoke from filtered cigarettes is connected to the inspiratory line. The control group is ventilated with same circuit, but the reservoir is filled with room air. Cyclic AMP and cyclic GMP are first isolated from samples of lung tissue which have been excised and rapidly frozen after various times of exposure, and are then measured by radioimmunoassay. There is no change detected in the cyclic AMP levels after up to 20 minutes (m). Compared to baseline, 35 femtomoles (fm)/mg, (n=28), the cyclic GMP levels are increased after 2 m. (88 fm/mg, n=5) and peak at 15 m. of exposure (150 fm/mg, n=20). By 20 m. of C.S. exposure the levels drop to 68 fm/mg (n=6). We conclude that cigarette smoking produces prompt increases in lung tissue cyclic GMP levels in vivo. (Supported by the Sellers Foundation, Winnipeg).

THE CORONARY VENOUS RESISTOR. G.A. Klassen and J.A. Armour. Department of Physiology and Biophysics, Dalhousie University Halifax, N.S., Canada, B3H 4H7

Using mongrel dogs anesthetized with α-chlorolose we have demonstrated that a significant systolic gradient exists between small epicardial coronary veins and the large veins (CVG) close to the coronary sinus. The presence of this gradient suggested that these veins might participate in regulation of coronary flow and myocardial function. We examined the effect of a number of interventions on this gradient. Right stellate stimulation augmented intramyocardial pressure, aortic pressure, and coronary artery pressure, but only slightly increased the pressure in the small coronary veins - thus the CVG was minimally effected. On the other hand, left stellate stimulation increased that gradient significantly while augmenting coronary artery pressure. Isoproterenol also increased CVG and minimally effected coronary artery pressure; noradrenaline increased all pressures. Acute aortic constriction increased coronary pressure but had little effect on CVG. Thus the CVG appears to be under significant sympathetic neural control and responds to α and β agonists. The coronary venous system has active neural and presumably metabolic regulation.

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*N.B.H.F. - New Brunswick Heart Foundation

STEADY STATE RELATIONSHIP BETWEEN CONTRIBUTION OF BONE ^{45}Ca AND DIET ^{40}Ca TO BLOOD CALCIUM IN EXTENSIVELY PRELABELLED ANIMALS. LeRoy Klein. Case Western Reserve University School of Medicine, Cleveland, Ohio 44106

To study the quantitative relationship between bone, diet, and blood calcium, rats, chicks, and dogs were extensively prelabelled with ^{45}Ca during early growth. The animals, while on a normal diet, were periodically sacrificed during weeks to months after labeling and the specific radioactivity (SA) of whole bone ^{45}Ca and serum ^{45}Ca were measured (dpm/mg calcium). While the SA of blood and bone ^{45}Ca decreased markedly with growth dilution, the ratio of blood SA to bone SA remained relatively constant (0.6-0.7) during the first month of age in rats, the first 4 months in chicks, and during the entire 14 months studied in dogs. With age the ratio decreased to 0.3 by 2.5 months in rats and to 0.4 by 8 months in chicks. During active growth the ratio shows that 2/3 of the serum's calcium is derived from bone and 1/3 from diet. In vitamin D-deficient chicks where influx of dietary calcium is inhibited, the blood-bone ratio approached 1.0, indicating isotopic equilibrium between bone and blood. Following parathyroidectomy in dogs, the ratio decreased in 1 week to 0.35 or after 4 weeks administration of a diphosphonate (EHDP, 10 mg/kg, which inhibits bone resorption) the ratio was 0.25. The isotopic data indicate that a constant relationship exists between contribution of bone and diet calcium to blood under normal conditions of growth. (Supported by NIH Grants AG-00361 and AG-00258)

ALTERATION OF THE INITIATION PHASE OF $HgCl_2$-INDUCED ACUTE RENAL FAILURE BY DITHIOTHREITOL. D.R. Klonne* and D.R. Johnson, Depts. of Environ. Health & Physiol., Univ. of Cincinnati Med. Cen., Cincinnati, OH 45267

Dithiothreitol (DTT), a sulfhydryl reducing agent, ameliorates the toxic effect of $HgCl_2$ on renal function measured 24 hrs after Hg administration (Kleinman, et al., Kidney Int. 12: 115, 1977). Since signs of acute renal failure (ARF) occur within 1 hr of $HgCl_2$ injection, we evaluated the effect of DTT on renal function and renal cortical protein bound sulfhydryl concentration (PBSH) during the first several hrs after Hg administration. Four hrs after $HgCl_2$ injection (3.0 mg/kg i.v.) urine flow rate ($\dot{V}$) was increased from 7.7 ± 0.6 (SEM) to 36.9 ± 4.5 µl/min and fractional excretion of Na (FE_{Na}) was elevated from 0.06 ± 0.01 to 2.49 ± 0.39%. In contrast, in Hg + DTT-treated rats (31 mg/kg i.p., 1 hr after Hg injection) $\dot{V}$ and FE_{Na} 4 hrs after Hg administration were significantly lower, 17.1 ± 6.5 µl/min and 1.09 ± 0.43%, respectively, and were not different from the values observed at the time of DTT administration, 23.8 ± 4.8 µl/min and 1.11 ± 0.26%, respectively. DTT alone had no effect on these parameters nor was there any significant difference in GFR between the Hg- and Hg + DTT-treated rats. Hg treatment depressed PBSH from 16.5 ± 0.3 to 13.9 ± 0.5 µmoles/g. However, PBSH was not as low in the Hg + DTT-treated group (14.9±0.2 µmoles/g). Therefore, the ability of DTT to reduce the effect of Hg on PBSH may be related to its ability to prevent severe loss of renal function. Supported by NIH grant ES 00159.

CARDIOVASCULAR RESPONSES TO ± 2G SINUSOIDAL ACCELERATION (< 0.3 Hz) IN NORMAL AND CARDIAC DENERVATED DOGS. C. Knapp*, D. Randall & J. Evans*. Wenner-Gren Lab. & Dept. of Physiol. & Biophys. Univ. of Ky., Lexington, KY 40506.

Cardiovascular regulation during whole body, sinusoidal acceleration (.006 to 0.25 Hz) was studied. Effectiveness of barostatic regulation was compared in normal (n=9) and cardiac denervated (n=8), chronically instrumented, tranquilized (Innovar-Vet, .075 cc/kg) dogs. Amplitudes of oscillations in aortic pressure in the normal dogs were smallest, about 30 mmHg, at the lowest frequencies, peaked at about 50 mmHg in the middle frequency range and tapered off to about 30 mmHg at the highest frequencies. Pressure oscillations in the cardiac denervated animals were larger, about 70 mmHg, across both the low and middle frequency range, tapering off sharply to 20 mmHg at the highest frequencies. This difference was due to a greater drop in aortic pressure during the +Gz portion of the cycle (i.e., as blood was being drained from the head to the feet) in the cardiac denervated vs. the normal animals. In both groups of animals, increases in peripheral resistance during +Gz were of comparable magnitude and were maximal at the lowest frequencies, diminishing monotonically thereafter. The principal difference between the pressure responses of the normal and cardiac denervated dogs was that cardiac output dropped to 1.5 L/min with +Gz stress in the normal vs. 1 L/min in the cardiac denervated dogs.

Supported by AFOSR #F44620-74-C-0012 and NIH #HL 19343.

AN INFORMATION CODING SYSTEM THAT SEEMS TO BE INDEPENDENT OF NOISE AND VARIABILITY. W.R. Klemm and C.J. Sherry*, Biology Department, Texas A&M University, College Station, TX 77843.

One of the major requirements for an effective information coding system, particularly a biological coding system, is that the code persist and be decipherable in the presence of noise and variability. We commonly analyze neuronal spike trains with a method that describes and preserves the serial order of 3-5 adjacent intervals. We wished to determine if treatment-induced changes in the incidence of such interval patterns were dependent on the interval variability, as commonly indicated by median duration, 15-85% range of durations, and skewness of the interval frequency distribution. Analysis was performed on spike trains from single cerebellar cortex neurons, before and after IV injection of ethanol. The incidence of certain serial-order patterns was changed with a high degree of statistical significance, but these changes (in terms of total, median, and average number) were independent of the conventional measures of interval variability. Thus, we have demonstrated a cybernetic coding mechanism that can operate independently of noise and variability and which coincidentally seems at the very least to be useful for a relatively complete and meaningful characterization of the interval patterns in a train of nerve impulses.

ADRENERGIC MODULATION OF Cl TRANSPORT ACROSS THE CORNEAL EPITHELIUM. S. Klyce and R.K.S. Wong* Div. Ophthalmology, Stanford Medical School, Stanford, CA 94305.

The modulation of Cl transport in the rabbit corneal epithelium by adrenaline has been demonstrated in vitro in our previous studies[1]. The presence of sympathetic nerves in the cornea has been suggested using histochemical techniques. Therefore the possibility that these adrenergic fibers may control Cl transport was considered. Using the retrograde transport of horseradish peroxidase we demonstrated that fibers from the superior cervical ganglion (SCG) innervate the adult rabbit cornea. The influence of the SCG on epithelial transport in vivo was examined following deep urethane anesthesia. Corneal potential and resistance was measured with the aid of a floating chamber designed to electrically isolate the tear side of cornea. Stimulation of the preganglionic trunk of the ipsilateral SCG with a cuff electrode usually produced mydriasis (indicating successful activation of sympathetic fibers). In 30% of these experiments, SCG stimulation led to the expected hyperpolarization of epithelial potential when the tear surface was bathed in Cl- free Ringer[1]. This mimicked the effect of application of 10^{-9}M adrenaline. These responses were blocked by 10^{-5}M propranolol. The present findings suggest that corneal epithelial transport is modulated by adrenergic fibers from the SCG.

[1] J. Physiol. 266: 777, 1977. Supported by EY 00915.

THE EFFECT OF EXERCISE ON CARDIAC ISCHEMIA. D. R. Knight* and H. Lowell Stone. Dept. of Physiology, Univ. of Oklahoma Health Sciences Center, Oklahoma City, OK 73190.

Previous data indicated that 4 weeks of repetitive exercise reduced the coronary hyperemic response and thus might improve coronary collateral blood flow. Myocardial segment length (SL) and heart rate (HR) response was examined in adult mongrel dogs before and after 2 minutes of coronary occlusion. Myocardial SL was determined by the implantation of piezoelectric crystals into the left ventricular free wall in the distribution of a major coronary vessel. A hydraulic occluder was placed around the vessel. The animals recovered for 3 weeks before coronary occlusion and were then subjected to 4 weeks of daily exercise. After 4 weeks of repetitive exercise, coronary occlusion was repeated. Resting diastolic SL was 1.34±0.21 cm and HR was 102±5 bpm. Coronary occlusion for 2 min resulted in a decrease in SL shortening or a paradoxical systolic lengthening with the average difference in shortening being 0.19±0.04 cm. HR increased to 121±4 bpm. Following 4 weeks of repetitive exercise diastolic SL was 1.41±.24 cm and HR was 87±1 bpm. Two minutes of coronary occlusion resulted in a difference in SL shortening of 0.11 ±.05 cm and a HR of 108±3 bpm. The difference in SL shortening following repetitive exercise was 46±14% of that during the control period. These data indicate that myocardial function during ischemia was improved following repetitive exercise either by an increase in collateral blood flow or by a decrease in ventricular compliance. (Supported by HL 22154)

COMPARING THE EFFECTS OF OUABAIN AND ISOPROTERENOL ON cAMP AND cGMP LEVELS, cAMP-DEPENDENT PROTEIN KINASE ACTIVITY RATIOS, AND ELECTROMECHANICAL PROPERTIES OF GUINEA PIG MYOCARDIUM. R.G. Knight*, S.L. Keely, and T.M. Nosek. Dept. of Physiology, Med. Coll. of Ga., Augusta, GA 30912.

The effects of a 2 min exposure to isoproterenol-I-($1X10^{-8}$M; n=7) and a 15 min exposure to ouabain-O-($5X10^{-7}$M; n=7) on contractility (max rate of tension rise-dT/dt), cAMP and cGMP levels, and cAMP-dependent protein kinase activity ratios (-cAMP/+cAMP) were compared in Langendorff perfused hearts attached by their apex to a strain gauge. Changes in the magnitude (AP) and duration (AP-D) of the slow response produced in K^+ depolarized muscle strips were used as indices of changes in electrogenic Ca^{++} influx (I(Ca)). Both I and O comparably increased dT/dt (75-97%). I significantly increased cAMP (37%) but not cGMP while O significantly decreased cGMP (75%) but did not affect cAMP. The -cAMP/+cAMP ratio was significantly increased from control levels of 0.22±.03 by both I (0.43±.01) and O (0.38±.02). I increased the AP by 13% and the AP-D by 30% while O decreased the same parameters by 18% and 44% respectively. These results suggest that the increase in -cAMP/+cAMP is involved in the increased contractility produced by both I and O. However, only the increase in -cAMP/+cAMP seen with I was associated with an increase in cAMP; O had no effect on cAMP but significantly decreased cGMP. Another difference between the modulatory actions of I and O was that I(Ca) was increased by I but decreased by O. Supported by Biomed. Res. Gr. 5S07-RR0-5365-17.

EFFECT OF SEX HORMONES ON STRIATED MUSCLE. James F. Knudsen and Stephen R. Max*. Univ. of Maryland, Baltimore, MD 21201

The mechanisms by which androgens exert their myotrophic influences are incompletely understood. We studied this question using glucose 6-phosphate dehydrogenase (G6PD), the rate-limiting enzyme of the pentose phosphate pathway, as an indicator of hormone action. We employed the hormone-sensitive levator ani muscle as a model system. Injection (i.p.) of testosterone propionate (TP) or estradiol-17β (E2) into immature (75 g. body wt.) male rats caused a 50% increase in the specific activity of G6PD in the levator ani muscle. Data to be presented elsewhere demonstrate that aromatization to E2 mediates the TP response (Neuroscience Abs., 5, 1979, In Press). The effect of E2 on G6PD was discernible at a dose of 0.025 mg/100 g. body wt., significant at 0.25 mg/100 g. body wt., and maximal at 2.5 mg/100 g. body wt. E2 increased G6PD by 50% as early as 8 h after injection, while TP required 12 h. Injection of E2 on two successive days increased G6PD by 80%. Simultaneous injection of actinomycin D abolished the increase in G6PD, suggesting enzyme induction rather than enzyme activation. Phlorizin, a glucose transport inhibitor, also prevented the effect of E2. Therefore, glucose uptake may be a necessary early event in G6PD induction. We conclude that E2 exerts an effect on striated muscle, viz., increased activity of G6PD, and further suggest that the mechanism of androgen action involves the conversion of T to E. (Supported by NIH Grant NS 14358).

ROLE OF PLASMA PROTEINS IN PLASMA AND RED CELL VOLUMES DURING A MARATHON. **M.A.Kolka* L.A.Stephenson* and J.E. Wilkerson. Human Performance Lab.,Indiana University, Bloomington, Indiana 47405**

Three adult males ran a competitive marathon (42.2 km). Before the race, and at 4.8 km intervals throughout the race, blood samples were drawn via an indwelling arm vein catheter. Samples were analyzed for erythrocyte count (EC), blood hemoglobin concentration (Hb), the hematocrit (Hct), total plasma protein concentration (PP), and plasma osmolality (PO). From these data the changes from pre-race (control) values of plasma (PV) and red cell (RCV) volumes, mean corpuscular volume (MCV), red cell (RCW) and plasma (PW) water concentration, and red cell (RCP) protein concentration were determined. PO was observed to increase linearly with distance run, with MCV being negatively correlated with PO. RCW averaged 0.71% above, and RCP 1.68% below control values during the race. Total RCV was constant throughout the race because of the negative relationship between EC and MCV. MCV remained constant during the race because of the balance between protein and water volumes in the red cell.

DENSITY-DEPENDENCE OF AIRWAY GAS TRANSPORT. A. Knoblauch, E.G. Honig, A. Sybert, and G.H. Gurtner. The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205.

We investigated the influence of the molecular weight of a gas on its exchange in the lung of anesthetized, mechanically ventilated dogs. A solution of three inert gases, two with similar molecular weights but different solubilities, and two with similar solubilities but different molecular weights, was infused intravenously until a steady state was reached. Inert gas concentrations in mixed venous and arterial blood and in expired gas were determined by gas chromatography using the technique of Wagner et al. (JAP 36:600, 1974). The two gases with high molecular weight, fluroxene (m.w. 126) and monochlorodifluoromethane (C1F2CH, m.w. 85.5) were taken as reference gases to predict Retention (R = arterial/mixed venous) and Excretion (E = mixed expired/mixed venous) for the less dense gas, acetylene (m.w. 26). Of 42 measurements in 16 dogs, 38 R values were higher for acetylene than predicted (mean 105.2%), while all 42 E values were lower than predicted (mean 89.8%). The physiologic dead space (R-E/R) was larger than predicted in every instance (mean 117%) indicating that the lighter gas is less efficently eliminated. The results are consistent with a Taylor dispersion mechanism operating in convective flow. (Supported by PHS Grant HL 10342, HL 07199 and the Parker B. Francis Foundation).

NEPHRON LOCALIZATION OF MINERALOCORTICOID ESCAPE. D.E. Kohan*, J.A.Haas*, and F. G. Knox., Dept. of Phys. & Biophysics, Mayo Clinic, Rochester, MN 55901

The nephron site(s) responsible for escape from the sodium retaining effects of mineralocorticoids appear to be distinct from those of mineralocorticoid stimulated Na reabsorption since no diminution of the enhanced Na reabsorption in the cortical collecting duct has been found during escape. In addition, Na delivery to the superficial late distal tubule is increased in rats that have escaped as compared to controls. In order to further localize the site(s) of mineralocorticoid escape, late proximal and early distal free flow micropuncture samples were obtained from 10% BW saline expanded Munich-Wistar rats, with or without 3 days of desoxycorticosterone acetate (DOCA) pre-treatment.

	Controls (n=12)	DOCA Treated (n=12)
Proximal Na delivery	59.7±1.8%	60.3±1.8%
Distal Na delivery	13.3±1.0%	19.9±1.6% *
Loop Na reabsorption	46.5±2.2%	41.4±2.1% **

*p <.005 **p <.05

FE_{Na}, GFR/kg BW and SNGFR/kg BW were not significantly different between the two groups. These studies suggest that the loop of Henle (defined as the nephron segment between the late proximal and early distal sites of micropuncture) plays a major role in escape from the Na retaining effects of mineralocorticoids. (Supported by HL 14133)

DETERMINATION AND HOMEOSTASIS OF FUNCTIONAL RESIDUAL CAPACITY (FRC) IN INFANTS. Philip C. Kosch* and Ann R. Stark* (Spon: Jere Mead) Dept. of Physiology, Harvard School of Public Health and Dept. of Pediatrics, Harvard Medical School, Boston, MA. 02115

To examine the determination and homeostasis of FRC, we measured airflow($\dot{V}$), tidal volume,(V_T)and inspiratory and expiratory time (T_i,T_e) in 7 sleeping, full term infants during the first 4 days of life. In contrast to adults, expiration is interrupted at substantial flows which immediately fall to and cross zero, indicating inspiratory interuption of relaxed expiration. In addition, expiratory braking often caused departure from the passive expiratory flow-volume curve. With this pattern of breathing, FRC is actively maintained at a higher lung volume than during spontaneously occurring apneic periods. When body position was changed from supine to upright, lung volume often increased up to about 1 V_T, mean T_i increased from 0.41 to 0.48($p < 0.025$) and mean T_e increased from 0.43 to 0.59 sec ($p < 0.025$). With prolonged T_e upright, infants expire more along their passive flow-volume curve before inspiring, thus effectively buffering the shift in lung volume. The active maintenance of FRC in newborns both benefits gas exchange and allows for compensation for shifts in FRC with change in posture.

(Supported in part by NIH Grant HL 21405 and HL 07118.)

NEUROANATOMICAL DISTRIBUTION OF CARDIOPULMONARY SYMPATHETIC AFFERENTS USING ^{3}H-LEUCINE AND AUTORADIOGRAPHY. D.R. Kostreva, J.L. Seagard, R.V. Purtock*, D.L. Van Horn, and J.P. Kampine. Med. Col. of Wisconsin and Wood VA Ctr., Milwaukee, WI 53193.

The distribution and number of cardiac and pulmonary sympathetic afferents with cell bodies in the upper thoracic dorsal root ganglia (DRG) were studied in mongrel dogs anesthetized with sodium pentobarbital. A thoracic laminectomy allowed direct access to the DRG for injection of 400 μCi of ^{3}H-leucine. One DRG was injected in each animal. The animals were allowed to survive for 10 days, after which the injected DRG with its dorsal and ventral roots, white rami, ansae subclaviae, ventrolateral, ventromedial, recurrent, and dorsal cardiac nerves, vagosympathetic trunk, and pulmonary nerves were excised and fixed in 4% gluteraldehyde. The nerves were then embedded in epoxy resin and sectioned for light and electron microscopy. The sections were then coated with a fine grain photo emulsion and refrigerated for 8 weeks. The sections were then developed, stained and photographed. The number of labelled axons were counted relative to the number of unlabelled axons in each of the nerves studied. The diameters of the labelled axons were measured using a sonic digitizer. The upper thoracic ventral roots were found to be primarily comprised of myelinated axons whereas the dorsal roots were primarily unmyelinated fibers. Large and small diameter labelled axons were found in the dorsal roots, DRG and peripheral cardiopulmonary nerves. (Supported by NIH Young Cardiovascular Investigator Grant HL 21042, Grant 16511, and VA).

EFFECT OF Ca^{2+} and Ni^{2+} ON CONTRACTILITY, METABOLISM AND CORONARY FLOW OF RAT HEART. Arisztid G.B. Kovách and Gábor Rubányi. Exp.Res.Dept., Semmelweis Medical University, Budapest, Hungary.

Mechanical and metabolic actions of Ca and Ni were investigated in the isolated rat heart perfused by modified Langendorff technique. Elevation of perfusate Ca concentration /Ca_p/ /0,3-7,8 mM/ produced positive inotropic effect and increase of O_2-consumption /MVO_2/. In the presence of 10 mM glucose, elevation of Ca_p was followed by and increase of tissue NADH fluorescence /reduction/,but with 10 mM pyruvate excess Ca_p produced NADH oxidation. 1 mM Ni abolished contractility, increased coronary resistance /CR/, reduced MVO_2 and caused NADH oxidation regardless of the substrate present. Elevation of Ca_p /from 1,3 to 3,9 mM/ in the presence of Ni restored contractility and MVO_2 but enhanced the increase of CR. NADH oxidation was antagonized by Ca in the presence of glucose only. Elevation of CR by Ni was maximal at 10^{-6} M concentration already. It is concluded that Ca adjusts myocardial metabolism to altered energy requirements by enhancing glycolysis and Ni inhibits the flow of reducing equivalents to the respiratory chain at site/s/ different from that where Ca enhances it.

ALTERATIONS IN AMINO ACID LEVELS IN CORTICAL BRAIN SLICES BY HIGH-PRESSURE OXYGEN. G.B. Kovachich* (SPON.: J.M. Clark). Inst. for Environmental Med., U. of Penn., Phila., PA 19104.

Rat brain cortical slices were incubated in normal or in 75 mM KCl Krebs Ringer phosphate (KRP) media for 30 min at 1, 5 and 10 atm O_2. Amino acids (μMole/g), pyruvate dehydrogenase (PDH) activity (nMole pyruvate/mg protein), and $^{14}CO_2$ production (μMole/g) from [U-^{14}C]glucose were determined (mean±SEM; n=3-6; *=statistical significance).

Normal KRP	1 atm	%	5 atm	%	10 atm	%
Glutamate	10.7±0.76	100	9.5±0.46	89	8.1±0.34*	76
Aspartate	2.4±0.32	100	2.3±0.45	97	2.6±0.61	110
Alanine	0.6±0.02	100	0.7±0.05	116	1.4±0.12*	234
PDH	12.4±0.32	100	12.3±0.43	99	11.4±0.42	92
$^{14}CO_2$	22.4±0.49	100	18.7±1.08*	83	17.7±0.66*	79
75mM KCl KRP						
Glutamate	7.2±0.70	100	6.9±0.37	96	3.4±0.16*	46
Aspartate	1.7±0.40	100	2.1±0.50	125	3.4±0.58*	203
Alanine	1.2±0.10	100	2.8±0.05*	224	3.9±0.27*	310
PDH	14.3±0.27	100	12.0±0.38*	84	10.8±0.38*	75
$^{14}CO_2$	42.0±2.60	100	30.8±1.98*	73	15.0±1.21*	36

10%O_2+90%He at 10 atm had no significant effect. Data indicate that high-pressure O_2 depresses glucose oxidation, probably at PDH level, and produces increased net breakdown and/or release of glutamate. These effects of O_2 are more marked in presence of 75 mM KCl medium. [Supported by NIH Grant HL-08899-15 and ONR Contract N00014-76-C-0248.]

CEREBELLA FASTICIAL, CAROTID SINUS BARORECEPTOR AND CARDIOPULMONARY BAROREFLEX COMPONENTS IN THE VASCULAR ADJUSTMENTS TO ORTHOSTATIC STRESS. S. Koyama*, W. S. Ammons* and J. W. Manning, Dept. of Physiol. Emory Univ. Atlanta, GA. 30322.

A two min. orthostatic stress of 30° head-up tilting in anesthetized cats results in compensitory changes in cardiovascular parameters. The dynamics of the response leads to a biphasic shift in systemic arterial pressure which has two distinct periods. The first compensitory phase is seen by a fall followed by a rise in systemic pressure with a period that does not exceed 50 sec. The phase of vascular adjustment which approximates a steady state change has a period which is better than twice the length of the first dynamic phase. Both arterial and cardiopulmonary baroreflex mechanisms adequately account for the dynamics of the near steady-state adjustment in peripheral resistance that has the longer time constant. Indeed, fixing carotid sinus pressure in the vagotomized cat at high, medium or low pressure levels only alters the steady-state pressure obtained with tilting but not the dynamics in either phase or period of the sympathetic induced vascular changes. By contrast, bilateral lesions of the fastigial nucleus of the cerebellum abates the first rapid phase of compensation leaving the animal with a single slower response to head-up tilting. In the vagotomized animals with fastigial lesions the steady-state change in arterial pressure to tilting is solely determined by carotid sinus baroreflex activity. (Supported by NIH Grant HL 16648-17)

SPINAL SITE OF SOMATIC AFFERENTS MEDIATING THE SOMATOSYMPATHETIC REFLEX IN DOGS. J. W. Kozelka* and R. D. Wurster. Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, IL 60153

The ascending spinal pathway of the somatosympathetic reflex was determined in anesthetized (pentobarbital 25 mg/kg or chloralose 100 mg/kg) mongrel dogs. Reflex increments in blood pressure and heart rate were elicited by right, left or bilateral stimulation of sciatic nerves at supramaximal intensities. Selective bilateral lesions were then made with fine scissors in the lumbar spinal cord (L-1, L-2) above the level of entry of the sciatic nerves. Heart rate and blood pressure alterations in response to bilateral carotid occlusion were unaffected by lesions at this level. In vagotomized or atropinized dogs the reflex pressor responses following peripheral afferent stimulation were eliminated by discrete dorsolateral sulcus (DLS) lesions. Conversely, the inhibitory effect of sciatic nerve stimulation upon phenylephrine-induced bradycardia was removed only following lesions of both the DLS and the dorsolateral funiculus. The interaction of peripheral afferent stimulation and phenylephrine-induced bradycardia was unaffected by beta-block (propranolol) prior to the lesions. While reflex amplitude is greatly depressed by the anesthetics chosen, lesions in chronic animals will require the use of such agents. The anatomical findings reported here may be used to determine the physiological significance of the somatosympathetic reflex in conscious dogs. (Supported by NIH Grant HL 08682.)

ADIPOSE TISSUE CHOLESTEROL STORAGE: EFFECT OF SATURATED AND UNSATURATED FAT DIETS. B.R.Krause, Mary Shannon Moore*, Margaret Balzer* and A.D. Hartman. LSU Medical Center, Dept. of Physiology, New Orleans, La. 70119.

The present experiments were designed to test the hypothesis that unsaturated fat diets result in a re-distribution of dietary and/or plasma cholesterol into adipose tissue. Fisher 344 rats were used since body weight and fat cell size, both of which influence adipocyte cholesterol storage, plateau after one year. Rats received for 90 days the following diets ad 11b: (A) chow, (B) chow +1% cholesterol, (C) chow +1% cholesterol +10% safflower oil and, (D) chow +1% cholesterol +10% stripped lard. Epididymal (Epi), perirenal (PR) subcutaneous (SC) and mesenteric (M) adipocyte cholesterol content (μg/10^6 cells) did not differ among the dietary groups except that Group C-PR cells contained 2-fold more cholesterol than the other groups at day 90. No notable changes occurred in the free/ester ratio in these depots. Lack of cholesterol accumulation may be related to the fact that plasma cholesterol did not become elevated until after 70 days in any group. Day 90 plasma cholesterols were 54,79,99 and 118 mg/dl for Groups A-D, resp. Liver cholesterol (43.4 mg/g) and triglycerides (6.98 mg/g) were highest in Group D. It is concluded that under these conditions the type of dietary fat does not alter adipose tissue cholesterol storage. (Supported by NIH grant AM-19995 and Cardiovascular Training Grant 410-22-5014).

CO-TRANSPORT OF CATIONS AND CL DURING THE VOLUME REGULATORY RESPONSES OF DUCK ERYTHROCYTES. Floyd M. Kregenow and Theresa Caryk* NIH, Bethesda, Md. 20205

Duck erythrocytes regulate their volume by utilizing ouabain-insensitive cation transport mechanisms. Enlarged cells lose K; shrunken cells gain Na & K via a Na+K co-transport process. We now find the unidirectional cation fluxes associated with these net movements are coupled to unidirectional Cl fluxes. Coupling even occurs when the cation fluxes do not generate net movement and describe instead a process resembling exchange diffusion. The Cl permeates the membrane through route(s) that appears to be separate from that used by the anion exchange mechanism. Of the anions, Br, I, NO_3, SCN and SO_4, all of which equilibrate across the membrane via the anion exchanger, only Br resembles Cl in permitting the cation process to operate. The reduction in cation flux seen with the rest of these inorganic anions is identical to that produced by an impermeant organic anion and is an inverse linear function of the Cl concentration. This finding suggests that these inorganic anions are unable to function as co-transport anions and inhibit by reducing Cl. SITS, an inhibitor of the anion exchanger, does not affect these cation transport processes and by reducing the rapid Cl fluxes associated with the anion exchanger unmasks the cation-coupled Cl fluxes. Thus when SITS is present manipulations which affect the cation transport processes, such as varying extracellular Na or K, produce similar changes in the unidirectional fluxes of both Cl and K.

THE CAUSE OF RED BLOOD CELL Na+ and K+ ALTERATIONS IN SHOCK. David J. Kreis, Jr.*, Arthur E. Baue and Irshad H. Chaudry. Dept. of Surgery, Yale University, New Haven, CT 06510.

Increases in RBC Na+ have been observed in several pathological conditions including uremia and shock. We have studied the effects of hemorrhagic shock and whole blood (WB) transfusions on RBC Na+, K+ levels using two shock models. Group A rats were bled to a BP of 40 mm Hg following which no further blood was removed or returned. The BP of those rats increased to 70 mm Hg within 30 minutes and remained at that level for 2 hours. Group B rats were bled to and maintained at 40 mm Hg for 1 1/2 hours. No significant changes in RBC Na+ or K+ levels were found during shock in either of these two models. In another study, rats were subjected to Group B shock and were transfused with rats WB which had been stored in cold ACD buffer for 6 days instead of their own shed blood. RBC Na increased from 3.5 + 0.1 to 8.4 + 0.7 and K+ decreased from 100.3 + 2.3 to 85.0 + 2.1 mM/L RBC in these animals. In an additional study, transfusion during shock with fresh WB mixed with ACD buffer produced no alterations in RBC Na+, K+ levels whereas transfusion with 3 day stored WB caused a 62% increase in RBC Na+. The RBC Na+ of stored WB itself increased by 75% and 127% at 3 and 6 days cold storage, respectively. These results indicate that: 1) hemorrhagic shock per se does not cause alterations in RBC Na+, K+ and 2) the changes in RBC Na+, K+ levels which have been reported previously are due to transfusion of stored blood.

MORPHOGENESIS OF HIGHER PLANTS FROM CULTURED TOTIPOTENT CELLS IN SPACE. Abraham D. Krikorian and F. C. Steward. Department of Biology, State University of New York, Stony Brook, N.Y. 11794.

The system will be described in which cultured free totipotent carrot cells have been exposed on semi-solid media in 50 mm diameter plastic petri dishes to the conditions of space flight. By these means it was shown on Cosmos 782 that such cells can give rise in darkness to somatic embryos with well-developed roots but with minimally developed shoots at near-zero gravity in 19.5 days. The embryos could be raised to maturity and were shown to be normal in phenotype. A sequel to the Cosmos 782 experiment was planned for late summer 1979. The objective was to extend the conclusions drawn from Cosmos 782 by testing whether the near-weightless space environment can support further development of shoots from already-developed later stages of somatic embryos. Some data from this experiment may be available for presentation. (Supported by the National Aeronautics and Space Administration)

RED CELL NA-K PUMP ACTIVITY AND HYPERTENSION. Donna L. Kropp* and Walter N. Durán, Dept. of Physiology, New Jersey Medical School, Newark, N.J. 07103.

A reduction of Na-K pump activity of vascular smooth muscle has been associated with hypertension by several investigators. We tested the hypothesis that red cell pump activity may also be modified by hypertension. Spontaneously hypertensive rats (SHR) and Wistar Kyoto normotensive rats (NTR) were lightly anesthetized for recording of their carotid arterial pressure. Subsequently, the rats were exsanguinated. Red cells were washed free of plasma and suspended in phosphate-buffered saline. Pump activity was determined using the ouabain-sensitive ^{42}K influx as an index. When diastolic pressure was significantly elevated, red cell pump activity of SHR was 60-70% of that of NTR. If systolic pressure of SHR was elevated but diastolic pressure was in the normal range, red cell pump activity of SHR was slightly reduced. A similar reduction of pump activity, compared to a normotensive individual, was found in red cells from a patient with diagnosed but yet untreated essential hypertension. Furthermore, hypertensive human red cells appeared to be more sensitive to pump inhibition by external Na than normotensive controls. We conclude that hypertension modifies pump activity of the red cell, and suggest that red cells are a convenient model to study the mechanisms by which Na-K pump activity is reduced in hypertension. (Supported in part by grants from the CMDNJ Foundation, USPHS NIH HL 20711 and AHA 78-896.)

CAN AMINOPHYLLINE REVERSE PROPRANOLOL-INDUCED CHANGES IN VENTRICULAR DIMENSIONS? S. Kunkes*, A. Strashun*, and B. Kent. Depts. of Surg and Med., Mt. Sinai Sch. of Med. and Bronx V.A. Medical Center, N.Y., N.Y.

Propranolol (Pr) inhibits production of cyclic AMP and aminophylline (Am) decreases its breakdown. To test the ability of Am to reverse the effects of Pr on left ventricular global function, 5 closed chest, anesthetized dogs previously instrumented with an electromagnetic flow probe on the ascending aorta, were studied using an EKG-gated scintillation probe to follow noninvasively the relative cardiac output (RCO), relative stroke volume (RSV), and ejection fraction (EF). After testing the beta receptor response with isoproterenol, 0.5mcg/kg (ISO_1), propranolol (≈2mg/kg) was given to establish a beta blockade by no significant response to the test dose, ISO_2. Am (5.6mg/kg in 20 min.) was then given. Results shown are mean and S.E.M.

	RCO	RSV	EF
Control	95±15	65±10	47±6
ISO_1	166±13	198±33	73±3
Pr	43±9	39±8	33±6
ISO_2	50±15	41±9	34±6
Am	92±17	75±14	53±8

The correlation between RCO and flow probe cardiac output was significant, $p < 0.001$. There is a significant increase in ejection indices in response to Am during beta blockade. The severe depression caused by Pr is reversed by Am and this change can be reliably followed with noninvasive techniques.

Effect of Carotid Body Denervation on Pacing in Unidirectionally Ventilated Chickens. A.L. Kunz, D.D. Tallman, Jr.*, E.K. Michal and R.K. Moore*. The Ohio State University, Columbus, Ohio 43210.

Respiratory movements in the unidirectionally ventilated chicken become synchronous with oscillations of $[CO_2]$. This is called pacing. Pacing can also be produced by O_2 oscillations with $[CO_2]$ held constant. We hypothesized: (1) the receptor mediating CO_2 pacing was the intrapulmonary chemoreceptor which is specifically sensitive to $[CO_2]$ and reported to be insensitive to $[O_2]$; and (2) that O_2 pacing was mediated only by the carotid bodies, which are known to be sensitive to $[O_2]$. Mature white leghorn males were surgically prepared for unidirectional ventilation. They were then paced with CO_2 and O_2 oscillations. Response to 4 sec. of hypoxia was tested. Then under Halothane anesthetic the carotid bodies were surgically denervated and the hypoxic test repeated. Little or no response indicated successful denervation. After awakening, attempts to pace the bird with CO_2 and O_2 were again made. We found birds could still be paced with either gas. These results strengthen the hypothesis that CO_2 pacing is mediated through intrapulmonary chemoreceptors, but refutes the hypothesis that O_2 pacing is mediated via the carotid bodies alone.

(Supported in part by the Central Ohio Chapter of the American Heart Association and the National Heart, Lung and Blood Institute Grant # HL23780.)

PERIVASCULAR H^+ AND K^+ ACTIVITIES AND PIAL ARTERIAL DIAMETER DURING CHANGES IN BLOOD PRESSURE. Wolfgang Kuschinsky* and Michael Wahl*. (SPON: B.R.Duling)
Department of Physiology, University of Munich, W. Germany.
The mechanism which enables the adjustment of cerebral arterial resistance to changes in arterial pressure (autoregulation) is still unknown. The contribution of perivascular H^+ and K^+ activities to this mechanism was investigated in chloralose anesthetized cats by inserting pH microelectrodes (Hinke type) or K^+ ion exchanger electrodes,respectively,into the perivascular space of single pial arteries. The cortical surface was kept under > 1 cm of warmed paraffin oil.Vascular diameter was measured by TV image splitting. Under control conditions, at a mean arterial blood pressure of 128±16(SD) mm Hg, perivascular pH was 7.25±0.11(SD) and K^+ activity was 2.46±0.65(SD) mM, respectively. Blood pressure was lowered down to 60 mm Hg by i.v. mecamylamine (2-10 mg/kg) or pentolinium (1-10 mg/kg) and increased up to 200 mm Hg by i.v. hypertensin (0.03-1.3 µg/kg .min). When blood pressure was decreased or increased, the dilations and constrictions of pial arteries were not accompanied by significant changes in either perivascular H^+ or K^+ activities. From our earlier studies with perivascular microinjections of H^+ or K^+(Circ.Res.31,240,1972),if the observed vascular reactions were induced by changes in extravascular H^+ or K^+ activity,then significant changes in the activities of either of these ions should have been found. It is concluded that H^+ and K^+ are not the triggers for the adjustment of pial arterial diameter during changes in arterial blood pressure.

EFFECT OF ATROPINE ON FATTY ACID INDUCED CHANGES IN JEJUNAL BLOOD FLOW, OXYGEN CONSUMPTION AND WATER TRANSPORT. P. R. Kvietys*, D. N. Granger, N. A. Mortillaro and A. E. Taylor.
Dept. of Physiology, Univ. of South Alabama, Mobile, AL 36688.
The aim of the present study was to assess the effect of atropine (0.2 mg/kg, i.v.) on the local intestinal hyperemic response to intraluminal placement of 20 mM oleic acid in 20% gallbladder bile (OA). We measured OA induced changes in venous outflow ($\dot{Q}_B$), oxygen consumption ($\dot{V}O_2$) and net transmucosal movement in canine jejunal segments in situ before and after atropine. One, 5 and 10 minutes after placement of OA, $\dot{Q}_B$ increased by 42.2, 41.5 and 30.8%, respectively, above the control (empty segment) value of 39.4 ml/min/100gm. When the animals were atropinized; 1, 5, and 10 minutes after placement of OA, $\dot{Q}_B$ was increased by 68.5, 45.8 and 26.9%, respectively, above a control value of 40.0 ml/min/100gm. Prior to cholinergic blockade intraluminal OA produced secretion in 5 and absorption in 2 of 7 dogs (0.28 ± 0.25 ml secreted/min/100gm). Atropine reverted net volume secretion to absorption or enhanced absorption (0.67 ± 0.19 ml absorbed/min /100gm). The increased (6-10%) $\dot{V}O_2$ induced by OA was not affected by atropine (N=3). In conclusion, atropine did not block the jejunal hyperemic response to luminal placement of OA and actually enhanced the hyperemic effect of OA during the first few minutes after placement. Cholinergic blockade, significantly altered net fluid movement induced by OA. Supported by HL 22569.

CONVERGENCE OF DOPAMINE, O_2 AND CO_2 CHEMORECEPTION IN AORTIC AND CAROTID BODIES. S. Lahiri, T. Nishino,* E. Mulligan and A. Mokashi.* Dept. of Physiol. and Inst. for Environmental Medicine, Univ. of Penn., Philadelphia, PA 19104.
Effects of dopamine (DA) and of a DA receptor blocker, haloperidol, on the responses of aortic and carotid chemoreceptors to hypoxia and hypercapnia were investigated in 12 anesthetized cats. Single or clearly identifiable paucifiber preparations were made from the peripheral ends of cut sinus and aortic depressor nerves. Intravenous infusion of DA (10-20 $\mu g \cdot min^{-1}$) decreased aortic and carotid body chemoreceptor responses to hypoxia and hypercapnia. The effect was greater at higher levels of stimulus. The magnitude of DA's inhibitory effect thus depended on the degree of both P_{O_2}- and P_{CO_2}-mediated receptor excitation. Haloperidol (0.5-2 $mg \cdot kg^{-1}$) potentiated the responses of both chemoreceptors to hypoxia and hypercapnia. This potentiating effect could result partly from a greater quantity of DA being released, which would normally inhibit the excitatory effect of hypoxia and hypercapnia. Haloperidol, having suppressed the inhibitory effect of DA, leaves the stimulation intact and consequently appears to potentiate it. The interaction of the inhibitory effect of DA with the excitatory effects of hypoxia and hypercapnia suggests their convergence in the chemoreception mechanism. DA, however, is not responsible for the initiation of O_2 and CO_2 chemoreception.
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PERIVASCULAR INTERSTITIAL FLUID PRESSURE MEASURED BY 2-5µ MICROPIPETS IN ISOLATED DOG LUNG. Stephen J. Lai-Fook.
Mayo Clinic and Foundation, Rochester, MN 55901

Saline-filled micropipets in conjunction with a servo-nulling electrohydraulic system (IPM Model 4) were used to measure the fluid pressure (Px) in the interstitium surrounding the partially exposed vein near the hilus of unperfused upper dog lobes. The pipets were inserted to depths in the interstitium of between 20 and 200µ with the lobe held at a constant transpulmonary pressure (Ptp) and constant venous pressure (Pv). Px responses to step changes in Pv occurred in less than 1 second. For Pv = 0 cm H_2O, Px relative to pleural pressure (atmospheric pressure) was -1.5 cm H_2O in lobes tested at 6 cm H_2O Ptp and decreased almost linearly to -8 cm H_2O in lobes tested at 25 cm H_2O Ptp. Reducing Pv from 0 to -10 cm H_2O resulted in a decrease in Px of 1 cm H_2O at 6 cm H_2O Ptp and 3 cm H_2O at 25 cm H_2O Ptp. Results agree with our previous measurements of Px using wick-catheters and open-ended needles, and are consistent with predictions from a continuum mechanics analysis of vascular interdepence.
(Supported by Grant HL 21584 form NHLBI)

PERSISTENCE OF INTENSITY FLUCTUATIONS OF SCATTERED LASER LIGHT FOLLOWING PHASIC ACTIVATION IN CARDIAC MUSCLE. Edward G. Lakatta and Donald L. Lappé*. Geronotology Res. Ctr., NIA, and Johns Hopkins Med. Inst., Baltimore, MD 21224.
A close correlation between steady levels of contracture force in non-beating rat cardiac muscle and the rate of intensity fluctuations of scattered He-Ne laser light (R) has suggested that R reflects contractile activation. The present study examines the decay of R and its relationship to the capacity for force development (DF) in the time period following steady state phasic stimulation at 60 min^{-1} (S60) in rat and cat papillary muscles. R was quantitated as $f_{\frac{1}{2}}$ which is derived from the half-decay time of the autocorrelation function for the scattered beam at 30°. After S60, $f_{\frac{1}{2}}$ was measured over 30 second intervals after which a single test stimulus enabled measurement of DF. Both $f_{\frac{1}{2}}$ and DF decayed with time in the cat but not in the rat.

Time after S60	Rat (n = 3) $f_{\frac{1}{2}}$ (Hz)	DF (g/mm^2)	Cat (n = 3) $f_{\frac{1}{2}}$ (Hz)	DF(g/mm^2)
30 sec	4.21±0.99	11.8±4.8	4.13±0.45	9.44±2.81
60 sec	4.17±0.94	12.2±5.10	2.58±0.54	7.32±2.87
90 sec	4.28±0.97	12.2±5.23	1.90±0.29	4.87±2.05

In the cat $f_{\frac{1}{2}}$, which continued to decay for 210 sec was highly correlated with DF: DF = {2.7 $f_{\frac{1}{2}}$ - 0.96}, r = .97, P< .001. The results demonstrate that the capacity for DF following phasic stimulation is related to $f_{\frac{1}{2}}$ and the decay of $f_{\frac{1}{2}}$ in the cat appears to be an integral feature of the Bowditch staircase.

ENDOTHELIAL CELL MORPHOLOGY AND HEMODYNAMIC STRESSES: AN SEM STUDY. B. Lowell Langille* (SPON: A. C. Groom). Univ. of Western Ontario, London, Can. N6A 5C1
Arterial endothelial cells of rabbits viewed with the SEM are aligned in the direction of blood flow both in straight segments of arteries and at branch sites. When local blood flow was surgically altered, by nephrectomy or coarctation of the aorta, changes in cell orientation followed predicted changes in local blood flow. Impressions of endothelial cells on plastic casts of arteries were also examined, to relate cell orientation to the three dimensional geometry of branches. At the origins of large aortic branches endothelial cells are arranged in helical patterns around the daughter branch. Further downstream axial alignment of cells was re-established. At smaller branches there is an abrupt change in cell orientation from the direction of the parent vessel to that of the daughter. These patterns mimic flow streamlines seen in glass model studies of arterial branches at high Reynolds number and low Reynolds number flow. Deformation of cells near branch sites during pressure distension of arteries was also examined. It is concluded that endothelial cells are sensitive to local haemodynamic stresses.
(Supported by the Ontario Heart Foundation).

INTENSITY FLUCTUATION OF SCATTERED LASER LIGHT IN NON-BEATING CARDIAC MUSCLE VARY WITH CONTRACTURE FORCE. Donald L. Lappé* and Edward G. Lakatta. Gerontology Research Center, NIA, and Johns Hopkins Med. Inst., Baltimore, MD 21224.

We have demonstrated that in non-beating rat cardiac muscle the rate of intensity fluctuations of scattered He-Ne laser light (R) and a portion of resting force (ΔRF) vary linearly over a tenfold range (0.4-4.0 mM) of $[Ca^{++}]$ in the bathing fluid. R was quantitated as ($f_{\frac{1}{2}}$) which is derived from the half-decay time of the autocorrelation function for the scattered beam at 30°. Since a good correlation was found between ΔRF and $f_{\frac{1}{2}}$ (r = 0.98) over that Ca^{++} range, it was hypothesized that $f_{\frac{1}{2}}$ reflected activation of the contractile proteins. The present study examines the relationship between $f_{\frac{1}{2}}$ and graded steady levels of contracture force (CF) caused by varying concentrations of ouabain in intact rat papillary muscles (n = 3), and of Ca^{++} in chemically skinned muscles (n = 3). Over 6 concentrations of ouabain ($2X10^{-6}$-$1X10^{-3}$), CF was increased an average of 2.3 g/mm^2 and $f_{\frac{1}{2}}$ by 30.4 Hz. CF = [0.07 $f_{\frac{1}{2}}$ -0.57], r = .95, ($P<.001$). In skinned fibers, over five $[Ca^{++}]$'s (pCA 6-3) the average of CF increased 2.9 g/mm^2 and $f_{\frac{1}{2}}$ by 15.2 Hz. CF = [0.15 $f_{\frac{1}{2}}$ +0.98], r = .86, ($P<.02$). The close correlation between CF, which is determined by the extent of Ca^{++} activation of contractile proteins, and $f_{\frac{1}{2}}$ extends the previous findings in the quiescent non-beating state and strongly suggests that $f_{\frac{1}{2}}$ reflects contractile activation in cardiac muscle.

OUABAIN-INSENSITIVE Na/Li EXCHANGE AND THE EFFECT OF ANTI-L IN LOW POTASSIUM (LK) SHEEP RED CELLS (SRBC). Peter K. Lauf, Bernhard F. Becker*, and Jochen Duhm*. Depts. Physiol. Duke University, Durham, N.C., USA, and University of Munich, W-Germany.

SRBC have a considerable ouabain-insensitive Na/Na exchange diffusion which is greater in LK than in high potassium (HK) SRBC (Tosteson & Hoffman, J.Gen.Physiol. 44:169,1960). Conversely, due to a smaller number of kinetically different pumps, ouabain-sensitive K-pump flux is smaller in LK than in HK red cells and may be stimulated by L-antibody binding to the L-antigen in LK cells (Joiner&Lauf, J.Physiol. 283:155&177,1978). We studied whether the two transport systems correlate on the molecular level by examining if anti-L also alters Na/Li exchange as mediated by the Na/Na exchanger. Li-uptake in isotonic choline chloride media containing 2 mM Li + 0.1 mM ouabain (Duhm et al. Pflüger's Arch. 364:147,1976) was 1.16 ±0.24 and 0.76 ±0.06 μmoles Li/ml cells x hr in 13 LK and 4 HK SRBC specimens, respectively. However, the 50% higher Li-uptake in LK cells can be accounted for by their higher Na-concentrations. Inhibitors of the Na/Na exchanger (NEM, PCMBS or phloretin) reduced Li-uptake to similar degree in both cell types Anti-L, which in choline media containing 5 mM KCl fully stimulated K-pump flux, failed to alter ouabain-insensitive Li-uptake. The similar Li-uptake by the Na/Na exchanger in both LK and HK cells, as well as the absence of the L-antigen on this system suggest that it is structurally different from the Na/K pump, and that only the latter is under control of the HK/LK genes. Supp.in part by NIH Grant 2 P01-HL 12.157.

The Effects of +Gz Acceleration Stress on Right Ventricular Pressures in Conscious Miniature Swine. M. H. Laughlin and J. E. Whinnery.* USAFSAM, Brooks AFB, TX 78235

Polyethylene catheters were chronically placed in the cranial vena cava of 5, 2-year old, female, 35-50 Kg, miniature swine. The catheters were large enough (O.D. 3.49mm and I.D. 2.67 mm) to allow the introduction of a 5 French PC-3.50 Millar pressure transducer into the venous system. After surgical recovery each animal was restrained, fitted with an anti-G suit, and placed in a fiberglass couch in the USAFSAM centrifuge. The Millar transducer was then passed through the chronic catheter and advanced into the right ventricular chamber in the fully conscious animal. Right ventricular pressures were measured during and after 30 sec exposures to +1G_z, +2G_z, +3G_z, +4G_z, +5G_z, +6G_z, +7G_z and +8G_z stress. Results presented below represent averages obtained over the last 10 seconds of each +G_z exposure.

	RSVP	RVDP	dP/dt	HR
Control	28±2	1±1	53±9	85±7
+2G_z	71±13	2±7	187±35	190±9
+5Gz	81±23	10±5	116±17	211±6
+8G_z	70±6	16±8	99±13	179±7

Mean ±Se's are presented (n=5). RVSP and RVDP are mean right ventricular systolic and diastolic pressures respectively (mmHg). dP/dt=mmHg/sec. HR=heart rate in beats/min. It is concluded the +G_z stress causes a significant increase right ventricular pressure work. This is probably the result of +G_z stress induced increases in sympathetic tone.

CIRCULATORY ADAPTATION FOR BIMODAL RESPIRATION IN THE DIPNOI LUNGFISH. Pierre Laurent, Richard G. DeLaney* and Alfred P. Fishman. CNRS-LPCR, Strasbourg FR. and Hosp. Univ. of PA Philadelphia, PA 19104

The African and South American Lungfish rely on gills and lungs for respiration during aquatic life and exclusively on lung ventilation during estivation. Aquatic gill O_2 exchange is low, but CO_2 exchange, acid-base balance and osmoregulation are still important functions. Morphologic studies have identified three areas of specialized vascular controls presumably for synchronizing perfusion of the aquatic and aerial gas exchangers in Protopterus and Lepidosiren: 1) gill bypasses via lamellar shunts (GS), 2) pulmonary artery vasomotor segments (PAVM) controlling lung perfusion, and 3) vasoactive arterial ducts (AD) which can channel blood directly from the gills to the systemic circulation bypassing the lungs. Utilizing these controls the fish can adjust the circulatory pattern from the aquatic fish gill mode to a mammalian like pulmonary circulation. Ultrastructure studies of the PVAM and AD demonstrated two types of nerve endings, i.e. cholinergic components and chromaffin cells, suggesting reciprocal nervous control. Pharmacological studies have shown that ACh constricts PAVM and dilates AD; α adrenergics constrict the AD. A nervous control of the GS has not yet been located and, like in other fish, the control may be purely local.

A GENETIC MODEL FOR THE STUDY OF STRESS-INDUCED HYPERTENSION IN RATS. J.E. Lawler,*, G.F. Barker,* and J.W. Hubbard.* (SPON: K.J. Kant) Univ. of Tennessee, Knoxville, TN 37916.

The spontaneously hypertensive rat (SHR) has elevated sympathetic drive to the cardiovascular system. However, as a model for psychological inputs to the development of hypertension (HT), the model is inappropriate, since HT develops whether or not stress is present. This study sought to investigate the effects of stress on systolic blood pressure (SBP) in animals which were offspring of HT and normotensive parents. The study utilized 48 male rats (F1 generation) of inbred SHR and inbred Kyoto-Wistars. At the beginning of study, all F1 rats had SBP between 140-160 mm Hg ($\bar{X}$=151 mm Hg). Animals were randomly assigned to 3 groups of 16 rats each: 1) conflict (restrained and stressed 2 hrs daily); 2) restraint control (restrained 2 hrs daily); and 3) maturation control (neither stressed nor restrained). After 3 wks of training and 12 wks of stress, the mean SBP (±SD) for each group was as follows: Group 1--186±8.8 mm hg; Group 2 -- 163±7.2 mm Hg; and Group 3--152±10.5 mm Hg. Analyses of variance revealed significant elevations in SBP for Group 1 across weeks. Group 1 animals were elevated when compared to either of the control groups. Since weekly SBP readings via tail cuff were taken a minimum of 2 hrs following stress (or restraint) sessions, it appears that stress in this genetic model leads to chronic elevations of SBP into the HT range. (Supported by Am Heart Assn and NIH grant HL 19680.)

DYNAMICS OF WEIGHT LOSS DURING PROLONGED SPACEFLIGHT. C. S. Leach, J. I. Leonard* and P. C. Rambaut*, NASA-Johnson Space Center and General Electric Co., Houston, TX 77058.

Loss of body weight of astronauts returning from space flight has been a consistent observation. The three Skylab missions have provided the data necessary to describe the dynamics of weight loss and its components during space flight lasting up to three months. An integrated analytical approach was used to examine cumulative metabolic balances for water, electrolytes and nutrients. The errors inherent in cumulative balance techniques were minimized by also using whole body measurements. The analysis resulted in a dynamic profile of the behavior of body water, lean tissue and fat and indicated that the equilibrium levels of these components are reached at quite different rates. An additional study was performed to estimate overall losses of lean body mass from several independent methods based on measurements of total body water, total body potassium, nitrogen balance and stereophotometric-body density. The results of these analyses indicated that of the total loss in weight (2.7± 1.5kg), little more than half can be attributed to lean body mass loss (1.5±0.3 kg), the remainder being derived from fat stores (1.2±0.3 kg). The loss in lean body tissue is attributed to a rapid loss of body water followed by a more gradual loss of nitrogenous constituents which appears to be self-limiting after about one month. Fat losses were more varied, being dependent on caloric intake and exercise levels.

REFLEX RESPONSES TO TEMPERATURE CHANGE IN THE MAIN PULMONARY ARTERIES OF THE DOG. J.R. Ledsome* and W.O. Kan* (SPON: F. Lioy). Univ. of B.C., Vancouver, B.C., Canada V6T 1W5

In the course of investigations into the function of sensory nerve endings in the walls of the pulmonary arteries we have noted reflex responses to small (2°C) changes in temperature. In chloralose anesthetized dogs a right atrium to left pulmonary artery, right-heart bypass was made. An isolated segment of the main and right and left main pulmonary arteries was perfused with venous blood. The temperature of the venous blood perfusing the isolated pulmonary arteries was varied in steps of 2°C over the range 30-41°C. Decreasing the temperature in the isolated pulmonary arteries caused a decrease in systemic vascular resistance and respiratory drive (phrenic electroneurogram). Increasing the temperature increased systemic vascular resistance and respiratory activity. The effects were present when the pressure in the isolated pulmonary arteries was low (20 torr) or high (80 torr). The responses to temperature change were prevented by cutting the vagosympathetic trunks in the neck. It is concluded that there are receptors in or close to the pulmonary arterial walls the activity of which is altered by temperature change. Stimulation of these receptors causes an increase in systemic vascular resistance and respiratory activity. (Supported by Medical Research Council of Canada and B.C. Heart Foundation.)

ADRENAL CONTRIBUTION TO CARDIAC RESPONSES ELICITED BY ACUTE HYPOXIA IN PIGLETS. J.C. Lee, J.C. Werner* and S.E. Downing Yale University School of Medicine, New Haven, CT 06510

The adrenal contribution to cardiac responses elicited by hypoxia was assessed in piglets, 1-12 weeks of age, anesthetized with pentobarbital (30 mg/kg). Hypoxia was produced by addition of N_2 to the respirator. External cardiac work was held constant and parasympathetic blockade was produced in each animal with atropine (1 mg). In a sham adrenalectomy group (N = 6) LV dp/dt max during hypoxia ($PaO_2 \sim 30$ mmHg) increased significantly to 3680 ± 414 mmHg/sec from control values of 2684 ± 318 mmHg/sec ($p < 0.01$). Heart rate rose from 171 ± 6 to 186 ± 7 beat/min ($p < 0.02$). These responses were not altered by ganglionic blockade with Arfonad (0.5 mg/kg/min). Equally large increases of LV dp/dt max appeared when heart rate was held constant by pacing. β-adrenoreceptor blockade with practolol (4 mg/kg) sharply reduced but did not eliminate the response. In contrast, no changes in LV dp/dt max or heart rate were observed during hypoxia in adrenalectomized piglets (N = 6). These findings indicate that the chronotropic and inotropic responses were dependent upon the integrity of the adrenal glands, and that there was minimal contribution from cardiac sympathetic fibers. Moreover, hypoxia appears to cause direct adrenal release of catecholamines, independent of neural activity.

CENTRAL INFUSION OF SARALASIN INHIBITS DRINKING TO INTRAVENOUS ANGIOTENSIN BUT NOT FOLLOWING CAVAL LIGATION IN RATS. Maw-Chang Lee*, Terry N. Thrasher and David J. Ramsay. Dept. Physiology, UCSF, San Francisco, CA 94143

The effects of intracerebroventricular (ICV) infusion of saralasin on drinking elicited by ICV injection of angiotensin II (AII), intravenous (iv) infusion of AII and caval ligation were investigated in rats with chronically implanted lateral ventricular cannulae. The infusion of saralasin at a rate of 5.2 ug/h began 75 min prior to the administration of the thirst stimulus and continued throughout the experiment. This treatment with saralasin reduced drinking induced by injection of 10 ng AII (ICV) from 6.91±1.33 to 0.49±0.26 ml (n=8, p<0.005) and by infusion of AII (100 ng/min iv for 20 min) from 3.26±0.51 to 0.09±0.09 ml (n=11, p<0.001). In contrast, saralasin ICV had no significant effect on drinking caused by ligation of the vena cava. Water intake at various times following ligation was:

ICV	n	2 h	4 h	5.5 h	
saralasin	20	.73±.19	1.23±.25	1.50±.28	(ml/100 gm)
saline	14	1.30±.23	1.69±.23	2.01±.26	

Even infusion of saralasin at two and ten times the dose did not attenuate drinking following caval ligation. These data show that administration of saralasin via the ventricular route is able to antagonize drinking elicited by systemic AII; in contrast the renin-angiotensin system does not play an essential role in the control of drinking following caval ligation in rats. (Supported by PHS Grant HL-18862)

SPECIFIC AIRWAY CONDUCTANCE IN ANAESTHETISED MAN. J.R.Lehane*, C.Jordan* and J.G.Jones*. (SPON: C.G. Caro) Clinical Research Centre, Harrow, England.

We have used the forced airflow oscillation method to determine respiratory resistance (Rrs) over a range of lung volumes (V_L) in supine anaesthetised patients. A computer analysis of the hyperbolic relationship between Rrs and V_L was used to determine the asymptotic resistance and yield a linear plot of conductance against V_L. Specific airway conductance was expressed as the slope of this line. Diazepam pre-medication was followed by thiopentone, pancuronium, endotracheal intubation and IPPV with 70% N_2O. After obtaining 3 measurements of SGaw, halothane 1.3% (n = 10) or enflurane 2.5% (n = 10) was added to the inspired gas mixture. During N_2O anaesthesia mean SGaw was 0.85 $cmH_2O^{-1}s^{-1}$, range 0.35 - 1.61. Following addition of halothane SGaw increased significantly in each of 5 patients ($P<0.05$, 2 sample t-tests), mean values increasing from 0.75 to 1.94 $cmH_2O^{-1}s^{-1}$, and decreased in 1 patient from 0.63 to 0.48 $cmH_2O^{-1}s^{-1}$ ($P<0.02$). In 4 patients there was no significant change. Following addition of enflurane SGaw increased from 0.98 to 1.84 $cmH_2O^{-1}s^{-1}$ in 3 patients ($P<0.05$). There were no significant changes in 7 patients. The average change after halothane was an increase in SGaw of 60% (n.s. $P=0.09$, paired t-test) and after enflurane was an increase of 43% ($P<0.02$). In conclusion, there was considerable individual variability in response to halothane. Enflurane produced smaller effects and did not cause bronchoconstriction.

DAILY LH PROFILES IN THE OVARIECTOMIZED, ESTROGEN IMPLANTED RAT AND BLOCKADE OF THE LH SURGE. Robert E. Leipheimer*, Timothy P. Condon*, and John J. Curry. Department of Physiology, The Ohio State University, Columbus, Ohio 43210

Plasma LH levels were determined over a 24 hr period in ovariectomized rats implanted with 5mm, 3mm, or 1mm silastic capsules containing 17β-estradiol. LH levels remained low at all times except during the LH surge, which peaked at 1700 hrs. The animals with 5mm capsules demonstrated an LH surge similar in magnitude to that seen in the intact rat. The rats with 3mm and 1mm capsules however, demonstrated a severely attenuated LH surge. Samples were also collected the next day at 1700 hrs to verify the daily occurance of the LH surge. The 1mm estrogen implanted, ovariectomized animal model was then used to study the effects of various neurotransmitter blocking agents on the LH surge. Each animal was given one of the following neurotransmitter blocking agents at 1100 hrs: pimozide (2mg/Kg), propranolol (20mg/Kg), atropine (70mg/100g), and methysergide (100mg/Kg). Each animal also received a subcutaneous injection of 17β-estradiol (20 ug) at 1200 hrs to elicit a full LH surge. Samples were collected at 1700 hrs by decapitation. The LH surge appeared to be inhibited by each of the blocking agents. The results suggest that the positive feedback of estrogen in this model can be disrupted by the blockade of various neurotransmitter pathways. This model may be useful in further examination of the control of the LH surge. (Supported in part by a grant from the Graduate School of The Ohio State University)

A MODEL FOR THE DETERMINATION OF THE INTERSTITIAL PO_2. Eugene A. Lentini, Carl DiJoseph* and Michael Venditto*. Dept. of Physiology/Pharmacology, Philadelphia College of Osteopathic Medicine, Philadelphia, Penn. 19131.

A variety of intracellular myocardial PO_2 determinations have been made with values ranging from 0-40 mm Hg. However no specific functional interstitial value of myocardial PO_2 has been determined which is associated with the activity of the tissue. Studies have shown that the developed tension of rat papillary muscle aerated with various percentages of oxygen was dependent on the particular aerating mixture. A graded contractile response was obtained which was dependent on the PO_2. The maximum developed tension occurred at 700 mm Hg. The data allowed for the determination of the myocardial diffusion coefficient of O_2 ($D'O_2$) which was 4.08×10^{-5} cm^2/min atm. The model was further developed and a minimal interstitial PO_2 value was derived. This determination indicated that, at equilibrium, for any developed tension to occur, the minimal PO_2 value of 21 mm Hg had to be exceeded. The information derived from this approach is in keeping with available intracellular PO_2 values.

REGULATION BY GABA-MODULIN OF GABA BINDING AND MEMBRANE PHOSPHORYLATION. A. Leon, A. Guidotti and E. Costa. Lab. Preclin. Pharmacol., NIMH, St. Elizabeths Hosp., Washington, D. C. 20032

Crude brain synaptosomal preparations have been shown to contain inhibitory material for GABA receptor binding. Various purification procedures including SDS polyacrylamide gel electrophoresis have made possible the identification of a thermostable, acidic protein (M.W. 15,000 dalton) termed GABA-modulin. Not only is this protein capable of inhibiting noncompetitively the Na^+-independent high affinity binding of GABA to synaptic membranes but also of inhibiting competitively the cyclic nucleotide-independent protein kinases.

GABA-modulin has been found to be present in high concentrations in cortex and cerebellum of different animal species and is associated with GABA receptors in synaptic plasma membranes obtained by sedimentation-flotation sucrose density gradient technique. On comparison to synaptic plasma membranes (SPM), synaptic junction (SJ) preparations, obtained by repeated freezing, thawing and Triton X-100 treatments of SPM, are characterized by a) a lower content of GABA-modulin, b) an increased high affinity binding of ^3H-GABA and c) a higher capacity to phosphorylate SJ proteins. Recombination experiments (SJ+ GABA-modulin) reduce both the endogenous phosphorylation and high affinity binding of GABA to SJ. These results suggest that GABA-modulin and membrane autophosphorylative capacity are implicated in the control of GABA receptor function.

SIZE OF WORKING MUSCLE MASS AND CIRCULATORY RESPONSE TO DYNAMIC EXERCISE. S.F. Lewis*, W.F. Taylor* and C.G. Blomqvist*, (SPON: J.H. Mitchell) Southwestern Med Sch, Univ of Tx Health Sci Ctr, Dallas, Tx 75235.

. The role of muscle mass as determinant of cardiac output (Q) (C_2H_2 rebreathing), heart rate (HR) and blood pressure (BP) were studied in 7 healthy sedentary ($\bar{x}$±SD $\dot{V}O_{2\ max}$=40.5± 2.5) young men who performed 1 arm cranking (A), 1 leg (L) and 2 leg cycling (LL), at loads requiring 25, 50, 75 and 100% $\dot{V}O_{2\ max}$ of each exercise mode. Regression analysis indicated that the slope of the line relating $\dot{Q}$ and HR to % $\dot{V}O_{2max}$ was steepest for LL, followed by L and then A. The order of slope steepness was reversed for diastolic (D) BP and total peripheral resistance (TPR). The slope of the line relating HR, systolic (S) BP and DBP to absolute $\dot{V}O_2$ was steepest for A, followed by L and LL. However, the relationship between $\dot{Q}$ and absolute $\dot{V}O_2$ was similar for A, L and LL. All variables were highly correlated (r^2>.40; p<0.05) with absolute $\dot{V}O_2$ and % $\dot{V}O_{2\ max}$ except TPR in A and DBP in LL. Results at maximal exercise were:

EX	$\dot{V}O_2$ l/min	$\dot{Q}$ l/min	HR bpm	SBP mmHg	DBP mmHg	TPR unit	Brackets = a difference
A	1.59	12.2	168	180	114	11.3	p < 0.05
L	2.30	14.2	181	188	96	9.1	
LL	2.98	16.7	193	192	84	7.3	

The circulatory responses to dynamic exercise appear to be critically dependent on the size of the working muscle mass.

ALTERATIONS OF TISSUE WATER AND ELECTROLYTES IN RABBITS AFTER AN INTRAVENOUS INJECTION OF CHOLERA TOXIN. C. T. Liu, M. J. Griffin* and J. W. Springer*. US Army Med. Res. Inst. Infect. Dis., Fort Detrick, Frederick, Md. 21701

Effects of cholera toxin on the intact gastrointestinal tract have been well documented. Death may ensue from massive, rapid intestinal losses of water and electrolytes. Increases in adenyl cyclase activity and cAMP concentrations in intestinal mucosal cells are believed to be the causes. Whether or not cholera toxin can be transported into the circulation from the intestine is still controversial. The purpose of this investigation was to measure changes in the water and electrolyte content of various tissues of rabbits given cholera toxin intravenously. A single dose (100 µg/kg) of purified cholera toxin was injected IV into each of 10 Dutch rabbits; an equal number of control rabbits received saline. Approximately 24 hr later, or shortly before death, the rabbits were anesthetized and killed for chemical analyses of their tissues and plasma (Am. J. Vet. Res. 39:1692, 1978). Cardiac and skeletal muscles showed a trend toward intracellular dehydration, while cerebellum and renal cortex demonstrated intracellular overhydration. In general, changes of tissue water followed the distribution of Na^+. However, total and intracellular Na^+ concentrations decreased in the thalamus-hypothalamus samples, without marked changes in intracellular water. It is postulated that these tissue changes are associated with increases in tissue cAMP values. This possibility is currently under investigation.

COMPUTER SIMULATIONS OF POSTURAL CHANGE, WATER IMMERSION AND BEDREST: AN INTEGRATIVE APPROACH FOR UNDERSTANDING THE SPACE FLIGHT RESPONSE. J. I. Leonard*, C. S. Leach and J. A. Rummel*, General Electric Co. and NASA-Johnson Space Center, Houston, TX 77058.

The use of mathematical models of physiological control systems is well suited for studying the spaceflight response because of the complex number of systems involved and the reasonable assumption that most alterations observed can be explained in terms of normal homeostatic function. The circulatory, fluid and electrolyte responses to weightlessness can be segmented into acute (hours), transitory (days) and adaptive (weeks) stages. The comprehensive Skylab studies focused primarily on the adaptive stage. Using a computer model of the circulatory, fluid and electrolyte system we have examined the complete temporal spectrum of fluid shift responses by simulating ground based studies which often provide more abundant data than spaceflight. Postural and water immersion studies provide clues to the acute reaction while bedrest allows examination of the longer term effects. This approach provides a framework for a systematic review of available experiments and can help explain conflicting results because of the bimodal response of many parameters. Simulation results suggest that headward fluid shifts can account for many of the circulatory, hematological, hormonal and renal effects observed in short term experiments. Longer term effects were found to be more dependent on adaptive cardiovascular and renal mechanisms and intracellular degradation.

EFFECTS OF PROTEIN LOADING ON INDIVIDUAL NEPHRON FUNCTION. Stan L. Lindstedt and Eldon J. Braun, Dept. of Physiology, University of AZ, College of Medicine, Tucson, AZ 85724

Because of the pronounced morphological heterogeneity within its kidney, we examined individual nephron function in the desert pocket mouse (Perognathus penicillatus, 17 g.). In these kidneys the largest juxtamedullary glomeruli (1.6 x 10^6 μ^3) may be four times the volume of the more abundant superficial-cortical glomeruli (4.0 x 10^5 μ^3). Likewise the longest proximal tubules (12 mm) may also be four times the length of the shortest (3 mm). In an attempt to explain the functional significance of this morphological heterogeneity, we measured single nephron glomerular filtration rates (SNGFRs) in hydropenic and protein-loaded animals by a modification of Hanssen's ^{14}C labeled sodium-ferrocyanide technique. All of the large juxtamedullary nephrons were found to be filtering maximally in animals maintained on a high protein (and no water) diet. In contrast, in hydropenic animals there was no measurable filtration in many of the largest nephrons. Those juxtamedullary nephrons which were filtering, did so at reduced levels (lower SNGFRs) relative to the protein-loaded animals. These results suggest that protein loading (high urea output) may cause a shift in filtration distribution toward the large juxtamedullary nephrons. Because of longer ascending limbs of Henle, these nephrons have a greater capacity to produce free water. Supported by NIH AM05738, AM16294 and NSF 77-04958.

TRANSFER OF ELECTROACUPUNCTURALLY INDUCED ANALGESIA BY BLOOD PLASMA. Y.K. Liu* and A.E. U. Edisen, Tulane University Medical Center, New Orleans, Louisiana.

Rabbits, unanesthetized and in the prone position, were given electroacupunctural stimulation through acupuncture needles inserted in points Bl 49 (hip region) and St 36 (motor point of tibialis anterior) on either right or left side. Frequency of stimulation varied between 8 and 60/sec.; the rate of variation being every 2 sec. as used by Claudie Terral. This stimulation elicited corresponding slow-fast muscle fasiculations in the limb affected. Analgesia, tested by lack of flexor withdrawal reflexes to pin pricks, appeared in 15-20 min. and was localized to the dorsal and lateral surfaces of thigh, leg and foot. Stimulation was maintained for 45-90 min. at which time the animal was sacrificed. Blood was withdrawn, kept at 0°C and centrifuged for 10 min. The donor rabbit's plasma was then infused through an ear vein of a naive recipient rabbit. Within 2 min. slow-fast muscle fasiculations similar to those of the donor were seen in the corresponding hind limb. Analgesia became established in 3-4 min. later, confined to the same regions of the thigh, leg and foot. When the plasma dose was high (doses varied from 9-40cc), the analgesia was noted to spread to the opposing limb, but not to the back, sides or forelimbs. Analgesic effects lasted for 28-42 minutes. (The support of the Edward G. Schlieder Foundation is gratefully acknowledged.)

EFFECT OF TRIIODOTHYRONINE (T_3) ON THE DEGRADATION OF THE SMALL SUBUNIT OF NaK-ATPase IN RAT RENAL CORTEX. C.S. Lo and T.N. Lo*. Dept. of Physiol., Uniformed Services Univ., Bethesda, Md. 20014 and Lab. of Cellular Metabolism, NHLBI, NIH, Bethesda, Md. 20205

T_3 administered to thyroidectomized rats promoted the de novo synthesis of the large subunit of NaK-ATPase and had no effect on its degradation (Lo and Edelman, J. Biol. Chem.251: 7834, 1976) and to the same degree T_3 augments the incorporation of methionine into both subunits of the enzyme in thyroidectomized rats (Lo and Lo, Endocrine Soc. Abs.892, 1979). The present study deals with the effect of T_3 on the rate of degradation of the small subunit (a sialoglycoprotein) of Na K-ATPase. Recently, surgically hypothyroid rats were labeled with (35_S) methionine 48h after the first injection of T_3 (50µg/100g b.w.) or the diluent and the renal cortices were resected 48h after either the second or third injections. The small subunit of NaK-ATPase (labeled with tritiated Na^+ borohydride) was quantified by electrophoresis in SDS-polyacrylamide gel. Forty-eight hours after the second injection, the isotope ratios ($35_S/3_H$) of the small subunit in the diluent and T_3- treated hypothyroid rats were 0.157±.04 and 0.138±.03 respectively ($p>.05$, n=5); 48h after the third injection, the ratios were 0.086±.02 and 0.084±02, respectively ($p>.05$, n=5). The results indicate that T_3 augments the de novo synthesis of the small subunit of NaK-ATPase and has no effect on its degradation, supporting the hypothesis that the small subunit is an active component of NaK-ATPase.

INSTANTANEOUS STROKE VOLUME IN MAN DURING LOWER BODY NEGATIVE PRESSURE (LBNP). J.A. Loeppky, K.L. Richards*, E.R. Greene*, M.W. Eldridge*, D.E. Hoekenga*, M.D. Venters, and U.C. Luft. Department of Physiology, Lovelace Medical Foundation, Albuquerque, NM 87108.

The precise temporal response of stroke volume (SV) during cardiovascular transients such as LBNP has remained in question because previous methods required a steady state. A unique 3.0 mHz pulse Doppler echocardiograph was used to noninvasively measure centerline blood velocities from the ascending aorta obtained from the suprasternal notch. Continuous SV was calculated from the systolic velocity integral in 6 male subjects during the first min and intermittently following the square wave onset of -50 Torr LBNP and its removal after 10 min. Although individual variations were evident, the mean results indicated that SV fell linearly from the onset of LBNP to 49% of the pre-LBNP value after 33 sec with the lowest value (-50%) seen during the 8th min. Immediately after LBNP, SV rose rapidly to the pre-LBNP level after 9 sec with the heart rate (HR) simultaneously falling by 22 bpm. SV then transiently fell by 20% but returned to and remained at baseline after 40 sec while HR continued to fall for 4 min. SV was inversely related to HR and Leg Volume throughout the procedure, however the tachycardia during LBNP did not prevent cardiac output from declining 40 and 50% after 33 sec and 8 min of LBNP, respectively. (Supported in part under contract NAS9-15483 with NASA.)

THE ROLE OF ANGIOTENSIN II AND PROSTAGLANDINS IN CONTROL OF RENAL HEMODYNAMICS DURING HEMORRHAGE. Mustafa F. Lokhandwala* and Bhagavan S. Jandhyala* (SPON: H.N. Sapru) Dept. of Pharmacol., Univ. of Houston, Houston, TX 77004

The interactions between the renin-angiotensin and the prostaglandin systems in the control of renal hemodynamics during hypotensive hemorrhage (HH) were evaluated in mongrel dogs. In the first group of animals, HH caused a modest decrease in renal blood flow (RBF) which had returned to almost control level 60 min after HH, and there was no change in the renal sympathetic nerve function. Administration of indomethacin resulted in significant decrease in the RBF in these animals. In a second group of animals where HH was carried out after inhibiting the prostaglandin synthesis with indomethacin, significant fall in RBF occurred which persisted for 60 min after HH. Renal sympathetic function was not affected during HH. Administration of SQ-20881 resulted in the return of RBF to pre-hemorrhage levels. In the last group of animals, HH was carried out after blocking angiotensin receptors with saralasin which produced very insignificant changes in RBF and in renal nerve function. Administration of indomethacin to these animals 60 min after HH resulted in a modest decrease in RBF. These results suggest that during HH, renal prostaglandins oppose the vasoconstrictor action of angiotensin II and act to maintain RBF to near normal level by acting direclty on the renal vasculature and do not modify renal sympathetic nerve function. (Supported in part by HL-22868).

RETICULOENDOTHELIAL SYSTEM FUNCTION AND HEMOLYSIS FOLLOWING THERMAL INJURY. D.J.LOEGERING and J.Turinsky. Dept. of Physiology, Albany Medical College, Albany, NY 12208

Previous studies from this laboratory have demonstrated that hemolyzed blood depresses reticuloendothelial system (RES) function and increases susceptibility to hemorrhagic and endotoxin shock. The present study relates the dose of hemolyzed blood required to cause an RES depression to the degree of hemolysis following thermal injury. Phagocytic index was determined in anesthetized rats (sodium pentobarbital, 30 mg/kg) after injection of rat blood hemolyzed by freezing at -20°. Phagocytic index was decreased 53.9% ($p<.01$) 30 min after injecting 0.3 ml hemolyzed blood/100g body weight, decreased 47.4% ($p<.02$) after 0.2ml/100g, and was unchanged after 0.1ml/100g. Plasma hemoglobin (Hb) was 5.4±0.4 (SE), 4.3±0.3 and 2.5±0.4 mg/ml 30 min after injecting the Hb equivalent of 0.3, 0.2 and 0.1 ml/100g hemolyzed blood, respectively. Plasma Hb 30 min following thermal injury (27% surface area scald) of 30, 20 or 10 sec duration was 4.7±0.5, 3.2±0.2 and 2.2±0.3 mg/ml, respectively. Mortality was 70% with the 30 sec burn and zero with the 20 and 10 sec burn. It is concluded that phagocytic clearance of erythrocyte debris may result in depression of RES function and that the hemolysis associated with thermal injury is sufficiently severe to contribute to the RES depression seen with this form of injury. (USPHS Grant GM-26102)

ALDOSTERONISM IS NOT CRITICALLY IMPORTANT IN THE MAINTENANCE OF SODIUM BALANCE OR ARTERIAL BLOOD PRESSURE DURING SODIUM DEPLETION. Thomas E. Lohmeier, Philip R. Kastner*, Manis J. Smith, Jr.*, and Arthur C. Guyton. Univ. Miss. Med. Cntr. Jackson, MS 39216.

To determine the quantitative role of aldosterone(ALDO) in the maintenance of arterial pressure and electrolyte balance during Na depletion(-Na), dogs were subjected to 2 wks of -Na while intact and 4 wks later following bilateral adrenalectomy. Mean arterial pressure(MAP) was recorded continuously 24 hrs/day. ALDO and cortisol(F) were continuously infused intravenously at maintenance levels in the adrenalectomized dogs. During the control period Na intake=50 mEq/day and K intake=45 mEq/day. The steady-state values were:

Intact	MAP	PRA	ALDO	F	P_{Na}	P_K
Control	96±4	1.0±.2	4.3±.4	1.4±.3	146±1	4.6±.1
-Na	96±4	6.2±.4	42±7	1.3±.3	144±1	5.1±.1
Adrenalectomy						
Control	99±6	0.6±.4	5.7±.5	1.5±.3	147±1	4.7±.1
-Na	90±5	8.7±.8	8.7±.7		140±1	5.7±.1

In both groups urinary Na excretion<2 mEq/day during the last 5 days of -Na although ALDO was 5 times higher in dogs with adrenal glands intact. Apparently, the aldosteronism which accompanies -Na does not play a potent role in the maintenance of Na balance nor of MAP. (Supported by NIH HL 11678).

"FATIGUE" OF GASTRIC SECRETORY AND MOTOR RESPONSES TO ELECTRICAL STIMULATION OF THE VAGUS NERVES IN CATS. Dale M. Lombardi and Frank P. Brooks. Dept. Physiology, University of Pennsylvania, Philadelphia, PA 19104.

Fatigue of the acid secretory response to constant electrical stimulation of the vagus nerves (ESV) in anesthetized dogs with reduction of acid output to 1/2 the maximal level occurred after 3 hours. (Cumming, J.D., Greetham, R.B. and Percival, H.G., J. Physiol. 200:61-62P, 1969). We have stimulated the distal crushed ends of the cervical vagi of cats anesthetized with chloralose-urethane at 5 Hz, 4 msec and 1 mamp for 3 hrs., collecting gastric content from a gastric fistula (pylorus ligated), and recording gastric antral contraction with an extraluminal strain gauge sewn to the gastric wall. We compared our results with similar observations in cats given bethanechol 300 µg/kg/hr i.v..

Acid output mM/hr	1st hr	2nd hr	3rd hr
ESV (7 cats)	2.23±0.17 SEM	3.16±0.19	3.59±0.40*
Beth (4 cats)	1.53±0.16	2.10±0.12	1.74±0.09
No. Antral Contr >15 Gm/hr			
ESV	172.0 ± 5.9*	119.0 ±6.3	74.7 ±4.3*
Beth	76.5 ±12.6*	131.8 ±2.1	134.7 ±9.5*

*p = <0.01

No fatigue was noted in acid secretion after 3 hours of ESV. The fatigue in gastric antral contractions is not due to decreasing smooth muscle responsiveness to acetylcholine. (Supported by USPHS NIAMDD Grant 2R01 AM14563)

EXTRACELLULAR AND INTRACELLULAR IONTOPHORETIC INJECTION OF MELANOCYTE STIMULATING HORMONE AND THE RESPONSE OF SINGLE MELANOPHORES IN FROG SKIN. M. A. Longshore*, J. M. Horowitz and G. M. Mikuckis*. Univ. of Calif., Davis, CA 95616.

A previous report introduced a model system whereby the effects of various compounds (e.g. cyclic AMP, cyclic GMP)can be seen within a single cell with nearby cells in the field serving as controls (J. Cell Biol. 74:928, 1977). In the present study, similar techniques were used to inject MSH within and outside Rana pipiens melanophores to determine if MSH injected within a cell would lead to melanosome dispersion. Injection currents were less than 200 namps, and the pH of injection solutions ranged from 6 to 8. In 46 cells intracellular MSH was ineffective in producing melanosome dispersion as viewed through the microscope. In order to verify that the electrode was in a melanophore, cAMP, shown to produce melanosome dispersion, was injected in 17 cells causing dispersion. In these 17 cells, prior injection of MSH caused no dispersion. To determine if adequate amounts of MSH were released, the electrode was withdrawn from the cell and placed near a group of melanophores and in all cases the cells close to the electrode tip showed melanosome dispersion after MSH injection. The results of this study remain consistent with the view that MSH receptors in frog skin melanophores are located on the external surface of the plasma membrane and MSH injected into the cytoplasm of the cell has no short term effect. [Supported by NIH Grant HD-003941]

RELEASE OF PANCREATIC POLYPEPTIDE (PP) BY CHOLECYSTOKININ (CCK) IN MAN. J Lonovics,* S Guzman,* P Devitt,* K Hejtmancik,* RL Suddith,* PL Rayford and JC Thompson. Dept Surg, Univ Texas Med Branch, Galveston, Texas 77550.

Previous studies have shown PP release by exogenous CCK in dogs. In man, PP has been released by the CCK analogue caerulein, but not by the pure compound. Methods: Six healthy fasting volunteers were studied. 99% pure CCK was sterilized by filtration and then checked for biologic activity by isolated rabbit gallbladder bioassay. Two doses of CCK were infused (Exp I, 0.25 µg/kg-hr;Exp II, 0.5 µg/kg-hr). Blood samples were taken for PP radioimmunoassay. PP levels released by CCK were compared to those seen after a food study in the same subjects (Exp III). Results: PP levels are expressed in pg/ml (mean ± SEM).

	Basal	15	30	45	60	75
I	165±47	376±80*	424±76*	401±66*	297±71*	225±57
II	208±51	442±126*	501±134*	504±129*	321±83*	222±47
III	147±32	922±318*	745±245*	645±169*	655±174*	661±152*

* = significantly different from basal (p <0.05).

Conclusions: Both doses of 99% pure CCK caused significant elevations in PP levels. Integrated values of PP were 36% (low dose of CCK) and 42% (higher dose) of integrated value of PP released by food. These results support the hypothesis that humoral mechanisms are involved in PP release and that CCK probably plays an important role in the intestinal phase of PP release in man.

RO 20-1724 RELAXATION OF TAENIA COLI IN THE PRESENCE OF IONOPHORE A 23187. Rodger Loutzenhiser* Philip Aaronson* and Cornelis van Breemen* (SPON: A.L.Bassett). University of Miami Sch. of Medicine Miami, Fl. 33101

We have studied the effect of the ionophore A 23187 upon tension and cellular calcium-45 (Ca_i) in the guinea pig taenia coli during the relaxation produced by Ro 20-1724, a phosphodiesterase inhibitor. Isotonic 80mM K produced a sustained contracture and increased Ca_i from 286±31 µM/kg to 636±28 µM/kg after 25 minutes. A 23187(10^{-6}M) was added to 80mM K depolarized tissue at 5 minutes. The ionophore produced no significant change in tension or in Ca_i (593±41 µM/kg at 25 minutes). Ro 20-1724(10^{-3}M) produced complete relaxation within 15 minutes and increased Ca_i (735±20 µM/kg), suggesting that the relaxation was mediated by a redistribution of cellular Ca. A 23187 did not effect the relaxation or Ca_i (623±59 µM/kg). Using ^{45}Ca efflux methods, we have previously demonstrated the presence of two cellular Ca compartments in taenia coli. Neither compartment is abolished in the presence of 10^{-6}M A 23187. These results suggest that A 23187 does not impair sequestration processes in smooth muscle cells. (Supported in part by NIH Grant 1 Ro1 HL 23559-01, and by NIH Grant HLT32 07188.)

EARLY CARDIOPULMONARY EFFECTS OF LOW-DOSE DAUNOMYCIN INFUSION. Jen Lucas*, Cheri Buchanan*, Bernard J. Rubal and Kim Barnard*. Cardiovas. Res. Lab., Texas Woman's University, Denton, TX 76204

Daunomycin is an anthracycline analog which is an effective anticancer agent. Unfortunately the use of anthracycline analogs is limited by their cardiotoxicity. In this study, ten mongrel dogs premedicated with morphine (5 mg/kg) and anesthetized with alpha chloralose (80mg/kg) were monitored for eleven hours. Five dogs were given an intravenous infusion of 2.5 mg/kg Daunomycin, and five dogs were used as controls. Arterial blood gases, heart rate, arterial diastolic pressure, percent change in left ventricular dP/dt, and percent change in Vmax were recorded hourly. No significant differences were found in arterial pH, PCO_2 or PO_2 between the two groups; nor were significant differences found in heart rate, arterial diastolic pressure, percent change in dP/dt or Vmax. However, a consistent depression in the mean percent change in dP/dt was noted from the fifth through eleventh hour post-Daunomycin infusion. These data suggest that significant cardiopulmonary impairment is unlikely in anesthetized dogs given a single dose of 2.5 mg/kg or less of Daunomycin. Further studies are needed to determine the earliest time of detectable cardiac depression induced by single or multiple dose regimes of anthracycline analogs. (Supported by Texas Woman's University Grant # 0936)

NOREPINEPHRINE AND RENAL FUNCTION AT EXTREMES OF SODIUM INTAKE. F.C. Luft, L.I. Rankin*, L.R. Willis*, D.P. Henry*, M.H. Weinberger*, Ind. Univ. Med. Ctr., Indpls., IN 46223.

To examine the effects of wide ranges in plasma norepinephrine (P_{Ne}) on renal function at extremes of Na intake, we infused Ne into 8 normal men in balance at 10 (A) or 800 (B) mEq/day. After two 30 min control periods, Ne was infused at 1,2,4,8 and 16 µg/min for 30 min. Ne was stopped if mean blood pressure (MBP) increased >25mm Hg. Arterial P_{Ne}, the clearances of inulin (C_{In}), PAH (C_{PAH}), Ne (C_{Ne}) and FE_{Na} were measured. Representative data (mean ± SEM):

Ne (µg/min)		0	1	4	8	ANOVA P
C_{In}	A	106± 5.0	102± 5.0	98± 6.0	93± 5.0	<0.05
	B	126± 6.0	105± 6.0	96± 7.0	95± 6.0	<0.05
C_{PAH}	A	630±28.0	574±37.0	493±22.0	425±22.0	<0.05
	B	651±44.0	540±43.0	450±34.0	422±26.0	<0.05
C_{Ne}	A	205±33.0	159±28.0	150±14.0	165±22.0	<0.05
	B	346±51.0	193±33.0	160±31.0	133±20.0	<0.05
FE_{Na}	A	0.4± 0.1	0.3± 0.1	0.3± 0.1	0.2± 0.1	NS
	B	3.3± 0.4	2.8± 0.3	2.4± 0.2	2.2± 0.3	<0.05

At 10 mEq/day, MBP increased 25mm Hg at 16 µg/min Ne, while at 800 mEq/day this increase occurred at 8 µg/min Ne. Ne in plasma and urine were highly correlated (r=0.9); the relationship was the same in both A and B. Ne decreased C_{In} and C_{PAH} independent of Na intake. Ne had an antinatriuretic effect independent of C_{In} and despite increased MBP. C_{Ne} exceeded C_{In} over a wide range of P_{Ne} irrespective of Na intake. (Supported by PHS HL 14159).

MUSCARINIC RECEPTOR DENSITY IN MYOPATHIC HAMSTER HEARTS. Donald D. Lund, Phillip G. Schmid, and Robert Roskoski, Jr.*. C.V. Center, Depts. of Biochem. and Int. Med., Univ. of Iowa and VA Hospital, Iowa City, Iowa 52240

Impaired parasympathetic modulation of sympathetic overactivity may explain the cardiomyopathy in Syrian Golden hamsters with skeletal myopathy. Previously we observed that acetylcholine synthesis in vitro was impaired in myopathic hearts (Physiologist 20:58, 1977). This study was done to examine cholinergic muscarinic receptors (CMR) in the myopathic heart. Specific ^{3}H-quinuclidinyl benzilate (QNB) binding to tissue homogenates was used to quantiate CMR density in ventricles of control (Bio 2.4) and myopathic (Bio 14.6) hamsters, 30, 90, 180, and 360 days old (n=6 for each group). Specific ^{3}H-QNB bound (fmol, mg. protein^{-1}) was similar (P>0.1) in myopathic and control hearts at 30 days (mean SEM) 34±2 vs 40±5; binding remained low in the myopathic ventricles and increased in the controls at later ages (P<0.05): 40±2 vs 70±5 (90); 41±2 vs 84±13 (180); and 46±3 vs 64±2 (360). The failure of CMR to increase normally in the myopathic heart with age may contribute to impaired parasympathetic modulation of sympathetic regulation. The defect could be related to acquired rather than genetic factors since QNB binding appears normal in young "premorbid" myopathic hamsters. (Supported by USPHS Grants HL-20768, HL-14388, and HL-24246).

EFFECTS OF 4-AMINOPYRIDINE (4AP) ON RODENT ADRENAL STEROID SECRETION,INVITRO. J.R.Lymangrover*(SPON: R.Lowe) Tulane Univ. Med. School New Orleans, La. 70112.

In order to ascertain the role that the transmembrane movement of K^+ plays in the control of steroidogenesis the action of 4AP (a specific K^+ blocking agent) on rat and mouse adrenal corticosterone secretion was studied. Rat or mouse adrenal cortical slices were superfused at a rate of 1ml/min with a Krebs-Henseleit-glucose solution maintained at 37°C. Corticosterone production by the tissue was continuously monitored by an on-line autoanalyzer-fluorometric procedure. The addition of a 10ml aliquot of a 10mM solution of 4AP to rat adrenal cortical tissue significantly inhibited basal steroid secretion. The simultaneous addition of 10mM but not 1mM 4AP significantly depressed (54.7% decrease) the response of the rat adrenal tissue to 10mU of ACTH. CAMP (1 to 20u mole) stimulated steroid secretion was also depressed (max 27% decrease) by the 10mM 4AP. A 10 ml aliquot of 0.1,1 or 10mM 4AP administered to mouse adrenal tissue resulted in substantial dose dependent transient elevations in basal adrenal corticosterone production. The continuous superfusion of 1,2 or 10mM 4AP reversably blocks ACTH stimulated steroid secretion from mouse adrenal tissue. The higher the concentration of 4AP the more effective was the blockade.These data suggest that alterations in the distribution and movement of K^+ across the adrenal cell membrane may play a role in the regulation of adrenal steroid secretion. (Supported by grants from E.D.Schlieder Fndn. and The Am. Heart Ass. of La.)

BONE REPAIR DURING IMMOBILIZATION. S.A. MacArthur*Technology Incorporated, P.C. Rambaut,*C.S. Leach , S.L. Pool* NASA/ Johnson Space Center, Houston, Texas 77058

The positive effects of functional weightbearing on bone repair has been accepted for some time; however, no reproducible method of inflicting a lesion with minimal trauma to the animal has been employed. In this study, reproducible bone lesions were made in the femurs of rats with a dremel drill and high speed carbon steel drill bits. Drill bits ranged in size from 0.5 to 1.0mm in diameter. Lesions made using this technique are easily visible on X-ray exposed film. Quantitative tetracycline labeling was used to distinguish pre and post-surgery osteoblastic formation. This surgical procedure may be accomplished with minimal body fluid loss and muscle trauma. Animals subjected to this experimental technique may regain their mobility within two hours after surgery and show rapid healing and recovery during the post operative period. Animals subjected to this technique and immobilized in plaster casts for 7, 14 or 21 days show a significantly increased calcium and potassium excretion over the mobile, non-casted animals. This increased excretion is similar to that seen in bed rested patients. Serum analysis did not indicate a significant difference in Hct., Ca, Mg, IPO_4, Na, K, or Cl between the casted and uncasted animals. After sacrifice, femurs were removed, then analyzed histopathologically to quantitate bone repair. The mobile animals healed more quickly than did the immobilized animals.

DIURNAL RHYTHMS OF PLASMA SEX STEROIDS IN THE KILLIFISH, FUNDULUS GRANDIS. Robert Macgregor III*, (SPON: J.W. Hudson) Dept. of Biology, University of Alabama in Birmingham, Birmingham, Alabama 35294

Diurnal rhythms of plasma corticosteroids have been reported in many teleost fish. However, diurnal rhythms of plasma sex steroids have not been identified in any teleost prior to the report. Daily peaks of plasma androgens (testosterone and dihydrotestosterone) in male and plasma estrogens (estradiol and estrone) in female gulf killifish were identified by radioimmunoassay technique. The killifish were maintained in aquaria (22°C, salinity 10 ppt) during a 15 hour daily photoperiod. Groups of fish (8-10) were bled and sacrificed at 3 to 4 hour intervals during a 24 hour period. A daily peak in plasma androgens (680 pg/ml ± 262) in males occurred 6 to 12 hours after the onset of the light cycle. In females, plasma estrogens rose sharply at the onset of darkness (600 pg/ml ±115) and remained elevated until the onset of light. Injections of O-LH caused an increase in plasma androgens (10-fold) and plasma estrogens (2-fold) in males and females, respectively. The occurance of daily rhythms of plasma sex steroids may reflect a daily cycle of plasma gonadotropins. (supported by UAB University College Faculty grant).

RESPIRATORY ACIDOSIS AND THE TWITCH CONTRACTION OF IN SITU SKELETAL MUSCLE. Brian R. MacIntosh and Wendell N. Stainsby, Dept. of Physiology, University of Florida, Gainesville, Fla.

Dogs anesthetized with pentobarbital were used to study the effects of respiratory acidosis on the mechanics of the twitch contraction. The left gastrocnemius-plantaris muscle group was isolated and the achilles tendon was secured to an isometric lever. The muscle's venous circulation was isolated to allow sampling of venous blood. The arterial circulation was left intact. Contractions were elicited by supramaximal (2-4v, .2 msec duration) stimulation of the cut sciatic nerve. In each experiment there were three ventilatory conditions: control, hypoventilation and hyperventilation (series A) or control, hyperventilation, hypoventilation (series B). During hypoventilation the inspired air mixture was enriched with O_2 to prevent hypoxia. Arterial PO_2 did not fall below 70 mm Hg. In series A, arterial pH changed from 7.37 ± .01 ($\bar{x}$ ± SEM) during control to 7.08 ± .03 during hypoventilation then 7.4 ± .02 during hyperventilation. In series B, pH changed from 7.36 ± .01 during control to 7.52 ± .02 during hyperventilation then 7.24 ± .03 during hypoventilation. Developed tension during hypoventilation was not significantly different from that during the control period. Developed tension during hyperventilation was significantly greater than developed tension during the control period. (Supported by American Heart Association, Florida Chapter, Grant #AG715.

5-THIO-D-GLUCOSE: THERMOREGULATORY EFFECTS IN MICE AT SEVERAL ENVIRONMENTAL TEMPERATURES. M. Mager and R. P. Francesconi. US Army Res. Inst. Environ. Med., Natick, MA 01760.

For several years we have been investigating the thermoregulatory effects of compounds which affect glucose metabolism both centrally and peripherally. The glucose analogue, 5-thio-D-glucose (5-TG), has been reported to be an effective competitive inhibitor of the glycolytic process with hypothetical thermoregulatory effects. Thus, adult, male mice were administered various doses of 5-TG at three environmental temperatures: 4°C, 22°C, and 35°C. Generally, intracerebroventricular or intraperitoneal administration of 5-TG resulted in significant hypothermic ($p<.05$ - $p<.001$) responses which were ordinarily dose-dependent. These hypothermic effects were significantly ($p<.005$) exacerbated by 18 h food deprivation prior to experimentation. The decrements in rectal temperature were accompanied by significant ($p<.001$) increments in circulating levels of glucose; in food deprived animals the increments were significantly ($p<.02$) attenuated. These results are highly suggestive that 5-TG is eliciting both central and peripheral glucopenia concomitant with circulatory hyperglycemia. Thus, at environmental temperatures below the thermoneutral zone, hypothermia may be the result of reduced availability of tissue glucose as well as competitive inhibition of glycolysis by 5-TG intermediates, both of which contribute to a decrement in heat production.

OXYGEN EQUILIBRIA IN WHOLE BLOOD CONTAINING MULTIPLE HEMOGLOBINS: IS THERE ISOHEMOGLOBIN INTERACTION IN INTACT SHEEP ERYTHROCYTES? L.A. Maginniss and R.B. Reeves. Dept. of Physiology, SUNY, Buffalo, N.Y. 14214.

Adult sheep (Ovis aries) exhibit Hb polymorphism (Hb A, Hb B, Hb AB). In heterozygotes the molar ratio Hb A/Hb B = 1. Sheep lack DPG-Hb interaction which simplifies the study of Hb A-Hb B interactions in intact red cells on whole blood O2 equilibrium curves (O2EC). We ask: can O2EC of AB cells be duplicated by superposition of O2EC from A and B blood? Continuous isocapnic O2EC were generated by dual wavelength spectrophotometry (430-453 nm) and electrode oximetry at 39°C. Blood pH was computed from a buffer line and the PCO2.

Hb	Animals/ Curves	P50 (7.5) torr	Hill's n	Δlog PO2/ΔpH
A	3/11	31.9 ± 1.1	3.01 ± .02	-.35 ± .03
B	4/16	40.5 ± 0.9	2.90 ± .03	-.36 ± .03
AB	4/16	35.9 ± 0.8	2.89 ± .06	-.37 ± .02
A + B	4/11	36.0 ± 0.7	2.88 ± .04	-.40 ± .02

O2 affinity of Hb AB blood was intermediate to Hb A and Hb B P50 values; the three phenotypes, however, exhibited similar curve shapes (n) and CO2-Bohr effects. No significant interaction between Hb A and Hb B within common red cells occurs. Identical O2EC from Hb AB cells and the red cell mixture (Hb A + Hb B) substantiate this conclusion. Sheep O2EC do not fit the Severinghaus (1979) equation for human O2EC. (Supported by NHLBI Grant HL-14414-07).

ROLE OF DECREASED MINERALOCORTICOID SECRETION IN THE CHRONIC HYPERTENSIVE EFFECTS OF SQ 14,225. Subir R. Maitra, Seiji Miyazaki, Alfonso G. Scicli, and Oscar A. Carretero*. Henry Ford Hospital, Detroit, MI, 48202.

The chronic antihypertensive effect of SQ 14,225 may be due to a decrease in mineralocorticoid secretion caused by blockade of angiotensin II (ANG II) formation. To study this hypothesis, changes in blood pressure (BP) were measured in the following three groups (gp) of spontaneous hypertensive rats (SHR): (A) adrenalectomized (ADX) with steroid support and treated with SQ 14,225 (100 mg/kg/day, p.o.),(n=7); (B) sham ADX treated with SQ 14,225, (n=7); and (C) ADX treated with steroid support (n=7). After three weeks of treatment, tail BP of gp A was 186 ± 2 mm Hg while that of gp B was 152 ± 2 ($p<.001$). BP of gp C was 205 ± 3 ($p<.001$, A vs. C). Plasma renin activity (PRA) of gp A was 13.6 ± 4 ng/ml/hr and that of gp B, 24.9 ± 5 ($p>.05$). Gp C had a PRA of 1.6 ± 1 ($p<.001$, C vs. A or B). Control studies with ADX and non-ADX SHR and Wistar-Kyoto rats showed that the doses of mineralocorticoids used had no hypertensive effects. Since the decrease of BP induced by SQ 14,225 was greater in non-ADX than in ADX receiving exogenous steroids we conclude that part of the chronic antihypertensive effects of SQ 14,225 are due to a decrease in mineralocorticoid secretion. Further, both non-ADX and ADX SHR responded to chronic blockade of ANG II formation with a marked rise in PRA.

TRANSMURAL DISTRIBUTION OF MYOCARDIAL BLOOD FLOW (MBF) IN UNANESTHETIZED PONIES WITH CHRONIC RIGHT VENTRICULAR (RV) SYSTOLIC HYPERTENSION. M. Manohar, G.E. Bisgard, V. Bullard*, and J.H.G. Rankin, Departments of Veterinary Science and Physiology, University of Wisconsin-Madison, WI 53706.

In 6 unanesthetized adult healthy ponies which had their main pulmonary artery banded (PAB) 1-3 months prior to the study, hemodynamics and MBF (15 μm radionuclide labeled micro spheres) were studied during control normoxemia (N) and during intravenous infusion (2 μg/kg/min) of isoproterenol HCl (I) at N (6), at hypoxia (H;4) and at hyperoxia (HY;2). PAB had resulted in marked RV hypertrophy. The mean RV systolic: aortic systolic (RVS:AOS) pressure ratio during N, N + I, H + I and HY + I was .67, .90, .93, and .90, respectively. At N, MBF was uniformly distributed across RV, septal, and the left ventricular (LV) myocardium. With I, MBF increased to all the subregions, but the Endo:Epi decreased significantly below unity in both ventricles. With I, heart rate, and the RV systolic pressure-time area (SPTA) had increased significantly while LV diastolic pressure-time area (DPTA) and aortic diastolic pressure (AOD) had decreased significantly. The RV coronary perfusion pressure-time area: RVS and LVDPTA: AOS were found to better predict the adequacy of respective ventricular subendocardial perfusion compared to the ratios obtained by using SPTA in the denominator. It is concluded that when RVS approaches AOS, a reduction in AOD along with a shortening of the RV diastolic duration may cause RV subendocardial ischemia once coronary autoregulation is abolished.

PULMONARY VENOCONSTRICTION CAUSED BY ELEVATED CSF PRESSURE (P_{CSF}) IN THE DOG. M.B. Maron* and C.A. Dawson. Dept. of Physiology, Med. Col. of Wisconsin, and Wood VA Med. Ctr., Milwaukee, WI 53193.

Previously we found that raising P_{CSF} caused pulmonary vasoconstriction which was caused by adrenal catecholamines. To localize the site of this vasoconstriction, we used the outflow occlusion technique, in which changes in vascular resistance are divided into changes in arterial and venous resistances. Experiments were conducted in 7 dogs in which the animal's left lower lung lobe (LLL) was denervated and perfused at constant flow and outflow pressure with blood pumped from the dog's pulmonary artery. Raising P_{CSF} to 208 torr caused the LLL arterial-venous pressure gradient (P_{A-V}) to rise 40.4% from 8.9 to 12.5 torr ($p < 0.001$). For comparison we infused epinephrine into the LLL at doses which caused similar increases in P_{A-V} to those observed with elevated P_{CSF}. The results are summarized below:

	Increase in Pressure Drop (torr)		
	Total	Arterial	Venous
P_{CSF}	3.6 ($p < 0.01$)	0.3 (NS)	3.3 ($p < 0.01$)
Epinephrine	4.0 ($p < 0.01$)	0.9 (NS)	3.0 ($p < 0.01$)

Thus the vasoconstriction caused either by elevating P_{CSF} or by infusing epinephrine resulted primarily from an increase in venous resistance. (Supported in part by the American Heart Assoc./Wisconsin Affiliate and NIH Grant HL 19298)

PROTECTIVE EFFECT OF CHRONIC SPLENECTOMY AGAINST EPINEPHRINE-INDUCED ACUTE RENAL FAILURE. Anil K. Mandal*, Jon Miller*, and Francisco Llach* (SPON: A.A. Yunice), VA Med. Ctr. and Univ. of Okla. Coll. of Med., Oklahoma City, Oklahoma, 73104.

We have reported that splenectomy is protective against epinephrine (Epi) induced acute renal tubular lesions (ATL). This report describes renal physiological studies in 7 intact dogs (Group I) and 7 chronic splenectomy dogs (Group II) receiving a 6 hr intravenous Epi infusion (4 μg/kg/min). The hourly measurements throughout the study included: Urine volume (UV), mean arterial pressure (MAP), glomerular filtration rate (GFR), effective renal plasma flow (ERPF), renal blood flow (RBF), urine sodium (UNaV), urine osmolality (UosmV), serum urea nitrogen (SUN) and creatinine (SCr). Kidney tissue was fixed for light and electron microscopy. Tubular lesions were scored from 0 to 4+. Group I had mean values (± SEM) in the 6th hour significantly different from Group II: UV .02 ± .04 vs .86 ± .19 ml/min, GFR 6 ± 5 vs 73 ± 14 ml/min, ERPF 7 ± 6 vs 133 ± 4 ml/min, RBF 48 ± 17 vs 176 ± 37 ml/min, UNaV 20 ± 8 vs 108 ± 26 mEq/L, UosmV 389 ± 34 vs 784 ± 116 MOsm/L, SUN 29 ± 1 vs 16 ± 1 mg/dl, SCr 1.94 ± .27 vs .9 ± .06 mg/dl and MAP 1st hr, 187 ± 6 vs 130 ± 9 mmHg. ATL were severe in Group I (3+ to 4+) and absent to mild in Group II (0 to 1+). In summary: 1) Group I was oliguric, had low GFR and ERPF with azotemia and severe ATL; 2) Group II was protected, having normal renal function, natriuresis, polyuria and low MAP; this may be explained by the presence of a vasodilator, possibly a prostaglandin-like substance.

CHOLINOCEPTIVE RECEPTORS IN INTRINSIC NEURONS OF RAT CAUDATE. L. A. Marco, J. C. Torri*, and J. A. Hirsch*. Dept. of Psychiatry, Med. Univ. of S.C. and VA Medical Center, Charleston, S.C. 29403.

We have previously shown (Marco et al., Brain Res. 53:291, 1973) that negative evoked compound potentials (ECP) and unit potentials (EUP) are generated in cat isolated caudate (CD) by activation of local interneuronal circuits (LIC). In this study rats were given 55 mg pentobarbital/kg intraperitoneally and the CD was surgically isolated from the rest of the neuraxis, except ventrally. EUP and ECP were recorded after full degeneration of extrinsic axons 6 or more days later with 5-barrel micropipettes. Two barrels were loaded with normal saline for recording and current neuralization and the other three with acetylcholine (ACh), dopamine (DA), and atropine for microiontophoresis. Single square pulse stimulation within 1.5 min. from the recording site triggered ECP and EUP of characteristics similar to those in cats at average latency of 10 msec. EUP often emerged from the ECP. Both were enhanced by iontophoresis of ACh but not of DA at the same or greater current strength. These results indicate that the synaptology of these LIC is ACh-sensitive, that ACh-sensitive neurons are aggregated in very discrete and neurochemically homogeneous clusters, and that a population of such neurons can be simultaneously activated by iontophorized ACh. (Supported by NINCDS Grant #NS14712-02.)

GLUCOSE TURNOVER DURING COLD STRESS IN A SMALL BIRD, THE AMERICAN GOLDFINCH (SPINUS TRISTIS). Richard L. Marsh* and William R. Dawson. The University of Michigan, Ann Arbor, MI 48109

With a single injection technique we have assessed glucose turnover (R_O in mg/min) in winter acclimatized goldfinches (body mass approx. 14 g) using 3-T-glucose. On the basis of metabolic rate ($\dot{V}O_2$), the resting glucose turnover is among the lowest reported for any vertebrate ($R_O/\dot{V}O_2$= 0.32 mg/cm$^3O_2$), even though plasma glucose levels are 3-4 times mammalian values. Unlike the mammals studied to date, glucose turnover does not increase proportionate to oxygen consumption during cold stress. At a $\dot{V}O_2$ of 2.35 times resting levels, R_O is the same as at rest, resulting in a substantial decline in $R_O/\dot{V}O_2$ (from 0.32 to 0.13 mg/cm$^3O_2$). At higher levels of $\dot{V}O_2$, R_O increases proportionately. Because carbohydrate is considered to be the limiting substrate during exercise or cold stress, the low levels of glucose turnover in this species are considered to be an important adaptation for winter survival. The low glucose turnover during shivering thermogenesis is correlated with the high capacities for β-oxidation and aerobic energy metabolism found in the muscles of this species. (Supported by NSF Grant DEB-77-25487 to W.R.D.).

DEPRESSION OF HYPOXIC PULMONARY VASOCONSTRICTION BY TRANSMURAL PULMONARY ARTERY PRESSURE. Bryan E. Marshall, MD,FRCP, and Carol Marshall, PhD*, Department of Anesthesia,University of Pennsylvania, Philadelphia, Pennsylvania 19104.

Published observations on hypoxic pulmonary vasoconstriction in man, dog, rat, cat, and guinea pig all fit a continuous expression for flow diversion from an hypoxic segment $(\dot{Q}_{SN} - \dot{Q}_{SH}/\dot{Q}_{SN}) = (\dot{Q}_{WN} - \dot{Q}_{WN}[K^4B/A])/(\dot{Q}_{WN} + \dot{Q}_{SN}[K^4B/A])$; where $\dot{Q}_{SN}$ and $\dot{Q}_{SH}$ are flow to test segment during normoxia and hypoxia, respectively; $\dot{Q}_{WN}$ is flow to rest of lung during normoxia; K = 0.749 and is the maximal vascular constriction; and B and A are changes in conductance of the test segment and rest of the lung, respectively, due to recruitment and/or distention. When transmural pulmonary artery pressure is increased (ΔPATM), then, also from published data, $K^4B/A = 0.8(\Delta PATM) - 0.12(\Delta PATM)^2 - 0.38$. Substitution in the flow diversion equation predicts progressive depression of flow diversion from an hypoxic segment as ΔPATM increases. This result is in agreement with experimental findings (Benumof et al: J Appl Physiol 38: 846, 1975) and compatible with clinical reports of pulmonary hypertension and arterial hypoxemia in respiratory distress syndromes (Zapol et al: N Engl J Med 296: 476, 1977). Clinical implication of this relation is that arterial hypoxemia may be improved if pulmonary hypertension is reduced.

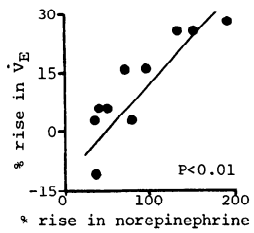
This work was supported by NIH, NHLBI 2 ROl HL 16916.

PLATELET RETENTION IN THE LUNG IN HYPOVOLEMIC SHOCK. B.A. Martin*, R. Dahlby*, I Nicholls* and J.C. Hogg. UBC Pulmonary Research Laboratory, St. Paul's Hospital, Vancouver, B.C.

We examined the removal of platelets by the pulmonary vascular bed during hypovolemic shock in dogs. Platelets and RBCs from each animal were labelled with ^{51}Cr and ^{99m}Tc, respectively, and were mixed in aliquots for rapid injection into the right atrium while blood was being sampled from the ascending aorta. From the concentration-time curves obtained, mean transit time (MTT), blood volume (BV) and % recovery were calculated from both RBC and platelet curves, and % extraction (ext) of platelets was calculated using the formula % ext = $^{C}RBC-^{C}$ platelets/^{C}RBC at the peak RBC concentration. In 9 control animals these injections were repeated at hourly intervals for 5 hours. In 5 experimental animals, two injections were performed at normal blood pressure (BP), one while lowering the BP, two during the period while BP was held at ~40 mmHg, and one after the shed blood was reinfused. The MTT and BV for platelets was greater than for RBCs and this difference increased in shock. The % recovery was less for platelets than RBCs and did not change in shock. The % extraction of platelets averaged 15% in control experiments and increased to 29% in shock (P<.02). Comparison of the platelet/RBC ratio in blood and in lung postmortem showed the lung to retain platelets after shock (P<.001). We conclude that hypovolemic shock causes the lung to remove platelets from the circulating blood.

VENTILATORY DRIFT DURING PROLONGED EXERCISE. Bruce J. Martin, Edward J. Morgan*, Clifford W. Zwillich*, and John V. Weil*. CVP Res. Lab., UCMC, Denver, CO 80262, and Indiana Univ. Sch. Med. Physiol. Sect., Bloomington, IN 47401

The mechanism by which ventilation ($\dot{V}_E$) steadily increases throughout prolonged exercise at constant work load remains unresolved. This $\dot{V}_E$ drift has implications for the adequacy of gas exchange during long-term exercise and for endurance exercise tolerance. In this study we examined a variety of proposed mediators of $\dot{V}_E$ drift. We found in 10 normal subjects that $\dot{V}_E$ increased 13% (P<0.01) from 12 to 60 minutes of cycle ergometer exercise at 2/3 $\dot{V}O_2$ max in parallel with two-fold increases in blood levels of both norepinephrine and epinephrine (P<0.01). Among subjects, increases in norepinephrine were positively correlated with the extent of $\dot{V}_E$ drift (P<0.01; see Figure). In contrast, $\dot{V}_E$ drift occurred in spite of unchanged or decreasing levels of a variety of other ventilatory stimuli, including CO_2 production rate and levels of arterial acidity and P_{CO_2}. These results suggest that rising blood norepinephrine levels may cause $\dot{V}_E$ drift during prolonged exercise at constant work rate.



(Supported in part by NIH Grant HL 14985)

RESPIRATORY MUSCLE FUNCTION IN INDUCED ASTHMA. J.G. Martin*, E.Powell*, S.Shore* and L.A. Engel, Meakins Christie Labs., McGill University Clinic, Royal Victoria Hospital, Montreal, Quebec, Canada.

We studied chest wall mechanics in 7 asthmatic subjects during progressive bronchoconstriction induced with increasing doses of inhaled histamine. Progressive hyperinflation was associated with persistent inspiratory muscle action throughout each expiration (Martin et al. Am. Rev. Resp. Dis 119:334, 1979). Prior to bronchoconstriction the minimum transdiaphragmatic (Pdi_m) and transthoracic pressures (Ptt_m) during expiration were reached after 78 ± 16% (mean ± 1 SD) and 81 ± 9% of the tidal volume had been expired (Vte). At maximum bronchoconstriction Ptt_m was reached at 73 ± 12% Vte, while Pdi_m was reached at 30 ± 16% Vte in 6 and 90% Vte in 1. Since diaphragmatic relaxation was usually complete early in expiration the persistent inspiratory muscle activity was due to the intercostal and accessory muscles. During increasing bronchoconstriction expiration was associated with a decrease in abdominal antero-posterior diameter while gastric pressure increased, reflecting abdominal muscle recruitment. We conclude that in acute asthma with hyperinflation there is persistent inspiratory muscle activity during expiration mainly due to intercostal and accessory muscles. Despite this, abdominal muscles are recruited. This interaction may serve to optimize diaphragmatic length.

Supported by the Medical Research Council of Canada.

STIMULATION BY HIGH K+-ARTIFICIAL SEAWATER (ASW) OF THE OUABAIN-INSENSITIVE SODIUM EFFLUX IN BARNACLE MUSCLE FIBERS. Drusilla Mason-Sharp* and E.E. Bittar, Department of Physiology, University of Wisconsin, Madison, Wisconsin 53706.

Depolarization of barnacle muscle fibers with high K+-ASW causes a stimulation of the ouabain-insensitive Na efflux. The magnitude of the response observed following exposure to 100mM-K+ depends on external $[Ca^{2+}]$ and $[Na^+]$ and on external pH, but is independent of external $[Mg^{2+}]$. External application of 10^{-4}M-verapamil virtually abolishes the stimulation. The response to depolarization is also significantly reduced by prior injection of 250mM-EGTA. These results suggest that the stimulation of the Na efflux involves a mechanism which is activated by the rise in myoplasmic Ca^{2+} that occurs following depolarization. Other maneuvers aimed at raising internal Ca^{2+} also stimulate the Na efflux: injection of 0.1M-$CaCl_2$ and external application of 10^{-5}M-A23187 cause stimulations measuring 186.3±9.7%, n=7 and 152.3±35.0%, n=4 respectively. Fibers injected with a pure inhibitor of cAMP-dependent protein kinase show a reduced response of the Na efflux to subsequent injection of 0.1M-$CaCl_2$ (124.1±9.7%,n=8,P<.001) or to exposure to 100mM-K+(429.0±40.1%, n=11 stimulation vs 834.9±76.3%, n=12, P<.001). External application of 5 x 10^{-4}M iodoacetamide and injection of 4 x 10^{-2}M-bongkrekic acid cause a 75% and a 45% reduction respectively in the response to subsequent depolarization (P<.001 for both). These findings suggest that the response to high K+ is at least partly coupled to a metabolic process.

RESPIRATORY ACIDOSIS IN CONSCIOUS SHEEP BREATHING 100% O_2 AT 1 ATA. S. Matalon and L.E. Farhi, Department of Physiology, State University of New York at Buffalo, Buffalo, N.Y. 14214.

To establish the chronology of cardiopulmonary changes that follow exposure to 100% O_2 at 1 atmosphere, we measured minute ventilation, end-tidal, arterial, and mixed venous gas tensions, arterial blood pH, cardiac output, heart rate, right and left atrial, and aortic and pulmonary arterial pressures in eight conscious sheep. Mean survival time was 90 hours. During the first 50 hours, all variables remained at control level, except for the expected rise in O_2 pressures. After 50 hours, there was a gradual increase in all CO_2 tensions, terminal arterial P_{CO_2} reaching as high as 200 torr, with no change in $(a-A)DCO_2$. Pa_{O_2} decreased but remained above 200 torr. Heart rate climbed, but all other circulatory variables and blood buffer base were maintained throughout. Thus, in our preparation, death was due neither to circulatory failure nor to hypoxemia, but occurred as a result of severe respiratory acidosis.

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VASOPRESSIN AND VASCULAR RESISTANCE IN DOC-SALT HYPERTENSIVE RATS. Hideyo Matsuguchi* and Phillip G. Schmid. C.V. Center and Dept. of Int. Med., Univ. of Iowa, Iowa City, Iowa 52240

Why do rats treated with desoxycorticosterone (DOC) and salt (S) develop hypertension? Is there a selective increase in vascular responsiveness to arginine vasopressin (AVP)? Is there an alteration in CNS regulation? Blood pressure (BP) responses to intravenous AVP, norepinephrine (NE), and angiotensin II (AII) were increased to a similar extent in 9 conscious DOC-S rats compared to 8 control (C) rats (by factors of 2.5, 1.8, and 3.6, respectively). BP responses to intracerebroventricular injections of AII were potentiated by a factor of 12 to 28, somewhat more than the potentiation of intravenous drugs. Increases in perfusion pressure (PP) in the hindquarters of 8 anesthetized DOC-S rats (vs 8 C rats) were augmented significantly and to a similar extent for AVP, NE, and AII. The dose of AVP required to produce a 50 mmHg increase in PP in C rats was 4 times that in DOC-S rats when the sympathetic innervation to the hindlimb was intact and 2.2 times that in DOC-S rats after lumbar sympathetomy. These results suggest DOC-S hypertension associated with 1) general increases in vascular reactivity, 2) more pronounced increases in responses to central as contrasted with peripheral stimuli and 3) possible facilitation of the vasoconstrictor influence of AVP in innervated vasculature. Thus, central mechanisms as well as general increases in peripheral vascular reactivity contribute to DOC-S hypertension.

ASSESSING THE RELIABILITTY OF RAT HEATSTROKE MORTALITY PREDICTIONS USING THE MAHALANOBIS D^2 STATISTIC W.T. Matthew* and R.W. Hubbard, US Army Research Institute of Environmental Medicine, Natick, MA 01760

We previously reported that the incidence of rat heatstroke mortality can be predicted from dose-response curves of the severity of body heating. Hyperthermia was assessed by either the T core maximum or the calculated hyperthermic exposure measured as an area in degree-minutes above a baseline core temperature of 40.4C. Prior to using this model to quantitate the effectiveness of treatment, it is necessary to further test the reliability of these predications. For this test, we used data from a prior report. A trial group of 82 fasted rats of approximately 500 g was selected. This group was heated to max core temperatures which ranged from 41.0 to 43.3°C. Total thermal area above baseline ranged from 7.5° min to 97.4° min. A third variable, a combined index, was calculated as the average of the lethal dose sustained according to previously published max T core and thermal area curves. These values ranged from 0.5 to 99. 60 animals survived and 20 animals died within 24 hrs. The reliability of each of the three variables in predicting mortality was evaluated by computing the Mahalanobis D^2 and the probability of correct classification was estimated by the area under the standard normal probability curve to the left of (D/2). The reliabilities of max T core, total area, and the combined index as predictors of mortality were found to be 0.75, 0.75, and 0.80, respectively. Thus, based on the Mahalanobis D^2 statistic, the use of the combined index enhanced the probability of a correct prediction of mortality.

EFFECT OF UREA ON ANGIOTENSIN II (A-II) AND BLOOD PRESSURE (BP). H. Page Mauck, Karl C. Corley Jr., James C. M. Chan.* Medical College of Virginia, Richmond, Virginia 23298

To test the hypothesis that urea enhances the vasoconstriction effect of A-II, experiments were carried out in 10 anesthetized cats, weighing 2.5 - 5 kg. Five of these animals were studied after receiving ibuprofen 30 mg/kg i.p. for two days or indomethacin 5 mg/kg i.v. at the time of the studies. Continuous BP was measured with a pressure transducer connected by a transfemoral cannula to the aorta. After the intra-arterial BP was stable, 5 minute infusions of A-II at a rate of 0.5 ml/min, alternating with 5 min infusions of D_5W were given at successive A-II dosage of 0.06, 0.12, 0.25, 0.5, 0.75, 1.25, 2.50, and 5.0 mcg/ml until an amount was reached which resulted in a sustained elevation of diastolic BP by 20 mm Hg above the averaged control values. This amount was the pressor dose of A-II. To achieve a blood urea concentration of 100±10 mg/dl, urea (40%) was then used as the vehicle in place of the D_5W. The studies were repeated to determine the pressor dose of A-II. The pressor dose of A-II was 0.15±0.19 mcg/kg/min with urea and 0.75±0.33 mcg/kg/min with D_5W. The effect of A-II was therefore, magnified seven-fold in the presence of urea ($p<0.02$). The use of PGE-inhibitors obliterated this difference. The data strongly suggest that this effect is mediated through prostaglandins, and obliterated with PGE-inhibitors.

LUNG FUNCTION OF RATS ANESTHETIZED WITH HALOTHANE OR PENTOBARBITAL AND BREATHING OXYGEN OR AIR. J. L. Mauderly and S. A. Likens*. Inhalation Toxicology Research Institute, Albuquerque, NM 87115.

The lung function of Fischer-344 rats was measured using halothane (HAL) or pentobarbital (PEN) during O_2 or air breathing by plethysmography. Measurements included spontaneous respiration, lung volumes, quasistatic compliance, forced expirograms and CO diffusing capacity. Data for HAL and PEN and for O_2 and air were compared. The average variability of the data was similar for all treatments. PEN gave larger values for tidal volume, functional residual capacity (FRC) and residual volume and a more convex flow-volume curve. HAL gave higher peak flows, better control of anesthetic depth, rapid induction and recovery, less airway secretion and more rapidly induced and longer lasting apnea. Air breathing gave larger values for respiratory frequency, tidal and minute volumes, FRC and diffusing capacity. Breathing O_2 gave a longer forced expiratory time and a greater safety margin for anesthetic depth. Anesthesia with HAL is preferable for routine, serial lung function tests. The small number of significant differences among the treatments suggests that data collected by any of the anesthetic-gas combinations studied are generally comparable, but that the few differences found should be considered. Five weekly measurements of 4 rats gave a mean coefficient of variation within individuals of 13% for 17 functional parameters. (Research performed under U.S. DOE Contract EY-76-C-04-1013.)

LACK OF "ACID REVERSAL" OF MYOFIBRILAR ADENOSINE TRIPHOSPHATASE IN MASTICATORY MUSCLE FIBERS OF RHESUS MONKEYS. L.C. Maxwell, D.S. Carlson* and C.E. Brangwyn*, Departments of Physiology and Anatomy, The University of Michigan, Ann Arbor, Michigan, 48109.

Myofibrillar adenosine triphosphatase (ATPase) activity was demonstrated in sections of masseter and temporalis muscles and selected limb muscles of rhesus monkeys. Incubations were performed with no pretreatment or after prior incubation in alkaline media (pH 10.2-10.4) or acidic media (pH 3.8-4.3). Without pretreatment, fibers having high or low ATPase activity were observed in limb and masticatory muscles. Following alkaline preincubation, the difference between high and low ATPase of limb muscle fibers is accentuated, whereas preincubation in acidic media (pH 4.3) results in inhibition of high and potentiation of low ATPase activities ("acid reversal"). While preincubation of masticatory muscle sections at pH 10.2 accentuates differences in ATPase activity, preincubation at pH 10.4 abolishes ATPase activity. Following acidic preincubation (pH 4.3), masticatory muscle fibers showed no reversal of ATPase activity. Preincubation at pH 3.8 abolished the ATPase activity of both limb and masticatory muscle fibers. The chemical basis for differences in ATPase histochemistry between masticatory and limb muscles is not known. (This research was supported by grants DE04227, DE05232 and contract DE52478 from the National Institutes of Health.

THE EFFECT OF NONIDEALITY UPON DIFFUSION KINETICS IN A FINITE TWO COMPARTMENT SYSTEM. M.E. May* and W.W. Fish* (SPON: J.G. Ondo). Depts. of Medicine and Biochemistry, Medical Univ. of South Carolina, Charleston, S. C. 29403

The purpose of this study was to ascertain the effect of diffusant nonideality, i.e., variation of the diffusion coefficient with concentration, upon the kinetics of mass diffusion from a finite compartment A to a finite compartment B through fixed channels. The fraction of the equilibrium amount of solute in B at any time t is given by

$$F = \frac{1-\exp(-\beta P t)}{1-\lambda\exp(-\beta P t)},$$

where λ and β depend on the diffusion coefficient and volumes of A and B while P is the total effective channel area/length. Simulations showed that diffusant nonideality results in concave plots of $\ln(1-F)$ vs t at large t but apparently linear semilog plots at small t ($F < .9$). However, interpretation of semilog plots of a nonideal diffusant in terms of an ideal solute significantly altered the "derived" values of P. The degree of error in P is enhanced at high ratios of volume A:volume B. We suggest that diffusant nonideality (e.g., for glucose, sucrose, urea) is an important consideration in the evaluation of experimental permeation data. (Supported in part by a NSF Predoctoral Fellowship and NIH Research Fellowship AM06015 to M.E.M.)

ONTOGENETIC ANALYSES OF ISOMETRIC CONTRACTILE PROPERTIES OF ALD AND PLD MUSCLES OF NORMAL AND DYSTROPHIC CHICKENS. Jacob Mazliah* and Ethel Cosmos, McMaster University, Hamilton, Ontario, Canada L8S 4J9

In vivo analyses of mechanical properties of the latissimus dorsi of dystrophic(D)birds (Storrs Line) from 15 to 600 days ex ovo support histochemical evidence that the slow tonic anterior(ALD)is spared dystrophic phenotypes whereas the fast twitch posterior(PLD)is the target for disease expression and they form the basis for similar analyses of the D-PLD cross-reinnervated by the nerve of the D-ALD(Cosmos et al.,1979, N.Y.Acad.Sci.,317:571). Physiological parameters of the D-ALD are not significantly different from those of the normal(N) ALD. In contrast, analyses of the PLD of N(n=40) and D(n=70)birds stress an inability of the D-PLD to develop both twitch(TwT)and tetanic tensions(TT)following indirect stimulation equivalent to those attained by the N-PLD. By 180 days, TwT/mw = 257±70(N)and 88±40(D); TT/mw(50Hz)=559±147(N)and 385±127(D). Twitch/tetanus ratio of the D-PLD is approximately one half that of the N-PLD. Although contraction and relaxation times are not different from those of the N-PLD, the rate of rise is reduced. In spite of structural and histochemical alterations, the ability of the D-PLD muscle to retain contraction times equivalent to the N-PLD supports its ability to respond to neuronal influences associated with contraction times. Grant support: MDA,MDAC (E.C.); predoctoral MDAC (J.M.).

EFFECTS OF TRANSPULMONARY AND VASCULAR PRESSURES ON THE SIZE OF THE PORES OF KOHN. R.W. Mazzone and S. Kornblau*. Dept. of Med., Univ. of Calif., San Diego, La Jolla, CA 92093.

The resistance to collateral ventilation can be influenced by lung volume. Since the pores of Kohn are possible pathways for collateral ventilation, we investigated the influence of transpulmonary (P_{tp}) and vascular pressures on the size of the pores. Isolated in situ dog lungs were perfused under Zone 2 or Zone 3 conditions then rapidly frozen following deflation to P_{tp} of either 5, 15 or 25 cmH_2O. Samples were freeze substituted and examined by transmission electron microscopy. From each sample of lung at least 5 pores were randomly selected and the minimum diameter visible on the cut section was measured. A total of 900 pores were examined. For Zone 2 and Zone 3 conditions increasing P_{tp} caused an increase in the size of the pores. No significant relationship was found between vascular pressures and the size of the pores over a range of capillary pressures from 0 to 40 cmH_2O. The mean minimum pore size for Zone 2 was 1.73, 2.11 and 2.79 µm and for Zone 3 was 1.2, 1.87 and 2.59 µm for P_{tp} of 5, 15 and 25 cmH_2O respectively. The increase in size with increasing P_{tp} suggests that the alveolar wall behaves as an elastic structure in which increasing stress is generated as lung volume is increased. Because of numerous collagen fibers present at the periphery of the pore, increases in vascular pressure cause the capillaries to bulge into the alveolar space rather than encroach upon the lumen of the pore. Hence vascular pressures do not significantly influence pore size. Supported by HL 17731 and HL 21943.

EFFECT OF PULMONARY HEMODYNAMICS ON EXTRAVASCULAR LUNG THERMAL VOLUME (Ve). D.R. McCaffree*, R.C. Allison*, E.D. Sivak*, H.T. McCurdy* and B.A. Gray. V.A. Medical Center and Dept. of Medicine, Univ. of Oklahoma, Okla. City, Okla. 73104

Using right (RA) and left (LA) atrial injections of 0°C green dye solution, pulmonary blood volume (PBV) and lung thermal volume (LTV) were calculated from aortic dye and thermal dilution curves in anesthetized, closed chest, dogs. Ve was calculated as the difference between LTV and PBV. Balloon inflations in the LA (LABI) or inferior vena cava (IVCBI) produced 15-30% decreases in cardiac output (CO) accompanied by 7-22 cm H_2O increases (LABI) or 4-10 cm H_2O decreases (IVCBI) in pulmonary artery pressure (Ppa). Nitroprusside (N) was used to produce similar decreases in Ppa without decreasing CO. Blood transfusion plus N was used to produce 35-70% increases in CO at constant Ppa. With increases in Ppa, providing LA pressure (Pla) did not exceed 35 cmH_2O, there were equal increases in LTV and PBV and no change in Ve. When Pla exceeded 35 cmH_2O there were increases in Ve which persisted after return of Ppa and Pla to control. With changes in CO at constant Ppa there were no changes in Ve. In 5/12 dogs with decreases in Ppa there were transient 10-50% decreases in Ve. We conclude that Ve, measured by the double injection method, is independent of hemodynamic changes excpt when derecruitment results in lung regions with no perfusion, or there is an actual increase in lung water. (Supported by the Veterans Administration and by USPHS NIH grants HL 7155 and HL 7210.)

EFFECT OF PULMONARY RECEPTOR STIMULATION ON LARYNGEAL AIRWAY RESISTANCE. Thomas V. McCaffrey and Eugene B. Kern.* Dept. of Otolaryngology, Mayo Clinic, Rochester, MN 55901.

The response of laryngeal airway resistance to pulmonary receptor stimulation was studied in 20 mongrel dogs anesthetized with alpha-chloralose (80 mg/kg). Stimulation of pulmonary stretch receptors by lung inflation to a pressure of 30 cm. H_2O inhibited the phasic reduction of laryngeal resistance during inspiration while producing a tonic reduction of laryngeal resistance which was related to lung inflation pressure. Stimulation of pulmonary J-receptors with capsaicin (10 mcg/kg) produced apnea and a marked increase in laryngeal resistance to 150 ± 30 SEM percent of control resistance. Capsaicin was effective in stimulating J-receptors only when injected into the pulmonary circulation and not when injected into the systemic circulation via the left ventricle. The effect of irritant receptor stimulation with histamine (10 mcg/kg I.V.) was tachypnea and a reduction in inspiratory laryngeal resistance to 59 ± 10 SEM percent of control resistance. Pulmonary receptor reflexes were abolished by sectioning the vagus nerves bilaterally below the origin of the recurrent laryngeal nerves. The action of pulmonary reflexes on the laryngeal airway may be important in the regulation of respiration by altering airway resistance on a breath to breath basis.

ASYMMETRY OF THE RESPONSE TO EXOGENOUS AMINES IN THE RABBIT EAR ARTERY. Thomas A. McCalden* and John A. Bevan, Department of Pharmacology, UCLA, Los Angeles, CA 90024.

Segments of rabbit ear artery were prepared in vitro with the adventitial (ADV) surface outwards or with the vessel everted to expose the intimal (INT). Norepinephrine (NE) and 5-hydroxytryptamine (5HT) were cumulatively added to the segments. With ADV NE the ED_{50} was 3.6± 1.3X10^{-7}M. The INT NE was more effective with an ED_{50} of 6.0± 1.1X10^{-8}M ($p<0.0005$). 5HT via the INT or ADV caused a biphasic response. The first part of the response occurred between 10^{-9} and 10^{-6}M. Above 10^{-6}M a further response due to alpha adrenoreceptor stimulation was found. With the adrenoreceptors blocked ADV 5HT showed an ED_{50} of 3.5± 1.4X10^{-7}M while INT 5HT was lower at 5.2± 1.3X10^{-8}M ($p<0.05$). The NE but not the 5HT difference was abolished by pretreating the arteries with desmethylimipramine (DMI) and deoxycorticosterone (DOC). However, both before and after this blockade of uptake mechanisms, the intimal stimulii produced faster initial responses than identical adventitial stimulii. The tension developed in 15 seconds with INT NE was 1.1± 0.13g (78.4% of plateau contraction at 3 minutes). ADV NE was slower at 0.29± 0.13g (32.9% of plateau). Similar differences for 5HT were observed (INT 0.48± 0.08g, ADV 0.15± 0.04g). These INT/ADV differences were not abolished by DMI and DOC. In contrast high potassium contractions were not significantly different with the two directions of application. These results suggest the presence of faster amine receptors at the intimal/medial border.

CCK SUPPRESSES FEEDING ELICITED BY NOREPINEPHRINE MICROINJECTION IN THE HYPOTHALAMUS OF THE RAT. M. L. McCaleb and R. D. Myers. Departments of Psychiatry and Pharmacology, University of North Carolina School of Medicine, Chapel Hill, N.C. 27514.

The gut hormone, cholecystokinin (CCK), is implicated in the mechanism underlying the cessation of feeding. Since direct application of norepinephrine (NE) to the hypothalamus evokes feeding, we determined whether CCK would alter catecholamine induced feeding. Seven rats given ground food ad lib were adapted to a regimen in which palatable wet mash was offered for 1.5 hr; during this interval 25% of the total daily food intake was recorded. Then a 23 ga stainless steel cannula was implanted stereotaxically in the rostral hypothalamus. At 30 min in the wet mash interval, 2.5 µg of NE was microinjected in a volume of 0.75 µl into this structure to elicit feeding. When either 0.5 or 1.0 µg/kg of CCK was injected intraperitoneally immediately prior to an intrahypothalamic injection of NE, the NE-induced feeding was suppressed significantly. A slight but significant enhancement of the NE-dependent component of water drinking was also noted. When either 75 or 150 ng CCK was microinjected directly into the NE sensitive site, food intake was either suppressed totally or virtually unaffected following NE injection. Thus, CCK may well act either directly or indirectly on the hypothalamic catecholamine system related to feeding. (Supported by NSF Grant BMS 75-18441).

DYNAMIC PROPERTIES OF MAMMALIAN SKELETAL MUSCLE: VARIATION WITH AGE. Roger McCarter, B. P. Yu and E. J. Masoro, University of Texas Health Science Center, San Antonio, Texas 78284.

Mechanical properties of the fast lateral omohyoideus muscle of rats were measured in vitro at 21°C. Muscles were obtained from rats (fed ad libitum) of 6, 12, 18, 24 and 27 months of age. Dynamic properties were measured using standard methods and sarcomere spacings were monitored by optical diffractometry. Indices of mechanical state such as contraction and relaxation times, maximum velocity of shortening, series compliance and maximum force per unit area exhibited little variation with age, even for muscles from extremely old rats. These results were correlated with histochemical and morphological examination of the same muscles. More than 80% of the fibers of muscles from rats of all ages were of type 2B. Major ultrastructural disarray of contractile filaments was obvious only for muscles from 27 month old rats. Fiber diameter decreased with age but fiber number increased, so that muscle mass remained relatively constant. The results indicate no major decline in performance of these muscles with advanced age. (Supported by NIH Grant RO1-AG00166 and by the Medical Research Service, V.A. Hospital, San Antonio, Texas)

CARDIOVASCULAR RESPONSES OF THE CHRONICALLY INSTRUMENTED MONKEY DURING SIMULATED SPACE FLIGHT. E.P. McCutcheon, E. Carlson, R.C.Mains*, N. Pace, D.F. Rahlmann*, and H. Sandler. Biomed. Res. Div., NASA, Ames Res. Ctr., Moffett Field, CA 94035, and Env. Phys. Lab., Univ. Cal., Berkeley, CA 94720.

To examine the feasibility of performing nonhuman primate space experiments, a test was conducted jointly by Ames Res. Ctr. and Johnson Space Ctr. Two adult male monkeys (Macaca nemestrina) were implanted with a telemetry unit for aortic (AP) and left ventricular pressures, ECG, and body temp. Pre-test preparation required intermittent monitoring of each animal, one for 4 mos and the other for 3 mos. For the simulated flight the animals were enclosed in a pod system (EPL, UC Berkeley), and monitored continuously, one for 9 and the other for 8 days. A graded lower body negative pressure (LBNP) stress test was performed daily on each animal. High quality data were obtained consistently throughout this demanding test sequence. In both animals, LBNP was well tolerated and the responses consistent. The LBNP responses also confirmed that the animal's condition was satisfactory and stable. The data also showed, in both cases, diurnal variations in heart rate (HR) (hourly mean ranges, HR 144 to 188 BPM, AP 84 to 114 mmHg). The results indicated that a confined, instrumented monkey is a feasible model for space experimentation, confirmed the value of ground control experiments simulating the flight environment, and showed the need for acquiring data for extended periods both before and after flight.

CORONARY EXTRAVASCULAR COMPRESSION IN TACHYCARDIA BEFORE AND AFTER CORONARY ARTERY OCCLUSION. Mary Ann McDonnell*, William J. Bugni*, Alexandros C. Kralios*, Theofilos J. Tsagaris and Hiroshi Kuida. University of Utah and VA Medical Centers, Salt Lake City, Utah 84132 and 84148

The mechanism of increase in coronary blood flow (CBF) after cessation of tachycardia is unclear. Sixteen dogs with controlled external workload were studied while continuously monitoring CBF index (I), coronary sinus O_2 content ($CcsO_2$) and myocardial O_2 consumption index ($M\dot{V}O_2I$). Seven of the dogs were also studied after occlusion (CAO) of the mid left anterior descending coronary branch. Heart rate (HR) was set at 120/min and then gradually increased to 240-300/min until left atrial pressure attained 12 mm Hg. $M\dot{V}O_2I$ increased by 3.81 ± 0.56 ml $O_2 \cdot min \cdot 100g^{-1}LV$ ($p<0.001$), CBFI increased by 22.1 ± 4.7 $ml/min \cdot 100g^{-1}LV$ ($p<0.001$) and $CcsO_2$ decreased from 7.76 ± 0.72 to 6.42 ± 0.53 vol% ($p<0.01$). Abrupt return of HR to 120/min resulted in further increase of CBFI by 55.3 ± 9.7 $ml/min \cdot 100g^{-1}LV$ ($p<0.001$), i.e. 48% above that attained during tachycardia although $M\dot{V}O_2I$ decreased by 2.65 ± 0.75 ml $O_2/min \cdot 100g^{-1}LV$ ($p<0.01$). Results obtained after CAO were similar. Since $CcsO_2$ remained above 5.5 vol% during tachycardia, the additional transient increase in CBFI in excess of $M\dot{V}O_2I$ requirements immediately after cessation of tachycardia is probably not the result of myocardial hypoxia. It may reflect removal of coronary extravascular compression, compensated by arteriolar vasodilatation during tachycardia.

INTESTINAL CAPILLARY WALL AS A CHARGE-SELECTIVE FILTER. P. M. McElearney* and D. N. Granger. Department of Physiology, Univ. of South Alabama, Mobile, AL 36688.

The lymph to plasma ratio (L/P) of lactate dehydrogenase isoenzymes (LD1-LD5) were used to study the charge selective properties of the intestinal capillary wall. The LDH isoenzymes exhibit the same molecular size yet have isoelectric points (pI) varying between 5.2 and 8.8. At control steady state lymph flows the L/P of endogenous LDH isoenzymes decreased as pI increased. The capillary osmotic reflection coefficient (σ_d) of each isoenzyme was estimated using 1 - L/P at lymph flows where L/P is filtration independent. Lymph flow was increased by stepwise elevation in intestinal venous pressure. In general, σ_d values increased as pI increased (σ_d = .70 when pI = 5.2, σ_d = .96 when pI = 8.8). These findings suggest the existance of a functionally significant electrostatic interaction between circulating charged molecules and cationic components of the intestinal capillary wall. Supported by HL 22569.

VENTILATION AND O_2 TRANSPORT IN RESTING AND ACTIVE CRAYFISH PROCAMBARUS CLARKI, ACCLIMATED TO COOL TEMPERATURE (10°). B.R. McMahon & C.D. Hassall*. Dept. Biology, U. of Calgary, Calgary, Alberta, Canada. T2N 1N4.

Ventilatory (scaphognathite, f_{sc}) and heart (f_H) pumping frequencies, % O_2 extraction from branchial water ($\%Extr_w$), pre- & postbranchial O_2 tensions, O_2 contents, and pH, were measured before & after 30 min enforced activity. Mean $\%Extr_w$ of quiescent animals was 42 but ventilation volume (V_w, calculated from f_{sc} and sc.stroke vol) and hence O_2 uptake (MO_2) were low (38ml. and 3.3 μ mol. Kg^{-1} mm^{-1}) at 10°. At extant pH (8.10) P_{50} was low (3-4 torr), hemocyanin (Hcy) of both pre- and postbranchial hemolymph was O_2 saturated, and dissolved O_2 accounted for most tissue oxygenation. During exercise f_{sc} and thus V_w rapidly increased 6-fold, $\%Extr_w$ decreased (to 23%) but nonetheless M_{O_2} increased 4 fold. 1 min after exercise V_b had increased 8 fold, postbranchial O_2 tension decreased slightly, and prebranchial O_2 tensions decreased markedly allowing substantial participation of Hcy bound O_2 in tissue oxygenation. pH falls markedly (to 7.55) allowing displacement of Hcy bound O_2 due to the Bohr effect ($\log P_{50} = -0.74$ pH). Just after activity the acidosis is mostly respiratory but a small metabolic component (partially lactic acid) occurs. 1h after, P_{CO_2} has decreased markedly but a slight acidosis remains. Restoration of hemolymph lactate and O_2 levels, MO_2 $\%Extr_w$ and V_w take 24-48 h. Increased Na^+ & Cl^- efflux accompanies increased V_w initially but rapid compensation prevents significant fall in hemolymph levels.

DEVELOPMENT AND RETENTION OF CONDITIONED TASTE AVERSION LEARNING IN RATS OF DIFFERENT AGES. M. Colleen McNamara and Ralph L. Cooper.* Center for the Study of Aging and Human Development, Duke University Medical Center, Durham, N.C. 27710

In our experiments we examined the influence of age on conditioned taste aversion (CTA) tasks. Male rats 3,6,10, and 19 months of age were conditioned to avoid a 0.1% saccharin solution by 3 sequential saccharin-amphetamine pairings. There was no difference in the rate at which this CTA response was acquired among the different age groups. However a significant age difference was observed in the retention of the CTA. Further studies indicate that peripheral factors (i.e., taste, illness following AMPH) are intact, whereas changes in the central nervous system and/or pituitary may contribute to the are-related decrements. (Supported in part by NIA Training Grant #AG00029 and Research Grant # AG0056)

CELL PROLIFERATION AT THE HUMAN TOOTH SURFACE.GROWTH PATTERNS AND CHARACTERISTICS. Herman Medak*, Charles E. Joseph* and Anwar A. Hakim. College of Dentistry. Univ. of Ill. Med. Center. Chicago. Illinois 60680.

Factors that influence cell-cell and cell-substratum interactions contribute to connective tissue proliferation and wound-healing. Human gingival fragments were explanted in culture bottles containing Eagle's minimal essential(MEM) supplemented with 20% fetal calf serum(FCS), 1 IU/ml insulin 50 u/ml penicillin and 50 ug/ml streptomycin. After 24h of incubation the explants became attached to the surface of the culture bottles. Enzyme treatment of the explants was deleated to maintain cell surface integrity, but caused several days delay in cellular release. Primary outgrowth occurred within 15 days of culture, and consisted primarily of epithelial-like cells. Once proliferation started, growth progressed to form cell monolayers. Growth was associated with the mitotic activity of migrating cells. Several weeks later fibroblast-like cells appeared on the outer limits of the outgrowth and migrated away from the explant and the epithelial outgrowth. When extracted human teeth(EHT) were carefully placed on a cell free but adjacent location to the monolayer outgrowth, cellular proliferation progressed to certain areas of the ETH-surface.The cells in contact with EHT appeared to elongate and join at their ends to form a cell cover. Cellular-spread-out, then continued in rays of elongated cells perpendicular to the initial cell layer. Cell-free areas on EHT were surrounded by cell-free zones.

SUPPRESSION OF FEEDING IN THE MONKEY BY INTRAVENOUS OR CEREBROVENTRICULAR INFUSION OF WOODCHUCK HIBERNATION TRIGGER. R.B. Meeker*, R. D. Myers, M.L. McCaleb, W.D. Ruwe, University of North Carolina, Chapel Hill and P.R. Oeltgen, V.A. Medical Center and University of Kentucky, Lexington.

An albumin fraction isolated from hibernating woodchuck serum by affinity gel chromatography on an Affi-Gel blue matrix was infused in a volume of 300-400 µl (1 mg/100 µl) into the cerebral ventricle of three macaque monkeys. Intake of food declined immediately and did not return to baseline for 48 hrs. Mean daily food intake fell 68%, from 162 g baseline to 52 g 24 hrs after infusion. Both total number and size of daily meals were reduced. A similar intraventricular infusion of an albumin fraction collected from non-hibernating woodchucks reduced food intake by 32%, but CSF control infusions had no effect. Intravenous infusion of 10 mg/2 ml of hibernation trigger into two macaques reduced food intake similarly, whereas the albumin fraction from non-hibernating woodchucks and bovine serum albumin were without effect. Thus, plasma from hibernating woodchucks apparently contains a constitutent which suppresses long-term food intake in the primate without notable side effects. The characterization of this substance may uncover a naturally occurring anorectic peptide with long-term biological potency.

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The Effects of Acute Hyponatremia on CSF and Brain Ions, Acid-Base Balance, and the Control of Breathing. J. Melton*, E.E. Nattie, M. Bergin*, and J. Daley*. Department of Physiology, Dartmouth Medical School, Hanover, NH 03755.

In acute hyponatremia (↓Na), the brain tissue response (K^+ loss) is known while the CSF response is incompletely characterized. We evaluated CSF in ↓Na and also asked whether the ionic changes altered CNS acid-base balance and/or the control of breathing. Isosmotic hyponatremia was produced in rats by ip injection of 5.5% glucose, 10 ml/100 g BW. Acid-base and electrolyte values were measured in blood, CSF and brain. $\dot{V}_E$ at rest and in response to 6.7% CO_2 was evaluated by whole body plethysmography. After 4 h, osmolality was decreased slightly in both plasma and CSF (9-12 mOsm) while mean plasma [Na^+] decreased from 141 to 125 mEq/l. In brain tissue (cortex and brainstem) the chloride space decreased 7-10%, cell space increased 2-4%, and cell K^+ decreased 5-6%. Mean changes in plasma and CSF values were:

	Na^+	K^+	Cl^-	HCO_3^-	PCO_2	pH
plasma	-16	NC	-18	-5.7	-6.9	NC
CSF	-11	NC	-13	+2.4	+3.9	NC

The decrease in CSF [Na^+] and [Cl^-] reflected 70% of the plasma change and CSF [HCO_3^-] increased while plasma HCO_3^- decreased. This ↑[HCO_3^-] could be due to the changes in CSF ions or PCO_2. In ↓Na at rest $\dot{V}_E$ was increased (+22%, P=.2) and $PaCO_2$ decreased (-17%, P=.06) while with CO_2 stimulation, $\dot{V}_E$ was increased (+40%, P<.007). The cause of this tendency for excitation of ventilation is unclear. (supported by HL 18351, RCDA 00364).

IN VITRO STUDIES OF DEPLETION, REPLETION, AND RELEASE OF PROLACTIN WITHIN THE LACTATING RAT PITUITARY. F. Mena, G. Forray*, G. Martinez-Escalera*, C. Clapp* and C.E. Grosvenor. Instituto de Investigaciones Biomedicas U.N.A.M. and Div. of Biol. and Health Sci., Unidad Ixtapalapa, U.A.M. Mexico City, Mexico

Fifteen min suckling caused a 35% depletion in electrophoretically detectable prolactin (Prl) from anterior pituitaries (AP) of lactating rats previously non-suckled for 8 h. AP tissue from these rats then was incubated at 37°C in 0.3 ml medium 199 in a metabolic shaker (125 rpm) in an atmosphere of 95% O_2-5% CO_2 for 30-240 min. The APs of suckled rats displayed an initial rapid repletion during the first 30 min of incubation, then a rapid (within 30 min) 55% depletion followed by an additional 15% depletion over the next 180 min. The APs of non-suckled rats placed in vitro underwent a 40% depletion of Prl within the first 30 min, followed by a 45% repletion during the next 30 min. A second depletion then occurred over the next 180 min (30% during the 30th-60th min and an additional 60% during the last 120 min). Prl was released into the medium during the first 90 min of incubation in proportionately greater amounts during "repletion" than "depletion" stages in all APs. The total Prl secreted into the medium in 240 min, however, was 30% less than that depleted in APs of non-suckled rats, but 40% more than that depleted in APs of suckled rats.

SEASONAL VARIABILITY IN THE RESISTANCE OF THE DOMESTIC FOWL, Gallus domesticus, TO EXPERIMENTAL ENDOTOXEMIA. G.F. Merrill and M. Rosolowsky*, Dept. of Physiol., Rutgers University, New Brunswick, N.J. 08903.

Several investigators have reported that the tolerance of experimental animals to stress and trauma is influenced by the season of the year. The objective of the current study was to determine if the resistance of the domestic fowl, Gallus domesticus, to experimental endotoxemia varies seasonally. Thirty-eight male white Leghorns (2.4±0.6kg) were divided into four treatment groups: fall (Oct), winter (Jan), spring (Apr), and summer (Jul). Each group was challenged with an i.v. bolus of E. coli endotoxin (2.5 mg/kg). Selected metabolic and hemodynamic variables were monitored for 24 hours. Only 4 of 11 fall birds survived (LD69), all winter (N=9) birds survived (LD0), and 2 each of the spring and summer birds survived (LD22).

Seasonal differences in arterial plasma glucose are given below:

	minutes postchallenge				
	C	120	480	1440	a = significantly less than values in other seasons.
Winter	247±14	260±17	286±15	228±17	
Spring	225±17	217±18	270±17	184± 9	
Summer	217±13	245±21	258±20	215±19	
Fall	151±6[a]	153±12[a]	159±10[a]	143±7[a]	

Circulating corticosterone increased less than 3-fold and greater than 10-fold in the fall and winter groups respectively. Supported by the NJAES and HATCH grant #763.

FAILURE OF HIGH DOSES OF SAR^1-ILE^8-ANGIOTENSIN II TO ABOLISH AUTOREGULATION OF RENAL BLOOD FLOW (RBF). J. Messick*, F. G. Knox and Wm. S. Spielman, Mayo Clinic and Foundation, Rochester, MN 55901

Recent work has demonstrated that angiotensin II antagonists (AIIA) inhibit the tubuloglomerular feedback mechanism. Studies in this laboratory indicate that the infusion of high doses of AIIA is capable of inhibiting renal vasoconstriction purported to be mediated by intrarenal angiotensin II (AII). To determine if intrarenal AII is a mediator of RBF autoregulation, we investigated the effects of intrarenal infusion of sar^1-ile^8-AII (50 µ g/kg per min) on autoregulation of RBF in seven renin-depleted dogs. Because prostaglandins may modulate RBF, AII antagonism was studied in the presence of prostaglandin blockade. Pressure-flow curves were obtained during the control period, following prostaglandin blockade (meclofenamate, 10 mg/kg, i.v.) and during intrarenal infusion of AIIA. The lower limit of autoregulation was determined from the inflection point of the pressure-flow curves and the slopes of the linear portions of the curves above the inflection points calculated by regression analysis. No significant differences were observed in the slopes during control, prostaglandin blockade, or AIIA infusion. Thus, intrarenal infusion of high doses of AIIA did not abolish RBF autoregulation in these renin-depleted, prostaglandin blocked dogs, militating against a major role for intrarenal AII and tubuloglomerular feedback in RBF autoregulation. (Supported by HL 14133).

ACETYLCHOLINE INFUSION RESULTS IN BLOOD FLOW TO LOW VENTILATION-PERFUSION AREAS IN DOGS. John F. Metcalf, Jose R. De Olazabal,* Michael J. Miller, and John C. Mithoefer. Medical University of South Carolina, Charleston, South Carolina 29403

The effect of infusion of acetylcholine (AcCh) on gas exchange was studied in a group of normal dogs. Airway pressure, pulmonary artery pressure and cardiac output were measured and the distribution of blood flow and ventilation versus ventilation-perfusion ratio ($\dot{V}_A/\dot{Q}$) was derived using the multiple inert gas infusion technique. At infusion rates between .1 mgm/minute and .5 mgm/minute, two types of response were observed. The commonest response (80% of dogs) consisted of the development of increased blood flow to an area of low ventilation-perfusion ratio. In this group of dogs, there was usually a small amount of blood flow to the low $\dot{V}_A/\dot{Q}$ area prior to infusion. The increase in blood flow to the low $\dot{V}_A/\dot{Q}$ area was usually associated with an increase in cardiac output but was not consistantly associated with a change in airway pressure or pulmonary artery pressure. In 20% of dogs the response showed no change in the blood flow distribution during the infusion of AcCh. In summary, the majority of dogs developed blood flow to a mode of low $\dot{V}_A/\dot{Q}$ (mean of approximately .1) in response to the infusion of a low dose of AcCh. The amount of increased blood flow in this low $\dot{V}_A/\dot{Q}$ mode correlates best with the increase in cardiac output. (Supported by USPHS, NIH Grant HL 22932-01.)

FETAL HEART RATE IS AFFECTED BY MATERNAL METHADONE ADDICTION. James Metcalfe, Marilyn Paul*, George Olsen.* Univ. Oregon Health Sciences Center, Portland, OR 97201.

End-tidal P_{CO_2} is significantly higher in pregnant methadone maintenance subjects than in normal pregnant women; their offspring weigh less than controls and have a high morbidity. Studies were performed between 30 and 41 weeks of pregnancy on 32 normal women and 4 women receiving daily oral doses of methadone (16-40 mg/day). Fetal heart rate (FHR) was recorded with an ultrasonic (Doppler) detector (Corometrics FM 111B). FHR, obtained continuously for 6 minutes of maternal rest and then for a 10-minute recovery period following 6 minutes of mild (50 Watt) bicycle ergometer exercise, was averaged for each minute. Mean FHR was 146 beats/minute when normal women were sitting at rest and 138 in methadone subjects, a significant difference ($p<0.001$). FHR was slower at 2 hours after the daily methadone dose than at 26 hours, but the difference is only significant in the 6th and 7th minutes following exercise. We have previously found slower than normal heart rates in young puppies subjected to uterine ischemia during gestation and in young guinea pigs exposed daily in utero to intermittent hyperthermia. (Supported in part by USPHS NIH Grant HD 10034 and the Oregon Heart Association).

REFRACTORY PERIOD OF THE HUMAN ESOPHAGUS, GW Meyer*, DC Gerhardt* and DO Castell, USU, Bethesda, MD.

In order to determine if there is a refractory period for peristalsis of the esophageal body, we studied five healthy subjects aged 29-43 using a multilumen motility catheter and a low compliance pneumohydraulic infusion system. The catheter was placed with its openings 2, 7, 12 and 17 cm above the lower esophageal sphincter (LES). Ten wet swallows were performed at each of 5, 10, 15, 20 and 30 second intervals with water boluses of 5, 10 and 15 ml. There was frequent absence of peristaltic response at the five second interval throughout the esophagus with all bolus sizes. In addition peristaltic amplitudes failed to achieve levels attained with longer time intervals. Mean amplitudes ± SE at each level using the 5 ml bolus are shown vs. the time interval between swallows.

SECS	17cm	12cm	7cm	2cm
5	30.6±4.5*	23.4±3.2*	13.8±4.5*	8.1±5.0*
10	34.4±9.2***	44.1±5.6*	44.9±7.3*	38.7±8.0*
15	42.9±13.5	56.3±9.8	55.4±11.2**	56.4±11.3
20	46.2±13.7	63.5±11.9	67.9±10.6	62.5±9.4
30	50.2±12.8	60.8±11.4	67.4±13.6	66.5±6.7

*P<0.001, **P<0.02, ***P<0.01

These data indicate the presence of a refractory period in the body of the esophagus at the 5 second time interval with recovery to normal by the 20 second interval, most evident in the distal esophagus. There was no significant difference between data acquired using 5, 10, or 15 cc boluses.

COMPARISON OF OVERALL AND REGIONAL LUNG MECHANICAL FUNCTION IN DOGS UPON OZONE EXPOSURE. P. Meyer*. Lawrence Livermore Lab., Livermore, CA 94550 and M. Morgan*, R. Holub* and R. Frank. School of Public Health and Community Medicine, University of Washington, Seattle, WA 98195.

Standard mechanical function tests were compared with radioactive nitrogen ($^{13}N_2$) ventilation measurements obtained with an Anger positron camera. Conventional tests measured flow resistance, dynamic compliance and multiple-breath nitrogen wash-out while the radioisotope technique determined regional and overall gas wash=in. Each dog was measured twice before and twice during the three-hour ozone exposure. Dogs were grouped according to ozone concentrations: 0.12, 0.22, and 0.45 ppmv. The animals were anesthetized and mechanically ventilated. With the positron camera and radioactive nitrogen we observed changes in the local distribution of ventilation following acute exposure to ozone. Inspired gas was delivered to the more central regions of the lungs, at the expense of peripheral areas, on exposure. The change occurred at all concentrations and its magnitude was concentration-dependent. Conventional tests of overall lung function were unaffected. We interpret these findings as evidence of slight changes in the calibre of peripheral airways. The relationship of this acute functional response to the long-term health of the lungs is uncertain.

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BRADYKININ INCREASES PULMONARY LYMPH FLOW IN ANESTHETIZED DOGS PRIMARILY BY INCREASING MICROVASCULAR PRESSURE. John Michael,* Hideaki Sakio,* Willie McFarland,* & Sami I. Said. VA Med. Ctr. & U. TX Hlth. Sc. Ctr., Dallas, TX 75216.

Bradykinin has been proposed as a mediator of increased vascular permeability in systemic & pulmonary microvessels. We investigated the effect of bradykinin infusions (5 µg/kg. min^{-1} for 2 hrs) on pulmonary vascular permeability & hemodynamics in 5 anesthetized dogs, as measured by changes in flow & protein concentration of right lymph duct (pulmonary) lymph. The thoracic duct was ligated above the diaphragm to eliminate collateral systemic lymph flow. We measured lymph flow ($\dot{Q}_L$), lymph & plasma protein concentrations, heart rate (HR), mean pulmonary arterial ($\bar{P}_{PA}$) & aortic pressure ($\bar{P}_{Ao}$) for at least 1 hr before & 2 hrs during bradykinin infusion. During the infusion, $\bar{P}_{Ao}$ decreased (from 146 ± 9 to 124 ± 10 mm Hg, $p<0.05$) & HR increased (from 158 ± 9 to 171 ± 10 beats/min, $p<0.05$). $\bar{P}_{LA}$ did not change, but $\bar{P}_{PA}$ increased (from 15.8 ± 1.4 to 17.4 ± 1.3 mm Hg, $p<0.02$). $\dot{Q}_L$ increased 85% (from 2.0 ± 0.3 to 3.7 ± 0.5 ml/hr, $p<0.02$) while lymph/plasma protein ratios decreased for albumin (from 0.70 ± 0.02 to 0.63 ± 0.03, $p<0.02$) and globulin (from 0.62 ± 0.03 to 0.56 ± 0.04, $p<0.02$). These results suggest that bradykinin: 1) is capable of increasing pulmonary lymph flow in anesthetized dogs, primarily by increasing effective microvascular pressure; & 2) under these experimental conditions, does not exert a potent influence on pulmonary vascular permeability. (Supported by Lung Center Award HL-14187 & Training Grant HL-05812).

THE INDUCTION OF PITUITARY TUMORS BY NEONATAL E_2 TREATMENT IN FEMALE MICE EXHIBITING ACCELERATED AGING OF THE REPRODUCTIVE SYSTEM. S.D. Michael*, O. Taguchi*, K. Yamashita* and Y. Nishizuka* (SPON: D.E. Murrish). Dept. Biol. Sci., SUNY, Binghamton, N.Y. 13901 and Aichi Cancer Center and Nagoya Univ., Chikusa-ku, Nagoya 464, Japan

One of the theories for pituitary tumor formation is the accumulation of PRL-secreting cells. Females of the SL/Ni strain of mouse show accelerated aging of the reproductive system characterized by the disappearance of all oocytes at about 8 months of age. At 12 months of age, PRL-secreting cells in the pituitaries became enlarged and increase in number. It is well known that E_2 injections during the neonatal period can cause irreversible changes in the hypothalamus and pituitary disturbing the normal secretion pattern of the pituitary hormones. The purpose of the present experiment with SL/Ni females was to attempt to further enhance the accumulation of PRL-secreting cells by neonatal E_2 injections and thus induce pituitary tumor formation. Mice were given daily subcutaneous injections of 0.5 µg E_2 from 0 to 4 days of age, killed at 13-14 months of age, then plasma hormones measured, and pituitary histology examined. E_2 injections increased the weight of the pituitary from 3.4±0.4 mg (n=9) to 8.6±0.9 mg (n=16), increased the hyperplasia of PRL-secreting cells resulting in tumor nodules in all animals, and increased circulating levels of PRL. In conclusion, E_2 injections during neonatal life can cause changes in the pituitary which result in the formation of PRL-secreting tumors in later life.

THE EFFECT OF HEMORRHAGIC SHOCK AND REINFUSION ON MICROVASCULAR PERMEABILITY IN DOGS. René P. Michel*, Mario Laforte*, and James C. Hogg. Lyman Duff Lab. McGill Univ., Montreal, P.Q., Canada. H3A 2B4

To elucidate the mechanisms involved in the "shock lung" syndrome, 10 anesthetized dogs were studied: systemic, pulmonary arterial (Ppa) and wedge pressures (Pw), right lymphatic duct (RLD) flows, and plasma and RLD lymph protein concentrations were measured. From the latter, capillary (Πc) and interstitial (Πis) oncotic pressures were calculated. Horseradish peroxidase (HRP) was injected intravenously and its concentration measured in plasma and lymph. One hour after HRP injection, the animals were hemorrhaged to 40-50 mm Hg for 2 h, reinfused and observed for a further 2 h. With shock, Pw and Ppa decreased and did not completely return to normal with reinfusion. The Πc decreased with shock and changed little with reinfusion; Πis remained relatively stable during shock, and fell with reinfusion of the shed blood. The RLD flow increased after 1 h of shock in 8 dogs and albumin and globulin lymph/plasma ratios increased during shock and reinfusion ($P<.05$). Pore radius (calculated with the Landis & Pappenheimer equation from HRP data) increased with reinfusion ($P<.05$) while pore number increased with both shock and reinfusion in 8 dogs. A small but significant increase in lung wet/dry weight ratios was observed compared to controls. We conclude that shock and reinfusion of the shed blood produces subtle alterations in microvascular permeability. (Supported by MRC of Canada Grant #MA-6474.)

GLOMERULAR PERMSELECTIVITY AND DYNAMICS IN DIABETES MELLITUS. L. Michels, W.F. Keane* and M. Davidman*, Univ. of Minn., Mpls., Mn. 55455.

Micropuncture measurements and fractional clearances of ^{3}H-neutral dextran (DN) and ^{3}H-anionic dextran sulfate (DA) were performed in male Sprague-Dawley rats, 4-6 weeks after induction of alloxan diabetes (D) and compared to age-matched sham animals (S). Plasma glucose levels were 138±5 mg/dl in S and 458±30 in D ($p<0.001$). Urinary albumin excretion (UAE) as measured by radial immunodiffusion was increased in D (0.35±0.02 mg/day/gKw) as compared to S (0.10±0.02, $p<0.05$), but total protein excretion was unchanged (D=12.2±1.2; S=9.7±1.2 mg/day/gKw). Fractional clearances of DN (C_{DN}/C_{IN}) and DA (C_{DA}/C_{IN}) were not significantly different between S and D over the range of molecular radii studied, 20-46A. Results mean ± SE: ($^{\dagger}p<0.01$):

	GFR (ml/min/gKw)	RPF	SNGFR (nl/min/gKw)	SNPF
S(N=11)	1.21±0.07	4.22±0.36	33.1±1.7	115±9
D(N=16)	1.08±0.07	3.11±0.19†	29.2±1.3	84±4†

Total arteriolar resistance increases by 28% (D=5.27±0.38 vs S=4.12±0.36x10^{10} dyne.S/cm^5, $p<0.05$) thereby decreasing single nephron plasma flow (SNPF) and renal plasma flow (RPF). Glomerular capillary pressure was also reduced (D=46.3±1.1 vs S=54.1±1.0 mmHg $p<0.01$). GFR and SNGFR are decreased slightly during this early diabetic period. The primary pathophysiologic alteration is an increase in arteriolar resistance with no detectable change in glomerular permeability, although a subtle change in UAE occurs.

25-HYDROXYCHOLECALCIFEROL (25-OH-CC) METABOLISM IN HEALING CHOLECALCIFEROL DEFICIENT CHICKS. R.J. Midgett*,M.Fintell.* LSU Med. Ctr. (SPON. R.A. Russell)

The measurement of 25-OH-CC metabolites in the blood of normal animals or humans is primarily limited to 1,25-and 24,25-dihydroxycholecalciferol (1,25-$(OH)_2$-CC, 24,25-$(OH)_2$-CC) as determined by binding assays. Here we report the serum metabolites found in chicks given 25-OH-[26,27-^{3}H]-CC for one week. Four week old white rock chicks fed a CC deficient diet were then given daily an oral supplement of either 1 nm or 5 nm 25-OH-CC. On the eighth day of this regimen the chicks were sacrificed. Lipid extracts of the serums were chromatographed on a precolumn of sephadex LH-20 then on a Tracor HPLC with a partisil 10 column eluted with hexane: *i*-propanol;90:10(v/v). The eluent fractions were dried and radioactivity determined. The results (see the table) show three metabolites of 25-OH-CC produced at both dose levels. In accordance with the current understanding of CC metabolism, 1,25-$(OH)_2$-CC serum level is relatively depressed and the level of 24,25-$(OH)_2$-CC relatively elevated in animals given 5 nm 25-OH-CC/day. The concentration of the third metabolite appears related only to the substrate concentration. (Supported in part by a Fred B. & Ruth B. Zigler Foundation grant from the American Heart Assoc. and General Research Support Grant #449-89-5146).

Dose	Metabolite [PMoles/ML (± S.D.)]			
	25-OH-CC	24,25-$(OH)_2$-CC	(25,26-$(OH)_2$-CC)	1,25-OH_2-CC
5 nmole	75.20(±20.1)	9.21(±1.16)	7.12(±0.87)	1.82(±0.29)
1 nmole	22.10(±8.15)	1.38(±0.44)	1.93(±0.72)	0.90(±0.24)

DISTINCTION AMONG ACTIVE TRANSPORT MODELS USING DYNAMIC SIMULATION. D.C. Mikulecky and B. Bunow*, Dept. of Physiology, Med. Col. of Va., Richmond, VA 23298 and Lab. of Applied Studies, DCRT-NIH, Bethesda, Md. 20014.

Question: Where does metabolic energy enter into the active transport cycle? Loosely speaking, there are four possibilities: 1) binding of the ligand, 2) transport of the bound ligand, 3) release of the ligand, and 4) return of the unloaded carrier. Recently, we have shown that neither net flux nor unidirectional flux experiments can distinguish among these biochemically distinct models without unjustified approximations (Bunow, 1979). Now we address distinguishing among them from observations of their internal dynamics in response to rapid perturbations (analogous to T-jump experiments). We suppose spectroscopic methods can be devised permitting simultaneous, dynamic measurement of the carrier populations in each of four distinguishable states. Starting from a steady state, each of the models is perturbed by changing the state distribution of the carrier. The relaxation can then be simulated using the circuit simulator SPICE2 Biophys. J. 25:87 (1979). In contrast to the usual T-jump analysis, which is restricted to a linearization about the steady state, our simulation is equally applicable to larger perturbations, since we solve the full non-linear dynamical equations for each model. We aim to determine the possibility of distinction among the four active transport models by the qualitative characteristics of their dynamic response.

THE INFLUENCE OF CARDIAC OUTPUT ON GAS EXCHANGE IN PATIENTS WITH COPD. Michael J. Miller,* William R. Cook,* and John C. Mithoefer. Medical University of South Carolina, Charleston, S.C. 29401

The effects of an increased cardiac output and associated alterations in mixed venous gas tensions on arterial gas tensions were studied in 5 patients with COPD. Ventricular afterload reduction with 75 mg. p.o. hydralazine increased cardiac output (mean 4.1 vs 5.7 L/min), mixed venous PO_2 (mean 33 vs 38 mm Hg), and arterial PO_2 (mean 60 vs 65 mm Hg) in every patient. Mixed venous PCO_2 fell (mean 59 vs 49 mm Hg), as did arterial PCO_2 (mean 53 vs 45 mm Hg). Calculated venous admixture in the lung (mean 19%), $\dot{V}O_2$, and $\dot{V}CO_2$ were unchanged. $\dot{V}_E$ increased (mean increase 0.52 L/min) despite a rise in arterial pH (mean 7.40 vs 7.44). The rise in $\dot{V}_E$, even if assumed to represent a rise in $\dot{V}_A$, was not sufficient to account for the observed alterations in arterial PO_2 and PCO_2. These findings support the hypothesis that changes in arterial PO_2 and PCO_2 can arise from changes in mixed venous blood gases, acting through ventilated alveoli, in the absence of variation in pulmonary venous admixture. Supported by a VA research grant.

EFFECT OF 16, 16 DIMETHYL PROSTAGLANDIN E_2 ON CANINE GASTRIC MUCOSAL BLOOD FLOW. Thomas A. Miller*, Julia M. Henagan* and André Robert. Univ. of Texas Medical School, Houston, TX 77030 and Upjohn Company, Kalamazoo, MI 49001

The effect of 16, 16 dimethyl PGE_2 (PGE_2) on mucosal blood flow (MBF) in the secreting (S) and nonsecreting (NS) canine Heidenhain pouch was assessed using ^{14}C aminopyrine clearance as an estimate of flow. After a 1 hr basal period, PGE_2 (2,10, and 50 µg/kg) was administered as an oral bolus and its effect on MBF in the NS pouch determined over the next 2 hrs. For studies on MBF in the S pouch, histamine dihydrochloride (HD) (1 mg/hr) was infused I.V. for 3 hrs. PGE_2 studies were identical except that 1 hr after commencing the HD infusion, PGE_2 (50 µg/kg) was given orally as a bolus. PGE_2 had no effect on MBF in the NS pouch with any dose employed. HD alone evoked a significant ($p<0.0005$) increase from basal in gastric acid secretion, volume output and MBF which remained constant for the duration of the experiment. In contrast, PGE_2 significantly decreased ($p<0.005$) HD-stimulated gastric acid production (1.4± 0.2 to 0.3± 0.1 mEq/15min), volume output (9.5± 1.4 to 2.1± 1.1 ml/15min) and MBF (22.6± 3.9 to 4.9± 2.4 ml/min) without altering the ratio (R) of MBF to volume rate of secretion. The observation that R was unchanged from HD control after administration of PGE_2 suggests that the reduction in MBF seen with PGE_2 was the result rather than the cause of the observed decrease in gastric secretion. Under the conditions of these studies, it is concluded that PGE_2 has no direct effects on MBF in the S or N canine stomach.

STIMULATION OF RESPIRATION BY AN ENDOGENOUS CENTRAL SEROTONINERGIC MECHANISM. D. E. Millhorn*, F. L. Eldridge and T. G. Waldrop*. (Spon: J. Perlmutt) Univ. of North Carolina, Chapel Hill, NC 27514

We reported (Fed. Proc. 38:1229, 1979) a brain stem mechanism, activated by carotid body and carotid sinus nerve(CSN) stimulation, which causes respiratory output(RO) to be increased for at least several hours after the immediate effects(the direct response and the respiratory afterdischarge) of the stimulation have dissipated. Since methysergide blocked this mechanism, we suggested that serotonin might be responsible. In the present study the central monoaminergic systems were examined in more detail. Paralyzed, vagotomized cats with cut CSN's were studied. $P_{ET}CO_2$ and temp were servo-controlled. RO was quantified from peak integrated phrenic activity. RO was facilitated by CSN stimulation. Three differently acting serotonin antagonists (methysergide, 1 mg/kg IV 40-60 min before; parachlorophenylalanine, 240 mg/kg i.p., on each of 2-3 days before; and 5'7-dihydroxytryptamine, 1 mg into the third ventricle 5 days before the experiment) were tested; all prevented the long-lasting increase in RO following CSN stimulation. A dopamine-norepinephrine antagonist (α-methyltyrosine, 75 mg/kg i.p., on each of 2 days before) did not prevent the increase in RO. We conclude that the long-lasting increase in RO following carotid body and CSN stimulation is caused by the activation of a central serotoninergic mechanism which facilitates respiration. (Supported by USPHS Grants HL-17689, NS-11132 and Pulm. Tr. Grant HL-07106)

RESPONSES OF PLASMA PROLACTIN TO ALTERATIONS IN AMBIENT TEMPERATURE AND HUMIDITY IN MAN. D. Mills* and D. Robertshaw. Med. Sci. Prog., Indiana Univ., Bloomington, In. 47401.

Following the positioning of skin and auditory meatal thermocouples, the insertion of a cannula in an antecubital vein, and a 1 h equilibration period, 6 men sat in an environmental room from 0900 to 1230 on 4 occasions. On each occasion a 1 h control period at 27°C dry bulb (db)/16°C wet bulb (wb) was followed by a 1.5 h experimental period at either 27°Cdb/16°Cwb, 13°Cdb/9°Cwb, 45°Cdb/26°Cwb, or 27°Cdb/26°Cwb, and a 1 h recovery period at 27°Cdb/16°Cwb. Blood and urine samples were taken every 30 min., and 100 ml tap water given every 15 min. to prevent dehydration. Plasma prolactin levels rose 53% ($p<.05$) in the heat, and fell 35% ($p<.05$) in the cold as compared to controls. No significant changes were observed during conditions of increased relative humidity alone. The plasma prolactin changes were associated with an increased mean skin temperature of 3.0°C in the heat and a decrease of 4.3°C in the cold. Corresponding changes in auditory meatal temperatures were +1.0°C, and -0.2°C, respectively. Temperatures during high relative humidity were not significantly different from controls. Plasma osmolality, serum Na^+ and K^+ levels did not change except in the cold, where there was an increase in serum K^+ from 3.8 mEq/L to 4.4 mEq/L ($p<.01$). These experiments suggest a direct relationship between ambient temperature and plasma prolactin levels in man which are not associated with changes in water and electrolyte status.

EFFECT OF PEEP IN CANINE LOBAR PNEUMONIA. S. Mink,*B. Light* and L.D.H. Wood.* (Spon: Victor Chernick). Sec. of Resp. Dis., University of Manitoba, Winnipeg, Canada.

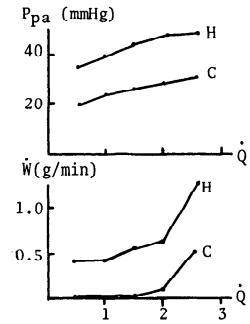
We studied 6 supine, ventilated dogs 48 hours after an inoculum of streptococcus pneumoniae was placed into a left lower lobe (LLL) bronchus. Measurements of pulmonary shunt (Qs/Qt), arterial pO2, and hemodynamics were made before (C_1), after (C_2), and during (P) 12 cm H_2O positive end-expiratory pressure (Peep). The dogs were volume loaded to maintain the lower lobes in zone III conditions and to keep cardiac output (CO) constant. Changes in perfusion (Q) to the right lower lobe (RLL) and LLL expressed as a percent CO were determined by radionuclide microspheres. The mean (±SD) results were:

	C_1	P	C_2
Q_{RLL}	33.3 ± 4.9	29.7 ± 4.6	30.3 ± 2.5
Q_{LLL}	18.5 ± 5.3	36.4 ± 4.1*	22.3 ± 1.2
Qs/Qt	25.5 ± 2.6	24.7 ± 4.0	33.8 ± 7.9

Compared to the normal Q_{RLL}, Q_{LLL} was reduced in conditions C_1 and C_2. Peep doubled the perfusion to the pneumonia lobe ($P<.05$)* but did not change the large Qs/Qt. We conclude that Peep increased Q_{LLL} either by improving ventilation to the LLL and thereby reducing hypoxic vasoconstriction, or by mechanically decreasing the vascular resistance in the pus filled lobe allowing perfusion to increase. The expected increase in Qs/Qt in the latter instance would be offset by a reduction in Qs/Qt in the non-pneumonic lung. (Supported by MRC of Canada and the Canadian Lung Association).

HYPOXIC CONSTRICTION AND FLUID FILTRATION IN PIG LUNGS. W. Mitzner, J. Sylvester, and R. Frank*. The Johns Hopkins Medical Institutions, Baltimore, Md. 21205.

In isolated ventilated blood perfused pig lungs, we measured the slow steady rate of change in weight ($\dot{W}$) as an index of fluid filtration during control (P_{O_2}=200) and hypoxia (P_{O_2}=50 mmHg) at several flow rates between 3 and 0.5 L/min. Lungs were in a zone II state with end-expiratory pressure fixed at 5 and venous pressure less than -15 cmH_2O. Compared with control (C), hypoxia (H) caused nearly parallel shifts in both the pulmonary artery pressure ($\dot{P}_{pa}$) vs. flow ($\dot{Q}$) and and $\dot{W}$ vs. $\dot{Q}$ relationships (see Fig.). This shift in the P_{pa} vs. $\dot{Q}$ curve suggests that hypoxia increased the effective back pressure to blood flow through the lungs. If this increase in back pressure were located at a locus downstream from permeable vessels, it would be consistent with the finding of a nearly constant increase in $\dot{W}$ at all flows. The non-linear shape of the $\dot{W}$ vs. $\dot{Q}$ relationship may be related to recruitment of filtration surface area at the higher flows. (Supported by NIH HL-10342 and 00347.)



STRETCH-INDUCED GROWTH IN CHICKEN WING MUSCLES: A NEW MODEL OF STRETCH HYPERTROPHY. P.A. Molé, R.G. Holly, J.G. Barnett*, C.R. Ashmore*, and R.G. Taylor*. Muscle Laboratory, University of California, Davis, CA 95616.

A new model of stretch-induced growth is evaluated in four chicken wing muscles stretched to different extents by a spring-loaded tubular assembly. Muscles grew in length and cross-section in proportion to the extent to which they were stretched. Longitudinal growth was essentially completed within 1 week while muscles grew in cross-section through at least 5 weeks of stretch. The muscles were neither denervated nor immobilized and muscle activity as measured by EMG was not increased. Oxidative enzyme activities increased substantially with stretch in the patagialis (PAT), a twitch muscle, but were relatively unchanged in the slow-tonic anterior latissimus dorsi (ALD). Stretch altered mitochondrial enzyme proportions in the PAT but had little effect in the ALD. Capillary density was unchanged with stretch in the PAT but decreased in the ALD. Capillary/fiber ratio, however, increased in both muscles. We conclude that muscles grow and adapt enzymatically due to stretch but that these responses are dissimilar in twitch and tonic muscles. (Supported in part by NIH #PHSY 5T01 GM01934-07 and AFOSR 78-3510A).

STIMULATION OF PEPSIN SECRETION (PS) IN THE DOG BY VARIOUS HISTAMINE (H) ANALOGS. E. Molina, B. I. Hirschowitz, J. Rentz. Gastroenterology, University of Alabama Medical Center and V.A. Medical Center, Birmingham, AL 35294.

Ten H analogs with different relative H-1 and H2 agonist activities were tested in stepwise 45min doses in 4 or 5 dogs drawn from a group of 6 gastric fistula dogs to define a role for H in PS in the dog. In each the output of pepsin, 525 KU/h, and acid, 24 mEq/h, with bethanechol (B) given in step-doses, 20-160 µg/kg.h, was used as 100% reference. All the H compounds with H2 action were more effective acid stimuli than B but none stimulated pepsin to more than 23% of B response.

	(PS) Dose*	Vm %B	(H^+) Dose	Vm %B		(PS) Dose	Vm %B	(H^+) Dose	Vm %B
Histamine	0.2*	3	0.9*	123	N'(Me)H	0.4*	6	0.8*	113
Betazole	2.3	13	45	103	N'N'(Me)$_2$H	0.7	8	0.7	122
Triazole	4.0	17	4.0	100	4,N'(Me)$_2$H	0.7	8	0.7	124
Dimaprit	0.6	23	0.6	153	4(Me)H	0.1	14	0.8	133
Impromidine	0.002	7	0.02	118	2PE	0.5	0	0.5	0
Bethanechol	0.7	100	0.7	100					

*=Dose, µMol/kg.h for max secretion

A bolus injection of 4(Me)H (100 µg/kg) during an infusion of B (80 µg/kg.h) increased H^+ output by 50% and inhibited PS by 50%. A similar bolus of the H-1 agent 2 Pyridylethylamine (2PE) had no effect on H^+ or PS. Conclusion: Low PS in the dog with H is due to combined H2 stimulation and inhibition. Regardless of structure the net effect is a low H efficacy for PS. (NIH AM09260)

PROSTAGLANDIN SYNTHETASE INHIBITION AS A MEANS OF PREVENTING CARDIOPULMONARY MANIFESTATIONS OF ENDOTOXIC SHOCK IN PONIES. J.H. Moore,* J.E. Shapland,* D. Hatfield,* and H.E. Garner. University of Missouri-Columbia, MO 65211.

Administration of 10 μg/kg of E. coli endotoxin to conscious unmedicated ponies caused acute arterial hypoxemia, pulmonary hypertension, increased pulmonary vascular resistance, decreased cardiac output, and lactic acidosis. In addition, diarrhea, cramping and colic were consistent signs exhibited. Pre-treatment with prostaglandin synthetase inhibitor, flunixin megulumine (1 mg/kg) abolished the cardiopulmonary sequelae of sublethal dosages of E. coli endotoxin. Outward signs of discomfort and diarrhea were also prevented. Cardiac output and arterial oxygen tension were consistently increased in animals pretreated with the prostaglandin synthetase inhibitor while pulmonary arterial resistance did not change significantly. Curiously, a decline in circulating white blood cells was measured in both the treated and untreated groups. These findings support a prostaglandin mediated mechanism for pulmonary vasoconstriction and hypoxemia following intravenous administration of E. coli endotoxin to conscious ponies.

A NEW RAT MODEL SIMULATING SOME ASPECTS OF SPACEFLIGHT. Emily R. Morey,* Eric E. Sabelman,* Russell T. Turner,* and David J. Baylink.* NASA-Ames Research Center, Moffett Field, CA 94035 and American Lake VA Medical Center, Tacoma, WA 98493.

A model system has been developed in which rats are suspended in an head-down mode but are free to move about a 360° arc on a plastic grid using their front paws while the rear limbs are totally unloaded but unrestrained. Suspended rats lose weight the first 2-4 days on the harness, then they begin to gain. Pair-fed controls gain about 20% more weight than suspended rats and weight-matched controls require about 20% less food than suspended animals to maintain parallel body weights. Similar results were noted during spaceflights of like duration, i.e., Cosmos 782 and Cosmos 936. The tibial bone formation rate decreased significantly, 44% or 37%, in suspended rats as compared to pair-fed or weight-matched controls, respectively. Within 10 days after release from the harness, bone formation rate returned to normal. Rats aboard Cosmos 782 or 936 showed similar changes in bone formation. Bone growth arrest lines were noted in suspended rats, but they were neither as distinct nor as extensive as those found in flight rats; the suspended rats did not appear to cease forming bone as indicated by tetracycline labeling. These results suggest that suspended rats gain weight similarly to flight rats and that unloading contributes to the decreased bone formation during flight but does not explain the cessation of bone formation noted during flight.

THE INFLUENCE OF THE THORAX ON TRAPPED GAS IN LUNGS. J.J. Morgan* and D.G. Frazer* (SPON: K.C. Weber). ALOSH, NIOSH, CDC, DHEW, and Dept. of Physiology and Biophysics, WVU, Morgantown, West Virginia 26506.

The intact lung and thorax were removed from rats (N=6) and ventilated in an air-filled plethysmograph. Five different pressure-volume (PL-VL) curves were recorded for every lung-thorax at a rate of 7.65cc/min. Each curve consisted of 4 cycles in which the minimum pressure PL(min) for cycles 1, 2, and 3 was either +7, +1, -2, -5, or -12cm H_2O. On the 4th cycle lungs were deflated to -12cm H_2O, where the volume of gas trapped in the lung, Vm, was measured and normalized with respect to maximum lung volume, VL(max). Based on the assumption that airways must close (menisci form in airways) during lung deflation for gas to be trapped in the lung, the relationship between Vm/VL(max) and PL(min) suggested that airway closure in a lung-thorax follows a normal distribution having a mean of -1.27cm H_2O and a S.D. of 2.25cm H_2O. This can be compared with a mean of +2.21cm H_2O and S.D. of 0.83 cm H_2O for a normal excised lung (Resp. Physiol, 36:121-129, 1979). The differences between the means of the two distributions reflect the negative intrapleural pressure generated in the intact lung-thorax at low lung volumes, while the difference in the S.D.'s likely results from the increased interdependence exhibited by the lung inside the thorax and/or a transpulmonary pressure gradient from the apex to base of the lung in the thorax. (Supported in part by DOE contract No. EY-77-C-21-8087).

BAROREFLEX STIMULATION OF RENAL NERVES AND THE EFFECT OF SALT DIET ON URINARY CATECHOLAMINE EXCRETION N.Morgunov* and A.D.Baines. University of Toronto, Toronto, Canada.

Rats with chronically denervated (DNX) left kidneys were placed on normal diet (ND), low salt diet (LS) or ND supplemented with 1% saline plus DOCA (1m) (HS-DOCA). Urinary excretion of dopamine (DA) and norepinephrine (NE) (ng/min/mlGFR) from the innervated (INX) and (DNX) kidneys was expressed as the difference between carotid ligation and control periods. Catecholamine excretion from the DNX kidney reflected systemic release (Sys) while INX-DNX renal nerve release (Ren).

	ND	LS	HS-DOCA
NE Sys	0.41±0.12 **	0.13±0.08 NS	0.20±0.06 *
Ren	0.17±0.03 **	0.13±0.05 *	-0.02±0.02 NS
DA Sys	0.07±0.03 *	-0.08±0.04 NS	-0.01±0.02 NS
Ren	0.34±0.07 **	0.17±0.05 *	-0.04±0.04 NS
	* p <0.05	** p <0.01	(n=7)

Baroreflex stimulation of renal nerves increased the systemic and renal release of NE but DA release was primarily from renal nerves. LS reduced the systemic release of NE without affecting the renal release, but significantly reduced ($p < 0.05$) the renal release of DA. HS-DOCA abolished the renal release of both NE and DA. In conclusion, renal nerves release both NE and DA. This release is regulated by salt diet and mineralocortecoid.

POTASSIUM AND FLUID SPACES OF CANINE CORTICAL BONE. M. A. Morris,* J. B. Day,* J. B. Bassingthwaighte, K.-N. An* and P. J. Kelly. Mayo Clinic and Mayo Foundation, Rochester, MN 55901 and University of Washington, Seattle, WA 98195

In cortical bone, lacunar and vascular volumes were measured by morphologic methods in Paragon-stained undemineralized bone sections. Potassium and fluid spaces were measured by the volume of distribution (V_D) technique. Under steady-state conditions, V_D = cpm tracer in 1 ml bone/cpm tracer in 1 ml plasma.

No.	Methods	Space	Results (ml/ml of bone ± SD)
6	Morphology	Haversian	0.015 ± 0.006
6	Morphology	Lacunar	0.015 ± 0.004
5	^{111}Indium	Plasma	0.008 ± 0.002
15	[^{99m}Tc]Rbc	Red blood cell	0.005 ± 0.002
9	[^{14}C]Sucrose	Extracellular	0.043 ± 0.010
4	[^{14}C]Inulin	Extracellular	0.042 ± 0.010
4	^{3}H	Total water	0.250 ± 0.030
10	^{42}K	Potassium, V_{DK}	1.270 ± 0.140

Assuming cell K^+ concentration of 150 meq/liter, hydration shell water of 0.16 ml/ml bone, and cell volume adjusted for canaliculi (0.015 + 0.027) of 0.042 ml/ml, bone cells could contain 150 x 0.042 or 6.3 meq/liter of K^+. Since plasma K^+ is 4.0 meq and V_{DK} is 1.27 ml/ml, cortical bone contains 4.0 x 1.27 or 5.1 meq/liter of rapidly diffusible K^+. Conclusion: Compartmentalization of K^+ in bone cells satisfactorily explains the previously observed K^+ ion gradient between bone and plasma, without postulating a K^+-rich bone fluid.

EFFECT OF GLUCAGON IN ILEAL TRANSCAPILLARY FLUID EXCHANGE. N. A. Mortillaro, P. R. Kvietys*, A. E. Taylor, W. H. Wilborn and D. N. Granger. Departments of Physiology and Anatomy, University of South Alabama, Mobile, AL 36688.

Systemic arterial pressure, superior mesenteric arterial and venous pressures, blood flow, lymph flow, lymphatic protein flux, net transmucosal volume flow, and interstitial volume were monitored from autoperfused loops of cat ileum to determine the effects of locally infused glucagon on intestinal transcapillary and transmucosal fluid exchange. Glucagon infusion caused a significant increase in intestinal blood flow (98%), lymph flow (6 fold), capillary filtration coefficient (38%), capillary pressure (22%), volume, and interstitial fluid pressure (from -2.1 to +4.6 mmHg). Precapillary (Ra) resistance and Ra/Rv decreased during the glucagon infusion. The transcapillary oncotic pressure gradient and the osmotic reflection coefficient were reduced suggesting that capillary permeability is significantly increased with glucagon. Ultrastructural analysis of tissue samples acquired during the infusion of higher doses of glucagon indicate disruption of the mucosal membrane. An alteration in mucosal structure is supported by the appearance of plasma proteins in the secreted fluid. The results of this study indicate that glucagon induced intestinal secretion results from an alteration in capillary fluid balance, i.e., an increased capillary pressure and permeability. Supported by HL 22392 and HL 22569.

BREATHING FREQUENCY AND BODY POSTURE IN NEWBORN DOGS AND RABBITS. Jacopo P. Mortola. Department of Physiology, McGill University, Montreal, Canada H3G 1Y6.

The breathing frequency (f) of anaesthetized newborn puppies and rabbits has been measured in different body postures (supine, prone, lateral, head down, 45° and 90° head up), either by changing the posture of the animal placed in a body plethysmograph or by tilting a board over which the newborn was positioned and f recorded with magnetometers. No differences were observed between postures except in the head up (UP) position; with 90° UP f decreased within the first 10 seconds after the tilting (transient) and was about 50% less than in the horizontal posture 1 minute after the tilting (steady state); with 45° UP f dropped during the transient and in a few cases was low also in steady state conditions. By moving the animal from the head up to the horizontal position a transient increase in f above the control pretilting value was noticed. After vagotomy no changes in f were observed, neither in transient nor in steady state conditions. The effect on f of the 45° UP posture was also tested in unanaesthetized newborns. In a few animals a small (10-20%) significant decrease in f was observed. In conclusion, f of anaesthetized newborns decreases during the head up tilting and remains low in the 90° UP posture as the result of a vagally mediated mechanism. This response is much less evident in unanaesthetized newborns.

(Supported by Canadian MRC).

EFFECTS OF METHYLPREDNISOLONE ON REGIONAL CONTRACTILE FUNCTION AND ULTRASTRUCTURE DURING CORONARY OCCLUSION AND REPERFUSION IN CONSCIOUS DOGS. Kriegh Moulton,* Hurley Myers, Lonnie Russell,* Sam Smith* and Kim Lindsey*. School of Medicine, Southern Ill. Univ., Carbondale, Ill. 62901.

The efficacy of methylprednisolone sodium succinate (MPSS) in protecting myocardial cells from the consequences of reperfusion remains questionable. Accordingly, we conducted a study in which the left anterior descending coronary artery of 9 conscious dogs was occluded for two hours and reperfused for six hours. MPSS (30 mg/kg, iv) or vehicle was given 15 min. before occlusion and again 4 hours later. Left ventricular (LV) hemodynamics (micromanometer) and normal zone and ischemic zone contractile function (ultrasonic segment-length crystals) were monitored throughout the study. Coronary blood flow was measured with radioactive microspheres before occlusion, 10 min after occlusion and at the end of the six hour reperfusion period. Dogs were sacrificed and LV samples were taken for light and electron microscopy. Systolic lengthening, which characterized the motion of the ischemic zone during occlusion, persisted during the six hours of reperfusion in all dogs. Thus, present results indicate that MPSS does not improve contractile function in the conscious dog. We have observed, moreover, that MPSS causes an increase in the incidence of ventricular arrhythmias during reperfusion. (This study was supported in part by the Upjohn Co.).

RELATIONSHIP OF EMG POWER SPECTRUM (PS) WITH LOW AND HIGH FREQUENCY FATIGUE IN HUMAN MUSCLES. J. Moxham*, A. DeTroyer*, G. Farkas*, P. Macklem, R. Edwards*, and C. Roussos.* Meakins Christie Labs., McGill Univ. Clinic, Royal Victoria Hospital, Montreal, Quebec, Univ. College Hosp., England.

Electrical stimulation of a fatigued muscle may result in a decrease in force, T, only at high frequencies (high frequency fatigue, F_h), or only at low frequencies (low frequency fatigue, F_l). Muscle fatigue is also associated with a shift of the EMG PS (ΔPS). In 3 subjects we correlated ΔPS with F_h and F_l by measuring T and PS during voluntary fatiguing, isometric contractions of the quadriceps and adductor pollicis, and T during surface electrical stimulation at 20 and 100 Hz. ΔPS was estimated as the ratio of the amplitudes of high frequency, H, (130-238 Hz) and low frequency, L, (20-40 Hz) components of the EMG. There was no change in H/L during F_l alone. However whenever F_h occurred in the presence of F_l, there was a decrease in H/L. We conclude that low frequency fatigue does not result in an EMG power spectral shift, whereas high frequency fatigue does. The inability of the muscle to respond to high frequency stimulation may be responsible, in part, for the change in power spectrum. Supported by the MRC of Canada.

PULMONARY ARTERY PULSATILE FLOW PATTERNS IN CANINE DIROFILARIAL DISEASE. P.V. Moulder, R.A. Brunswick*, B. Flauto*, B. Gallet* and J.A. Alexander*. Veterans Administration Hospital and University of Florida, Gainesville, FL 32610

Pulmonary artery pulsatile flow patterns (F_{PA}) have been compared to standard dynamic and resistance data for evaluation of the vascular obstructive characteristics of the dirofilarial infested dog. The signal from a ring type electromagnetic flow probe (Biotronix) on the main pulmonary artery was low pass filtered at 50 or 25 Hz and displayed on an optical recorder chart at 100 mm/sec. for pattern analysis. Standard right and left heart and vascular pressures were obtained along with indicator dilution cardiac output in 32 anesthetized, open-chest preparations. The severity of the pulmonary arterial involvement with the dirofilaria imitis was judged according to the mass of worms and the presence of intimal disturbance. The F_{PA} was characterized by slope changes, reversal and peaking. In baseline and hyperdynamic state (open large, systemic arteriovenous fistula) only the severely involved animals manifested marked changes in F_{PA} pattern. With obstructions to lobar arteries further correlation occurred; thrombus embolization a further step correlative occurred. No useful sensitivity was manifested. When elevated resistance and a cardiac index of 2 or more liters/min. were combined, the flow pattern changes manifested the closest level of correlation. (Supported by the Medical Research Service of the Veterans Administration)

DOSE-RESPONSE RELATION OF CSF SODIUM AND RENAL SODIUM EXCRETION, AND ITS ABSENCE IN HOMOZYGOUS BRATTLEBORO RATS. **David R. Mouw, Arthur J. Vander, Claudia Landis*, Sandra Kutschinski*, Nancy Mathias* and Deborah Zimmerman*. Dept. of Physiology, U of Mich. Med. Sch. Ann Arbor 48109.**

Constant intraventricular infusion(3.3-6.6 ul/min) of artificial CSF with sodium concentrations of 100, 150, 200, 250, 300, and 350 mM produced a linear dose-related change in renal sodium excretion in conscious, unrestrained Sprague-Dawley rats. The periventricular receptors stimulated were able to evoke substantial changes in body sodium balance; the 350mM Na CSF produced an estimated 14% deficit in the content of Na in the ECF over a five-hr period. This is the first demonstration of such a dose-response relation over a wide range of CSF Na concentration (above and below normal) in conscious animals. Both the dose-response relation, and the magnitude of the effects, suggest an important physiologic role for this control mechanism. The natriuresis in response to 300mM sodium infusion was identical in Long-Evans Brattleboro rats, but was completely absent in homozygous animals. Although the experimental methods (conscious unrestrained rats)precluded simultaneous evaluation of efferent pathways other than ADH, the evidence from the DI rats suggests that ADH may be the efferent pathway for the response. (Supported in part by USPHS NIH Grant 1 R01 NS 12825 and by a grant from the Mich. Kidney Fdn.)

ULNAR ARTERY TENSION DEVELOPMENT BY POTASSIUM DEPOLARIZATION AND DIRECT ELECTRICAL STIMULATION. S. Mras*, J.M. Price and D.L. Davis. Dept. of Physiology, College of Medicine, Univ. of South Florida, Tampa, FL 33612

Dose-response curves from dog ulnar arteries were obtained using norepinephrine (NE) at 10^{-3}-10^{-10} M, potassium depolarization (K) at 5-120 mM, and direct electrical stimulation (DS) at 50-250 ma. Two mm wide rings were mounted in bicarbonate-buffered PSS for recording isometric tension, treated with 6-OHDA, and equilibrated at 3 g resting tension. Stimulus-response curves to K and DS and responses to ED_{50} levels of NE ($3x10^{-6}$ M) were compared in the presence of 10^{-4}-10^{-8} M verapamil (V) or nitroprusside (NP). Responses to NE were decreased in a dose dependent fashion by both V and NP. Decreases were larger and more consistent with V. Responses to K were decreased in a dose dependent fashion by both V and NP. The highest doses of V abolished responses, whereas the highest doses of NP decreased responses by 50-75%. Responses to DS were affected similarly by V and NP with lower concentrations potentiating responses and higher concentrations decreasing responses. Responses to ED_{50} levels of K (45 mM) and DS (150 ma) in Ca-free PSS showed similar time courses of decay. Corresponding curves for NE exhibited 3-fold longer time courses of decay. These results indicate that DS and K produce tension development in vascular smooth muscle by similar but not necessarily identical mechanisms. Supported in part by grants from the American Heart Assoc., Palm Beach County Chapter, and USPHS grant HL-18866.

GENERATION OF PLASMA HEPARIN ACTIVITY DURING EXTRACORPOREAL PERFUSION IN THE DOG. T. Murphy*, F.J. Walker*, F. Taylor III*, S. Sofer*, and L.B. Hinshaw. VA Medical Center and Depts. Medicine & Exptl. Path., Univ. of Oklahoma Health Sci. Ctr., Oklahoma City, OK 73104.

Dogs perfused in our laboratory with an arteriovenous extracorporeal perfusion system without added heparin developed whole blood clotting times (WBCT) greater than 24 hr (Surg. Gynec. Obstet. 148:689, 1979). Further studies to define this coagulation defect have demonstrated the appearance of a plasma inhibitor of thrombin and Factor Xa clotting of bovine plasma. This inhibitor stimulated the inactivation of Factor Xa by antithrombin III (ATIII) but not by o-methylisourea modified ATIII. Thrombin inhibition by ATIII was also stimulated. Six perfused dogs developed an equivalent to 0.98 to 6.15 U/ml of heparin activity determined by inhibition of thrombin-induced clotting of normal canine plasma. This activity was heat stable, adsorbed by $BaSO_4$ and neutralized by protamine. Infusion of protamine sulfate into two perfused dogs reversed the anticoagulant activity and brought the WBCT from greater than 24 hr to less than control. The activity did not develop in saline, citrated whole blood, or non-anticoagulated blood circulated in the perfusion system. We conclude that dogs perfused on our extracorporeal perfusion system without added heparin develop an endogenous heparin activity in their plasma which is a major contributor to their autoanticoagulated state. (Supported by Med. Res. Service of the VA and NIH Grants HL17812 and HL07207.)

REDUCED CORONARY VASOCONSTRICTION WITH BARORECEPTOR UNLOADING IN SEVERELY HYPERTROPHIED RIGHT VENTRICLES OF CONSCIOUS DOGS. P.A. Murray and S.F. Vatner, Dept. of Med., Harvard Med. Sch. and Peter Bent Brigham Hosp., Boston, MA 02115

While severe right ventricular hypertrophy (RVH) is associated with attenuated reflex increases in peripheral vascular resistance in response to carotid sinus hypotension, caotid baroreceptor control of the coronary circulation in the presence of RVH is unknown. Accordingly, 5 normal (N) dogs and 6 dogs with RVH, induced by chronic (4-6 mos) pulmonary artery stenosis, were instrumented with aortic catheters, Doppler ultrasonic flow transducers on the R main coronary artery, pacing electrodes, and hydraulic occluders on both carotid arteries below the carotid sinus. RVH was characterized by an approximate doubling in RV mass and resting R coronary artery blood flow. With heart rate held constant, levels of R coronary vascular resistance (mmHg/ml/min) were measured during control and after 45 seconds of carotid sinus hypotension induced by bilateral carotid occlusion. Despite a significantly lower ($p<0.01$) control level of R coronary resistance in RVH (2.59±.29) than N (5.72±.41), the increase in R coronary resistance during carotid sinus hypotension observed in N (1.10±.11) was sharply reduced in RVH (0.49±.14). Thus, unloading the carotid sinus baroreceptor reflex results in vasoconstriction of the normal R coronary circulation even with beta adrenergic activity intact. This carotid sinus baroreceptor induced coronary vasoconstriction is depressed following the development of RVH.

TEACHING FIRST-YEAR MEDICAL STUDENTS THE PHYSIOLOGICAL BASIS OF CARDIOLOGY IN A COMPETENCY-BASED PROGRAM. Hurley Myers, Roger Robinson,* and Robert Colvin*. Southern Illinois University, School of Medicine, Carbondale, Ill. 62901.

We believe that cardiovascular (CV) problems are solved better when physicians combine skills and knowledge of both basic and clinical science; thus, we introduce our first-year students (Ss) to the CV system using clinical problem units. These units are composed of clinical cases and related basic science learning modules, which contain behavioral objectives, evaluation criteria, learning resources, and study guides. Ss receive all materials in advance of the course. Although Ss are encouraged to use independent study, we have found that strategically scheduled activities, such as introductory or summary lectures, films, help sessions, dog labs, and clinical case discussions, improve learning and encourage student-faculty contact. Learning progress is determined by demonstrated competence and not by grades or time accumulated. If a student has inadequate knowledge of unit material at first evaluation, a new test is scheduled. If, however, there are minor content errors or questions about test organization or expression of thought, Ss meet individually with the instructor. In six years of experience we have found that only 45% of Ss complete each unit evaluation without some form of retesting. In spite of this, course organization, content, and personal satisfaction are highly rated by most Ss (>80%).

CENTRAL β-ADRENERGIC RECEPTOR SENSITIVITY IN CONSCIOUS SPONTANEOUSLY HYPERTENSIVE RATS. Hurley Myers, Sam Durr,* Mark Smith* and Ronald Browning*. Southern Illinois University, School of Medicine, Carbondale, Ill. 62901

Several studies report that brainstem catecholamine turnover in spontaneously hypertensive rats (SHR) is lower than that of Wistar-Kyoto (WKY) controls. This condition could cause enhanced central adrenergic receptor sensitivity in the SHR. To test this possibility, we measured heart rate (HR) and blood pressure (BP) in 20 SH and 23 WKY rats after central β-adrenergic receptor stimulation. Three doses of isoproterenol (ISO) were used (1μg, 5μg and 10μg in 10μl). Each dose was given intracerebroventricularly (icv) to conscious rats while femoral arterial BP and HR were recorded for 60 min. In both groups, the 5 and 10μg doses of ISO caused a decrease in BP and an increase in HR, which was significant ($p<.05$) by 30 sec and maximum between 5 and 10 min after injection. These changes were attributed to direct cardiac and vascular β-receptor stimulation since they were not prevented by ganglionic blockade with hexamethonium (25mg/kg, iv). The 1μg dose of ISO did not lower BP, but did increase HR significantly ($p<.05$) by 30 sec. This early increase in HR was centrally mediated, however, since it could be blocked by hexamethonium or icv propranolol (10μg in 10μl). These findings suggest that central β-receptor sensitivity to ISO is not different in SH and WKY rats and that ISO, when given centrally in a dose that does not leak rapidly into the peripheral circulation, increases HR, but does not affect BP.

FLUID SHIFTS AND THE MOBILIZATION OF PLASMA FREE FATTY ACIDS OBSERVED IN MIDDLE-AGED MEN AND WOMEN MARATHON RUNNERS. Loren G. Myhre, Sarah A. Nunneley, and G. H. Hartung*. USAF School of Aerospace Medicine, Brooks AFB TX 78235.

Hematological responses of 6 male and 5 female runners were studied during a marathon in cool weather (T_a 14.4° to 17.8°C) at sea level. Ages ranged from 45 to 58 yrs and from 32 to 50 yrs for the men and women, respectively. Venous blood samples were obtained at 0, 4, 17, and 26.2 miles. Mean values for finish time, fluid intake, wt loss, and Δ plasma volume were: 3.58 hrs, 1120 ml, 2.26 kg (-3.2%), and -5.5% for the men; 4.17 hrs, 1195 ml, 1.63 kg (-2.9%), and -6.5% for the women. Initial and final values for plasma glucose averaged 111 and 106 mg/dl; corresponding values for plasma free fatty acids (FFA) were 69 and 321 μg/ml. Intermediate blood samples indicated that (1) the reduction in plasma volume was complete at 4 miles remaining relatively constant thereafter in spite of progressive wt loss, and (2) plasma glucose showed a marked initial rise followed by progressive decreases which were accompanied by corresponding increases in FFA. These results support previous work indicating that, during prolonged moderate exercise in a cool environment, plasma volume may be maintained with fluid intake which replaces less than half the water lost by sweating. It appears that circulating FFA provide an abundant source of energy, thus sparing blood glucose during prolonged exercise in trained distance runners.

LOAD CARRYING AT SELF-PACED WORK RATES. W.S. Myles* (SPON: R.J. Shephard)
DCIEM, Downsview, Ontario, M3M 3B9

Nine male subjects walked on a treadmill with back pack loads equal to 10% and 40% of their body weight. Although the treadmill speed was selected so that measured oxygen consumption was the same for both load conditions, the heavier load was perceived by all subjects as harder work than the lighter load. When the subjects worked at their own pace, walking on a level road or climbing stairs with load weights equal to 10% and 40% of body weight, they compensated for the heavier load by decreasing walking speed and climbing rate. Although the energy costs estimated for self-paced walking and stair climbing were the same for both load conditions, subjects perceived the heavier load as harder work. In these experiments perceived exertion was not a significant cue determining voluntary work rates.

Rheogenic Na transport in frog skin. Wolfram Nagel Dept.Physiol.Univ.Munich, Germany

Intracellular potentials of frog skin were measured under conditions of zero transcellular current flow (mucosal Amiloride or Na-free solution). The potential difference across the basolateral membrane was found to be hyperpolarized by 20 mV above steady state potentials of 93 mV. The hyperpolarization disappeared within 15-25 min. Hyperpolarization was absent in the presence of Ouabain. Magnitude and/or duration of hyperpolarization correlate directly with the amount of Na accumulated in the intracellular space during preceeding periods of Na uptake from the mucosal side. A fraction of the intracellular potential is missing during Na transport after disappearance of the hyperpolarization but reappears within 10-20 min. The data demonstrate existance of rheogenic Na transport across the basolateral membrane of the frog skin at normal rates of transepithelial transport (not experimentally elevated intracellular Na content). The transport dependent electrical potential accounts for 30-50 % of the intracellular potential during transepithelial Na transport. Na-K exchange through the pump pathway at rate of 2:1 is suggested from estimates of the rheogenic pump current and comparison with the short circuit current. (Supported by DFG)

CSF and Brain Ions in Acute Hypercapnia. E.E. Nattie (SPON. D. Bartlett, Jr.) Department of Physiology, Dartmouth Medical School, Hanover, NH 03755.

The dramatic response of CSF and brain tissue total CO_2 (TCO_2) to acute hypercapnia is well described. In both sites the increase in TCO_2 is rapidly in excess of the existing buffer characteristics. The corresponding ionic changes in the CNS have been less thoroughly studied. To evaluate these, rats were exposed to 11% CO_2 or air for 20 min. or 3 hrs. Blood, CSF, and brain tissue Na^+, K^+, Cl^-, and TCO_2 were measured in each animal. Brain TCO_2 was evaluated by in vitro CO_2 titration, electrolytes after acid digestion. The mean changes in CSF ions at 20 min. and 3 hrs. are:

	Na^+	K^+	Cl^-	TCO_2
20 mins.	+5	+.4	0	+5.4
3 hrs.	+1	+.2	-6	+9.0

In blood, at 20 mins. TCO_2 increased 3.2 mM/l with little change in ions, and at 3 hrs. TCO_2 increased 6.9 mM/l while Cl^- decreased 5 mM/l. In brain, tissue water, Cl^- space, and tissue ions did not change with the exceptions of Na^+ and the CO_2 titration curve. Tissue Na^+ was increased ≈2 mM/kg tissue at 20 mins. and 3 mM/kg tissue at 3 hrs. and the titration curve was displaced upward in a roughly parallel fashion also by ≈ 2 mM/kg tissue at 20 mins. and 3.3 mM/kg tissue at 3 hrs. The tissue values allow two tentative conclusions: 1) the initial increase in CSF Na^+ and later decrease in CSF Cl^- reflect net exchange with blood, 2) the upward displacement of the tissue titration curve is accompanied by an equimolar change in tissue Na^+. (Supported by HL 18351; RCDA 00364.)

Chloride-Dependent Sodium Uptake by Rat Small Intestine. Hugh N. Nellans and Joan E. Popovitch* Columbia University, New York, N.Y. 10032

The uptake of sodium by isolated microvillus membrane vesicles of rat small intestine was investigated using a rapid filtration technique. Employing sucrase as a marker enzyme, typical purification of this membrane fraction is 20 to 25 fold. Initial rates of sodium uptake into an osmotically active intravesicular space range from 5 to 6 n Eq/mg protein min. In the presence of 2 mM NaCl and 98 mM KCl, with isosmotic mannitol in the intravesicular compartment, an "overshoot" of sodium uptake is demonstrable. D-glucose induces an increment in the sodium uptake "overshoot" under similar conditions. Valinomycin preincubation abolishes the initial Na accumulation above equilibrium levels suggesting a potential-dependent component of influx. Further, valinomycin treated vesicles exhibit an anion dependence of sodium uptake in the following sequence of efficacy: $Cl=SCN>NO_3>SO_4$. These results suggest that sodium transport across the microvillus membrane of rat small intestinal epithelial cells entails at least three mechanisms. Potential-sensitive sodium influx in both the presence and absence of D-glucose are consistent with diffusional and sodium-dependent glucose entry, respectively. The chloride-dependent, potential-independent sodium influx has not, however, been previously demonstrated in an isolated membrane preparation and suggests that this system may resemble the neutral, coupled sodium-chloride influx of in vitro rabbit ileum. (Supported by NIH Grant AM-19945.)

EVIDENCE FOR THE ROLE OF H_2 RECEPTOR IN THE MODULATION OF PERIPHERAL VAGAL TRANSMISSION IN PENTOBARBITAL ANESTHETIZED DOG. Premanand Nandiwada*, Mustafa F. Lokhandwala, and Bhagavan S. Jandhyala, (Spon: G. J. Grega), Inst. for Cardiovasc. Studies, Univ. of Houston, Houston, Texas 77004

Role of H_1 and H_2 receptors in vagally mediated alterations in the cardiac rate is examined in these studies. Intravenous infusion of histamine (3 µg/kg/min) significantly inhibited reflex bradycardic responses to phenylephrine in the anesthetized dogs, while the pressor effects were essentially unaltered. Bradycardic responses to electrical stimulation of right vagus were also reduced during histamine infusion. Metiamide, an H_2 receptor antagonist, potentiated bradycardic effects to vagal stimulation, and antagonized histamine-induced inhibition of bradycardia to phenylephrine as well as to vagal stimulation. However, pyrilamine, an H_1 receptor antagonist, failed to alter the inhibitory effect of histamine on responses to vagal stimulation and to reflex bradycardia. Histamine infusion did not affect reductions in the heart rate produced by exogenous acetylcholine. The results of this investigation indicate that histamine could modify release of acetylcholine from vagal efferents by an action mediated via H_2 receptors. Physiological significance of these findings merits further consideration. (Supported by USPHS Grant No. HL22868).

ADRENOCORTICOTROPIC HORMONE AND CORTICOSTERONE MAINTENANCE OF OOCYTE MATURATION IN THE PREPUBERTAL RAT FOLLOWING ADRENALECTOMY. Mary V. Nekola,* Sharon K. Smith,* and Lynn G. Nequin. School of Medicine, Southern Illinois University, Carbondale, Illinois 62901.

The present work was undertaken to determine if the inhibitory effects of adrenalectomy (A) on oocyte maturation in the prepubertal rat (Nekola et al., SSR Abstracts, 1979) were explicable by the action of adrenocorticotropic hormone (ACTH) rather than the absence of corticosterone (B). Sprague-Dawley rats were A or sham A (S) on day 20 of age. Three groups of A animals were given 160 µg/ml B in 7% ethanol (ETOH) in water while the S animals were exposed to 7% ETOH in water. A dose of 0.1 ml saline was administered subcutaneously (s.c.) at 1800 hours in the S group and in one of the A groups. The 2 remaining A groups received 3 IU or 12 IU (post A levels) of 1-18 ACTH (Organon, 2001) from day 21 to day 25 s.c. at 1800 hours. All animals were sacrificed on day 25 between 4 and 6 p.m. The oocytes were collected and cultured under standard conditions. After 9-11 hours the oocytes (46-65 oocytes/group, 6 animals) were examined for intact nuclei (germinal vesicles, GV), GV breakdown without polar body formation (GVB), and extruded polar bodies (PB). χ^2 analysis revealed no changes in any stage of maturation between groups. PB formation ranged between 54-66% GVB 23-27%, GV 10-21% and total maturation (PB and GVB) 79-90%. It does not appear that ACTH is responsible for the reduction in maturation following adrenalectomy.

ADAPTATION OF MOTILITY IN THE FUNCTIONING SMALL BOWEL OF RATS FOLLOWING JEJUNOILEAL BYPASS. P.R. Nemeth*, D.J. Kwee*, and N.W. Weisbrodt. Univ. of Texas Med. School, Houston, Tx 77025.

Rats fail to gain weight for the first week following 70% jejunoileal bypass. By the second week, these animals begin to gain weight at the same rate as sham operated animals. The small bowel in continuity was studied in rats 3 and 14 days after operation to determine if an adaptation in motility occurs. Jejunoileal bypass was performed with the bypassed segment anastomosed to the distal colon. During surgery, one end of a catheter was sutured into the proximal duodenum and the other end exteriorized. Animals were fasted 24 hours before study and then force-fed 1.0 ml/100 g body weight of an isosmotic elemental diet. After 15 minutes, $Na_2{}^{51}CrO_4$ was instilled into the gut lumen. Animals were sacrificed at 15, 50, and 150 minutes following introduction of the isotope and the intestines removed to determine the distribution of ^{51}Cr. The percentage of radioactivity reaching the colon was as follows with the number of animals in ( ).

Days following bypass	min. ^{51}Cr in bowel 15'	50'	150'
3	2.6 ± 0.8(4)	13.9 ± 2.8(6)	68.5 ± 5.3(4)
14	0.3 ± 0.1(4)	1.6 ± 0.9(7)	63.1 ± 5.2(7)
Significance	P < 0.025	P < 0.0005	NS

These results indicate that an adaptation in motility occurs in rats within 14 days of jejunoileal bypass. The adaptation involves a delay in transit in the earliest times following a meal when some nonabsorbed material may be present.

FLOW DEPENDENCE OF PHASE FIVE IN SINGLE-BREATH TESTS. C.M.Nichol*,H.J.B.Guy* and D.B.Michels.Depts.of Med.Christchurch Clinical School of Med. Christchurch,New Zealand and Univ. of Calif. San Diego, La Jolla, Ca. 92093.

A downward-deflecting phase five (Ph V) is commonly seen following the terminal rise (Ph IV) in single-breath tests. This was studied in 33 normal non-smoking men aged 19-65 using a test in which the instantaneous respiratory exchange ratio was measured during a VC exhalation while breathing air (SBR test). The volume of phase five (VP5) increased with expiratory flows from 0.3-0.7 l/sec, and was significantly correlated with the volume at which flow limitation occurred (VFL). Phase five was demonstrated in all subjects over age 22 and increased with age. VP5 was shown to be less than VFL by a fixed amount approximately equal to the anatomical dead-space in repeated SBR tests on a single subject at a variety of flow rates between 0.1 and 1.0 l/sec. Similar results to these were obtained in preliminary studies with both the single-breath nitrogen washout test and single-breath washouts of boli of inert tracer gas inhaled at RV. This behaviour is predicted by a model of lung emptying in a gravitational field similar to that of Hyatt et al (J. Appl. Physiol.35:411-419). In these models progressive flow limitation occurs from bottom to top of the lung with phase five beginning when all parts of the lung become flow-limited. Supported by the Medical Research Council (N.Z.), the North Canterbury Hospital Board and NASA grant NGL 05-009-109.

EFFECT OF PLASMA FIBRONECTIN (OPSONIN) DEFICIENCY ON PULMONARY MICROVASCULAR PERMEABILITY DURING PSEUDOMONAS SEPTICEMIA. G.D.Niehaus*, P.T.Schumacker* and T.M.Saba. Dept. Physiology, Albany Medical College, Albany, NY 12208

Opsonic (plasma fibronectin; CIg) deficiency correlates with pulmonary failure in trauma patients during sepsis (Science 201:622,1978). Reticuloendothelial (RE) clearance of microparticulates is inefficient in sheep with low opsonin levels (184.6±13μg/ml) and increased lung microembolization. We studied the effect of plasma fibronectin deficiency on lung microvascular permeability during septicemia in the anesthetized, ventilated sheep lung lymph preparation. Pulmonary wedge pressure (P_w), pulmonary arterial pressure (P_{pa}), lung lymph flow ($\dot{Q}_L$), lymph and plasma protein ratios (L/P) were measured. Plasma fibronectin has a high affinity for denatured collagen and was depleted 50% by gelatin infusion (16mg/kg) as tested by immunoassay. Its level was also depleted by Pseudomonas alone. Plasma fibronectin deficiency did not alter lung microvascular permeability or pressures. Pseudomonas caused a sustained 2-3 fold increase in $\dot{Q}_L$ (control=6-7ml/hr); a transient increase in P_{pa}; and a transient decrease in L/P protein ratio. In contrast, Pseudomonas septicemia during plasma fibronectin deficiency resulted in a persistent 600-700% increase in $\dot{Q}_L$ even though the elevation in P_{pa} was transient. Also, the L/P protein ratio increased to a new steady-state 20% above control. Thus, opsonic deficiency can potentiate septicemia induce increased pulmonary microvascular permeability. (GM-21447; T32-GM-07033; HL-07194)

ALVEOLAR SUBPHASE pH MEASURED IN VIVO IS LOWER THAN ARTERIAL pH. D. Nielson, J. Goerke and J.A. Clements†. UCSF, San Francisco, CA 94143.

The pulmonary alveolar subphase, found between the surfactant film and the alveolar epithelium, has an estimated volume of 5 to $20x10^{-12}$ liter/alveolus. We have used H^+ sensitive glass microelectrodes to measure the pH of the subphase in stable, open chest rabbits. Subphase pH in three animals was 7.04 (n=2), 7.14±.12 (n=4) and 7.21 (n=2) when arterial pH was 7.46, 7.45 and 7.49 respectively. pO_2 was >100 torr, and pCO_2 was 30-35 torr while mean carotid arterial blood pressure was maintained at 90-100 torr. Thus the pH of the alveolar subphase was significantly lower than the simultaneous arterial pH, but not as low as the pH (6.3) of fetal lamb lung fluid (Adamson et al., 1969). Using a 3M KCl microelectrode in each experiment we found a potential difference (PD) of -2.5 to -3.5 mV between the pleura (taken as zero reference) and the alveolar subphase. A small correction of .04 to .06 pH units was thus applied to arrive at the above pH values. Measurements of the PD between the trachea and visceral pleura in fetal lambs and in adult rats (Engleberg and Radin, 1977) yield values similar to the alveolopleural PD measured by micropuncture. Supported by USPHS NHLBI grants no. HL-06285 and HL-07159.
† Career Investigator, American Heart Association.

INTERACTION OF TEMPERATURE AND HYPERCAPNIA IN THE CONTROL OF BREATHING IN THE SNAKE, COLUBER CONSTRICTOR. W.F. Nolan* and H.M. Frankel. Bureau of Biological Research and Dept. of Physiology, Rutgers University, New Brunswick, N.J. 08903.

Steady-state and off-transient ventilatory responses to 0, 4 and 7% CO_2 in 21% O_2, balance N_2 were examined at body temperatures (T_b) of 15, 25 and 35°C in unanesthetized, restrained black racer snakes. Arterial blood samples were obtained via posterior dorsal aorta catheters and analyzed for Po_2, Pco_2 and pH. HCO^-_3 and OH^-/H^+ were calculated. The temperature effect on blood gases and pH was also examined in vitro. Minute volume ($\dot{V}_T$), Pco_2 and OH^-/H^+ increased and pH and HCO^-_3 decreased with increased T_b at 0% CO_2. In vivo dpH/dT and $dPco_2/dT$ were significantly less than the in vitro observations. Steady-state $\dot{V}_T$ increased during hypercapnia at 25° and 35° but not 15°. Off-transient maximum $\dot{V}_T$'s were greater than their respective steady-state averages in all cases at 15° and in most cases at 25°. Results indicate that ventilatory response to CO_2 and/or H^+ is altered by temperature. Our observations suggest that some factor other than the maintenance of a constant relative alkalinity (OH^-/H^+) is the primary stimulus which determines ventilation when T_b is changed in these animals. In addition, the increase in off-transient $\dot{V}_T$ compared to steady-state suggests the involvement of an airway or intrapulmonary chemoreceptor in the ventilatory response to CO_2. (Supported in part by the C & J Busch Fund).

SOME FURTHER OBSERVATIONS ON HOW INJECTED GTP STIMULATES THE Na EFFLUX IN ALDOSTERONE PREEXPOSED BARNACLE MUSCLE FIBERS. Jude Nwoga* and E. Edward Bittar, Department of Physiology, University of Wisconsin, Madison, Wis. 53706

The starting point of this work is the observation that the response of the ouabain-insensitive Na efflux to the microinjection of $GTPNa_2$ in barnacle muscle fibers preexposed overnight (in vivo) to a large dose of aldosterone is not only greater than in unexposed fibers but also sustained. Whereas injection of EGTA(100mM) causes a partial reversal, injection of 0.5M $MgCl_2$ causes complete reversal of the response.(KCl is ineffective).By contrast, injection of 0.5M $CaCl_2$ causes stimulation of the already stimulated efflux.Overnight preexposure of the barnacle specimen to aldosterone and 5μg/ml actinomycin D does not lead to a reduced response to GTP nor to a change in kinetics. Since the binding constants of $GTPNa_2$ and $ATPNa_2$ for Mg are practically the same, experiments with $ATPNa_2$ were done. Injection of .5M $ATPNa_2$ stimulates the ouabain--insensitive Na efflux but not to the same extent as an equimolar solution of $GTPNa_2$. These results support DeWeer's view that the Na efflux e.g. in squid axon, is suppressed by cytosolic pMg. Furthermore, choleragen (10^{-4}M) when injected leads to a prompt but slow rise in efflux averaging 185=±20%[n=6] 80 mins after injection. Choleragen-injected fibers show 52±10%[n=6] stimulation following injection of 0.5M $GTPNa_2$, a value significantly less than that observed with controls. This finding is consistent with the view that while choleragen increases adenylate cylase activity, it has the opposite effect on guanylate cyclase.

POSSIBLE NEURAL CONTRIBUTION TO POSTPRANDIAL INTESTINAL HYPEREMIA. R. Nyhof* and C. Chou. Depts. of Physiology and Medicine, Michigan State Univ., East Lansing, MI 48824

To see if the local mucosal nerves play a role in the postprandial intestinal hyperemia, the effects of luminal placement of various nutrients were compared before and after exposing the mucosa to 0.4% dibucaine HCl (DIB) in in situ canine jejunal segments (n=25). Digested food increased local venous outflow before and after DIB but the former (+50±14.5%) was significantly greater than the latter (+16.8 ±8.5%). Solutions of 5.4% glucose and 40 mM oleic acid, each mixed with 10% gallbladder bile, were then tested. The hyperemic effect of glucose (+13.4±2.7%) was completely blocked, while that of oleic acid (+32.6±4.7%) was attenuated (to+9.7±3.0%) by DIB. The increase in oxygen consumption ($\dot{V}_{O_2}$) (+22.1±9.1%) by oleic acid was blocked after DIB (+1.8±1.8%). The increase in $\dot{V}_{O_2}$ (21.2±4.6%) by glucose was less after DIB (+10.7±3.8%), as was the glucose absorption rate (31.8±5.0 to 21.2±3.1 mg/min·gm^{-1}). The attenuation in $\dot{V}_{O_2}$ and glucose absorption was primarily due to attenuation or inhibition of the hyperemia by DIB since the arteriovenous differences of glycose and O_2 were unchanged. Thus, local mucosal nerves seem to play a role in intestinal hyperemia during digestion. (Supported by grant HL-15231 from NHLI.)

†The percentage values in parenthesis are the changes from precontrol during which normal saline was in the lumen.

AIRWAY EFFECTS OF RESPIRATORY HEAT LOSS (RHL) IN NORMAL SUBJECTS. C.F.O'Cain*, N.B.Dowling, Jr.*, A.S. Slutsky*, K.P. Strohl*, E.C. Deal, Jr.*, E.R. McFadden, Jr., R.H. Ingram, Jr. Peter Bent Brigham Hospital and Harvard Medical School, Boston, MA 02115

Although normal and asthmatic subjects have similar degrees of airway cooling with exercise, normal subjects fail to show changes in usual measures of lung mechanics even after exhausting work breathing cold air (mean $\dot{V}_E$=80 l/min). To investigate whether this lack of response represents a higher threshold value for the RHL stimulus in normals, we studied nine non-asthmatic subjects in whom we produced greater RHL than obtainable by exercise by having them perform eucapnic hyperventilation(mean $\dot{V}_E$=120 l/min) with -10^{0}C air for 4 min. In contrast to exercise, with its lower $\dot{V}_E$ and RHL, all subjects responded to this stimulus with significant but modest changes on FVC maneuvers (mean ±SD % decrease FEV_1=5±2; MMF=14±6). Larger changes were seen on two measurements initiated near FRC: $\dot{V}_{max}$ at 30% VC fell 22±9% and the slope of phase III on single-breath N_2 tests increased 79±54%. After hyperventilation with air at BTPS conditions, there were no changes in any variable. This study demonstrates that normal subjects can be made to respond to airway cooling, but it requires much larger values of RHL than normally obtained by exhausting exercise. (Supported in part by an MRC(C) fellowship, and NHLBI Grants 16463, 17382, and 19170.)

THE HYDRODYNAMIC DRAG AND MAXIMAL SWIMMING SPEEDS OF BLUEFISH (POMOTAMUS SALTATRIX) WITH NEUTRAL OR NEGATIVE BOUYANCY IN LAMINAR AND INDUCED TURBULENT FLOW. Christopher S. Ogilvy* and Arthur B. DuBois, John B. Pierce Fndn, Yale Univ. New Haven, CT., and Marine Biological Lab., Woods Hole, Mass.

A transition from laminar to turbulent flow over a rigid streamlined body increases the drag of that body. To see if this is true for a flexing body we presented laminar and induced turbulent flow conditions to swimming bluefish. The force of body drag was measured using a miniature body accelerometer where F_D = body mass x peak to peak acceleration ÷ $2\sqrt{2}$. At any given swimming speed (N_R 10^5-10^6) the drag remained the same regardless of the flow conditions. Similarly, the maximal swimming speed of the fish remained unchanged in laminar or turbulent flow. To alter the bouyancy in three fish, the swimbladder was replaced with a balloon and catheter which connected to a syringe outside the water tunnel. At a swimming angle of 33°, 45cc of air was removed from the swimbladder. The force of drag at zero speed was 0.44N indicating that the force of "induced drag" was equal to the body's weight in water. The body drag decreased to 0.33N at 0.38 $M \cdot s^{-1}$ and then increased with water speed. At neutral bouyancy, a practically linear relationship was found between body drag and swimming speed and represents only forces of frictional (parasitic) drag. By flexing the body, the bluefish may be able to achieve boundary layer reattachment which is unaffected by turbulence. (NIH HL-17487).

ARACHIDONATE INCREASES LUNG MICROVASCULAR PRESSURE AND TRANS VASCULAR FLUID FILTRATION IN UNANESTHETIZED SHEEP. M.L. Ogletree* and Kenneth Brigham. Vanderbilt University Medical Center, Nashville, Tennessee 37232.

Prostaglandins (PG) and thromboxane derived from arachidonic acid (AA)can cause pulmonary hypertension, but effects of AA on lung fluid balance have not been measured. We infused purified AA into unanesthetized sheep prepared for collection of lung lymph. AA(25 and 50µg/kgxmin)produced dose related increases in pulmonary artery pressure(Ppa)and lung lymph flow(Qlym)with corresponding decreases in the lymph to plasma protein concentration ratio(L/P).Indomethacin(I)(5mg/kg+3mg/kg x hr)inhibited responses to AA.Steady state responses to AA in the presence and absence of I are shown in the table (mean±S.E.M., N=5).

	Ppa cmH_2O	Qlym ml/hr	L/P		Ppa	Qlym	L/P
Base	21±3	9±2	0.56±0.07	I alone	19±2	12±3	0.56±0.06
AA(25)	31±3*	13±3	0.51±0.06*	I+AA(25)	20±1+	12±2	0.57±0.05
AA(50)	38±4*	22±5*	0.42±0.05*	I+AA(50)	23±2+	14±3+	0.54±0.04+

*p<0.05 compared to baseline; + p<0.05 compared to AA alone

Lung lymph responses to AA were like those caused by mechanically increasing left atrial pressure. We conclude that arachidonate, by conversion to PG endoperoxides, increases lung vascular pressures, but not permeability.

INFLUENCE OF ELECTRODE POSITION AND GASTRIC BALLOON ANCHORING ON ESOPHAGEAL DIAPHRAGMATIC EMG IN HUMANS. E. Önal*, M. Lopata* and M.J. Evanich, Univ. of Illinois and West Side VA Hospitals, Chicago, IL. 60680

The effects of electrode position and gastric balloon anchoring on esophageal diaphragmatic EMG (EMG_{di}) response to CO_2 rebreathing were studied in seven normal, sitting humans using an esophageal catheter that consisted of four platinum wire coils enabling simultaneous recording of three EMG_{di} signals from three different sites in the esophagus. A gastric balloon attached to the distal end of the catheter allowed anchoring of the catheter. Two rebreathing experiments were performed on the same day with and without balloon anchoring. EMG_{di} signals were quantitated as a moving time average. Maximum EMG_{di} activity was approximately 2cm above the gastroesophageal (GEJ) junction in sitting humans. Changes in electrode position of at least 2cm above the site of maximum EMG_{di} activity caused minimal changes in recorded diaphragmatic activity and did not significantly effect the quantitated EMG_{di} response to CO_2 rebreathing. In every subject the EMG_{di} responses obtained within 4cm distance above the GEJ were statistically similar for anchored and unanchored runs. These results indicate that: 1) EMG_{di} response to CO_2 rebreathing can be reliably quantitated within 4cm above the GEJ, 2) gastric balloon anchoring offers no advantage in quantifying this response in upright humans and 3) EMG_{di} responses to hypercapnia shows intraindividual reproducibility on the same day. (Supported by NIH Grant HL 14735

REGIONAL CEREBRAL BLOOD FLOW (rCBF) INCREASES WITH INTRACEREBROSPINAL FLUID (CSF) INFUSIONS OF NOREPINEPHRINE (NE). J.T. O'Neill* and R.J. Traystman. Dept.of Environ. Hlth.Sci. Johns Hopkins Med. Insts., Baltimore, Maryland 21205.

r-CBF responses to CSF infusions of NE (20 and 100 µg/ml) were studied in 24 anesthetized, paralyzed, ventilated dogs. Mock CSF was infused (0.5 ml/min) into the lateral ventricle and drained from the cisterna magna. r-CBF was measured with the radioactive labeled microsphere (15 ± 3µ) technique. The ipsilateral brain hemisphere was sectioned into 17 regions for measurement of r-CBF. r-CBF was measured before (t=0), 90, 180 and 270 min after NE was added to CSF solutions. 20 µg NE/ml CSF did not alter r-CBF. 100 µg NE/ml CSF increased r-CBF to the rostral spinal cord (81%), medulla (95%), pons (80%), midbrain (53%), diencephalon (61%), caudate nucleus (86%) and periventricular white matter (33%) by 270 min. Total hemispheric blood flow, however, remained unchanged. Increases in r-CBF were attenuated by addition of Propranolol (4.5 µg/ml CSF) 15 min prior to t=0 blood flow measurements. We have demonstrated that CSF-NE infusions increase rCBF in certain regions of the brain and that these increases are attenuated by beta-adrenergic blockade. The mechanism of these r-CBF changes may be direct by stimulation of vascular adrenergic receptors or central neurogenic pathways, or indirect by affecting cerebral metabolism. (Supported by NIH HL-10342 and HL-07199)

CITRATE UPTAKE AND OXIDATION BY TISSUE SLICES FROM AD LIBITUM-FED AND STARVED RATS. M. Onwochei and A. Gold, Dept. of Physiology, Howard Univ. College of Medicine, Washington, D. C. 20059

Tissue slice studies were conducted to ascertain differences in citrate uptake and oxidation by the kidney from ad libitum-fed (control) rats and those starved for seven days. Kidney slices from each group were incubated at 38°C for one hour in Krebs Ringer bicarbonate buffer (KRB) containing 1 or 3 mM citrate. A pH of 7.4 was maintained by gassing the medium in a closed incubation flask for 10 min with 95% O_2-5% CO_2. Citrate uptake and tissue citrate level were determined fluoroenzymatically. In another experiment, 0.15 uCi ^{14}C-citrate was added to KRB-citrate medium at pH 7.4. $^{14}CO_2$ was collected with phenethylamine mixed with methyl alcohol in a 1:1 ratio and analyzed by liquid scintillation spectrometry. Preliminary results from these studies indicate the following: (1) citrate uptake is slightly higher and tissue citrate level lower in the starved rat kidney slice; (2) citrate oxidation in both groups are similar. The data therefore suggest that the machinery for citrate uptake and oxidation is relatively intact in the starved rat kidney. Citrate uptake data are also similar to those obtained in prior in vivo experiments. (Supported by NSF Research Grant #PCM-7619916)

FILTRATION (Kf) AND REFLECTION (σ) COEFFICIENTS OF PULMONARY CAPILLARIES BY INDICATOR DILUTION: VALIDATION IN THE ISOLATED LOBE. L. Oppenheimer*, H. Goldberg*, R. Holland*, and W. Macedo*. (Spon: John A. Hildes). Univ. of Man., Winnipeg.

We measured Kf and σ in isolated canine left lower lobes suspended from a force transducer and perfused with plasma stained with indocyanine green ($6x10^{-3}$g/%). Experiments were conducted in zone III of West. During the slow weight gain phase following a step change in capillary pressure (ΔPiv), a 4 ml H_2O bolus was injected into the inflow cannula without a change in Piv. Weight changes (ΔVis'), inflowing and outflowing reciprocal dye-dilution curves were obtained. The procedure was repeated in isogravimetric conditions. The flux (Qf_2) across the membrane following the hypotonic bolus in isogravimetric conditions is ($Qf_2=\Delta Vis''/\Delta T=\sigma x Kf x \Delta\pi$). The flux ($Qf_1$) when the hypotonic bolus is given during the hydro-static gradient is ($Qf_1=\Delta Vis'/\Delta T=Kf x \Delta P+\sigma x Kf x \Delta\pi$), therefore, after obtaining ΔP, ($Kf=Qf_1-Qf_2/\Delta P$, and $\sigma=Qf_2/Kf x \Delta\pi$). $\Delta\pi$ reflects mostly the crystalloid concentration difference across the membrane. Mean capillary crystalloid concentration was obtained from the dye-curves while it was assumed unchanged in the interstitial space. By comparing the dye curves of the water boli to dye curves following reference boli of N.S., we calculated ΔVis' and ΔVis'', Kf (.123+.051g/min x cmH_2O/g dry weight and σ (.011+.001). These results compare well with Kf (.122+05g/min $\bar{x}$ cmH_2O/g dry weight) and σ (.007 + .0011) obtained from the weight changes. (Supported by MRC of Canada).

ROLE OF HIPPOCAMPUS IN SHORT-TERM MEMORY DURING AGING. J. M. Ordy and K. R. Brizzee, Delta Regional Primate Research Center, Covington, La. 70433.

The hippocampus has been implicated in short-term memory, spatial orientation, and neuroendocrine regulation of endocrine and autonomic function. Prominent manifestations of aging include loss of short-term memory, disturbance in spatial orientation, and alterations in autonomic arousal. The specific aims of this study were to examine the effects of aging on short-term memory in C57/Bl/6 mice and Fisher 344 rats in relation to neurochemical and morphological changes in the hippocampus as a major convergent multimodal sensory and reward integration center involving entorhinal, thalamic, and frontal cortex information processing pathways. Compared to young and middle aged mice and rats, aged animals were significantly inferior in short-term retention or memory in passive-avoidance tests. In the aged animals, there was also a significant decline in cell populations and cholinergic receptors, as well as a significant accumulation of intraneuronal lipofuscin age pigment in the CA-1 zone of the hippocampus. These findings indicate that significant age-related cellular alterations occur in the hippocampus, representing one of the primary convergent multimodal sensory centers concerned with mediation of short-term memory. (Supported by NIH Grant RR00164-17.)

MEDULLARY RESPIRATORY NEURON ACTIVITY: RELATIONSHIP TO TONIC AND PHASIC REM SLEEP. John Orem. Texas Tech University School of Medicine, Lubbock, Tx. 79430

This study analyzed the relationship of brain stem respiratory neuron activity to the tonic and phasic events of rapid eye movement (REM) sleep. Dorsal and ventral medullary respiratory neurons were recorded in sleeping cats. Discharges of inspiratory and expiratory cells increased in number and average frequency with increases in ponto-geniculo-occipital (PGO) spiking (phasic REM activity). The correlations between PGO wave frequency and respiratory neuron activity were positively related to the discharge levels of the neurons: the more active the cell, the greater the relationship to PGO activity. Tonic REM influences on respiratory neurons were calculated by extrapolating from the regression line relating PGO frequency and neuron activity to the hypothetical state of no PGO activity. These calculated levels, when compared to non-REM sleep levels, showed that tonic REM mechanisms decruited some neurons and activated others. Decruited cells tended to be found in the ventral medullary respiratory group; activated cells were generally in the dorsal group. These results demonstrate an association of brain stem respiratory activity to non-respiratory REM sleep variables.

EFFECT OF $PaCO_2$ SET-POINT ON THE MAGNITUDE OF THE VENTILATORY RESPONSE TO EXERCISE. A.Oren*, K.Wasserman, B.J.Whipp & J.A. Davis*. Harbor-UCLA Medical Center, Torrance, CA 90509.

If the ventilatory control mechanism behaves as a system to keep $PaCO_2$ from deviating from its set-point, then a greater ventilatory response will be expected for the same work rate if $PaCO_2$ were low rather than high due to the metabolic-$PaCO_2$-$\dot{V}_E$ interrelationship. To determine the contribution of the $PaCO_2$ set-point on the ventilatory response to exercise, 5 normal adults were studied during chronic metabolic alkalosis, acidosis and a control state. These states were achieved by a 3-day ingestion of 0.7 $NaHCO_3$, 0.3 NH_4Cl and 0.1 $CaCO_3$ gm/kg/day, respectively, and verified by measuring arterialized venous blood bicarbonate (meq/L) and $P_{ET}CO_2$. Each subject cycled on an ergometer to a constant load (75±15 watts). $\dot{V}_E$, V_T, f, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, R, $P_{ET}CO_2$ & $P_{ET}O_2$ were determined breath-by-breath. The ventilatory response during steady-state (ss) and dynamic square-wave forcing (characterized by the half time of response(s), i.e. $t_{\frac{1}{2}}$) were:

	$H\overline{C}O_3$	$P_{ET}CO_2$	$\dot{V}_E/O_2$	$\dot{V}_E$ss	$t_{\frac{1}{2}}$
Alkalosis	33.3±4.3	38.2±5.5	14.2±5.3	26.1±1.8	60.8±43.2
Control	22.1±1.6	35.2±6.0	15.8±4.8	29.0±4.9	52.5±39.1
Acidosis	15.0±2.8	27.6±3.6	17.6±6.2	36.5±8.9	41.2±20.8

Our findings support the concept that the ventilatory control mechanism during exercise provides a ventilatory response for a fixed work rate which varies inversely with the pre-exercise $PaCO_2$ set-point.

SURFACE CABLES ON HEART MUSCLE CELLS. J. Orenstein* and S. Bloom. Geo. Wash. Univ. Med. Ctr., Washington, D.C. 20037

The surface of hamster heart muscle cells prepared by mechanical disaggregation was studied by SEM and TEM. The sarcolemmae of these cells, unlike those isolated after enzyme digestion, were covered with glycocalyces. Although some cells showed focal avulsion of the sarcolemma and glycocalyx, these structures were generally intact. A striking SEM finding was the presence of fine, longitudinally oriented, fibrils, partially embedded in the glycocalyx. These fibrils, or "cell surface cables", were conspicuous in contracted cells where there were transverse depressions, or grooves, at the level of each Z disc, with the intervening sarcolemma formed into ridges or mounds over the adjacent cytoplasm. Surface cables extended longitudinally from one ridge to the next, bridging the grooves. They were found, by SEM, to be about 24nm thinner than nearby collagen fibrils. Since TEM studies revealed that collagen fibrils close to the cell surface were 37nm in diameter, the thickness of a surface cable was calculated to be 13nm. TEM of cells stained en bloc with uranyl acetate showed uniform, 12nm, unbanded fibrils in the same anatomic loci expected of the surface cables. These fibrils emanated from, but could not be identified within, the glycocalyx. Similarity in thickness and location of the 12nm fibrils observed by TEM and the 13nm cables observed by SEM suggests that they are identical. These cables may function to limit cardiac distention. (Supported in part by N.I.H. Grant HS 22137).

Changes in Histamine and Histidine Decarboxylase (HD) distribution in rat aortic endothelial and smooth muscle cell under streptozotocin-induced diabetes. Alicia Orlidge* and T. M. Hollis. Biology Dept., Penn State University, University Park, Pa. 16802.

The distribution of histamine and histidine decarboxylase within the thoracic aorta has been examined in male Wistar rats rendered diabetic by IV injection of streptozotocin (55 mg/kg). Specific wall components examined were endothelial (EC) and smooth muscle cells (SMC) of the same animal. Within 3 days following streptozotocin injection these animals showed fasting IPGTT 2hr values from 300-600 mg/dl, while corresponding control and saline-injected sham values were 88-110 mg/dl. Within control animals there were no apparent differences in histamine, expressed in terms of nmol/mg cell protein, between EC and SMC. However, in the diabetic animals, EC showed a 2-3 fold increase in histamine content as compared to control EC; a similar increase is also present in vascular smooth muscle. The overall cell histamine content appears related to the HD activity of the cell involved. Results support the concept that large vessel injury occurs during diabetes mellitus, and that such injury may be one of the important factors responsible for increased severity of atherosclerosis among individuals having diabetes mellitus.
Supported by Public Health Service grant HL20460.

IS CONTINUITY OF THE BOWEL WALL REQUIRED FOR PROPAGATION OF THE MIGRATING MOTOR COMPLEX FOLLOWING MOTILIN? H.S. Ormsbee, G.L. Telford*, and G. Robert Mason Univ. of Md., School of Medicine, Balto., Md.21201

This study evaluated the mechanism of the apparent aborad propagation of the motilin-induced canine migrating motor complex (MMC). Four mixed-breed dogs each had eight force transducers sewn to the gastrointestinal tract on the antrum, the pylorus, and at 10,50,120,130 200 and 250 cm from the pylorus on the small intestine. Motor activity was recorded in the 18-hour fasted animals to observe naturally occurring and motilin induced MMC's (100 ng/Kg IV). After these studies a 30 cm Thiry-Vella loop (TVL) of jejunum was surgically constructed in each dog and recordings were repeated. In 11 control studies the motilin-induced activity front passed the intended TVL 31.2 ± 7.5 min after injection. After TVL this measurement was 43.1 ± 35. 7 min for 14 studies. In 7 of these the values differed from the control mean by greater than 2SD. Apparent propagation of the motilin-induced activity fronts to the ileum was also altered by formation of the TVL but responses of the proximal intestine to motilin were unaffected. These responses to motilin were not further changed by the addition of a transthoracic truncal vagotomy. Continuity of the bowel wall appears to play a role in the appropriate timing of the MMC's induced by exogenous motilin.

EFFECT OF LOW LEVEL RENAL NERVE STIMULATION DURING AORTIC CONSTRICTION ON RENIN SECRETION IN FILTERING AND NON-FILTERING KIDNEYS. Jeffrey L. Osborn* and Gerald F. DiBona, Univ. Ia. Col. Med. and V.A. Med. Ctr., Iowa City, IA 52242

Previous studies in denervated filtering kidneys showed that low level renal nerve stimulation (LLRNS) augmented renin secretion (RS) after aortic constriction to 50 mmHg. In the present experiments, the mechanism of the effect of LLRNS on RS using both filtering and non-filtering kidneys was investigated. RS was determined in control (C), aortic constriction (AC) and recovery periods both before and during LLRNS (10 V, 1 ms, 0.25 Hz). In filtering kidneys, AC to 80 mmHg equally increased RS before and during LLRNS. Glomerular filtration rate (GFR) remained constant and renal vascular resistance (RVR) decreased during both AC periods. In non-filtering kidneys, AC to 80 mmHg did not change RS or RVR either before or during LLRNS. In contrast, AC to 50 mmHg in non-filtering kidneys decreased RVR and increased RS from 126 ng/min during C to 192 ng/min after AC. Similarly, during LLRNS, AC to 50 mmHg reduced RVR and increased RS from 37 ng/min in C to 80 ng/min following AC. Conclusions: In the non-filtering kidney, LLRNS does not enhance RS following AC to 80 or 50 mmHg. In the filtering kidney, LLRNS does not alter the RS response after AC to 80 mmHg when both GFR and RBF are autoregulated. LLRNS augmentation of RS during AC to 50 mmHg does not result from an interaction with the renal vascular baroreceptor. (NIH AM 15843, HL 07121, VA Merit)

RELATIVE CONTRIBUTION OF STARLING FORCES AND REABSORPTION COEFFICIENT ON CAPILLARY REABSORPTION FOLLOWING VOLUME EXPANSION. Cobern E. Ott, Dept. of Physiology and Biophysics, University of Kentucky, Lexington, Kentucky 40536.

In steady state conditions uptake by the peritubule capillaries equals reabsorption by the proximal tubule. This study determined the relative importance of changes in Starling pressures vs pertubule capillary permeability surface area (PS) on the diminished reabsorption following extracellular volume expansion in the dog. All measurements were made in hydropenic conditions (HC) and repeated after volume expansion (VE). Micropuncture techniques were used to measure capillary and tubule reabsorption, capillary hydrostatic pressure (CP) and efferent capillary oncotic pressure (πE). Interstitial hydrostatic pressure (IP) was measured from chronically implanted polyethylene capsules. Interstitial oncotic pressure (πI) was determined from renal lymphatic protein. Net reabsorption pressure (NRP) was calculated and divided by capillary reabsorption (CR) to determine PS. Results are mean ± SEM.

	CP mmHg	πE mmHg	IP mmHg	πI mmHg	NRP mmHg	CR nl/min	PS nl/min/mmHg
HC	11.3	32.8	5.9	5.2	18.7	44.9	2.40
	1.1	4.0	1.0	.3		9.2	
VE	13.7	20.8	10.4	4.0	12.2	28.7	2.36
	1.4	4.2	1.2	.2		8.6	

PS was changed less than 2% by VE. The results show that the diminished capillary reabsorption can be explained by changes in Starling pressures while the capillary PS was unchanged.

HORMONAL, BLOOD GLUCOSE, LACTATE, AND HEMATOLOGIC CHANGES IN YOUNG BEAGLE DOGS DURING HYPER-G STRESS EXPOSURES AND ADAPTATION TO CHRONIC CENTRIFUGATION. J. Oyama, B. C. Daligcon*, L. Q. Chan*, and L. C. Keil. NASA-Ames Res. Ctr., Moffett Field, CA 94035

Unrestrained, 20-week-old, male Beagles were centrifuged for 1,4,8 or 21 hrs. at $-2.5G_x$ on a 50-ft. diameter centrifuge. Each test group of 4 dogs was bled from the jugular vein before, immediately after, and 1 and 4 hrs. after each run. Blood levels of catecholamines, cortisol, insulin, vasopressin, glucose, lactate, and total leukocytes were increased significantly by centrifugation while T_4 and T_3 were decreased. The changes effected were critically dependent on the exposure duration. Eight of the dogs were subsequently chronically centrifuged at $-2.5G_x$ on the same centrifuge which was run continuously except for brief bi-weekly or monthly stoppages. After two weeks of centrifugation, plasma T_3 levels remained significantly below baseline values and of noncentrifuged control dogs. Growth of the centrifuged dogs which was initially suppressed resumed after 4 weeks of exposure at which time many of the above parameters had been restored to pre-exposure values. Results of this study provide for the first time the dynamic sequence of elaboration of a number of important hormones involved in the physiological and metabolic stress response of dogs to hypergravity and during the course of their adaptation to chronic centrifugation.

SCALING OF MUSCULOSKELETAL SYSTEM, VISCERA AND SKIN AS A FUNCTION OF TOTAL BODY MASS IN TERRESTRIAL MAMMALS. Nello Pace, Donald F. Rahlmann* and Arthur H. Smith. Univ. of California, Berkeley CA 94720 and Davis CA 95616.

In general terms, the musculoskeletal system may be considered to represent the weight-bearing organ of the body. The scale relationship of this system to total body mass among homologous animals, such as terrestrial mammals, is of basic interest in gravitational physiology. As part of a broader study, mass determinations have been made of the viscera, skin and skinned eviscerated carcass in groups of 6 animals each of male and female laboratory mice, hamsters, rats, guinea pigs and rabbits of ages ranging from 30 days to 1 year. The total body masses in the animal series ranged from 0.02 kg to 4.5 kg. The skinned, eviscerated carcass (SEC) essentially comprises the musculoskeletal system of the body, and its mass displayed a statistically significant hypergonic scale relationship to total body mass (TBM): $SEC,kg = 0.503(TBM,kg)^{1.055}$. In contrast, the visceral mass (VIS) displayed a significant hypogonic scale relationship to total body mass: $VIS,kg = 0.158(TBM,kg)^{0.871}$. Skin mass did not yield a simple scale relationship to total body mass, because of interspecies differences, and is treated separately. Overall, intraspecies differences of sex and age had little effect on the scale relationships for skinned, eviscerated carcass and for viscera. Thus, the importance of the continuous loading imposed by gravity in shaping body proportions is reaffirmed. (Supported by NASA Grant NSG-7336.)

SENSORY DISCHARGES RECORDED IN AFFERENT MAMMARY NERVE OF LACTATING RATS. P. Pacheco*, L. Muzquiz*, C. Clapp* and G. Martínez-Escalera*. (SPON: M. Salas) Inst. of Biomed. Inv., Univ. of Mexico. México, D.F.

The segmental nerve supplying the first abdominal mammary gland (consisting of 3 branches: superficial, medial and deep) was dissected in urethane-anesthetized lactating rats for recording. The following stimuli were applied: a) cutaneous tapping and "scanning", b) tapping and traction of the nipple, c). 05 ml saline into a cannulated duct, d). 5-5 mU i.v. oxytocin. Overlapping fields of medial and deep branches were observed. Phasic "on-off" or phasic "on" discharges were provoked on each branch, by tapping and "scanning" respectively. Tapping on the nipple was ineffective, whereas traction elicited two types of discharges only on the medial branch. One lasted only as the traction was maintained while the other continued as an afterdischarge. Oxytocin elicited a 15-30 sec discharge in medial and deep branches. Duct dilatation provoked a 2-6 sec activity on medial branch. In conclussion, mechanical and parenchymal receptors of the mammary gland transmit impulses mainly through the medial branch of the segmental nerve.

HEAT INTOLERANCE AS A FUNCTION OF PERCENT OF BODY SURFACE INVOLVED WITH MILIARIA RUBRA. K. B. Pandolf, T. B. Griffin*, E. H. Munro* and R. F. Goldman. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760.

Previous work from this Institute has shown that one bout of artificially induced miliaria rubra (heat rash) resulted in a marked reduction in heat tolerance for the rashed subjects (57% of average surface area rashed) compared to matched controls. Miliaria rubra was induced on the experimental subjects by wrapping them for 3 days in polyethylene plastic. Twenty-four heat acclimatized male volunteers were wrapped as previously described but to produce miliaria rubra in specific regions of the body. Three experimental rash groups were involved: 1) the torso (17% total skin surface rashed, n=6), 2) torso and arms (38%, n=8), or 3) legs (41%, n=6), while four subjects served as controls. All subjects were re-exposed to walking (1.56 m/s) for 100 min in the heat (T_a=48.9°C, 20% rh) on the 7th day after unwrapping, and again 14, 21 and 28 days after unwrapping. When compared to responses for the last acclimatization day, tolerance time and sweat rate were significantly lower and mean body temperature and Δ heat storage significantly higher for experimental rash subjects contrasted to the controls for up to 21 days; however, no significant differences between the three rashed groups were found. The critical amount of surface area for heat intolerance from heat rash appears related to the specific region of the body and associated sweating responses; smaller rashed areas of the trunk, because they have greater potential for abundant sweating, may produce similar responses to heat stress as larger rashed areas of the limbs. Heat intolerance due to rash was not resolved until after 21 days.

MYOCARDIAL NOREPINEPHRINE DEPLETION IN ENDOTOXIN SHOCK: ROLE OF HYPOGLYCEMIA AND NEURAL MEDIATION. B. J. Pardini*, S. B. Jones and J. P. Filkins. Dept. of Physiology, Loyola Univ. of Chicago, Stritch Sch. Med., Maywood, Il 60153

Endotoxin (ET) elicits hemodynamic and metabolic responses resulting in activation of the sympathetic nervous system and depletion of tissue norepinephrine. Present studies examined the nature of myocardial norepinephrine (MNE) depletion in endotoxicosis. Male Holtzman rats (300-350 gms) were administered 5 mg of S. enteritidis ET or saline, iv. Ventricular muscle and plasma samples were obtained at 5 hrs after treatment or near death. The ET group was divided into early and late shock stages on the basis of plasma glucose (PG) levels. Compared to controls, early stage rats (PG>40 mg%) demonstrated a 17% decrease ($p<.01$) in MNE (ug/gm wet wt.) while late stage rats (PG≤40 mg%) had a 68% decrease ($p<.001$) in MNE. Regression analysis for MNE vs PG for all ET rats yielded $r=.74$ ($p<.01$). Insulin hypoglycemia (IH) was used to test whether the singular effect of low PG would deplete MNE. Neither mild (PG>40 mg%) nor severe (PG≤40 mg%) IH altered MNE ($p>.05$). Regression analysis for MNE vs PG for all IH rats yielded $r=.15$ ($p>.05$). To assess neural involvement of MNE depletion, ganglionic blockade (chlorisondamine, 5 mg/kg, iv) was induced 1 hr after ET treatment. Blockade sensitized rats to ET shock and hypoglycemia, but MNE was not depleted ($p>.05$). It is concluded that MNE depletion in ET shock: (1) is related to, but not solely dependent on hypoglycemia, and (2) is neurally mediated. (Supported by NIH Grant HL 08682.)

THE EFFECTS OF SYSTEMIC VENOUS HYPERTENSION ON LUNG WATER AND PULMONARY MECHANICS IN DOGS. P.D. Paré* and L.A. Brooks* (SPON: C.F. Cramer). UBC Pulmonary Research Laboratory, St. Paul's Hospital, Vancouver, Canada.

Systemic venous hypertension (SVH) and fluid overload could result in pulmonary edema and altered lung function by increasing pulmonary transcapillary fluid flux and retarding pulmonary lymphatic flow. To test this hypothesis we studied 22 anesthetized dogs in a volume displacement body plethsymograph. We measured subdivisions of lung volume, pulmonary resistance (R_L), dynamic compliance (C_{DYN}), phase III of the single breath nitrogen washout, vascular pressures and arterial blood gases before and four hours after: Gp I, n=5, no treatment; Gp II, n=5, elevation of systemic venous pressure to 25 cm H_2O with a right atrial balloon; Gp III, n=6, fluid overload (100 ml/kg/hr); and Gp IV, n=6, a combination of venous hypertension and fluid overload. Gravimetric lung water (PEW) was measured at the end of each experiment. SVH alone did not result in significant changes in PEW (Gp I - 3.46±.16; Gp II - 3.44±.18 gm H_2O/gm dry tissue) or pulmonary function. SVH combined with fluid overload, when compared with fluid overload alone, resulted in increased PEW (Gp III - 4.24±.3; Gp IV - 4.78±.42) and significant alteration in pulmonary function (decreased TLC, FRC, VC, C_{DYN} and PO_2; increased RV and R_L). We conclude that SVH favors the formation of pulmonary edema under conditions of increased pulmonary transcapillary fluid exchange.

ALTERATIONS IN THE PLASMA LH MOLECULE OF SENESCENT C57BL/6 MICE AND GOLDEN HAMSTERS. T. A. Parkening, T. J. Collins* and E. R. Smith*. Univ. Texas Medical Branch, Galveston, Tx. 77550

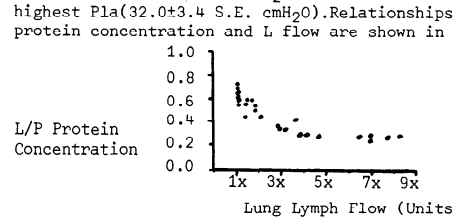
Recent RIA studies conducted in our laboratory have shown that significantly higher levels of plasma LH exist in aged mice and hamsters than those found in younger mature females. To test if the higher levels of LH detected by RIA were as biologically active, a radioreceptor assay (RRA) was used consisting of membrane fractions of luteinized ovaries of rats or mice (Lee and Ryan, Proc. Nat. Acad. Sci. 69:3520, 1972). Blood was obtained from aged constant diestrous C57BL/6 mice (16-20 mo old), anestrous golden hamsters (13-17 mo old), repetitive pseudopregnant Wistar rats (14-18 mo old) and younger mature females (2-5 mo old) of each species. Plasma LH levels measured by RIA for younger mice, hamsters and rats were 40.2 ± 2.2, 4.8 ± 0.7 and 20.4 ± 5.9 ng/ml and for older females 57.9 ± 5.8, 16.3 ± 1.4 and 7.2 ± 1.4 ng/ml respectively. Levels of LH were significantly higher in aged mice ($P<0.01$) and hamsters ($P<0.001$) and statistically lower in aged rats ($P<0.05$). For the same females plasma LH levels determined by RRA for younger animals in each group were 56.0 ± 2.4, 26.9 ± 4.9 and 30.9 ± 6.4 ng/ml and for aged females 47.2 ± 3.2, 29.7 ± 3.8 and 13.2 ± 1.5 ng/ml respectively. Levels of LH by RRA were significantly higher ($P<0.05$) in younger mice and rats. These data suggest that the LH molecule of older C57BL/6 mice and hamsters is altered with advancing age. (Supported in part by NIH Grant AG00757).

EFFECT OF INCREASED PULMONARY VASCULAR PRESSURE ON ALBUMIN EXCLUDED VOLUME IN THE LUNG. J. C. Parker and A. E. Taylor., Dept. of Physiology, University of South Alabama, Mobile, AL 36688.

The effect of increased pulmonary vascular pressure on the excluded volume fraction for interstitial albumin (F_E) was studied in the lungs of dogs during a steady state period of increased left atrial pressure. A tracheo-bronchial lymphatic was cannulated for recording lymph flow, (Q_L), lymph total protein, and albumin ($C_L(A)$) concentrations. Lung tissue samples were collected and analyzed for tissue blood volume using ^{51}Cr labelled red cells, interstitial fluid (V_I) using the $^{99m}T_c$-DTPA (diethylenetriaminepenta acetic acid) space, and the ^{125}I labelled extravascular albumin (Q_A). Control values for 7 experiments (means ± S.E.) were capillary pressure (P_C) = 8.7 ± 8 cmH_2O, $\dot{Q}_L$ = 20.6 ± 6.7 μl/min, $C_L(A)$ = 1.33 ± .12 gm %, V_I = 2.18 ± .12 ml/g dry wt., F_E = .33 ± .04 and Q_A/V_I = .95 ± .11 gm %. When P_C was increased to 25.6 ± .9 cmH_2O (N=6), the mean steady state values were; $\dot{Q}_L$ = 57.6 ± 21 μl/min, $C_L(A)$ = 1.02 ± .16 gm %, V_I = 3.23 ± .41 ml/g dry wt., F_E = .15 ± .03, and Q_A/V_I = .98 ± .08 gm %. These data indicate that F_E decreased at high vascular pressures and contributed to the reduced colloid osmotic pressure of tissue fluid in the lung. (Supported by NIH HL 22549-02).

LUNG MICROVASCULAR PROTEIN SIEVING DURING ACUTELY ELEVATED LEFT ATRIAL PRESSURE IN SHEEP. R.E. Parker*, R.J. Roselli*, K.L. Brigham and T.R. Harris. Vanderbilt University Medical Center, Nashville, Tennessee 37232.

To see how lung microvessels sieve proteins, we measured plasma (P) and lung lymph (L) protein concentrations in unanesthetized sheep at several left atrial pressures (Pla). While measuring Pla, pulmonary artery pressure and L flow, we inflated a left atrial balloon, increasing Pla in steps and allowing steady state to occur at each Pla(2-5hrs). L flow increased more for a given pressure change at high pressures: Maximum L flow reached 8 times baseline. L/P total protein concentration decreased from a baseline value of 0.645±0.020 S.E.(Pla=2.88±0.85 S.E. cmH_2O) to 0.276±0.009S.E. at the highest Pla(32.0±3.4 S.E. cmH_2O).Relationships between L/P protein concentration and L flow are shown in the figure:



Electrophoretic separation of L and P proteins showed more sieving of larger proteins. Lung microvessels sieve proteins according to size and sieving persists even at very high Pla.

A POSSIBLE VASOCONSTRICTOR ROLE OF VASOPRESSIN IN WATER REGULATION. R. H. Parsons, L. M. Ziemek* and M. J. Saslawsky*, Department of Biology, Rensselaer Polytechnic Institute, Troy, N.Y. 12181

The osmotic water permeability and tritiated water exchange of Rana pipiens measured one day after hypophysectomy increased when compared to control values from 0.38±0.04(34) to 0.66±0.88(33) $g \cdot 100cm^{-2} \cdot hr^{-1} \cdot 200mOsm^{-1}$ and from 0.136±0.03(34) to 0.165±0.06(33) $ml \cdot hr^{-1}cm^{-2}$, respectively. The osmotic water permeability of normal frogs injected with 0.2 ml 1 M NaCl/5g increased from 0.33±0.66(17) to 0.73±0.06(17) $g \cdot 100cm^{-2} \cdot hr^{-1} \cdot 200mOsm^{-1}$ while tritiated water exchange was not significantly affected. Five days following hypophysectomy there was a decrease in the osmotic water permeability and tritiated water exchange such that values did not vary significantly when compared to control data, 0.46±0.08(14) compared with 0.38±0.42(34) $g \cdot 100cm^{-2} \cdot hr^{-1} \cdot 200$ $mOsm^{-1}$ and 0.141±0.12(14) compared with 0.136±0.03(34) $ml \cdot hr^{-1} \cdot cm^{-2}$, respectively. The increase in osmotic water permeability due to hypophysectomy is different from that caused by NaCl or ADH injection since values for tritiated water exchange increased only after hypophysectomy. Since tritiated water is circulation dependent (Mahany and Parsons, 1978, Am. J. Physiol. 234:R172-R177), this data suggests a vasoconstrictor role for endogenous pituitary hormone. If the hormone is removed (i.e., hypophysectomy), vasodialation occurs which results in increased circulation which in turn causes an increased osmotic water exchange.

DEHYDRATION AND RENAL ORNITHINE DECARBOXYLASE (ODC) ACTIVITY IN MICE. K.A.Pass*, H.L.Vallet*, and J.E.Bintz*. (SPON: J.Turinsky). NYS Dept. Health, Birth Defects Inst., and Albany Med. Coll., Albany, N.Y. 12201.

With chronic dehydration pituitary stores of antidiuretic hormone (ADH) and oxytocin are depleted, which suggests an increased secretion of these hormones. When administered to rats, arginine vasopressin increased renal ODC activity (Scalabrino and Ferioli, Endocrinology, 99:1058, 1976), implicating polyamines in the tropic hormonal control of the kidney. No data is available on the effects of dehydration on renal ODC activity. In the present studies in vitro production of $^{14}CO_2$ from 1-^{14}C-ornithine was used as a measure of renal ODC activity. In mice dehydrated for 60 hours, there was a 70% reduction in kidney ODC activity when compared to controls, whereas mice which received only 1.5% NaCl for 60 hours showed no change in renal ODC. In normally hydrated mice both ADH (3 IU/100g) and oxytocin (30 IU/100g) caused large (7X) and significant increases in renal ODC. When given to dehydrated mice, ADH and oxytocin stimulated the already depressed renal ODC although not as greatly as in non-dehydrated animals (1.5 vs. 7X). These results suggest that during the stress produced by water deprivation, renal ODC activity is reduced by mechanisms other than those induced by the normal secretory products of the posterior pituitary.

EPOCH AVERAGING OF THE EVOKED VISUAL RESPONSE. Samuel M. Peacock, Jr. Eastern Pennsylvania Psychiatric Institute, Phila., Pa. 19129

The technique of epoch averaging of the evoked visual responses to two second trains of photic stimulation at various frequencies and intensities reveals a fractionation of the compound visual potential into at least two components. Under certain conditions, a third component is evident which appears to be tightly linked to the alpha rhythm and is quite indistinguishable from it. Brief trains of photic stimulation evoke a variety of parametric dependent responses over most of the "available" cortex. The dependence of these response component characteristics on flash repetition rate and/or intensity suggests differential sensitivities of components of the compound evoked visual potential. These sensitivities infer different anatomical substrates. Of the six divergent fiber groups of the optic tract, three have more or less direct routes to cerebral cortex, the dorso-lateral geniculate or primary visual pathway projecting to the primary visual area 17, a parallel path from superior colliculus to pulvinar to secondary visual areas and frontal eye fields, and a more indirect pre-tectal path to the medial inter-laminar nucleus and from there diffusely projecting to many cortical areas. These three inputs may be represented in these fractionated responses. The data suggests that the evoked visual response is most complex involving at least three pathways and projecting to multiple areas of the cerebral cortex.

CEREBRAL VENOCONSTRICTION IN VITRO. William J. Pearce, Dept. of Physiology, UCLA School of Med., Los Angeles, CA 90024.

Previous studies in our laboratory have demonstrated that the retroglenoid vein, an extracranial continuation of the canine temporal sinus, possesses a dense adrenergic innervation. The present study was undertaken to determine the potential for retroglenoid venoconstriction. The 5 mm of the retroglenoid vein immediately adjacent to the cranium was excised and placed in a bath for measurement of resting and developed tension. When stretched to an optimum resting tension of 1.75 to 2.0 g, these rings produced 1.08 ± .30 g of active tension in response to 10^{-7} M norepinephrine. Electrical stimulation at 8 Hz, 100 v, and pulse duration of .3 msec produced an active tension of 1.01 ± .57 g. Because the effects of electrical stimulation were blockable by phentolamine and tetrodotoxin, it is concluded that the retroglenoid vein constricts in response to sympathetic stimulation. This suggests that constriction of this vein may contribute to the variations in the observed effects of sympathetic stimulation on cerebral blood flow. (Grant support: AHA-CLAA 437IC.)

A DUAL ROLE FOR INSULIN IN CELLULAR TRANSPORT. T.W. Pearson and S.B. Horowitz*. Cell Physiology Lab., Michigan Cancer Foundation, Detroit, MI 48201.

We find that insulin increases α-aminoisobutyric acid (AIB) and 3-*O*-methyl-D-glucose (3*O*MG) uptake from media by *Rana pipiens* oocytes. This allows utilization of cryomicrodissection to study the hormone's specific influences on nucleus and cytoplasm. Cells were incubated in 1.6 mM ^{14}C-AIB, 1.0 mM ^{3}H-3*O*MG Ringers at 20°C in the absence and presence of insulin (sodium-insulin, 1U/ml) for various times, frozen in liquid nitrogen to prevent subsequent solute redistribution, and the nucleus and cytoplasmic samples isolated at -45°C and analyzed for water, K^+, Na^+, ^{3}H-3*O*MG and ^{14}C-AIB contents. Insulin and time dependent shifts in K^+, 3*O*MG, and AIB concentrations are observed in nucleus and cytoplasm. These can be attributed to two cellular responses: (1) a change in the membrane-determined steady state levels of diffusive (or free) solute concentrations, and (2) a decrease in the cytoplasmic water volume accessible to these solutes. Insulin's "transport" effects therefore include modulation of the cell membrane as well as modulation of solute distributions in the intracellular space. The significance of this dual role to the hormone's multifaceted metabolic actions will be considered. (Insulin was a gift of Eli Lilly & Co. Supported by NIH grants GM19548 and HD12512 and an institutional grant from the United Foundation of Greater Detroit.)

The mechanism of lipidosis in the hearts of rats fed a high fat-high erucic acid diet. S.D.Peckett, S.C.Vasdev and K. J.Kako, Dept. of Physiol., Univ. of Ottawa, Ottawa, Ont.

This study deals with triglyceride (TG) accumulation which occurs in the hearts of rats which have consumed a high fat diet containing a large amount of erucic acid (22:1) as a component fatty acid. Rats of weaning age were fed for 1 week a synthetic diet containing 20 % by weight of corn oil (C-rats) or mustard seed oil (M-rats). The cardiac TG content of the M-rats increased to a level 5-times greater than that of the C-rats; nearly a half of the TG fatty acids consisted of erucic acid. Furthermore, erucic acid was localized almost exclusively at positions 3 and 1 of the TG molecules of the M-rats, and there was little accumulation of normal TG containing C-16 and C-18 fatty acids. The enzyme activity of phosphatidate synthesis was increased significantly in the hearts of the M-rats, but a negligible amount of erucic acid was incorporated into position 2 of the glycerol molecule. The rate of TG lipolysis of the M-rats was greater than that of the C-rats. These results, together with our previous findings, suggest i) that fatty acids accumulate in the hearts of the M-rats because erucic acid is oxidized slowly and because it inhibits the oxidation of other fatty acids, and ii) that the turnover rate of cardiac TG in the M-rats is increased; moreover, fatty acids,derived from the hydrolysis of the TG, are oxidized at an unequal rate, leaving the heart tissue with a greater quantity of TG molecules containing erucic acid.

SERUM DIGOXIN CONCENTRATIONS IN DOGS BEFORE AND DURING CONCOMITANT ADMINISTRATION OF FUROSEMIDE. W. M. Pedersoli,* and R. F. Nachreiner* (SPON: S. D. Beckett). Auburn Univ., Auburn, AL 36830 and Michigan State Univ., East Lansing, MI 40909.

Healthy dogs were treated once a day for 16 days with a liquid, oral dosage form of digoxin (0.022 mg/Kg). From day 9 to 16 they were also injected intramuscularly with furosemide (4.4 mg/Kg). Serum digoxin was measured by a radioimmunoassay technique. Eight hours after the 8th dose of digoxin had been administered, serum digoxin was in the accepted therapeutic range. After 8 days of concomitant administration of digoxin and furosemide serum digoxin was found to be in the accepted moderate to severe toxic range. Clinical signs of digitalis toxicosis were consistently observed during the combined digoxin plus furosemide treatment period. There was no significant ($P>0.05$) difference between the serum concentrations of potassium, sodium, and osmolality during digoxin treatment alone. Serum creatinine concentrations remained within the accepted normal range for dogs. Serum sodium concentration was significantly ($P<0.05$) lower during combined digoxin plus furosemide treatment when compared to digoxin treatment only. Results indicate that an interaction between digoxin plus furosemide occurred which led to significantly ($P<0.05$) higher concentrations of serum digoxin during combined digoxin and furosemide treatment. (Supported in part by funds from the Scott-Ritchey Program, A.U.)

EFFECT OF STEROIDS ON INTRAVENOUS SODIUM ARACHIDONATE. J.C. Penhos, M. Montalbert-Smith, E. Ramey and P. Ramwell. Georgetown University Medical Center, Department of Physiology and Biophysics, Washington, D.C. 20007.

Previously we have shown that (i) corticosteroids protect mice treated (i.v.) with arachidonic acid (50 mg/kg) and (ii) there is a significant increased mortality of the male mice. To determine the effect of the gonads, the following groups of castrated mice (3 weeks before) were treated with estradiol (0.1 mg/kg), testosterone (1 mg/kg), progesterone (1 mg/kg) or cortisol (2.5 mg/kg) twice a week during two weeks. Estradiol treatment significantly reduced the mortality in normal and castrated males. Testosterone and progesterone significantly increased the mortality in these groups and in castrated females. Cortisol treatment significantly reduced mortality in all four groups. It is suggested that sodium arachidonate has a dual effect: (1) a thromboembolic action in the lung capillaries which is reduced by estradiol (or absence of androgens) and (2) a stressing effect which is attenuated by cortisol. In contrast, both testosterone and progesterone exacerbated the effect of arachidonate. It is possible that arachidonate metabolism may be modified by gonadal hormones. (Supported in part by NIH Grant HL 18718-04.)

CARDIAC CELL ALTERATIONS IN PRE- AND POSTNATAL CARBON MONOXIDE (VOLUME OVERLOAD)-INDUCED CARDIOMEGALY. D. Penney, C. Doyle*, M. Baylerian*, K. Fanning* & G. Davis*, Depts. of Physiol. & Anatomy, Wayne St. Univ. Med. Sch., Detroit, MI 48201

Pregnant rats were exposed to 200 ppm CO for 18 days. Newborns inhaled 500 ppm CO for 32 days. As previously reported (Penney), cardiomegaly was seen in the 1st group at birth (b.) and was maximal in the 2nd group 14-21 days after b. Whole heart DNA conc. was lower at b. in CO fetuses than in controls. Changes in DNA conc. 1 and 2 weeks after b. suggest that both hypertrophy and hyperplasia take part in early postnatal cardiomegaly. DNA conc. fell after b. in both CO and controls, with a transient rise at 14 days, a time when muscle cell binucleation increases most rapidly. DNA conc. 76 days following postnatal CO was about 10% that at b., but DNA conc. in left ventricle (LV) and interventricular septum in CO hearts was higher than controls. DNA content reached a plateau 14 days after b. Hydroxyproline (hypl.)(an index of collagen) conc. was lower in newborns treated with CO as fetuses. Hypl. conc. increased gradually 3-fold from b. to 105 days of age in both postnatal CO and control rats. Hypl. content was unaltered by cardiomegaly, rather increasing as in normal development. Hypl. conc. was higher in right ventricle than LV. Histological examination of the hearts showed an increase in cell size, binucleation, mitochondria and connective tissue with age. Mitotic activity is common in both muscle and non-muscle cells. Non-regressive cardiomegaly seen earlier cannot be explained by changes in DNA and hypl. (NIH gr. HL-22859-01)

HORMONAL INFLUENCES ON THE SECRETION OF LUNG FLUID IN THE FETAL GOAT. Anthony M. Perks and Sidney Cassin. Dept. Physiol., Univ. of Florida Coll. Med., Gainesville, Fla, 32610.

Fetal lungs secrete fluid in volumes which approach those of the kidneys; however, little is known of any controls, and the following study investigated the possible effects of hormones. Fetal goats (95-148 days gestation) were delivered by Caesarian (chloralose, 50 mg/kg), and the umbilical circulation was left intact. Fluid production was determined by the rate of dilution of Blue Dextran 2000 (Pharmacia), added directly to the lungs (200 mg/fetus); 0.5 ml samples were withdrawn every 10 mins from a tracheal cannula. Prolactin (NIH, P-S-11, ovine), added directly to the lung fluid, at 2.5-10.0 μg/ml, stimulated flow. At 10 μg/ml, rises averaged 1.1, 1.4 and 2.6-fold in succeeding hours (significant at $P< 0.01$ and < 0.001, last two hours, respectively). There was a parallel increase in the secretion of Na^+ and Cl^-, but not of K^+. Saline controls gave no effects. Synthetic pentagastrin (0.1-2.5 μg/kg/min, i.v.) did not stimulate flow. Epinephrine (0.1-2.5 μg/kg/min, i.v.) gave increasing periods of reabsorption. Vasopressin (Pitressin; 38-1258 mU/ml), added directly to the lung fluid, produced reabsorption for periods up to 20 mins. Synthetic arginine vasopressin (AVP; Sigma), infused i.v. at 10-20 mU/kg/min, gave a prolonged reabsorption of fluid, which was increased by lung expansion, or epinephrine. It is suggested that prolactin may stimulate lung secretion, while AVP, epinephrine and inflation may combine to remove fluid at birth.

BIPHASIC ALTERATIONS IN TRANSMITTER RELEASE INDUCED BY LIPID A AT THE FROG NEUROMUSCULAR JUNCTION. Robert J. Person. Dept. of Physiology and Biophysics, Univ. of Oklahoma Health Sciences Center, Oklahoma City, OK 73190.

Previous work has shown that derivatives of the cell wall of gram negative bacteria depress neuromuscular transmission by reducing quantal release; spontaneous release is depressed although crude extracts (ie, endotoxin) may transiently increase release rates. Standard intracellular recording techniques were used to record spontaneous miniature endplate potentials (MEPPs) and evoked endplate potentials (EPPs) at frog sartorius neuromuscular junctions. Muscles were superfused with a suspension of Lipid A derived from S. Minnesota Re-595 in phosphate-buffered Ringer's with various levels of [Ca]. MEPP frequency transiently increased, peaking at 12±5 times control (19 junctions), then decreased to 0.1-10% of control at concentrations of 1-10 μg Lipid A/ml bath. No significant change in MEPP amplitude was observed. EPP amplitude transiently increased to 1.5-2 times control then declined to an asymptotic value or to complete failure of evoked release as a function of concentration of Lipid A. Changes in EPP amplitude were accompanied by corresponding changes in quantal content; the facilitation ratio of paired EPPs increased as EPP declined. These results suggest that Lipid A, presumably, the membrane-toxic component of the bacterial cell, may transiently increase Ca permeability across the presynaptic terminal membrane prior to isolating the membrane. (Supported by Biophysics Section, ONR, N00014-77-C-0630).

EFFECT OF BARORECEPTOR DENERVATION ON $+G_z$ TOLERANCE IN DOGS D. F. Peterson and V. S. Bishop. Oral Roberts Univ. Med. Sch. Tulsa, OK, 74171 and UTHSCSA, San Antonio, TX 78284

Nineteen of 27 mongrel dogs underwent sterile surgery in order to either selectively denervate carotid sinus baroreceptors (CSD:N=9) or to totally denervate arterial baroreceptors (TD:N=10). After 10 days recovery, under light alpha chloralose anesthesia, a solid state Millar catheter was passed via the femoral artery to measure aortic arch pressure. ECG and heart rate were obtained. Each dog was then immobilized on the end of a 4m centrifuge arm for one minute exposure to constant $+G_z$ acceleration. Transient hypotension was observed during $+3G_z$ for control (C) and CSD dogs with gradual return to control. Initially tachycardia occurred in both groups. TD dogs underwent a sudden, dramatic drop in blood pressure (-67 ± 11%) which persisted until $+G_z$ acceleration ended. Bradycardia (-28 ± 8% maximum) persisted in TD dogs. The ability of a bladder-type, anti-G suit to extend $+G_z$ tolerance was tested by observing responses to $+6G_z$ during suit inflation. Maintenance of aortic arch pressure was obtained at $+6G_z$ for both C and CSD dogs with the suit inflated. TD animals underwent a dramatic, persistent fall in blood pressure. Results indicate that totally baro-denervated dogs cannot control aortic arch pressure during $+3G_z$ acceleration whereas both control dogs and those with intact aortic arch receptors maintain pressure. Additionally, the anti-G suit cannot maintain aortic arch pressure at $+6G_z$ unaided by functional arterial baroreceptors. Supported by AFOSR 73-2525.

Electrical & Mechanical Correlates of Isometric Fatigue in Cat Skeletal Muscle

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The height and duration of muscle fiber action potentials, motor nerve action potentials, the rise time, height, and half relaxation time of a muscle twitch, and maximum velocity of shortening for isotonic contractions were measured before, during and after fatiguing isometric contractions of the medial gastrocnemius muscle of the cat. Fatiguing isometric contractions were induced in these muscles by sequential electric stimulation of groups of axons from the L6, L7, and S1 ventral roots with the appropriate stimulus amplitude and frequency to sustain the tensions. The results of these experiments showed that although the action potential frequency and height were uneffected by fatigue, the twitch characteristics and velocity of shortening were markedly effected by the fatigue process. The implication of these findings is that isometric fatigue is not due to electrical fatigue.

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BLOOD PRESSURE, ADH, WATER AND ALCOHOL DRINKING LEVELS WITH CHRONIC CENTRAL ANGIOTENSIN INFUSIONS. M. Ian Phillips, Valerie Kalter,* Robert Lewis,* and Louise Rosenbaum,* Dept. of Physiology, University of Iowa, Iowa City, Iowa 52242

Numerous studies have shown that acute injections of angiotensin II (AII) into brain ventricles (IVT) reliably elicit drinking and pressor responses. Here we report the effects of chronic AII infusions IVT over 7 days. Gronan and York (1977) showed no increase of blood pressure (BP) to 100 ng/hr AII. We have used two higher doses infused via Alzet osmotic pumps. Rats cannulated in the lateral ventricle had baseline levels of drinking water or alcohol (12%) and of BP determined over three days. Pumps were then implanted subcutaneously. Controls received saline (1ul/hr) or were unoperated. Experimentals received 1ug/hr or 6ug/hr AII.

With the low dose, water drinking rose progressively from 35ml to 130ml per day, ANOVA $p<.001$ but BP did not rise. Urine flow increased then leveled out despite increased drinking. Vasopressin levels measured at day 7 by RIA (n=5) were elevated ($p<0.02$) over control levels. Drinking lasted 24 hours after pumps had expended. Alcohol drinking (12-27ml/day) was induced by AII in 40% rats. At high dose, water drinking was 160+ml per day. BP rose above control levels at days 5 and 6 (130-200mmHg).

Thus, chronic AII infusions increase ADH release and drinking at a lower dose than BP is increased. This may reflect baroreceptor reflex regulation. Alcohol drinking to chronic AII was not consistently elevated. (Supported by NSF).

ALVEOLAR-CAPILLARY EQUILIBRATION KINETICS OF CO_2: MEASUREMENTS BY REBREATHING IN MAN AT REST AND DURING EXERCISE. J. Piiper, M. Meyer and P. Scheid. Abteilung Physiologie, Max-Planck-Institut für experimentelle Medizin, D-3400 Göttingen, FRG

Alveolar-capillary equilibration of CO_2 was measured by a rebreathing technique using the stable isotope $^{13}CO_2$. The rebreathing mixture contained 0.07% $^{13}CO_2$, 1% He, 1% C_2H_2, 3% O_2 and 7.5% $^{12}CO_2$. The partial pressures of all these gases were continuously recorded by mass spectrometry. From the kinetics of $^{13}CO_2$ equilibration (and other parameters) the following average values for the alveolar-capillary CO_2 conductance (in $ml \cdot min^{-1} \cdot torr^{-1}$) were obtained in 3 healthy males (28 - 33 years): at rest, 180; during bicycle ergometer exercise (75 watt), 310. Comparison with D_L for CO and O_2 measured in the same subjects and with in vitro data on CO_2, equilibration kinetics in blood suggests that alveolar-capillary CO_2 equilibration is mainly limited by $CO_2/HCO_3^-/H^+$ equilibration between red cells and plasma. Calculations show that the limitation to CO_2 transfer resulting from finite equilibration kinetics is slight at rest, but of considerable extent in heavy exercise.

ENERGY EXPENDITURE WHILE STANDING OR WALKING SLOWLY UPHILL OR DOWNHILL WITH LOADS. Nancy A. Pimental* and Kent B. Pandolf. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760

Eight males (24 yr, 176 cm, 79 kg) stood, or walked 0.5 or 0.9 m/s for 20 min on grades of −10 to +25% with loads of 20 or 40 kg. Energy expenditure (watt) was not significantly different in any of the standing conditions; grade and load increased energy expenditure while standing but not sigificantly. Although the standing energy expenditure means were relatively low, high perceived exertion ratings suggest limits to tolerance time in some conditions. All standing means were significantly lower than walking means. Walking 0.9 m/s on a -10% grade was significantly lower than walking 0.5 m/s on a +10% grade, which was significantly lower than walking 0.9 m/s on a +10% grade. While walking, there was a significant difference between loads: means for the 20 kg loads were lower than means for the 40 kg loads. As the condition became more strenuous by increasing load, speed, and/or grade (while walking), energy expenditure became more sensitive to changes in these variables. The current energy expenditure prediction formula (Pandolf et al., J. Appl. Physiol. 43:577, 1977) was found to predict slightly high for standing conditions, low for walking 0.5 m/s on a +10% grade, and accurately for walking 0.9 m/s on a +10% grade. In the standing conditions the deviation between predicted and measured was higher at the 40 kg load than the 20 kg load. The formula is not equipped to predict for negative grades. This study suggests that the prediction formula may place too much emphasis on the effects of speed and load while standing and walking slowly.

CREATION AND HEMODYNAMIC CHARACTERIZATION OF CHRONIC VOLUME OVERLOAD. W.W. Pinsky*, R.M. Lewis*, C.J. Hartley*, M.L. Entman* (SPON: L.H. Michael). Depts. Pediatrics (Lillie Frank Abercrombie Sec. Cardiology) and Medicine (Cardiovascular Sciences) Baylor Coll. of Med., Houston, Texas.

Chronic ventricular volume overload (CVVO) results in cardiac dysfunction that may not be reversible by surgical repair. To study the altered function and its reversibility, we instrumented 18 previously healthy dogs (27-31 Kg) so that in the awake state, the following could be measured: LV systolic and end-diastolic pressures (LVP and LVEDP); first derivative of LVP (LVdP/dt); systemic arterial pressure (SBP); circumflex coronary artery blood velocity (CBF); LV systolic (ESL) end-diastolic (EDL) muscle segment lengths. An 8-10mm dacron conduit was inserted between the infrarenal abdominal aorta and the IVC. At weekly intervals for 10-12 wks the indices were recorded in the awake state at rest, followed by α stimulation (phenylephrine), and by β stimulation (isoproterenol). The conduits were then ligated, and the measurements repeated for another 8 wks. Compared to control (C) at rest, after shunting EDP, CBF, ESL and EDL ↑ ($p<0.02$) and dP/dt/EDP ↑ ($p<0.02$). With α stimulation, the shunted dogs' EDP ↑ more, dP/dt and dP/dt/EDP ↓ more and ESL, EDL and CBF ↑ less than C ($p<0.02$). With β stimulation dP/dt and dP/dt/EDP ↑ less than C ($p<0.02$). Eight wks following the ablation of the overload no improvement was observed at rest or with α and β stimulation. CVVO causes ↓ contractility with ↓ compliance that does not ameliorate after correction.

DIMETHYLBENZANTHRACENE SUPPRESSION OF MAMMARY GLAND NUCLEIC ACID SYNTHESIS AND LACTATION. Howard S. Pitkow, Charles Rice*, Robert Christman*, and Debra Scalpato*. Penna. Col. of Podiatric Med., Phila., PA 19107

In order to determine the effects of Dimethylbenzanthracene (DMBA) on mammary gland growth and function, female adult Long-Evans rats (12 animals/group) were intraperitoneally injected daily with 1 mg DMBA in sesame oil on days 8 through 12 of pregnancy. On days 1, 6, 11, 21 post-partum mothers were autopsied and their abdominal-inguinal mammary gland dry weights and nucleic acid contents determined. On days 1 and 21 of lactation the gland dry weight, RNA, and DNA were significantly less in the DMBA injected groups when compared to control values. No significant differences in these parameters were found on days 6 and 11 post-partum. However, the litter weight of the experimental group was significantly less on day 6 ($p<0.01$). Our data suggests that small amounts of DMBA in pregnancy significantly decreases mammary gland growth and secretion by day 1 of lactation. Milk was not yet readily available to the pups as indicated by the retarded pup growth on day 6 ($p<0.01$). Since no significant differences existed between gland weights and nucleic acid contents on days 6 and 11 we feel that a mammary gland rebound phenomena occurs enabling the DMBA pup weights to become comparable to that of controls by day 11. By day 21 post-partum the significant differences between the gland weight and nucleic acid contents suggest that DMBA enhances mammary gland involution.

A MODEL OF THE ROLE OF PROSTAGLANDINS (PG) AND OXYGEN (O_2) IN VASCULAR SMOOTH MUSCLE (VSM) CONTRACTION. R. N. Pittman. Dept. of Physiol.,Med. Coll. of Va., Richmond, VA 23298

Data from several VSM preparations suggest that altered contractile activity in response to changes in bathing fluid PO_2 may be mediated by PG. Usually decreases in solution PO_2 below a critical level cause graded relaxation. Kalsner has measured increased release of a vasodilator PG-like substance in response to hypoxia in bovine coronary artery. To assess the link between available O_2 and PG production, a mathematical model was developed relating the concentrations of O_2, arachidonic acid (AA) and PG in a slab of VSM. It is assumed that anoxia leads to increased AA production and PG synthesis requires O_2 and AA. Thus, in hypoxic VSM most AA is formed in the central anoxic core and diffuses to the surrounding normoxic tissue where AA and O_2 are utilized in PG synthesis. An equation expressing PG output as a function of solution PO_2 was derived. Qualitative agreement was obtained between the model and Kalsner's data. In the lamb ductus arteriosus and bovine pulmonary artery, severe hypoxia leads to a return of force to pre-hypoxic levels. These findings are consistent with this model but were not observed by Kalsner. Experimental tests of the model will require the determination of AA formation and PG synthesis in VSM as a function of PO_2 as well as an assessment of energy limitation and the involvement of other vasoactive substances. (Supported in part by NIH grant HL18292)

IMPAIRED CORTICAL MICROPRESSURE AUTOREGULATION IN CONTRALATERAL KIDNEYS OF GOLDBLATT HYPERTENSIVE RATS (GHR). D. Ploth, R. Roy* and L.G. Navar. Univ. of Alabama Medical Center, Birmingham, Alabama 35294.

The impaired autoregulation of GFR and renal blood flow (RBF) of contralateral kidneys of two kidney GHR was further evaluated by testing the efficiency of autoregulatory adjustments of microvascular and tubular pressures during acute reductions in blood pressure (BP). Cortical micropressures were measured with a servo-nulling device in GHR and in normal rats prepared with pentobarbital anesthesia. Renal BP was altered by constricting a clamp between the renal arteries. At spontaneous BP of 169±5 mmHg ($\bar{x}$±SEM), kidney GFR in the GHR was 1.35±.07 ml/min, sodium excretion ($U_{Na}V$) was 1.60±.66 µEq/min, and urine flow rate (V) was 22±6 µl/min. At a clamped renal BP of 120±1 mmHg kidney GFR, $U_{Na}V$, and V were reduced to .78±.07 ml/min, .071±.021 µEq/min, and 5±1 µl/min. At spontaneous BP proximal tubule pressure was 16.0 ±.7, peritubular capillary pressure was 11.7±0.6 and distal tubule pressure was 11.4±1.6 mmHg. All decreased significantly to 13.0±.3, 10.1±.3, and 8.8±.8 mmHg, respectively, with acute BP reduction to 120 mmHg. Normal animals autoregulated GFR, RBF, and micropressures efficiently when renal BP was reduced from 130 to 115 mmHg. The micropressure observations provide further evidence for impaired ability to adjust intrarenal vascular resistances in the contralateral kidney indicating that normal renal hemodynamic function can be achieved only at elevated BP.

THE EFFECT OF PROSTAGLANDIN E_1 (PGE_1) ON PULMONARY VASCULATURE IN MICROEMBOLISM SYNDROME (MES) IS TIME DEPENDENT. Poddar, P.K.*, E.C. Peirce II, and B. Kent. Depts. Surg & Physiol. Mt. Sinai Sch. Med. & Bronx V.A. Med. Center, N.Y.,N.Y.

PGE_1 is a known potent vasodilator. Pretreatment with PGE_1 (1mcg/kg/min) increases the survival rate in dogs in which MES is produced by raising pulmonary artery pressure (PAP) by 300% of baseline with injection of microfibrillar collagen. To establish the time course of effectiveness, PGE_1 was infused at 5, 30 and 60 min. after MES in 3 groups of 5 dogs (groups I, II, and III respectively). A control group (C) of 7 dogs was not given PGE_1. The results are shown as mean changes in pulmonary vascular resistance (PVR) and PAP after a 30 min. PGE_1 infusion. The controls are changes at comparable times without PGE_1.

			I	II	III
PVR	mmHg/L/kg	C	-3.0*	1.6	0.7
		PGE_1	-5.2*	0.4	0.1
PAP	mmHg	C	-5.7*	-2.2	-0.3
		PGE_1	-15.4*	-8.0	-2.8

*$P < 0.01$

The significant decrease in PVR and PAP in group I correlates with a significant increase in survival (control, 7/7; I, 1/5 died, $P<0.05$). The loss of the ability of PGE_1 to lower PVR and PAP with delayed administration in II and III is accompanied by a decrease in survival (II, 3/5; III, 4/5 died). The mechanism by which PGE_1 increases survival in MES is linked to pulmonary vasodilatory effects which are lost with time.

HEMODYNAMIC EFFECTS OF DOPAMINE AND DOPAMINE-GLUCAGON FOLLOWING HEMORRHAGE AND BLOOD REPLACEMENT. T. C. Poder*, J. P. Rosborough*, and S. I. Deavers. Texas Woman's University and Baylor College of Medicine, Houston, Texas 77030

Two groups of anesthetized dogs were bled to a mean arterial pressure of 50 mmHg. This pressure was maintained for 90 minutes and then the shed blood was replaced. In Group I, after an interval of 60 minutes, dopamine (6 µg/kg/min) was infused for 60 minutes. In Group II, dopamine (3 µg/kg/min) and glucagon (0.4 µg/kg/min) were infused for 60 minutes. No significant changes in cardiac output were observed in the preinfusion period between the groups. Postinfusion cardiac outputs were significantly ($p < 0.025$) different between the groups: in Group I, after dopamine alone, cardiac output decreased, whereas in Group II, after dopamine and glucagon, cardiac output increased. Renal blood flow was significantly different between the groups, both before ($p < 0.025$) and after ($p < 0.01$) drug infusion. In addition, renal blood flow increased significantly both after the infusion of dopamine ($p < 0.05$) and after the infusion of dopamine-glucagon ($p < 0.01$). (Supported by TWU Grant #0932.)

INFLUENCE OF A HIGH CARBOHYDRATE DIET ON GLYCOGEN REPLETION AFTER EXERCISE IN RAT MUSCLES. James L. Poland and Carolyn Trowbridge* Med. Coll. of Va., Richmond, VA 23298

The supercompensation of human skeletal muscle glycogen during recovery after exhaustive exercise, is reportedly greatest with a high carbohydrate diet. In experimental rats fed standard laboratory chow (51% carbohydrate), exercise induced glycogen supercompensation has been observed in cardiac but not skeletal muscle. The current study was made to determine if a high carbohydrate diet (70% carbohydrate) would facilitate glycogen supercompensation in rat skeletal muscles. Though the high carbohydrate diet produced in resting rats an elevation in liver glycogen (70 vs. 50 mg/mg), there were no significant increases in the glycogen levels of cardiac, soleus, red vastus lateralis (RVL), or white vastus lateralis (WVL) muscles. Also unchanged were the levels of blood glucose, plasma free fatty acids (FFA), and triglyceride concentrations in cardiac, soleus, RVL and WVL muscles. The rats on the high carbohydrate diet displayed no greater glycogen depletion during swimming and no alterations in the pattern of glycogen repletion at 0, 4 and 7 hours following the exercise. During recovery both groups showed constant levels of blood glucose and no glycogen supercompensation in skeletal muscles, but similar increases in myocardial glycogen and in plasma FFA. It is concluded that even with a high carbohydrate diet, exercise in rats sufficient to produce myocardial glycogen supercompensation does not generate glycogen supercompensation in skeletal muscles. (Supported by a grant from Muscular Dystrophy Association)

SEROTONIN POTENTIATES NERVOUS STIMULATION OF MUCUS GLAND SECRETION IN CANINE TRACHEA IN VIVO. D. Popovac*, R. Chinn*, P. Graf*, J. Nadel and B. Davis. CVRI and Depts of Physiology and Medicine, UCSF, San Francisco, California

We prepared dogs with cut superior laryngeal nerves (SLN) on stimulating electrodes and cannulae in both cranial thyroid arteries for drug infusion. We exposed the upper tracheal mucosa and sprayed it with powdered tantalum. Secretions from the mucus glands caused elevations (hillocks) in the tantalum layer. In an area (1.2 cm^2) of tantalum coated epithelium, we counted the hillocks and measured the dia of 6 round hillocks after stimulating a SLN electrically with increasing frequency (5 V, 0.5 - 20 Hz, 15 sec) A) before, B) during, and C) after a subthreshold infusion of serotonin (1 mg/ml).

Hertz		0.5	1	2	4	6	8	10	20	
Number of Hillocks	A	3	5	14	28	33	43	48	45	B>A
	B	12	17	31	51	50	65	63	71	$p<0.01$[1]
	C	2	4	11	26	40	46	59	68	
Diameter of Hillocks (mm)	A	0	0	0.1	0.2	0.2	0.3	0.4	0.5	B>A
	B	0.1	0.1	0.2	0.3	0.3	0.4	0.4	0.5	$p<0.01$[1]
	C	0	0	0.1	0.2	0.2	0.3	0.3	0.4	

The table shows mean values from 6 dogs. These studies show that serotonin potentiates nervous stimulation of mucus gland secretion in canine trachea. (Supported in part by NHLBI Grants HL-06285 and HL-21150 and the Cystic Fibrosis Foundation) ([1]analysis of covariance)

EFFECT OF LEVODOPA ON ARTERIAL BLOOD PRESSURE DURING REWARMING FROM HYPOTHERMIA. Pava Popovic,* Vojin Popovic and A. Dimova.* Dept. of Physiology, Emory Univ., Atlanta, Ga. 30322

Levodopa administered in large doses induces hypertension in normothermic and in hypothermic rats. In this work, the effect of levodopa on mean arterial blood pressure was studied in hypothermic rats during rewarming. Twenty-eight unanesthetized female Sprague-Dawley rats were used in experiments. Levodopa or norepinephrine were administered through the chronic aortic cannula in doses that produced similar hypertensive response. In hypothermic rats (body temperature 17°-18°C), norepinephrine induced hypertensive response lasted 15 min. The pressor response after levodopa administration lasted much longer, 4 hrs or as long as the animal was kept at a low body temperature of 17°-18°C. When the animal was rewarmed, the arterial blood pressure decreased as soon as the body temperature reached 21°C. At this temperature one observes first shivering, and the thermoregulatory mechanisms are again in full action. Our results demonstrate that with the onset of shivering the levodopa induced long lasting hypertensive response in hypothermic animals is terminated. Body cooling below a temperature of 20°C seems to inactivate the enzyme dopamine beta hydroxylase.

PULMONARY VASCULAR HISTAMINE-1 RECEPTOR: A FUNCTIONAL SUBUNIT OF THE ALPHA ADRENERGIC SYSTEM. R.J. Porcelli, D.F. Ventura*, E.J. Guidi*, E.H. Bergofsky, SUNY, Stony Brook and VAMC, Northport, N.Y. 11768

The pharmacologic blockade or release of alpha receptors greatly affects histamine-stimulated H-1 responses in pulmonary vascular smooth muscle (JAP, 34:483-8, 1973). To analyze further the inter-relations of these 2 important receptors, we studied the effect of diminished availability of alpha receptors in the histamine-induced pulmonary vasoconstriction in the perfused feline lobe utilizing two approaches: 1) enhanced beta activity, achieved by epinephrine or isoproterenol infusions, raised lobar venous c-AMP effluent and reduced pulmonary vasoconstrictor responses to histamine by 80%, 2) norepinephrine, designed to leave residual agonist at the alpha receptors after a series of infusions also greatly reduced histamine vasoconstrictor responses (by 52%); this effect was not mediated by beta enhancement, since c-AMP generation, compared to that produced by EPI or ISO, was meager. The effect of diminished availability of alpha receptors on pulmonary vasoconstriction was limited to histamine; pulmonary vasoconstrictor responses to other agents, such as serotonin, were unaffected by limited alpha receptor availability. These data suggest the pulmonary vascular H-1 receptor is a functional sub-unit of the alpha receptor. (Supported by NHLBI Grant #HL-17711 and HL-23210, the Veterans Administration, and the James S. Mountain Memorial Fund.)

EFFECTS OF LEAD (Pb) ON THE RENAL RESPONSE TO EXTRACELLULAR VOLUME EXPANSION (VE). W.J. Powers* and E.C. Foulkes, Depts. of Environ. Health & Physiol., Univ. of Cincinnati Col. of Med., Cincinnati, Ohio 45267

Rats given 0.5% lead acetate for 3 weeks show a depressed natriuretic response to VE with 0.9% saline IV (5% body wt.). In 4 control animals, VE increased urine flow from 6 ± 1 (SEM) to a maximum of 66 ± 16 µl/min, and Na excretion similarly from 0.5 ± 0.2 to 11.3 ± 0.9 µEq/min. Corresponding values in 8 Pb-exposed animals were: urine flow 6 ± 1 to 30 ± 7 µl/min, Na excretion 0.9 ± 0.3 to 7.8 ± 1.9 µEq/min. GFR changed in control animals from 2.0 ± 0.4 to 2.4 ± 0.3 ml/min and in the Pb group from 1.8 ± 0.2 to 2.6 ± 0.4 ml/min. Blood Pb levels were: control, 3.3 ± 0.3 µg%; exposed, 56.9 ± 6.4. Because depression of the natriuretic response in the Pb group could not be explained on the basis of a reduced GFR, influence of mineralocorticoids was next tested. Control and Pb-exposed animals were pretreated with 25 mg/kg DOCA. In 9 DOCA-treated controls, VE increased urine flow from 5 ± 1 to a maximum of 46 ± 6 µl/min; similarly Na excretion rose from 0.6 ± 0.2 to 13.1 ± 1.7 µEq/min. Nine DOCA-treated Pb-exposed animals showed maximal changes of 5 ± 1 to 27 ± 3 µl/min and 0.5 ± 0.1 to 8.4 ± 1.3 µEq/min. Since depression of the natriuretic response by Pb cannot be explained by changes in either GFR or circulating mineralocorticoid, these preliminary studies suggest that Pb interferes with the "third factor" response to VE. Supported by NIH grant ES 00159.

DOES END SYSTOLIC PRESSURE (ESP) DETERMINE END SYSTOLIC VOLUME (ESV)? R.M. Prewitt*, L. Oppenheimer*, H. Goldberg*, J. Rabson*, J. Sutherland*, and L.D.H. Wood*. (Spon: J.A. Moorhouse). University of Manitoba, Winnipeg, Canada.

We measured left ventricular (LV) ESV and ESP in 7 anaesthetized ventilated dogs pretreated with propranolol (1.5 mg/kg) before (1) and 5 minutes after (2) opening a large arteriovenous shunt and expanding plasma volume with dextran infusion. Thermal dilution cardiac output and stroke volume (SV) doubled between 1 and 2. Real size biplane ventricular areas were obtained at end-diastole using R-wave gated equilibrium nuclear cardiology techniques, and end diastolic volume (EDV) were calculated according to the area-length equation. Then ESV=EDV-SV. Although mean (±SD) ESP increased ($P<.05$) from 1 (120±32) to 2 (132±23), ESV (ml) decreased ($P<.005$) from 1 (29±8) to 2 (19±10). These results indicate that ESV is not uniquely determined by ESP, and suggest an alteration in the LV systolic pressure-volume relationship as a function of outflow impedance. Since mean ejection velocity also doubled in 2, left ventricular force-velocity characteristics also vary with outflow impedance. One explanation is that contractile element velocity is unchanged between 1 and 2, but the velocity and extent of muscle shortening is increased in 2 because there is less opposition to shortening of the series elastic elements during ejection against a reduced resistive afterload. (Supported by the Canadian Heart Foundation).

THE EFFECTS OF THE INTRINSIC CARDIAC NERVES (ICN) ON ATRIAL ELECTRICAL CONDUCTION. D.V. Priola and M.B. Curtis*. Univ. of New Mexico, School of Medicine, Albuquerque, NM 87131.

Nicotinic (NIC) stimulation of the ICN has previously been shown to depress atrial and ventricular contractility and slow AV nodal conduction; no effects were noted on the specialized ventricular conduction system. The present study was done to determine the influence of the ICN on electrical conduction in the atrium. Ten dogs were placed on cardiac bypass and recordings were taken during atrial pacing (P) from the right atrium (RA), both proximal (RA_p) and distal (RA_d), Bachman's bundle (BB), left atrium (LA) and the bundle of His (h). Potentials recorded from BB were usually compound, consisting of an early (BB_1) and a later (BB_2) component. NIC, acetylcholine (ACh) and tetrodotoxin (TTX) were injected intracoronary. ACh usually produced a modest (~10%) shortening of the p-RA_d and p-BB intervals along with the expected increase in AV nodal conduction time. NIC also tended to shorten the p-RA interval but usually lengthened the p-BB intervals while also slowing AV nodal conduction. After neural blockade with TTX, the effects of NIC on the RA and the AV node were abolished, while the changes in BB conduction were inconsistently affected. TTX did not change the responses to ACh. The data suggest that the ICN are capable of decreasing intra-atrial conduction time via NIC-stimulated release of ACh. The slowing of inter-atrial conduction may be mediated directly by nicotinic receptors in the specialized cells of BB. (Supported by NHLBI Grant No. HL 18517).

OBSERVATIONS ON BEHAVIORAL CONTROL OF WATER BALANCE AND RESPIRATION IN THE TERRESTRIAL SLUG, LIMAX MAXIMUS. David J. Prior. Univ. of Kentucky, Lexington, KY. 40506

Behavioral responses to dehydration which involve reduction in exposed respiratory surfaces lead to a physiological dilemma: reduction of oxygen uptake as well as water loss. Such behaviors must therefore be a balanced response to dehydration and oxygen demand. Using the slug, Limax, we have begun studying neural control of behavioral responses to dehydration and oxygen demand. The pneumostome(opening to lung) of a hydrated slug is kept continually open. The lung can be responsible for 50%(4-5ul/gm/5 min) of total O_2 uptake and 50% of total water loss(quiet animals). Following dehydration(10% loss of body weight) the pneumostome begins to open and close rhythmically, an activity that can reduce water loss from the lung. Progressive dehydration results in a linear increase in blood osmolality; hydrated being 135-145 mOsm/Kg. HOH and 10% dehydrated, 150-160 mOsm/Kg.HOH. Variation in blood osmolality may be involved in the onset of the rhythm. This is supported by the fact that several identified pneumostome motor cells have a specific sensitivity to variation in osmolality. (Supported in part by NSF BNS 74-15217-A01 and an Alfred P. Sloan Fellowship.

CONTROL OF INTESTINAL BLOOD FLOW DURING HEAT STRESS. D.W. Proppe* (SPON: B.P. Yu). Dept. of Physiology, Univ. of Texas Health Science Ctr., San Antonio, Texas, 78284.

The objective of this study was to determine the adrenergic mechanisms involved in controlling intestinal blood flow in unanesthetized, chronically instrumented baboons during heat stress. Five baboons, each with a Doppler flow probe around the superior mesenteric artery and arterial catheters for measurement of blood pressure and blood temperature (T_{bl}), were subjected to environmental heating (T_a = 40-45°C) for 40-130 minutes. During this heating, T_{bl} gradually rose 2-3°C, superior mesenteric artery blood flow (SMF) gradually fell, and superior mesenteric vascular resistance (SMR) gradually rose. At peak T_{bl}, SMF had fallen 29.2 ± 0.7% (mean ± SE) and SMR had risen 49.6 ± 3.3%. During heating after induction of α-adrenergic blockade by phenoxybenzamine or phentolamine, SMF and SMR changed very little, i.e., at peak T_{bl}, SMF had fallen only 2.5 ± 5.4% and SMR had risen only 7.0 ± 3.9%. During heating after induction of β-adrenergic blockade by propranolol, the % fall in SMF and % rise in SMR was smaller than in the unblocked, heat-stressed baboon. However, the absolute changes in SMF and SMR in the heat-stressed, β-receptor blocked animal were not significantly different from those seen in the unblocked animal. These data suggest that stimulation of intestinal α-adrenergic receptors plays a major role in producing intestinal vasoconstriction in the heat-stressed baboon. (Supported by NIH Grant #HL-20766)

EFFECTS OF OSMOTIC STRESS ON VARIOUS PROTEINS IN THE SERUM OF PARATELPHUSA HYDRODROMUS. T.S. Rajeswari* (SPON: E. Radha). Department of Zoology, Bangalore University, Bangalore-560 001, India.

Acclimation of the fresh water field crab Paratelphusa hydrodromus from its natural medium to one with a higher concentration (1%, 2% and 3% sodium chloride media) resulted in a significant decrease in the amount of serum total proteins and globulin and an increase in albumin and copper containing proteins. These changes have correlation to the body size of the animal and are influenced by the concentration of the medium. The causes and physiological implications of these changes are discussed with reference to salinity stress.

AUTONOMIC INFLUENCES ON ATRIAL PACEMAKERS. W. C. Randall, J. X. Thomas, J. M. Loeb and J. F. Moran*. Depts. of Physiology and Med., Loyola Univ. Med. Ctr., Maywood, IL 60153

In relating sinoatrial nodal (SAN) discharge to atrioventricular conduction, we examined the relative importance of sympathetic and parasympathetic influences at these regions of the heart. There is paucity of information on this in the quietly resting undisturbed dog. Standard limb lead ECGs were recorded by holter monitoring over a 24-hr period while the animal was isolated in his cage. The experimental groups consisted of control unoperated dogs, dogs sustaining intrapericardial cardiac denervation, dogs with surgical excision of the SAN, and dogs with ischemic infarction of the SAN and perinodal regions. Average 24-hr "holtered" heart rates were highest in the totally denervated animals with progressive decrement in controls, surgically excised, and in infarcted models. Intrinsic heart rate, as defined in animals with a surgically denervated heart, was consistently high. Marked instability in heart rate, with recurring long periods of asystole, characterized animals sustaining excision or infarction of the SAN region. Animals with totally denervated hearts exhibited markedly stable heart rates over the 24-hr period. These results may be interpreted to indicate a continually functioning autonomic modulation of both SAN and subsidiary pacemakers during a 24-hr period, with minimal parasympathetic input during activity, and maximal parasympathetic and minimal sympathetic input during rest. (Supported by NIH Grant HL 08682.)

PRESENCE OF ANGIOTENSIN II (AII) IN THE PRIMATE BRAIN. J.T. Quinlan,* M.I. Phillips, and J.A. Weyhenmeyer,* Dept. of Physiology, University of Iowa, College of Medicine, Iowa City, IA 52242

The presence of AII has been measured in the rat brain by radioimmunoassay, indirect immunofluorescence and immunocytochemistry. If AII in the brain is of biological significance in the mammalian system, then it should be present in the primate brain. We have tested this hypothesis and wish to report the presence of AII immunoreactivity within the brain of the monkey.

Six rhesus monkeys were anesthetized with pentobarbital and perfused via the aorta with saline followed by phosphate buffered picric acid-paraformaldehyde, pH 7.4. Vibratome sections, 100u, were pretreated with Triton X-100 and incubated with a 1:1000 dilution of rabbit anti-AII, titered at 1:95000 by RIA at 50% binding for 24 hr at 4°C. Sections were then incubated in a goat anti-rabbit IgG solution folowed by rabbit peroxidase/anti-peroxidase. Fibers with varicosities were found in the hypothalamus, thalamus, anterior commissure, midbrain, pons, medulla and spinal cord. These fibers tend to occur in isolation and often in intimate contact with small arteries. This study indicates the existence of a central AII system in primate brain. (Supported by NSF grant #BNS77-24415 to MIP. JAW is a PMA fellow.)

We wish to thank Dr. Detlev Ganten (University of Heidelberg) for the AII antibody and Dr. S.S. Hayreh (University of Iowa, College of Medicine) for supply of the monkeys.

GRAPHIC SIMULATIONS WITH AN INTEGRATED MICROCOMPUTER SYSTEM James E. Randall, Medical Sciences Program, Indiana Univ. School of Medicine, Bloomington, IN, 47401.

Continuing microcomputer developments provide programming conveniences for mathematical simulations at a reasonable cost but the diversity of hardware and operating systems has discouraged exchange of teaching exercises. Rather than expect universal compatibility the growing popularity of one economical unit having the necessary features suggests that it should be considered for teaching simulations. Some of the features include integration of high-resolution graphic vector commands into BASIC and replacement of floating point subroutines with a numerical processor chip to provide rapid displays of the dynamic nature of physiological variables. Superimposed lines of text which scroll as plotting progresses can display numerical values or comments. The low-cost floppy disk drive has a flexible operating system which can be initiated and used without technical skills. Such a unit will be demonstrated with graphic solutions of the following models: the interaction of glucose and insulin for different pancreatic sensitivities following a test dose of glucose; ventricular and axon action potentials; factors determining the central arterial pulsatile pressure; and the relationship between vectorcardiographic loops and the scalar limb leads.

FETAL HEART RATE AND UMBILICAL RESISTANCE. J.H. Rankin, T. Phernetton*, M. Stock*, D. Anderson* and M. McLaughlin*. Dept. Physiol. Univ. of Wis. Med. School, Madison, WI 53706.

It has been suggested (Biol. Neonate 33:225, 1978) that norepinephrine (NE) does not change umbilical vascular resistance (R) but does change umbilical blood flow (Q) by changing fetal heart rate (FHR). This invokes the concept of impedance matching between the fetal and placental circulations in which FHR is an important determinant of Q. We have tested this in 10 near-term chronically catheterized sheep fetuses. 50 ug/min of NE was infused into a hindlimb vein for 150 sec. At that time blood pressures were observed and blood flows were measured using radioactive microspheres. Observations were made in the control state where the infusion of NE decreased FHR from 174 ± 8 (mean ± SEM) to 126 ± 9. After the administration of 1.5 mg atropine, FHR was 200 ± 12 and in this condition NE increased FHR to 282 ± 10. Umbilical resistance was defined as (arterial - venous pressure)/Q. NE caused umbilical vasoconstriction in the presence of both bradycardia and tachycardia. The response during tachycardia was less than that seen during bradycardia but the fetal renal circulation behaved in the same way and this difference cannot therefore be ascribed to impedance matching between the fetal and placental circulations. We conclude that NE exerts an effect on Q via changes in fetal arterial pressure and slight changes in the caliber of the umbilical vessels and that R can be defined as pressure drop/Q. Supported by NIH grant HD06736.

RESPIRATORY RESPONSES TO TRACHEAL DISTENSION. S. V. Rao*, F. B. Sant'Ambrogio* and G. Sant'Ambrogio. Department of Physiology and Biophysics, UTMB, Galveston, TX 77550

In ten dogs, anesthetized with pentobarbital (30 mg/Kg) and spontaneously breathing through an endotracheal tube, short segments (3 cm) of either intrathoracic (ITT) or extrathoracic trachea (ETT) were distended by overinflation of the sealing cuff within the first half of inspiration and maintained for at least the next cycle. Phrenic electroneurogram, its integral, arterial pressure and end-tidal CO_2 were recorded. Distension of the ITT led to a significant ($P < 0.05$) prolongation of expiratory duration (Te = 219% of control) in 9 of the dogs; ETT distension prolonged Te in 6 of the dogs (206%). An inhibition of inspiration was found in 8 dogs resulting from either a shortening of inspiratory time (Ti = 48% of control) together with a reduction of peak phrenic amplitude (PPA = 48%) or as an initial decrease of the phrenic discharge which immediately resumed. After vagotomy distension of ITT shortened Te (58% of control) in 7 dogs, while the same challenge was ineffective when given through ETT. No significant effects were elicited on Ti and PPA by ITT and ETT distensions. Some of these results can be interpreted in the light of known behavior of tracheal stretch receptors, and indicate also the presence of extravagal influences. (Supported by NIH grant RO01-HL-20122-02).

VENTRICULAR FIBRILLATION THRESHOLD DECREASES WITH MODERATE LEVELS OF ETHANOL: COMPUTER CONTROLLED DETERMINATION IN THE CLOSED CHEST DOG. Julia S. Rasor,* James Foerster,* Perry Gee,* Zakauddin Vera,* and Dean T. Mason. University of California, Davis, California 95616.

The only other study on the effects of ethanol on ventricular fibrillation threshold (VFT) reports no change in VFT with blood alcohol concentrations (BAC) of 0.12 - 0.14g%. We found a significant decrease ($p<0.01$) in VFT with a BAC of 0.12g%. Intoxication occurs above 0.10g% BAC. Twelve dogs were anesthetized with methoxyflurane and ventilated with 100% O_2. Blood pH and body temperature were maintained. Mean arterial blood pressure was held constant (100±10 mm Hg). A right atrial pacing wire and right ventricular fibrillation catheter were intoduced intravenously. A computer paced the atrium at 180 beats/min for 12 beats then automatically delivered a train of 15 square wave current pulses (4 msec duration at 100 Hertz) to the ventricle during the vulnerable period. A three second delay between cycles followed to allow fibrillation. The train was incremented 1 ma with each cycle. Defibillation was accomplished within 3 seconds of onset with external paddles. VFT was determined just before and every 15 minutes after intravenous infusion of ethanol (8 dogs) or saline (4 dogs).

Ethanol (g%)	0.00	0.08	0.10	0.12	Saline Infusion
VFT±SD(ma)	24±11	26±9	20±9	18±12	VFT±SD(ma) 25±5 27±3 27±2 27±5

MECHANISMS OF INCREASED GLUCOSE UPTAKE BY GRACILIS MUSCLE DURING ENDOTOXIN SHOCK IN THE DOG. R.M. Raymond*, J.M. Harkema* and T.E. Emerson, Jr. Dept. of Physiology and Surgery, Michigan State Univ., E. Lansing, MI 48824

Recent reports from this laboratory have shown that under natural flow conditions, canine gracilis muscle glucose uptake is increased during endotoxin shock, but that this does not happen if muscle blood flow is held constant. These data suggest that in this shock model, the increased glucose uptake by skeletal muscle is associated with tissue ischemia and/or hypoxia. The present study was completed to determine whether tissue ischemia, hypoxia, or both contribute to the increased skeletal muscle glucose uptake during endotoxin shock. Mongrel dogs of either sex were anesthetized with Nembutal, anticoagulated with heparin and ventilated spontaneously. The isolated, innervated, constant flow perfused gracilis muscle was used. An isolated lung was used in the extracorporeal system to control the O_2-CO_2 tensions of the blood perfusing the gracilis muscle (lung ventilated with either 0% O_2, 95% N_2, 5% CO_2 or 95% O_2, 5% CO_2). Muscle blood flow was: 1) constant and hypoxemic (P_aO_2 = 10-20 mm Hg); or 2) ischemic and hyperoxic (P_aO_2 = 450-550 mm Hg). During constant flow-hypoxia, skeletal muscle glucose uptake increased significantly throughout the 6 hr. protocol, whereas under ischemic-hyperoxic conditions muscle glucose uptake decreased throughout the protocol. These data suggest that the increased glucose uptake by skeletal muscle during endotoxin shock in the dog is caused by tissue hypoxia and not ischemia. (Supported by NIH Grant RO1 GM26394).

PANTOTHENIC ACID AND COENZYME A CONTENT OF ORGANS FROM NORMAL AND DIABETIC RATS. D. K. Reibel, B. W. Wyse*, D. A. Berkich*, and J. R. Neely. Dept. of Physiology, Hershey Med. Cent., Penn. State Univ., Hershey, PA 17033

Coenzyme A (CoA) content was significantly increased in hearts from diabetic rats. The CoA and pantothenic acid (PA) content of heart and several other organs were measured to determine if alterations in CoA were associated with changes in tissue pantothenic acid. Diabetes was induced by intravenous injection of alloxan (60 mg/kg). Forty-eight hours later, organs were excised and quickly frozen. PA content was measured in tissue extracts by radioimmunoassay and CoA was measured enzymatically. CoA levels of heart and liver from diabetic animals were 130 and 200% of control, respectively. In contrast, PA content of the heart was 50% of control while no change in liver PA was observed. CoA in the pancreas was approximately 50% and PA was 200% of control. Although no changes were found in CoA levels in the kidney, PA levels were only 25% of control. No changes were observed in either CoA or PA in the diaphragm or skeletal muscle. PA concentration in the blood of diabetic animals was approximately 200% of that found in control animals. These data indicate that changes in CoA content of diabetic organs is not directly related to changes in PA content suggesting that diabetes has an effect on the pathway of PA conversion to CoA. (This work was supported by grant #HL-20484).

A COMPARISON OF THE CONTRACTILE PROPERTIES OF NORMAL AND DYSTROPHIC EMBRYONIC CHICK MUSCLE. Peter J. Reiser* and Bradford T. Stokes. Dept. of Physiology, The Ohio State University, Columbus, Ohio 43210.

The mechanical properties of isolated posterior latissimus dorsi (PLD) muscles from chick embryos of normal and genetically dystrophic strains (lines 412 and 413, Univ. of Calif., Davis) were studied from day 14 to day 20 of incubation. Isometric twitch and tetanic contractions elicited by direct supramaximal stimulation were characterized during this developmental period. Both peak twitch and tetanic (40 Hz for 4 sec) forces per cross sectional area produced by muscles from the dystrophic strain were consistently less. The greatest difference was observed at day 18 in ovo when the twitch force generated by the dystrophic muscles was approximately 50% of that produced by muscles from the normal strain. In addition, the developmental patterns of the twitch tensions of normal and dystrophic PLD are different. The force of the normal PLD increased from days 16 to 18 and subsequently declined until day 20. The dystrophic PLD, however, showed no change in twitch force from days 16 to 19 but decreased from day 19 to day 20. Additionally, the time to complete relaxation following both twitch and tetanic contraction was greater for the muscles from the dystrophic than the normal strains. The data relate to both the normal development of these muscle systems and the inability of the dystrophic PLD to produce normal twitch and tetanic forces. Supported in part by Muscular Dystrophy Association, Inc.

AGE-DEPENDENT CHANGES IN RENAL PROXIMAL TUBULE BRUSH BORDER MEMBRANE MALTASE ACTIVITY. Uzi Reiss* and Bertram Sacktor. NIH, NIA, GRC, Baltimore, MD 21224

The specific activity of maltase in isolated brush border membranes of aged (>11 yrs) dogs is decreased about 70% compared to the activity in young adults (1-4 yrs), 57 and 188 nmoles/min/mg prot, respectively. Enrichments, relative to cortex homogenates, in brush border marker enzymes were identical in both age groups. Maltase specific activities in the homogenates have the same age-decrement, 70%. The enzyme, when selectively solubilized with papain and chromatographed on Sepharose 4B, shows a similar age decrement, 2565 vs 8610, in the "old" and "young", respectively. These findings rule out the possibility that the decrease in brush border membrane activity with age is due to differences in homogeneity of the membrane preparations. The partially purified (400-fold) enzymes from the two age groups do not differ in Km, mol. wt, nor net charge. Maltase from the two age groups does differ in sensitivity to temperature. At 54°, both the partially purified and membrane-bound "old" enzyme is more stable. The "old" enzyme also has a biphasic temperature inactivation curve whereas the "young" enzyme shows a linear relationship. These findings suggest that the enzyme undergoes a conformational change in the kidney of the aged dog. An analogous age-dependent decrease in maltase activity is seen in the 24 mo rat compared to the 6 mo animal. Maltase activity in kidneys of male is twice that of female rats, in both the aged and young adult.

PLASMA GLUCOSE RESPONSES TO INSULIN IN NORMOTHERMIC AND HYPOTHERMIC HAMSTERS. Garth Resch* and Eric Sollars* (SPON: L. Langley). Univ. of Missouri, Kansas City, Mo. 64110

The control of blood glucose in hypothermic hamsters became of interest after the role of glucose in survival during hypothermia was demonstrated (Resch and Musacchia, 1976). Four groups of Syrian hamsters weighing 100 to 120 gm were kept on feed and water ad lib, on a 12:12 light dark cycle, and at an ambient temperature of 26°C. Half were controls, injected with saline, and half were experimentals, injected with 0.01 U/kg insulin. Half of the controls and experimentals were normothermic (NT)(Tre 38°C) and half were made hypothermic (HT)(Tre 7°C) by the helium-cold method. All animals received a carotid cannula. Blood samples were drawn for the determination of plasma glucose before and at 10, 20, 30, 40, and 60 min after insulin injection. Plasma glucose in NT control animals increased 15% above initial values. The maximum fall in blood glucose after an insulin bolus occurred at 30 min in NT animals, but was not well defined in HT animals. Within 60 min the maximum change in plasma glucose was 26.56 ± 6.95 (SEM) in HT animals compared to 59.98 ± 9.05 at 30 min in NT animals ($P < 0.025$). Preliminary data suggests an increased threshold and reduced sensitivity of plasma glucose responses to insulin in HT. The data indicates that the HT hamster plasma glucose is responsive to insulin and that the response is reduced compared to NT controls. (Supported in part by FRG 2401-2100).

INTRACELLULAR K^+ ACTIVITY (aK_i) AND CELL MEMBRANE POTENTIALS IN NECTURUS GALLBLADDER (NGB) EPITHELIUM. L. Reuss, S.A. Weinman* and T. P. Grady*, Washington Univ., St. Louis, Mo.

Cell membrane potentials (apical: V_{mc}, basolateral: V_{cs}), transepithelial potential (V_{ms}) and aK_i were measured in NGB epithelial cells under control conditions and during exposure to amphotericin B (5 μM, mucosal side) or ouabain (0.1 mM, serosal side). Amphotericin B produced immediate decreases of V_{mc} and V_{cs} and increase (mucosa-negative) of V_{ms} (ΔV^a_{ms}); after a delay of 1 to 2 min, aK_i fell, reaching values close to equilibrium distribution in 5 to 10 min. Replacement of mucosal Na with K in the presence of amphotericin B resulted in an immediate increase of aK_i. Ouabain produced slow cell depolarization, and a fall of V_{ms}; aK_i fell slowly over a period of 120 min. Exposure to a high-K mucosal medium restored partially and transiently aK_i and cell potentials. The effect of amphotericin B on potentials can be entirely explained by an initial loss of apical membrane K selectivity followed by a rapid decrease of aK_i, which depolarizes the basolateral membrane. The effect of ouabain is mostly due to the slow decrease of aK_i. ΔV^a_{ms} was reduced by ouabain (30-60 min exposure). This effect was corrected by pre-exposure to high-K mucosal medium, indicating that the low aK_i, and not the inhibition of the Na pump, is responsible for the smaller ΔV^a_{ms} in presence of ouabain.
(Supported in part by USPHS. NIH Grant AM 19580).

OPIATE RECEPTOR BLOCKADE IMPROVES CARDIAC PERFORMANCE IN HEMORRHAGIC SHOCK. D.G. Reynolds, R.B. Lechner*, N.J. Gurll and T. Vargish*. Dept. of Surgery, Univ. of Iowa, Iowa City, IA 52242.

In previous studies we demonstrated that naloxone, 2mg/kg bolus plus 2mg/kg·hr infusion, improved cardiovascular function and survival in hemorrhagic and endotoxic shock. In this study we evaluate the efficacy of naloxone at reduced doses. Four groups of 5 anesthetized dogs were bled to a MAP of 45mmHg which was maintained for 1 hr using a reservoir. The reservoir was then clamped and therapy initiated; the shed blood was never returned and drug infusion continued until the animals expired. Group I dogs were given saline i.v.; Group II, naloxone, 0.5mg/kg bolus and 0.5mg/kg·hr infusion; Group III, 1mg/kg plus 1mg/kg·hr; Group IV, 2mg/kg plus 2mg/kg·hr. Naloxone increased MAP (mmHg), LV dp/dt (mmHg·10^3/sec), and CO(L/min) and prolonged survival (S in hrs). Initial values for each parameter did not vary significantly between groups.

	MAP		LVdp/dt		CO		S	
Group	O*	Rx*	O	Rx	O	Rx		
I	44±1	34±4	1.0±.1	1.2±.1	0.5±.1	0.5±.1	1.4±0.1	
II	45±1	48±6	1.1±.1	1.5±.1	0.6±.1	1.1±.3	1.8±0.2	
III	45±1	72±9†	0.9±.1	1.7±.3	0.7±.1	0.9±.2	3.0±0.4**	
IV	45±1	81±5†	1.0±.1	2.1±.1†	0.7±.1	1.3±.1†	5.0	0.8*†

*O-oligemia, Rx-treatment **p<.05 to Group II
† -p<.05 *†p<.05 to Group III

The improvement of myocardial performance afforded by naloxone is a dose related phenomenon. The mechanism of action may involve blockade of β-endorphin effects on opiate receptors.

RELATION OF INSPIRATORY UNITS IN PHRENIC AND RECURRENT LARYNGEAL NERVES TO WHOLE NERVE ACTIVITIES IN THE CAT. Charles Richardson* and Robert A. Mitchell, Depts of Physiol and Anesthesia, and CVRI, Univ. of Calif., San Francisco CA

We reported (Physiologist 21(4):99) that power spectral densities (PSDs) of the phrenic nerve had peaks at 86Hz and at 36Hz and the recurrent laryngeal nerve had peaks at 82Hz and 52Hz during inspiration. To determine if these peaks represented differences in single fibers, we compared the PSDs of individual units with the PSDs of the whole nerves of six decerebrate, paralyzed, artificially ventilated cats. Of 19 recurrent laryngeal units, 5 had PSDs similar to the phrenic nerve PSDs, 13 had PSDs similar to the recurrent laryngeal nerve PSDs, and 1 was not classified. Of 105 phrenic units, 73 had PSDs similar to the phrenic nerve PSDs, 22 had PSDs similar to the recurrent laryngeal nerve PSDs, and 10 were not classified. Time interval histograms and instantaneous rate plots for each unit provided poor measures of the unit's rhythmic drive as measured by its PSD because the units did not fire on every cycle of the central drive. Our results indicate that the differences between whole phrenic nerve PSDs and whole recurrent laryngeal nerve PSDs is due to differences of individual units. We suggest that these differences in PSDs for the phrenic and recurrent laryngeal units may reflect differences in the respiratory pattern generators driving them.
(Supported by USPH grants HL-06825 and GM15575).

CHARACTERISTICS OF BLOOD FLOW IN THE HUMAN CALF MUSCLE FOLLOWING STATIC AND RHYTHMIC CONTRACTIONS. D. R. Richardson, R. Shewchuk*, and J. T. Kearney*, Department of Physiology, University of Kentucky, Lexington, Kentucky 40536.

Six consenting males of mean age 27.5 years were trained to exert maximum voluntary contractions (MVC) of their calf muscles. Subjects sat in a chair with their knee immobilized by a support strap, and pressed the ball of their foot against a load cell. Calf muscle blood flow (BF) was measured via a Whitney gauge in response to static contractions of 30, 40,60, & 80% MVC. The latter 3 levels were taken to fatigue. During the 30 & 40% MVC contractions BF did not vary from control values. During higher MVC contractions BF could not be measured. Maximal post exercise hyperemia (PEH) following 30,40,60, & 80% MVC averaged: 36.7, 40.6, 55.3, & 39.8 ml/min X 100 ml respectively. At 30 & 40% MVC, PEH was a significant linear function of the force exerted among the subjects. The subjects also engaged in rhythmic isometric contractions of 30% MVC for 3 minutes at frequencies of 20,50, & 80 strokes per minute. Average PEH values for these frequencies were respectively: 25.7, 41.6, & 47.7 ml/min X 100 ml. At each frequency PEH among the subjects was a significant linear function of the force exerted per stroke. These results support a model in which PEH of the calf muscle is determined by an interaction during contraction of muscular compression vs active vasodilation (Supported by Ky. Tobacco & Health Res. Inst. Grant 24016).

DROMOTROPIC INFLUENCES OF THE CARDIAC NERVES AT THE A-V JUNCTION. L. E. Rinkema*, J. X. Thomas and W. C. Randall. Dept. of Physiology, Loyola Univ. Med. Ctr. Maywood, IL 60153

Autonomic influences on the chronotropic and dromotropic properties of the heart are well recognized but contributions of individual cardiac nerves in matching A-V nodal conduction to sinoatrial firing rate are almost totally unknown. In this study their modulation of A-V nodal conduction was examined using a His bundle catheter in the non-coronary cusp of the aorta. Stimulation of the following cardiac nerves produced decreases in A-H interval from an average control of 81 msec in all dogs (n=5); left ansa subclavia (37%↓), Innominate (21%↓), ventrolateral (21%↓), right ansa subclavia (26%↓), and right stellate cardiac (18%↓). These changes were eliminated by propranolol while atropine had no effect. A-V block was seen with stimulation of the left thoracic vagus (LTV), right thoracic vagus (RTV), and caudovagal (CaV). Following atropine the RTV had no effect but LTV and CaV stimulation produced A-H interval shortening (13↓,19%↓). The remaining cardiac nerves (ventromedial, recurrent, and cranio-ovagal) lengthened the A-H interval in 1/2 the dogs and decreased it in the rest. These effects were reversed after appropriate blockade with atropine or propranolol indicating that these nerves contain both sympathetic and parasympathetic fibers. Thus the A-V junction receives input from all of the cardiac nerves, those of the left side being predominately sympathetic and those from the right being mixed.
(Supported by NIH Grant HL-08682.)

THE EFFECT OF RUBELLA VACCINATION DURING PREGNANCY ON CELLULAR IMMUNITY IN NEW ZEALAND WHITE RABBITS. Cynthia S. Ritter*, Martha S. Ellert, Ginger W. Miller*. Southern Illinois University, Carbondale, Ill. 62901.

The live attenuated rubella virus prophylactically used to immunize humans against rubella has been shown to possess immunosuppressive properties. Immunosuppression has also been implicated as a factor in preventing rejection of the fetus during pregnancy. The present study evaluated the effect of attenuated rubella virus HPV-77DE5 (Meruvax) vaccination during pregnancy on cellular immunity in rabbits. Measurement of the proliferative capabilities of T-lymphocytes after phytohemagglutinin (PHA) stimulation was performed on blood samples collected every 7 days for 7 weeks from rabbits that were treated as follows: 1) pregnant, not vaccinated 2) vaccinated, not pregnant and 3) vaccinated during pregnancy. Pregnant rabbits exhibited significantly ($p<0.01$) lower lymphocyte proliferation at 28 days post-mating than nonpregnant rabbits. Rabbits vaccinated on the 17th day of the experiment showed significantly ($p<0.01$) lower lymphocyte proliferation 11 days post-vaccination than did nonvaccinated rabbits. Rabbits vaccinated during pregnancy exhibited lack of lymphocyte proliferation in response to PHA stimulation more frequently than did rabbits that were only vaccinated or pregnant. These results suggest that rubella vaccination during pregnancy decreases cellular immune responses in rabbits.

LOBAR DIFFERENCES IN COLLATERAL RESISTANCE AND INTERDEPENDENCE IN EXCISED DOG LUNGS. N. E. Robinson and R. Milar*. Depts. of Physiology, and Large Animal Surgery and Medicine, Michigan State University, East Lansing, MI 48824

Lobar variations in the time constant for collateral ventilation (Tcoll), collateral flow resistance (Rcoll) and effective segment compliance (Cs) were measured in each lobe of freshly excised dog lungs at transpulmonary pressures (P_L) = 2 and 5 cm H_2O using a wedged catheter technique (J. Appl.Physiol. 44:63, 1978). The pleural surface area (A) and volume (Vs) of segments isolated by the wedged catheter were calculated after air drying lungs at P_L = 30 cm H_2O. Right middle, left upper, and accessory lobe segments had a high A/Vs ratio whereas right upper, and right and left lower lobes have a low A/Vs ratio. Lobar segments with high A/Vs had longer Tcoll than segments with low A/Vs of both P_L = 2 and 5 cm H_2O. At P_L = 5, the longer Tcoll of high A/Vs segments was due to higher Rcoll with no difference in Cs. At P_L = 2, the longer Tcoll was due to higher Cs with no difference in Rcoll. At P_L = 2, high A/Vs segments were relatively independent of the adjacent lobe but at P_L = 5 became more interdependent. In contrast, low A/Vs segments were less interdependent at P_L = 5 than at P_L = 2 cm H_2O. These findings suggest that lobar segments with high A/Vs ratio are prone to atelectasis because of a long Tcoll and lack of interdependence with adjacent lung parenchyma. (Supported in part by USPHS NIH grant #HL 17768 and by a BRSG grant from the College of Veterinary Medicine.)

DIAPHRAGM ENERGY METABOLISM IN ACUTE RESPIRATORY FAILURE. D.F. Rochester, N.S. Arora*, S.K. Goldberg*, J. McCormack*, and D. Moore*. Univ. of Virginia, Charlottesville, VA 22908.

Acute obstructive respiratory failure (AORF) is characterized by increased work of breathing, progressive hypoxemia, and respiratory acidosis. To assess the impact of AORF on diaphragmatic energy metabolism, we used a dog model in which transvenous stimulation of the left phrenic nerve caused the left hemidiaphragm (LHD) to contract for 400 msec 60 times a minute, while the non-contracting right hemidiaphragm (RHD) served as a control. Moderate (M) or severe (S) inspiratory resistances were used to decrease tidal volume and produce hypercapnia. One hour after LHD pacing and resistance breathing, PO_2 and pH were measured in arterial and left diaphragmatic venous (LDV) blood, and portions of LHD and RHD were rapidly excised, frozen, and analyzed for [ATP] and phosphocreatine ([PC]). In 8 group M and 9 group S dogs, LDV blood PO_2 was 32 and 19 torr, and [H+] was 55 and 79 nmol/l ($P<.05$). RHD [ATP] and [PC] were essentially the same in both groups. By way of contrast, in group M dogs LHD[ATP] and [PC] were 73% and 64% of the corresponding RHD values ($P<.05$), while in group S dogs LHD [ATP] and [PC] fell to 63% and 39% of RHD levels ($P<.001$). The decreases in LHD [ATP] and [PC] correlated with the degree of hypoxemia. We conclude that in AORF the combination of severe contractile effort, hypoxia and acidosis progressively depletes diaphragmatic energy reserves, whereas hypoxia and acidosis alone have relatively little effect. (Supported by USPHS NIH grant HL-21500).

Dietary Carbohydrate Depletion Increases Anaerobic Threshold. H. Thomas Robertson, Alan Chait* and John Brunzell*. Univ. of Washington, Seattle, WA 98195 (Spon. M.P. Hlastala).

The anaerobic threshold (AT) has been postulated to represent a point where oxygen delivery to exercising muscle becomes inadequate, with ensuing lactic acidosis. As muscle glycogen stores represent the source of lactate during exercise, depletion might alter lactate production. Four male subjects (age 24-57, VO_2 max 24-50 ml O_2/Kg min) underwent progressive incremental exercise tests on a cycle ergometer following a 12 hour fast on 3 occasions: on a normal diet, after 4 days on an isocaloric 80% lipid, 5% carbohydrate diet (low CHO), and after 3 days on an isocaloric 85% carbohydrate diet (high CHO). Maximal exercise times were decreased only after the low CHO diet, by 3 to 9%. Tidal fluctuations in N_2 were measured at the mouth, and the AT was most reproducibly defined as the point where mean P_{EN_2} became equal to P_{IN_2}. The AT was lowest in each subject following the high CHO diet (62.2 ± 4.1% of maximal effort, mean ± S.D.), and highest following the low CHO diet (79.0 ± 7.5% of maximal effort). Venous lactate levels measured during exercise were lower at each corresponding work load on the low CHO diet compared to the high CHO diet. Although the AT is a reproducible finding under specified conditions, a decrease in muscle carbohydrate stores caused a 10 to 25% increase in the AT, suggesting that its link to tissue oxygen utilization is not as direct as had been suggested. (Supported by NIH grant HL-18687.)

ENHANCEMENT OF HYPOTHERMIC CARDIAC PERFORMANCE WITH PRYUVATE. Janet D. Robishaw*and Roy F. Burlington. Dept. Biol. Central Michigan Univ. Mt. Pleasant, MI 48859.

Ischemia depresses cardiac contractility by depleting energy stores. Treatment of myocardial ischemia with pyruvate (Pyr) enhances cardiac performance while preserving cellular energy levels (Liedtke et al., Circ.Res.39:378,1976). During hypothermia myocardial function is depressed and subendocardial lesions may occur. Pry may partially alleviate these dysfunctions. To test this hypothesis we perfused the aorta of isolated, isovolumic working rat hearts with oxygenated ($95\%O_2$-$5\%CO_2$) Krebs Ringer Bicarbonate containing 5mM glucose (G) of 5mM G + 7.5mM Pyr. Hearts were initially perfused at 21°C for 30 min followed by decreasing temperature until cardiac arrest occurred. Perfusion pressure was maintained at 60 mm Hg during all experiments. Pry significantly augmented left ventricular pressure (LVP) ($P=<.001$ at each temperature) but it did not alter arrest temperature (12°C).

Temp. (°C)	21(5)	20(6)	19(6)	17(6)	15(6)	14(6)	13(4)
LVP(mmHg)-G	70±5*	77±5	78±6	87±8	92±10	92±4	92±4
LVP-G + Pyr	131±8	138±8	141±6	151±6	158±6	156±7	156±7

*X ± SE for number of hearts in parentheses

Coronary flow was maintained and spontaneous heart rate decreased with progressive hypothermia in both control and treated hearts. Pry may provide substrate for a better maintenance of the energy state in cardiac tissue during hypothermia.

NITROGLYCERIN EFFECTS ON CEREBRAL HEMODYNAMICS. M.C.Rogers* and R.J. Traystman. Depts. of Anesthesia and Environ. Hlth. Sci., Johns Hopkins Med. Insts., Baltimore, Md. 21205.

Cerebral hemodynamic effects of sublingual (SL) and intravenous (IV) nitroglycerin (NTG) were studied in 5 anesthetized, paralyzed, ventilated dogs, at normal and artificially elevated cerebrospinal fluid pressures (Pcsf). Cerebral blood flow (CBF) was measured with the venous outflow technique. Cerebral perfusion pressure (CPP) was calculated as the difference between mean arterial pressure (Pa) and Pcsf. In animals with normal Pcsf (10-20 mmHg), SL (0.3 mg) or IV (5,25,50 µg/kg) NTG decreased Pa to 70-80% of control and elevated Pcsf to 150-250% of control, thus decreasing CPP. However, CBF remained unchanged. With artificially elevated Pcsf (40-50 mmHg) SL or IV NTG produced similar decreases in Pa and increases in Pcsf (up to 80 mmHg). This marked increase in Pcsf and moderate decrease in Pa lowered CPP below the autoregulatory range and reduced CBF to 50% of control. Nitroprusside (NPR)(5,25,50 µg/kg IV)resulted in similar hemodynamic changes both at normal and elevated Pcsf. However, NTG produced a more marked decrease in Pa and delayed increase in Pcsf over all ranges of systemic hypotension than did NPR. We conclude that NTG and NPR may have deleterious effects on CBF by reducing CPP. The mechanism for the elevation in Pcsf with NTG or NPR is probably related to a change in cerebral venous capacitance leading to an increase in cerebral blood volume. (Supported by HL 10342)

COMPARISON OF MODEL AND SHEEP LUNG PROTEIN EXCHANGE IN RESPONSE TO VASCULAR PRESSURE CHANGES. R.J. Roselli*, R. Parker* and T.R. Harris. Vanderbilt University School of Medicine, Nashville, Tennessee 37232

A multiple pore model was used to predict lung lymph flow (L) and lymph to plasma protein ratios (R) as a function of transcapillary pressure drop. Characteristic model pore sizes and numbers were determined previously from two levels of vascular pressure (1). The theoretical values compared favorably with data collected from 8 different sheep where left atrial pressure was elevated in 3 to 4 steps from baseline to as high as 45 cm H_2O. We plotted LR/(1 - R) vs. L for each protein as described by Renkin et al. (2). The relationship is non-linear, characteristic of a heteroporous system, and is reproduced by the model. We conclude that transvascular fluid and protein exchange in the lung can be simulated in considerable detail with a porous membrane model of the pulmonary endothelium composed of three pore populations: small pores which admit solvent only, large shunts and intermediate sieving pores. (Supported in part by USPHS HL-22933 and NIH HL-19153 Grants.)

1) Harris, T.R. and Roselli, R.J. Proc. 31st ACEMB, 20:14, 1978.

2) Renkin, E.M. et al. Microvas. Res., 14:191-204, 1977.

CAPTOPRIL AND THE INTESTINAL RESPONSE TO HEMORRHAGIC SHOCK

Leonard M. Rosenfeld and Harry S. Cooper.* Depts. of Physiology and Pathology, Thomas Jefferson Univ., Phila., PA. 19107

Adult male cats, anesthetized with pentobarbital sodium (30 mg/kg), underwent a hemorrhage protocol in which arterial blood was withdrawn until a mean arterial blood pressure (MABP) of 40 mm Hg developed. Oligemia was maintained for a period of 2.5 hours, after which time, all remaining shed blood was reinfused and the cats observed for an additional 2 hours. Coincident with the large reduction in MABP, superior mesenteric artery flow (SMAF) was similarly reduced as recorded by a noncannulating electromagnetic flow probe fitted around the artery. Post-oligemic plasma activities of cathepsin D (CD) and alkaline phosphatase (AP) were elevated 11-fold and 3-fold respectively; intestinal morphological damage was graded at 2.8 ± 0.4 on a 0-4 scale of increasing severity (control 0.03 ± 0.02). Captopril, an angiotensin converting enzyme inhibitor (SQ 14,225) was administered at an initial priming dose of 0.5 mg/kg followed by infusion of 0.5 mg/kg/hr from the onset of oligemia until the conclusion of the 4.5 hour experimental period. Improved post-reinfusion maintenance of MABP and SMAF was noted. Plasma elevations in enzyme activity were more moderate: 8-fold for CD, 1.5-fold for AP. Intestinal morphologic damage was graded at 2.5 ± 0.3. Blockade of angiotensin II formation by captopril thus demonstrates beneficial effects on post-oligemic hemodynamic status and on the degree of cellular enzyme release without significant improvement in intestinal morphology.

BIPHASIC RESPONSE OF DOG CORONARY ARTERIES TO ALPHA-ADRENERGIC STIMULATION. Gordon Ross, V.S.R. Krishnamurty* and Sylvie Teper-Edelstein*. Dept. of Physiology, UCLA School of Medicine, Los Angeles, CA 90024.

Ring segments of large coronary arteries from dogs were mounted on force transducers in Krebs-bicarbonate solution containing propranolol 10^{-6}g/ml at 37° and pH 7.4. Norepinephrine induced biphasic contractures with an initial fast component reaching a peak within 30s and a slow component which reached a maximum in 120-240s. Verapamil 10^{-7}g/ml, EGTA (1 mM) and low external calcium concentrations reduced the slow component to a greater extent than the fast component. Ouabain 10^{-6}M, potassium-free Krebs solution and reduction of the bath temperature to 24° augmented the slow component of the norepinephrine response but had variable effects on the fast component. It is concluded that the fast component of the alpha adrenergic response is mainly due to intracellular calcium release. The slow component appears to be dependent upon calcium influx which is modulated by Na^+, K^+-ATPase. (Supported by AHA-GLAA grant #538IG.)

OTOCONIAL COMPLEXES AS ION RESERVOIRS IN ENDOLYMPH. Muriel D. Ross and Thomas Williams. The University of Michigan, Ann Arbor, Michigan 48109.

Otoconia of the gravity receptors and their membranes are complex mineral deposits of calcite crystals and organic substance. $^{45}Ca^{++}$ uptake and exchange in these complexes and in bone mineral were studied in adult Wistar rats using microdissection procedures, pooled otoconial samples (from 6 rats), and the sensitive method of liquid scintillation spectrometry. Intraperitoneal injection of $^{45}Ca^{++}$ (4 mCi/kgm body weight) resulted in rapid uptake into saccular complexes (15 mins) but uptake into utricular complexes took longer (up to two hrs). Although retention of $^{45}Ca^{++}$ was higher in saccular complexes throughout the experimental period (one month), maximal uptake occurred in both complexes by 4 hrs. This time frame is consistent with that for maximal uptake into bone. $^{45}Ca^{++}$ declined quantitatively in otoconial complexes after 4 days but remained high in bone mineral. An ancillary finding was that a sex factor may influence $^{45}Ca^{++}$ uptake both in otoconial complexes and in bone. The results indicate that the otoconial complexes are dynamic mineral deposits but that they function in distinct environments at the two sites. It is suggested here that otoconial complexes are not only weight-lending devices in gravity receptors but also act as ion reservoirs, contributing to the ionic stability of the endolymph. (Supported by NASA Grant NSG 9047).

NATRIURETIC EFFECTS OF ANGIOTENSIN II (A_{II}) AND RENIN SUBSTRATE (RS) IN THE ISOLATED RAT KIDNEY. S.G. Rostand*, S.C. Hebert*, and L.G. Navar, Birmingham, Alabama.

A_{II} is known to exert a biphasic action on urinary sodium excretion. We studied the natriuretic effects of A_{II} and RS in isolated rat kidneys perfused at 37°C and at normal and elevated perfusion pressures with KRB buffer containing 7.5% BSA, 5 mM glucose, and 5 mM urea and gassed with 95% O_2:5% CO_2. In paired experiments at constant perfusion pressure of 100 mm Hg, the addition of A_{II} (5 ng/ml) reduced perfusate flow rate by 80% and had no effect on GFR. $U_{Na}V$ rose from 0.62 ± 0.13 μEq/min to 4.5 ± 1.3 μEq/min (SE) and F_RNa fell from 99.2 ± 0.03% to 92.8 ± 0.09%. Similar results occurred when RS (1 μg/ml) was added. When perfusion pressure was increased to 140 mm Hg, in another series of experiments, $U_{Na}V$ was 8.3 ± 1.3 μEq/min for control kidneys, but was 27.5 ± 4 μEq/min with A_{II} and 29 ± 1.8 μEq/min in the presence of RS. GFR rose under all three conditions, but $\Delta T_{Na}/\Delta GFR$ remained unchanged (∿ 130). However, $\Delta U_{Na}V/\Delta GFR$ in the presence of A_{II} or RS was twice that of controls. We conclude that the natriuresis seen following the addition of A_{II} or RS is independent of changes in perfusion pressure. Our data also demonstrate an augmented pressure natriuresis seen in the presence of A_{II} or RS which was more than could be explained by changes in GFR. These data suggest that the observed natriuresis is in part the result of a direct tubular action of these peptides.

CHANGES IN PULMONARY TISSUE VOLUME (V_t) DURING CARDIOGENIC EDEMA. Alan F. Rothfeld* and Mitchell Friedman. University of North Carolina, Chapel Hill, N.C., 27514.

A repeatable and rapid method for measuring changes in lung H_2O would be useful for the early detection of pulmonary edema (PE). We have used a rebreathing method (RB) in canine PE induced by balloon obstruction of the mitral valve and varying rates of saline infusion. The animals were rebreathed with 900 ml of a gas mixture containing 0.3% $C^{18}O$, 10% He, 1.0% C_2H_2, 21% O_2, Bal N_2. RB parameters include V_t, pulmonary capillary blood flow ($\dot{Q}c$) and diffusing capacity (D_L). Also, lung microvascular hydrostatic (Pmv) and oncotic pressures (πmv) were measured. The mean results were:

	C*	B**	30 min†	60 min†	90 min†
n	19	19	19	12	7
V_t(ml/kg)	8.6	10.6†	10.1	9.4	10.8
Pmv-πmv(mmHg)	-5.0	4.1†	13.1†	12.9†	13.6
Qc(L/min)	1.41	1.34	2.44†	2.48	2.41
D_L(ml/min x mmHg)	10.7	12.9†	11.7†	10.7†	9.6†

[*Control;**Post-balloon inflation;†Time after saline infusion; †Significant ($p<.05$) differences from previous value.]

4 additional dogs developed severe PE during the study (3-fold increase in V_t). Mean V_t in all dogs was 104% of autopsy lung H_2O values. Thus, RB measurements of V_t are accurate and sensitive in moderate and severe states of cardiogenic PE. In addition, a steady state model of PE has been developed which allows studies of therapeutic interventions. (Supported by NIH grants HL-21168 and HL-07106.)

SUBSTRATE UTILIZATION IN POST-ISCHEMIC RAT HEARTS; INCREASED RATIO OF CALCULATED ENERGY PRODUCTION TO MECHANICAL WORK

M.J. Rovetto and R. Werkman.* Department of Physiology, Jefferson Medical College, Philadelphia, PA. 19107.

The effect of 2 hrs low flow whole heart ischemia (coronary flow 20% of aerobic flow) in the isolated working rat heart on post-ischemic substrate utilization and mechanical function was determined. Glycolysis was increased 2-fold in both aerobic and post-ischemic hearts after 2 hrs perfusion with 11 mM glucose as the only exogenous substrate. Aerobic hearts oxidized 30% more glucose, and lactate production was doubled. Increased glucose utilization in post-ischemic hearts was accounted for by increased lactate production. With 1 mM octanoate or palmitate as substrate, glycolysis in aerobic hearts remained constant but increased 2-fold in post-ischemic hearts. This latter increase was accounted for by increased lactate production and was likely due to decreased tissue ATP concentrations. Post-ischemic oxygen consumption and the calculated ATP production rates also were not changed by ischemia regardless of the substrates used. Because mechanical function was depressed about 50% in all post-ischemic hearts, they had a similar percentage reduction in work efficiency. The data are consistent with either uncoupling of oxidative phosphorylation or increased levels of internal work in the post-ischemic heart. Supported in part by NIH grant Nos. HL 17895 and HL 00289.

INSULIN SECRETION RATE AND OXYGEN CONSUMPTION ARE ALTERED BY BUFFER FLOW IN THE PERFUSED CANINE PANCREAS. Mark W. Roy*, M. Sue Jones* and Ralph E. Miller, Univ. Kentucky, Lexington, KY 40536.

The purpose of this work was to examine the importance of buffer flow rate to insulin secretion rate (ISR) from the perfused canine pancreas. Pancreata of mongrel puppies (2-4.5 kg) of both sexes were completely isolated in situ and perfused with modified Krebs Ringer bicarbonate (0.2% albumin, 3.3% Dextran 70) at flow rates of 0.2 to 2.8 ml/min.g wet pancreas. Pancreatic O_2 consumption, pH change across the pancreas and ISR were determined at several flow rates. At autopsy, pancreata were removed, weighed, dried, and re-weighed. At buffer flow rates up to 0.75 ml/min.g (wet), ISR remained ca. 1.5 ng/min.g, then increased linearly to 11 ng/min.g as flow was increased to ca. 1.75 ml/min.g (wet). Flow rates greater than 1.75 ml/min.g (wet) represented a plateau during which ISR and O_2 consumption did not change. O_2 consumption increased linearly to 21 µl/min.g as flow was increased to 1.75 ml/min.g (wet) (perfusion pressure 90-100 mm Hg). As flow was increased from 1 to 11 ml/min.g dry weight, arterio-venous pH difference decreased linearly from 0.22 to 0.02. The absence of significant edema was demonstrated by dry to wet weight ratios comparable to those found in normal blood perfused organs. These results indicate that, at buffer flow rates less than ca. 1.75 ml/min.g (wet), flow dependent hypoxia may result. This hypoxia may be responsible for the diminished ISR. (Supported by NIH #5-AM17082-06)

BONE STRAIN AS A FUNCTION OF SPEED. C.T.Rubin* and L.E.Lanyon* (SPON:C.R.Taylor). Harvard University, Cambridge, MA 02138

The size and shape of bone reflects the strains imposed during normal activity. However, because of the mechanical dissimilarities of walking, trotting and galloping, one expects strain orientation to be different, creating contradicting stimuli for bone growth. Ideally, if an animal could maintain a unique loading axis throughout these gaits, this would optimize a bone's architecture. Local strains acting on bone can be measured by rosette strain gauges, determining both the axes of loading and the magnitude of strain imposed during locomotion. Gauges were attached to the cranial and caudal surfaces of the tibial and radial midshafts in 2 ponies and 2 dogs. Recordings were taken at speeds up to 30 km/hr. Throughout this range only a minor shift of loading orientation occurred, and always at the walk-trot transition. This shift was approx. five degrees in the medial-lateral plane, towards the long axis of the bone. Peak strain magnitude was not simply proportional to speed, but instead related to the mode of locomotion e.g. caudal tibial strain of a dog increased 41% from a walk to trot (-1080 to -1840 microstrain) at 4 km/hr, but dropped 30% from a trot to a gallop (-2100 to -1400 µε) at 12 km/hr. Bone strain, proportional to the muscle and ground forces which act upon it, plateaus off at a high speed gallop, and well within measured in vitro yield strains. The axes in which bones are loaded are maintained by coordinated muscles throughout the speed range, creating a unique stimulus to bone growth. (Supported by NIH AM18140 and NIH AM05658).

DEVELOPMENT OF THERMOREGULATION IN INDIVIDUALS AND BROODS OF THE AMERICAN GOLDFINCH. Richard D. Rowlands and Henry D. Prange. Indiana University, Bloomington, IN 47405

Thermoregulatory ability (maintenance of body temperature (T_b) above ambient temperature (T_a) over an ambient temperature range of 19 to 37°C) of individual goldfinches (*Carduelis tristis*) typically becomes apparent on the third day of nestling life and homeothermy (T_b maintained between 36 and 40°C over a T_a range of 10 to 40°C) is attained by the seventh day. Multiple regression analysis indicates that the ability to increase metabolic rate in response to a decrease in T_a is the most important factor contributing to this development in individuals, while improvement of insulation through plumage development, and decrease in surface to volume ratio with increased body size are less important. Preliminary analyses of data from broods comprised of 2 to 6 individuals shows that broods attain homeothermy at a younger age than single individuals and that larger broods do so earlier than smaller broods. The greater reduction in surface area for heat loss per unit of thermogenic tissue results in a greater importance of surface to volume ratio for broods in comparison with individuals.

COMPARISON OF CARDIAC VOLUME AND MASS MEASUREMENTS IN WOMEN SPRINTERS AND SEDENTARY SUBJECTS. B. Rubal, J. Rosentswieg*, K. Barnard*, C. Buchanan*, and B. Hamerly*. Cardiovas. Res. Lab., Texas Woman's University, Denton, TX 76204

Left ventricular volume and muscle mass measurements were evaluated in twelve women ranging in age from 19 to 28. Six women were conditioned sprinters and six were sedentary subjects. Left ventricular total volume (muscle + cavity volumes), end-diastolic volume, muscle volume, and muscle mass calculations were derived from measurements obtained via M-mode echocardiography. Also, the ratio of left ventricular chamber volume/muscle volume was calculated. All subjects were examined in the left lateral decubitus position and measurements were standardized for body surface area. Although mean values for left ventricular total volume, muscle volume, muscle mass and the ratio of cavity volume/muscle volume was greater in the athletes than the sedentary subjects, no significant differences were observed. End-diastolic volumes were significantly greater ($P = .022$) in the sprinters than the control group. The mean values ± SEM for the athletes and the sedentary subjects were 68.3 ± 5.6 ml/m^2 and 49.8 ± 3.8 ml/m^2, respectively. These data suggest that cardiac volume and/or muscle mass measurements may be of value in assessing the effects of conditioning programs. (Supported in part by Texas Woman's University Regional Development Center and Life Mark, Inc.)

HISTOCHEMICAL LOCALIZATION OF NUCLEOSIDE PHOSPHORYLASES (NP) SELECTIVE FOR PURINE (Pu) AND PYRIMIDINE (Py) COMPOUNDS IN HEART, KIDNEY AND LIVER. Rafael Rubio and Robert M. Berne, Dept. of Physiology, Univ. of Virginia, Charlottesville, VA 22908.

Histochemically Pu-NP activities appears to be highly concentrated in the cytoplasm of capillary endothelium. Hence, it has been suggested that adenosine released by parenchymal cells becomes degraded to inosine and hypoxanthine as it passes through the endothelium toward the capillary lumen. This interpretation depends largely on the reliability of the histochemical results. To provide greater assurance of the selectivity of this histochemical technique for Pu-NP localization, Pu-NP was compared to Py-NP in cells which are known by biochemical assay to contain nuclear and cytoplasmic components of Py-NP enzymes that are highly specific for ribose-1-phosphate (R-1-P). Tissues were incubated in a medium containing R-1-P and a Pu or Py base. The reaction proceeds toward the formation of the corresponding nucleoside and release of inorganic phosphate (P_i) which is trapped with lead to mark the site of enzyme activity. Py-NP activity was detected largely in the nuclei and slightly in the cytoplasm of endothelial cells of the three organs, and replacement of R-1-P by 2-deoxy R-1-P showed no activity. These results indicate that these histochemical techniques are reliable because they are in agreement with biochemical studies and clearly discriminate between Pu-NP and Py-NP activities. Supported by grant NHLBI 10384.

GASTRIC CYTOPROTECTION BY PROSTAGLANDINS (PG): POSSIBLE MEDIATION BY MUCUS SECRETION. H Ruppin, B Person, A Robert, and W Domschke. Dept of Medicine, University of Erlangen, Germany, and Dept of Experimental Biology, The Upjohn Co, Kalamazoo, Michigan USA.

Topical PG stimulate gastric mucus secretion in rats (Surg forum 27:402,1976) and protect the gastric mucosa from necrotizing agents (GE 72:1121,1977). Basal gastric electrical potential difference (PD), in mV, and gastric mucus secretion (GMS), in μmoles/hr of N-acetylneuraminic acid, were determined in 6 healthy volunteers after PGE_2 (1 mg topically), 40% ethanol ("E," 50 ml topically), and both. The studies consisted of 4 consecutive instillations of 50 ml of test solution (NS, PGE_2, E, NS. NS, vehicle, E, NS. NS, PGE_2, NS, NS) and being terminated by complete aspiration of gastric contents. Results (mean+SEM; PD: mV, lumen negative):

	NS	Vehicle	PGE_2		Vehicle	PGE_2
PD	43 ± 4	41 ± 4	53 ± 4*	ΔPD	-25 ± 3	-27 ± 3*
GMS	25 ± 2	26 ± 2	41 ± 8*	ΔGMS	+48 ± 9	+80 ± 24*

*:p< 0.05 vs vehicle. Δ:change during E when mucosa pretreated by either the vehicle or PGE_2. The increase in PD due to PGE_2 was accompanied by a significant increase in gastric pH from 2.4 to 2.9 while no change in pH occurred during E. CONCLUSIONS: 1. The parallel augmentation of PD and GMS by PGE_2 suggests gastric cytoprotection through mucus secretion, 2. the opposite directions of ΔPD and ΔGMS during ethanol indicate epithelial cell damage and consecutive mucus discharge from injured gastric mucosa.

BLOOD FLOW RESPONSES OF THE HUMAN CALF AND FOREARM. Nancy J. Rusch, R. Clinton Webb, John T. Shepherd and P.M. Vanhoutte. Universitaire Instelling Antwerpen, Wilrijk, Belgium and Mayo Foundation, Rochester, Minn., U.S.A.

Earlier work has shown that the blood vessels of calf and forearm react differently during isometric contralateral handgrip and during emotional stress. The present study was designed to compare the reactivity of these two vascular beds during various cardiovascular adjustments. Forearm and calf blood flow were measured with a plethysmograph; mean arterial pressure was measured indirectly. Calf and forearm showed a comparable vasodilatation after arterial occlusion (reactive hyperemia). During compression of the carotid arteries, the forearm and calf blood flow increased; following Valsalva maneuver blood flow in both vascular beds decreased. During isometric exercise of the contralateral forearm, resisted breathing and headdown tilt the calf blood flow did not change, but the forearm blood flow increased. Following coughing calf blood flow decreased but forearm blood flow was augmented. These changes in blood flow reflected changes in resistance of the respective vascular beds. These findings demonstrate that the blood vessels of calf and forearm can behave differently during cardiovascular adjustments to stress.

ANALYSIS OF BLOOD-LYMPH TRANSPORT IN RESTING AND PASSIVELY FLEXED DOG HIND-LEG. G. Rutili*, D. N. Granger, N. A. Mortillaro, J. C. Parker, and A. E. Taylor. Dept. of Physiology, University of South Alabama, Mobile, AL 36688.

In dogs the hind-leg lymph preparation has been used to characterize the transport of different proteins across the blood-lymph barrier. In previous studies, lymph flow in this preparation has usually been maintained by passive movement of the leg and the purpose of this study is to evaluate this effect on protein transport. The superficial saphenous lymphatics in both hind legs were cannulated and the lymph flow and protein concentrations determined at spontaneous lymph flow (one leg) and at forced (contralateral leg; 100 flection/min) lymph flow for comparison purposes.

A new theoretical approach was used to characterize the protein transport and sieving properties of this preparation. Evaluation of the transport was based on calculating the osmotic reflection coefficient (σ_d) and the solvent drag reflection coefficient (σ_f). For the purpose of calculation, σ_d was assumed to equal $1-C_L/C_P$ at the maximal experimental lymph flow which was achieved by graded increases of venous pressure. σ_f was estimated by using the cross-point method.

σ_d for total proteins was approximately 0.9. By using σ_f it was found that convection dominates the transport of large molecules even at resting lymph flows. Passive movement of the leg at the frequency used in this study does not seem to alter the transport and sieving characteristics of the blood-lymph barrier. Supported by HL 22569.

SINO-VAGAL INTERACTION IN ARTERIAL PRESSURE RESTORATION AFTER 10% HEMORRHAGE. Kiichi Sagawa and Hiroshi Hosomi. The Johns Hopkins Medical School, Baltimore, Md. 21205

The summation between the carotid sinus baroreceptor reflex system (CS-system) and the vagally mediated reflex system (V-system) was studied as they restore mean arterial pressure (MAP) after 10% quick hemorrhage in splenectomized conscious dogs chronically instrumented with catheters for pressure measurement and hemorrhage. The experiment was repeated under nerve intact condition (INTACT), with cold block of the vagi ([V]), after carotid sinus denervation ($\overline{CS}$), and $\overline{CS}$ plus [V] situations. MAP falls at 1.5 min after the hemorrhage were 7.2 in INTACT, 24.7 in [V], 36.0 in $\overline{CS}$, and 67.6 in CS + [V] mm Hg. When we calculated the open-loop gains of CS- and V-systems assuming a simply additive summation between them a self contradiction occurred. To avoid this contradiction, it was necessary to assume that CS- and V-systems interact in a facilitatory manner. Mean open-loop gains calulated under this assumption were 1.64 for the CS-system alone, 0.89 for the V-system alone, and 6.59 for the synergistically interacting component between them. These intriguing results warrant further studies of the summation between the two reflex systems.

EFFECT OF ATHLETIC TRAINING ON PHYSICAL FITNESS UNDER HYPODYNAMICS. Hisashi Saiki, Masayuki Nakaya*, Masamichi Sudoh* Mizuho Abe*, and Masaru Naruse*. Space Medicine Laboratory, Jikei University, Tokyo, Japan 105

Since 1969, when decreased orthostatic tolerance of athletes was noticed, many studies have been performed in connection with the selection on training of astronauts or PS, but still no clear conclusions have been obtained.

In this paper, using as subjects, healthy, adult male "non athletes" in good physical condition, fluctuations of their physical fitness during 2 weeks' vigorous athletic training were measured in many parameters, and the effects of 6 hours' water immersion exposure on the functions were compared before and after training.

The results obtained were as follows :

(1) As a result of training, many functions such as $\dot{V}o_2$ max, flicker fusion value, HPA reaction level (urinary excretion levels of cortisol), etc. showed an increase of the physical fitness capacity. But no decrease of orthostatic tolerance ability was found.

(2) Water immersion exposure after training showed negative stress effects from the point of view of mineral and hormonal metabolism.

These results seem to suggest that during the process of training, a state of body condition where there is an increase in physical fitness capacity, including orthostatic tolerance, is attainable.

UNEQUAL EFFECTS OF K ON VMAX AND CONDUCTION VELOCITY IN CANINE PURKINJE AND VENTRICULAR MUSCLE FIBERS. Tomoaki Saito*, J.L. Hill* and L.S. Gettes. University of North Carolina, Chapel Hill, N.C. 27514

Myocardial conduction velocity (θ) is determined by the maximal rate of rise of the action potential upstroke ($\dot{V}$max) and other properties including resting and threshold potentials and longitudinal resistance. In guinea pig (GP) papillary muscle, increasing extracellular K speeds θ until $\dot{V}$max is decreased by 30% when θ slows. To determine if the 30% decrease is critical in other species and fibers, we studied the effects of increasing K on canine Purkinje (P) and ventricular (V) fibers. θ slowed when K=7 mM in P and 9 mM in V fibers. In both, as in GP, the slowing occurred when $\dot{V}$max was decreased by 25-30%. To explain the different sensitivities of P and V fibers to K^+, we studied them simultaneously in a single-chambered bath. Increasing K caused a greater change in resting potential (RP), $\dot{V}$max, and their relationship in P than in V fibers. Increasing K from 5 to 10 mM caused a decrease in RP of 19 mV in P and 16 mV in V. The RP associated with a 50% decrease in $\dot{V}$max was -71 mV in P and -65 mV in V. This occurred at a K=8 mM in P and 10 mM in V. Our results indicate that in both P and V fibers a 25-30% decrease in $\dot{V}$max is required to overcome the θ speeding effects of increasing extracellular K. The differing sensitivity of P and V fibers suggest differences in membrane properties and Na conductance variables in the two fiber types.

ANALYSES OF THE RECOVERY OF FORCE DEVELOPMENT FROM THE RESTED STATE AND FROM PRIOR CALCIUM DEPLETION IN RABBIT HEART. W.G. Sanborn* and G.A. Langer. UCLA School of Medicine, Los Angeles, CA 90024 and Wadsworth, VA Center, Los Angeles, CA 90073.

Rabbit papillary and trabecular muscles were subjected to three protocols that markedly depressed steady state isometric force development (SSFD). These protocols were: 1) brief perfusion (BP) in Ca-free medium for 2 to 5 min, 2) extended perfusion (EP) in 0.1 mM Ca medium for 50 min, and 3) interruption of SSFD for 15 min, a rest interval sufficient to yield the rested state (RS). The time to recover from RS was not dependent on muscle cross-sectional area whereas the time to recover from RS, $[Ca]_o$=constant, the rate limiting step is most likely associated with an excitation-dependent movement of coupling Ca into stores critical for force development. Time to recover to SSFD after BP and EP was statistically equivalent and more rapid than the time to recover to SSFD from RS for the thinnest muscles. These results suggest: 1) that recovery after BP and EP was rate limited by the entry of Ca into the extracellular space (ECS) and 2) that during BP and EP the loss of coupling Ca was either kinetically inseparable from the loss of Ca from ECS, alone, or retained in an additional inexchangeable compartment. (Supported by USPHS Grant #11351-12 and a Grant from the American Heart Association, Greater Los Angeles Affiliate.)

INTAKE AND RENAL EXCRETION OF WATER AND ELECTROLYTES DURING 7 DAYS OF ETHANOL ADMINISTRATION. William Q. Sargent, John R. Simpson, and James D. Beard. Univ. of Tenn., Memphis, 38104

In dogs, an acute dose of ethanol (2.5 g/kg) has been shown to produce water, Na and Cl retention. The present study was undertaken to ascertain the effects of a 7-day administration. Dogs were given either 2.5 g/kg of a 33% ethanol solution or an isovolumetric, isocaloric dose of dextrose solution. Urine was collected by bladder catheterization prior to the first dose and at the end of days 1,3,5, and 7. Water intake and food consumption were measured daily. Urine and food were analyzed for Na, K, Cl, and Mg. A sulfate space was determined on day 7. There was a significant increase in body weight and the volume of distribution of sulfate in the ethanol treated animals. The table expresses the mean difference between treatment groups (ETOH - DEX) for the entire 7 days.

	INTAKE	OUTPUT	BALANCE
Water	4460 ml*	2777 ml*	1683 ml*
Na	118 mEq*	30 mEq	88 mEq*
K	118 mEq*	82 mEq*	36 mEq
Cl	137 mEq*	43 mEq	94 mEq*

Renal magnesium excretion was also elevated in the ethanol group. The results suggest that chronic ethanol intake also produces Na, Cl, and water retention with resultant extracellular volume expansion. (Supported by USPHS Grant AA02670 and an agreement with the State of Tenn., Dept. of Mental Health and Mental Retardation). *$P < 0.05$

PHYSIOLOGICAL RESPONSES TO MAXIMAL EFFORT WHEELCHAIR AND ARM CRANK ERGOMETRY. M.N. Sawka*, R.M. Glaser, M.F. Brune*, S.W. Wilde* and A.G. Suryaprasad*. Wright State Univ. Sch. of Med., Dayton, OH 45435 and VA Med. Ctr., Dayton, OH 45428

The purpose of this investigation was to compare physical work capacity (PWC), oxygen uptake ($\dot{V}O_2$), heart rate (HR), pulmonary ventilation ($\dot{V}E$) and blood lactate concentration (LA) for maximal effort wheelchair ergometer (WERG) and arm crank ergometer (ACE) exercise. Wheelchair-dependent (N=2) and able-bodied (N=7) subjects completed a progressive intensity, discontinuous test for each method of exercise on separate days. Exercise bouts were 4 min in duration interspersed by 5 min rest periods. The initial workrate was extrapolated from submaximal HR vs power output (PO) data. This PO corresponded to 75% of each subject's predicted age adjusted maximal heart rate corrected (-10 bpm) for arm exercise. Each test was terminated by (1) physical exhaustion and/or (2) an inability to maintain a flywheel velocity of 180 $m \cdot min^{-1}$. A significantly ($P<0.05$) higher PWC was found for ACE than WERG exercise. No significant differences were found for $\dot{V}O_2$, HR, $\dot{V}E$ and LA between the two exercise modes. Mean values during WERG and ACE exercise for PWC were 395 and 610 $kpm \cdot min^{-1}$, for $\dot{V}O_2$ were 2.01 and 1.97 $l \cdot min^{-1}$, for HR were 157 and 165 bpm, for $\dot{V}E$ were 85.6 and 79.8 $l \cdot min^{-1}$, and for LA were 6.9 and 8.3 $mmol \cdot l^{-1}$, respectively. These data suggest that arm crank propulsion should be studied as a method to increase PWC for wheelchair activity. (Supported in part by the Medical Research Service of the VA).

EFFECTS OF TWO EXERCISE PROGRAMS ON PERFORMANCE AND SKELETAL MUSCLE OXIDATIVE CAPACITY. W.R. Sandel*, P.A. Mole*, and E. Bockman, U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760 and L.S.U. School of Medicine, New Orleans, LA 90112.

Preliminary studies indicated a 6-75 min range in run times to exhaustion (RTE) among untrained rats. Since other studies did not determine pre-training RTE (RTE_1) and match animals by these values, bias in performance capacity may have been introduced when animals were separated into trained and control groups. We paired 232 g rats into 2 groups (n=14 each) with statistically identical RTE_1 (40 min). One group (designated as long duration run time, LD) began running at 50% RTE_1 and increased 4% weekly for 13 weeks until 100% RTE_1 was achieved and maintained for 5 weeks. The second group (designated as short duration run time, SD) ran 10 min daily, 27 m/min, 10% grade, 18 weeks. In spite of differences in exercise programs, group body weights increased identically by the end of training (about 65 g, 28%), and final run times (RTE_2) of groups increased about 3.5 fold ($p < 0.05$). Although this represents an increase in work done of approximately 283 kg • m for both groups at RTE_2, neither exercise program enhanced skeletal muscle oxidative capacity as measured by malate dehydrogenase and cytochrome c. It is hypothesized that the LD exercise program was not sufficient to increase RTE or oxidative capacity above those of SD animals. SD animals had greater RTE_2 (111 min) than controls in other studies (26 min) because they began with greater performance capacity. Therefore, our results indicate an exercise range in which RTE is enhanced independently of skeletal muscle oxidative enzyme adaptations.

STRONTIUM SUBSTITUTES FOR CA^{++} IN STIMULUS-SECRETION COUPLING IN THE ECCRINE SWEAT GLAND BUT ENTERS THE CELL BY TWO DIFFERENT MECHANISMS. Kenzo Sato and Fusako Sato*. Univ. of Iowa, Iowa City, Ia. 52242.

Isolated and cannulated single eccrine sweat glands of the monkey palm were used to study the role of Ca^{++} and Sr^{++} in the secretory response to cholinergic stimuli (MCH). Evidence indicates that the secretory response to MCH is mediated by influx into the secretory cell of Ca^{++}; namely, removal of Ca^{++} from the bath reversibly abolishes secretion and A23187(10^{-5}M), but not X537A, induces secretion, which is then inhibited by D600(1mM). Sr^{++} can replace Ca^{++} in the bath but seems to enter the cell by both MCH-mediated and nonmediated processes producing the secretory rate comparable to that seen in Ca^{++} medium with MCH. In Ca^{++} free 4mM Sr^{++} Ringer, MCH at $5x10^{-7}$M instantaneously triggers secretion, which is inhibited by atropine only at a huge concentration, $5x10^{-4}$M. Spontaneous secretion in the Sr^{++} medium without MCH is minimal at time zero but gradually increases over the 60 min period to reach the sweat rate seen under MCH stimulation. This spontaneous secretion is not inhibited by atropine or adrenergic antagonists but is instantaneously inhibited by addition to the bath of Ca^{++}(2mM), however, secretion is resumed by the subsequent addition of MCH. Both A23187 and X537A behave like MCH and thus may be carriers of Sr^{++} but the latter does not carry Ca^{++} across the membrane. The data are consistent with the thesis that Ca^{++} is a mediator of MCH stimulation and is also important in maintaining the stability of the cell membrane.

FACTORS INFLUENCING AORTIC PRESSURE AND FLOW DURING MECHANICAL POSITIVE PRESSURE VENTILATION (V). Steven M. Scharf and Robert Brown. West Roxbury VA Medical Center and Harvard Medical School, Boston, MA 02132

In 14 anesthetized mongrel dogs we studied the factors which influenced aortic systolic pressure (Pao) and peak systolic flow (Qao) during V at three different respiratory rates: slow (8/min); medium (14/min) and fast (25/min), at constant tidal volume (300cc). The mean increase in pleural pressure (Ppl) was 5.3 ± .5(SE) Torr. At all three respiratory rates Qao fell during inspiration reaching a nadir at end-exhalation (the point at which Ppl returned to baseline) (at slow and medium rates to 85 ± 2% and at the fast rate to 93 ± 2.4% of baseline. Pao rose more during the early part of inspiration at the medium and fast rates (5 ± .9 Torr) than at the slow rate (3 ± .7 Torr); then Pao fell to a nadir at end-exhalation: -5.6 ± 1.6 at slow; -2.3 ± 1 at medium; .1 ± .5 Torr at fast rate. Impedance (Iao) to systemic flow (Pao/Qao) increased throughout the respiratory cycle reaching a peak by end-exhalation. When Ppl was increased in a square wave manner, Qao did not change for .75sec and then decreased exponentially. A model was developed which predicted the major qualitative features of the changes in Qao during V at different respiratory rates. Changes in Pao result from the interaction between the decreases in Qao and the transmitted increases in Ppl, and are modified by changes in Iao.

Supported by VA funding.

CORONARY AND COLLATERAL RESISTANCES IN THE BEATING AND FIBRILLATING HEART. Konrad W. Scheel, Jack L. Wilson*, and Leslie A. Ingram*. University of Tennessee Center for the Health Sciences, Memphis, TN 38163

The effects of fibrillation on the coronary resistances (6 dogs) and coronary collateral resistances (9 dogs) were investigated. The circumflex (C), anterior descending (A), and right (R) coronary arteries were cannulated in an isolated, blood perfused preparation with the left ventricle vented to atmosphere. Blood flows were simultaneously recorded with electromagnetic flow meters during vasodilation. In the beating heart coronary resistances were determined from perfusion pressure and late diastolic flow values. Collateral resistances were calculated using the double retrograde flow method. The resistances of C and R before and after fibrillation were not significantly different ($P = 0.4$, $P = 0.7$, respectively). Beating: C = 0.36 ± 0.04 (mean ± SEM) mm Hg/ml/min/100 g; R = 1.05 ± 0.08. Fibrillating: C = 0.35 ± 0.03; R = 1.05 ± 0.07. There was a small but significant ($P < 0.01$) increase in resistance of A following fibrillation. Beating: A = 0.51 ± 0.06. Fibrillating: A = 0.56 ± 0.06. There was no significant difference in collateral resistances between the two states. It was concluded that myocardial contractions without ventricular load (pressure) have a minimal effect on collateral resistance. (Supported by the American Heart Association.)

BICARBONATE TRANSPORT IN THE URINARY BLADDER OF THE TURTLE AS A FUNCTION OF LUMINAL HCO_3 CONCENTRATION. Theodore P. Schilb. L.S.U. Medical Center, New Orleans, LA.

It has previously been reported that the urinary bladder of the turtle transports HCO_3 from lumen to serosa, resulting in the acidification of the luminal fluid, and that in the absence of exogenous CO_2 and HCO_3 the transport rate as a linear function of luminal pH, that is independent of serosal pH and transmural pH gradients. Present data show that the transport rate is a saturable function of luminal bicarbonate concentration in the presence and in the absence of exogenous bicarbonate and that this function vanishes when the tissue is anoxic.

INHIBITION OF LIPOLYSIS BY ALPHA ADRENERGIC AGENTS: EVIDENCE OF TWO CLASSES OF ALPHA RECEPTORS R.J. Schimmel, College of Med. & Dent. of N.J.-NJSOM, Piscataway, N.J. 08854

Previous data from this and other laboratories have provided strong evidence for an α adrenergic sensitivity on hamster fat cells that acts to suppress lipolysis and cAMP levels. The purpose of the present investigation was to characterize the effects of α adrenergic stimuli on lipolysis and cAMP levels in hamster adipocytes exposed to various lipolytic stimuli. Adipocytes were prepared by collagenase digestion of epididymal fat bodies. The α adrenergic agents used were: clonidine, methoxamine, phenylephrine and methyl norepinephrine. Lipolysis activated by methyl xanthines or adenosine deaminase was most strongly inhibited by clonidine and less strongly inhibited by methoxamine and methyl norepinephrine and not by phenylephrine. In contrast, lipolysis activated by isoproterenol or norepinephrine was strongly inhibited by phenylephrine and only weakly inhibited by methoxamine, clonidine and methyl norepinephrine. cAMP levels were lower in the presence of clonidine, methoxamine and methyl norepinephrine but higher in the presence of phenylephrine. The different rank order of potency of these α agents to inhibit methyl xanthine or adenosine deaminase activated lipolysis as compared to isoproterenol activated lipolysis suggests the presence of two populations of α receptors on fat cells: one is selective for clonidine, methoxamine and methyl norepinephrine; the other for phenylephrine. (Supported by NIH Grant AM-21431.)

THE EFFECT OF VARYING THE RESISTANCE OF OBSTRUCTED SMALL AIRWAYS ON PHASE DIFFERENCE. Evelyn H. Schlenker* and Marc J. Jaeger. (Spon: D. M. Travis). University of Florida, Gainesville, FL 32610

In a two compartment model of the lung, the phase difference (PD) between mean alveolar pressure and flow of the mouth varies as the ratio of the resistance of the obstructed (Ro) compartment to the resistance of the normal compartment. Using 22 smokers with a PD, we attempted to decrease Ro by having them breathe at increased lung volume (one liter above functional residual capacity) or by administering a β-adenergic bronchodilator (metaproteronal sulphate). PD did not decrease significantly with either increased lung volume or metaproteronal in II of the heaviest smokers (mean pack year (P/Y) = 38 years) going from 12.0 ± 6.1° to 10.2 ± 5.5 and 12.0 ± 6.1° to 8.0 ± 7.1° respectively. The II lighter smokers (P/Y = 14.3 years), however showed a significant decrease of PD with increased lung volume or metaproteronal from 12.8 ± 5.4° to 1.4 ± 4.5° and 12.8 ± 5.4° to 1.4 ± 4.5°. We interpret this to mean that the small airways of heavy smokers are less able to dilate in response to increased lung volume or to metaproteronal then are those of light smokers. (Supported by the Parker B. Francis Foundation and NIH Grant T01HL0579).

EFFECT OF CHANGES IN CHEST WALL MOTION ON 133-Xe CLEARANCE IN SUPINE DOGS. E. R. Schmid,* T. J. Knopp,* K. Rehder and R. E. Hyatt. Mayo Graduate School of Medicine, Rochester, MN 55901.

We have previously shown in supine dogs that chest wall motion is different with spontaneous respiration (SR) and mechanical ventilation (MV) during anesthesia. To determine whether there was an altered ventilation per unit lung volume associated with this, we studied regional 133-Xe clearances in 7 anesthetized (enflurane, 1.5 MAC) supine dogs during SR and MV. Following equilibration of the lungs with 133-Xe, regional clearances were determined in duplicate from apical nondependent (AND), basal nondependent (BND), and basal dependent (BD) regions. Functional residual capacity (FRC) was determined by ethane dilution. Cumulative inspired fresh gas volumes ($\Sigma\dot{V}_I$) necessary to reduce original counts to 75, 50 and 25% were defined and expressed as $\Sigma\dot{V}_I$/FRC. Tidal volume/FRC ratios were not different between SR and MV.

$\Sigma\dot{V}_I$/FRC to Reduce Counts to 75, 50, 25% of Original Counts

% Original Counts	Spont. Resp.			Mech. Vent.		
	AND	BND	BD	AND	BND	BD
75%	0.84	0.75	0.38	0.88	0.78	0.35
50%	2.01	1.84	1.00	2.11	2.01	1.04
25%	4.00	3.72	2.45	4.21	4.15	2.61

Mean $\Sigma\dot{V}_I$/FRC ratios were not significantly different ($P > 0.2$) between SR and MV. We conclude that changes in chest wall motion are not necessarily associated with an altered ventilation per unit lung volume. (Supported by USPHS, NIH grant HL-21584, and the Parker B. Francis Foundation.)

REGIONAL CARDIAC NOREPINEPHRINE TURNOVER IN GUINEA PIGS WITH PULMONARY ARTERY CONSTRICTION (PAC). Janine A. Schmidt*, Phillip G. Schmid, Robert Oda*, and Howard Mayer*. C.V. Center and Dept. of Int. Med., Univ. of Iowa, Iowa City, Iowa 52242

Selective pressure overload of the right ventricle in guinea pigs leads to reduced tyrosine hydroxylase activity (TOH) in the right but not the left ventricular wall (Circ. 56(Suppl.III):228, 1977). Therefore, we determined regional norepinephrine turnover (NE-TO) in the same model to assess whether another index of sympathetic neural function exhibited a corresponding change. NE-TO was quantitated from the rate of disappearance of tracer amounts of ^{3}H-NE overtime, k_{NE} hr^{-1}. Control (C) guinea pigs (n=12) had higher values of k_{NE} in the right atrium (RA) than in the left atrium (LA) or right (R) and left (L) ventricles (0.0547± 0.0101 vs 0.03991±0.01166, 0.03881±0.00948, 0.04096±0.00851) ($\bar{x}$±SEM, $P<0.05$). Guinea pigs with PAC had marked RV hypertrophy and either normal (n=12) or reduced (n=11) RV catecholamines. In the former group, k_{NE} was high and uniform in the four heart chambers. In the latter group, k_{NE} was low and also uniform. These results indicate disparate changes in the regional pattern of TOH and NE-TO in guinea pigs with PAC and suggest two possible mechanisms of altered sympathetic neural function, one affecting synthesis and another affecting storage of neurotransmitter.

COMPARATIVE EFFECTS OF ARACHIDONIC (AA) ACID METABOLITES ON TRACHEAL SPIRALS AND PARENCHYMAL STRIPS. M.W.Schneider* and J.M.Drazen,Dept.Physiol.,Harvard Sch.Publ.Hlth.and Dept.Med. Peter B.Brigham Hosp.and Harvard Med.Sch.,Boston, MA 02115.

Many oxidative products of AA metabolism are synthesized by guinea-pig lungs during immediate type hypersensitivity reactions. Because prominent pathobiologic changes occur in the airways during these reactions, we compared the pharmacological activity of several AA metabolites to that of histamine (HIST) using guinea-pig tracheal spirals (TR) and parenchymal strips (PS). The AA metabolites tested were; Prostaglandin (PG)$F_{2\alpha}$,PGD_2,PGI_2,6-keto-$PGF_{1\alpha}$,9α,11α and 11α,9α cyclic ether endoperoxide analogues. HIST was the most effective constrictor of the TR. PGD_2 and the 9α,11α and 11α,9α cyclic ether analogues had maximal effects between 40 and 60% of the maximal HIST response of this tissue,while $PGF_{2\alpha}$,6-keto-$PGF_{1\alpha}$ and PGI_2 had minimal effects on TR. The most effective constrictor of the PS was the 11α,9α analogue, eliciting contractions twice as great as those achieved with HIST or KCl. The 9α,11α analogue was the next most effective agent, contracting the PS to 90% of HIST, followed by PGD_2=73% and $PGF_{2\alpha}$=39%. PGI_2 and 6-keto-$PGF_{1\alpha}$ had little contractile effects on the PS. PGE_2 relaxed both tissues, previously constricted with HIST. PGI_2 and PGD_2 relaxed the TR at high concentrations,but none of the PGs were as effective a bronchodilator as isoproterenol. This suggests that AA metabolites may play an important role in the peripheral airway constriction which is evident during hypersensitivity reactions. (Supported by HL-17382).

RESPIRATORY DRIVES AND EXERCISE VENTILATION IN THE MENSTRUAL CYCLE. R.B. Schoene*, D.J. Pierson*, H.T. Robertson, University of Washington, Seattle, Washington 98195.

Progesterone (PG) administered to males augments resting ventilation ($\dot{V}_E$) ventilatory drives and exercise $\dot{V}_E$ (Clin. Res. 27:58A,1979). We studied the effect of the fluctuation of endogenous PG on resting $\dot{V}_E$, hypoxic(HVR) and hypercapnic ventilatory(HCVR) responses,and $\dot{V}_E$ during exercise testing on a bicycle ergometer in six menstruating females. Subjects were tested once in mid-follicular (F) and once in mid-luteal (L) phases. Daily basal-body T° were recorded; serum progesterone levels were drawn fasting on the morning of testing and at exhaustive exercise. HVR was evaluated by the shape parameter A;HCVR was assessed by $S=(\Delta\dot{V}_E/\Delta P_ACO_2)$. Standard determinations of ventilation and mouth occlusion pressures were measured. The results in the first six subjects (4 non-athletes, 2 trained runners:

Menst. Phase	Resting P_ACO_2	Rest $\dot{V}_E$ (L/min)	HVR A	HCVR S	$\dot{V}_E$ (L/min) at exercise of: $\dot{V}CO_2$ 1 L/min	$\dot{V}CO_2$ 2 L/min	$\dot{V}CO_2$ max
F	43.6 ± 0.8*	7.7 ± 0.7*	73.1 ± 30.8*	1.3 ± 0.0*	28.5 ± 0.8*	56.2 ± 1.8*	76.0 ± 2.9*
L	41.2 ± 0.9*	9.3 ± 0.8*	148.4± 36.2*	2.2 ± 0.5*	29.8 ± 1.8*	63.0 ± 3.8*	83.5 ± 3.7*
P	<.02	<.01	<.05	<.05	NS	<0.1	<.02

Menstruating women in the luteal phase have augmented $\dot{V}_E$, ventilatory drives,and exercise $\dot{V}_E$. This finding is consistent with stimulation of the central respiratory centers by the fluctuation of progesterone during the menstrual cycle. Supported by NIH grant # HL05761 * S.E.M.

A LINKAGE OF ACTIVE TRANSPORT TO THE FRANKENHAEUSER-HUXLEY CONSTANT FIELD EQUATIONS. G. M. Schoepfle and J. T. Tarvin. Dept. of Psychiatry, Lab. of Membrane Biol., Dept. of Physics University of Alabama in Birmingham, Birmingham, AL 35294

The Frankenhaeuser-Huxley constant field leak current equations (J. Physiol., 171:302, 1964) are set to a 3/2 ratio for the resting state in the Xenopus node and are coupled to an electrogenic pump current term which is proportional to an emf derived from classical thermodynamics. This active transport term I_p is identical with that derived by Rapoport (Biophys. J., 10:246, 1970) in terms of a much more generalized argument of irreversible thermodynamics. At all times

$$I_p = g_pV - 3g_p(RT/F)\ln[(Na)_o/(Na)_i] + 2g_p(RT/F)\ln[(K)_o/(K)_i] - g_p(RT/F)\ln[(ADP)(P_i)/(ATP)(H_2O)] - g_p(\Delta H/F) - g_p(T/F)[S^o_{ATP} + S^o_{H_2O} - S^o_{ADP} - S^o_{Pi}]$$

where V is membrane potential, g_p = .0303 mho/cm^2 and the last three terms which include standard entropies are assumed to be constant. A small increase in $(Na)_i$ coupled with a corresponding decrease in $(K)_i$ induces post spike voltage changes which correspond to those observed during tetanization. Progressive hyperpolarization continues well beyond time of normal post spike undershoot, despite the fact that the curves are fairly close to one another prior to this time. NIH Support

PULMONARY GAS EXCHANGE DURING PSEUDOMONAS SEPTICEMIA WITH ASSOCIATED PLASMA OPSONIC (FIBRONECTIN) DEFICIENCY IN THE SHEEP. P.T.Schumacker*, G.D.Niehaus* and T.M.Saba. Dept. of Physiology, Albany Medical College, Albany, NY 12208

Opsonic glycoprotein (plasma fibronectin; CIg) deficiency correlates with pulmonary failure in trauma patients during septicemia. Reticuloendothelial (RES) dysfunction exists during opsonic deficiency, and during RES depression aggregates of fibrin, platelets and collagenous debris are localized in the lung. The present study evaluated the effect of opsonic deficiency on gas exchange impairment during septicemia. Anesthetized, ventilated sheep were challenged with Pseudomonas; Pseudomonas plus gelatin (16mg/kg), or gelatin alone. Gelatin (denatured collagen) was chosen due to its high affinity for opsonic protein. Opsonin levels were acutely depressed after gelatin, but bacterial challenge itself also decreased opsonin levels. Sepsis with and without gelatin decreased fibrinogen and increased fibrin degradation products (FDP). Shunt was not altered after gelatin, but was transiently elevated during sepsis. Cardiac output was unaltered after gelatin but declined with septicemia during opsonic deficiency. Pulmonary vascular resistance was transiently elevated after bacterial challenge with sustained elevation after bacterial challenge during opsonin deficiency. Thus, the similar but minimal gas exchange impairment may be due to the septicemia-induced opsonic depletion. Alternatively, gas exchange insufficiency may only develop as a later sequel to lung injury. (GM-21447; HL-07194; T32-GM-07033)

METABOLISM OF EXOGENOUS ADENINE NUCLEOTIDES IN LOCKE-RINGER PERFUSED RAT LUNG. J.B. Scott, and B.H. Selleck* (SPON: W.D. Collings). Department of Physiology, Michigan State University, East Lansing, MI 48824.

Exogenous adenine nucleotide metabolism was studied in the isolated perfused rat lung to determine if venous plasma adenine nucleotides can pass through the lung vasculature and reach the systemic arterial circulation. In eleven rat lungs the pulmonary arterial ATP was increased in increments from 0 to 110 μg/ml and at each level of ATP infusion pulmonary venous ATP was assayed (method sensitivity < 1 ng/ml). Pulmonary arterial ATP levels up to 10 μg/ml resulted usually in no detectable pulmonary venous ATP and in no case was the pulmonary venous ATP greater than 10 ng/ml. Less than 0.1% of pulmonary arterial ATP levels from 10 to 110 μg/ml was observed in the pulmonary venous effluent. Ion exchange chromatography of the pulmonary venous effluent (N=7) indicated that virtually all of the pulmonary arterial ATP or ADP was converted to AMP on a single pass through the lung vasculature. In lung preparations free of edema (N=4) no nucleosides, cyclic 3,5-AMP, IMP or ADP were observable in the venous effluent during pulmonary arterial ATP infusion. Intrapulmonary arterial AMP, cyclic 3,5-AMP and IMP passed through the lung vasculature without breakdown. These findings suggest that venous plasma adenine nucleotides other than cyclic 3,5-AMP would recirculate through the lungs as AMP. (Supported by HL10879 from NHLI)

THE ROLE OF CRANIAL NERVES IN CHOLINERGIC CEREBRAL VASODILATATION. O. U. Scremin*, R. R. Sonnenschein and E. H. Rubinstein. Dept. of Physiology, UCLA School of Med., Los Angeles, CA 90024.

The increases in cerebral blood flow (CBF) associated with cortical arousal and hypercapnia have an important cholinergic component. Cholinergic fibers can reach the brain vessels via central pathways or, alternatively, via the cranial nerves that contribute fibers to the carotid plexus. Also, visceral afferents in the IX and X nerves have been proposed by some to play a role in the cerebrovascular response to CO_2. To evaluate the possible involvement of cranial nerves in the cholinergic vasodilatation, the increases in internal carotid blood flow induced by physostigmine (0.15 mg/kg, i.v.) or hypercapnia ($ETCO_2$=8%) were studied before and after bilateral intracranial division of the VII, VIII, IX, X and XI nerves in halothane/N_2O anesthetized, mechanically ventilated rabbits. The multiple denervation did not affect the cerebrovascular responses under study. Moreover, electrical stimulation of the III and VII nerves with parameters adequate to activate their parasympathetic fibers, as revealed by constriction of the pupil and lacrimal secretion respectively, did not induce changes in CBF. It is concluded that cranial nerves are not involved in the cholinergic vasodilatation and do not contribute to the effect of CO_2 on CBF. (Grant support: NIH HL 17903 and AHA-GLAA 437IG.)

CARDIAC REFLEX REGULATION OF VASCULAR RESISTANCE. J.L. Seagard, S.R. Bachhuber*, Z.J. Bosnjak*, and J.P. Kampine. Med. Col. of Wisconsin and Wood VA Ctr., Milwaukee, WI 53193

The present investigation was performed to determine the contribution of cardiac receptors (CR) with vagal or sympathetic afferents to reflex regulation of vascular resistance (VR) in the isolated hindlimb and kidney. 15 mongrel dogs were anesthetized with either sodium pentothal (25 mg/kg) + halothane or sodium pentobarbitol (35 mg/kg), and placed on an isobaric system to maintain blood pressure constant. The left external iliac artery or left renal artery was cannulated and the otherwise isolated bed was perfused at constant pressure via a servo-control unit which gave on-line readings of flow and resistance. The CR were stimulated by either coronary occlusion or topically applied nicotine or cryptenamine. Stimulation was repeated following vagotomy and sympathectomy. Coronary occlusion produced a consistent dilation of 5-25% in the isolated hindlimb and 9-14% in the kidney. Vagotomy eliminated the reflex in the hindlimb, but a small response remained in the renal bed of several dogs. Sympathectomy eliminated all responses. Application of nicotine to the heart of vagotomized dogs produced either renal constriction or dilation, depending on the areas of the heart involved. Cryptenamine application produced a consistent dilation. Vagal CR were shown to have a dominent role in the regulation of VR while the sympathetic CR produced consistent changes only in response to pharmacologic stimulation. (Supported by NIH Grants HL 16511 and 1F32 HL 05882, and the VA).

CHANGES IN AORTIC ACTOMYOSIN AND FORCE WITH HYPOTENSION. Charles L. Seidel and Rebecca Bowers*. Baylor College of Medicine, Houston, TX 77030

Previous work from this laboratory suggested that the absolute amount of actomyosin (AM) in aorta from SHR rats was greater than in aorta from WKY rats. The purposes of these experiments were to determine if AM content was decreased by a reduction in systolic blood pressure and if such a reduction is reflected in a reduction in maximum contractile response (MCR). Ten wk old WKY and SHR rats were given hydralazine (80mg/l) in their drinking water for 2 wks. At the end of this time, the MCR to phenylephrine and KCl, the AM content (SDS-PAGE) and total protein content of thoracic aorta were determined and compared to aorta from untreated rats. The systolic blood pressure of treated animals was significantly reduced by the end of the first week. There was no change in aortic wet weight or total protein content, but AM content and MCR to both agonists were significantly reduced. An analysis of the ratio of MCR to AM content indicated: that the ratio is lower in aorta from SHR rats; treatment does not change the ratio, and SHR aorta undergo a smaller reduction in MCR for a given reduction in AM than do aorta from WKY rats. These results suggest that in both normotensive and hypertensive rats; the net production of aortic AM, and therefore, MCR are sensitive to hydralazine induced hypotension.
(Supported by grants HL 17269, HL 23185 and the American Heart Association Texas Affiliate)

METABOLISM OF EXOGENOUS ADENINE NUCLEOTIDES IN LOCKE-RINGER PERFUSED INTESTINE. B.H. Selleck*, C.C. Chou, R. Nyhof*, and J.B. Scott. Department of Physiology, Michigan State University, East Lansing, MI 48824

To determine if adenine nucleotides released by cells of the intestine can be recovered in the intestinal venous outflow, the metabolism of intraarterial ATP was studied in non-recirculating, Locke-Ringer, constant flow perfused dog intestinal segments (N=4) and in constant pressure perfused rat intestinal tract (N=5). Arterial ATP was increased in increments from 0 to 250 µg/ml and at each level of ATP infusion intestinal venous ATP was assayed using firefly luminescence (sensitivity < 1 ng/ml). Intraarterial ATP levels up to 10 µg/ml resulted in almost all cases in no detectable venous ATP; and less than 0.1% of arterial ATP levels from 10 µg/ml to 250 µg/ml was observed in the intestinal venous effluent. Breakdown products of intraarterial ATP (80-250 µg/ml) were analyzed by gradient elution ion exchange chromatography. In both dog and rat intestine the major products of extracellular ATP metabolism were AMP and nucleosides with no observable formation of either ADP, cyclic 3,5-AMP or IMP. Intraarterial cyclic 3,5-AMP (40-150 µg/ml) was not observably degraded on a single pass through the rat intestinal circulation (N=4). These findings suggest that endogenous adenine nucleotides, other than cyclic 3,5-AMP, released by cells of the intestine would appear in the intestinal venous effluent primarily as AMP and nucleosides.
(Supported by grant HL 15231 from NHLI.)

CONTRIBUTIONS OF THE RENIN-ANGIOTENSIN SYSTEM AND BODY FLUID VOLUME TO THE DEVELOPMENT OF RENOVASCULAR HYPERTENSION. A.A. Seymour*, J.O. Davis, R.H. Freeman, J.M. DeForrest, B.P. Rowe*, and G.M. Williams.* Univ. MO Sch. Med., Columbia, MO 65212.

A .22 mm clip was placed on the renal artery of each 150 gm rat in 3 groups of one-kidney animals. The increase in systolic blood pressure (SBP) of 6 sodium replete rats (from 93±5 to 153±11 mm Hg) within 12 days was the same as the rise observed in 8 sodium restricted and, presumably, volume deplete rats (from 97±4 to 149±7 mm Hg). During continuous infusion of the converting enzyme inhibitor SQ 14225 (80 µg/hr) in 6 clipped sodium deplete rats, SBP did not increase (96± 4 and 101±4 mm Hg, control and day 12, respectively). Within a week of termination of the SQ 14225, SBP rose to 149±11 mm Hg. In addition, SQ 14225 (35 mg/kg/day) completely abolished the pressure response to renal artery constriction(RAC) in 3 sodium deplete one-kidney dogs. During angiotensin blockade, mean arterial pressure (MAP) did not change following RAC (83±5 and 68±5 mm Hg, control and day 7 values). MAP significantly increased to 113±2 mm Hg within a week of terminating SQ 14225 treatment. The data demonstrate that development of renovascular hypertension depends on both increases in renin activity and changes in body fluid volume.
(Supported by PHS Grant HL 07094-04.)

EFFECTS OF INTERCOSTAL AND ABDOMINAL MUSCLE AFFERENTS ON MEDULLARY RESPIRATORY NEURON(NA,NRA) ACTIVITY. R. Shannon, D.L. Freeman* and B.G. Lindsey*. Dept. of Physiology, Col. of Med., U. of So. Florida, Tampa, Fla. 33612

Intercostal nerve afferent fibers (Group I) were shown to inhibit phrenic activity(PA) and inspiratory neurons located near the nucleus tractus solitarius (Shannon, Physiologist 21(4):108,1978). Studies were conducted to determine if this reflex activity affected inspiratory(I) and expiratory(E) neurons in the nucleus ambiguous(NA) and nucleus retroambigualis(NRA). Anesthetized (Dial), vagotomized, paralyzed, artificially ventilated cats were used. PA (C_5), NA and NRA extracellular activity, and thoracic dorsal root action potentials were monitored during electrical stimulation of T_5-T_{10} external or internal intercostal nerves(INS). PA and I cells in the NA (15) and NRA (27) were inhibited by INS; no I cells were facilitated. INS during I shortened I time(Ti) and decreased the subsequent E time(Te); the duration of E cell (29 of 30) activity decreased. INS during E prolonged Te and the duration of activity of 15 of 25 E cells; no E cells were facilitated. Some (14 of 28) E cells also transiently decreased their rate of activity. It is concluded that 1) the dominant effect of intercostal and abdominal muscle proprioceptor afferents on central respiratory activity is inhibition of inspiration, 2) the changes in duration of central expiratory activity results from the effects of I on E neurons, and 3) there may also be some minor inhibition of E neurons by muscle afferents. (Supported by USPHS, NIH Grant HL-17715).

SEX DIFFERENCES IN HEAT TOLERANCE AND ACCLIMATIZATION. Yair Shapiro*, Kent B. Pandolf, Barbara A. Avellini* and Ralph F. Goldman. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760

Sex differences in heat tolerance and acclimatization were studied in 10 males and 9 females. Subjects acclimatized for 7 days walking 1.34 m/s for 100 min at 49°C, 20% rh. Subjects were then exposed to 2 hot dry conditions (54°C, 10% rh; 49°C, 20% rh) and 2 hot wet conditions (37°C, 80% rh; 35°C, 90% rh). Exposures lasted 120 min: 10' rest, 50' walk (1.34 m/s), 10' rest, 50' walk. Physiological measurements included: heart rate (HR), rectal temperature (T_{re}), and sweat loss ($\dot{m}_{sw}$). During acclimatization, mean final HR dropped 27 in females and 30 b/min in males, final T_{re} dropped 0.70 and 0.46°C respectively, and $\dot{m}_{sw}$ remained unchanged. Although females maintained higher HR and T_{re} than males, both sexes showed similar trends during acclimatization. During the hot dry exposures HR and T_{re} were significantly lower for males than females by 20 and 13 b/min and by 0.32 and 0.25°C for the two days; no significant differences in $\dot{m}_{sw}$ were observed. During the hot wet exposures both mean final T_{re} and $\dot{m}_{sw}$ were lower in females than males; by 0.24 and 0.34°C and by 159 and 106 g/m²·h respectively (males sweated 40 and 25% more than females). None of the above differences correlated with $\dot{V}O_2$ max of the subjects. Several conclusions can be drawn: (a) both sexes react similarly during heat acclimatization, (b) males tolerate hot dry climates better than females, (c) females tolerate hot wet climates better than males, (d) during hot wet conditions females conserve body water better than males by reducing inefficient (non-evaporative) sweat loss.

A MUCUS BARRIER TO WATER MOVEMENT IN THE PANCREAS - APPLICATION TO CYSTIC FIBROSIS (CF). Mitchell L. Shiffman*, Mary J. Gillon* and William R. Galey, Univ. of New Mexico, Dept. of Physiology, Albuquerque, N.M. 87131.

The formation of the water and electrolyte secretion by the pancreatic ducts is thought to occur by the active transport of solute and the accompanying movement of water to produce a final iso-osmotic secretion. However, rabbits treated for 7 days with reserpine produce a hypertonic final pancreatic secretion. Increased (Ca^{++}) and (protein) are also observed. It, therefore, appears that osmotic water is prevented from flowing across this epithelia into the duct lumen. One such barrier to water movement may be a decreased osmotic water permeability of the ductal cells. However, red cells obtained from these animals showed no alteration in this parameter. Another barrier to water movement may be mucus. It has been demonstrated that the water permeability through a mucus sheet is inversely proportional to the mucus concentration (Digestion 17 (1978) 234). Since the mucus concentration appears to be elevated in treated animals, we propose that this mucus coats the pancreatic ductal system and perturbs osmotic water movement. The reserpine treated animal has been proposed as a model for CF based upon many similarities in exocrine gland morphology and secretion. Therefore, this observation is particularly relevant to CF and may help explain the paucity of water observed in CF secretions (NEJM 295 (1976) 481). (Supported by NIH grant #R01-AM17843).

OVARIAN STEROIDOGENESIS IN THE EARLY BOVINE FREEMARTIN L.S.Shore and M.Shemesh* Kimron Vet. Inst. Beit Dagan P.O.B. 12, ISRAEL

Gonads from eight heterosexual twins and 1 set of sextuplets were incubated for 24h in tissue culture medium 199 supplemented with 5% calf serum. Five testes from freemartin males of crown-rump length (CRL) 3.8-12.4 cm produced testosterone(T),0.26-0.53 ng/24h, and progesterone, 0.5-2.9 ng/24h, but no detectable estradiol(E) (<50 pg). These values are within the normal range produced by 44 singletons previously studied. In contrast, 8 of 10 freemartin ovaries produced measurable amounts of T(0.14-0.59 ng/24 h) whereas in 32 normal ovaries T was undetectable (<50pg). Estradiol however was undetectable in all freemartin ovaries examined, whereas measurable amounts of estradiol were found in 23 cultured normal ovaries from of 3.3-10 cm CRL(0.1-5.1 ng/24h). Progesterone secretion by the freemartin ovaries were not significantly different from normal ovaries. The finding of high T and no detectable E in ovaries from heterosexual twins suggest that a male inducer substance from the co-sib causes a biochemical change in the ovary at the level of aromatase enzyme system and the affected ovary is independently responsible for the subsequent masculinization of the internal and external genitalia characteristic of the freemartin.

HYDRAULIC MODEL SIMULATION OF BARORECEPTOR REFLEX CONTROL OF THE ENTIRE CIRCULATION. Artin A. Shoukas and Kiichi Sagawa The Johns Hopkins University, School of Medicine, Baltimore, Md. 21205

A hydraulic model made from common laboratory instruments is used to simulate the entire circulatory system of a 25-kg dog. The basic model comprises a single flow pump representing the heart-lung section, a large and a small bore cylinder representing arterial and venous compliances, and a hydraulic resistor representing total peripheral resistance. A variable unstressed volume is built in the venous compartment, which determines the venous pressure-volume relation together with the venous compliance. We have used this basic model to demonstrate overall circulatory mechanics as well as arterial baroreceptor reflex control of cardiac pumping ability, peripheral resistance, and venous capacity (compliance and unstressed volume) in the maintenance of arterial pressure in the control condition and after mild and severe hemorrhage. Students initially quantitate the effects of hemorrhage on the areflex model, and then repeat the experiment after the reflex control is added. The basic model can be easily expanded to add elements such as two separate sides of the heart, the pulmonary circuit, a collapsible venous segment, or a leaky capillary segment. The hydraulic model has been well received by students and is an important teaching tool for their understanding of overall circulatory mechanics and its control by the baroreceptor reflex.

HEART RATE AND TOLERANCE TIME DURING EXERCISE IN DIFFERENT CLIMATES. Esar Shvartz* and Eliezer Kamon. Douglas Aircraft Company, Long Beach, CA 90846

Thirteen of the present author's previous studies, and 2 other studies, where heart rates (HR) and tolerance times (TT) were recorded were reviewed. These studies included 26 different conditions of climate, exercise type and load, and clothing, with TT ranging from 7 min. to 3.3 hrs. In addition, four men were tested while running to exhaustion for 7 and 14 min. at 10°C, and while performing muscular endurance type exercises at 23°C with TT ranging from 30 sec. to 2 min. Final HR was found to present a poor indicator of TT. However, the rate of HR increase (from resting value of 70 beats·min^{-1}) expressed as beats·min^{-1}·hr^{-1} correlated r = -0.982 with TT in the above 30 different conditions. These results showed a power curve with $y = 88.5x^{-0.97}$ where y = TT and x = HR in beats·min^{-1}·hr^{-1}. The above relationship could also be expressed as TT(hr) X SI = 100 beats·min^{-1}, where SI is stress index in beats·min^{-1}·hr^{-1}. Thus, the rate of HR increase presents an excellent indicator of TT during exercise regardless of the condition of climate, clothing, or exercise type, load and duration.

CONTRACTILE ACTIVITY AND cAMP DEPENDENT KINASE ACTIVATION IN BOVINE CORONARY ARTERIES. P. Silver, C. Schmidt and J. DiSalvo., Dept. Physiology, U. of Cinti., Cinti, O 45267

Since cAMP-mediated β adrenergic relaxation has been implicated in vascular tissue, the purpose of this study was to determine if changes in contractile activity in bovine circumflex coronary arteries (BCA) were related to changes in the activation of cytosolic cAMP dependent protein kinase (s) (PK). Activity ratios (AR), $\frac{PK\text{activity-cAMP}}{PK\text{activity+cAMP}}$, were used to assess PK activation. With .5M NaCl in the PK extraction buffer, unstimulated BCA tested in this manner had AR=.47±.02 ($\bar{X}$±SEM). Contraction of strips with 30 mM KCl increased isometric tension (8g.) but no change occured in AR (.47±.05). Similarly, relaxation (94%) of strips by removal of KCl was not associated with any change in AR. (.48±.03). However, dose dependent relaxation of KCl contracted BCA by isoproterenol was related to concomitant increases in AR (5×10^{-8}M-20% relax.-AR=.54±.03; 1×10^{-6}M-70% relax.-AR=.85±.06). Without .5M NaCl in the extraction buffer, unstimulated AR dropped to .23±.02 and there were no differences in AR among treatments. Using methods previously described for aortic tissue (Fed. Proc.1243, Spr., 1979), 2 peaks of cytosolic PK were also identifiable in BCA. In conclusion, since increases in AR were seen only during relaxation resulting from β stimulation, the results suggest that such relaxation is associated with activation of PK. Moreover, the evidence suggests type II isozymic form of PK is involved in this phenomenon.
Supported by HL 20196

RESPIRATION AND ION TRANSPORT IN RABBIT URINARY BLADDER. S.U. Silverthorn and D.C. Eaton*. Univ. Texas Medical Branch, Galveston TX 77550.

Respiration (Q_{O2}) was measured in 20-40 mg pieces of rabbit urinary bladder using a standard polarigraphic oxygen probe. Short-circuit current (I_{SC}) was measured concurrently in a piece of tissue mounted in a Ussing-type chamber. Average control Q_{O2} was 24.4 ± 6.7 nl O mg wet wt.$^{-1}$min^{-1}; average I_{SC} was 5.5 μA cm^{-1}. Average change from control Q_{O2} rates caused by 10 min exposure to various drugs or ion-free Ringer's is summarized below:

Nystatin (NYS)	+23.8 ± 10.3%	0-Na	-41.4 ± 11.4%
Ouabain (OUB)	-20.4 ± 9.1%	0-K	-19.8 ± 7.1%
Amiloride (AML)	-15.3 ± 7.0	0-Cl	-15.8%
SITS	no effect	0-Cl + OUB	-39.4%

AML is not as effective as OUB in inhibiting Q_{O2}. OUB added to a preparation containing AML depressed Q_{O2} further to -20%. Na-free Ringer is the most effective inhibitor of Q_{O2}. However, the combination of Cl-free Ringer's and OUB is almost as effective in depressing respiration. This may reflect a neutral NaCl pump such as suggested by Reuss et al. (JGP 73: 385,'79). (Supported by DHEW 1 ROI-AM20068)

THE EFFECT OF CONTROLLED HAEMORRHAGE ON OXYGEN EXTRACTION IN THE DOG ISCHAEMIC HIND LIMB. S. Simha, J. Grayson and M. Leveson. Department of Physiology, University of Toronto.

In seven nembutal anaesthetized dogs a polyethylene loop was established in the left femoral artery and used to occlude the artery and to measure the pressure distal to the occlusion. A similar loop was created in the femoral vein and used for measurement of venous outflow and for venous blood sampling. Arterial samples were taken from the opposite femoral artery. The mean arterial pressure was 154 mm Hg and the mean venous outflow was 57 ml/min. The a-v oxygen difference was 4.2 ml/100 ml; the extraction ratio was 21%. In these experiments controlled haemorrhage was performed, 300 to 400 ml of blood was withdrawn over a period of 2 to 3 mins. The systemic arterial pressure fell to 85 mm Hg and the venous outflow to 28 ml/min. The a-v oxygen difference rose significantly to 10.2 ml/100 ml and the OER to 44%. The femoral arterial loop was occluded. The distal pressure (peripheral femoral pressure) was 50 mmHg The venous outflow remained unchanged but the a-v oxygen difference rose further to 16.2 ml/100 ml and the OER to 68%. It is of interest to note that despite the fact that femoral occlusion produced no change in venous outflow the OER increased by 40%.

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A TOPOLOGICAL ANALYSIS OF THE VERTEBRATE CONE RETINA BASED ON A REALISTIC MODEL. R. Siminoff 705 Sycamore Terrace, DeWitt, N.Y. 13214

A model of the vertebrate cone retina has been developed from which ensues the annular organization of the bipolar cell (BC)--higher visual neural elements are derived from the BC. The model is organized into unit hexagons (UH) acting as the spatial building blocks for the receptive field (RF) organization of retinal elements. There are 2 types of UHs, the unit red hexagon (URH) and the unit green hexagon (UGH), which form 4 variations of the center/surround fields of the BC--URH/UGH, URH/URH, UGH/URH and UGH/UGH. Each cone within the UH has a weighted input (a_x) resulting from stray light effects and electrical coupling of like-cones. Each UH has surrounding rows of cones which do not have direct inputs to the BC but can produce polarization changes via stray light effects and electrical coupling. A general formula for the a_x is derived permitting a topological analysis which defines 5 variations of each of the 2 types of UHs--2 trichromatic, 1 red dominant, 1 green dominant and 1 blue dominant forms. Symmetries of the cone mosaic produce definite patterns in the topology of the UHs.

EFFECT OF CHRONIC EXERCISE ON MYOCARDIAL CONTRACTILE PERFORMANCE IN ADULT MALE RATS. Richard Simmons*, Harold A. Spurgeon, and Edward G. Lakatta. Gerontology Research Center, NIA, Baltimore, MD 21224.

Adult male rats, 5 months of age, underwent treadmill and swimming training 5 days/week for 26-30 weeks. Physical conditioning was evidenced by a relative decrease in body wt. in the exercised animals (E) compared to sedentary controls (S) (E = 499.6±12.3 g, S = 626.7±12.9 g, $P<.001$), and relative bradycardia in E (E = 271±3, S = 299±7 beats/min, $P<.005$). Contractile performance was studied in a perfused septal preparation (29°, 80 beats/min) at the peak of the Starling curve. Developed force (DF), maximum rate of force development, and contraction duration were not different in S vs E over a range of perfusate Ca^{++} of 0.3 to 2.0 mM. Maximum DF (Ca^{++} 2.0 mM) was 30.6±2.5 g in E and 29.1±2.4 g in S. The maximum DF response to isoproterenol ($5X10^{-7}$M), paired stimulation (PS) and 30 min. acidosis (pH 6.8) were not different in E vs S.

	Control DF (g)	% Control		
	(Ca^{++} 0.3 mM)	Isoproterenol	PS	Acidosis
E	11.9±1.3	163.5±9.4	183.4±27.0	60.6±8.8
S	13.7±1.7	173.4±10	164.5±19.3	63.0±3.9

The absence of a conditioning effect on performance over a wide range of contractile states differs from other reports and may relate to the age at which training began (adult rather than neonate), sex, and/or duration of the conditioning protocol.

HISTAMINE (H_1, H_2) EFFECTS ON PULMONARY MECHANICS AND GAS EXCHANGE IN THE CALF. R.F. Slocombe*, N.E. Robinson. Depts. of Large Animal Surgery & Medicine, and Physiology, Michigan State University, East Lansing 48824

We measured static compliance (C_{stat}), lung pressure volume hysteresis (P-V_{Hyst}), dynamic compliance (C_{dyn}), airway resistance (Raw) and alveolar arterial oxygen difference (ΔAaP_{O_2}) in anesthetized ventilated calves. Histamine was administered by continuous intravenous infusion to three groups of calves. Group 1 received histamine alone, Group 2 was treated with tripelennamine (H_1 antagonist) and Group 3 with metiamide (H_2 antagonist) prior to histamine. Histamine caused no change in C_{stat}, increased P-V_{Hyst}, decreased C_{dyn} from 95±31.1 to 38±6 ml/cm H_2O and increased Raw. Vital capacity maneuvers reversed the effects of histamine on P-V_{Hyst} and C_{dyn} but did not alter Raw. ΔAaP_{O_2} increased from 43±10 mmHg to 77±13 mmHg during histamine. All parameters returned to control 15 min after cessation of histamine. H_2 blockade did not reduce the effect of histamine on the lung. H_1 blockade prevented the histamine induced decrease in C_{dyn}, increase in Raw and increased ΔAaP_{O_2}. P-V_{Hyst} decreased following H_1 blockade and histamine, suggesting a weak H_2 mediated dilation of small airways. We conclude histamine H_1 receptors cause large and small airway constriction and impaired gas exchange in calves. The lack of collateral ventilation in calf lungs does not appear to delay recovery from histamine in ventilated calves. (Supported by HL 17768 and USDA Animal Health funds.)

BLOOD SAMPLING TECHNIQUE (AORTIC AND PORTAL VENOUS) IN UNANESTHETIZED UNRESTRAINED RATS. C.H. Sloop and B.R. Krause. L.S.U. Medical Center, New Orleans, LA 70119.

Techniques have been developed to allow blood sampling from the distal aorta and portal vein in unanesthetized, unrestrained rats. A chronic intraduodenal cannula enabled us to infuse substances into the lumen of the duodenum. The aortic and portal cannulas were constructed from polyvinylchloride (PVC) tubing drawn to a fine tip (0.008" OD) and polyethylene tubing (PE 50). The portal vein was cannulated via a mesenteric vein. The aorta was cannulated by a method similar to that reported by Weeks (PSEBM 104:646, 1960). The intraduodenal cannula (ID) (silicone rubber 0.031" OD) was threaded through a purse string suture in the membraneous portion of the stomach. The PE ends of the aortic and portal cannulas were closed with 23 g plugs and secured to the rats neck with wound clips. The ID cannula was buried under a wound clip on the rat's back. These techniques were used to simultaneously sample aortic and portal vein blood during absorption of labelled amino acids (AA) in the unanesthetized rats 3-5 days post-surgery. Portal vein AA concentrations peaked within two minutes after the ID injection and were approximately twice the aortic values. The portal vein cannulas can be used to study absorption, GI hormone secretion and to selectively infuse compounds into the portal vein. The aortic cannula could be used to measure mean arterial blood pressure, to sample arterial blood, or infuse the caudal part of the rat. (Supported- NIH Grant HL 20954)

IMPAIRED CAPABILITY TO SUSTAIN SYNAPTIC TRANSMISSION IN AGED RATS. Dean O. Smith. Univ. of Wisconsin, Madison, WI 53706

Synaptic transmission at the neuromuscular junction of the rat phrenic nerve-diaphragm muscle was studied in aged and young, control rats; their ages were 24-26 mos. and 12-13 mos., respectively. The resting potential of the diaphragm muscle cells was found to be consistently lower in the old animals than in the controls. Membrane input resistance and capacitance were not significantly different. The rate of occurrence of miniature end-plate potentials (m.e.p.p.s) in old rats was 1.75 times higher than in the controls; the distribution of intervals between the times of occurrence of successive m.e.p.p.s was exponential in both cases, however. In Mg^{2+}-blocked preparations, facilitation and post-tetanic potentiation were observed; differences between data obtained from both age groups were not significant. In curare-blocked preparations, synaptic depression occurred during repetitive nerve stimulation. The depression was more severe in the aged animals; this difference was consistent and independent of the rate of stimulation. Repetitive nerve stimulation led to action potential conduction block in the presynaptic terminals of both age groups; however, failure occurred at lower frequencies and shorter times of stimulation in the aged animals. The block appeared to be associated with membrane depolarization. It is concluded that the capability to sustain transmission is diminished at the neuromuscular junction of aged rats; this could underlie the deterioration of synaptic structures observed during senescence.

PRESERVATION OF ISCHEMIC MYOCARDIUM BY PINANE THROMBOXANE A_2

Edward F. Smith III, Karsten Schror, Michael Bickerton, J. Bryan Smith, Kyriacos C. Nicolaou, Ronald Magolda and Allen M. Lefer. Depts. of Physiology and Pharmacology, Jefferson Medical College, and Dept. of Chemistry, Univ. of PA., Phila., PA.

Pinane-thromboxane A_2 (PTA_2), a thromboxane A_2 analog, has been shown to antagonize the vasoconstriction and platelet aggregation induced by thromboxane A_2, and to specifically inhibit thromboxane synthesis. Since thromboxane A_2 generation would be detrimental in acute myocardial ischemia (MI) by decreasing coronary blood flow and increasing platelet aggregation, inhibition of thomboxane production and action may be beneficial in MI. In pentobarbital anesthetized cats, the left anterior descending coronary artery was ligated, and PTA_2 ($0.5\ \mu moles \cdot kg^{-1} \cdot h^{-1}$) or a Na_2CO_3 vehicle was infused 30 minutes post-MI for 270 minutes. Compared to vehicle treated MI cats, PTA_2 prevented the increase in plasma thromboxane levels seen at 2 through 5 hours ($p<0.005$) and prevented the large increase in plasma CK activities at 4 and 5 hours ($p<0.025$). In addition, PTA_2 abolished the differences in myocardial CK activities between ischemic and non-ischemic regions, and prevented the decrease in bound cathepsin D in the ischemic region. Moreover, ECG analysis revealed a decreased incidence of premature beats in PTA_2 treated MI cats as compared to MI-vehicle cats. These data indicate that PTA_2 protects the ischemic myocardium and suggests that inhibition of thromboxane actions is beneficial during the early stages of acute MI.

CARDIOVASCULAR RESPONSE OF CORONARY HEART DISEASE (CHD) PATIENTS TO ISOMETRIC EXERCISE. James J. Smith, C. Vincent Hughes*, Felix E. Tristani*, Karel J. Kotrly* and Jill A. Reinke*. Medical College of Wisconsin, Milwaukee, WI 53226 and Veterans Administration Medical Center, Wood, WI 53193

Previous studies have shown that the circulatory responses to certain preload stresses are altered in CHD. The objective of the present study was to test the response of 11 male CHD patients and 17 age-matched normal, male subjects to a standard isometric exercise (IE)--an afterload stress. The subjects held one third of maximal tension on a handgrip dynamometer for five minutes. Circulatory responses were monitored with non-invasive methods; stroke volume was estimated by means of transthoracic impedance cardiography.

In both groups there were progressive increases in heart rate (HR), arterial blood pressure (ABP), double rate product (DRP=HR x systolic pressure) and ejection time (ET) and decreases in preejection period (PEP). There were also, in both groups, progressive increases in cardiac index due mainly to the HR increase. The CHD patients showed somewhat greater increases in HR, ABP and DRP and a decrease in the rapid ejection period (beginning of ejection to peak dz/dt). The results indicate a stronger cardiac response to the IE in the CHD patients compared to the control subjects.
(This study was supported by the Veterans Administration).

EFFECTS OF INTRAHYPOTHALAMIC INJECTIONS OF THYROTROPIN RELEASING HORMONE AND NOREPINEPHRINE ON CONTROL OF BREATHING IN RATS. R. M. Smith*, D. R. McCaffree*, C. V. Gisolfi and J. P. Farber. Univ. of Oklahoma Health Sciences Center, Oklahoma City, OK 73190.

Norepinephrine (NE) and thyrotropin releasing hormone (TRH) can depress the activity of the same cells in the rostral portion of the hypothalamus (Brain Research 150:205-209, 1978). Previously published data also suggest that ventilatory output can be modulated from this region. Using haloperidol tranquilized (2 mg/kg) adult rats with chronically implanted guide tubes, we measured the ventilatory effects (using whole body barometric plethysmography) of unilateral or bilateral .25 ul injections of NE bitartrate (40-80 µg/ul) or TRH (.015-.050 µg/ul) into the rostral hypothalamus. Injections were performed over a 30 sec interval and cannula patency was checked during the injection as well as after the injection. The typical response consisted of an increase in breathing rate with inconsistent effects on tidal volume. The response reached a peak during the 5 min post-injection measurement period. Effects on breathing were not obtained by injecting solutions having similar osmolarity and/or pH. These data lead to the suggestion that inhibition of cell discharge in the rostral hypothalamus can mediate tachypnea.

MELATONIN TRANSPORT BY THE CHOROID PLEXUS. Anthony P. Smulders*, Ernest M. Wright, UCLA and Loyola Marymount University, Los Angeles, CA 90024.

In vitro preparations of the IIIrd and IVth ventricle choroid plexuses and the arachnoid of the bullfrog were used to study transport of ^3H-melatonin. There was a net flux across the IVth ventricle plexus from CSF to blood. The unidirectional flux from CSF to blood at 10-30 nM was twice that in the opposite direction. Thin layer chromatography showed that the transported ^3H is in fact ^3H-melatonin and not metabolic breakdown products. The unidirectional fluxes across the arachnoid were not significantly different. Accumulation of melatonin by the IVth ventricle plexus is asymmetrical, the T/M ratio (tissue water concentration of melatonin/incubation media concentration of melatonin) was 2.1 ± 0.2 (5) from the ventricular side and 0.6 ± 0.1 (4) from the vascular side. The steady state T/M ratios for the IIIrd ventricle plexus, the IVth ventricle plexus and the arachnoid were 18 ± 8 (4), 4.2 ± 0.9 (4) and 6.5 ± 1.2 (4) respectively, at a melatonin concentration of 2 nM. In the IIIrd ventricle plexus the T/M ratio decreased to 4.8 ± 1.5 (4) at 450 µM. Accumulation of melatonin in these tissues was reduced at 0°C, and inhibited by the addition of substrates in the sequence melatonin > serotonin > N-acetylserotonin. We conclude that melatonin is actively transported from CSF to blood by the choroid plexuses and the results suggest that the IIIrd ventricle plexus plays the major role in this process. **(Supported by USPHS NS09666).**

ULTRA-HIGH IMPACT FREE-FALL SURVIVAL. Richard G. Snyder. University of Michigan, Ann Arbor, Michigan 48109.

Human tolerance limits to extreme deceleration forces and the influence of various environmental factors have been studied during the past 18 years. Of 30,000 free-fall cases collected to date, over 500 have been subjected to intensive biomedical investigation at the scene. Selected cases are presented in which survival has been documented at decelerations far exceeding levels generally considered to be survivable. These data extend current known limits obtained in voluntary investigations on human subjects and provide a further basis for correlations with data from animal, dummy, cadaver, or other surrogates, or mathematical model simulation. Despite survival or transient recovery from calculated impact velocities of 53.7 meters per second, wide variations have been found. Biological effects of trauma are evaluated and critical biophysical factors that may influence survival tolerance are discussed. In certain cases involving ultra-short impact time durations (<600 microseconds), subjects have survived extremely high impact forces, for reasons still unknown. Solutions of the parodox of why certain individuals have ly tolerated ultra-high deceleration forces theoretically ly considered non-survivable may have significant application to future design of impact protection.

EFFECTS OF INHALED CO_2 ON THE RESPONSE OF NEWBORN LAMBS TO MASSIVE HEMORRHAGE. A. Sola*, M. Schlueter* and R. Phibbs* (SPON: J.A. Clements). U of Calif, S F, San Francisco 94143

We studied 15 unanesthetized lambs less than 8 days old, 11 breathing room air (RA) and 4 breathing 4.5% CO_2 (CO_2). We measured blood volume with CsCl labelled RBCs then hemorrhaged (H) 50% of the measured blood volume over 30 m. No volume was reinfused. We measured heart rate (HR), arterial pressure (BP), PaO_2, pH, $PaCO_2$, cardiac output (CO) and organ blood flow (microsphere method) before, at 2/3 and the end of H and 90 m. after H. 4 of 11 in RA survived (S). In all 11, HR and BP fell at 2/3 H, pH and $PaCO_2$ decreased, PaO_2 increased. The average $PaCO_2$ was 26 torr in S and 22 torr in non-S at end H. CO in all in RA was 22% of baseline (BL) at the end of H and, in S, 50% of BL at 90 m. post H. Myocardial blood flow (Q_m) changed directly with BP, falling to 40% of BL at end H and returning to BL at 90 m. post H. Brain blood flow (Q_b) was unchanged in S and only fell just before death in the non-S. Adrenal blood flow rose to 160% of BL in S and was unchanged in non-S. CO_2 did not change CO or organ flow before H. In CO_2 all 4 survived. Changes in HR, BP and PaO_2 were similar to the survivors in RA. $PaCO_2$ remained at BL level (35 torr) and pH was lower. Q_m was only 8% below BL at 2/3 H and rose to 19% above BL at end H and 40% at 90 m. post H. Q_b was 40% above BL throughout H and 90 m. post H. Preventing hypocarbia appears to protect Q_m during massive hemorrhage in newborn lambs. Supported by HL-19185.

CEREBRAL BLOOD FLOW (CBF) OF DOGS WITH EXPERIMENTAL DIABETES MELLITUS (EDM). Sparks, H.V. and D'Alecy, L.G. Michigan State University, East Lansing, MI 48824 and University of Michigan, Ann Arbor, MI 48109

The purpose of this study was to determine if dogs with EDM exhibit altered control of CBF. Dogs were given alloxan, which caused a sustained increase in blood glucose to greater than 200 mg/dl. After one month they were anesthetized with α-chloralose. End tidal pCO_2 was held constant by mechanically respiring the animals. CBF was measured by injecting radioactive microspheres into the left atrium and drawing a reference sample from the brachial artery. Microspheres were injected during a control period and during infusion of epinephrine (E) at a rate which caused the largest achievable rise in mean aortic pressure (MAP). E infused at 2.13±.4 μg/min·kg caused an increase in MAP from 112±8 to 144±11 mm Hg in dogs with EDM, whereas .91±3 μg/min·kg caused MAP to increase from 112±7 to 180±4 mm Hg in control dogs. Cerebral vascular resistance of dogs with EDM did not increase when E was infused and so CBF increased from 39±4 to 48±5 ml/min·100g. Resistance of control dogs increased so that CBF changed from 29±2 to 38±2 ml/min·100g. This difference could not be explained by differences in blood pCO_2 or PO_2. We conclude that the most likely explanation of this result is that autoregulation of CBF is impaired in experimental DM. (Supported by USPHS Grant HL24672).

EFFECTS OF CEREBELLECTOMY AND CO_2 ON THE INTERCOSTAL NERVE ACTIVATION OF THE INSPIRATORY OFF-SWITCH. D.F. Speck* and C.L. Webber, Jr. Department of Physiology, Loyola University of Chicago, Maywood, Illinois 60153

Stimulation of intercostal afferents demonstrates the time-dependency of off-switch excitability observed with both lung inflation and pneumotaxic center stimulation. Since intercostal afferents are known to project to the cerebellum, the present study examined the possibility that this intercostal effect is mediated through cerebellar inhibition of inspiration. Decerebrate, vagotomized, paralyzed, and artificially ventilated cats were used. The left sixth intercostal nerve was stimulated centrally with a 3-pulse train (0.1 msec, 200 Hz) delivered at different intervals (Ti) after the onset of phrenic neural activity. At each delay, the stimulus intensity was adjusted to the minimal level (mA) required to elicit a phase switch to expiration. In each cat, mA vs Ti plots were obtained before and after cerebellectomy at both 4% and 5% CO_2 levels. The results clearly demonstrated that the off-switch threshold is elevated by an increase in the end-expiratory $\%CO_2$. Cerebellectomy, however, did not affect the off-switch excitability at either of the CO_2 levels. Therefore, although the cerebellum is known to affect respiration, this study shows that the intercostal activation of the off-switch is not dependent upon an intact cerebellum, but is probably mediated directly on brainstem respiratory neurons. (Supported by NIH Grant HL08682)

CALCIUM-PHOSPHORUS-MAGNESIUM INTERACTIONS IN MAN. Herta Spencer, Lois Kramer*, Carol Gatza*, Clemontain Norris*, and Margaret Lesniak*. Metabolic Section, Veterans Administration Medical Center, Hines, IL 60141

Calcium and phosphorus, used singly and combined, decrease the intestinal absorption of magnesium in animals. However, little is known on this subject in man. The effect of these minerals on magnesium metabolism was studied in man under controlled conditions. The constant diet and the urinary and fecal excretions were analyzed for Ca, P, and Mg for several weeks in all study phases. In the control study the dietary intake of Ca averaged 200 mg/day, of P 800 mg/day, and of Mg 250 mg/day. In the experimental studies, calcium intakes ranged from 800 to 2000 mg/day. Increasing the intake of Ca from 200 to 1400 or 2000 mg/day did not affect the urinary or fecal Mg excretions or the Mg balance. Added P resulted in a moderate increase of the fecal Mg excretion during different Ca intakes, while urinary Mg did not change. During a high Mg intake of 850 mg/day the added Ca or P also did not affect Mg metabolism. Added P decreased urinary Ca during all intakes of Ca and Mg and decreased the Mg balance in some but not in all cases. Added magnesium did not affect the intestinal absorption of Ca, while it decreased urinary P and increased fecal P slightly. (Supported in part by USPHS grant DE-02486 and in part by ERDA CONTRACT ER(11-1)-1231-127.)

EFFECT OF SPACEFLIGHT ON BONE STRENGTH. Daniel M. Spengler,* Emily R. Morey,* Dennis R. Carter,* Russell T. Turner,* and David J. Baylink.* University of Washington, Seattle, WA 98195, NASA-Ames Research Center, Moffett Field, CA 94035, and American Lake VA Medical Center, Tacoma, WA 98493.

The effect of spaceflight on whole bone mechanical properties of stationary and centrifuged rats both immediately following and 25 days after an 18.5 day flight aboard Cosmos 936 was determined. The left femur was used for measurement of mechanical parameters which were determined by a standard torsion test; ultimate torque, deformation to failure, energy, and stiffness were measured. After 18.5 days of spaceflight, a significant decrease in bone torsion strength, including torque (17.5 ± 4.4 vs 26.1 ± 6.9 10^5 cm-dynes), stiffness (2.97 ± 0.22 vs 4.15 ± 0.39 10^3 cm-dynes/radian), and energy (1.8 ± 0.9 vs 2.6 ± 1.3 10^5 erg radians) was observed. Inflight centrifugation appeared to prevent these changes. All significant differences produced by spaceflight on bone strength recovered 25 days postflight. The decrease in bone strength appears primarily due to changes in bone geometry since body weights of the rats and lengths of the left femora revealed no consistent effect of flight. However, the presence of a signficant bone growth arrest line in bones from flight rats must also be considered. (Supported in part by NASA contracts RA18698B and RA36687B)

EFFECT OF ADENOSINE ON THE DISTRIBUTION OF RENAL BLOOD FLOW Wm. S. Spielman, S. L. Britton and M. J. Fiksen-Olsen*, Dept. of Physiology, Mayo Foundation, Rochester, MN 55901

Intrarenal infusion of adenosine (ado) results in a relatively greater fall in superficial nephron glomerular filtration rate (GFR) than whole kidney GFR. This nonuniform decrease in GFR occurs despite a concomitant increase in total renal blood flow (RBF), thus the present study was undertaken to assess the effect of adenosine on RBF distribution. Whole kidney blood flow and RBF distribution were studied in anesthetized dogs (n=8) before and during the intrarenal artery infusion of ado (0.3 μmol/min) using an electromagnetic flowmeter and radiolabeled microspheres (15μ). No change was observed in outer cortical flow ($4.36\pm.50$ vs. $4.41\pm.63$ ml/min per g), but ado infusion resulted in a significant increase in inner cortical blood flow ($1.54\pm.34$ vs. $2.99\pm.52$ ml/min per g). Whole kidney blood flow was increased during ado from $2.61\pm.29$ to $3.08\pm.43$ ml/min per g. Additional experiments were performed using indomethacin (or meclofenamate) treated (n=14) or phenoxybenzamine treated (n=5) dogs to determine if the deep cortical vasodilation is mediated by increased prostaglandin production or inhibition of norepinephrine release. No effect on the increase in deep cortical flow during ado was detected in either prostaglandin synthesis blocked or α-adrenergic blocked dogs. These data suggest that adenosine per se acts to preferentially dilate vessels of the inner cortex. (Supported by HL14133).

ARSENIC FOR PHOSPHORUS SUBSTITUTION: USE IN BONE-SEEKING AGENTS FOR IMAGING AND THERAPY. Pavanaram K. Sripada,* Parvathi Hosain,* Richard P. Spencer, Fazle Hosain*. Univ. Connecticut Health Center, Farmington, CT 06032.

While phosphorus is a key element in the bone matrix and in intermediary metabolism, it does not possess readily available radionuclides which emit gamma rays or positrons. Arsenic is in the phosphorus "family" in the periodic table and can be substituted in a number of biochemicals. Hence, the arsenic analogues of methylene diphosphonate (MDP) were studied. Both the monoarsenic substituted arsonomethylphosphonic acid (AMPA) and the disubstituted methylenediarsonic acid (MDA) bound the radiolabel Tc-99m(Sn) and delivered it to bone. The ratios of activity of AMPA/MDP and MDA/MDP were essentially 1, showing no difference between these agents in bone uptake. Synthesis of As-76-AMPA was accomplished by Na2O3 condensation with monochlorophosphonic acid, with purification via the cyclohexylamine salt. The As-76-AMPA had blood clearance and bone localization identical to Tc-99m-MDP. The results of double tracer studies with As-76-AMPA and Tc-99m-AMPA showed nearly identical values. Arsenic does possess a number of radionuclides which are positron or gamma ray emitters. Hence, there are potential applications in following bone turnover, and in tomography with either single photons or positrons. In addition, beta particle emissions from other arsenic radionuclides may permit therapy. (Supported by USPHS CA 17802 from the National Cancer Institute).

CENTRAL AND PERIPHERAL EFFECTS OF CAPTOPRIL ON ARTERIAL PRESSURE AND HEART RATE OF THE SPONTANEOUSLY HYPERTENSIVE (SH) RAT. J.F. Stamler,* M.J. Brody, and M.I. Phillips. Depts. of Physiology and Pharmacology, Univ. Iowa, Iowa City, Ia. 52242

Captopril (SQ 14,225) is an orally active inhibitor of angiotensin converting enzyme. Intravenously (IV), it lowers mean arterial pressure (MAP) in SH rats, but not in normotensive Wistar-Kyoto (WKY) rats. The small size of the molecule suggests that it may be able to cross the blood-brain barrier and lower MAP via a central mechanism.

To determine if Captopril has a central depressor action, the IV and brain intraventricular (IVT) routes of administration were investigated. Captopril (225μg/kg) was administered IVT and IV to six male SH rats. After IVT injection, MAP decreased 35.3 ± 10.6 mmHg (mean ± SD), $P<.01$ and 16.3 ± 10.7 mmHg, $P<.05$ after IV. The difference between the IVT and IV routes was significant, $P<.05$. This result suggests that there is a central component to the hypotensive action of Captopril. There was no significant change in heart rate in either case. The lack of reflex tachycardia indicates an inhibition of the baroreceptor reflex.

The central action of Captopril is not due to the accumulation of bradykinin in the brain since IVT injections of bradykinin increase MAP. However, the ability of competitive antagonists of AII to lower MAP in SH rats suggest that the central hypotensive action of Captopril, proposed here, is due to the inhibition of the central angiotensin system.
(Supported by NIH PPG HL 14388)

CHARACTERIZATION OF AN ANDROGEN BINDING COMPONENT IN THE HUMAN PLACENTA AT TERM. Rita L. Stanley*, Ariel Milwidsky* and Paige K. Besch. Dept. of Ob/Gyn, Baylor College of Medicine, Houston, Texas 77030

A high affinity, saturable, binding component for androgens (K_d=1.9±0.21x10^{-9}M, DHT; K_d=4.9±2.4x10^{-9}M, testosterone 0.6±0.18x10^{-9}M, R1881; 4.6x10^{-9}, DHEA) was identified in human placental cytosol at term. The binder was degraded by protease and precipitated at 30-35% $(NH_4)_2SO_4$ saturation, negating plasma contamination. H^3-progesterone and H^3-R5020 did not bind significantly in cytosol, nor could the radioinert compounds significantly displace androgens, ruling out progesterone receptors. R1881 binding exhibited thermolability at 45°C for 30 min, decreasing to 11% of control valves whereas testosterone binding was only depressed to 84%. H^3-R1881 associated at 0°C within 2 hrs and was stable at least 18 hrs; relative displacing abilities by radioinert competitors were: androstenedione,20%; R5020,3.1%; DHT,3.0%; T, 2.1%; progesterone,1.0%; E_2,<0.1%; cortisol,0%. The relative displacing ability of R1881 for H^3-DHT was 0.5%; H^3-T,0.21%; H^3-progesterone,0%; H^3-DHEA,13% and H^3-pregnenolone, 346%. R1881 binding sites represented 13% of total testosterone binding sites. Half-life of dissociation was 32 min for R1881 and 15 min for testosterone. The data suggest 2 binding proteins, one for structures related to T, the other to pregnenolone. Speculations as to nature include transport and receptor functions.

VENTILATORY AND CARDIAC CHANGES DURING EARLY STAGES OF AROUSAL IN S. LATERALIS. J.M. Steffen and M.L. Riedesel. Dept. Biol., University of New Mexico, Albuquerque, N.M. 87131

A plethysmographic technique was used to follow changes in ventilation during the first hour of arousal at a T_a of 8-10°C. Heart rate (HR) was monitored by recording of the ECG from silver wires implanted subcutaneously over the scapular region. Increased breathing frequency (f) and HR were the first signs of arousal, with HR/f dropping from 6.5 in hibernation to 2.0 or less within the first ten minutes of arousal. This change was consistent and persisted throughout the time course of the study. This indicates the usefulness of HR/f in assessing the depth of hibernation in these animals or in anticipation of an imminent arousal. The following changes were noted after one hour of arousal: 1) f increased by 40-50 fold; 2) HR rose to 10 times the hibernating value; 3) tidal volume revealed only a modest 25% increase; and 4) expiratory minute ventilation increased 50 fold. This would indicate that stimulation of breathing frequency is of much more importance during the early stages of arousal than an increase in tidal volume.

EFFECTS OF SODIUM BICARBONATE AND CALCIUM ON THE CARDIOVASCULAR RESPONSE TO SEVERE RESPIRATORY ACIDOSIS. C.R. Steinhart*, S. Permutt, G.H. Gurtner, and R.J. Traystman. Johns Hopkins Medical Insts., Baltimore, Maryland 21205.

We reported (Fed. Proc. 38:891, 1979) that hypercapnic heart failure is prevented by beta-adrenergic stimulation and hastened by beta-blockade. These results are consistent with a model of Ca^{++}-H^+ antagonism which has been further investigated in this study. Arterial CO_2 ($PaCO_2$) was raised by increasing the percent inspired carbon dioxide (F_ICO_2) in O_2 in anesthetized, paralyzed, ventilated dogs. In 5 control dogs (CO_2 only), cardiac output ($\dot{Q}$) increased (20%) at moderate levels of $PaCO_2$, and decreased (49%) at high $PaCO_2$ levels. Left ventricular function (LVF) curves were markedly depressed at the high $PaCO_2$ level. In 5 dogs, propranolol and sodium bicarbonate were administered (I.V.) as $PaCO_2$ was elevated. $\dot{Q}$ increased (50%) and LVF curves were not depressed from control at high $PaCO_2$. In 6 additional dogs, propranolol and Ca^{++} were administered (I.V.) as $PaCO_2$ was elevated. $\dot{Q}$ again increased (89%) and LVF curves suggested improved cardiac performance. We conclude that hypercapnic heart failure is prevented by attenuating the decrease in arterial pH or by administration of Ca^{++}. Our results remain consistent with a Ca^{++}-H^+ antagonism. (Supported by NIH HL-10342 and HL-07199.)

EFFECT OF HALOTHANE ON MEMBRANE DIFFUSING CAPACITY FOR O_2 (DMO_2) IN THE LUNG. John K. Stene*, Raymond B. Laravuso* and Barry Burns. J. Hopkins Sch. Med., Dept. Anes., Balto., Md. 21205

If cellular lipids pose a significant diffusion resistance to gas exchange, then agents like halothane which dissolve in the lipid fraction of cell membranes should alter the diffusion properties of the alveolar-capillary membrane. We have used the Na dithionite (DTT) method (JAP 46:100,1979) for DMO_2 in excised, perfused left-lower lobes (dog 20kg, ketamine anesthesia). Studies were done at 5-25 °C. Following control measurements, halothane was given via ventilator and gas exchanger for 6-8 min, generally reaching 2-3% as measured by mass spec during rebreathing for DMO_2. Halothane caused a reversible decrease in DMO_2 (70% of control- 50 ml/min/torrSTPD $P<.001$). Despite this approx. 30% reduction in DMO_2 with halothane, DMO_2 is still sufficiently large that gas exchange in vivo would continue to be perfusion limited. While these results rule out "melting" of the lipid clathrate in membrane micelles (since this would increase DMO_2), several possible alternative explanations remain - including: structering of intracellular water, constriction of low diffusion resistance aqueous membrane pores, swelling of membrane lipoproteins or cell interior, etc. Supported by USPHS grants and American Heart Association.

DETERMINATION OF PLASMA RENIN ACTIVITY IN THE TURTLE. PSEUDEMYS SCRIPTA ELEGANS. G. A. Stephens and J. S. Creekmore*. Univ. of Delaware, Newark, DE 19711

The physiological role of the renin angiotensin system in lower vertebrates is presently unresolved. To study the system in reptiles we developed a radioimmunoassay procedure for determination of plasma renin activity (PRA) in the turtle. Blood from conscious turtles was collected by cardiac puncture in Na_2EDTA. After centrifugation at 2-4°C the plasma was pooled and stored at -20°C. Angiotensin was generated by incubation of 0.5 ml of plasma for 1 or 2 hr at 25°C with phenylmethylsulfonylfluoride and dimercaprol. The pH of the samples was adjusted to the pH optimum of 4.2 with acetic acid. Angiotensin generation increased with incubation time up to 12 hr and with temperature to a broad peak at 25-35°C. Angiotension was quantified by radioimmunoassay of a 25 ul sample of incubated plasma using human angiotensin I antibody (Immutope, Squibb). After equilibration for 24 hours at 4°C, the unbound angiotensin was removed with charcoal and the supernatant was counted. Five turtles maintained in tap water and fed twice weekly on trout food (Purina) had an average PRA of 10.10± 0.65 ng angiotensin I/ml/hr. Preliminary results suggest that acclimation of the animals to distilled water produced a fall in PRA while maintenance in dilute salt water (2.5 g NaCl/L) produced an elevation in PRA. (Supported by the Univ. of Del. Res. Foundation)

COLCHICINE BINDING ACTIVITY OF GASTRIC MUCOSA. H.E. Stewart* and D.K. Kasbekar, Department of Physiology and Biophysics, Georgetown University, Washington, D.C. 20007.

Colchicine inhibits acid and pepsinogen secretion by the in vitro frog gastric mucosa (Am. J. Physiol. 236:E550, 1979). To study the mechanism of inhibition, colchicine binding activity was determined in oxyntic cell enriched mucosal homogenates and oxyntic cells held in tissue culture. Incubation of the 25,000 x g (25K) fraction at 25° with radioactive colchicine in Na-phosphate buffer (pH 6.8) containing GTP yields a DE 81 (anion exchange filter) - absorbable increase in bound radioactivity during the initial 40 minutes followed by a subsequent loss of the label with increasing time. The bound label does not appear in the void volume of DEAE Sephadex column and can be eluted with 0.8 M KCl containing phosphate buffer, suggesting tubulin-like properties of the binding protein. The binding is linear with increasing protein concentration, is not significantly inhibited by lumicolchicine and appears to be a biphasic function of colchicine concentration. The high affinity K_a for colchicine is of the order of 20μM, whereas that for low affinity is in the mM range. These data indicate the presence of a tubulin-like protein in the oxyntic cells of the gastric mucosa, and suggest the need for additional studies on the relationship of colchicine-binding activity vis à vis inhibition of gastric secretory function. NSF support.

BRONCHODILATOR EFFECT OF ISOCAPNEIC HYPERVENTILATION IN PATIENTS WITH ASTHMA. David R. Stirling*, David J. Cotton*, Brian L. Graham* and James A. Dosman. Division of Pulmonary Medicine, Department of Medicine, University Hospital, University of Saskatchewan College of Medicine, Saskatoon, Canada S7N OXO

We have previously shown that bronchoconstriction induced by inhaled histamine was inhibited during exercise in asthmatic patients (Federation Proceedings, 38:1110, 1979). To explore the mechanism of these findings we measured the change in pulmonary resistance (R_L) following 5 rapid inspiratory capacity breaths of histamine at rest, during isocapneic hyperventilation (IH) and during steady state treadmill exercise in 3 asthmatic patients. We measured transpulmonary pressure using an esophageal balloon, flow using a pneumotachygraph and obtained R_L by an electrical subtraction method. End-tidal CO_2, minute volume of ventilation, and respiratory rate were similar during IH and exercise, but heart rate was lower during IH (83 ± 13 beats/min) than during exercise (143 ± 8). At rest R_L increased 121% following histamine while R_L increased only 49% ($p < .05$) during IH and 28% ($p < .01$) during exercise. We conclude that the inhibition of histamine-induced bronchoconstriction during exercise may be related to lung volume changes rather than metabolic factors. (Supported by MRC Canada 5618, the Saskatchewan Anti-Tuberculosis League and the John Moorhead Fund)

FETAL PLACENTAL VASCULAR RESPONSE TO PARTIAL OCCLUSION OF MATERNAL PLACENTAL VASCULATURE. M. Stock*, D. Anderson*, T. Phernetton*, M. McLaughlin* and J.H. Rankin. Dept. Physiol., Univ. of Wis. Medical School, Madison, WI 53706.

Local regulation of fetal placental blood flow was studied in 5 near-term sheep. Maternal blood flow was reduced or eliminated to 8-17% of the placenta by ligation or embolization. Radioactive microspheres (15u) were administered to mother and fetus before and after placental vascular occlusion. Relative activities (RA) defined as (% total placental radioactivity)/(% total placental weight) were calculated for each isotope. Change in RA for individual cotyledons was used to confirm occlusion and to assess fetal response at 24 hours post-occlusion. The results below represent the difference in fetal RA (control - 24 hr test) for occluded and non-occluded cotyledons (mean ± SEM). The number of cotyledons is in parentheses. P values for paired t-tests indicate change in fetal RA is significant only for the occluded cotyledons.

Sheep	Occluded		Non-occluded	
1	.37 ± .09 (7)	P<.01	.01 ± .02 (54)	NS
2	.15 ± .04 (10)	P<.01	<.01 ± .02 (52)	NS
3	.32 ± .01 (11)	P<.001	.04 ± .03 (47)	NS
4	.47 ± .05 (12)	P<.001	.02 ± .02 (63)	NS
5	.33 ± .04 (13)	P<.001	-.01 ± .01 (80)	NS

These values represent a 28% decrease in fetal RA in response to maternal occlusion. We propose the existence of a mechanism whereby local fetal placental blood flow is dependent upon the adjacent maternal flow. Support: NIH grant HD06736.

RENAL TRANSPORT OF N-(4-AZIDO-2-NITROPHENYL)-2-AMINOETHYL-SULFONATE (NAP-TAURINE). M.F. Stokols*, F.J. Koschier*, J.M. Goldinger*, and S.K. Hong. Dept. of Physiology, SUNY at Buffalo, Buffalo, New York 14214.

The organic anion, NAP-taurine, contains an azido group that upon photoactivation becomes a highly reactive nitrene radical. The present study was undertaken to determine if NAP-taurine is transported by the renal organic anion system. The study utilized rabbit kidney cortical slices incubated in a modified Cross-Taggart medium at 25°C in an O_2 atmosphere and under a red safelight to avoid photoactivation. NAP-taurine inhibited p-aminohippurate (PAH) transport (I_{50} = 25 µM) without affecting tissue accumulation of the organic cation tetraethylammonium (TEA) or the tissue distribution of water and electrolytes. NAP-taurine at 10 µM was accumulated by cortical slices, achieving a steady state slice-to-medium concentration ratio (S/M) of ≈14 and metabolic inhibitors reduced this value to ≈2. NAP-taurine transport (Km = 30 µM) was inhibited by PAH, probenecid, 4,4'-diisothiocyanostilbene-2,2'-disulfonate (DIDS), zero Na^+, and ouabain. The inhibition by PAH was competitive. NAP-taurine transport was unaffected by TEA and was strongly stimulated by acetate. In the isolated perfused rat kidney, using a dextran perfusate, NAP-taurine had a clearance ≈10 times the GFR. DIDS significantly reduced this secretion. In conclusion, NAP-taurine has a specific interaction with the renal organic anion transport system and thus may be useful as a covalent label for this system. (Supported by USPHS Grants AM-18918 and AM-05437)

ISOPROTERENOL RESPONSE OF THE HYPERTROPHIED DOG HEART. H. Lowell Stone, R. T. Dowell, and L. A. Sordahl, Dept. of Physiology, Univ. of Oklahoma HSC, Oklahoma City, OK 73190.

The response of the heart to the infusion of isoproterenol (I) was determined in 10 adult mongrel dogs before and after supravalvular aortic constriction. The animals were instrumented 4 weeks prior to control studies to measure left ventricular pressure (LVP), left circumflex coronary blood flow (LCV), and heart rate (HR). An adjustable constrictor device was placed around the ascending aorta. Following the infusion of isoproterenol during a central period, the cross-sectional area of the aorta was reduced 40% and 6 weeks later the study repeated. At the latter time, left ventricular mass had increased an average of 24±3% for the group. The results were as follows:

	LVP (mm Hg)	dP/dt (mm Hg/sec)	HR (bpm)	LCV (cm/sec)
Control	138± 8 /2±2	3729±401	98±4	28±2
I-0.25 µg/min kg^{-1}	154±11 /0±2	6774±648	178±7	49±6
Constricted	157±16 /5±2	3016±314	114±6	33±4*
I-0.25 µg/min kg^{-1}	200±25*/1±2	5222±679*	181±9	62±7*

*=P<0.05 compared to preconstriction values.

A significant elevation in LV systolic pressure and LCV occurred with the infusion while dP/dt was reduced. These data indicate a reduced contractile response in the non-failing hypertrophied heart to isoproterenol associated with a significant increase in coronary blood flow. The decrease in contractile response could result from a change in the contractile proteins or endocardial blood flow. (Supported by HL 23206).

THE RELEASE OF CARDIAC ENZYMES DURING PERFUSION HYPOTHERMIA. William B. Strawn* and David R. Redden* (SPON: M.G. Levitzky). Dept. of Biological Sciences., North Texas State Univ., Denton, TX 70012.

Heart-specific creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) levels, which are elevated following myocardial tissue damage, were measured in coronary sinus blood of anesthetized dogs undergoing selective hypothermic perfusion of the left anterior descending (LAD) branch of the coronary artery to determine if lowered temperatures cause enzyme release. Cooled whole blood was provided to the LAD from a carotid artery via an extracorporeal circuit immersed in a constant temperature water bath. Blood temperatures were measured at the point of entry into the LAD and maintained at one of three temperature ranges (19-25 C, 25-31 C, 31-37 C) for 4 hrs. Blood samples were collected from the coronary sinus and serum CPK and LDH isoenzyme activities were determined by spectrophotometry and electrophoresis. Animals in the 19-25 C group showed an initial rapid release of enzymes after 2 hrs of perfusion, while those in the other two groups showed no significant elevation. This increase in enzymatic activity was unrelated to cardiac mechanical function which remained unchanged from control throughout the experiment. The results suggest a temperature dependent alteration of myocardial membrane integrity allowing for leakage of enzymes across the membrane.

ACTIVATION OF UPPER AIRWAY MUSCLES BEFORE THE ONSET OF INSPIRATION IN NORMAL MAN. K.P. Strohl*, M.J. Hensley*, M. Hallett*, N.A. Saunders* and R.H. Ingram, Jr. Peter Bent Brigham Hospital and Harvard Medical School, Boston, MA 02115

Animal studies have demonstrated that activation of upper airway muscles precedes the onset of inspiration. To investigate whether this sequence occurs in man, we studied three healthy males in the supine position during quiet wakefulness and non-REM sleep. We measured electromyographic (EMG) activity of the alae nasi (AN), genioglossus (GG), and diaphragm (DI) by surface, fine wire and intraesophageal electrodes, respectively. Onset of inspiration was determined by EMG-DI, airflow by facemask and pneumotachograph, or transdiaphragmatic pressure. Sleep state was determined by electroencephalography. During sleep, phasic activity in AN (3 subjects) and GG (2 subjects) consistently preceded the onset of respiration by up to 600 msec. (mean 200 to 300 msec.). During wakefulness, phasic activity in AN and GG could not be detected in many breaths due to the presence of tonic activity: when present during quiet breathing, phasic activity in GG and AN preceded inspiration by a shorter and more variable period when compared to sequences observed during sleep; voluntary breaths produced simultaneous onset of AN/GG and inspiration. These findings suggest that in man a sequence of respiratory muscle activation occurs which is more apparent and less variable during sleep. (Supported by grants from NIH (HL 16463, HL 20968, GM 07560-02), PGMF Syd. Uni. and RACP)

MECHANICS OF BREATHING DURING EXERCISE IN AIRFLOW OBSTRUCTION. *D. G. Stubbing*, J.L.C. Morse*, L.D. Pengelly, N.L. Jones, St. Joseph's Hospital/ McMaster University, Hamilton, Ontario, Canada.*

We used an exercise body plethysmograph to study pulmonary mechanics in 6 subjects with chronic obstructive lung disease at rest and in steady state exercise at 200 and 400 kpm/min. The mean age was 51 years and mean FEV_1 63% of predicted. The flow rates during tidal breathing at rest reached the maximum expiratory flow volume (MEFV) curve in most subjects; on exercise they all reached the MEFV curve during tidal breathing. During exercise functional residual capacity and total lung capacity did not change, but residual volume (RV) increased to 113.3% of the value at rest. Dynamic compliance (Cdyn) fell to 52.8% of the control value but static compliance was relatively unchanged at 90.2% of control. Expiratory resistance (Rlex) increased to 118% of control value. The MEFV curves did not change. The fall in Cdyn may be due to increases in tidal volume and/ or respiratory frequency. The increase in Rlex is probably due to increased expiratory pressure generated when breathing on the MEFV curve during exercise. Despite these marked dynamic changes there was no change in static pulmonary mechanics (Supported by the Canadian Lung Association).

PRODUCTION OF MONOCLONAL ANTIBODIES TO HUMAN GASTRIN. R.L. Suddith,* C.M. Townsend,* P.L. Rayford and J.C. Thompson. Department of Surgery, The University of Texas Medical Branch, Galveston, Texas 77550.

Hybrid cells which secrete gastrin-specific antibody have been derived from fusions between mouse myeloma cells and spleen cells from mice immunized with synthetic human gastrin I (SHG I). Gastrin antibodies produced by hybridomas were detected in the culture supernates by solid phase radioimmunoassay. Spleen cells (10^8) from Balb/c mice immunized with SHG I were fused to myeloma cells (10^7) of either the P3x63xAg8 or the nonsecretory P3-NS-1 cell line using polyethylene glycol. The initial fusion progeny were plated into 96-well microtiter plates. Hybrids were selected by their ability to grow in hypoxanthine aminopterin thymidine medium. Conditioned media from hybridomas were transferred to polystyrene tubes. Protein from these media is passively bound to the wall of the tubes. The presence of gastrin-specific antibodies was measured by the amount of ^{125}I gastrin bound in each tube. Background binding was 2% of input counts (12,000/tube). Hybrids producing antibodies which bound at least 4 times background were selected. 41 of 1080 (4%) of P3x63xAg8 cell hybrids secrete gastrin-specific antibody, whereas 11 of 540 (2%) of the hybrids with P3-NS-1 did so. These studies show that it may be possible to develop monoclonal antibodies to peptide hormones; this development will facilitate studies on molecular heterogeneity.

ANALYSIS OF GI MOTOR ACTIVITY USING A GRAPHIC-TO-DIGITAL CONVERTER. Charles M. Suter*, Herbert S.Ormsbee, Gordon L. Telford*, and G. Robert Mason. U. of Md. Hosp. Baltimore, Maryland 21201

Recently, several low cost graphic-to-digital converters have become available which translate strip chart records into computer readable format.The practicality of using such a device for analysis of GI motility data is reported here.Precalibrated extraluminal strain gage force transducers were sewn to the GI tract of 6 anesthetized dogs.Contractile activity was recorded on an 8-channel strip recorder for a variety of experimental conditions.The strip chart was placed on a graphic-to-digital converter and selected points were converted to sets of computer readable coordinates by positioning a manual cursor over the points.The coordinates of the base and peak of each contraction were used to calculate motility indices, areas under the contraction curves, and tonic shifts. These were printed in tabular form or graphed on the computer plotter or graphic display. Comparison with manual analysis of the same data revealed excellent agreement (r=0.871).The use of a computer oriented graphic-to-digital analysis of GI motility data has increased the speed, accuracy, and amount of information obtained.(Supported in part by the Frank C. Bressler Research Fund)

EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE RAT BLOOD-BRAIN BARRIER. Carl H. Sutton* and Frederick B. Carroll.* (SPON: V. Popovic) Dept. of Neurological Surgery, Univ. of Miami, Miami, Fla. 33152

Sprague-Dawley male rats were used to study the tolerance of the blood-brain barrier (BBB) to microwave irradiation. The rat brains were locally heated with microwaves (2450 MHz) under chloral hydrate anesthesia, while the body of the animals was shielded with Eccosorb. The brain and body temperatures were monitored with thermocouples. Horseradish peroxydase was administered (i.v.) 30 min prior to the animal sacrifice in order to determine possible BBB disruption by microwave heating. After perfusion with 5% PVP in saline at 4°C, the excized brains were homogenized for biochemical and histochemical studies. In normothermic (37°C) rats BBB was disrupted after brain heating for 10 min at 45°C, after 15 min at 42°C and after 60 min at 40°C. In hypothermic (30°C) rats the BBB integrity was lost after heating brains for 15 min at 45°C, after 30 min at 42°C, and after 180 min at 40°C. It is concluded that microwave hyperthermia disrupts the integrity of the BBB to protein (horseradish peroxydase) in the selectively heated rat brain. The tolerance of the BBB to microwave energy is dose-related, depending upon the temperature of brain and the length of the heating. The BBB received significant protection from body core hypothermia, probably through the contact of endothelial cells with cooled blood.

VENTILATORY AND METABOLIC RESPONSES TO STEADY STATE AND PROGRESSIVE SUPINE EXERCISE. O. Szekely, R. Foster, J.M. Kinney, J. Askanazi, S. Rosenbaum and P. Silverberg (Sponsored by H.H. Bendixen) Dept. of Surgery and Anesthesiology, College of Physicians & Surgeons of Columbia University, New York, NY 10032

This study was conducted to differentiate the ventilatory and metabolic behavior with supine exercise at low levels (VO_2<1000 ml/min) from the well documented response to high level upright exercise. Using a canopy system (J. Appl. Physiol 33:523, 1972) for non-invasive measurement of breathing patterns and gas exchange, 9 male subjects were studied while performing steady state (SSE) and progressive exercise (PRE). Work loads were: SSE 1.5 Kgm/sec for 17 min; PRE 1.5, 2.5, 3.75 and 5.0 Kgm/sec with 2 min. increments. Total work was the same (1548 Kgm) in both types of exercise. With steady state exercise tidal volume (V_T) and respiratory rate (f) rose 26% and 60% resp. Minute ventilation (VE) increased 115%. With progressive exercise f rose during the 1st and 2nd work level (36%), then remained constant while V_T and V_E increased during all 4 levels (to 146% and 256%). In both cases inspiratory time (T_I) remained fairly constant, but expiratory time (T_E) decreased (SSE: —27%. PRE: —37%). At the same time inspiratory flow increased 73% and 186% in SSE and PRE. The O_2 consumption reached a stable level in 4 minutes in SSE but rose continuously in PRE. This finding shows that in SSE both the V_T and f accounted for the increases in V_E while in PRE the V_T is the dominant factor.

IS THE CENTRALLY MEDIATED PRESSOR RESPONSE TO ANGIOTENSIN II (AII) INFLUENCED BY OPIATE RECEPTORS? Julianna E. Szilagyi* and Carlos M. Ferrario. Cleveland Clinic Research Division, Cleveland, Ohio 44106.

The present study was designed to investigate a possible interconnection between central effects of AII and opiate receptors in the area postrema. Nine male mongrel dogs were anesthetized with chloralose (60 mg/kg, iv) after premedication with morphine (2 mg/kg, im). Mean arterial pressure (MAP) was monitored during three-minute infusions of AII (Dose: 10,20 ng/kg/min) and norepinephrine (NE: 100,200 ng/kg/min) given intravenously (IV) and intravertebrally (VA). At the highest dose tested AII introduced VA and IV produced a 26 ± 2 mmHg and 18 ± 2 mmHg increase in MAP respectively. NE (200 ng/kg/min) given VA and IV caused a 13 ± 4 and 16 ± 3 mmHg pressor response respectively. After the intravenous administration of 0.8 mg of the morphine antagonist naloxone hydrochloride, the VA pressor response to AII was reduced by 50% ($p < 0.01$); those to IV AII were unchanged while NE (IV, VA) responses were increased but not significantly. Morphine given into the VA of dogs anesthetized with chloralose alone resulted in a two-fold increase in the pressor response to AII (VA). These data suggest that naloxone blunts the centrally mediated pressor response to AII without reducing its direct vasoconstrictor action. (Supported by NHLBI grant #HL-6835 and American Heart Association Advanced Fellowship).

MITOCHONDRIAL ROLE IN THE STIMULATION OF Na EFFLUX BY ALDOSTERONE IN SINGLE MUSCLE FIBERS. R.B. Tallitsch, Dept. of Biology, Augustana College, Rock Island, Il. 61201

Work with single muscle fibers from the barnacle Balanus nubilus loaded with 22-Na by microinjection has revealed that these fibers can be rendered sensitive to external aldosterone by pre-exposing the barnacle in vivo. External in-vitro application causes a delayed stimulation of the Na efflux (latent period av. 60 min). This transitory stimulation is abolished by transcription and translocase inhibitors, as well as oxythiamine or spironolactone application prior to external application of aldosterone. ATPMg or pyruvate injection prior to aldosterone application augments the stimulatory response. More recent work shows that preinjection of flurocitric acid, malonic acid, antimycin-A or 2,4-DNP, but not rotenone, abolished the response to aldosterone. Internal application of alpha-ketoglutaric acid after flurocitric acid, or S-succinyl CoA after rotenone augments the delayed response. This is not seen with oxaloacetic acid injection following malonic acid. Augmentation is also observed in fibers injected with FADH. Injection of NADH is ineffective. These results suggest that aldosterone modulates Na efflux by influencing mitochondrial function, presumably at the level of succinic dehydrogenase. (Supported by Ill. Heart Assoc. & Augustana Faculty Research Comm.)

pH CHANGES INDUCED BY ELECTRICAL STIMULATION. Pei Chin Tang. Dept. of Physiology, Univ. of Health Sciences/The Chicago Medical School, Chicago, Illinois 60612

As reported previously, monophasic square-wave pulses applied to platinum electrodes generated polarization potential and caused gas release when immersed in a physiological solution (Fed. Proc., 38:1402, 1979). In present experiments, platinum electrodes were placed in a gel composed of 2.5% gelatin and 9% Universal Indicator in a phosphate buffered saline solution. Application of monophasic square-wave electric pulses elicited pronounced pH changes. In the vicinity of the positive electrode the Indicator showed a pH value of 4-5 while showing a pH value of 10-11 in the vicinity of the negative electrode. Change of pH occurred before the appearance of gas bubbles on the electrode surfaces. This extreme pH change could be a major cause of necroses that often occur in chronic stimulation of nervous tissues. The pH change was not observed when the stimulation was made with capacitor-coupled pulses, 60 Hz. AC or balanced biphasic square-wave pulses. Capacitor-coupled pulses and 60 Hz AC appear useful for avoiding pH change and gas release in chronic nerve stimulation. Biphasic pulses are not as useful since they can cause pH change and gas release if the pulses are unbalanced. (Supported by NIH Grant NS15353-01 and Easter Seal Research Foundation Grant R-7623.)

Ventilatory Kinetics in the Exercising Dog. P.C. Szlyk, D.R. Pendergast and J.A. Krasney. Dept. of Physiology, SUNY, Buffalo, NY 14214

The total ventilatory ($\dot{V}E$) on-response to dynamic exercise was analyzed breath-by-breath in 4 tracheostomized dogs over a range of $\dot{V}O_2$ from 25 to 95 $ml \cdot min^{-1} \cdot kg^{-1}$. At the onset of exercise, $\dot{V}E$ increased abruptly ($\dot{V}E_{FAST}$), then either remained constant or decreased. Following this time delay (TD), $\dot{V}E$ rose more slowly ($\dot{V}E_{SLOW}$) to attain a stable plateau (Flandrois, Dejours). The amplitude of $\dot{V}E_{FAST}$ was similar at all $\dot{V}O_2$ levels. The TD averaged 46.6 (±6.5)sec, 30.6 (±1.4)sec, and 21.9 (±1.5)sec at $\dot{V}O_2$ levels of 30-40, 55-65, and >75 $ml \cdot min^{-1} \cdot kg^{-1}$, respectively. As $\dot{V}O_2$ increased, the average $\dot{V}E$ value during the TD represented a smaller fraction of the total $\dot{V}E$ response (69%(±5), 53%(±3), and 41%(±4), respectively). Also, the $t_{½}$ of $\dot{V}E_{SLOW}$ decreased as the $\dot{V}O_2$ was raised (28.9(±2.8)sec, 26.5(±3.8)sec, and 21.6(±1.7)sec, respectively). $\dot{V}E_{FAST}$ was associated with an increase in respiratory frequency (f). $\dot{V}E_{SLOW}$ was characterized by a further rise in f when $\dot{V}O_2 < 45$ $ml \cdot min^{-1} \cdot kg^{-1}$, but above this $\dot{V}O_2$ level, increases in tidal volume (V_T) primarily mediated the increments in $\dot{V}E_{SLOW}$. In summary, the $\dot{V}E_{FAST}$ is the major component of $\dot{V}E$ at low $\dot{V}O_2$, whereas at higher $\dot{V}O_2$, $\dot{V}E_{SLOW}$ is engaged earlier and makes a greater contribution to the total $\dot{V}E$ response.

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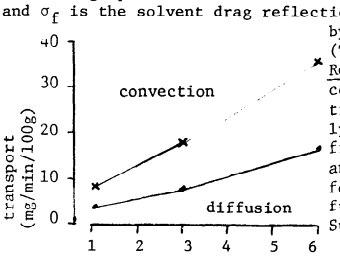
SCHEDULE-INDUCED HYPERTENSION: EFFECT OF CHRONIC ETHANOL INGESTION. Maisy Tang* and John L. Falk. Rutgers Univ., New Brunswick, N. J. 08903

Previously (Psychosomat. Med. 39:252, 1977) we have shown that exposure to daily intermittent-food-delivery sessions produced excessive 0.9% saline intake and hypertension in hungry mononephrectomized rats. The same level of food and saline intake and mononephrectomy without the intermittency of the feeding schedule did not produce hypertension. In the present study, 2 groups of 49-day-old rats (day 1) were food restricted (80% free-feeding growth rate) and exposed to an around-the-clock intermittent feeding regimen: a 1-hr session (one 45 mg food pellet/2 min) every 4 hr. The alcohol group (EtOH) drank 2.5% EtOH made in saline. The glucose group (Glu) drank saline with glucose added to equate caloric intakes between groups. Mononephrectomy was performed between days 167-174. Indirect blood pressure slowly increased in both groups to 145 (EtOH) and 160 (Glu) by day 232. Direct mean carotid pressures were 156 (EtOH) and 170 (Glu). The EtOH group had lower pressures by both measures, but these differences were not statistically significant. Thus, an ethanol intake of 10g/kg/day did not alter the course of development in this type of hypertension. (Supported by USPHS NIH grants HL19612 and AA00253)

CONVECTIVE AND DIFFUSIVE TRANSPORT OF ENDOGENOUS PROTEINS IN LUNG LYMPH. A. E. Taylor, J. C. Parker, and D. N. Granger. Dept. of Physiology, University of South Alabama, Mobile, AL 36688.

The relative contributions of convection and diffusion to protein transport between plasma and lung lymph were determined for six endogenous protein fractions with effective radii ranging between 37Å and 120Å. Total flux (J_D) for each fraction was determined from the product of lymph flow (J_V) and lymph concentration for each fraction. Convective flux (J_C) was calculated by; $J_C = J_V (1-\sigma_f) \bar{C}_p$; where C_p is the average protein concentration between plasma and lymph, and σ_f is the solvent drag reflection coefficient determined by the cross-point method (Taylor, et al., Microvasc. Res. 13:297, 1977). Both convective and diffusive transport increased as lymph flow increased. The figure shows convective and diffusive transport for albumin (37Å) as a function of lymph flow. Supported by NIH HL 22549.



RESPONSE OF THE 2-KIDNEY YUCATAN MINIATURE BOAR TO DOCA AND d-ALDOSTERONE. J.M. Terris and R.C. Simmonds*. Dept. of Physiol., Uniformed Services Univ., Bethesda, MD 20014.

It has been shown that the uninephrectomized pediatric male pig will respond to chronic implantation of DOCA with a rise in mean arterial pressure (MAP), hypokalemia, polyuria, polydipsia, and a suppressed plasma renin activity (Terris et al., Clin. Sci. Mol. Med. 51:303S-5S, 1976). We have now demonstrated that the 2-kidney adult Yucatan miniature boar will respond similarly not only to chronic implantation of DOCA but also d-aldosterone (aldo). These animals also develop a marked hypochloremic metabolic alkalosis. All animals were 18-28 months old (70-100 Kg) at the time of implant. Pre-study observations were conducted in 6'X 6' indoor holding pens or 5'X 35' indoor-outdoor kennels. Experimental animals were housed individually in eight 4'X 6' metabolic cages. They received tap water ad libitum, and a pre-measured quantity of food with sodium chloride added to approximate the intake of the pediatric pigs. Blood pressures and blood samples (indwelling carotid catheter) and metabolic data were obtained daily. After 7-10 days of stable baseline measurements, silicon rubber strips (control, with DOCA, or with aldo, 5 animals each group) were placed subcutaneously under Surital anesthesia. After 2-4 days MAP, serum sodium, pH and bicarbonate rose. Serum potassium, chloride, and plasma renin activity fell. 1± week after implant water intake and urine output increased. We conclude that both DOCA and aldo are effective in this animal and that uninephrectomy is unnecessary.

VAGAL AFFERENT ACTIVITY INHIBITS SPINAL NEURONS RELAYING NOCICEPTIVE INPUT FROM THE HEART. Roger Thies, Robert D. Foreman, and Neal Weber*. Dept. of Physiology and Biophysics, Univ. of Oklahoma Health Science Center, Oklahoma City, OK. 73190.

Previous studies from this laboratory have shown that nociceptive information from the heart is transmitted by neurons of the spinal cord that project to the brainstem. These neurons begin to discharge or accelerate their discharge rate in response to coronary artery occlusion, application or injection of bradykinin to the heart, and noxious stimulation of the forelimb and chest wall skin and muscle. Such neurons were identified in chloralose anesthetized cats by brief latency responses to electrical stimulation of the left sympathetic chain, and in most by antidromic activation from the spino-medullary junction. Stimulation of vagal afferent fibers, especially unmyelinated ones, inhibited spontaneous and sympathetic-elicited activity of these thoracic neurons. A tonic vagal inhibitory effect is also suggested, since firing of these thoracic neurons elicited by bradykinin (0.2ml. of 0.1mg/ml) into the heart was often potentiated after section of both vagi in the neck. Similarly, in some neurons firing in response to CAO was much more pronounced after vagal section. This vagal activity is the afferent limb of a response which descends to inhibit spinal neurons responding to noxious stimuli transmitted by sympathetic afferent fibers. (Supported by NIH Grant HL22732 and Biomedical Research Support Grant 5S07-RR05411.)

RENAL GLUTATHIONE LEVELS, GSH, AND ELECTROLYTE EXCRETION. Denyse Thornley-Brown* and T.C. Welbourne. LSU Medical Center, Shreveport, La. 71130

To determine if a relationship exists between renal GSH levels and electrolyte excretion, adult male Sprague-Dawley rats were anesthetized with nembutal, 30mg Kg^{-1} ip., and prepared for clearance, ^{14}C-inulin, measurements. After a control clearance period, rats were administered i.v. either 10mg acetazolamide, Az, or 75mg D-glutamate, D-Glu, followed by two 15 min. collections. Az is a well known diuretic whose site of action is proximal and whose effect on GSH levels is unknown; D-glu blocks the synthesis of GSH but is not known if it affects electrolyte excretion. As expected, D-glu lowered renal GSH levels 33 percent, $P<.05$, and interestingly, induced a 4 fold increase in H^+, Na^+ and K^+ excretion (all significant $P<.05$). Az, as expected, decreased H^+ excretion and increased Na^+ and K^+ excretion about 3 fold and interestingly, lowered GSH levels. The results are consistent with a relationship between renal GSH metabolism and the renal handling of electrolytes.

EFFECT OF D- AND L-PROPRANOLOL ON CARDIAC MECHANORECEPTOR C-FIBERS. M.D. Thames*. CV Center & Dept. of Int. Med., Univ. of Iowa, Iowa City, Iowa 52242.

dl-propranolol has both beta adrenergic receptor blocking (BB) and nonspecific membrane stabilizing (local anesthetic) effects. The purpose of this study was to determine if the discharge of left atrial (n=8) and left ventricular (n=5) mechanoreceptors with nonmyelinated vagal afferents is altered by the BB or the membrane stabilizing (MS) effect of dl-propranolol in open chest pentobarbital anesthetized cats. The locations of the receptors were established by probing the open heart. Graded occlusion of the ascending aorta (AoO) resulted in increases in the firing of atrial endings, which were linearly related to atrial pressure (1.5 imp/sec/mmHg), and in the firing of ventricular endings, which correlated best with diastolic pressure (0.69 imp/sec/mmHg). d-propranolol (0.3-0.6 mg/kg), which has MS but not BB properties, did not alter the response of atrial or ventricular endings to AoO. The response of atrial endings to AoO was not changed during isoproterenol (6 mcg bolus). l-propranolol (0.3-0.6 mg/kg) which has both MS and BB effects markedly decreased the sensitivity of ventricular (0.25 imp/sec/mmHg) but not atrial endings. This effect was the result of l-propranolol-induced changes in contraction mechanics due to BB. Although the response of ventricular endings is altered by l-propranolol, atrial endings are not influenced by the BB or MS effects of dl-propranolol nor are they influenced by beta receptor stimulation. (Supported by HL 21158).

A-V CONDUCTION IN THE CONSCIOUS DOG. J. X. Thomas, Jr., W. C. Randall, M. J. Barber and J. F. Moran*. Depts. Physiol. and Med., Loyola Univ. Medical Center, Maywood, IL 60153

A previous report from this laboratory demonstrated that following total autonomic blockade, with atropine and propranolol, 1:1, A-V conduction was maintained up to 290-310 bpm. These studies also indicated that the predominant neural influence at the A-V junction in the dog was mediated by parasympathetics. The present experiments were designed to determine whether under resting and completely isolated conditions, spontaneous alterations in autonomic tone to the A-V junction could affect conduction. Experiments were performed on two groups of mongrel dogs, control dogs with normally innervated hearts and a second, cardiac denervated group. All dogs underwent a similar protocol in which a Lead II EKG was recorded intermittently for 24 hrs using a Cardiodyne programmable holter monitor. Average heart rates of each dog were computed. Each dog was "holtered" again and then paced via a previously implanted right atrial electrode, using a Medtronic pacemaker at a rate 30-40 bpm above the average heart rate of the preceding 24 hr. Normally innervated dogs had frequent episodes of varying degrees of A-V block, particularly during periods of minimal activity. The denervated group showed no deviation from the paced rhythm. These data suggest that the changes in sympathetic and parasympathetic outflow occurring in the conscious dog affect A-V conduction. (Supported by NIH Grant HL 08682.)

ACUTE REDUCTION IN VENOUS RETURN LEADS TO DRINKING AND VASOPRESSIN SECRETION IN DOGS. Terry N. Thrasher, Lanny C. Keil and David J. Ramsay. Dept. Physiol., UCSF, San Francisco Ca 94143 and Ames Research Center, Moffett Field, CA 94035.

Constriction of the thoracic vena cava in dogs leads to the development of edema, associated with an increase in water intake. This chronic preparation is often used as a model of congestive cardiac failure. In the present study, the acute effects of caval constriction were studied. Dogs were surgically prepared with inflatable cuffs around the thoracic vena cava and with femoral arterial cannulae. After recovery from surgery, the cuff was inflated enough to reduce mean arterial pressure by 30 mmHg. In the first 60 min following constriction, water intake was 183±33 ml with a latency of 22±6 min. compared with zero intake during control periods. Twenty min following constriction, plasma vasopressin concentration had increased from 1.6 ± 0.2 to 31.5 ± 10.0 pg/ml and plasma renin activity from 4.2 ± 0.3 to 20.3 ± 3.5 ng/ml/3h. Mean arterial blood pressure was reduced initially by 27 ± 14 mm Hg with an associated increase in heart rate from 76 ± 5 to 142 ± 12 beats/min. Blood pressure and heart rate returned towards normal during the next hour. These data indicate that an acute reduction in venous return is a potent stimulus to drinking and renin and vasopressin secretion in the dog.

Supported by USPHS Grant HL-18862.

EXERCISE TRAINING AND PERIPHERAL VASCULAR RESPONSES OF SHR GROUPS. C.M. Tipton, R.D. Matthes*, K.A. Rowlett*, J.G. Edwards*, and R.A. Oppliger*. Exercise Physiology Laboratory, University of Iowa, Iowa City, Iowa 52242.

Recent studies with SHR groups (Med. Sci. Sports. 11:78, 1979) have reinforced the concept that endurance training (ET) will lower, but not normalize, resting systolic blood pressure. To determine whether training would modify the responses of the peripheral vascular beds, the hind limb perfusion technique of Brody et al., (J.A.P. 18:645, 1963) was used with 16 female SHR assigned equally to nontrained (NT) and ET groups. They had been exercising for longer than six months and their VO_2 max results proved that they were trained. Training was associated with lower (26%) resting peripheral resistance and less responsiveness (21%)* to bilateral carotid occlusion. Tilting and asphyxia experiments did not exhibit any ET effects. When either tyramine, norepinephrine, isoproterenol, propranolol or phentolamine were injected with varied dosages, there were no significant peripheral changes in blood pressure that suggested an ET influence. Wall and lumen plus thickness of the iliac artery were measured and ET was associated with larger lumen areas, no differences in wall thickness, and a smaller wall/lumen ratio. These collective results suggested that vascular responsiveness was not a major factor in explaining ET changes. On the other hand, structural aspects might be worthy of further investigation.
(*denotes statistical significance at .05 level, supported in part by HL 21245-02 and GM-07045-01)

THE RESPONSE OF THE PERINATAL PULMONARY CIRCULATION TO PROSTAGLANDIN D_2. M.L. Tod*, J.E. Frisinger*, J.B. Philips*, J.A. Jordan* and S. Cassin. Dept. Physiology, Univ. Of Fla., College of Medicine, Gainesville, Fl. 32610.

Prostaglandin D_2 (PGD_2) has been reported to cause pulmonary vasoconstriction in adult animals. However, we have found that PGD_2 yields dose-related vasodilatation in the pulmonary circulation of fetal goats. Studies were performed on ten fetal goats which were delivered by cesarean section with umbilical circulation undisturbed. The left pulmonary artery was perfused at constant flow with blood from the inferior vena cava. Pulmonary, left atrial and systemic pressures were monitored, as well as pulmonary flow, heart rate, blood gases and pH. Infusions of PGD_2 directly into the pulmonary artery in doses of 0.03-3.4 µg/kg/min produced decreases in the pulmonary vascular resistance (PVR) of 4-53%, with an insignificant ($P > .50$) effect on the mean systemic blood pressure, as compared with the systemic hypotension seen with PGE_2 and PGI_2 (Cassin et al, Physiologist 21:17, 1978). Similar experiments were performed on five newborn lambs, ranging in age from 2-14 days. In newborn lambs doses of 0.03-0.79 µg/kg/min gave decreases in PVR of 5-34%, while doses greater than 10.0 µg/kg/min produced up to a 42% increase in PVR. The maximum dose given was 40.26 µg/kg/min. The response of the pulmonary circulation to PGD_2 appears to be related to development, resulting in a vasodilatation in the fetus, a biphasic response in the neonate, and the reported vasoconstriction in the adult.

QUANTITATIVE EEG ANALYSIS OF PRECONVULSIVE PERIOD IN RATS EXPOSED TO HIGH OXYGEN PRESSURE. D. Torbati,* A.J. Simon* and A. Ranade* (SPON.: B.T. Storey). Inst. for Environmental Medicine, Univ. of Penn., Philadelphia PA 19104.

The EEG of rats exposed to high oxygen pressures displays electrical discharges preceding onset of generalized clinical convulsions (GCC). To establish characteristics of pre- and post-electrical discharge activity, awake, unrestrained rats were exposed to 3, 4 and 5 ATA O_2. Quantitative electrocortical activity (ECoG) was monitored continuously until GCC developed. ECoG was analyzed using a hybrid analog-digital system. The "energy" contents (time integral of rectified voltage) of the individual Δ, θ, α, β_1 and β_2 bands and the total energy content were individually plotted versus time (10-sec intervals). The results showed that the energy content of either individual frequency bands, or total energy content, or both rose above control levels before onset of the first electrical discharge (FED). These changes occurred 1-10 min before FED at 5 ATA O_2; 2-30 min at 4 ATA O_2; and 2-60 min at 3 ATA O_2. The FED latency was 13-73 min at 5 ATA O_2; 26-103 min at 4 ATA O_2; and 78-215 min at 3 ATA O_2. Total ECoG energy content also rose between FED and first GCC. ECoG changes before the first GCC may correlate with alterations in cortical tissue P_{O_2} and cerebral oxygen consumption: this requires further investigation. [Supported by NIH Grant HL-08899-15 and ONR Contract N00014-76-C-0248.]

ATTENUATION IN CENTRAL NEURONS: ITS RELATIONSHIP TO INCREASED INTRACYTOPLASMIC FREE CALCIUM AND MEMORY STORAGE. Clara Torda. Res.Dpt.,N.Y.C.PA.Training,New York,N.Y.,10028.

According to current concepts attenuation (the decrease of amplitude and increase of duration of subsequent spikes during a spike burst) plays some role in memory storage. Theoretical considerations based on experimental evidence (Torda, Soc.Nsci.Abstr.,4,111,1978; IRCS Med.Sci.:Nervous system, 7,138,1979) suggested that attenuation may result from intracellular accumulation of free Ca inside neurons that depend on Ca influx for spike generation (e.g. spikes of dendritic origin). Therefore, bioelectric processes have been intracellularly recorded from special neurons of the pontine nucleus reticularis gigantocellularis following the method described by Segundo, Takanaka & Encabo, J.Neurophysiol., 30, 1194,1967). These neurons responded with attenuation to high frequency stimulation. First it was observed that in these neurons spiking generated at the dendritic trigger zones depended on Ca influx (Ca gating mechanism).Experimentally induced independent changes of Ca influx and removal of the intracytoplasmically accumulated free Ca led to the conclusion that attenuation resulted from intracellular increase of free Ca.Under physiological conditions this increase resulted from the differences of the ratio of Ca influx (fast) and Ca removal(slow). Since the intracellular free Ca is mainly removed by binding on proteins and/or polypeptides, this stimulus-dependent intracytoplasmic accumulation of free Ca partakes in memory storage processes through its binding.

BICARBONATE-STIMULATED ATPASE IN PLASMA MEMBRANE AND MITOCHONDRIAL FRACTIONS OF FIDDLER CRAB (UCA MINAX) GILL. David W. Towle and E. Franklin DePew*. Univ. of Richmond, Va. 23173

Since active chloride uptake from seawater by fiddler crabs may depend on bicarbonate as a counterion, a search for a chloride-bicarbonate-stimulated ATPase was made in subcellular fractions of homogenized gill, the tissue most likely responsible for monovalent ion regulation in crabs. A bicarbonate-stimulated ATPase, inhibited by thiocyanate but enhanced only slightly by chloride ions, was found in mitochondrial and microsomal membrane fractions obtained by differential centrifugation. Several investigators have suggested that bicarbonate-stimulated ATPase in other tissues is exclusively mitochondrial. Since our initial membrane fractions were heavily contaminated with mitochondria, we employed density gradient centrifugation through 20-40% sucrose to separate mitochondria from a plasma membrane-rich fraction. Assays of the mitochondrial enzyme cytochrome oxidase and the plasma membrane-bound enzyme sodium-plus-potassium-dependent ATPase showed that cross contamination between these two fractions was less than 5%. Nevertheless, the plasma membrane fraction as well as the mitochondrial fraction exhibited substantial bicarbonate-stimulated ATPase activity, supporting the concept that this enzyme is not exclusively mitochondrial and is situated in the plasma membrane where it may play a direct role in chloride transport by Uca gill epithelium.
(Supported by the John Neasmith Dickinson Memorial Research Fund)

INCREASED ACTIVITY OF INTRAMUSCULAR PROTEASES IN THE HYPERTHYROID STATE. Teruhiko Toyo-oka* and John Ross, Jr. BSB-2013 Division of Cardiology, Department of Medicine, University of California, La Jolla, California 92093

Muscle atrophy accompanies the hyperthyroid (H) state. To determine whether or not the activity of endogenous muscle proteases is involved, activities were analyzed of 3 different proteases known to degrade myofibrillar proteins. L-thyroxine (200 µg/Kg, i.m. in saline) was administered to rabbits (N=9) for 2 weeks, while control rabbits (N=8) received only saline. Activities in skeletal muscle of cathepsin B1 and D (which are mainly located in lysosomes and degrade both myosin and actin) were increased twofold in H animals ($p<0.001$). The activity of calcium-activated neutral protease (which is in the cytosol fraction, activated by Ca^{2+} ions at neutral pH and degrades both troponin and tropymyosin) was increased threefold in H skeletal muscle ($p<0.05$). The increased activity of lysosomal proteases did not result from increased fragility of lysosomes, since comparison of the activities from the cytosol and lysosomal fractions showed retained activity in the lysosomes to be higher in the H groups ($p<0.01$). The cause of the increased activity of these proteases was due to increased amount of enzyme, as estimated from activities expressed per weight of muscle and per mg protein, and from enzyme kinetics. The findings suggest that increased activities of these 3 proteases could play a role in skeletal muscle atrophy in the H state.
(Supported by NIH Research Grant HL 12373).

CONTROL OF BREATHING IN NEWBORN KITTENS. Teresa Trippenbach. McGill University, Montreal, Canada, H3G 1Y6

To study the control of breathing in newborn kittens, I investigated, 1) the effects of CO_2 on inspiration (T_I), expiration (T_E), and 'integrated' phrenic activity (3% CO_2 in O_2 was given for 1 min.); 2) the Hering-Breuer expiratory-promoting reflex (the airway was occluded at the end inspiration). 26 kittens from 1-21 days old were anesthetized with pentobarbital (20 mg/kg. i.p.), tracheostomized and breathed spontaneously. In the majority of kittens, CO_2 produced a decreased in T_I together with an increase in the rate of rise and peak amplitude of phrenic activity. This was not always followed by a shortening of T_E; in fact, in some kittens, T_E was prolonged. The changes in T_E were more pronounced than those in T_I. The breath-to-breath relations between T_E and T_I, both during control and CO_2 inhalation, were not significant or negative in most of the animals. The Hering-Breuer reflex was stronger in kittens with higher respiratory frequencies. There was no developmental changes in CO_2 effects, however, the Hering-Breuer reflex was strongest in the oldest animals. The results indicate that in newborn kittens, the mechanisms controlling inspiration and expiration are similar to those described in adult cats. However, the functional linkage between these two phases has not yet matured by the third week of life. (Supported by the Medical Research Council of Canada).

MEAN CIRCULATORY FILLING PRESSURE AND WHOLE-BODY VENOUS TONE IN CONSCIOUS RATS. Nick C. Trippodo and Jin Yamamoto.* Ochsner Medical Institutions, New Orleans, LA 70121.

To test the hypothesis that at any given blood volume (BV), mean circulatory filling pressure (MCFP) is influenced mostly by venous rather than arterial characteristics and thus provides a means to assess whole-body venous tone, we determined the effects of norepinephrine (NE, 0.75 µg/kg/min, IV), hexamethonium (HX, 15 mg/kg plus 1.3 mg/kg/min, IV), and hydralazine (HL, 0.5 mg/kg, IV) on MCFP in conscious male rats. MCFP was measured by inflating an indwelling right atrial balloon to briefly arrest the circulation. BV was estimated by dilution of radioiodinated albumin and hematocrit.

	C	NE	HX	HL
N	13	11	12	10
MAP(mm Hg)	110±3	146±2*	93±3*	94±2*
BV(ml/kg)	67±1	64±1*	70±1	69±1
MCFP(mm Hg)	7.9±0.2	9.4±0.3*	6.1±0.1*	7.9±0.2

$\bar{x}$ ± SE, MAP=mean arterial pressure, C=control, *p<0.05 against control.

NE and HX, known to affect both arteriolar and venular tone, increased and decreased MCFP, respectively, while causing opposite or insignificant effects on BV. HL, known to have little effect on veins, did not significantly change MCFP or BV. The results support the concept that at a given BV, MCFP is a reliable index of whole-body venous tone. (Supported in part by NIH HL22261).

REVERSIBLE DECREASE OF AEQUORIN RESPONSES IN MUSCLE FIBERS BY PROLONGATION OF A TRANSVERSE D.C. STIMULUS. Gerhard Trube*, J. Rafael Lopez*, Laurel A. Wanek*, and Stuart R. Taylor. Mayo Foundation, Rochester, Mn. 55901

Contractions of skeletal muscle fibers are depressed by transversely-applied d.c. stimuli of long duration. We microinjected the Ca^{++}-sensitive photoprotein aequorin into single fibers isolated from frog (Rana temporaria) twitch muscle to determine if this stimulus-related decrease in tension is associated with a change in intracellular Ca^{++} release. There was a reversible, graded decline of force and aequorin luminescence when the strength of a stimulus was increased above 1.5 times rheobase and its duration was 5 ms or longer (15°C). At 3 times rheobase and 10 ms pulse duration peak twitch force was 30-60% and peak luminescence 40-70% of control (1 ms pulse duration). The fibers were injected only from one side, but we found no significant difference among decreased aequorin responses when the polarity of the stimulating electrodes was reversed; the aequorin seems to have reached equal concentrations in both sides of the fiber when the first of these records were taken (20 min after the injection). We conclude that the decrease in force and luminescence is due to a decrease or lack of Ca^{++} release in the region of the fiber adjacent to the anode, since it has been shown that the myofibrils in this region do not shorten actively after a long stimulus (Rüdel and Taylor, J. Physiol., 1969, 205:499). (Supported by NSF 77-22442, CONICIT of Venezuela, NS 14268 from the USPHS, and 77-983 from the AHA.)

ATP-DEPENDENT CALCIUM TRANSPORT IN SARCOLEMMAL MEMBRANE VESICLES. W.R. Trumble*, J.P. Reeves* and J.L. Sutko*. (SPON: L. Krulich) U. Texas Hlth. Sci. Ctr., Dallas, TX 75235

Membrane vesicles highly enriched in sarcolemma (SL) were prepared from dog ventricular tissue. The vesicles accumulated Ca (10-15 nmoles/mg protein) in the presence of 160 mM KCl, 5 mM $MgCl_2$ and 3 mM Tris-ATP (pH 7.4). Ca accumulation was reduced 5- to 10-fold when either Mg or ATP was omitted. The accumulated Ca was released by osmotic shock or by treating the vesicles with the Ca-ionophore A23187 (1 µM). Inhibitors of mitochondrial Ca transport such as ruthenium red (0.033 mM), azide (5 mM), 2,4-dinitrophenol (1 mM), carbonyl cyanide m-chlorophenylhydrazone (0.01 mM) and oligomycin (25 µg/ml) had no affect on Ca uptake by the SL vesicles. Oxalate, in contrast to its behavior in sarcoplasmic reticulum (SR) preparations, did not stimulate Ca uptake in the SL vesicles. The presence of Na markedly inhibited Ca uptake in the SL vesicles but did not inhibit oxalate-supported Ca accumulation by SR. Moreover, addition of 50 mM Na caused a rapid efflux of Ca from preloaded SL vesicles. The results suggest that Ca accumulation reflects the activity of an ATP-dependent Ca pump in SL vesicles with an "inside-out" orientation. The effects of Na are attributed to the Na-Ca exchange system in the SL vesicles. (Supported by NSF Grant No. PCM78-16130).

DIFFERENTIAL EFFECT OF SEX IN EXPERIMENTAL HYALINE MEMBRANE DISEASE (HMD). W.E. Truog*, D.L. Kessler*, S. Palmer*, J.Murphy*, D.E. Woodrum*, and W.A. Hodson. Dept. of Pediatrics, University of Washington, Seattle, WA 98195.

The influence of sex on the surface active properties of the immature lung is presently unknown. Utilizing a primate model of HMD (Ped.Res. 13:654,1979), the effect of sex on lung phospholipid (PL) composition, Type II cell number, lung volume, and severity of disease was examined in 44 M.nemestrina (23 female(F), 21 male(M)). The animals were delivered by C-section at a mean of 80% of term and sacrificed at 7±8 ($\bar{x}$ ± SD) hrs after birth. A respiratory distress score (RD) of 1 (severe) to 6 (normal), based on blood gas and radiographic criteria, was assigned to each animal. There were no sex differences in gestational age (GA) (F=140±4 d, M=139±4 d) or body weight (F=337±59g, M=363±42g). Females had more severe disease (RD=2.7) than males (RD=3.8)(P<0.05); F accounted for 70% of animals with scores of 1 or 2 but only 33% of those with scores of 5 or 6 (P<0.05). There were no sex differences in mean maximum lung volume (Vmax), % Vmax at 10 cm H_2O pressure, total lung PL, or number of Type II cells/alveolus. Both lung lavage PL and surface concentration were lower in F (F=7±8, M=17±14 mg/g dry lung)(P<0.025),and (F=2.6 ±7.5, M=7.3±5 cm^2/mg dry lung)(P<0.05). Lavage PL and RD score did not correlate with GA over the range examined. The more severe RD of the female is unexplained by differences in lung distensibility, number of Type II cells, or total lungPL. The results imply a M advantage in PL secretion or turnover.

HYDROPHOBIC DETERGENT BLOCKS INTESTINAL TRANSPORT OF LIPID INTO LYMPH. P. Tso*, J.B. Rodgers*, and J.A. Balint. Albany Medical College, Albany, New York, 12208.

Previous findings from this laboratory demonstrated that when rats were fed diets with 10% fat and 1% cholesterol by weight for two months, the experimental group which had 0.5% Pluronic L-81 (hydrophobic detergent) supplemented in the diet had significantly lower serum cholesterol and triglyceride levels. This investigation was undertaken to study the lymphatic transport of triglyceride and cholesterol in rats with or without Pluronic L-81 in their infusate. A lipid emulsion containing glycerol tri [9,10 ^3H (n)] oleate (40 µmol), [4-^{14}C] cholesterol (7.8 µmol), phosphatidylcholine (8.8 µmol) and sodium taurocholate (49.5 µmol) per 3 ml/h was infused for 8 h with 0.5 mg/h of Pluronic L-81 added in experimental rats. Triolein digestion and absorption were not impaired in the experimental rats, but lymphatic output of both triglyceride and cholesterol in lymph was greatly impaired as compared to the control rats as shown below:

	% infused radioactivity - ^3H (^{14}C)		
	Luminal	Mucosa	Lymph
Experimental	4.6 (15)	47.4 (66.2)	6.2 (7.0)
Control	2.8 (17.6)	22.4 (21.5)	52.3 (45.1)

The ^3H lipid in the mucosa was 80-85% esterified. Thus L-81 produces a block in exit of esterified triglyceride and of cholesterol from mucosal cells into lymph.

POTENTIATION OF HYPOXIC PULMONARY VASOCONSTRICTION BY OXATOMIDE, A NEW ANTIHISTAMINE. Alan Tucker. Wright State University School of Medicine, Dayton, OH 45435.

Oxatomide (OX), an orally active anti-allergic drug, has been suggested to inhibit mast cell discharge and to antagonize any histamine (HIS) which is released. These unique properties make OX a useful drug for studies of the pulmonary circulation. Six dogs (12 to 16 kg) were studied twice, one week apart, both 1) untreated and 2) after OX (10 mg/kg, p.o.) given prior to anesthesia. Three dogs received OX first. The dogs were then anesthetized, intubated, and allowed to breathe spontaneously. Measurements of pulmonary arterial pressure (PAP), cardiac output (CO), and pulmonary vascular resistance (PVR) were made before and during hypoxia (8 to 11% O_2 for 20 min) and progressive HIS infusion (1.25, 2.5, 5, and 10 µg/kg/min for 2 min at each dose) in duplicate. After OX, hypoxia induced greater increases in PVR (+74% vs +19%) and PAP (+49% vs +22%), and decreases in CO (-4% vs +8%) and stroke volume (-12% vs -1%). Arterial blood gases and pH were unchanged by OX during either normoxia or hypoxia. HIS, after OX, induced decreases in PVR (-17% vs +22%) and PAP (-6% vs +12%), and increases in CO (+35% vs +14%) and stroke volume (+10% vs -3%). These results confirm that OX acts as a HIS H_1-receptor antagonist, and demonstrate that hypoxic pulmonary vasoconstriction is potentiated after OX. If OX does indeed prevent HIS release, then hypoxia appears to cause the release of HIS, which in turn opposes vasoconstriction. (Supported by the Miami Valley Heart Chapter, AHA)

EFFECT OF PARATHYROID HORMONE (PTH) ON ESOPHAGEAL SMOOTH MUSCLE (ESM). S.N. Tuma & A.K. Mukhopadhyay. Dep. Medicine, Baylor College of Medicine, Houston, Texas 77030.

Gastrointestinal Symptoms are common in patients with hyperparathyroidism. The purpose of the present investigation was to evaluate the effect of PTH (bovine extract, Lilly) on longitudinal (LS) and Circular (CS) strips (12mmx 5mm) of opossum ESM. The strips were mounted in oxygenated baths (25 ml) containing Krebs-Ringer solution at 37°C. Electrical field stimulation of the LS & CS produced respectively a response during stimulation (DR), and a response after stimulation - the "off" response (OR). Both the DR & OR were dependent on voltage, frequency & pulse width of stimulation. Addition of 0.1, 0.4, 0.7 & 1.0 u/ml of PTH produced 21, 44, 78, and 93% increases in the amplitude of OR in circular strips. Higher doses (3.0, 5.0, 8.0 u/ml) produced initial stimulation followed by inhibition of OR. Tetrodotoxin (TTx) produced dose dependent inhibition of both OR & DR. After complete inhibition of OR with TTx, PTH did not show any effect. However, after ED50 inhibitory dose of TTx, PTH still stimulated the OR significantly. Atropine (10^{-7}M) did not block the stimulatory effect of PTH on OR. In higher doses (3.0, 5.0, 8 u/ml) PTH produced a dose dependent inhibition of DR and a dose dependent increase in tension in LS. In conclusion PTH has a stimulatory effect on the OR of CS of opossum ESM. This effect presumably is related to stimulation of the "cryptogenic" nerves responsible for the OR. The effects of PTH on ESM is of physiological interest.

ALTERED BONE TURNOVER DURING SPACEFLIGHT. Russell T. Turner,* Emily R. Morey,* Chung Liu,* and David J. Baylink.* American Lake VA Medical Center, Tacoma, WA 98493 and NASA-Ames Research Center, Moffett Field, CA 94035.

The effect of spaceflight on bone turnover was studied on growing rats. During 19-day spaceflights aboard Cosmos 782 and Cosmos 936, periosteal bone formation rate at the tibiofibular junction was reduced 47% and 43%, respectively, as compared with ground controls ($p<0.001$ in both cases). Inhibition of bone formation was accompanied by an arrest line at the periosteum suggesting that formation ceases during flight. The periosteal bone formation rate returned to or exceeded normal values 25 days after flight. Spaceflight did not appear to alter endosteal bone parameters: no significant changes occurred in net formation rate, osteoblast number, medullary area or osteoclast number, either immediately after flight or 25 days postflight. Similarly, no changes were seen in the longitudinal growth of the tibia, femur, or humerus. Lacunar-canalicular diameter was only slightly increased in the humerus after spaceflight (Cosmos 782) and not changed in the femur (Cosmos 936). Also, no changes were detected in vascular volume in either femur or humerus. The results suggest that near-weightlessness during orbital spaceflight results in reduced bone formation at the periosteum but not at the endosteum or the growth plate and that mechanical unloading of bone during spaceflight does not enhance resorption at the endosteum. (Supported in part by NASA contracts RA18698B and RA36687B)

RELATIONSHIPS OF GLOMERULAR ONCOTIC (π_g) AND HYDROSTATIC (ΔP) PRESSURES AND NEPHRON PLASMA FLOW (RPF), WITH THE GLOMERULAR PERMEABILITY COEFFICIENT (L_pA). B.J. Tucker* and R.C. Blantz. Univ. of Calif., San Diego, La Jolla, Calif. 92093 and VA Medical Center, San Diego, Calif. 92161

Several studies have appeared in the literature linking increases in L_pA with increases in systemic protein concentration (C_A) and oncotic pressure (π_A). In the present study in rats (n=24) utilizing micropuncture techniques we have examined the correlations of π_g (integrated π), π_A, C_A, rpf, glomerular hydrostatic pressure gradient (ΔP) and systemic hematocrit (Hct) to L_pA. Three 2-period protocols were utilized to examine within animal changes of the above parameters: 1) hydropenia to 10% body weight (BW) saline expansion (SE) (n=9), 2) SE to 1% BW of concentrated rat plasma protein (25g %) solution (HP) with removal of 1.5% BW whole blood (n=6) and, 3) SE to 1% BW HP with 2.5% BW whole blood removed with reinfusion of the removed red blood cells (n=9). Utilizing multiple regression analysis to ascertain which factors best correlated to changes in L_pA we found that π_A, π_g, C_A correlated positively ($p<0.01$) and that ΔP and the glomerular capillary hydrostatic pressure correlated in the inverse to L_pA ($p<0.01$ and $p<0.02$ respectively). There was no correlation to rpf or nephron blood flow. There was no consistent correlation of L_pA to Hct, however, when correlations did occur, L_pA tended to rise with reductions in Hct. These results do not show causality but indicate correlations in π_g and ΔP to changes in L_pA.

ENERGY METABOLISM AND BLOOD FLOW IN BURNED LIMB MUSCLE. J. Turinsky, I.H.Chaudry, D.J.Loegering and K.M.Nelson. Dept. Physiology, Albany Med. Coll., Albany, NY 12208 and Dept. Surgery, Yale Univ. School of Medicine, New Haven, CT 06510

We have previously shown that 3 days following a 3-sec scald of one hind limb, in vitro glucose utilization is markedly increased in soleus muscle from the burned limb but not from the contralateral unburned limb. The aim of the present study was to evaluate whether hypoxia might be contributing to this local metabolic alteration. Three days following a 3-sec scald of one hind limb of the rat, blood flow through soleus and gastrocnemius muscles of the burned limb as measured with labelled microspheres was increased 70% ($p<0.02$) and 48% ($p<0.01$), respectively. Calf muscles of the burned limb, frozen in situ, showed 48% decrease in ATP ($p<0.001$), 37% decrease in ADP ($p<0.001$), 192% increase in AMP ($p<0.01$), 45% decrease in total adenine nucleotides ($p<0.001$), 377% increase in lactate ($p<0.001$) and 132% increase in pyruvate ($p<0.001$). Blood flow and ATP levels of calf muscles of unburned limb of burned rats did not differ from controls. The decrease in ATP and increase in lactate in the burned limb suggest increased rate of glycolysis in vivo which may be due, in part, to the decrease in ATP-induced inhibition of phosphofructokinase. Low ATP and high lactate may also suggest that muscles of the burned limb are hypoxic in spite of the increase in blood flow. The increased flow may be mediated by vasodilatory effects of increased leakage of AMP and lactate. (Supported by USPHS Grant GM-22825)

FACTORS AFFECTING OSMOTIC FLUID SHIFTS IN ANURIA. Antonios H. Tzamaloukas* (SPON: K.D. Gardner, Jr.) University of New Mexico, Albuquerque, NM 87131.

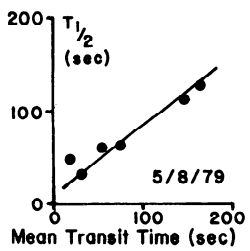
Changes in the amount of extracellular (ECF) solute result in osmotic fluid shifts between intracellular (ICF) and ECF spaces. In order to further the understanding of this phenomenon we analysed according to a mathematical model the factors regulating the magnitude of the osmotic shifts. Three parameters were found to affect this function: (1) The initial distribution of body water between ICF and ECF spaces; for comparable changes in ECF solute, osmolality changes and fluid shifts will be smaller in ECF volume contracted rather than in ECF volume expanded states. (2) The initial relationship of body solute to body water; all other factors being equal, fluid shifts in subjects with relative water excess will be greater than in subjects with relative water deficit. (3) The magnitude of change in the amount of solute; it bears a linear relationship to the osmolality change and a non-linear one to the magnitude of the fluid shift. Conclusions: When the amount of ECF solute changes, (a) calculations of osmotic fluid shifts and of osmolality changes should take into account the pre-existing status of body solute and water and the magnitude of the solute change, and (b) with similar gains or losses in solute, changes in osmolality and in body fluid distribution are greater in edematous rather than in non-edematous states.

AGE-RELATED DECREMENT OF GROWTH HORMONE SECRETION IN RESPONSE TO MAXIMAL MUSCULAR WORK. S.P. Tzankoff* and A.H. Norris. GRC/NIA/NIH, Baltimore, MD 21224

The role of growth hormone (GH) in growth and development in man and other species obscures less dramatic effects the hormone may have through adult life. Most evidence which shows man retains the capacity for GH secretion to very old age was derived from clinical testing using pharmacologic stimuli such as insulin-induced hypoglycemia or arginine infusion. Those tests may not reflect changes in GH secretion in response to normal stimuli such as muscular work. The present study was undertaken to examine age-related effects on exercise-induced GH secretion for the purpose of evaluating factors which might mediate aging losses in skeletal muscle mass. Sixty-three healthy participants of the Baltimore Longitudinal Study aged 21-81 underwent maximal treadmill tests. Heparinized blood for GH assay was obtained after 7 min of recovery from maximal effort. Basal samples were obtained on 42 of the men. Subjects were selected by age into decade groups (20-29,30-39,etc). Mean post-exercise GH values were 8.5, 5.3, 3.2. 3.2, 1.6, and 1.9 ng/ml, respectively. Mean basal GH values ranged between 1.4 and 1.8 ng/ml and did not differ with age. GH is well known to stimulate skeletal muscle anabolism. To the extent that exercise-induced GH secretion may mediate post-exercise muscle protein replication for maintenence or even hypertrophy, the present data suggest that even the relatively young men in their 40's are at a disadvantage.

TEMPORAL DELAY OF VENOUS BLOOD CORRELATES WITH ONSET OF EXERCISE HYPERPNEA. Karyl M. VanBenthuysen*, G. D. Swanson, C. VanWay*, J. V. Weil*, and C. W. Zwillich*. Cardiovasc. Pulm. Res. Lab, Univ. of Colo. Health Sciences Center, Denver, Colo. 80262

Exercise hyperpnea may be dependent on neural and/or humoral factors. If a humoral signal is important in causing exercise hyperpnea, then delaying the arrival of blood from exercising limbs should delay the onset of hyperpnea. In 11 chloralose-anesthetized dogs, exercise produced by electrical stimulation of hind limb muscles resulted in a 40% increase in $\dot{V}O_2$ and $\dot{V}CO_2$ with a proportional increase in ventilation such that arterial PCO_2 remained unchanged. An extracorporeal circuit removed blood from the inferior vena cava and returned it to the superior vena cava. A delay was introduced by varying the length of this circuit and mean transit time (MTT) was measured from arrival in the pulmonary artery of green dye injected intravenously in an exercising limb. In 5 of 7 dogs, the half time of the ventilatory response ($T_{½}$) was directly correlated with MTT (cumulative $p < .001$) (see figure for typical dog). This relation persisted following L_2 spinal cord transection in 3 of 4 additional dogs (cumulative $p<.001$). These data indicate that humoral factors contribute to the onset of exercise hyperpnea.



EFFECTS OF SEX AND AGING ON THE APOLIPOPROTEIN PROFILE OF MALE AND FEMALE RATS. Brian J. Van Lenten*, Christine H. Jenkins*, and Paul S. Roheim. (SPON: R.A. Russell). Louisiana State University Medical Center, New Orleans, LA 70119.

The influences of aging and sex on apolipoprotein profiles have not been well established. Adult Wistar rats of 12, 60, 76 and 96 weeks of age were used to study sex differences in plasma cholesterol and apolipoprotein concentrations during aging. Estrous cycles of female rats were monitored. At 12 weeks, males had higher concentrations of apo B and cholesterol than females. The male/female (M/F) ratio for apo B increased with age through 96 weeks as a result of the apo B increasing in males and remaining unchanged or decreasing in females. In contrast, at 12 weeks there was no difference between males and females for apo A-I, but the M/F ratio decreased through 76 weeks due to the increasing A-I concentrations in the female. At 96 weeks, after the female rats had stopped cycling, the M/F ratio for apo A-I increased. No significant sex differences occurred for apo E, A-IV, or C-III at 12 weeks, however males appeared to have higher apo E concentrations than females at 96 weeks, and the absolute concentrations of apo E and C-III were greater than at 12 weeks. It appears that sex and aging may result in selective changes in apolipoprotein concentrations. Work is currently being conducted to complete the apolipoprotein profiles and to study the underlying changes in metabolism. (Supported: NIH Grant HL 20954).

THE ROLE OF NH_4^+ EXCRETION BY THE SKIN OF *RANA PIPIENS* IN ACID-BASE BALANCE. J.C. Vanatta and L.W. Frazier. U. of Tx Southwestern Med. Sch. and Baylor College of Dentistry, Dallas, Texas 75235; 75246.

The skin of *Rana pipiens* was mounted between leucite chambers and incubated with Ringer solution on each side. In 7 control experiments and 6 experiments using skins from frogs in metabolic acidosis, the serosal and epithelial media were 1.5 mM PO_4 Ringer solution, pH 6.7-6.8, with 0.6 mM glutamine in the serosal media. In the remainder of the experiments the serosal media was 10 mM PO_4 Ringer solution, pH 6.9-7.0 containing 0.6 mM glutamine and the epithelial media was 0.6 mM PO_4 Ringer solution, pH 6.5-6.6. Frogs in normal acid-base (I) balance were fasted and kept in deionized water. Frogs in metabolic acidosis (II) received 6 doses of 120 mM NH_4Cl, 0.02 ml/g body weight injected into the dorsal lymph sac over a 48 hour period. Incubation periods were 222 to 255 minutes. The skin excreted ammonia with the final concentration in the epithelial media greater than in the serosal media. In 15 skins from I, excretion averaged 0.609 ± 0.067 (± SEM) and in 17 skins from II the average was 0.884 ± 0.089 nanomoles (100 mg wet weight)$^{-1}$ (min)$^{-1}$. $P/2 < 0.025$. In addition the skins acidified the epithelial media, but we were unable to show an increased rate of acidification in acidosis. The skin of *Rana pipiens* increases ammonia excretion in response to metabolic acidosis thereby aiding in the correction of the acidosis. (Supported in part by NIH General Research Grant 5 SO 1-RR05426-14, and by NIH Grant AM 18689).

ROLE OF APPLIED PLEURAL PRESSURE IN VENTILATION DISTRIBUTION DURING CYCLIC BREATHING: A NONLINEAR MODEL SIMULATION. A. van Grondelle* and H.K. Chang, Biomedical Engineering Unit and Dept. of Physiology, McGill University, Montreal, Canada.

To delineate the recently suggested role of different applied pleural pressures in ventilation distribution, a nonlinear model of the respiratory system has been used to simulate cyclic breathing under various conditions by varying the model parameters. The model consists of a common pathway, represented by a resistance, and two parallel compartments, each represented by a resistance and a compliance in series. The resistances depend non-linearly on instantaneous flow and volume, the compliances on instantaneous volume. Two cyclic pleural pressure swings, which may differ by a constant vertical difference (ΔP) and may vary in amplitude, are the driving pressures for the lung compartments. When published data on resistances, compliances and pleural pressure swings of normal young adults are used, the predicted ventilation distribution conforms to recognized experimental data. When the pleural pressures are varied, it is shown that the distribution of ventilation (1) depends on the magnitude of ΔP, (2) for a given ΔP is insensitive to the amplitudes of equal pleural pressure swings, and (3) is more dependent on the ratio of the applied pleural pressures than on the time constants.

(Supported by the Medical Research Council of Canada.)

RESPIRATORY MECHANICS OF A SMALL CARNIVORE: THE FERRET. A. Vinegar, E.E. Sinnett* and P.C. Kosch*. Dept. of Physiology, Harvard School of Public Health, Boston, Ma. 02115

The ferret, Mustela putorius furo, is a small, relatively inexpensive carnivore with minimal housing requirements. Lung morphology shows many similarities to the human lung (Hyde et al., 1979). Measurements were made from anesthetized (pentobarbital sodium), tracheotomized, supine males. Six animals weighing 576.2±11.5g, had tidal volumes, V_T=6.06±0.30ml; respiratory frequencies, f=26.7±3.9 min^{-1}; dynamic lung compliance, C_{DYN}=2.48±0.21 ml cmH_2O^{-1}; pulmonary resistance, R_L=22.56±1.61 $cmH_2O\ L^{-1}$ sec^{-1}. Volume-pressure curves from nine ferrets revealed almost infinitely compliant chest walls so that lung and total respiratory system curves were essentially the same. Total lung capacity (TLC) (89±5ml) and functional residual capacity (FRC) (17.9±2.0ml) were determined by gas freeing the lungs in vivo. The TLC of these ferrets is about the same as in 2 kg rabbits. Maximum expiratory flow-volume curves showed peak flows of 10.1 vital capacities (VC) sec^{-1} at 75%VC and flows of 8.4 and 5.4 VC sec^{-1} at 50 and 25%VC. (Supported in part by NIH HL-07118 and HL-17382)

INDUCTION OF SLOW CHANNELS BY MICROINJECTION OF CYCLIC AMP (cAMP) INTO HEART CELLS. Stephen Vogel* and Nick Sperelakis, University of Virginia Medical School, Charlottesville, VA 22908.

To further clarify the relation between cAMP and the myocardial slow inward current, cAMP was microiontophoresed into heart cells. Short canine Purkinje fibers were made by crushing. The preparation was suffused (10 ml/min) with Krebs-Henseleit solution (37°). Only fibers having resting potentials >-70 mV and normal action potentials were tested. The fast Na^+ channels were voltage inactivated by elevating $[K]_o$ to 20 mM, rendering the cells inexcitable. Hyperpolarizing current was passed using a bridge circuit through microelectrodes filled with 1 M Na-cAMP. cAMP injection (100-200 nA for 3-60 sec) induced slow action potentials (APs) in about one-third of the preparations tested. The size and rate of rise of the response was proportional to the injected cAMP. The slow APs persisted for up to 2 min after the injection. cAMP also potentiated the theophylline (1 mM)-induced slow AP in 2 preparations tested. The most marked effect was an increase in the maximal rate of rise which persisted up to 15 min. Similar results were obtained for the theophylline-induced slow AP in 2 guinea pig papillary muscles. Control injections of AMP, acetate, of Cl^- were ineffective. Thus, cAMP injections mimic the effect of catecholamines and some other positive inotropic agents. The results support the hypothesis that the phosphorylated slow channel is the form available for voltage activation. (NIH grant HL-18711)

SIMULATED GRAVITATIONAL FIELD INFLUENCES ON AGEING PROCESS. Alexandru Vrăbiescu. National Institute of Gerontology. Bucharest, 78178, Romania.

Rats were submitted whole life on 2 or 5g centrifugation. They became earlier adults and premature ageds; their life span was consequently shorter. The pathological changes were: arthritis, decalcification, scleroatrophy of the skin, an invasion of connective tissue in the somatic muscles as in the heart muscle, an intensive interstitial sclerogenic reaction, a coronarian arterio-sclerosis, an increased mucopolysaccharidic content of the aortic wall. The collagen of the tail fibers showed a much more advanced biological age. Histogical changes occured too, similar with those found in stress, at the level of pituitary and adrenal glands. At the heart level changes pathognomonic for hemodynamic disorders and insufficiency occured too; the cell divisions in the hematopoetical marrow were inhibited. Our data show an increase of the ontogenic speed in direct relation with the strength of the simulated gravity. The author discusses about the role of earth gravity as factor interferring in the ageing process.

CARDIOVASCULAR RESPONSES OF WOMEN DURING PROLONGED WORK AT ALTITUDE. J.A. Wagner, D.S. Miles*, and S.M. Horvath. Inst. Environ. Stress, U. of Cal., Santa Barbara, 93106.

Five women (23-32 yrs) performed bicycle work in a hypobaric chamber for 2 h at 41% of their respective altitude maximal oxygen uptake at 758, 586, 523, and 446 Torr barometric pressures (P_B). Oxygen uptake remained at a constant level for 2 h. Mean ± SE cardiac output ($\dot{Q}_C$ = 8.5 ± 1.4 L/min), stroke volume (Q_S = 75 ± 13 ml), and heart rate (f_C = 115 ± 6 beats/min) were similar at all altitudes, generally increasing with time, but time-related changes differed with altitude. Blood pressures were not affected by altitude or duration of work. Total peripheral resistance decreased from 1130 to 920 dynes·sec/cm^5 after 1 h at 758 Torr P_B but was constant throughout work at 586 (890 dynes·sec/cm^5), 523 and 446 Torr (830 dynes·sec/cm^5). Between 60-120 min at 446 Torr P_B mean f_C declined and Q_S increased, while $\dot{Q}_C$ continued to increase at a slower rate than at lower altitudes. Blood epinephrine levels, measured only at 758 and 446 Torr P_B, were not affected by work at 758 Torr, but a threefold increase occurred at 446 Torr. Blood norepinephrine levels increased with work but not altitude and may have been responsible for the time-related increases in $\dot{Q}_C$, f_C, and Q_S.

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ALTERATIONS IN HEMOGLOBIN OXYGEN AFFINITY FOLLOWING THE ADMINISTRATION OF d-ALPHA TOCOPHEROL ACETATE (VITAMIN E) IN DOGS. John H. von Colditz*, Rochelle L. von Colditz*, S. Bert Litwin*, (SPON: J.P. Kampine). Department of Thoracic and Cardiovascular Surgery of the Medical College of Wisconsin at Milwaukee Children's Hospital, Milwaukee, WI 53233

Eight dogs (17-21 kg) were given Vitamin E by mouth for 21 days, each receiving daily doses for 7 days of 200, 800, and 2000 IU respectively. Venous blood samples were drawn prior to treatment, 12 hours, 1-7, 14 and 21 days after starting treatment and weekly for 5 weeks after stopping the drug. Hemoglobin (Hgb), hematocrit, P_{50} (P_{O_2} at 50% saturation), 2,3-diphosphoglycerate (2,3-DPG), erythrocyte intracellular pH (pH_{ic}) and venous P_{O_2}, P_{CO_2} and pH were determined. By day 4 after starting Vitamin E, P_{50} increased from 29.8±.57 ($\bar{X}$±SE) to 33.88±.86$^+$ mmHg. It then fell to 30.45±.59$^+$ mmHg on day 7. On day 14 (800 IU) and day 21 (2000 IU) P_{50} increased to 31.43±35$^+$ and 31.76±43$^+$ mmHg, respectively. 2,3-DPG was significantly increased on days 4, 7, 14, and 21 from control of 15.1±.8 umol/g Hgb to a maximum of 20.3±.7$^+$ umol/g Hgb on day 21. pH_{ic} differed significantly from control only on day 21 (7.25±.02 v 7.14±.03$^+$). All other parameters remained unchanged. During five weeks after stopping the drug, 2,3-DPG and pH_{ic} returned to control values. The results suggest Vitamin E causes reversible changes in P_{50} which may be mediated by changes in 2,3-DPG and H^+. This may be useful in the treatment of many disease states which include deficiencies of oxygen transport. (+ = p<.05).

CYSTEINE TRANSPORT BY THE BLOOD-BRAIN BARRIER. Lester A. Wade* and Helen M. Brady* (SPON: J.C. Pisano). Tulane Univ. Med. Sch., New Orleans, La. 70112

Cysteine uptake by brain capillaries was studied using Oldendorf's carotid injection technique, in which a labeled compound and tritiated water were simultaneously injected into the right carotid artery of a rat, the rat decapitated at 5 or 15 seconds, and the brain prepared for liquid scintillation counting. Thin layer chromatography studies indicated that reduced DL-dithiothreitol (DTT) (.25 - 10mM) converts cystine (the oxidized form of the amino acid) to cysteine (the reduced form), although over long periods of time, cysteine was not stable even with the higher DTT concentrations. The oxidized form of DTT, which may be formed in the reaction, had no effect on the uptake of cysteine (.01mM). Neither oxidized DTT (2mM) nor reduced DTT (10mM) had any effect on the uptake of ^{14}C-cycloleucine (.025mM), a neutral amino acid transported primarily by the L system. In the absence of DTT, ^{35}S-cystine (25uM to .1uM) did not show any significant uptake using the carotid injection technique. However, in the presence of DTT, ^{35}S-cysteine (.01mM) did show uptake which was partially inhibited by cycloleucine (4mM), and by L-alanine (4mM), a neutral amino acid transported primarily by the A and the ASC systems. Cysteine appears to be taken up by one or more neutral amino acid transport systems. (Supported in part by USPHS, NIH Grant NS 13914)

INFLUENCE OF MIXED VENOUS P_{O_2} ON RATE OF DIFFUSION OF O_2 INTO THE PULMONARY CAPILLARY. P.D. Wagner. Dept. of Medicine, Univ. of California, San Diego, La Jolla, CA 92093

Conventional teaching concerning diffusion limitation of pulmonary O_2 exchange is that alveolar P_{O_2} ($P_{A_{O_2}}$) is the most important factor to consider, but recent analyses suggest that $P_{A_{O_2}}$ is important only insofar as it determines the slope of the O_2 dissociation curve. If this slope is the critical factor, mixed venous P_{O_2} ($P_{\bar{v}_{O_2}}$) should also be important. This notion was examined in theoretical calculations of oxygenation along the capillary in a homogeneous lung model of normal diffusing capacity. For $P_{A_{O_2}}$ = 100 torr, halftime of rise of P_{O_2} between $P_{\bar{v}_{O_2}}$ and $P_{A_{O_2}}$ ($T_{½}$) increased from 0.09 sec ($P_{\bar{v}_{O_2}}$ = 50) to 0.32 sec ($P_{\bar{v}_{O_2}}$ = 10), while for $P_{A_{O_2}}$ = 60, $T_{½}$ increased from 0.18 sec ($P_{\bar{v}_{O_2}}$ = 50) to 0.43 sec ($P_{\bar{v}_{O_2}}$ = 10). At $P_{A_{O_2}}$ = 60, diffusion equilibration after 0.75 seconds was virtually complete if $P_{\bar{v}_{O_2}}$ >40 torr, but was only 80% complete for $P_{\bar{v}_{O_2}}$ = 10. These calculations show that at any given $P_{A_{O_2}}$, $P_{\bar{v}_{O_2}}$ has considerable influence on the rate of diffusion equilibration of O_2. Thus, situations in which $P_{\bar{v}_{O_2}}$ is low (for example, when cardiac output is low in relation to O_2 uptake) are associated with considerably increased vulnerability of O_2 exchange to diffusion limitation. (Supported by NIH HL 00111 and HL 17731.)

LONG-LASTING INHIBITION OF RESPIRATION FOLLOWING CALF MUSCLE STIMULATION. T. G. Waldrop*, D. E. Millhorn* and F. L. Eldridge. Univ. of North Carolina, Chapel Hill, NC 27514

We have reported a serotoninergic brain-stem mechanism, activated by carotid sinus nerve (CSN) or carotid body stimulation, which causes a prolonged (hours) increase in respiratory output (RO) (Fed. Proc. 38(3):1229, 1979). The present study was done to determine if neural input from peripheral muscles did the same. Anesthetized, paralyzed cats whose vagus and carotid sinus nerves had been cut were used; RO was quantified from peak integrated phrenic activity. Body temperature and PET_{CO_2} were kept constant by servocontrollers. Bilateral calf muscle stretching caused RO to increase and led to a respiratory afterdischarge; both effects were similar to those of CSN stimulation. Unlike CSN stimulation, however, calf muscle stretching did not result in the prolonged increase in RO. In fact, RO was decreased for up to thirty minutes following muscle stimulation. This prolonged post-stimulation inhibition was not prevented by prior treatment with antagonists of serotonin, dopamine or endorphin. We conclude that stimulation of peripheral muscle receptors does not activate the endogenous serotoninergic mechanism which facilitates respiration. Instead, calf muscle stretching seems to activate a long-lasting inhibition of respiration; the mechanism is not yet identified. (Supported by USPHS Grants HL-17689, NS-11132 and Pulmonary Training Grant HL-07106)

EFFECTS OF HIGH-G ON VENTILATION/PERFUSION IN THE DOMESTIC FOWL. Sue C. Walgenbach*, R. E. Burger*, and A. H. Smith. Animal Physiology, University of California, Davis, CA 95616.

Exposure of man and other mammals to high $+G_z$ forces causes pulmonary distortion and results in ventilation/perfusion ($\dot{V}/\dot{Q}$) inequalities. Respiratory anatomy of birds, however, is fundamentally different from that in mammals; the bird lung is relatively small and inelastic, and ventilation is not a function of lung compliance. The purpose of this experiment was to determine if $\dot{V}/\dot{Q}$ inequalities exist in the bird during exposure to high sustained G. Birds were exposed to 5, 6, 8 and $10+G_z$ of duration ranging from 1 to 5 minutes. Just prior to termination of acceleration, arterial blood samples were drawn via a carotid artery catheter. These samples were analyzed for P_aO_2 and P_aCO_2 and compared to Earth-gravity controls. At 5, 6 and 8 G, P_aO_2 did not fall below control values. At 10 G, hemoglobin remained at least 80% saturated. P_aCO_2 did not increase during acceleration exposures of 5, 6 or 8 G. A slight increase did occur in two birds at 10 G. This evidence tends to indicate that no significant $\dot{V}/\dot{Q}$ abnormalities occur in the bird lung during a 1 to 5 minute exposure to 5, 6, 8 or 10 G. Also, this data supports earlier work from this laboratory, indicating that ventilation does not influence tolerance of birds to high-G exposures. (Supported by AFOSR 77-3430)

DIURESIS DURING ACUTE HYPOXIA IN THE CONSCIOUS DOG. Benjimen R. Walker* and Robert F. Grover. Cardiovascular Pulmonary Research Laboratory, University of Colorado Medical Center, Denver, Colorado 80262

The renal response to acute hypoxia in the conscious dog is not clear. We therefore monitored the effect of 40 minutes of hypocapnic hypoxia (PaO_2=43±2 (SEM) mmHg; $PaCO_2$=23±1 mmHg) on renal function in 5 conscious dogs. Urine flow increased by 21±5% ($p<.01$) upon hypoxic exposure. This diuresis was accompanied by an increase in renal plasma flow of 10±3% ($p<.05$) and a similar (9±4%) increase in glomerular filtration rate. Since arterial blood pressure was elevated, renal vascular resistance was unchanged. Total solute excretion rate was raised by 22±3% ($p<.01$) and the C_{osm}/C_{in} ratio was also elevated (13±8%, $p<.025$), suggesting that tubular solute transport may be partially inhibited. Since prostaglandins are known to have effects on both renal hemodynamics and tubular function, urinary PGE_2 was assayed in 4 experiments in 3 dogs. PGE_2 excretion rate was seen to increase coincident with the diuresis. In a pilot experiment, meclofenamate (2 mg/kg iv with 2 mg/kg/hr infusion) blocked both the diuresis and the renal hemodynamic alterations. It can thus be concluded that acute hypoxia induces a diuresis in the conscious dog. This diuresis is attributable to a combination of increased filtration and reduced tubular solute transport. These changes appear to be at least in part prostaglandin mediated.

OVARIAN SEROTONIN AND MONOAMINE OXIDASE LEVELS IN RELATION TO OVULATION. Pamela Y. Walker* and Karam F. A. Soliman, School of Pharmacy, Florida A & M University, Tallahassee, FL 32307.

In the mature cyclic female rat, analysis for ovarian serotonin (5-HT) reveals comparatively high levels. Fluctuation of serotonin content was observed during the ovulation cycle. Peak for serotonin was observed during estrus. Analysis for monoamine oxidase (MAO) levels also revealed peak levels of the enzyme during estrus. In immature females treated with PMSG there was no serotonin detected in the ovaries using this procedure. When MAO activities were determined in immature, PMSG treated animals, MAO levels were low and the levels declined up to 48 h after PMS injection. On the other hand, 9 ovaries from patients admitted to the hospital for various gynecological problems were analyzed for 5-HT. Data obtained indicated that patient with follicular cysts has higher levels of 5-HT than ovaries with corpora albicana. Ovaries with copora lutea were found to contain the least amount of 5-HT. Results from this experiment indicated that 5-HT might be involved in the ovulation process of the mature ovary as well as cyst formation. (Supported by a grant from NIH, #RR8111)

MEASUREMENT OF AORTIC PRESSURE-DIAMETER RELATIONSHIPS IN CONSCIOUS HYPERTENSIVE PIGS. D.O. Walterhouse*, D.M. Cohen, O.S. Randall*, and D.F. Bohr. Univ. of Mich., Med. Sch., Ann Arbor, MI 48109.

Piezoelectric crystals were surgically embedded in the wall of the descending thoracic aorta to determine aortic diameter (AD) and aortic pressure (AP) was monitored via an indwelling catheter. A distensibility index [DI=(pulse diameter)/(pulse pressure x diastolic diameter)] was calculated. AD and DI were determined in three conscious pigs before and at intervals after the subcutaneous implantation of the mineralocorticoid, DOCA and in one silastic-implanted control pig. AD increased with growth in both control and in DOCA hypertensive pigs. In hypertensive pigs, the increase in AP produced a further increase in AD. Whereas DI did not change in the control pig (pre vs post-implant), DI decreased in DOCA hypertensive pigs. However, when phenylephrine was infused to elevate AP in pre-DOCA and DOCA hypertensive pigs, aortas from hypertensive pigs were more distensible than those from pre-DOCA pigs at any given AP. When placed on a lowered sodium diet, AP fell to normotensive levels in 2 of 3 hypertensive pigs and DI returned toward pre-implant values. It is concluded that the mechanical properties of aortas from conscious pigs change as hypertension develops and that these changes are reversible. This study was supported by a grant from the NHLBI, Grant #HL-18575.

LUNG GAS STORES AND THE KINETICS OF GAS EXCHANGE DURING EXERCISE. S.A. Ward, J.A. Davis*, M.L. Weissman, K. Wasserman and B.J. Whipp. Div. Respiratory Physiology & Medicine, Harbor-UCLA Medical Center, Torrance, CA 90509 and Dept. Anesthesiology, UCLA, Los Angeles, CA 90024.

The extent to which changes in lung gas stores dissociate gas exchange at the mouth from that obtaining at the alveolar-capillary membrane during the non-steady-state of moderate cycle ergometer exercise was determined in 4 air-breathing adults. Accordingly, the influence of the temporal behavior of functional residual capacity (FRC) on O_2-uptake ($\dot{V}O_2$) and CO_2-output ($\dot{V}CO_2$) was assessed. Subjects performed 6 end-inspiratory (I) and 6 end-expiratory (E) step-transitions to 100 watts (4 min. duration) from both prior rest (R) and unloaded pedaling(U). Air flow, PO_2 and PCO_2 signals underwent A-to-D conversion and were processed by a digital computer to yield breath-by-breath values for $\dot{V}O_2$, $\dot{V}CO_2$, and the change in FRC (ΔFRC, the difference between inspiratory and expiratory tidal volumes). The fall in FRC (0.1-0.8L) which occurred during the first 10 sec. of exercise was consistent for each subject; this effect being greater for I-transitions (cf.E) and for R-transitions (cf.U). Thereafter, FRC changed only at a slow rate, increasing in some and decreasing in other subjects. Consequently, the effects of FRC-induced changes in lung gas stores on the kinetics of gas exchange at the mouth were appreciable only during the first few breaths of exercise, resulting in the underestimation of $\dot{V}O_2$ and the overestimation of $\dot{V}CO_2$. (Supported by NIH grant HL11907).

EFFECTS OF HEPES AND BICARBONATE BUFFER ON REACTIVITY OF ARTERIAL SMOOTH MUSCLE. William H. Waugh. Depts. of Med. and Physiol., East Carolina Univ. Sch. Med., Greenville, NC 27834

HEPES buffer in place of HCO_3 buffer is reported to depress contractile responses in rat aorta and portal vein (Altura et al. Fed. Proc. 38, 1979). Yet, HEPES buffer mixed with HCO_3 buffer did not depress rabbit ear arterial responses to adrenergic nerve stimulation (Gillespie & McKnight J. Physiol. 259, 1976). Paired rings of rabbit femoral artery were incubated at 37°C in solution containing Na 141, K 4.0, Ca 1.5, Mg 0.5, PO_4 1.0, SO_4 0.5, glucose 7.2, creatine 0.2, $CaNa_2EDTA$ 0.026, and neomycin 0.055 (all in mM) plus either 16 mM HCO_3 (Cl 131) with 5% CO_2-95% O_2 or 10 mM HEPES (Cl 141) with 100% O_2 regassing. Using 1.0-ml volumes, bath pH's remained within 0.02-0.03 units of initial pH of 7.36±0.02 at 37°C during cumulative studies over 55 min with µl additions of l-norepinephrine (norepi) in 154 mM NaCl. Low dose (10 nM norepi) responses were 15.9±4.4% of maximal isometric tension responses (10 µM norepi) of 9.03±0.64 gf in HCO_3 buffer and 17.0±5.3% of the maximal responses of 9.42±0.57 gf (mean ± SEM, n=8) in HEPES buffer solution. Respective ED_{50} values were 125±42 nM & 89±24 nM norepi (P>0.2). Mean dose-response curves did not differ significantly. Thus, 10 mM HEPES buffer substituted for a $NaHCO_3$/5% CO_2 buffer system at the same pH did not depress arterial reactivity. Neither HCO_3 anion nor a $NaHCO_3/H_2CO_3$ buffer appears essential for full sensitivity & contractility of rabbit femoral artery muscle in vitro during cumulative dose-response studies with norepi.

EFFECT OF POTASSIUM ON NERVE ENDINGS AND EFFECTOR CELLS IN ISOLATED VASCULAR SMOOTH MUSCLE. R.C. Webb and P.M. Vanhoutte. Universitaire Instelling Antwerpen, Wilrijk, Belgium.

Experiments were performed to determine the effects of elevated potassium concentration on isometric contractions of isolated rat tail artery strips in respons! to exogenous norepinephrine and electrical stimulation. Contractile responses to norepinephrine were determined in strips denervated with 6-hydroxydopamine. The concentration of potassium in the bathing solution was altered by equimolar substitution of NaCl with KCl. Contractile responses to low concentrations of norepinephrine (3×10^{-9}M) and low frequency electrical stimulation (0.5 Hz) were potentiated when the concentration of potassium was increased from 5.9 to 41.2 mM. Further increases in potassium concentration caused a small reduction in the potentiation to norepinephrine and caused an inhibition of responses to 0.5 Hz electrical stimulation. Contractile responses to high concentrations of norepinephrine (3×10^{-7}M) were progressively decreased when the potassium concentration was elevated. Contractions induced by high frequency electrical stimulation (16 Hz) were unaltered by increasing the potassium concentration to 41.2 mM. At higher concentrations of potassium, the contractions in response to 16 Hz electrical stimulation were inhibited. These results suggest that increases in the potassium concentration of the extracellular fluid alter the functional properties of both effector cells and adrenergic nerve endings in the blood vessel wall.

AN EXPERIMENTAL MODEL OF BIOT PERIODIC BREATHING IN THE CAT. C.L. Webber, Jr. and D.F. Speck*. Department of Physiology, Loyola University of Chicago, Maywood, Illinois 60153

The present experiments represent a follow-up on the fortuitous observation in another study that brainstem lesion placement in anesthetized cats often induced a periodic breathing pattern of the Biot type (cluster breathing). Cats were anesthetized with pentobarbital (PB, 30 mg/kg,i.v.) and were instrumented for the recording of several respiratory and cardiovascular parameters. Experiments were designed to study the spontaneous breathing patterns before and after pneumotaxic center lesion placement. Biot breathing was induced in about half of all attempts. Two factors turned out to be crucial for success. First, PB levels exceeding 35 mg/kg decreased the probability of Biot to near zero. Biot breathing could be favored in some of these preparations, however, by continuous central vagal stimulation. Second, pneumotaxic center lesion placements had to be accurate. Lesions falling outside of the critical area, either by design or default, also encouraged low probabilities for Biot breathing. In spontaneous Biot cats, the periodic breathing could be reversed by hypoxic and potentiated by hyperoxic gas inhalations. In addition, computer analysis demonstrated that as compared to control, expiratory duration became distinctly bimodal; inspiratory duration remained more stable. These results are significant in that a new model may now be available for the detailed examination of the control of expiratory timing. (Supported by NIH Grant HL08682)

EFFECTS OF AIRWAY OPENING AND CLOSING ON THE SHAPE OF LUNG PRESSURE-VOLUME CURVES. K.C. Weber and D.C. Frazer*. ALOSH, NIOSH, CDC, DHEW, and Dept. of Physiology and Biophysics, WVU, Morgantown, West Virginia 26506.

Excised rat lungs were inflated-deflated in an air-filled plethysmograph for 2 cycles at an average rate of 3.82cc/min. In cycle 2 a sinusoidal volume perturbation (4cc, 0.5Hz) was added to the average increase in lung volume during inflation. The sinusoidal volume variations caused small pressure-volume (PL-VL) loops to be formed within a quasi-static like pressure-volume envelope. The maximum and minimum pressures during each loop were designated PL(max) and PL(min) respectively. As the lung was slowly inflated PL(max) and PL(min) increased. When PL(min) increased above 0.5cm H_2O during a given sinusoidal cycle, the shape of the PL-VL loops changed in the following manner: 1) the characteristic knee in each loop gradually disappeared, 2) there was an initial reduction in PL(max) and, 3) the amount of hysteresis exhibited by each small loop was greatly reduced. The transition zone in which the PL-VL loops were affected occurred when PL(min) was between 0.5 and 2.5cm H_2O. Since this zone corresponds with the same range of pressures at which the airways close in the rat (Resp. Physiol. 36:121-129, 1979), it appears likely that the closing and reopening of airways is primarily responsible for many of the predominant characteristics normally associated with pressure volume curves. (Supported in part by DOE Contract No. EY-77-C-21-8087.)

ELECTROLYTE PERMEABILITY OF THE FROG PERINEURIUM. A. Weerasuriya*, S.I. Rapoport and R.E. Taylor, NINCDS, NIH, Bethesda, Md. 20205; NIA, NIH, Baltimore, Md. 21224.

The perineurial sheath of the frog sciatic nerve was removed as a cylinder and mounted in Ringer's at room temperature, directly or inside-out on cannulae that allowed continuous perfusion for measurement of transperineurial tracer flux (Weerasuriya et al., Brain Res., in press). Na permeability equalled 1.68×10^{-6} cm/sec, when flux was measured in either direction across the perineurium. Na and K fluxes in either direction were unaffected by ouabain, amiloride or by Ringer in which Na was substituted by choline. Simultaneous measurement of transperineurial fluxes of Na, K and Cl showed that the Cl/K permeability ratio (1:1.00) did not differ significantly (P>0.05) from the ratio of limiting conductances in free solution (1:0.95), but that the Na/K permeability ratio (1:1.67) differed significantly (P<0.01) from the limiting conductance ratio in free solution (1:1.46). Bathing the perineurium in hypertonic Ringer's increased the permeability coefficients of all three ions but did not alter the permeability ratios among the ions. The results show that the perineurium is a diffusion barrier to ions with low permeability coefficients of the order found in epithelia with tight junctions. Furthermore, Na and K fluxes probably are passive and follow, as does ^{14}C-sucrose flux, a paracellular as opposed to a transcellular pathway. This pathway appears to be more selective to K than to Na, and equally selective to K and Cl.

ENHANCED RESPONSE TO NEAR THRESHOLD β-ADRENERGIC STIMULATION IN HYPERTHYROID CARDIAC MUSCLE: ELECTRO-MECHANICAL CORRELATES. Jeanne Y. Wei*, Harold A. Spurgeon, and Edward G. Lakatta. Gerontology Research Center, NIA, and Johns Hopkins Medical Institutions, Baltimore, MD 21224.

It has been previously shown that contractile response to near threshold concentrations of isoproterenol (I) is increased in ventricular muscle from hyperthyroid (H) vs. euthyroid (E) rats. To examine whether this may be mediated by increased transsarcolemmal calcium influx, we measured transmembrane action potentials (TMP) and contractile response to I (5×10^{-9} M) in right ventricular papillary muscles from H (thyroxine 6.4 mg/kg/day i.m. X7 days) and E rats. The muscles, at L_{max}, were superfused with Krebs bicarbonate at 29°. Baseline values: maximal rate of tension development (dT/dt): H=33.5±5.8 g/mm^2, E= 14.4±2.7 g/mm^2 (P<.01); resting TMP (RMP): H= -71.3±1.4 mV, E= -69.8±1.5mV; integrated area above -40mV (A-40): H= 585.6±78.6 mV-ms, E= 545.1±55.6 mV-ms; Time to 75% repolarization (T75): H= 46.5±4.4 ms, E= 35.9±3.5 ms. Responses to I, as % of baseline ± SEM, were:

	N	RMP	A-40	T75	dT/dt
H	7	1.9±1.1	29.8±7.2	21.1±7.4	46.7±18.4
E	8	-0.1±0.4	10.8±2.1	4.2±2.2	3.2±3.8
		NS	<.05	<.05	<.05

These findings suggest in H relative to E, a greater increase in Ca^{++} influx, reflected by A-40 and T75, is induced by I and may account for greater contractile responses observed in H.

EFFECTS OF ALTITUDE ACCLIMATION ON TEMPERATURE REGULATION AND O_2 TRANSPORT AT HIGH ALTITUDE IN PIGEONS. Y. Weinstein*, D. V. Gonzales*, and Marvin H. Bernstein. New Mexico State University, Las Cruces, New Mexico 88001.

To provide information about acclimation effects on responses to high altitude in birds, we exposed pigeons (Columba livia, mean mass 0.38 kg) at rest to simulated altitudes between 1.2 and 9 km above sea level and to air temperatures (T_A) of 6 and 23°C in a darkened hypobaric chamber. Group I (controls) had been acclimated to 1.2 km and Group II to 7 km for at least 4 weeks at 23°C, 12L:12D photoperiod. At 1.2 km, steady-state colonic temperature (T_C) averaged 40-41°C in both groups. T_C decreased slightly with altitude in both groups, but fell below normothermic levels only at 6°C and 9 km in controls. Oxygen uptake ($\dot{V}O_2$) did not change with altitude in Group I but doubled between 1.2 and 9 km in Group II at both T_A. $\dot{V}O_2$ in Group II was higher than that of Group I at 5 km and above. At 1.2 km, heart rate (f_h) was 140 min^{-1} in Group I and 225 min^{-1} in Group II. Above 5 km, f_h in Group I increased until equal to that of Group II at corresponding T_A. Above 7 km O_2 pulse increased in Group II but decreased in Group I. These results suggest an increase in stroke volume, O_2 content of blood, or both in GroupII and the opposite in Group I at high altitudes. With the increase in f_h, this represents an increase in O_2 transport with altitude. (Supportedby NSF Grant PCM78-08130 and NIH Grant GM07667.)

THE EFFECT OF SYMPATHETIC NERVE STIMULATION ON OVARIAN PROGESTERONE LEVELS. G.K. Weiss, W. Dail* and A. Ratner. Univ of New Mexico, School of Medicine, Albuquerque, N.M. 87131

The rat ovary is innervated by sympathetic nerves through two separate pathways. One pathway, the ovarian plexus, accompanies the ovarian artery; the second is a newly described nerve which reaches the ovary by its suspensory ligament (superior ovarian nerve). Previous in vitro experiments and microscopic observations suggest that sympathetic nerves may have a direct control of ovarian steroidogenesis. An in vivo study was done to determine if direct stimulation of sympathetic fibers alters ovarian progesterone levels. Rats in diestrus were anesthetized and either the left ovarian plexus nerve (OPN) or the left superior ovarian nerve (SON) were stimulated for 30 min using bipolar electrodes (alternating 30 sec on and 30 sec off). Progesterone levels in the ovary were determined using a radioimmunoassay with the right ovary serving as a non-stimulated control Stimulation to the OPN in 10 rats produced an increase of 94% over controls (± 32 SEM). Prior administration of an alpha adrenergic antagonist (phentolamine) blocked this increase. Stimulation of the SON in 12 rats produced a decrease in progesterone (31% ± 6 SEM) which was blocked with a prior administration of phentolamine. Other experiments were done to test if these changes occurred in response to changes in ovarian blood flow. The results are consistent with the hypothesis that sympathetic nerves exert a direct control of ovarian steroid production. Supported by NIH Grant RO1-HD09475

CARDIODYNAMIC GAS EXCHANGE AT THE START OF EXERCISE. M.L. Weissman, K. Wasserman, N. Lamarra,* J.A. Davis* and B.J. Whipp. Harbor-UCLA Medical Center, Torrance, CA. 90509

The rapid increase in cardiac output following exercise onset would lower the $\dot{V}_A/\dot{Q}$ ratio of the lungs if ventilation did not increase concomitantly. To determine the effect of such a reduced $\dot{V}_A/\dot{Q}$ on pulmonary gas exchange following the transition from rest to constant-load exercise, subjects exercised for 30-60 sec. on a Lanooy ergometer at various fixed work rates (50-300 watts), while ventilation was maintained constant at the resting level. On-line measurements of inspired and expired airflows (pneumotachography) and the PCO_2 and PO_2 of respired gas (mass spectrometry) were analyzed by computer to yield breath-by-breath plots of expired ventilation ($\dot{V}_E$), CO_2 output ($\dot{V}CO_2$) and O_2 uptake ($\dot{V}O_2$), end-tidal PCO_2 ($P_{ET}CO_2$) and PO_2 ($P_{ET}O_2$) and the gas exchange ratio (R). $P_{ET}CO_2$ was increased in the first breath of exercise and thereafter continued to rise progressively, paralleling a similar time course of heart rate increase. $P_{ET}O_2$ and R fell progressively during the exercise, beginning with the first breath. These changes were typically greater in magnitude the higher the work rate. These data indicate that the increased cardiac output at exercise onset can produce significant changes in pulmonary blood composition beginning with the first breath of exercise. Thus, a transient humoral error signal generated at the lungs, caused by the increase in cardiac output, could stimulate known arterial chemoreceptors before blood from the working muscles has reached them.

FLUID TRANSPORT ACROSS THE CANINE TRACHEAL EPITHELIUM. M.J. Welsh*, J.H. Widdicombe, and J.A. Nadel. C.V.R.I., UCSF, San Francisco, California 94143

Active ion transport by the dog's tracheal epithelium is believed to underlie respiratory tract fluid production. Therefore, it is important to correlate changes in active ion transport with changes in volume flow. We have measured the rate of fluid movement (J_v) by an electrical method. Six tissues were mounted in modified Ussing chambers. A capacitance probe measured the level of fluid in a teflon tube on the submucosal side of the chamber. Changes in the volume of the submucosal chamber produced changes in the fluid level in the tube which is measured as changes in capacitance. The average baseline J_V was 44 ± 23 $nl \cdot min^{-1}$ (mean ± SE). In only three of the tissues was the resting J_V significantly greater than zero. After stimulation with aminophylline (a drug which is known to stimulate Cl secretion under short-circuit conditions), J_V increased to a mean of 137 ± 29 $nl \cdot min^{-1}$ ($p<0.001$). The hydraulic conductivity (measured by increasing osmolarity by 57 ± 6 mOsm with sucrose) was 9.2 ± 0.8 x 10^{-5} $cm \cdot sec^{-1} \cdot Osm^{-1}$. Thus, fluid secretion into the airway is minimal in the control state. The increase in fluid secretion with aminophylline is consistent with the increase in Cl secretion which this drug produces under short-circuit conditions. (Supported in part by NHLBI Grants HL-07159 and HL-06285)

EVALUATION OF THE NORMATIVE FAR FIELD AVERAGED AUDITORY EVOKED RESPONSES IN THE CANINE. S.J. Whidden* and R.W.Redding (SPON:D.D. Gilboe) . Univ. of Wisconsin,Madison, WI 53706

Thirty normal adult dog's short-latency averaged monaural auditory evoked potentials were recorded in response to click stimulation.These early far field acoustic responses were analyzed by a computer program ,statistically to determine the normative values for the wave number,latency,amplitude and magnitude (vertical local). The electrode array was from the vertex of the skull to the proximal caudal convex of the pinna.The results indicate that the mean latency in milliseconds of each potential were: Wave I, 1.8±.08; Wave II, 2.69±.12; Wave III, 3.49±.15; Wave IV, 4.92±.11; Wave V, 5.8±.11; and Wave VI, 7.26±.39 . The amplitude mean(from the trough to the subsequent positive peak) in microvolts for each evoked potential were: Wave I, .661±.15; Wave II,.44±.13 Wave III, .28±.08; Wave IV,.22±.12; Wave V, .36±.24 and Wave VI, .39±.17. The mean magnitude in millimeters for each evoked response was : Wave I, 23.±4.; Wave II, 29.±3.7; Wave III, 36.±4.; Wave IV, 9.±10.; Wave V,10.±5.; and Wave V I , 15.± 5. . All data was treated by analysis of variance and plotted by a Versatec Electrostatic Plotter. The results suggest that the amplitude latency and magnitude did vary between subjects,and the ears of the subjects, but the wave form was consistent from run to run in the same subject.

The Effect of G_z Acceleration on Pulmonary Perfusion in the Miniature Swine. James E. Whinnery* and M. Harold Laughlin. USAFSAM, Brooks AFB, TX 78235

The effect of increased G_z acceleration on the distribution of pulmonary blood flow in 4 conscious miniature swine was measured with a gamma scintillation camera using 99mTc labeled human macro-aggregated albumin and human albumin microspheres. The radiolabeled albumin was injected by a remote-controlled injection system via a chronically implanted silastic catheter placed in the cranial vena cava such that the first capillary bed encountered was that of the pulmonary system. Multiple studies with G_z levels from $-4G_z$ to $+8G_z$ were performed in the same animal allowing accurate comparison of the effects of acceleration stress on the distribution of pulmonary blood flow. The animals were fitted with abdominal anti-G suits and instinctively performed straining maneuvers both of which simulate the environment of pilots flying advanced fighter aircraft during the increased stress of aerial combat maneuvering. Marked shifts in pulmonary flow were observed with both $+G_z$ and $-G_z$ acceleration. Compared to baseline conditions ($0G_z$, $-1G_x$) the perfused lung area seen on anterior scans decreased by 5%, 18%, 21% and 27% in going to $+2G_z$, $+4G_z$, $+6G_z$ and $+8G_z$ respectively, and increased by 4%, 17% and 41% in going to $-1G_z$, $-2G_z$ and $-4G_z$ respectively. The comparison of the relative flows from zero G_z to $+8G_z$ revealed a decrease in flow not only in the cranial areas bilaterally but also a decrease in flow in the most dependent caudal areas bilaterally. The changes in perfusion distribution in the lungs are a major determinant in the blood oxygen desaturation that occurs during $+G_z$ acceleration.

BLOOD FLOW OF MASTICATORY MUSCLES OF RHESUS MONKEYS. T. P. White, S. Pachtman*, J.F. Villanacci*, J.A. Faulkner and J.A. McNamara*. Depts. of Physical Education, Physiology and Anatomy, University of Michigan, Ann Arbor, MI 48109

Skeletal muscle blood flow (MBF) of Rhesus monkeys (n=7) were measured by a radioactive microsphere technique. Measurements were made at rest and during direct twitch stimulation (2, 4, 6, 8 or 10Hz) of the masseter (MST), temporalis (TMP), and extensor digitorum longus (EDL) muscles. When MBFs of the MST and TMP were measured a 7mm bite-opening appliance was placed at the first molar to maintain constant muscle fiber length during contractions. The EDL was attached to a force transducer. Resting MBFs ($\bar{X}\pm$SEM) were 7.2±1.9, 7.3±2.1, and 3.5±1.6 ml·100g^{-1}·min^{-1} for the MST, TMP and EDL muscles, respectively. For the MST a maximum MBF of 163.2± 25.1 ml·100g^{-1}·min^{-1} was reached at 8Hz. The maximum MBF of the TMP, obtained at 8Hz was 79% of the maximum MST value ($p < .05$). Within a given muscle, there was considerable variability in regional MBF during contractions. The high maximum MBF in masticatory muscles is contrasted with a maximum MBF of 16.0±2.1 ml·100g^{-1}·min^{-1} for the EDL. The value for the EDL is approximately 20% of the limb MBF of other mammalian species. The monkeys were in captivity for several years, and the differences in maximum MBF might result from a relative disuse of the limb muscles compared with the muscles of mastication. (Supported by grants DE04227, DE05232, and contract DE52478 from the National Institutes of Health.)

BIOCHEMICAL ADAPTATIONS TO COLD IN THE WHITE-FOOTED DEER MOUSE (PEROMYSCUS LEUCOPUS). Steven J. Wickler* (SPON: W.R. DAWSON). The University of Michigan, Ann Arbor, MI 48109

The maximal aerobic capacity for thermogenesis ($\dot{V}O_2max$) in freshly captured Peromyscus increases from an average value in summer (June-Aug.) of 11.5 cc O_2(g·hr)$^{-1}$ to an average winter (Dec.-March) value of 19.5. One mechanism for increased heat production is to move substrates through oxidative pathways more rapidly, possibly by increasing activity of oxidative enzymes. Samples of the two, primary thermogenic tissues of Peromyscus, skeletal muscle and brown adipose tissue (BAT), were taken on a seasonal basis and assayed for the maximum catalytic activity ($\dot{V}max$) of two oxidative enzymes. The $\dot{V}max$ of citrate synthase (CS), a TCA cycle enzyme, and β-hydroxy acyl CoA dehydrogenase (HOAD), an enzyme of β-oxidation, were taken to indicate flux through oxidative pathways. $\dot{V}max$ values expressed below are in μmoles substrate (g tissue·min)$^{-1}$ and were measured at 25°C. When summer vs winter comparisons are made, CS increased from 60.7 to 113.8 in muscle and from 102.5 to 284.6 in BAT. HOAD increased from 30.2 to 53.4 in muscle and from 83.2 to 1393 in BAT. Cytochrome c concentrations, determined simultaneously with CS and HOAD measurements, paralleled changes observed in CS. Cytochrome c increased in muscle from 6.6 nmoles (g)$^{-1}$ to 11.8 and from 16.3 to 52.3 in BAT. (Supported by an NSF Dissertation Grant, DEB-7822787).

A NEW TECHNIQUE FOR PRODUCING MICROANATOMICAL CASTS. Robert F. Wideman, Jr.* and Eldon J. Braun. Department of Physiol., College of Medicine, U. of Arizona, Tucson, Arizona 85724.

Microanatomical casts are used to study structure-function relationships in organs and tissues. These casts are produced by injecting an opaque compound into anatomical and vascular spaces, followed by clearing or maceration of the surrounding tissues. An injection compound now has been developed which: a) Initially has the viscosity of plasma; b) Hardens rapidly and without shrinkage; c) Is stable in water, alcohol, and organic solvents; d) Can be embedded and sectioned using routine microtechniques; and e) Utilizes inexpensive and readily obtainable materials. This compound consists of 5% gelatin (Gelatin, U.S.P., J.T. Baker Chemical Co., Phillipsburgh, N.J. 08865) to which colored pigments (Speedball Pigmented Opaque Inks, Hunt Mfg. Co., Statesville N.C. 28677; in proportions of 1ml ink per 5ml 5% gelatin) and glutaraldehyde (25%, Electron Microscopy Sciences, Box 251, Fort Washington, PA. 19034; 4-8μl per ml gelatin-ink mixture) have been added. After intravascular injection of this mixture, microvascular casts consisting of permanently fixed protein are formed as a result of the crosslinking action of glutaraldehyde upon gelatin. This process has been used to demonstrate for the first time the microanatomical architecture of the avian renal portal system. (Supported by NIH Grant HL-07249 to RFW and NSF Grant PCM 77-04958 to EJB.

INTERACTION OF ESTRADIOL AND DAYLENGTH IN THE CONTROL OF SERUM PROLACTIN IN FEMALE HAMSTERS. E. P. Widmaier* and C. S. Campbell, Northwestern University, Evanston, Il. 60201.

Changes in serum levels of prolactin (PRL) have been implicated in the induction of reproductive quiescence in male hamsters. Serum PRL is depressed in males exposed to non-stimulatory (short-day) light cycles, and this response is not altered by testosterone. In the present study, groups of intact short-day (SD) acyclic or long-day (LD) cyclic metestrous female hamsters were decapitated at one of six time-points over 24 hours. Other LD and SD-exposed hamsters were ovariectomized (OVX), given Silastic implants that were empty or were filled with 10 mm of estradiol benzoate (EB), and decapitated in the morning 4 weeks later. PRL was never detectable in serum of SD acyclic females; in cyclic metestrous females, PRL was elevated during the light phase of the 24 hour day ($p < .005$). EB dramatically enhanced PRL in both LD and SD OVX females; OVX without EB treatment resulted in low levels of PRL, but these levels were still higher in long-days than in short-days. The results suggest that in female hamsters: 1) a stimulatory photoperiod, without gonadal intervention, can maintain serum PRL at higher levels than can a non-stimulatory photoperiod; and 2) ovarian estradiol is capable of enhancing serum PRL in female hamsters. These phenomena, together with the loss of the diurnal pattern of PRL secretion in anestrous females, may play an important role in the loss of estrous cyclicity in the female Syrian hamster. (Supported by NIH grant PHS HD-10050 to C. S. Campbell)

CHANGES IN ELECTRICAL RESISTANCE OF TURTLE BLADDERS EXPOSED TO $HgCl_2$. T. Wilczewski*, J.H. Durham*, W. Nagel, & W.A. Brodsky. Dept. Physiol. & Biophys., Mt. Sinai Sch. Med., N.Y.C. & Dept. Physiol., Univ. Munich, West Germany.

The mucosal addition of $HgCl_2$ (10^{-5}M) to turtle bladders bathed by Na Ringer media induces a biphasic change in resistance (R_t) which doubles in 30 min, then decreases to half-control levels between 30 and 240 min. Concomitantly Isc and PD decrease monotonically to reach 10% of control levels. Changes during the phase of increasing R_t (5-30 min post-Hg) are reversed by replacing the Hg-containing mucosal fluid with Hg-free mucosal fluid or by mucosal addition of dithiothreitol. Changes during the later phase (90-240 min post-Hg) could not be reversed. Microelectrode impalements reveal that the electronegativity of cell to mucosal fluid increases in the first 30 min after addition of $HgCl_2$ while partial resistance of the apical membrane (R_a/R_t) doubles.

It is suggested that the reversible phase of these Hg^{++} effects, is due to formation of dissociable SH group-reactive Hg complexes with constituents of apical membrane and cytoplasm; and the irreversible phase, to the formation of covalent Hg complexes with constituents essential for Na pumping and general cell function.

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DETECTION AND MAGNITUDE ESTIMATION OF INSPIRATORY RESISTIVE LOADS WITH ABDOMINAL RESTRICTION. R. L. Wiley, L. A. Mayers* and F. W. Zechman. Miami Univ., Oxford, OH 45056 and Univ. of Kentucky Med. Ctr., Lexington, KY 40506

We previously reported (The Physiologist) 21(4):128, 1978) the ability of subjects to estimate the magnitudes of inspiratory resistive loads (ΔR) and express their perception by squeezing a handgrip dynamometer. The slope of the regression curve of a log-log plot, applying Steven's power law, describes the relation between stimulus (ΔR) and response (handgrip). Detection threshold is the fractional resistance change needed to achieve detection 50% of the time; ΔR50/Ro. In the present study we compared ΔR50/Ro and slopes of magnitude estimation (ME) in control and with abdominal restriction. A plywood clamp similar to our earlier chest clamp restricted abdominal movement so that VC was reduced 15.5% and ERV 36%. Subjects were presented 6 loads from 0.25 - 1.8cm$H_2$0/L/s for ΔR50 scoring and 7 loads from 1.24 - 20.99cm$H_2$0/L/s for magnitude estimation. Mean ΔR50/Ro with abdominal clamping (0.35) was not significantly different ($p < .05$) from control (0.42). Mean slope of magnitude estimation with clamping (1.06) was not different from control (1.18). Altering diaphragmatic mechanics and proportional contributions of respiratory muscles to development of pressure, flow and volume in this way does not change the ability of subjects to detect or estimate magnitudes of inspiratory resistive loads. (Supported by NIH Grant #16878)

EFFECT OF PHENOXYBENZAMINE ON IN VIVO VENOUS MEMBRANE POTENTIAL IN SPONTANEOUSLY HYPERTENSIVE RATS. W.J. Willems, S.J. Contney* and W.J. Stekiel. Department of Physiology, The Medical College of Wisconsin, Milwaukee, WI 53226.

This study was designed to clarify the role of α and β adrenergic mechanisms in maintenance of venous membrane potentials (E_m) in vivo in spontaneously hypertensive rats (SHR) and Wistar Kyoto control rats (WKY). Following anesthesia, mesenteric loops with circulation and innervation intact were placed in a suffusion chamber. E_m of small veins (300-600 μm) was measured with flexibly mounted glass microelectrodes (40-80 Mohm) and diameters measured with split-image optics. Significant venoconstriction produced by norepinephrine suffusion was converted to venodilation by addition of phenoxybenzamine (PBZ) to the suffusate. E_m (mv) are listed below.

Strain	Control	10^{-6} gm/ml PBZ	PBZ + 10^{-6} gm/ml Propranolol
SHR E_m	-33 ± 1.5	-47 ± 1.7	-40 ± 1.7
WKY E_m	-52 ± 1.5	-49 ± 1.4	-39 ± 0.8

Control E_m's were significantly less in SHR. PBZ significantly hyperpolarized E_m only in SHR. After PBZ E_m's in both strains were similar to E_m's measured previously following neural blockade with tetrodotoxin. Addition of propranolol to the PBZ suffusate depolarized venous E_m in both strains. The data indicate that the relatively depolarized venous E_m in SHR derives from increased α adrenergic input. The relatively hyperpolarized E_m in WKY and in both strains after PBZ derive from β adrenergic, non-neural factors--possibly humoral catecholamines. (Supported in part by NHLBI HL16454)

SYMPATHETIC VASOCONSTRICTION IN THE FOREARM DURING BRIEF ISOMETRIC CONTRACTIONS. C.A. Williams, J.G. Mudd* and A.R. Lind. Depts. of Physiology and Medicine, St. Louis Univ. School of Medicine, St. Louis, MO 63104

Successive isometric handgrip contractions, each for 4 sec at 60% MVC resulted in fatigue with an increased MAP to 152 ± 11 mm Hg, but forearm blood flows, measured during the 8 sec periods between contractions, increased to about half-maximal, 22.3 ± 2.0 ml/min·100 ml. Experiments were performed to determine whether sympathetic constriction could account for the steady-state flow. The brachial artery of 4 trained subjects was catheterized and connected to a pressure transducer. Forearm blood flows were measured with a Whitney gauge. After infusing 0.5 mg INDERAL, resting forearm flows did not increase above control levels. As subjects exerted successive contractions at 60% MVC to fatigue, blood pressure increased as before but forearm flows averaged only 26.0 ± 4.1 ml/min·100 ml, levels that were not different from control values. Immediately after infusion of 1 mg REGITINE, resting forearm flows increased to 9.2 ± 0.9 ml/min·100 ml. During fatiguing exercise, forearm blood flows increased to maximal levels, 37.3 ± 1.5 ml/min·100 ml, as blood pressure increased. These data suggest that α-adrenergic vasoconstriction competes with metabolic vasodilatation to control blood flow in the forearm during isometric exercise. Supported by NIH Grant HL07050, A.F. Grant # AFOSR-76-3084C.

AUTOREGULATION OF THE PERIPHERAL CORONARY BED SUPPLIED BY COLLATERALS. Jack L. Wilson*, Konrad W. Scheel and Leslie A. Ingram*. University of Tennessee Center for the Health Sciences, Memphis, TN 38163

The purpose of this study was to determine if the collateralized coronary bed exhibits blood flow regulation and if this capacity (coronary reserve) increases with collateral proliferation. The experiments were performed on 4 control dogs, 4 dogs with 1 month, and 4 dogs with 5 months of circumflex Ameroid occlusion. In the anesthetized intact animal, the circumflex was cannulated distal to the occluder, and blood flow was routed to this vessel from the brachiocephalic artery. Following interruption of this bypass flow, BF, for 60 sec, a hyperemic response, HR, was observed in all control animals. A HR was also observed following a retrograde flow measurement. In 1 month animals, the HR was very small to absent after interruption of BF, but present in all dogs after the retrograde flow measurement (coronary steal). In the 5 month Ameroid group, there was no HR after BF interruption. Following retrograde flow measurements, only 1 of the 4 dogs showed a HR. We concluded that collateral supply to the occluded vascular bed can become so extensive that coronary flow in the resting state may be limited not by collaterals but by the regulating peripheral coronary bed. (Supported by the American Heart Association.)

CARDIAC DYNAMICS I. Burl R. Williams, Jr.*, Martin G. Heltai*, and Bernard J. Rubal. Department of Biology, Texas Woman's University, Denton, Texas 76204.

A video tape was produced demonstrating basic principles of cardiopulmonary function. The material is designed for use in teaching physiology, pathophysiology, and clinical physiology where laboratory experience is not possible. Pulmonary topics discussed include thoracotomy, pneumothorax, atelectasis, positive pressure ventilation, and sighing. Cardiac principles demonstrated include response to vagal stimulation, arrhythmias, hypoxia, coronary artery occlusion, and ventricular fibrillation and defibrillation. The tape presents visual demonstration of these principles with simultaneous intraventricular heart sounds and accompanying narrative. The video tape is 25 minutes in duration.

INHIBITION OF AKR LYMPHOMA BY GLUCAN IMMUNOTHERAPY. D. Williams*, R. McNamee*, A. Kitahama* and N. Di Luzio, Dept. of Physiology, Tulane University School of Medicine, New Orleans, LA 70112.

Glucan, an immunostimulant polyglucose, was evaluated for its ability to alter the course of a transplantable murine lymphoma, which spontaneously occurred in an AKR/J retired breeder. For survival studies, lymphoma was induced by the ip injection of 1 x 10^3 syngeneic lymphoma cells. The initiation of glucan therapy, both iv and ip, was on day 7 post-tumor cell challenge. Peripheral leukocyte counts were employed to monitor the onset of the malignant episode. By day 15, the control group showed a leukocyte count of 145.0 ± 8.0 x 10^3/cu mm. In contrast, the glucan group had a normal peripheral leukocyte count of 11.3 ± 0.3 x 10^3/cu mm. Survival data indicated that glucan markedly altered the course of malignant disease. The median survival time of the control group was approximately 15 days, at which time the glucan-treated group showed a 100% survival. A 100% mortality occurred on day 17 in the control group, whereas the glucan group manifested a long-term 60% survival. Histopathological observation on day 16, post-tumor, revealed marked tumor growth, with hepatic and pulmonary metastases in the control mice. In contrast, tumor growth was markedly reduced as were metastatic lesions in the glucan group. These data denote that glucan immunotherapy is effective against a syngeneic murine lymphoma. (Supported in part, by American Cancer Society, MECO Cancer Research Fund and NCI-CA-13746.

REDUCTION OF HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY BY WATER DEPRIVATION IN YOUNG SPONTANEOUSLY HYPERTENSIVE RATS. M.F. Wilson, P. Tompkins*, D.J. Brackett*, C.F. Schaefer*, and C.L. Hall*. Veterans Administration Medical Center and Depts. of Medicine and Anesthesiology, OUHSC, Oklahoma City, Oklahoma 73104

Cardiac hypertrophy was studied in water deprived (WD) versus non-deprived (ND) young spontaneously hypertensive rats (SHR) and their normotensive progenitor strain, Wistar Kyoto (WKY). A 23.5 hr/day WD schedule was maintained from 5 to 13 weeks in 23 SHR and 8 WKY rats to compare with ND controls. Body weight (BW), blood pressure (BP), heart rate (HR), hematocrit (Hct), left and right ventricular (LV, RV) weights (W), LV and RV protein (Prot), desoxyribonucleic acid (DNA), and hydroxyproline (HP) were measured. LV index and ratios of LV/RV for all parameters were calculated. In WD versus ND SHR and WKY, BP was lower with no change in HR. There was no significant effect of WD on WKY LVW nor on biochemical indices of LV hypertrophy. There was a significant effect of WD in SHR, which had a lower LVW, LV total Prot and HP, with the same LV total DNA and higher LV DNA concentration than ND. The RVW and biochemical indices were the same for all groups. In WD versus ND SHR the LVW/BW and LVW/RVW ratios were lower and the ratio of LV/RV DNA concentration was higher. These data are consistent with the hypothesis that WD in SHR reduced the rate of development of hypertension, shown by a significantly lower BP, LVW, and smaller LV cell size with no change in the total number of cells.

INFLUENCES OF HORIZONTAL HYPOKINESIA ON PERFORMANCE AND CIRCADIAN PHYSIOLOGICAL RHYTHMS IN FEMALE HUMANS. C.M. Winget and C.W. DeRoshia.* Biomedical Research Division, NASA, Ames Research Center, Moffett Field, CA 94035

Dissociation of circadian rhythms from the environment has been observed in young males during hypokinesia (bedrest). In this study rectal temperature (RT) and heart rate (HR) were sampled every .5 hour from 8 female subjects (35-45 years old) during 9 days ambulatory (I), 9 days bedrest (II) and 5 days postbedrest (III). The data were characterized by relatively large inter-individual variability. RT acrophase occurred 1 hour later in II than in I or III but HR acrophase remained constant. HR daily mean and integrated amplitude (IA) decreased in all subjects in II relative to I and III. The RT phase changes in II were correlated ($P \leq .02$) with baseline RT IA levels. Performance was measured twice daily and pre- and post 1.5 G_z centrifugation using an ATC-510 flight simulator tracking test. No significant changes were found in group performance levels during the study although certain individuals exhibited significant changes. The results indicate that the transition from II to III is more disruptive of circadian rhythmicity than the transition from I to II as a result of orthostatic stress in III following deconditioning in II. Differences between RT and HR circadian parameters observed in response to II probably reflect separate coupled oscillatory systems which are differentially sensitive to the reduced effectiveness of zeitgeber during hypokinesia.

REFLECTION COEFFICIENT, PS PRODUCT, MEAN TRANSIT TIME AND DISTRIBUTION VOLUME IN LUNGS OF GOATS WITH CHRONIC LYMPH FISTULAE. R. Winn*, J. Gleisner*, B. Nadir* and J. Hildebrandt (Spon: Y-L. Lai), Virginia Mason Res. Ctr., Seattle, WA 98101.

Goats were prepared with chronic lung lymph fistulae to allow study of the microvascular barrier and the interstitial space. Lymph was collected from the caudal mediastinal lymph node preceding and following the injection of FITC-labeled albumin. The reflection coefficient (σ) and permeability surface area product (PS) were determined as suggested by Brace, et al. (Microvas. Res. 16:297, 1978) assuming no concentration occurs in the lymphatics. Mean transit time ($\bar{t}$) was found from the appearance of FITC-albumin in the 15 min lymph collections. These curves were adequately represented by a 15 min delay and a single exponential. Thus, the simplest model for the interstitial space was a single well mixed region. The volume of distribution can be shown to be: $V_d = \sigma \bar{t} Q_f/(1-R)$ where $R = C_L/C_p$ = lymph-plasma protein ratio, Q_f = lymph flow, and the term $\sigma/(1-R)$ accounts for the effect of a varying diffusional flux of the labelled albumin across the microvascular barrier. The concentration gradient is C_p-C_L, where C_L of the label increases from zero initially to some steady level . The mean σ of total protein was found to be 0.65 and the mean PS product 4.34 ml/h. Mean $\bar{t}$ for albumin was 1.88 resulting in a V_d for albumin of 24.6; σ for albumin was .49 and PS 16.9 ml/h. (Supported by NRSA HL 05421, and NIH grants HL 22369, HL 20652, and HL 20773.

THE EFFECTS OF TESTOSTERONE, DIHYDROTESTOSTERONE, ESTRADIOL, 5α-ANDROSTAN-3α,17β-DIOL ON PLASMA LUTEINIZING HORMONE LEVELS IN THE ACUTELY ORCHIDECTOMIZED DOG. M.L. Winter*,J.C. Pirmann* A.A. Gil*, and R.E. Falvo. Southern Illinois University School of Medicine, Carbondale, Illinois, 62901.

In order to investigate the effects of testosterone(T) and its metabolites on luteinizing hormone(LH) secretion in the male dog the following study was done. Five dogs were castrated and allowed to recover from surgery for 7 days. On days 7,11,19, and 23 post-castration, the dogs were randomly injected with T, dihydrotestosterone(DHT), estradiol(E_2), 5α-androstan-3α,17β-diol(3α-diol), and corn oil according to a Latin-square design. The doses of the androgens and E_2 were 250μg/kg and 50μg/kg, respectively. Blood samples were taken every 20 min 1 h pre-injection and for 3 h post-injection. Samples were also taken at 6,9,12, and 24 h post-injection. The plasma LH rise after castration was significantly reduced by injection of T or E_2. Results also showed that the plasma LH levels were not significantly reduced by injecting DHT or 3α-diol. Corn oil had no effect on LH levels. The T and E_2 suppression of LH levels agreed with our previous findings. These data indicate that the plasma LH levels in the acutely orchidectomized dog are not suppressed by DHT, 3α-diol, or corn oil injections. These data, which are supported by studies in the human male, indicate that DHT may not suppress LH secretion. It is concluded that the male dog may be the animal of choice to study the effects of T and its metabolites on gonadotropin regulation.

ELEVATION OF LEFT VENTRICULAR DIASTOLIC PRESSURE BY PEEP IN THE ISOLATED IN-SITU HEART. R.A. Wise*, J.L. Robotham*, B. Bromberger-Barnea, W.R. Taylor*, S. Permutt. The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205.

Positive end-expiratory pressure (PEEP) elevates left ventricular diastolic pressure (LVDP) for a given cardiac output. Possible mechanisms are: 1) decreased compliance of the left ventricle (LV) due to interdependence with the right ventricle (RV); 2) impaired LV contractility due to neural or humoral factors; 3) mechanical interaction of the heart and lungs. To evaluate this, we used an open chested, in situ, isovolumic, coronary-perfused dog heart preparation with minimal RV volume. The non-perfused lungs were ventilated with constant tidal volume (TV) at 0 and 15 cmH_2O PEEP. With no PEEP, TV ventilation caused little change in LVDP. With PEEP, LVDP increased 3.5 to 5.0 mmHg at end-expiration, and with tidal ventilation increased 2.5 to 6.0 mmHg. In a similar preparation with the heart and lungs removed from the thorax, lung inflation had a variable effect on LVDP. When a circumferential binder was placed around the lungs, the results were similar to those with the chest wall present. Since ventricular interdependence; and neural and humoral variables were controlled, we conclude that PEEP increases LVDP by mechanical compression on the heart by the lungs constrained by the chest wall even in the open chested dog. (Supported by NIH HL-10342 and The Maryland Thoracic Society.)

IMIDAZOLE IMPROVED SURVIVAL FROM ENDOTOXIC SHOCK IN RATS. W.C. Wise, J.A. Cook,* and P.V. Halushka*. Departments of Physiology, Pharmacology, and Medicine, Medical University of South Carolina, Charleston, South Carolina 29403.

Previous studies in essential fatty acid-deficient rats suggested a possible pathogenic role for thromboxane A_2(TxA_2) in endotoxin (ENDO) shock. We have investigated the effect of a Tx synthetase inhibitor, imidazole (Im), on the pathogenesis of ENDO shock. Im was administered (i.p. 18mg/kg) 1 hr pre- and 3 hr post-iv administration of S. enteritidis ENDO (20mg/kg) and also at 30mg/kg, 1 hr pre-ENDO in Long-Evans rats. By 5 hrs, mortality in the control group was 50% (N=48) as compared to only a 10% mortality (N=11) in Im treated rats ($P<.01$). At 24 hrs this dose of ENDO produced 90% mortality in controls, but only a 36.4% mortality in both Im treated groups. ENDO induced a significant 77% reduction in platelet counts in control animals at 15 mins whereas in Im pretreated rats the thrombocytopenia was significantly less ($P<.05$). Additionally Im significantly decreased ($P<.01$) ENDO induced elevations in serum acid phosphatase, β-glucuronidase, GOT and GPT. The lower serum lysosomal hydrolase activity and minimal increases in plasma transaminase activity in the Im-treated group indicate a maintenance of hepatic integrity relative to shocked controls. This data demonstrates that Im protects against the lethal endotoxic shock. The observations support the hypothesis that TxA_2 may play a significant role in the pathogenesis of endotoxic shock. (Supported by AHA #77731 &NIH, GM 20387)

GLUCOCORTICOID ANTAGONISM OF IN VITRO STIMULATION OF ADIPOSE TISSUE GLUCOSE OXIDATION BY ENDOTOXIN. L. Witek-Janusek* and J. P. Filkins. Depts. of Physiology and Maternal Child Health Nursing, Loyola Univ. of Chicago, Maywood, IL 60153

Endotoxemia in rats increases glucose oxidation (GO) by epididymal fat pads (EFP) and dexamethasone (DXM) antagonizes this effect (Circ. Shock 5: 317, 1978). Current studies were aimed at, 1) developing an in vitro model of endotoxin (ET) stimulation of GO in EFP and 2) examining the DXM antagonism. Paired EFP of fed male Holtzman rats were pre-incubated for 120 min at 37°C with and without ET (100 μg/ml) in Krebs-Ringer-Bicarbonate (KRB) with 1% albumin and 1% D-glucose. EFP were then rinsed (0.9% NaCl) and assayed (180 min) for GO in a media of ^{14}C-glucose (0.5 μCi/ml) KRB with 5.55 mM unlabeled D-glucose. ET significantly increased GO (168 ± 4.8 vs 268 ± 7.3 DPM/g/180 min x 10^3). Chilling of EFP before incubations reduced this response. DXM (100 μg/ml) blunted ET stimulated GO when coincubated with ET (94 ± 7.8 vs 117 ± 9.1 DPM/g/180 min x 10^3); however, it had no effect when added after the initial preincubation with ET (94 ± 4.6 vs 145 ± 7.6 DPM/g/180 min x 10^3). These in vitro results correspond with in vivo data in that ET stimulates GO and that antagonism by DXM requires its presence during the early stage of ET insult. In conclusion, this system has the potential to serve as a model for investigating the mechanism of ET action and its antagonism by glucocorticoids. (Supported by USPHS Grant HL08682)

THE EFFECT OF PROLONGED ACTIVITY ON THE CONTRACTILE PROPERTIES OF FAST AND SLOW SKELETAL MUSCLE. F.A. Witzmann*, D.H. Kim*, and R.H. Fitts* (SPON: B.E. Piacsek). Biology Dept., Marquette Univ., Milwaukee, WI 53233.

Contractile properties of the slow, type I, soleus (SOL), the fast, type IIB, superficial vastus lateralis (SVL), and the mixed fast, type IIA and IIB, extensor digitorum longus (EDL) muscles were determined in vitro(21°C) in both control and fatigued rats. The rats were fatigued by 7 hrs. of swimming. The contractile properties of the EDL and SOL but not the SVL were altered by the prolonged swim. The EDL isometric contraction and one-half relaxation time were shortened significantly to 77% and 66% of control values. Both twitch(P_t) and tetanic(P_o) tension were significantly depressed in EDL (fatigued P_t 205±67, P_o 633±190 vs control P_t 636±36, P_o 2397±171 g/cm^2) and SOL (fatigued P_t 243±36, P_o 1651±228 vs control P_t 374±36, P_o 2466±76 g/cm^2). The maximal rates of tension development(+dP/dt) and decline(-dP/dt) were also significantly depressed in both the fatigued EDL and SOL.The greatest decrease occurred in the EDL where P_t, +dP/dt of 13.3±4.6 g/msec/cm^2 and P_o, +dP/dt of 14.6±4.4 g/msec/cm^2 were 43% of the control. The maximal velocity of isotonic shortening (Vmax) was relatively fatigue resistant in both EDL and SOL compared to the changes in P_o. In summary, alterations in the contractile properties during prolonged submaximal work appears related to the degree of contractile activity and thus is primarily confined to muscles with a high percentage of type I and/or IIA fibers. (Supported by Marquette Univ. Faculty Research Grant.)

CLONIDINE ADMINISTRATION IN HYPERTENSION. Robert L. Wolf, Lora L. Rice*, and Stanley Reichman*. The Mount Sinai Medical Center and The Hospital for Joint Diseases and Medical Center, New York, New York 10029

The hypotensive effects of clonidine hydrochloride (Catapres (C)), administered either thrice daily (Method I) or twice daily (Method II) were compared to placebo (P) and to each other. Alterations of blood pressure (BP), pulse rate (PR) (dependent variables), weight, height, age, sex, race, and duration and severity of hypertension (independent variables) were recorded. The results demonstrate: A) a very high correlation between dosage levels of C and BP for Method I but not for Method II; B) virtually flat dose-BP response curves for all treated patients; C) significance levels generally above 99% for all regression equations; D) that Methods I and II, when tested by analysis of variance, significantly reduce the BP from P by the same amount; E) that Method II is not significantly different from Method I. Calculations were based on an alpha-level of 0.01 and a power of 0.99.
(Supported in part by Syracuse China Corporation, Syracuse, New York and by Boehringer Ingelheim Ltd., Ridgefield, Connecticut)

PERIPHERAL CORTICOSTEROID (11OHCS) RESPONSE TO 5 MIN STEPS OF 6 DOSES ACTH INFUSED WITH OR WITHOUT HEMORRHAGE IN THE CONSCIOUS DEXAMETHASONE-TREATED DOG. C.E. Wood*, J. Shinsako*, and M.F. Dallman. Univ. Calif., San Francisco, CA 94143.

Hemorrhage (HEM. 15 ml/kg) in the conscious dog increases plasma ACTH 11pg/ml and 11OHCS 2.8ug/dl above control. These studies were performed to test whether HEM increases adrenal sensitivity to ACTH. Dogs (7) with femoral arterial catheters were pretreated with dexamethasone (4mg sc, at -12 and -2 h). (This pretreatment was shown not to affect the 11OHCS response to ACTH step infusions compared to saline-injected controls.) Each experiment consisted of saline or ACTH α1-24 (6 steps, 7.6-382 ng/min, 5 min each) with or without HEM (15ml/kg). ACTH (±HEM) but not saline (±HEM) raised plasma ACTH and 11OHCS. Plasma ACTH correlated linearly with ACTH infusion rate (r^2=.99). The slope of the regression line was increased by hemorrhage ($p < .001$).

ACTH INF. RATE	ACTH(pg/ml)		11OHCS(ug/dl)	
(ng/min)	+HEM	-HEM	+HEM	-HEM
7.6	18±3	13±2	.4±.1	.5±.1
15	19±3	14±3	.6±.1	.6±.1
38	29±3	21±5	2.5±.7	1.6±.8
76	57±3	48±6	3.8±.7	2.6±.7

CONCLUSIONS: 1) In dexamethasone-pretreated dogs, the 11OHCS response to infused ACTH is not changed by hypovolemia; 2) At threshold (38 ng/min ACTH), the adrenal is exquisitely responsive to ACTH. (Supported in part by USPHS grant AM06704 and NASA-University Consortium NCA2-OR665-806.)

NEUROMODULATORY FUNCTION OF SUBSTANCE P AND SEROTONIN IN THE MYENTERIC PLEXUS. J. D. Wood, P. Grafe* and C. J. Mayer*. Dept. of Physiol., Kansas Univ. Med. Ctr., Kansas City, KS 66103 and Physiologisches Institut der Universität München, Munich, Germany.

Slow excitatory processes were studied with intracellular recording methods in myenteric neurons of guinea-pig small intestine. Electrical stimulation of presynaptic fibers to the neurons evoked prolonged excitatory potentials (slow EPSPs) which continued for periods lasting as long as 8 min after termination of stimulation. Substance P (1 nM) in the superfusion solution mimicked the slow EPSP in most respects, except it did not reduce the characteristic hyperpolarizing after-potentials that follow action potentials in these neurons (refer to Wood and Mayer, J. Neurophysiol. 42:569, 1979 for characteristics of the slow EPSP). Serotonin mimicked all aspects of the slow EPSP when it was applied either iontophoretically or in the superfusion solution (50 nM). The serotonin antagonist, methysergide (10 μM), blocked reversibly both the stimulus - evoked slow EPSP and the action of serotonin. The action of substance P was not blocked by methysergide. The results suggest that serotonin is the neurotransmitter for slow synaptic modulation of excitability in myenteric neurons and that modulation of excitability by substance P may be a paracrine function. (Supported in part by NIH Grants AM 70727 and AM 16813)

A METHOD FOR MEASURING GASTRIC VASCULAR PERMEABILITY TO PLASMA PROTEINS. John G. Wood* and Horace W. Davenport. University of Michigan, Ann Arbor MI 48109

The purpose of this work was to develop a meathod for measuring gastric vascular permeability to plasma proteins in normal and plasma-shedding states. An isolated segment of a dog's stomach was perfused with donor blood at constant flow. Maximal vasodilatation was produced by intra-arterial infusion of papaverine. Venous pressure was increased by 15 mm Hg. Plasma containing 131-I albumin and 125-I fibrinogen was infused intra-arterially. Venous effluent blood was collected in consecutive 1-min samples. Filtration was calculated as the difference between arterial inflow and venous outflow. Extraction of labeled proteins was calculated as the difference between arterial delivery and venous efflux. During control infusions lasting 60 min when the mucosa was bathed with phosphate buffer, pH 7, initial PS products for albumin and fibrinogen were 6.5 and 2.3 $cm^3 10^4$ sec^{-1} gm dry w t^{-1} respectively. Filtration and PS products gradually fell. Intra-arterial histamine infusion (0.09 to 0.9 μg ml^{-1}) caused increased filtration and permeation by both proteins. Pyrilamine maleate (5 mg kg^{-1}), an H_1 receptor antagonist, prevented the increases caused by histamine.

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ACID-BASE BALANCE DURING HEATING AND COOLING IN THE LIZARD, VARANUS EXANTHEMATICUS. S.C. Wood, K. Johansen, M.L. Glass* and R.W. Hoyt*. Aarhus University, Aarhus, Denmark

Our original report (J. comp. physiol. 116:287, 1977) showing invariance of arterial pH with body temperature in Varanus (an exception to the "relative alkalinity" concept) has been criticized on several legitimate bases. The present study re-evaluated this question taking account of these objections. Five lizards were studied over a wider range of body temperature (15 to 38°C vs. 25 and 35° in the original study). Arterial blood was sampled during heating and cooling at various rates, using restrained and unrestrained animals with and without face masks. Arterial pH shows a very slight, but significant temperature dependence, i.e., pH = 7.66 - 0.005 (T). The slope, while significantly greater than zero ($p < 0.005$) is much less than reported for most other ectotherms ($dpH/dT \simeq 0.016$). The original conclusion that this species maintains a constant arterial pH (instead of a constant OH/H ratio) as temperatures changes must be modified, but only slightly. The mechanism of this regulation, and what distinguishes this species from most other ectotherms, is the temperature-independent ratio of ventilation to CO_2 production (V_E/V_{CO_2}). Consequently, arterial P_{CO_2} rises only slightly, and insignificantly, more than predicted from the iso-pH change in P_{CO_2} required by the disparate temperature-induced changes in pK'_2 and CO_2 solubility. (Supported by NSF Grant No. PCM 77-24246).

ELECTROPHYSIOLOGIC CHARACTERISTICS OF THE ISOLATED, ARTERIALLY PERFUSED ATRIOVENTRICULAR NODE OF THE PUPPY HEART.

W. Thomas Woods and Thomas N. James*, University of Alabama Medical Center, Birmingham, Alabama 35294

The atrioventricular (AV) node in the canine heart lies beneath a 1 mm layer of endocardium making electrophysiologic study with microelectrodes difficult. To obviate dissection of surrounding tissue, we developed a preparation in which we could record from proximal and distal AV node cells as well as His bundle cells. The isolated right atrium was perfused with physiologic solution through the AV node, septal, and sinus node arteries; this allowed us to manipulate independently the proximal AV node, distal AV node, and sinus node respectively. Pacing sites were the sinus node, AV node, or from a movable pacing electrode. Action potentials underwent a transition when specially sharpened microelectrodes were moved from proximal to distal AV node; first they resembled those of atrial muscle and then gradually they came to resemble pacemaker cells in the most distal AV node. This transition corresponded to the region of slowing impulse transmission. More distal impalements abruptly encountered the characteristic His bundle cell action potentials. These normal AV node action potentials confirmed the viability of this preparation, a similarity to the rabbit AV node, and the anatomical correlation with the 4 major cell types of the AV node (Sherf and James, Circulation 37:1049, 1968).

ADJUSTMENTS OF BODY FLUID pH IN RESPONSE TO DAILY CHANGES IN BODY TEMPERATURE OF COLLARED LIZARDS. Stephen A. Worsham* and Graeme S. Maclean* (SPON: A. F. Bennett). Dept. Biology, Univ. Texas at Arlington, Arlington, Tx. 76019.

A micro-pH electrode, encased in a 21 gauge stainless steel shaft, was implanted in the hind leg of the lizard Crotaphytus collaris to obtain continuous recordings of interstitial fluid pH as body temperature was varied at rates similar to those occurring in the natural environment. Animals were maintained at 20°C - 30°C for 24 h prior to insertion of the electrode. After pH had remained stable for at least 2 h, Tb was either increased or decreased between 35°C and 5°C at rates of 3 - 6°C/h. This resulted in a pH change of -0.018 $\Delta pH/\Delta°C$. Total CO_2 content of mixed venous blood remained relatively constant. Measurements taken after 4 h acclimation at 8°C and 32°C were 23.3 ± 1.4 (mean ± SE) and 20.2 ± 1.3 (mean ± SE) mM/L respectively. Simultaneous measurements of oxygen consumption rate and minute ventilation showed that relative hyperventilation occurs at lower temperatures. We conclude that ventilatory adjustments are sufficiently rapid to maintain constant relative alkalinity of the extracellular fluid in these lizards during the normal diurnal cycles of body temperature. (Supported by grant # 15-650 from Organized Research funds of The University of Texas)

EFFECTS OF SANDFLY FEVER ON MUSCLE STRENGTH. J.E. Wright*, J.J. Knapik*, W.L. Daniels*, D.S. Sharp*, J.A. Vogel, G. Friman*, & W.R. Beisel*. U.S. Army Rsch Inst of Env Med, Natick, MA 01760 and U.S. Army Rsch Inst of Inf Dis, Ft. Detrick, MD 21701.

In documenting the effects of a brief standardized infectious illness on physical performance capacity, 9 healthy male volunteers were studied. Inoculation of 7 individuals with Sicilian type Sandfly Fever Virus reproduced previously reported subjective symptoms and clinical findings including headaches, myalgia, anorexia, generalized malaise, leukopenia and fever ($\bar{x}$ peak T_{re}: 39.5 ± 0.2°C) lasting 46 ± 2.8 hours. During fever, isometric strength of grip, upper torso and leg muscle groups decreased by 10, 12 and 23%, respectively ($p < 0.05$ for each). Peak torque during isokinetic contractions of knee extensors at 36 and 180°/sec decreased by 19 ($p < 0.05$) and 16% (NS), respectively. Peak torque during identical contractions of arm flexors was unaffected by fever. Strength values 48 hours after subsidence of fever, though still reduced, were not significantly different from those obtained prior to inoculation. Clinical and performance changes in the two saline-injected control subjects were minimal. Our results support previous suggestions that work performance during illness may be more closely related to subjective perceptions of symptomatology than to the standard clinical indications of illness. No relationships were apparent between strength decrement and peak fever temperature, fever duration or absolute initial strength capacity.

NONLINEAR REACTION-DIFFUSION SYSTEMS WITH MULTIPLE STATIONARY STATES: NETWORK MODELLING AND NUMERICAL SOLUTION USING SPICE2. J.L. Wyatt, Jr.*, D.C. Mikulecky, J.A. DeSimone, Physiol. Dept., Med. Coll. of Va., Richmond, Va. 23298

Using the network thermodynamic paradigm and the circuit analysis package SPICE2, we can simulate reaction-diffusion systems with much less effort than more conventional methods require. The following examples are given in detail: an n-th order reaction in a porous catalytic slab, substrate inhibition kinetics with multiple steady states, and a cellular metabolic scheme involving Michaelis-Menten kinetics and membrane transport. In these examples we show how various nonlinearities can be readily incorporated by using polynomial controlled sources in the network model. To represent a spatially distributed system, we reticulate the domain of interest into subregions sufficiently small that spatial variations within any subregion can be neglected. The simulation results exemplify the tradeoff of accuracy against programming effort and computer time. Transient effects are easily included in these models by use of capacitors to model storage phenomena.

DISCONTINUITY OF PULMONARY MUCOCILIARY TRANSPORT DUE TO METAPROTERENOL SULFATE. D.B. Yeates,* D. Spektor, and B.R. Pitt Section of Environmental Medicine, University of Illinois at Medical Center, Chicago* and Institute of Environmental Medicine, New York University Medical Center, New York, New York.

Mucociliary transport was measured using radioaerosol techniques in the trachea with a six-detector probe and in the lung with a pair of scintillation detectors. Twelve healthy nonsmoking adults were studied on two occasions. After the second aerosol inhalation, 20 mg. of metaproterenol was administered orally. The rate of bronchial clearance at the time the first bolus reached the most caudal tracheal detector (RTB_1's) and the fraction cleared in 2 hours (TB_{120}) were used as indices of lung clearance. Tracheal mucociliary transport rates (TMTR's) in the control studies (mean 4.2±2.5 mm/min) were significantly correlated with RTB_1's (mean (5.9±3.3) x 10^{-3}/min) ($r=0.70$) and TB_{120} mean (0.48±0.19) ($r = 0.68$). In contrast, after administration of metaproterenol there was a significant inverse correlation between TMTR's which were increased (mean 6.4±4.5 mm/min) and RTB_1's which were decreased (mean (3.4±2.7) x 10^{-3} mm/min) ($r = 0.66$). In addition there was no correlation between TMTR's and TB_{120}'s which were not significantly altered (0.44±0.14) ($r^2 = 0.1$). These data show that increasing tracheal mucociliary transport is not necessary a consequence of faster lung clearance and suggest that some agents may result in opposing effects on mucus transport in different airway generations

INSULIN HYPERSECRETION FOLLOWING RETICULOENDOTHELIAL SYSTEM (RES) DEPRESSION. Michael R. Yelich and James P. Filkins. Dept. of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153

Endotoxemia has been shown to elicit a hypersecretion of insulin (Circ. Shock 6: 174, 1979). Since endotoxin is removed from the circulation by the RES, the present study investigated the status of insulin secretion from pancreata of rats treated 4 hours previously with either colloidal carbon (CC, 100mg iv) or lead acetate (PbAc, 5mg iv) - agents known to depress the RES. The isolated perfused pancreas model of Grodsky was employed using fasted, 330g, male Holtzman rats and secretion of immunoreactive insulin (IRI) was measured during a 40 min perfusion period. Total IRI secretion from pancreata of 6 CC-injected donors was 177% higher ($p \leq 0.01$) than that from 6 sham controls (2802±530 vs 7750±1323 µU IRI, Mean±SE). In similar experiments using pancreata from PbAc-injected donors (n=5), IRI secretion was increased 77% ($p \leq 0.01$) relative to that from 6 control donors (3163±290 vs 5608±334 µU IRI). These results indicate that RES depression by CC or PbAc results in a marked hypersecretion of insulin from the isolated pancreas in response to a glucose stimulus. It is suggested that altered states of insulin regulation relate to the increased sensitivity to endotoxin shock caused by RES depression (J. RE Soc. 22: 461, 1977). Lastly, these data point out a potentially important control mechanism whereby the RES can modulate pancreatic insulin secretion. (Supported by NIH Grant HL08682)

INDUCTION AND EARLY DETECTION OF VITELLOENESIS IN FISH GIVEN ESTROGENS ORALLY. Sandra Yosha and Paul Cardeilhac. Col of Vet Med and Whitney Marine Lab, U of FL, Gainesville, FL 32610.

Pinfish (Lagodon rhomboides) treated during the resting phase of the reproductive cycle with 5 µg estrogen/g fish were sacrificed within ten days after treatment and evaluated for presence of oocyte proteins in the liver, ovary, and serum. Serum alkali labile protein phosphorus (SALPP), an indicator of vitellogenin, increased in response to estradiol-17-β(E_2) to 14.8 µgP/ml and in response to the synthetic estrogens, 17-α ethynl estradiol (157.3 µgP/ml), ethynl estradiol-3-methyl ether (144.0 µgP/ml), and diethylstilbestrol 223.8 µgP/ml). Estrone and estriol failed to increase SALPP above basal levels (<10 µgP/ml). In addition to SALPP, oocyte proteins were identified by an immunodiffusion test using antiserum raised against partially purified pinfish oocyte homogenate. The antiserum detected oocyte proteins in liver and ovary homogenates, and in sera from treated fish,including fish treated with estrone or estriol. The major immunoreactive protein, which is thought to be vitellogenin, has the following properties: 1) estrogen induced, 2) present in liver, serum, and ovaries of estrogen stimulated fish, 3) absent from males and non-vitellogenic females, 4) contains both lipid and phosphorus, 5) produces radial immunodiffusion rings that are directly proportional to SALPP levels ($y=0.06x + 8.16$; $r^2=.91$; n=42). Both immunodiffusion and SALPP analysis indicate that estrogens given orally are effective in stimulating vitellogenin synthesis by the liver.

RADIOLOGICAL EVIDENCE OF TIBIAL BONE MASS LOSS IN HYPODYNAMIC MONKEYS (M. NEMESTRINA). Donald R. Young. NASA, Ames Research Center, Moffett Field, CA 94035

During hypodynamic restraint, local areas of atrophy develop in the tibiae of monkeys. Experiments were conducted to draw comparisons between three non-invasive radiological techniques used to monitor the osteopenia which occurs in disuse osteoporosis. The techniques involved X-rays, photon absorptiometry, and gamma ray computer tomography. Three animals were studied during six months of restraint, and six months of rehabilitation with a high calcium diet and a program of physical exercise. X-rays of the tibiae showed bone loss intracortically and at the endosteal surface in the proximal anterior tibia. Measurements made by photon absorptiometry showed a 17-21% decline of bone mineral content in the proximal tibia within five months. Gamma ray tomography demonstrated a thinning of the cortex and widening of the medullary space in the anterior tibia. During recovery, osteoid tissue formation and mineralization in the cortex proceeded at a slow rate, and therefore the bone mineral content in the tibia remained depressed. The three procedures agreed in demonstrating that regional loss of bone is associated with intracortical resorption cavities as well as endosteal bone resorption, and that bone mass loss is not readily reversed during recovery and rehabilitation in the adult animal.

COMPARATIVE EFFECTS OF ASCORBIC ACID AND ETHANOL INFUSION ON URINARY EXCRETION OF CATIONS IN THE DOG. A. A. Yunice and C. C. Haygood*, VA Hosp., Medical Service, and Depts. of Med. and Physiol., Univ. of Okla., Okla. 73104

Our previous studies have shown that chronic ingestion of ascorbic acid (ASA) have significant effect on reducing kidney tissue zinc concentrations in the rat. To gain further insight into the renal hemodynamics involved, we compared the effect of ASA infusion with that of ethanol (EtOH) on plasma and urinary cations concentration. Eighteen mongrel dogs were divided into three groups: saline control (6), 100mgASA/Kg body weight (6) and 33% EtOH at the rate of 4.0 ml/min (6). Conventional methods for quantifying glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were utilized. Analyses of urine and plasma samples for I^{125}-Iothalamate, PAH, osmolality, Na, K, Ca, Mg, Zn, and Cu were performed. The average of pre-fusion samples was compared with the average of infusion and post-infusion samples. Results indicate that during acute ascorbic acid infusion, urinary excretion of all metals tested was significantly increased and all returned to pre-infusion levels during post-infusion period with the exception of Na and K. There was a two-fold increase in urinary flow with GFR and ERPF remaining unchanged in both experimental groups. Cationic concentrations of plasma were unaltered. It is concluded that large doses of ascorbic acid may enhance urinary excretion of essential metals by altering tubular membrane transport rather than renal hemodynamics. (Supported by the VA Research Service)

ANALYSIS OF LONG-TERM EFFECTS OF EXTRACELLULAR POTASSIUM CONCENTRATION ON RENAL POTASSIUM EXCRETION. David B. Young, Dept. Physiol. & Bioph., Univ. Med. Cntr., Jackson MS 39216.

The effects of long-term changes in extracellular K concentration (P(K)) on renal K excretion independent of changes in aldosterone were studied in 7 adrenalectomized dogs. The dogs, whose weight averaged 21.7±1.0 kg, were fed a diet containing 30 mEq Na and 10 mEq K and received continuous i.v. infusion of 50 µg/day aldosterone and 1 mg/day methylprednisolone. K intake was increased from 10 to 30, 100 and 200 mEq/day by continuous i.v. infusion of KCl, each rate maintained for 7 days by which time the dogs were in electrolyte balance and P(K) was stable. On the 7th day measurements of the following variables were made: plasma Na and K, urinary Na, GFR, and mean arterial pressure (MAP). Plasma Na, urinary Na excretion, arterial pH, GFR and MAP were unchanged by increasing K intake. The steady-state levels of P(K) and urinary K excretion were 3.13 mEq/L, 10 mEq/day;4.18 mEq/L, 27 mEq/day; 4.13 mEq/L, 66 mEq/day; 4.75 mEq/L, 170 mEq/day. Below the normal level of P(K)(4.18 mEq/L), there is a weak relationship between P(K) and K excretion, (16 mEq/day)/mEq/L. Above the normal level the effect of P(K) on K excretion is very powerful, (251 mEq/day)/mEq/L. These data, obtained in the absence of changes in aldosterone, Na excretion, GFR, arterial pressure and pH demonstrate that extracellular K has an important role in control of renal K excretion. Supported by NIH HL 21435, HL 11678 and a Grant-in-Aid from Miss. Heart Assn.

EFFECTS OF PROSTAGLANDIN E_1 (PGE_1) AND PROSTAGLANDIN $F_{2\alpha}$ ($PGF_{2\alpha}$) ON THE DIURETIC RESPONSE TO ACETYLCHOLINE (ACh) IN INDOMETHACIN (INDO)-TREATED DOGS. J.C.H. Yun, Dept. of Physiology, Howard Univ., Coll. of Med., Wash. DC 20059 and NIH, Bethesda, Md. 20014.

We have reported that the diuretic response to renal arterial infusion of ACh in anesthetized dogs was shortened by INDO (5mg/kg,I.V.) (Group I). To determine whether PGE_1 or $PGF_{2\alpha}$ would restore the diuretic response to ACh in INDO-treated dogs, PGE_1 (Group II) or $PGF_{2\alpha}$ (Group III) was infused into the renal artery at 1.9 µg/min before and during renal arterial infusion of ACh.

		V(ml/min)
Group I	Control	0.33 ± 0.07
N = 6	INDO	0.48 ± 0.22
M ± SEM	ACh 40 min	2.78 ± 0.47***
	ACh 100 min	1.11 ± 0.34*
Group II	Control	0.21 ± 0.07
N = 11	INDO + PGE_1	1.16 ± 0.23***
M ± SEM	PGE_1 + ACh 40 min	3.43 ± 0.50***
	PGE_1 + ACh 100 min	3.57 ± 0.50***
Group III	Control	0.21 ± 0.08
N = 11	INDO + $PGF_{2\alpha}$	0.53 ± 0.16*
M ± SEM	$PGF_{2\alpha}$ + ACh 40 min	1.86 ± 0.44**
	$PGF_{2\alpha}$ + ACh 150 min	0.84 ± 0.42*

*** P<0.001 ** P<0.01 * P<0.05

The data suggest that PGE_1 but not $PGF_{2\alpha}$ helps to maintain the diuretic response to ACh in INDO-treated dogs.

DICHLOROACETATE (DCA) DECREASES PLASMA LACTIC ACID (LA) OBSERVED DURING EXERCISE IN DOGS. Edward J. Zambraski, Gary F. Merrill, and Steven M. Grassl*. Dept. of Physiology Rutgers Univ., New Brunswick, N.J. 08903.

DCA has been reported to reduce the lactacidemia associated with diabetes, hypoxia and other clinical conditions. To determine whether DCA would influence the accumulation of LA seen during exercise, chronically instrumented dogs were exercised with and without DCA. Dogs (n=8) were run on a treadmill at light (L), moderate (M) and heavy (H) exercise workloads. The tests were repeated after DCA (100 mg/kg i.v.). Mean arterial pressure (MAP) and heart rate (HR) were recorded. Arterial plasma LA was determined at each workload. Values are mean ± SEM. († P < .05 vs. control test).

	Control			DCA		
	MAP	HR	LA	MAP	HR	LA
	(mmHg)	beats/min	(mg/dl)			
Rest	120±3	109±6	19±2	107±5	104±8	11±2
L	133±4	168±8	26±4	127±5	151±8	15±2
M	144±3	203±11	38±5	130±4	†169±7	20±4
H	151±6	211±9	52±6	139±7	210±9	†23±3

In additional experiments dogs (n=6) performed prolonged moderate exercise (50 min). LA, 24±1 mg/dl at rest, increased to 41±6 mg/dl at 10 min. and 50±5 mg/dl at 50 min. In repeat tests when DCA was given at 12 min, LA at 50 min was 60% lower when compared to the control run (P\ < .05). Thus DCA attenuates the increase in LA during exercise. Supported by NJAES.

THE CONTRACTILE PROPERTIES AND FUNCTIONS OF SINGLE MOTOR UNITS OF THE THYROARYTENOID (TA) MUSCLE IN CATS. David L. Zealear* (SPON: James C. Houk). Dept. of Physiology, U.C., San Francisco, CA 94143

Because of the difficulty in penetrating and holding laryngeal motoneurons with micropipettes in the brainstems of spontaneously breathing cats, a technique was developed for penetrating axons in the recurrent laryngeal nerve. It provided a less damaging and more stable approach to studying these motoneurons. The contractile properties of single TA motor units were determined by stimulation of their axons while monitoring muscle fiber tension development. Upon recording from these same axons during stimulation of mucosal afferents of the internal laryngeal nerve, axon spiking revealed the extent to which motor units participated in gag vs. expiratory contractions of the muscle. Motor units were of two types: fast-red and slow. Approximately 70% were fast-red and were distinguished by their faster contraction times, faster conducting axons, presence of sag, larger size, and presence of facilitation during the first minute of fatigue. Both types were extremely fatigue resistant. All units participated in the gag reflex while only slow units could be "aroused" to exhibit expiratory activity, presumed preparatory to vocalization. (Funded by NIH Grants EY01474-03 and NS14103-02)

FOURIER ANALYSIS APPROACH TO MEASUREMENTS OF IMPEDANCE OF THE RESPIRATORY SYSTEM BY FORCED OSCILLATION. S. Zoledziowski, (Spon. G.J.A. Cropp), State Univ. of New York and Children's Hospital, Buffalo, N.Y.

We have developed a new analytical approach to the measurement of impedance of the respiratory system (Z_{rs}) by forced oscillations (FO) in which the signals are processed digitally. Only 4 basic arithmetic operations are needed so that processing can be done in real time with an inexpensive microprocessor (TMS 9900). Since the excitation frequency is known, the pressure (P) and flow ($\dot{V}$) signals can be digitized at a rate of 12 samples per period. A 12 point Fourier analysis is then performed, giving the cophase (c) and quadrature (s) components of the fundamental frequency and its harmonics up to the sixth. Z can be computed from the following formula:
$Z = P/\dot{V} = R+jX = [(Pc\dot{V}c + Ps\dot{V}s) + j(Ps\dot{V}c - Pc\dot{V}s)]/(\dot{V}c^2+\dot{V}s^2)$, where R is the resistance and X the reactance. One value of Z is obtained for each FO cycle. Using physical models, resistances from 0.1 to 40 cm $H_2O/l/s$ were measured. In the midrange, coefficients of variation were < 1%; at the high and low extremes, coefficients of variation were < 6%. Measurements of R_{rs} were also performed on human subjects and correlated well with values of airway resistance measured with a body plethysmograph (r = 0.70).

(Supported in part by the Parker B. Francis Foundation)

EFFECT OF VAGAL PULMONARY AFFERENT DISCHARGE ON EXPIRATORY TIME. E.J. Zuperku, F.A. Hopp*, and J.P. Kampine. Med. Col. of Wisconsin and Wood VA Ctr., Milwaukee, WI 53193

The effects of pulmonary afferent (PA) discharge (present only during T_E) on the control of T_E was studied in anesthetized (Nembutal, Halothane) paralyzed, open-chested vagotomized dogs. Electrical pulse trains of various frequencies, widths, and delays were used to stimulate the largest A fibers in the central end of the vagus nerve. The phrenic neurogram, $\overline{PNG}(t)$, was used to measure T_I and T_E and to synchronize the stimulator. Mechanical ventilation had no noticable effect on T_I and T_E and it was possible to maintain blood gases constent independent of breathing pattern. To establish a non-vagotomized control breathing pattern and to minimize hysteretic effects, respiratory center was paced by a stimulus pattern which consistently terminated T_I ($T_I<T_{IO}$) and consistently prolonged T_E ($T_E>T_{EO}$). Single breath test patterns were separated from each other by 4 to 6 control breaths. The study shows that: 1) For trains lasting throughout T_E, the T_E vs. stim. freq. plot has a hyperbolic shape (higher freq. markedly increase T_E) which is asymptotic to the frequency which causes apnea. 2) T_E is a linear function of train width {$T_{EO}<W<T_E$ max (f)}. 3) The delay time from end-of-train to next breath, (T_{Id}), is constant and independant of T_E. 4) T_{Id} increases with train freq. 6) Pulse trains early in T_E ($W<T_{EO}$) produce small increases in T_E. These studies suggest that PA activity during T_E is a sensitive regulator of T_E in the dog. (Supported by the VA).

CARDIOVASCULAR EFFECTS OF VOLUME LOADING IN TRANQUILIZED BABOONS. M. Zimpfer*, W.T. Manders* and S.F. Vatner, Dept. of of Med., Harvard Med. Sch. and Peter Bent Brigham Hosp., Boston, MA 02116

Volume loading elicits marked reflex tachycardia (Bainbridge reflex) in lower species, but the extent to which this occurs in primates is controversial. The goal of this study was to determine the extent to which rapid volume loading (1000 ml saline) increased heart rate and decreased regional vascular resistances. Accordingly, 4 baboons were instrumented with catheters in the aorta and left atrium and Doppler or electromagnetic flow probes on the mesenteric, renal, and iliac arteries. Several weeks after operation the animals were tranquilized with Ketamine, 5 mg/kg. Volume loading increased left atrial pressure by 20.0±0.1 from 7.6±0.7 mmHg, heart rate by 33±4 from 92±4 beats/min, and blood flows to all beds, while mean arterial pressure did not change significantly, and resistance fell in the mesenteric (52±5%), renal (40±8%) and iliac (63±3%) beds. Thus, in the tranquilized baboon, volume loading elicits striking cardiovascular effects, characterized by significant tachycardia and intense peripheral vasodilation.

VASCULAR AND RESPIRATORY EFFECTS OF SERATONIN (5HT) IN CONSCIOUS AND ANESTHETIZED DOGS. Irving H. Zucker and Kurtis G. Cornish, Dept. of Physiol. and Biophysics., Univ. of Neb., College of Medicine, Omaha, Nebraska 68105.

A comparison of hypotensive, hypertensive, chronotropic and respiratory effects of left atrial or left ventricular injections of 5HT(50-200 µg) was undertaken in 8 conscious (CS) dogs, in 13 pentobarbital or chloralose anesthetized closed chest (ACC) dogs and in 9 anesthetized open chest dogs (AOC). There were no differences in left atrial or left ventricular injections. The response in the CS dogs was an initial respiratory stimulation followed by hypotension and then a later hypertension. Concomitant with hypotension was a bradycardia followed by tachycardia. The changes in blood pressure and heart rate are shown in the table. In AOC dogs the hypertensive response was accompanied by a significant increase in renal sympathetic nerve activity. Right vagotomy did not attenuate the response. Left vagotomy attenuated but did not abolish the response. Atropine abolished the initial hypotension. It is concluded that the response to 5HT is primarily a hypotensive, bradycardiac response followed by a small hypertension in the conscious dog. Supported by NIH Gr.#HL22594A.

Change in Blood Pressure (mm Hg)

CS		ACC		AOC	
HYPOT.	HYPERT.	HYPOT.	HYPERT.	HYPOT.	HYPERT.
22.6±1.9	21.5±2.7	8.3±1.8	32.7±5.2	0±0	67.2±5.5

Change in Heart Rate (BPM)

BRADY	TACHY	BRADY	TACHY	BRADY	TACHY
58.5±3.9	23.3±3.9	46.6±6.5	18.3±5.5	26.5±6.7	40.6±6.7

SPACE ENVIRONMENT WORK SHOP

The following ten abstracts result from a series of mini-seminars presented by the National Aeronautics and Space Administration by invitation of the Commission on Gravitational Physiology.

NUTRITION AND MUSCULOSKELETAL METABOLISM IN SPACE. Steven I. Altchuler, NASA-Johnson Space Center, Houston, TX 77058.

The results of the Skylab bone and muscle experiments are reported. Skylab consisted of 3 flights up to 84 days long. The data obtained were used to predict the effects of long-term exposure to weightlessness upon the skeleton.

Metabolic balance studies were performed on calcium (Ca), phosphorous(P04), nitrogen, and several other nutritional components. The mineral mass of the calcaneous and the forearm were measured by -ray absorption. At 1 week intervals, serum samples were collected for Ca, P04, parathormone (PTH), and protein analysis.

Space flight induced a Ca loss. The overall loss accelerated for 50 mg/day at 1 week to 300 mg/day after 12 weeks. Hypercalciuria increased to a plateau at 4 weeks; fecal Ca losses increased throughout the missions. Alterations in bone mineral content were seen. Losses from the calcaneous were slightly correlated with total Ca balance. No correlation was found in the forearm. These results are similar to those found in bedrest.

Present research attempts to define exactly what changes occur in the skeleton during space flight or bedrest. Various treatments for reducing the Ca loss are being studied: exercise, diphosphonates, electromagnetic fields; dietary changes, and statically-applied longitudinal forces. Possible areas of Earth medicine that may be affected by this research include fracture healing, disuse and senile osteoporosis, and treatment of skeletal deformities.

LIFE SCIENCES EQUIPMENT AND FACILITIES CONCEPTS. William H. Bush, Jr. NASA-Johnson Space Center, Houston, TX 77058.

To support investigators who have approved experiments for Shuttle Spacelab missions, the Life Sciences Experiments Program will provide flight-worthy general purpose Life Science Laboratory Equipment (LSLE). This LSLE will be developed after analysis of all experiment proposals to identify common equipment which can be used to support more than one experiment and used on more than one mission. After the experimenter has been selected, available LSLE equipment will be provided to the investigator to incorporate in his experiment development. General purpose items such as mass measuring devices, inflight blood collection systems specimen holding facilities, refrigerators and freezers, etc. are typical examples of this type of equipment.

After the investigator has developed his experiment, he will forward the completed hardware to the development center: Ames Research Center generally for animal and biological investigations or to Johnson Space Center for human investigations. Upon completion of the development center activity all experiments and related LSLE equipment will be forwarded to JSC Life Sciences Integration Facility where the total payload will be assembled and combined with additional LSLE and flight equipment. This flight equipment includes racks, data system interface units, power units, etc. Final tests will be performed with discipline oriented payload specialist training, final science testing and preparation for shipment to the Kennedy Space Center.

NASA PRINCIPAL INVESTIGATORS INTERFACES FLIGHT OPPORTUNITIES/ ADVANCED MISSIONS. William E. Feddersen, NASA-Johnson Space Center, Houston, TX 77058.

The NASA is engaged in developing a series of physiological experiments selected for flight on Spacelab I. These experiments proposed by Investigators from Universities and the Johnson Space Center are part of an overall complement of life sciences experiments that includes investigators from Europe and the United States. The role of Investigator in the Space Shuttle Program has expanded from previous manned space flight programs. The Investigator Working ing Group is composed of Principal Investigators who are responsible for establishing recommendations for time-sharing, selection of Payload Specialists, and resolving operational conflicts among experiments.

Flight opportunities are available on Spacelab in the early 1980's. An Announcement of Opportunities for Life Sciences Experiments was issued and responses were received in July 1978. These proposals are currently undergoing scientific and technical evaluation. From these proposals experiments will be selected for definitive studies and later assignment to specific Spacelab missions. A series of Spacelab Mission Simulations have been conducted at NASA in preparation for future life sciences Spacelab flights.

Advanced missions and future life sciences programs are being studied and include such activities as orbiting space stations, large construction platforms, and space solar power stations.

NEUROPHYSIOLOGY. Jerry L. Homick, NASA-Johnson Space Center, Houston, TX 77058.

A description of the Neurophysiology Research Program at the Johnson Space Center will focus on the issues of neurosensory adaptation to weightless space flight and observed problems, primary space motion sickness, attendant with such adaptation. A general overview of past space flight findings in this area, as well as current and planned research activities will be presented.

The presentation will highlight pre-, in-, and post-flight vestibular system related data obtained on the crews of the three long duration Skylab missions conducted during the early 1970's. The implications of the space motion sickness syndrome for the operational success of the upcoming Space Shuttle flights will be addressed. A broad based program of basic and applied research which seeks to elucidate the causes of, and develop means for the prediction, prevention and treatment of this syndrome is in progress. Certain key elements of these current research programs will be described in detail with data and pictorial information. Also, new and improved techniques for the measurement and analysis of vestibular system related responses will be described in summary fashion.

HEMATOLOGY STUDIES DURING EXTENDED MANNED SPACE FLIGHT. Stephen L. Kimzey, NASA-Johnson Space Center, Houston, TX 77058.

Consistent reductions in circulating red blood cell mass have been observed during all American and Russian space flights since the Gemini missions.

Initially it appeared that this resulted from the near 100% oxygen atmosphere of spacecraft. Similar red cell changes were observed in a chamber study using an atmosphere identical to Gemini and later Apollo spacecraft. Studies also revealed subtle changes in red cell membrane integrity consistent with the concept at mild oxygen toxicity result ing in intravascular hemolysis.

Data from Skylab do not support this concept. Apparently another factor (weightlessness?) in space flight suppresses red cell production.

Several factors suggest a complex relationship between red cell loss and duration of weightlessness. A reduced plasma volume and changes in the function and structure of red blood cells were also observed.

This review will address questions about blood volume regulation during spaceflight and causes of its apparent failure.

BIOCHEMICAL PROCESSES DURING EXTENDED MANNED SPACE FLIGHT. Carolyn S. Leach, NASA-Johnson Space Center, Houston, TX 77058.

Skylab offered the first opportunity to observe biochemical changes caused by 84 days of weightless space flight. A series of biochemical investigations were undertaken as part of the Skylab Program. These included blood sampling as well as metabolic data under controlled dietary conditions inflight. Several hormonal and other biochemical changes in the crewmen occurred.

Changes reported are consistent with the hypothesis that an increase in thoracic blood volume occurs upon entry into weightlessness. This acts upon the stretch receptors in the walls of the great vessels and the atria. This stimulation is interpreted as volume expansion, which then causes water and electrolyte losses. These losses cause a reduction in blood volume and an increase in renin and aldosterone secretion. Fluid balance is thus re-established at a new level appropriate to weightlessness.

Such adaptation does not occur with calcium and nitrogen. These constituents of bone and muscle leave the body faster than they can be replenished. This new homeostatic set point in metabolism of electrolytes and water stresses the crewman, which is reflected in increased levels of cortisol and other endocrine parameters.

Future research is aimed at determining whether this depletion of man's biochemical reserves is tolerable over a prolonged period of time.

SPACE LIFE SCIENCES ARCHIVAL LIBRARY. John A. Mason. NASA-Johnson Space Center, Houston, TX 77058.

The Space Life Sciences Archival Library (SLSAL) was conceived and developed to disseminate to the biomedical scientific community, for the purpose of research and investigation, all life sciences factual information relevant to the study of manned space flight. The SLSAL serves as the primary depository for life sciences biomedical and bioengineering information derived from manned space flight programs.

The library collection is multi-media in scope, reflecting the total complement of information and data media that have been generated during a space program or manned mission. The collection is characterized by five basic types of information sources: (1) Life sciences data, raw and processed, obtained during space flight and related biomedical ground testing. (2) Technical and analytical information aiding in the production, support, and interpretation of life sciences data. (3) Written or published analyses and interpretations of life sciences data by a research scientist. (4) Technical information related to the design, maintenance, and operation of life sciences equipment used during a manned mission or ground-based biomedical tests. (5) Program documentation citing the objectives, requirements, management, and evaluation of a space program or manned mission. The Archival Library facility and services are available to all persons and are free. The facility and its data bank can be accessed by phone, letter, and computer terminal.

BIOMEDICAL APPLICATIONS. Dennis R. Morrison, NASA-Johnson Space Center, Houston, TX 77058.

The Space Bioprocessing Program is exploring the novel effects of weightlessness (no buoyancy or sedimentation or convection) on such processes as electrophoresis and suspension cell culture which may have industrial applications.

Separations: Studies have shown that a substantial increase in electrophoresis resolution and/or throughput is possible in the absence of gravity induced sedimentation or thermal convection. Current research is emphasizing the isolation of pancreatic cells, pituitary, cells kidney cells, and purification of medically important proteins such as antihemaphilic factor (AHF).

Suspension Culture Biosynthesis: Weightlessness allows unique behavior of fluids and suspensions. Some cells have demonstated increased growth rates, cell size, and metabolism under weightless conditions. Preliminary studies have indicated that liquid suspension cell cultures, under microgravity conditions, may avoid some of the technical problems of current ground-based biosynthesis systems. Living cells attached to microcarriers would not sediment nor would oxygen bubbles rise to produce foam. Current studies are exploring new possibilities for synthesizing high value biologicals using suspension cell culture systems which are not plagued by sedimentation nor other gravity induced problems.

ENVIRONMENTAL PARAMETERS OF SPACE. Michael A. Reynolds, NASA-Johnson Space Center, Houston, TX 77058.

Many potential users of Space Shuttle whose research could benefit from near zero-g environment are not equipped with the required intuitive and quantitative understanding of the near zero-g environment necessary to design their experiment.

With this in mind we will give a qualitative presentation of some physical phenomena emphasizing behavior of liquids (surface tension and mechanical stability). Surface tension will be shown as a dominant force in fluid behavior. Other phenomena that will be discussed are friction and multiphase systems. The handling and contamination of fluids will also be discussed.

CELL BIOLOGY. Gerald R. Taylor, NASA-Johnson Space Center, Houston, TX 77058.

A summary of the important investigations of cell systems in space will be displayed. Cell studies originated with measurements of the survival rates of fungal spores aboard the high altitude balloon flight of Explorer 2 in 1935. In the ensuing years, the effect on cell systems of irradiation vacuum, changing periodicities, and reduced gravitational force have been studied in space. Special emphasis will be placed on the bacteriophage induction studies and high-altitude microbial captures conducted by the Soviet Union, the radiation response experiments performed by the Federal Republic of Germany, and several studies conducted by American scientists. An analysis of the composite results will be presented with comments on fertile areas for future research.

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for

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15-19 October 1979

New Orleans, Louisiana

Group space has been reserved on the following regularly-scheduled flights. All fares and schedules are current as of 1 March 1979 and are subject to change.

Groups originating in Dallas, Denver, and St. Louis require a minimum of 10 persons to operate. Group flights from Detroit, Miami, Cleveland, Pittsburgh, Los Angeles, and San Francisco must have at least 20 persons participating. And groups originating in Boston, Chicago, New York, and Washington require 40 persons traveling together. Additionally, Boston, Chicago, New York, and Washington participants must be members of the American Physiological Society (spouse, dependent children, or parents living in the same household as the member may also accompany the member) in order to participate in the group flight from each of these respective cities.

A deposit of $50 per person is required to secure reservations on any group flight. Your confirmation will include your final invoice for which payment is due on or before 14 August 1979. No subsequent invoice will be sent unless there is a change in the airfare for your particular flight. NOTE: Any reservations postmarked after 14 August 1979 must be accompanied by full prepayment in order to be accepted. Absolutely no reservations can be made after 21 September 1979. Tickets will be mailed to you approximately three weeks prior to departure--provided that your payment in full has been received. Reservations are accepted on a first-come, first-served basis (no telephone reservations can be accepted.)

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Group #1: Boston				PRICE=$207	(Normal Fare=$284)
Boston to New Orleans	Delta	# 129	14 Oct	Lv. 4:03PM/Ar. 7:02PM	
New Orleans to New York	Delta	# 416	19 Oct	Lv. 5:55PM/Ar. 9:23PM	
New York to Boston	Delta	# 332	19 Oct	Lv.10:55PM/Ar.11:39PM	
Group #2: Chicago (O'Hare)				PRICE=$164	(Normal Fare=$198)
O'Hare to New Orleans	Delta	# 109	14 Oct	Lv. 3:08PM/Ar. 5:10PM	
New Orleans to O'Hare	Delta	# 514	19 Oct	Lv. 6:00PM/Ar. 8:03PM	
Group #3: Denver				PRICE=$189	(Normal Fare=$236)
Denver to New Orleans	Texas	# 939	14 Oct	Lv. 2:30PM/Ar. 6:59PM	
New Orleans to Denver	Texas	# 960	19 Oct	Lv. 7:27PM/Ar.10:17PM	
Group #4: Dallas				PRICE=$104	(Normal Fare=$134)
Dallas to New Orleans	Delta	# 628	14 Oct	Lv. 3:30PM/Ar. 4:34PM	
New Orleans to Dallas	Delta	# 541	19 Oct	Lv. 7:15PM/Ar. 8:27PM	
Group #5: Los Angeles				PRICE=$231	(Normal Fare=$330)
Los Angeles to New Orleans	National	# 152	14 Oct	Lv.11:45AM/Ar. 5:01PM	
New Orleans to Los Angeles	National	# 35	19 Oct	Lv. 7:05PM/Ar. 8:56PM	
Group #6: New York/LaGuardia				PRICE=$185	(Normal Fare=$254)
LaGuardia to New Orleans	Delta	# 535	14 Oct	Lv.12:25PM/Ar. 2:18PM	
New Orleans to LaGuardia	Delta	# 416	19 Oct	Lv. 5:55PM/Ar. 9:23PM	
Group #7: St. Louis				PRICE=$125	(Normal Fare=$162)
St. Louis to New Orleans	Delta	#1765	14 Oct	Lv. 5:21PM/Ar. 6:50PM	
New Orleans to St. Louis	Delta	#1756	19 Oct	Lv. 7:35PM/Ar. 9:05PM	
Group #8: San Francisco				PRICE=$258	(Normal Fare=$368)
San Francisco-New Orleans	National	# 46	14 Oct	Lv.12:25PM/Ar. 5:55PM	
New Orleans-San Francisco	National	# 73	19 Oct	Lv. 6:55PM/Ar. 8:59PM	
Group #9: Baltimore				PRICE=$160	(Normal Fare=$222)
Baltimore-New Orleans	Delta	# 129	14 Oct	Lv. 5:35PM/Ar. 7:02PM	
New Orleans-Baltimore	Eastern	# 126	19 Oct	Lv. 6:45PM/Ar.11:15PM	
Group #10: Detroit				PRICE=$144	(Normal Fare=$214)
Detroit to New Orleans	Delta	#1749	14 Oct	Lv. 1:30PM/Ar. 3:52PM	
New Orleans to Detroit	Delta	# 846	19 Oct	Lv. 5:58PM/Ar. 9:00PM	
Group #11: Pittsburgh				PRICE=$148	(Normal Fare=$212)
Pittsburgh-New Orleans	United	# 231	14 Oct	Lv. 3:55PM/Ar. 5:20PM	
New Orleans-Pittsburgh	United	# 79	19 Oct	Lv. 6:10PM/Ar. 9:14PM	
Group #12: Cleveland				PRICE=$148	(Normal Fare=$212)
Cleveland-New Orleans	United	# 297	14 Oct	Lv. 6:40PM/Ar. 8:08PM	
New Orleans-Cleveland	United	# 79	19 Oct	Lv. 6:10PM/Ar.10:31PM	
Group #13: Miami				PRICE=$120	(Normal Fare=$172)
Miami to New Orleans	National	# 25	14 Oct	Lv. 5:10PM/Ar. 6:01PM	
New Orleans to Miami	National	# 196	19 Oct	Lv. 6:50PM/Ar. 9:19PM	

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Chevy Chase Travel reserves the right to change any or all flight numbers, flight times, and/or departure airports in order to preserve the greatest conveniece for the greatest number of participants. Due to frequent airline schedule changes, the above changes may be necessary in order to provide the group flights at acceptable times.

CANCELLATION AND REFUND: Full refund (minus a $5 per person handling fee) will be made up to twenty-one (21) days prior to departure, after which time a 25% (plus $5 per ticket handling fee) cancellation penalty will be assessed on the total roundtrip airfare for flights originating in Boston, Chicago, New York, and Washington. For Los Angeles, San Francisco, Miami, Detroit, Pittsburgh, and Cleveland full refund (less $5) up to seven (7) days prior, subsequently a 10% (plus $5) penalty will prevail. Full refund at any time for Denver, Dallas, and St. Louis (less $5). No refund at all for any group within 21 days prior to departure if cancellation results in an insufficient number of persons to operate the group.

*I agree to the terms noted and accept for all persons listed on reverse.

SIGNATURE_____ DATE_____

XXVIII
INTERNATIONAL CONGRESS OF PHYSIOLOGICAL SCIENCES

WELCOME TO BUDAPEST

The Hungarian Physiological Society extends a heartfelt invitation to all scientists working in the physiological sciences and to their friends to attend the XXVIII International Congress of Physiological Sciences to be held in Budapest, Hungary, July 13–19, 1980. Since 1889, the first International Physiological Congress in Basle, physiologists the world over have assembled almost every three years. This is the first occasion that the International Congress of Physiological Sciences is being organized in Hungary. We sincerely hope that this large meeting will once again foster the understanding and friendly relations amongst research workers engaged in the various areas of physiology.

Budapest – with more than two million inhabitants – is one of the most beautifully situated cities in the world. The natural ambience and the relation between hills and lowlands that make up the city, truly reflect the whole country. Budapest is the political, economic and cultural centre of Hungary – and at the same time is a major attraction for tourists.

A large variety of interesting monuments recall the historic past: remains from the Roman era still exist at Aquincum, while baths and sepulchral chapels have survived in Buda from the 150 year Turkish rule. And, of course, there are many buildings in the classic 19th century style. The Buda Castle Hill District is an open air museum, reflecting the history of the Capital and the whole country, for it includes monuments from almost every period of Hungarian history.

The organizers of the Congress will do their best to provide an interesting programme and memorable experiences for the participants of the Congress during their stay in Budapest.

KÁLMÁN LISSÁK
President of the Congres

XXVIII
INTERNATIONAL CONGRESS OF PHYSIOLOGICAL SCIENCES

The XXVIII International Congress of Physiological Sciences will be held under the high patronage of

PÁL LOSONCZI

the President of the Presidential Council of the Hungarian People's Republic

under the patronage of

EMIL SCHULTHEISZ

the Minister of Health of the Hungarian People's Republic, and

JÁNOS SZENTÁGOTHAI

the President of the Hungarian Academy of Sciences

HONORARY COMMITTEE

The Minister of Foreign Affairs
The Minister of Culture
The Minister of Education
The Minister of Heavy Industries
The Minister of Home Trade
The President of the State Office for Technical Development
Mayor of the City Council of Budapest
General Secretary of the Hungarian Academy of Sciences
Secretary of the Science Policy Committee
President of the Federation of Hungarian Medical Societies
Rector of the Semmelweis University Medical School
Rector of the Eötvös Lóránd University
Rector of the University of Veterinary Science

INTERNATIONAL UNION OF PHYSIOLOGICAL SCIENCES

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E. NEIL (United Kingdom)

Vice-presidents:

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NATALIA P. BECHTEREVA (U.S.S.R.)

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INTERNATIONAL SCIENTIFIC COMMITTEE

NATALIA P. BECHTEREVA (U.S.S.R.)
P.O. BISHOP (Australia)
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Y. KATSUKI (Japan)

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J. SALÁNKI
E. STARK
E. VARGA

NATIONAL PROGRAMME COMMITTEE

Chairman:

L. TAKÁCS

Co-chairman:

G. PETHES

Chairmen of the sections:

1. J. SALÁNKI
2. E. VARGA
3. ZSUZSA HOLLÁN
   G. GÁRDOS
4. A. G. B. KOVÁCH
5. L. HUTÁS
6. L. TAKÁCS
7. T. GÁTI
8. E. STARK
9. B. FLERKÓ
10. J. SZENTÁGOTHAI
    M. PALKOVITS
11. E. GRASTYÁN
12. G. ÁDÁM
13. F. OBÁL
14. G. PETHES

LOCAL ARRANGEMENT COMMITTEE

Chairman:

T. GÁTI

Co-chairman:

L. SZOLLÁR

MOTESZ; OFFICE FOR CONFERENCE ORGANIZATION

Secretary:

ÁGNES RUBÁNYI

Members:

ERIKA HOLLÓS
JOHANNA KÜNNLE

GENERAL INFORMATION

1. CONGRESS VENUE

The Premises of the Budapest International Fair Centre of Hungexpo (Budapest X., Dobi István út 21.).

2. REGISTRATION

Registration Forms A (two cardboard copies) are enclosed.* They should be completed and mailed no later than **December 10, 1979** (as per postmark) to the CONGRESS SECRETARIAT, Budapest POB 370, H-1445 – Hungary.

This is an essential condition for your participation in the Congress.

The payment of registration fees and other items including hotel deposit shown on Order Form D enclosed* with this Second Announcement should be effected by means of a cheque drawn in favour of IBUSZ Rcs. No. 551 001 and sent to the CONGRESS SECRETARIAT (Budapest POB. 370, H-1445 – Hungary).

If you should effect a bank transfer, make it in favour of Account No. IBUSZ Rcs. 551 001 at the Hungarian National Bank, Budapest V., Szabadság tér 8. H-1054 – Hungary and please let us have a copy of the bank draft.

3. REGISTRATION FEES

Active Members $ 150., U.S.	– including the Programme, the Volume of Abstracts, the Directory, the Get-together Party and the Congress Reception.
Affiliates $ 100., U.S.	– including Associates' programme, the Get-together Party and the Congress Reception.

4. INCREASED RATES FOR REGISTRATIONS RECEIVED WITH A POSTMARK AFTER DECEMBER 10, 1979

Active Members $ 170., U.S.
Affiliates $ 120., U.S.

5. FINANCIAL AID

There will be a limited number of modest grants available which will be reserved mostly for young physiologists. Only those active members who have submitted an abstract and have paid the registration fee postmarked no later than **December 10, 1979** can be financially supported. Notification of acceptance or rejection of Financial Aid Application (Form C)* will be forwarded on the Programme Confirmation Return Card by March 1980.

*Forms referred to are in a Supplemental Packet - See Request Form provided on page 169.

6. REGISTRATION HOURS AND OFFICE

The Registration and Information Office will be located in Building "K" of the Congress Centre and will be open from Saturday, July 12, 1980 from 11:00 A.M. until 7:00 P.M., and every subsequent day from 8:30 A.M. until 6:00 P.M. during the Congress. Participants are requested to register in person immediately after arrival, if possible on Saturday, July 12, 1980, at the above office. Phone number of the Registration Office during the Congress: 573–555.

7. BADGES

In addition to being a means of identifying the participants, the badge is your admission card to scientific sessions and social events. Only those wearing their badges will be admitted.

8. MAIL AND TELEPHONE SERVICE

A post office will be set up in Building "K" next to the Registration Office.

9. RECEIPT OF MAIL

Prior to the Congress, participants' mail should be sent to the CONGRESS SECRETARIAT, Budapest, POB 370, H-1445 – Hungary. *During* the Congress, to the CONGRESS CENTRE, c/o HUNGEXPO, Budapest, POB 44, H-1441, Hungary, or to the SECRETARIAT.

10. CANCELLATION

Should intending participants cancel their registration, all fees will be returned on application up to March 31, 1980, subject to a deduction of 20 per cent. No fees will be returned after this deadline.

11. MEALS, REFRESHMENTS, SNACKS

Light meals and refreshments will be available in various cafeterias and restaurants in the Congress Centre. Lunch tickets ($5.00 per day) are to be paid in advance (see enclosed Order Form D)*. Participants are advised to order lunch in advance.

12. ACCOMMODATION

The Organizing Committee entrusted the IBUSZ Touring Company Ltd, Congress Department (Budapest, Felszabadulás tér 1, H-1053, Hungary) to provide accommodation for the participants in hotels of various categories, as well as in students' hostels (see enclosed Order Form D)*. Reservations can be made only upon receiving the hotel deposit, no later than **December 10, 1979.**

13. CAMPING SITES

Camping sites, which are rather crowded in summer, are available in the vicinity of Budapest. For details please make direct contact with the Hungarian Camping and Caravanning Club, Budapest POB 224, H-1444, Hungary – before **November 30, 1979.**

14. DRESS

will be informal for all occasions.

15. ELECTRIC CURRENT

Line voltage is 220 V, 50 Hz

*Forms referred to are in a Supplemental Packet - See Request Form provided on page 169.

16. WEATHER

The weather in July is generally pleasant and sunny. The average temperature ranges from 24 to 28°C.

17. EXCHANGE OF CURRENCY

Foreign currency can be brought into Hungary without restriction. Hungarian currency up to a total amount of 100.–Ft in coins can be brought into the country and taken out. An exchange office will be set up in the Registration Office.

18. VISAS

can be ensured in advance from the Hungarian Embassies or can be obtained at Ferihegy Airport and highway border crossings. *Visas cannot be obtained at the railway border stations.*

ADVICE TO THE PARTICIPANTS FOR APPLICATION OF ENTRY VISA

Due to the expected great number of participants – in order to avoid an unnecessary loss of time at the airport and traffic jam at road frontier crossings – participants are advised to apply for their entry visa in advance from the local Hungarian Embassy or Representation, respectively.

Participants coming from countries where there is no Hungarian Representation, may apply for entry visa at any Hungarian Embassy or Representation, respectively.

If participants wish to receive their entry visa at another place than with which they filed the application, they are requested to state the Hungarian Embassy or Representation where it would be easiest for them to collect their visas. The granting of an entry visa for participants from countries where there is no Hungarian Representation, requires a longer time, therefore participants are asked to file their visa application and to enclose a letter of invitation no later than March 31, 1980.

19. TRAVEL

For information and travel arrangements please contact the nearest MALÉV Hungarian Airlines office. A shuttle bus service will be provided for transportation from Ferihegy Airport to the centre. A Congress reception desk will be located at the Airport.

20. RENT A CAR

service is at your disposal at Ferihegy Airport and at all hotels.

21. LOCAL TRANSPORT IN BUDAPEST AND PARKING

In Budapest trams and buses operate without conductors. Tickets must be purchased in advance at tobacco shops "Dohánybolt" and Metro stops – blue tickets for buses (1.50 Ft) and yellow tickets for trams (1.–Ft). Tickets are valid for one journey only and must be punched inside the vehicles. For the Metro a one forint coin is to be inserted into the slot at the barrier. The Congress Centre can be reached from the terminal "Örs Vezér tér" of the Metro line by bus 100.

For participants in the Congress a weekly ticket valid from July 13 to 19, 1980 for an *unlimited* number of journeys on buses, trams, electric buses, the metro, and the suburban railway within the limits of Budapest will be provided. Tickets may be reserved and paid in advance (see the enclosed Order Form D).*

There is a parking lot for participants at the Congress Centre. In Hungary drivers are not supposed to drink alcoholic beverages, even a glass of wine; fines are high and drinking may entail court procedure.

*Forms referred to are in a Supplemental Packet - See Request Form provided on page 169.

22. SHOPPING HOURS

are generally 10:00 A.M. to 6:00 P.M. on weekdays, with shorter hours on Saturday.

23. EXHIBITION AND ADVERTISEMENTS

An exhibition of pharmaceutical products and medical scientific instruments related to the topics of the Congress is to be held during the meeting. The Organizing Committee entrusted the HUNGEXPO Hungarian Foreign Trade Office for Fairs and Publicity (Budapest, POB 44, H-1441 Hungary, Mrs. J. Győrffy or Mrs. J. Pártos) with the organization of the exhibition. The exhibition will take place at the Congress area.

Advertisements can be placed in the Catalogue for Exhibitors.

For information please contact HUNGEXPO or the MOTESZ Congress Bureau (Budapest, POB 32, H-1361-Hungary).

24. SOCIAL PROGRAMME

included in the registration fee of active members and affiliates

Sunday, July 13, 1980

8:00 P.M. Get-together Party at the Congress Centre

Tuesday, July 15, 1980

7:00 P.M. Reception in the Premises of the Congress Centre

Additional social programmes not included in the registration fee are listed in Order Form D.* Applications for tickets with the appropriate remittance, should be made on Order Form D.*

25. ASSOCIATES' PROGRAMME

included in the registration fee of affiliates

- Sightseeing coach tour of Budapest
- Visit to Szentendre, an old, charming town situated 20 km north of Budapest on the right bank of the Danube
- Journey to the Buda Hills
- Visit to the Castle Hill District including the Semmelweis Medical History Museum and the Old Pharmacy called the "Arany Sas" as well as the National Gallery in the Royal Castle
- A full and exciting tour of Parliament and the Museums of Budapest including the National Museum, the Museum of Fine Arts and the Ethnographic Museum followed by a walk on Margaret Island and refreshments.

Coaches with the above destinations will run periodically from Monday, July 14, 1980 until Friday, July 18, 1980.

The exact time of departure of the buses as well as the daily programme will be marked on the Associates' programme ticket.

*Forms referred to are in a Supplemental Packet - See Request Form provided on page 169.

SCIENTIFIC PROGRAMME

1. OPENING AND CLOSING SESSIONS

The Scientific Programme of the XXVIII International Congress of Physiological Sciences will begin in the afternoon on Sunday, July 13, 1980, with a Plenary Session as part of the opening ceremony in the Convention Hall at the Congress Centre.

The Congress will close at about 11:00 A.M. on Saturday, July 19, 1980, with a final Plenary Session.

2. STRUCTURE OF THE SCIENTIFIC PROGRAMME

The Scientific Programme of the Congress will be built around 14 Sections covering the major fields of Physiological Sciences (see Sections and Topic Category List).

The programme of each Section extends from 9:00 A.M. to 12:30 P.M. and from 2:00 to 5:30 P.M. on Monday–Friday and from 9:00 to 11:00 A.M. on Saturday and will include Invited Lectures, Congress Symposia and Free Communications selected either as posters or slide (oral) presentations.

Organizers of the Satellite Symposia will have the opportunity to introduce or summarize their Symposia in the Section Programme on Monday afternoon and Saturday morning.

A Teaching Workshop as well as exhibition of teaching materials, biomedical laboratory equipment, scientific publications, etc. will also be arranged.

2.1 INVITED LECTURES

About 70 scientists are being invited to deliver 60 minute lectures incorporated into the programme of the Sections. These lectures will cover recent advances in special fields of Physiology, and also provide an opportunity to the Invited Lecturers to present their contributions to that particular field (to be listed in the Programme).

2.2 CONGRESS SYMPOSIA

About 120 Congress Symposia will be held throughout the week, every day, as part of the Section programmes. At each Symposium, after an introduction by the Chairman, four or five Invited Speakers will deliver 20 minute oral presentations, each followed by 10 minute discussions. Four or five free communications (10 minute oral presentation plus 5 minute discussion) selected by the Programme Committee will complete the Symposium programme (see Tentative List of Congress Symposia).

A Congress Symposium on the *History of Physiology* will be organized by I. Hutás. Members interested in the Symposium are requested to contact I. Hutás (National Korányi Institute for TBC and Pulmonology, Budapest, Pihenő út 1. H-1529, Hungary) for further information.

2.3. SHORT PRESENTATIONS

The Programme Committee will select and group the volunteer papers into appropriate sessions and schedule them for poster or slide (oral) presentation, taking the authors' preference into consideration as far as possible (to be numbered and listed in the Programme).

2.4. TEACHING WORKSHOP AND EXHIBITION

This session will be organized by I. Forgács. Members who wish to participate in the workshop and exhibitors are requested to contact the Congress Secretariat for further information.

2.5. SCIENTIFIC FILM PRESENTATIONS

Members intending to show a scientific film should write to the Congress Secretariat by **December 31, 1979**, and provide the following information:

- title and author(s);
- short description of content;
- time needed for showing;
- with or without sound;
- size of the film (16 or 35 mm).

Intentions are to organize an independent film session.

3. LANGUAGE

Each participant may use the language of his/her choice during the presentations. However, since no simultaneous translation service will be available authors are encouraged to choose a language reaching the largest possible audience. All authors are requested to submit their abstracts in English.

4. SUBMISSION OF ABSTRACTS

Abstracts of Short Presentations have to be submitted on Abstract Form B/1 enclosed*with this Announcement. Abstract Form B/2 with two abstract pages is available for the Chairmen and Invited Speakers of the Congress Symposia and Abstract Form B/2 with four abstract pages for Invited Lecturers. A spare copy of the Form is attached. Authors are requested to follow carefully the instructions for the preparation of abstracts outlined in the Abstract Form.

Each Active Member is entitled to submit one abstract for Short Presentation. Invited Lecturers and Invited Speakers may not submit abstracts for Short Presentations. No limit is imposed on co-authorship of additional communications.

Abstracts will be accepted only from those who have paid the Registration Fee for Active Membership ($150) by **December 31, 1979 (December 10, 1979**, as per postmark).

In order to be accepted for programming the original abstract with 6 copies and the related forms indicated on the Abstract Form have to be postmarked on or before **December 10, 1979.**

Notices of acceptance or rejection and programme confirmation will be forwarded by March 1980.

5. PUBLICATIONS

Abstracts of poster and slide presentations will be published in the Proceedings of the IUPS, Vol. XIV., together with abstracts of Invited Lectures and Congress Symposia papers.

The following publications will be distributed to Active Members upon registration at the Congress:

- Programme
- Volume of Abstracts (Invited Lectures, Congress Symposia, Free Communications)
- Directory of Participants.

6. INSTRUCTIONS FOR POSTER PRESENTATION

Mount your poster on the board assigned to you during the 30 minutes immediately preceding your scheduled poster session.

The poster board surface area is approximately 1.2 m high and 1.8 m wide.

*Forms referred to are in a Supplemental Packet - See Request Form provided on page 169.

Prepare for the top of your poster space a label indicating the programme number of your abstract, its title, authors, city and country, to facilitate ready identification of your presentation. The lettering for this heading should be no smaller than 5 cm high. All illustrations must be prepared beforehand. Your illustrations must be readable from distances of about 2 m. Major headings should be in heavy lettering at least 2 cm high; minor lettering should be at least 0.5 cm high. Simple use of color can add emphasis. Keep illustrative material simple.

It is advisable to have on hand sketch paper and two felt marking pens. Please do not write or draw on the Poster Boards.

The posters must be removed within 30 minutes after the closing of the session.

A poster assistant will help you with any information or technical aid you may need.

7. INSTRUCTIONS FOR SLIDE PRESENTATION

Ten minutes will be available for short oral presentations, followed by five minute discussion. Facilities will be available for projection of 5 X 5 cm slides.

With a red or black felt pen mark all slides in the upper right corner of the frame facing the screen. Add sequence numbers and name of presenting author.

8. MAILING INSTRUCTIONS AND CHECK LIST

Before mailing, please check all material carefully against this list to ensure that you submit a correctly prepared abstract and related forms.*Mail to Congress Secretariat for receipt before **December 31, 1979 (December 10, 1979** postmarked).

1. Abstract Form B/1 for short communications (poster or slide presentation) or Abstract Form B/2 with No 1–2 abstract pages for Chairmen and Invited Speakers of Congress Symposia or Abstract Form B/2 with No 1–4 abstract pages for Invited Lecturers.

– Is abstract correctly typed within the designated space? See Instructions on Abstract Form.

– Have you stated the mailing address of the first (presenting) author?

– Have you indicated on the Abstract Form B/1 the numbers of three Section Topics, in order of preference, under which your paper could be presented? See Sections and Topic Category List.

– Have you indicated your presentation preference (poster or slide) in the appropriate box on the Abstract Form B/1?

2. Copies of Abstract Form

– Have you supplied six copies (xerox or unglazed print) of the face of the entire Abstract Form; and in the case of Invited Lecturers and Speakers, also additional abstract pages?

3. Author Index Cards

– Have you completed the enclosed Author Index Card?

– Have you prepared additional 10 X 15 cm white file cards for each co-author named in the abstract?

– Have you typed the family name (surname) first, followed by first name(s) in the upper left corner?

4. Abstract Identification Card 1 and 2

– Have you entered the title of your paper and the names of all authors exactly as they appear in your abstract?

– Have you indicated numbers of Section Topic Category as they appear on the Abstract Form?

– Have you indicated your presentation preference (poster or slide) in the appropriate space?

– Have you underlined a maximum of 5 key words in red pencil in your abstract title on the Abstract Identification Card 2?

*Forms referred to are in a Supplemental Packet - See Request Form provided on page 169.

5. Programme Confirmation Return Card

– Have you completed both sides of the self-addressed postcard for receipt of abstract, programme confirmation, and financial support approval?

6. Registration Form A (two copies)

– Have you filled in both Registration Forms A ? Did you include cheque or copy of bank draft covering payments?

7. Order Form D

– Have you filled in Order Form D ? Did you order accommodation, lunches, weekly ticket and excursion?

8. Financial Aid Application Form C

– If appropriate, have you filled in the Financial Aid Application Form C ?

9. SATELLITE SYMPOSIA

About 50 Satellite Symposia are scheduled to be held before and after the Congress. These Symposia are organized and financed independently of the Congress, but participants should be Active Members of the main Congress. The list given below is, in part, still tentative, and may be subject to change. For further information, please write directly to the respective organizer (see List of Satellite Symposia).

SECTIONS AND TOPIC CATEGORY LIST

01 GENERAL CELL PHYSIOLOGY
(Chairman: J. SALÁNKI)

0101 Cell particles
0102 Regulatory enzymes of the cell
0103 Mechanism of secretion, neurosecretion
0104 Pinocytosis
0105 Membrane transport
0106 Transepithelial transport of substances
0107 Intracellular transport, axoplasmic flow
0108 Electrophysiology of non-excitable cells
0109 Electrophysiology of excitable cells, ionic channels
0110 Interneuronal transmission
0111 Monoaminergic mechanisms
0112 ACh as transmitter
0113 Amino acids as transmitters
0114 Cellular function of cyclic nucleotides
0115 Glia
0116 Cell and tissue cultures
0117 Varia

02 MUSCLE (SKELETAL, SMOOTH)
(Chairman: E. VARGA)

0201 Electrical properties of muscular membrane
0202 Ionic permeabilities and transport in muscle
0203 Excitation-contraction coupling
0204 Structure proteins
0205 Energy transformation in muscles
0206 Contractile responses
0207 Molecular and functional aspects of muscular differentiation
0208 Innervation, denervation
0209 Neuromuscular transmission
0210 Comparative physiology of muscles
0211 Muscle and gravitation
0212 Varia

03 BLOOD – HAEMATOLOGY – IMMUNOLOGY
(Chairman: ZSUZSA HOLLÁN
Co-Chairman: G. GÁRDOS)

0301 Haemopoiesis
0302 Red cells
0303 Leukocytes
0304 Platelets
0305 Haemoglobin structure and functions
0306 Development of the haemoglobin molecule
0307 Lipids of blood cells and plasma
0308 Plasma membrane: structure and functions
0309 Membrane transport in blood cells
0310 Blood groups
0311 Plasma proteins
0312 Haemostasis, haemorheology and thrombosis
0313 Lymphocyte receptors
0314 Macrophages in immune phenomena
0315 Soluble factors in immune phenomena
0316 Structure of major histocompatibility complex gene products
0317 Immune complexes and the complement system
0318 Autoimmune phenomena
0319 Varia

04 CARDIOVASCULAR PHYSIOLOGY AND LYMPHATIC SYSTEM
(Chairman: A.G.B. KOVÁCH)

Heart

0401 Heart muscle biophysics, bioelectricity, electromechanical coupling, biochemistry
0402 Cardiodynamics, cardiac output
0403 Local and humoral control of heart function

Peripheral Circulation

0404 Vascular structure and function, vessel wall blood supply
0405 Microcirculation, rheology of the blood, capillary transport
0406 Lymph formation and flow, interstitial fluid, edema
0407 Cerebral blood flow
0408 Pulmonary circulation
0409 Muscle blood flow (coronary and skeletal)
0410 Organ blood flow: liver, gastro-intestinal tract, skin, adipose tissue, bone marrow, glands, reproductive organs
0411 Venous circulation
0412 Local and humoral blood flow regulation, autoregulation

Overall Control of the Circulation

0413 Reflex control of the heart and peripheral circulation
0414 Humoral control
0415 Cortical, emotional, behavioural control

Applied Physiology and Pathophysiology of Circulation

0416 Shock, anoxia, haemorrhage, hypotension
0417 Hypertension
0418 Space, gravitation, exercise, hypo- and hyperthermia
0419 Fetal, neonatal circulation, aging
0420 Methodology and new approaches
0421 Varia

05 RESPIRATION
(Chairman: I. HUTÁS)

0501 Blood gases
0502 Regulation of respiration
0503 Pulmonary sensory afferents and defense reflexes
0504 Tracheobronchial smooth muscle
0505 Pulmonary surfactant
0506 Mechanics of breathing
0507 Gas exchanges and V_A/Q
0508 Respiration in exercise
0509 Metabolic functions of the lung
0510 Regulation of acid-base balance
0511 Varia

06 KIDNEY AND BODY FLUIDS
(Chairman: L. TAKÁCS)

0601 Structural organization of the kidney
0602 Renal blood flow and glomerular filtration rate
0603 Renal interstitium and lymph
0604 Nephron heterogeneity
0605 Electrophysiology
0606 Tubular transport mechanisms
0607 Mechanisms of urinary concentration and dilution
0608 Neural and hormonal control of renal functions
0609 Control of extracellular fluid volume
0610 Renal hormones
0611 Renal metabolism
0612 Ammoniagenesis
0613 Adaptive renal functions
0614 Onto- and phylogenesis of renal functions
0615 Kidney and hypertension
0616 Experimental renal diseases – pathophysiology of the kidney
0617 Varia

07 NUTRITION – DIGESTION – METABOLISM
(Chairman: T. GÁTI)

0701 Control of ingestion
0702 Vitamins and trace elements
0703 Saliva and salivation
0704 Electrical activity of gastrointestinal muscle
0705 Neural and hormonal control of gastrointestinal motor function
0706 Basic mechanism of HCl production
0707 Neural and hormonal control of gastric secretion
0708 Hormonal receptors in the gastrointestinal tract
0709 Factors influencing splanchnic blood flow
0710 Ion transport in intestinal tract
0711 Mechanism of the intestinal absorption and metabolism of proteins and carbohydrates
0712 Fat absorption and metabolism
0713 Liver
0714 Bile acids and pigments
0715 Pancreatic exocrine function
0716 Digestive enzymes
0717 Malnutrition and malabsorption
0718 Hyperalimentation and obesity
0719 Drug metabolism in the digestive system
0720 Varia

08 ENDOCRINOLOGY – NEURO-ENDOCRINOLOGY – NEUROPEPTIDES
(Chairman: E. STARK)

0801 Hypothalamic hormones in endocrine regulation
0802 Neuroendocrine regulation and limbic system
0803 Hormone receptors in endocrine regulation
0804 Mode of action of hormones
0805 Developmental endocrinology
0806 Hormones and behaviour
0807 Endocrine rhythms
0808 Neuropeptides as neurotransmitters
0809 Non-peptide neurotransmitters in the regulation of hypophyseal function
0810 Endogenous neuropeptides and hypophyseal function
0811 Metabolism of neuropeptides
0812 Peptide analogues as tools in endocrinology
0813 Entero-pancreatic peptides in hormonal regulation
0814 Neurohypophysis
0815 Thyroid
0816 Adrenal cortex
0817 Parathyroid
0818 Varia

09 REPRODUCTION – DEVELOPMENT
(Chairman: B. FLERKÓ)

0901 Hormones and brain development
0902 The LH–RH neuron system and its development in mammals
0903 Pituitary cytodifferentiation
0904 Neurotransmitters involved in the regulation of pituitary-ovary axis
0905 Neurotransmitters involved in the regulation of the pituitary-testis axis
0906 Androgen receptors
0907 Estrogen and progestogen receptors
0908 Regulation of reproductive behaviour (sexual, maternal, etc.) in mammals
0909 Action of endorphins-enkephalins in reproduction
0910 Humoral factors involved in capricitation, fertilisation, implantation
0911 Hormonal control of oocytes
0912 Factors involved in early pregnancy
0913 Endocrine function of blastocytes
0914 Prostaglandins and pregnancy
0915 Interaction between fetus, placenta and mother
0916 Contraception
0917 Varia

10 REGULATORY FUNCTIONS OF CNS
(Chairman: J. SZENTÁGOTHAI
Co-Chairman: M. PALKOVITS)

1001 Supraspinal control of circulation, respiration and digestion
1002 Motor control and locomotion
1003 Striatal mechanisms
1004 Cerebral cortex
1005 Callosal functions, lateralisation of the brain
1006 Sleep and wakefulness
1007 Programme control in the CNS
1008 Dynamic patterns in the CNS, statistical neurodynamics
1009 Cerebellar mechanisms
1010 Limbic system
1011 Local circuits; functions of interneurons
1012 Central actions of biogenic amines
1013 Animal navigation and orientation
1014 Critical periods during maturation of CNS regulatory function
1015 Organization of thalamic functions, thalamo-cortical interaction
1016 Cholinergic mechanisms in CNS, nicotinic and muscarinic receptors
1017 Physiology of autonomic nervous system
1018 Physiology of the vestibular system
1019 Spinal reflexes
1020 Varia

11 SENSORY FUNCTIONS
(Chairman: E. GRASTYÁN)

1101 Physiology of receptors. Transducer mechanisms and coding
1102 Peripheral and central somatosensory mechanisms
1103 Vision (including anthropoids), peripheral and central mechanisms
1104 Hearing, peripheral and central mechanisms
1105 Taste, peripheral and central mechanisms
1106 Olfaction, peripheral and central mechanisms
1107 Visceral sensations, peripheral and central mechanisms
1108 Muscle and joint receptors, peripheral and central mechanisms
1109 Thermoreceptors, peripheral and central mechanisms
1110 Electoreceptors, peripheral and central mechanisms
1111 Pain
1112 Association systems and sensory-motor integration
1113 Adaptive plasticity of sensory functions
1114 Neurophysiological basis of perception
1115 Sensory information processing in "nonsensory" areas (reticular formation, nonspecific thalamic nuclei, fronto-parieto-temporal cortices, etc.)
1116 Central processing of information
1117 Centrifugal control of sensory transmission
1118 Varia

12 BEHAVIOUR – HIGHER FUNCTIONS OF CNS
(Chairman: G. ÁDÁM)

1201 Genetics and evolution of higher nervous functions
1202 Physiology of instinctive behaviour
1203 Psychophysiology of perception and attention
1204 Physiological bases of emotion
1205 Psychophysiology of motivation
1206 Mechanisms of classical (pavlovian) and of operant (instrumental) learning
1207 Ethological aspects of learning
1208 Molecular bases of learning, memory storage and retrieval
1209 Visceral learning
1210 Neurotransmitters and behaviour
1211 Physiological aspects of cognitive processes
1212 Physiological basis of consciousness
1213 Brain mechanisms of nonconscious processes

1214 Pharmacological influence on higher nervous functions
1215 Psychophysiology of sensory-motor integration
1216 Communication and social behaviour in animals
1217 Verbal behaviour and speech
1218 Ontogenesis of behaviour
1219 Varia

13 ENVIRONMENTAL PHYSIOLOGY
(Chairman: F. OBÁL)

Thermoregulation

1301 Integration of thermal signals
1302 Neuropharmacological aspects of temperature regulation
1303 Ontogenetic and comparative aspects of thermoregulation
1304 Effector mechanisms in thermoregulation
1305 Neurohumoral mechanisms in thermoregulation
1306 Fever
1307 Hibernation

Adaptation to the environment

1308 Adaptation to the environment (heat, cold, hypoxia, acceleration, high and low pressure)
1309 Physiological effects of combined environmental stressors
1310 Alteration of physiological functions due to mechanical and electromagnetic oscillations
1311 Alteration of physiological functions due to chemical agents in the environment

Sports and work physiology

1312 Physiology of static and dynamic exercise
1313 Assessment of occupational stress and strain
1314 Neurohumoral mechanisms of adaptation to work stress
1315 Integration of motor patterns
1316 Age-related differences in physical fitness and performance

Chronophysiology

1317 Circadian rhythms, infradian and ultradian components
1318 Regulation of circadian activities
1319 Circannual rhythms, seasonal variables
1320 Varia

14 COMPARATIVE PHYSIOLOGY – FARM ANIMALS
(Chairman: G. PETHES)

1401 Comparative environmental physiology
1402 Comparative behavioral physiology (including farm animals)
1403 Developmental neurobiology
1404 Invertebrate neurobiology
1405 Adaptation mechanisms
1406 Comparative physiology of circulation and heart
1407 Comparative physiology of respiration
1408 Neuronal modelling in invertebrates
1409 Comparative physiology of synaptic receptors and transmitters
1410 Comparative endocrinology
1411 Physiology of lactation of farm animals
1412 Perinatal physiology of farm animals
1413 Fetal homeostasis
1414 Avian physiology (domestic birds)
1415 Growth
1416 Comparative aspects of parturition in farm animals
1417 Metabolism of farm animals (energy, heat, vitamins, organic, mineral and trace constituents)
1418 Digestion in ruminants and non-ruminant herbivorous domestic animals
1419 Adaptations in domestic animals to environmental stress (including metabolic disorders)
1420 Varia

S1 TEACHING WORKSHOP
(Chairman: I. FORGÁCS)

S2 SYMPOSIUM ON HISTORY OF PHYSIOLOGY
(Chairman: E. SCHULTHEISZ)

CONGRESS SYMPOSIA

TENTATIVE LIST

01 SECTION • GENERAL CELL PHYSIOLOGY

1. Charge movement in nerve membrane
2. Optical changes during electrogenesis
3. Calcium electrogenesis
4. Transmission in autonomic ganglia
5. Synaptic transmission and modulation
6. Cell motility in non-muscle cells
7. Time in cell physiology
8. Epithelial transport
9. Models of iso-osmotic transport
10. Cell-to-cell communication

02 SECTION • MUSCLE

1. Calcium exchange and compartmentalization
2. Smooth muscle
3. Cross-bridge mechanism and energetics
4. Molecular and functional aspects of muscle differentiation
5. Physiological studies on muscle diseases

03 SECTION • BLOOD – HAEMATOLOGY – IMMUNOLOGY

1. Development of human blood cells
2. Regulation of differentiation of haemoglobin structure and function
3. The role of calcium in red cell membrane transport processes
4. Structure and function of blood cell membranes
5. Molecular basis of blood coagulation
6. Cell receptors in the regulation of immune responses

04 SECTION • CARDIOVASCULAR PHYSIOLOGY AND LYMPHATIC SYSTEM

1. Cation regulation in the myocardium
2. Factors regulating myocardial substrate metabolism
3. Neural reflex control of the heart
4. Biomechanical properties of arteries
5. Reflex control of the circulation in human
6. The integrative role of the autonomic nervous system in the regulation of cardiovascular function
7. Circulatory actions of prostacyclin and thromboxane
8. Routes of transcapillary transport: correlation of structure and function
9. Blood brain barrier
10. Starling forces: with emphasis on single capillary studies
11. Cardiovascular fetal physiology
12. Control of vascular capacitance in man and animals
13. Neural control of the microcirculation
14. Cerebral blood flow regulation
15. Non-invasive optical monitoring of cardiovascular and cerebral metabolism

05 SECTION • RESPIRATION

1. Respiratory muscles in man (mechanics and control)
2. Comparative physiology of respiration
3. V_A/Q distribution
4. Breathing control during exercise
5. Prostaglandins in the lung
6. Arterial chemoreceptors and chemoreflexes
7. Defense reflexes from the respiratory tract

06 SECTION • KIDNEY AND BODY FLUIDS

1. Ontogenetic aspects, compensatory hypertrophy
2. Renal cell cultures
3. Renal blood flow
4. Glomerulo-tubular balance
5. Tubular handling of calcium and phosphate
6. Cell ionic activity and element analysis
7. Electrophysiology and epithelial transport
8. Tubular acidification
9. Extracellular volume control
10. Regulation of water balance

07 SECTION • NUTRITION – DIGESTION – METABOLISM

1. Electrophysiology of gastrointestinal epithelia
2. The gastric mucosal barrier to Na and H ions
3. Molecular changes during metabolic processes of gastrointestinal peptide hormones
4. Factors involved in the integrated mechanism of intestinal absorption
5. Lipoprotein metabolism, apolipoproteins, lipid constituents

6. Intestinal polypeptides and peptidergic nerves
7. Vitamins and trace elements
8. Role of cyclic nucleotides in stimulus-secretion coupling of exocrine glands
9. Mechanisms of gastrointestinal exocrine secretion
10. Gastrointestinal motility

08 SECTION • ENDOCRINOLOGY – NEUROENDOCRINOLOGY – NEUROPEPTIDES

1. Hormonal receptors and decoding of genetic information
2. Preprohormones, prohormones, hormones
3. *In vitro* systems for studying neuroendocrine regulation and steroid hormone action
4. Suspected hypothalamic releasing and inhibiting hormones: localization, biochemistry, physiology
5. Neurotransmitters in the control of anterior pituitary function
6. Extrahypothalamic structures in neuroendocrine regulation
7. Pituitary and gastrointestinal hormone-like material in brain
8. Effects of endogenous opioid peptides on the neuroendocrine system
9. Neuropeptides as neurotransmitters
10. Behaviour and hormonal balance

09 SECTION • REPRODUCTION – DEVELOPMENT

1. The role of the hypothalamus in the regulation of LH and FSH
2. Gonadotropin and steroid hormone receptors
3. Secretory proteins of the male reproductive tract
4. Contraception
5. Reproduction and development

10 SECTION • REGULATORY FUNCTIONS OF CNS

1. Neural mechanisms of voluntary movements and precentral motor area
2. Neuronal mechanisms of subcortical sensory processing
3. Cortical interconnectivity (extrinsic)
4. Ontogenetic development and differentiation of CNS
5. Modular organization principles in CNS
6. Cerebellum
7. Mechanism of transmission in the monosynaptic reflex pathway in spinal cord
8. Eye movement and pursuit control system
9. Locomotion
10. Sleep

11 SECTION • SENSORY FUNCTIONS

1. Comparative experimental analysis of habituation
2. How is sensory information presented to the brain?
3. Visceral sensory mechanisms and sensations
4. Pain mechanisms
5. Thermoreception
6. Processing of sensory information in the hippocampus
7. Chemical sensations and their perception
8. Joint and muscle receptor system and kinesthesis
9. The electrophysiology of auditory perception
10. Depth perception

12 SECTION • BEHAVIOUR – HIGHER FUNCTIONS OF CNS

1. Developmental plasticity of CNS
2. Learning in isolated neuronal structures
3. Mechanisms of conditioning, learning and memory
4. Visceral learning
5. Cortical sensory-motor integration
6. Functions of mammalian associative cortex
7. Psychophysiology today and tomorrow
8. Electrophysiological basis of verbal and cognitive behaviour
9. Psychophysiology of altered states of consciousness
10. Psychophysiology of motivation

13 SECTION • ENVIRONMENTAL PHYSIOLOGY

1. Exercise physiology (human exercise physiology)
2. Osmoregulation
3. Gravitational physiology I.
4. Gravitational physiology II.
5. Physiology of static effort
6. Regulation of the sleep-waking rhythm by environmental and endogenous factors
7. The mammalian nervous system at pressure

14 SECTION • COMPARATIVE PHYSIOLOGY – FARM ANIMALS

1. Diving I: metabolism, physiology and control
2. Diving II: metabolism, physiology and control
3. Phylogenesis of hormones and hormone receptors
4. Neuromuscular transmission in invertebrates
5. Fetal homeostasis
6. Control of *corpora lutea* function of ruminant and non-ruminant domesticated animals
7. Comparative physiology of lactation in farm animals
8. Digestion in non-ruminant herbivorous animals

SATELLITE SYMPOSIA

Title	Chairman/ Organizer	Location	Time	Information
01 SECTION • GENERAL CELL PHYSIOLOGY				
The serotoninergic neuron	M. JOUVET A. CALAS	Marseille France	July 9–11	A. CALAS Departement de Neurobiologie Cellulaire, INP, CNRS 31, ch-J-Aiguier, F-13274 Marseille Cedex 2, France
Ionselective microelectrodes and their use in excitable tissues	L. VYKLICKY EVA SYKOVÁ	Prague Czechoslovakia	July 7–11	JIRINA ZÁKOVÁ Institute of Physiology of the Czechoslovakian Academy of Sciences Budejovicka 1083 Prague 142 20 Czechoslovakia
4th international conference on cyclic nucleotides	J. E. DUMONT G. A. ROBISON	Brussels Belgium	July 22–26	G. A. ROBISON Department of Pharmacology University of Texas Medical School Houston, Texas 77025 P.O.B. 20708, U.S.A.
Neurotransmitters in invertebrates	KATALIN S. RÓZSA L. HIRIPI	Veszprém Hungary	July 9–12	L. HIRIPI Biological Research Institute of the Hungarian Academy of Sciences H-8237 Tihany, Hungary
Amino acid transmitters	P. MANDEL F. V. DEFEUDIS	Strasbourg France	July 10–11	F. V. DEFEUDIS Centre de Neurochimie 11 Rue Uhmann F-67085 Strasbourg Cedex France
02 SECTION • MUSCLES				
Mechanism of muscle adaptation to functional requirement	G. MARÉCHAL F. GUBA	Szeged Hungary	July 20–21	F. GUBA Dept. of Biochem. Univ. Med. School H-6701 Szeged, Dóm tér 9. Hungary

Title	Chairman/ Organizer	Location	Time	Information
Membrane control of skeletal muscle function	P. HOROWICZ E. VARGA	Debrecen Hungary	July 10–12	E. VARGA Dept. of Physiol. Univ. Med. School H-4012 Debrecen, P.O.B. 22 Hungary

04 SECTION • CARDIOVASCULAR PHYSIOLOGY AND THE LYMPHATIC SYSTEM

Oxygen transport to tissues (ISOTT)	A. G. B. KOVÁCH B. CHANCE E. DÓRA	Budapest Hungary	July 9–12	E. DÓRA Experimental Research Department Phone: 343-162, 339-983 H-1082 Budapest, Üllői út 78/a, Hungary
Homeostasis in injury and shock	J. J. SPITZER H. B. STONER A. G. B. KOVÁCH ZSUZSANNA BIRÓ	Budapest Hungary	July 21–24	ZSUZSANNA BIRÓ Experimental Research Department Phone: 343-162, 339-983 H-1082 Budapest, Üllői út 78/a, Hungary
Cardiovascular system dynamics: models and measurements	E. WETTERER T. KENNER H. HINGHOFER-SZALKAY	Graz Austria	July 10–12	H. HINGHOFER-SZALKAY Department of Physiology University of Graz Phone: 31581 Harrachgasse 21/V A-8010 Graz, Austria
Symposium on vasomotion	P. M. VAN-HOUTTE	Antwerpen Belgium	July 24–26	P. M. VANHOUTTE Dept. Interne Geneskunde Universitet Antwerpen Universitetsplein 1. Phone: Phone: 031/28-25-28 2610 Wilrijk, Belgium
Symposium on coronary circulation	W. LOCHNER W. SCHARPER E. BASSENGE	Bad Nauheim Federal Republic of Germany	July 5–7	D. W. LOCHNER Physiologisches Institut I. Universität Düsseldorf Phone: 0/211/311-2672 2670 Moorenstrasse D-400 Düsseldorf, FRG
Factors influencing adrenergic mechanisms in the heart	M. SZENTIVÁNYI S. JUHÁSZ-NAGY	Budapest Hungary	July 21–24	S. JUHÁSZ-NAGY Institute of Vascular Surgery Phone: 154-080 Városmajor u. 68. H-1122 Budapest, Hungary

Title	Chairman/ Organizer	Location	Time	Information
The cardiac electric field: its measuring and modelling	E. SCHUBERT	Dresden German Democratic Republic	July 6–9	E. SCHUBERT Physiologisches Institut Hessische Str. 3-4 104 Berlin, GDR
Pathophysiology and pharmacotherapy of cerebral disturbances	E. BETZ J. GROTE R. WÜLLENWEBER D. HEUSER	Tübingen Federal Republic of Germany	July 22–25	D. HEUSER Physiologisches Institut Phone: 07071/292194 Gmelin Str. 5. D-7400 Tübingen I., FRG
05 SECTION • RESPIRATION				
Airway irritability	M. A HAXHIU	Prishtina Yugoslavia	July 21–22	M. A. HAXHIU Institute for Clinical Physiology, Medical Faculty 38000 Prishtina, Yugoslavia
Exercise bioenergetics and gas exchange	P. CERRETELLI B. WHIPP	Milano Italy	July 7–10	P. CERRETELLI Istituto di Fisiologia (III) Università di Milano. via Mangiagalli, 32 20133 Milano, Italy
Gas exchange function of normal and diseased lungs (by invitation)	J. PIIPER P. SCHEID	Göttingen Federal Republic of Germany	July 9–11	J. PIIPER Max-Planck Institut für Experimentelle Medizin Hermann Rein Str. 3 D-3400 Göttingen, FRG
06 SECTION • KIDNEY AND BODY FLUIDS				
Regulation of sodium excretion by hormones	B. LICHARDUS J. PONEC	Bratislava Czechoslovakia	July 9–12	J. PONEC Institute of Exp. Endocrinology, Slovak Acad. Sci. Vlarska 3, Kramare 80936 Bratislava, Czechoslovakia
Renal transport of organic substances	P. DEETJEN	Innsbruck Austria	July 22–24	P. DEETJEN Institut für Physiologie und Balneologie der Universität Innsbruck, F. Pregl Str. 3. A-6010 Innsbruck, Austria
Prostaglandins and the kidney	J. C. FRÖLICH A. S. NIES R. W. SCHRIER	Stuttgart Federal Republic of Germany	July 23–24	J. C. FRÖLICH Department of Clinical Pharmacology Auerbachstr. 112 Phone: 0711/81 01 700 D-7000 Stuttgart 50, FRG

Title	Chairman/ Organizer	Location	Time	Information
07 SECTION • NUTRITION-DIGESTION-METABOLISM				
Hydrogen-ion transport in epithelia (by invitation)	IRENE SCHULZ	Frankfurt/M Federal Republic of Germany	July 8–12	IRENE SCHULZ Max-Planck-Institut für Biophysik Kennedyallee 70, D-6000 Frankfurt/Main, FRG
Saliva and salivation	Y. KAWAMURA T. ZELLES	Székesfehérvár Hungary	July 10–12	T. ZELLES Research Group of Oral Biology, Semmelweis University Medical School Nagyvárad tér 4. H-1445 Budapest, Pf. 370. Hungary
Fluoride metabolism	M. HOHENEGGER	Vienna Austria	July 10–11	M. HOHENEGGER Department of General and Experimental Pathology, University of Vienna Währingstr. 13. A-1090 Vienna, Austria
International symposium on hormones, lipoproteins and atherosclerosis	M. PALKOVIC NINA SKOTTOVÁ	Bratislava Czechoslovakia	July 21–23	NINA SKOTTOVÁ Institute of Experimental Endocrinology, Center of Physiological Sciences, Slovak Academy of Sciences Vlárska 3, Kramare 80936 Bratislava Czechoslovakia
Gastrointestinal defence mechanisms	K. HARTIALA T. JÁVOR	Pécs Hungary	July 20–22	T. JÁVOR 1st Department of Medicine University Medical School Ifjúság útja 31. H-7643 Pécs, Hungary
Ionic mechanisms in glandular secretion	J. GRAF	Vienna Austria	July 11–12	J. GRAF Department of General and Experimental Pathology, University of Vienna Währingstr. 13 A-1090 Vienna, Austria
VIIth International conference on the physiology of food and fluid intake	S. KOZLOWSKI ELZBIETA FONBERG	Warsaw Poland	July 7–10	ELZBIETA FONBERG Center of Clinical and Experimental Medicine Jazgarzewska ul. 17 Phone: 41–32–39 00–730 Warsaw, Poland

Title	Chairman/ Organizer	Location	Time	Information
09 SECTION • REPRODUCTION-DEVELOPMENT				
Placental transfer: methods and interpretations	M. YOUNG GY. TELEGDY	Szeged Hungary	July 10–12	M. YOUNG Department of Gynaecology St. Thomas' Hospital Medical School London, SE1 7EH, U.K.
Gonadal steroids and brain function	F. NEUMANN J. MEITES W. WUTTKE	West-Berlin	July 10–11	W. WUTTKE Max-Planck-Institut für biophys. Chemie Postfach 968 D-3400 Göttingen, FRG
10 SECTION • REGULATORY FUNCTIONS OF CNS				
Structural and functional aspects of dorsal horn mechanisms	A. IGGO M. RÉTHELYI	Keszthely or Veszprém Hungary	July 10–13 or July 20–23	A. G. BROWN Royal (Dick) School of Veterinary Studies, Summerhall, Edinburgh, EH9 1QH, U.K.
Neural communications and control. Facts and theories (by invitation)	A. DAMJANOVICH D.M. MacKAY G. SZÉKELY	Debrecen Hungary	July 21–24	E. LÁBOS 1st Department of Anatomy Semmelweis University Medical School, Tűzoltó u. 58. H-1450 Budapest, Hungary
Central nervous control of autonomic nervous system	H. SELLER	Heidelberg Federal Republic of Germany	July 7–9	H. SELLER I. Physiologisches Institut, Im Neuenheimer Feld 326 D-6900 Heidelberg, FRG
Physiology and pharmacology of epileptogenic phenomena	M. R. KLEE H. D. LUR E. J. SPECKMANN	Frankfurt/M Federal Republic of Germany	July 5–9	M. R. KLEE Max-Planck-Institut für Hirnforschung, Neurobiologische Abt., Deutschordenstr. 46. D-6000 Frankfurt/Main, FRG
Intervertebrate neurobiology: mechanisms of integration	J. SALÁNKI	Tihany Hungary	July 20–23	J. SALÁNKI Biological Institute of Hungarian Academy of Sciences H-8237 Tihany, Hungary
Systems theoretic approach to visual-motor functions	H. DRISCHEL	Leipzig German Democratic Republic	July 22–24	H. DRISCHEL Karl Ludwig Institute of Physiology, Phone: 7167222 Liebig str. 27. 701 Leipzig, GDR

Title	Chairman/ Organizer	Location	Time	Information
11 SECTION • SENSORY SYSTEMS				
Sensory physiology of aquatic lower vertebrates with special focus on electroreception	T. SZABÓ	Keszthely Hungary	July 21–23	T. SZABÓ CRNS Laboratoire de Physiologie Nerveuse, Department de Neurophysiologie Sensoriel F 91190 Gif sur Yvette France
Cellular analogue of conditioning and neural plasticity	O. FEHÉR	Szeged Hungary	July 21–22	O. FEHÉR Department of Comparative Physiology, Attila József Univ. of Sciences H-6726 Szeged Hungary
Neuronal plasticity in sensorimotor systems	H. FLOHR	Bremen Federal Republic of Germany	July 10–12	H. FLOHR Department of Neurobiology Univ. of Bremen NW2 D-2800 Bremen FRG
Neuronal mechanisms of hearing	J. SYKA	Prague or High Tatra Czechoslovakia	July 20–23	J. SYKA Institute of Experimental Medicine Czechoslovak Academy of Sciences U. Nemocnice 2 128 08 Prague 2 Czechoslovakia
Information processing in the retina	A. KAFKA-LÜTZOW	Vienna Austria	July 10–12	A. KAFKA-LÜTZOW Physiologisches Inst. der Universität Wien Institutszentrum Schwarzspanierstr. 17. A-1090 Wien Austria
Visual neurophysiology	O. CREUTZFELDT B. B. LEE	Göttingen Federal Republic of Germany	July 8–10	B. B. LEE Max-Planck-Institut f. Biophysikalische Chemie Pf. 968 D-03400 Göttingen FRG
Joint congress ECRO IV/ISOT VII on chemoreception	E. P. KÖSTER H. VAN DER STARRE	Noordwijkerhout Holland		H. VAN DER STARRE Dept. of Animal Physiology Zoölogisch Laboratorium der Rijksuniversiteit Phone: 31-71148333 ext. 7660 Leiden, Kaiserstraat 63. Postbus 9516 2300 RA Leiden Holland

Title	Chairman/ Organizer	Location	Time	Information
13 SECTION • ENVIRONMENTAL PHYSIOLOGY				
Developmental and environmental factors in thermoregulation	SZ. DONHOFFER S. KOVÁCS	Pécs Hungary	July 10–12	S. KOVÁCS Dept. Pathophysiology Szigeti u. 12. H-7643 Pécs Hungary
Sports physiology (hormonal and pharmacological aspects in present day exercise physiology)	R. FRENKL	Budapest Hungary	July 10–12	R. FRENKL Dept. Medicine, Hungarian University of Physical Education Alkotás u. 44. H-1123 Budapest Hungary
Metabolic and functional changes during exercise	V. SELIGER	Prague Czechoslovakia	July 6–8	V. SELIGER Faculty of Physical Education and Sport, Charles University, Ujezd 450 Praha 1-Mala Strana Czechoslovakia
Underwater physiology	A. BACHRACH	Athens Greece	July 7–9	BARBARA C. NICHOLS Federation of American Societies for Experimental Biology 9650 Rockville Pike Bethesda, Maryland 20014 USA
14 SECTION • COMPARATIVE PHYSIOLOGY – FARM ANIMALS				
Comparative physiology: perspectives	K. JOHANSEN R. C. TAYLOR	Sandbjerg Denmark	July 22–27	K. JOHANSEN Department of Zoophysiology University of Aarhus Aarhus C Denmark
Recent progress in avian endocrinology	G. PETHES F. HERTELENDY I. ASSENMACHER	Budapest Hungary	July 9–12	G. PETHES Department of Physiology, University of Veterinary Science Phone: 22-30-44 H-1400 Budapest POB. 2. Hungary
MATHEMATICAL AND COMPUTER MODELLING OF BIOLOGICAL SYSTEMS				
	L. FEDINA B. KANYÁR	Budapest Hungary	July 21–24	L. FEDINA Computing Group of the Semmelweis Univ. Med. Sch. Phone: 130–436, 341–550/5 Kulich Gyula tér 5. H-1089 Budapest, Hungary
IBRO SYMPOSIUM				
Brain mechanisms of perceptual awareness and purposeful behavior In honor of Professor Moruzzi	C. AYMONE-MARSAN O. POMPEIANO	Pisa Italy	July 10–12	O. POMPEIANO Instituto di Fisiologia Umana Umana Cattedra II- Universita di Pisa Via S. Zeno N. 31 56100 Pisa, Italy

IMPORTANT NOTICE

All forms referred to in this Announcement (registration forms, abstract forms, etc.) are available as a Supplemental Packet, which can be obtained by completing the request form below.

All persons who pre-registered for the Congress have been sent the Announcement and Supplemental Packet directly.

Please note that the deadline for *receipt* of registration is *December 31, 1979.*

Please note Travel Awards Announcement on page ii.

Dr. Orr E. Reynolds
American Physiological Society
9650 Rockville Pike
Bethesda, MD 20014

Dear Dr. Reynolds:

Please send me the Supplemental Packet for participation in the XXVIII International Congress of Physiological Sciences.
My mailing address is:

Name _____

Address _____

_____

_____

_____

City_____ State_____ Zip _____

COUNCIL OF ACADEMIC SOCIETIES BRIEF

ASSOCIATION OF AMERICAN MEDICAL COLLEGES • 1 DUPONT CIRCLE NW • WASHINGTON DC
(202) 828-0400 SUMMER, 1979 VOL. 4., NO. 4

The CAS Brief is prepared by the staff of the AAMC Council of Academic Societies and is distributed through the auspices of your member society.

THE RESEARCH OUTLOOK. Although the academic year began on a hopeful note with the President vowing more support for basic research and Secretary Califano enunciating clearly his desire to correct many of the problems about which researchers have been concerned for the past several years, events have not borne out these promising statements:

The NIH/ADAMHA Budget. The fiscal year 1980 budget for NIH and ADAMHA will almost certainly be set at a level below the amount required to keep pace with inflation. If the Carter Administration expected the Senate to follow its traditional pattern of substantially increasing the President's request for biomedical research and medical education, they were as surprised as everyone else when that did not occur. This year, in fact, the House surpassed the Senate in largesse when it came to funding for biomedical research. The House bill, which was approved by the full House on June 26, provides an increase in the total NIH budget of $202.6 million (6.3%) over last year's appropriation. ADAMHA is funded in the House bill at a level slightly below the 1979 appropriation. An attempt on the House floor to increase the NIH budget to provide additional funds for investigator-initiated grants was unsuccessful. Similar attempts to raise the NIH budget are expected to be made on the Senate side when the bill is marked up in the full Appropriations Committee and on the Senate floor, but these efforts will probably meet with strong opposition. Since the Senate bill is now lower than the House version for NIH and equal to the House version for ADAMHA, it is unlikely that the final Labor-HEW Appropriations bill will provide the necessary inflationary increases for biomedical research.

Decline in Clinical Researchers. A threatened decline in the numbers of MDs entering research training in preparation for academic careers has now become a clear reality. Only 1200 MDs entered postdoctoral research training in 1977 as compared to 3500 in 1974. The number of clinical researchers in the pipeline is far less than the number needed to maintain the national biomedical research effort and to meet the future needs of the medical schools for clinical faculty. The AAMC Executive Council discussed these trends in clinical research manpower at a recent meeting and authorized the immediate formation of an *ad hoc* committee to formulate a concerted plan to address this problem.

Compensation of Injured Research Subjects. Also in the clinical research area but with wider funding implications for all of biomedical and behavioral research is the threat of DHEW to require that all research institutions provide compensation to human subjects injured in the course of research. A coalition of researchers, university administrators and insurance executives is studying the problem intensively. AAMC has written to Secretary Califano delineating the myriad of unresolved questions in this area and asking DHEW to seriously consider the implications for research institutions if compensation plans are required.

HEALTH SCIENCES PROMOTION ACT OF 1979--(S.988). This bill, introduced in Senator Kennedy's Subcommittee in May, would restructure the Public Health Service Act to enshrine each of the National Institutes of Health in statute; encourage a reduction in paperwork and the administrative burden of research grants; and establish a Council to plan research, to annually critique the President's health science budget, and to provide science advice to the Congress. The goals are praiseworthy but the means proposed to achieve them are questionable. Hearings on the Health Science Promotion Act have been held by Senator Kennedy's Subcommittee, and it is clear that considerable debate is yet to come. Reaction to this legislation has been mixed. While few clinical investigators would disagree with efforts to reduce the paperwork associated with biomedical research, most question the need to extensively restructure one of the few entities of the federal government which has functioned well. Perhaps one of the most widely-held contentions with the bill is the inclusion of sunset provisions for all Institutes except the National Cancer Institute and the National Heart, Lung and Blood Institute. Although the future course of this legislation is uncertain, it will undoubtedly be a bill which is watched with keen interest by the entire biomedical research community.

1979 MEDICAL SCHOOL GRADUATES. In June, approximately 15,000 members of the 1979 graduating class from United States medical schools embarked on their graduate medical education. Based on data from the National Resident Matching Program, 60% of these entered programs in the primary care specialties of family practice (14%), internal medicine (36%), and pediatrics (10%). Six percent chose programs in obstetrics and gynecology. Another 16% entered surgery and surgical specialty programs. The medical specialty programs of dermatology, neurology, and psychiatry took in 4% of the class, and the support specialties 6%. The remaining 8% entered flexible first year graduate positions. This proportional distribution amongst the specialties is about the same as for the graduating classes during the past four years, during which the size of the graduating class has grown by over 2,400.

The Class of 1979, which entered in 1975, was selected from a pool of 42,624 applicants, the largest ever. There were 2.8 applicants for each position. The number of applications has declined each year since. In 1978, 36,636 applicants competed for 16,527 positions, a ratio of 2.2:1. This trend of a decline in the number of applicants is expected to continue. The rapid increase in the number of graduating college seniors has plateaued, and the demographic data for the 80's show a decided downward slope for the number of citizens reaching college age.

ACCREDITATION WORKING GROUP REPORTS. The Working Group on Accreditation of the AAMC Task Force on Graduate Medical Education has completed its work. Its Report, with recommendations for changes in approach to the accreditation of graduate medical education will be distributed to the constituent members of the Council of Academic Societies in the near future. Copies can be obtained by contacting August G. Swanson, M.D., Director, Department of Academic Affairs.

REVISION OF REQUIREMENTS FOR GRADUATE MEDICAL EDUCATION. The Coordinating Council on Medical Education approved a revision of the general requirements for Graduate Medical Education and forwarded it to its parent organizations for ratification. When ratified by the AAMC, AMA, American Board of Medical Specialties, Council of Medical Specialty Societies and American Hospital Association, the revision will become a new standard for accreditation of graduate medical education. It will require institutions sponsoring graduate medical education programs to assume greater responsibility for their quality.