AMERICAN PHYSIOLOGICAL SOCIETY

PROCEEDINGS

FALL MEETING, AUGUST 25-29, 1969

UNIVERSITY OF CALIFORNIA, DAVIS, CALIFORNIA

ABSTRACTS OF PAPERS

An asterisk following an author's name denotes "by invitation." Abstracts are arranged in alphabetical order by first-named author.

IS THERE STAGNANT BLOOD IN THE LUNG CAPILLARIES? R.Abboud*,G.Andersson* and R.F.Coburn. Dept. Physiol., Div.Grad.Med., U. of Pa., Phila., Pa.

We have studied the variables that influence the simultaneous alveolar uptake of the two CO isotopes, ^{12}CO, ^{14}CO, when blood has been previously loaded with one of the isotopes. Under these conditions, in capillaries with blood flow limited CO uptake, there is a preferential uptake (P.UP.) of the non-loaded isotope relative to its P_{ACO}. This is due to differences in relative back pressures of the 2 isotopes as capillary [COHb] approaches saturation and to displacement of the loaded isotope from COHb by a rate limited reaction. Both processes could also occur in capillaries with stagnant blood and could result in up to 15-60% P.UP. of the non-loaded isotope. In 11 experiments on closed chest anesthetized dogs without prior CO loading, both isotopes were absorbed proportional to their P_{ACO}. In 8 open chest dogs loaded with ^{12}CO, the uptake of the 2 isotopes determined in one lung whose blood flow was stopped showed that the P.UP. of ^{14}CO during 10 sec. breath-holding was 54 $\pm$ S.E. 11% of that theoretically expected at kinetic equilibrium. 9 paralyzed anesthetized dogs 15-17 Kg. were first loaded with ^{12}CO (mean [COHb] 20.5% sat.) and then made to inhale the 2 isotopes (mean $P_A{}^{12}CO_0$ 8 mmHg) and hold their breath for 8-11 sec. at a transthoracic pressure of 12 cmH_2O and a mean lung volume of 61.5% of TLC. ^{14}CO was preferentially taken up relative to ^{12}CO (mean P.UP. 2.0 $\pm$ S.E. 0.39%, $p<0.001$). Of the ^{14}CO taken up from alveolar gas 99.3 $\pm$ S.E. 1.3% ($p>0.5$) could be accounted for in serially sampled arterial blood; thus P.UP. of ^{14}CO occurs mainly in capillaries with flowing blood. There was no apparent effect of position (vertical vs. horizontal), pulmonary arterial pressure or height of lung in Zone 1. Two similar experiments with ^{14}CO loading gave equivalent results. Considering the errors, we conclude that under our experimental conditions there is less than 3-5ml of stagnant blood in the pulmonary capillaries.

COMPARISON OF RESPONSES OF MUSCULAR AND CUTANEOUS VESSELS TO LOCAL TEMPERATURE CHANGES. Wadie Abdel-Sayed* and Francois M. Abboud. Dept. of Med., Univ. of Iowa Coll. of Med., Iowa City, Iowa.

The isolated gracilis muscle and the isolated hind paw of dogs were denervated and perfused with blood at constant rates using Sigmamotor pumps. The temperature of the perfusate was reduced from 37° C to an average of 27° C and then increased to an average of 41° C. Changes in perfusion pressure (PP) and in small vein pressure (SvP) reflected changes in total and in venous resistances respectively. During cooling, PP in the muscle decreased (average -20%) whereas PP in the paw increased (+50%); SvP in the muscle did not change significantly whereas SvP in the paw increased (+42%). Responses were reversed by rewarming of the perfusate. Increases in PP in the muscle during sympathetic nerve stimulation (NS, average +56 mm Hg) and during intraarterial norepinephrine (NE, +56 mm Hg) were reduced by hypothermia (+39 and +39 mm Hg respectively) and restored by rewarming (+48 and +55 mm Hg respectively). Corresponding increases in PP in the paw averaged +79 and +96 mm Hg during NS and NE respectively at normal temperature; +56 and +67 mm Hg at low temperature and +67 and +101 mm Hg at high temperature. Venous responses to NS and NE were negligible in the muscle but were prolonged and augmented in the paw during cooling. The results indicate that the effect of cooling on resistance vessels in cutaneous and muscular beds favors redistribution of blood flow away from cutaneous and into muscular vessels. It appears also that an augmentation of constrictor responses to NS and NE occurs selectively in venous segments of the paw during cooling; arterial responses to these adrenergic stimuli are reduced in magnitude in both muscle and paw during cooling. These effects are reversed rapidly by rewarming.

PROPRIOCEPTIVE RELAYS TO THE CEREBRAL CORTEX, AND THEIR SIGNIFICANCE IN INTRASPINAL ORGANIZATION. V. C. Abrahams, D. Butler* and J. Daynes*, Department of Physiology, Queen's University, Kingston, Ontario, Canada.

Previous experiments in chloralose anaesthetized cats have shown that a profound and prolonged facilitation of lumbosacral monosynaptic reflex activity follows stimulation of neck and forepaw muscle nerves. Structures critical to the interaction lie supratentorially. It has now been found that electrical stimulation of the post-cruciate dimple and the suprasylvian gyrus (both cortical regions receiving proprioceptive input) has similar effects on lumbosacral reflex excitability to neck and forepaw nerve stimulation. Ablation of the post-cruciate dimple only transiently affects cervico-lumbar interactions, whereas ablation of the anterior pole of the suprasylvian gyrus reduces or abolishes cervico-lumbar interactions for the duration of acute experiments. Thus the suprasylvian gyrus may play some role in integrating spinal reflex excitability and hence may be regarded as part of the cortical mechanisms for regulating posture. Such a view is supported by the known connections in this region which include input from many sensory systems, including the vestibular system.

Supported by grants from the Medical Research Council of Canada.

TEMPERATURE DIFFERENCES IN UMBILICAL BLOOD VESSELS OF SHEEP FETUS IN UTERO. R. M. Abrams, D. Caton*, J. Clapp* and D. H. Barron. John B. Pierce Fdn. Lab. and Depts. of Epidem. & Pub. Health, Anesthesiology and Physiology, Yale Univ. Sch. of Med., New Haven, Conn.

As determined by means of indwelling thermocouples, the temperature difference between umbilical artery and umbilical vein of the sheep fetus in utero during the last month of gestation ranges between 0.1-0.4°C. In general, smaller differences were found during the first few days following surgery. After the post-operative period, wider temperature differences became the rule. A larger difference was noticed also when the thermocouples were found at delivery to be at the body wall of the fetus. 3 of 7 fetuses showed no temperature difference after surgery and they were delivered dead. From data on average O_2 consumption and average umbilical blood flow rates of fetal lambs in utero (Meschia, et al., Crenshaw, et al., Quart. J. Exper. Physiol., 1967, 1968), we calculated that all the fetal metabolic heat could be lost via the umbilical circulation if a temperature difference of 0.2-0.3°C could be maintained between umbilical artery and umbilical vein.

This study was supported by USPHS Grants HD03575-01 and HD02300-08.

HYPOTHALAMIC CONTROL OF BEHAVIORAL TEMPERATURE REGULATION IN THE SQUIRREL MONKEY. Eleanor R. Adair (intr. by - J.A.J. Stolwijk). John B. Pierce Foundation Laboratory, New Haven, Conn.

Thermode and thermocouple re-entrant tubes were implanted unilaterally in the medial preoptic area of the hypothalamus of squirrel monkeys (Emmers and Akert coordinates: A 12.5, L 0.5, D + 1.0). Placements were verified by X-rays and histologically. The tubes emerging from the skull were countersunk in acrylic making postoperative restraint of the monkeys between experiments unnecessary. Water perfusion of the thermode shifted brain temperature within the range 35 - 43C. Hypothalamic, ambient, rectal and three skin temperatures were monitored during behavioral temperature regulation. Convective heating and cooling of the animal's chamber was achieved by a valve system that allowed air from one of two thermostatically-controlled sources to circulate through the chamber. Monkeys learned to pull a chain to operate the valves, thus selecting between two aversive air temperatures, 10 and 50 C. Typical behavior produced cycling between the two to achieve an average ambient temperature of 33 - 35 C. Cooling the hypothalamus 0.5 - 4.0 C below neutral (39.5 C) motivated the monkey to immediately select the hot air for a duration linearly related to the magnitude of the brain temperature displacement. Rectal and skin temperatures rose. Conversely, warming the hypothalamus 0.5 - 3.0 C above neutral motivated the animal to lower the air temperature immediately and caused a subsequent fall in rectal and skin temperatures. The monkeys resumed behavioral cycling of air temperature to achieve thermal balance, often at a new average ambient temperature.

Supported by USPHS Grant ES-00354.

THE EFFECT OF AGE UPON CARDIORESPIRATORY RESPONSE TO A MULTISTAGE TREADMILL WALK TEST. William C. Adams, Edmund M. Bernauer, and Malcolm M. McHenry (intr. by A. H. Smith). Human Performance Laboratory, Physical Education Department, University of California, Davis, California.

Eighty normal, sedentary middle-aged males undertook a progressively intensified (via increased speed and grade) treadmill walking test which was terminated by the subject's inability or unwillingness to continue (usually due to severe shortness of breath or faltering gait and general muscular fatigue), or by completing 45:00 of walking. EKG tracings, heart rate, blood pressure, pulmonary ventilation and oxygen consumption were taken serially during the walk and for 15 minutes postexercise. Grouping into 20 subjects in each of 4 decades from 30-69 yrs yielded the following age related observations: 1) No significant difference between groups in resting oxygen uptake (ml/min/kg); 2) Resting blood pressure was significantly higher in the two older groups (146/86 vs. 127/77); 3) Maximum walk time decreased with age (39.0, 36.3, 34.5 and 29.5 min., respectively) in direct proportion to maximum oxygen uptake; 4) Maximum ventilation was significantly lower in Group IV, who also demonstrated higher oxygen ventilatory equivalents throughout the walk; 5) Terminal blood pressure was not significantly different, although Group IV had higher blood pressures throughout the test; 6) Maximum heart rate was 184, 178, 171 and 155, respectively; and 7) Oxygen uptake (ml/min/kg) did not differ by more than 5% among groups at any stage of the test, although when expressed as ml/min/kg (LBW), the older subjects had higher values. No ischemic ST segment depressions greater than 0.1 mv. were noted. Postexercise recovery values showed similar age relationships. Although an r of -0.70 between age and walk time was noted, a much stronger relationship was found between maximum oxygen uptake and walk time (r=0.93), indicating that physiological factors other than those indicated by chronological age alone, are responsible for work capacity.

CORTICAL NEURONAL AND SILENT CELL MEMBRANE POTENTIALS AFTER EXCESS CALCIUM IONS. W. Ross Adey & Elizabeth M. Rovner*
Dept. of Anatomy & Space Biology Laboratory, University of California, Los Angeles.

We have studied membrane potentials (MPs) in 601 neurons and 285 silent cells of conscious cats. Silent cells (SCs) were first seen at depths of 200u and neurons at 400u. MPs of neurons were typically 30 to 50mV, with lower values in brief penetrations. MPs of SCs ranged from 20 to 85mV. SCs depolarized 10-15mV when aleolar CO2 increased from 4 to 6 percent. Calcium chloride (60 or 90uEq in 0.1ml) was applied topically every 10 min. (total dose 500uEq). With 60uEq doses, SCs were rarely detected 90 mins after Ca in the outer 1.0mm cortex. Neuron MPs were simultaneously shifted to higher values (50 to 85mV). MPs of neurons and SCs at greater depths were unchanged. After 2 h, SCs again appeared in the outer 1.0mm, often with high MPs (80 to 95mV). By contrast, after 90uEv doses, very few MPs of either neurons or SCs were seen in the outer 1.0mm in the first 90 mins, and hyperpolarized neurons were rare. Neuronal MPs gradually reappeared here after 2 h, together with silent MPs in the range 20 to 45mV. Deeper SCs showed MPs from 55 to 75 mV. Electron microscopy showed no major changes after Ca. Thus, raised calcium levels that hyperpolarize neurons may also depolarize certain silent membranes. These studies were assisted by PHS Grant MH-03708 and USAF Contract 49-638-1387.

EFFECTS OF MORPHINE ON THE CONVERSION OF ^{14}C TRYPTOPHAN (TP) AND ^{3}H TYROSINE (TY) INTO TELENCEPHALIC SEROTONIN (5-HT), NOREPINEPHRINE (NE), AND DOPAMINE (DM). S. Algeri*, A. Revuelta*, and E. Costa. Lab. of Preclinical Pharmacology, Natl. Inst. of Mental Health, Saint Elizabeths Hospital, Washington, D.C. 20032.

We implanted male rats with two 75 mg pellets on day 1 and 3. On day 6 these rats were hyperthermic and lethargic. Nalorphine (50 mg/kg i.p.) elicited hypothermia, salivation, lacrimation, diarrhea, restlessness, increased motor activity, and "wet dog" shakes in morphine implanted but not in normal rats. Six days after morphine implantation, we infused intravenously 8 treated and 6 normal rats with ^{14}C TP (2 μc/kg/min) and ^{3}H TY (48 μc/kg/min). After 45 min. of infusion, we measured the specific activity (SA) of various compounds in plasma (PL) and telencephalon (TL).

	dpm/mμmol ± S.E.									
	(PL)	(TP)	(TL)	(5-HT)	(PL)	(TY)	(TL)	(NE)	(TL)	(DM)
Control	2996 ± 318		430 ± 66		8182 ± 1022		1123 ± 192		912 ± 56	
Morphine	2116 ± 145		451 ± 53		8802 ± 2061		747 ± 95		851 ± 102	

The infusion did not change TP and TY steady state levels in PL or TL. Moreover, we found that morphine neither changes the SA of TY and TP nor the steady state level of 5-HT, NE, and DM in TL. Hence, the ratio between the specific activity of 5-HT, NE, DM, and plasma, TP, and TY reflects the amine turnover rate. Our results suggest that morphine accelerates the turnover rate of 5-HT but slows that of NE.

ROLE OF CALCIUM IONS IN THE PHENOMENON OF DRUG-INDUCED UNEQUAL MAXIMUM CONTRACTILE RESPONSES OF VASCULAR SMOOTH MUSCLE (VSM). Burton M. Altura, Bella T. Altura* and R. Zeman*. Albert Einstein Col. of Med., Bronx, New York 10461

Considerable evidence has accrued which suggests that calcium ions (Ca) are necessary for contraction of all types of muscle including VSM. A property common to VSM is the ability of different drugs to induce unequal maximum contractile (UMCR) responses. It is not unreasonable to assume that different drugs could induce UMCR in VSM either through unequal utilization of the same cellular Ca fraction or use of different Ca fractions. Helically cut rabbit aortic strips were set up isometrically in-vitro. Maximal or supramaximal concentrations for 7 drugs revealed the following descending order of per cent maximum contractile response in normal Krebs-Ringer (K-R): epinephrine (E)>histamine$\cong$barium (Ba)>serotonin$\cong$potassium (K)>angiotensin>acetylcholine. Cumulative log-dose response curves revealed that the relative order of drug potency shows no relationship to the relative order of per cent maximum response (epinephrine). Exposure of rabbit aorta to Ca-free K-R containing EDTA for various intervals of time revealed that the 7 drugs exhibit different rates of loss of contractility with time and different relative order of maximum response. Although readmittance of Ca cumulatively (up to 10mM), after either 0.5hr or 2hrs in Ca-free K-R, failed to restore most of the drug induced responses to their maximums, Ca did restore the order of relative maximum response, except for K. Ba ions could only substitute for Ca in K and E-induced contractions. The data suggest that although all drugs probably require Ca for contraction of VSM, different drugs can utilize different bound stores of Ca (some are depleted sooner than others); E and K can utilize both bound and extracellular Ca ions. (Supported by 1-K3-GM-38, 603-01, HE-12462 and HE-11391).

THE "PROTECTIVE" EFFECT OF METABOLIC ALKALOSIS ON MYOCARDIAL MUSCLE DURING ACUTE ANOXIA. G. Anderson*, J. Souhrada*, R. W. Bullard, and J. J. McGrath*. Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

Several studies have shown that heart and skeletal muscle preparations isolated from rats adapted to high altitude maintain function longer in anoxia and recover faster after anoxic depression. In looking at mechanisms of this anoxic tolerance we decided to study the effect of altered pH, an important factor in the control of glycolytic rate. This was done using both the right ventricular strip preparation (RV) and the heart lung preparation (HL). Metabloic alkalosis (MA) was induced using NaOH, $NaHCO_3$ and Tris buffer. Experimental anoxia was brought about by switching the aerating gas mixture from 100% O_2 to 100% N_2 in RV and from 95% O_2 - 5% CO_2 to 95% N_2 - 5% CO_2 in the HL. Oxygen tension was followed continuously in the IRV bathing medium. The pH during experimental anoxia ranged from 7.5 to 7.7 in the experimental groups and 7.1 to 7.2 in control groups. Measurements of myocardial contractility and static cardiac work were made in the RV and HL respectively. Alkalinity increased the resistance of both preparations to anoxia as evidenced by a prolonged period of contraction during oxygen deprivation and a greater recovery of function afterwards in both types of preparation. These data indicate that alkalosis has a marked protective effect on the rat heart muscle during acute anoxia, and suggest the possibility that increased tissue buffering capacity could explain some of the functional changes even in tissues following adaptation. (Supported by U.S. Air Force Contract F 44620-68-C-0014)

DISTORTION OF THE HEART DIPOLE MOMENT. E. T. Angelakos, C. V. Nelson, P. G. Hugenholtz* and P. R. Gastonguay*. Maine Medical Center and New England Regional Primate Center.

Studies were made in 17 dogs and 11 rhesus monkeys using the Nelson lead system for obtaining the spatial dipole moment vector based on surface intergals and taking into account the dimensions of the torso (Nelson et al. Circ. Res. 17:168, 1965). Three peaks were identified as M_1, M_2 and M_3 at mean times of 30%, 48% and 63%, of QRS duration, corresponding to septal, LV transmural and LV epicardiac excitation. The resistivity of the blood is normally 1/3 that of myocardium (150 vs 450 ohm-cm). Increasing hematocrit (by exchange transfusion of packed cells) increased blood resistivity (creating more homogenous heart-blood electrical conditions), and generally decreased the magnitude of M_1 and M_2 and increased the magnitude of M_3. These changes were of the order of 25% to 40%. It is concluded that the presence of the intracardiac blood distorts the magnitude of the recorded spatial QRS voltages by enhancing those associated with septal and LV transmural excitation (radial spread) and attenuating voltages due to LV epicardiac excitation (tangential spread). This conforms with expected changes for radial and tangential dipoles near a highly conductive mass.

EVIDENCE FOR CHOLINERGIC PARTICIPATION IN CENTRALLY-INDUCED NATRIURESIS. Jose Antunes-Rodrigues*, Janice Dorn* and S.M. McCann. Dept. Physiol., Univ. Tex. Southwestern Med. Sch., Dallas, Texas 75235.

Although the dipsogenic properties of carbachol implanted in the hypothalamus have been well documented, no systematic study of its effects on electrolyte excretion appears to have been made. For this purpose, carbachol was injected through chronic, indwelling cannulae into either the 3rd or lateral brain ventricle of conscious, water-loaded male rats. Animals were placed in individual metabolism cages with no food or water, and 20 min urine samples were measured and analyzed for Na^+ and K^+. In a series of 30 rats, 3rd ventricular carbachol in doses from 0.1μg-2.0μg (2μl) consistently produced a 6-9 fold increase in Na^+ excretion. This natriuresis was not seen after intraventricular isotonic NaCl, or following intramuscular administration of carbachol. Low doses of carbachol which were effective in the 3rd ventricle were ineffective if injected into the lateral ventricle, although higher doses (1-2μg) in this location evoked natriuresis. Despite the fact that urinary K^+ was elevated during the natriuresis, the Na/K excretion ratio increased, and urinary volume remained essentially unchanged. Rats completely hypophysectomized 1-2 weeks previously still manifested a natriuretic response to 3rd ventricular carbachol. The natriuresis seen in both intact and hypophysectomized rats was abolished by injecting 150μg atropine at the time of the water loading (1 hr 20 mins prior to carbachol treatment). Elicitation of large increases in sodium excretion by carbachol and blockade of the response by atropine implies a role for a cholinergic mechanism in centrally-mediated natriuresis. The natriuresis is not dependent on the presence of the hypophysis and may reflect the activity of some specific natrioceptive system, perhaps involving a natriuretic hormone. (Supported by NIH grant #10073-04)

DISUSE OF STRETCH AFFERENTS BY CHRONIC TENOTOMY AND DE-EFFERENTATION. R.S. April* and W.A. Spencer, New York University Medical School, NYC (Supp. USPHS NB-05980, NB-113-02).

Previous work indicated that, several weeks following combined tenotomy and ventral root transection, there was an increase in the effectiveness of group I fiber actions on the cells of Clarke's Column. These findings suggested that chronic afferent fiber disuse is associated with increased effectiveness of these same fibers in discharging these post-synaptic cells; but it was necessary to rule out the possible existence of trophically induced tonic activity. Therefore, we measured resting discharge frequency and functional properties of 112 group I and II afferents supplying previously tenotomized and de-efferented triceps surae muscles. There was no evidence of any increase in resting discharge frequency of such units; the mean frequency (5.2/sec.) was nearly identical to that of afferents of normal muscle (6.5/sec.). Moreover, in experiments in which the experimental muscles were not exposed, passive rotation of the ankle joint (through a range similar to that of normal postural movements) produced no or very little increase in unit discharge. In contrast, very slight ankle rotation in comparable normal control preparations was associated with the usual large increases. We may therefore assume that, in tenotomized and de-efferented muscles, postural ankle rotation would fail to increase discharge frequency in muscle stretch afferents to a level comparable to that occurring on the normal, control side; hence the experimental stretch sensitive afferent fibers would be relatively disused. These control experiments further support the inference that disuse is associated with increased synaptic effectiveness at this relay.

ELECTRO-MECHANICAL CORRELATES OF PAPILLARY MUSCLE CONTRACTION. J.A. Armour and W.C. Randall. Department of Physiology, Loyola University, Chicago, Illinois.

Strain gauge arches containing an insulated unipolar electrode on one foot were applied to the longitudinal surface of the anterior and posterior papillary muscles and to overlying epicardial segments of the left ventricle. During a normal cardiac cycle, the papillary muscle showed electrical activation concurrently with the initial deflection of the Q-wave of the standard ECG, followed in 5 to 10 msec. by similar activation of the epicardium. However, mechanical contraction occurred first in the epicardial segments followed in 25 to 30 msec. by contraction of the papillary muscles. Intraventricular pressure began to rise an average of 10 msec. before detectable contraction appeared in the papillary muscles. This contractile sequence can be altered by ectopic stimulation of the epicardium or endocardium. In control circumstances, papillary muscle contractile force is of relatively low magnitude with only moderate increases resulting from increased preload or afterload on the left ventricle. Direct electrical excitation of the stellate ganglia or norepinephrine injections induced eight to ten-fold increase in contractile force and dF/dt. Stimulation of small branches of the sympathetic cardiac nerves often elicited separate augmentation of contraction in only one of the papillary muscles within the left ventricle while another may augment only the remaining muscle. *(Supported by NIH Grant HE 08682)*

EFFECT OF SIMULATED ALTITUDE ON GLUCOSE KINETICS IN SHEEP. M.E. Augustine* and R.W. Phillips. Colorado State University, Fort Collins, Colorado 80521

The effect of altitude exposure on glucose utilization was studied using six intact young adult male sheep. Glucose biokinetics were determined at 1500 m, ambient elevation in Fort Collins. The sheep were then placed in a hypobaric chamber and maintained at a simulated altitude of 6200 m for 32 days. Additional measurements of glucose utilization were carried out during acute acclimation, after 4 weeks at simulated altitude and following return to ambient elevation. Plasma glucose concentration decreased from 82 to 69 mg/100 ml after the 4 week acclimation period. Plasma glucose concentration during the acute and recovery phases was not significantly different from the control values. During the chronic phase glucose space as a percent of body weight increased from 28.5 to 35.9. The entry rate increased nonsignificantly from 2.11 to 2.42 mg/min/kg body weight after the 4 week acclimation. There was a corresponding nonsignificant decrease in the turnover time from 116 to 108 minutes. The pool size increased by 15% during this 4 week period. The seeming paradox of an increasing pool size and decreasing glucose concentration may be explained by the marked increase in glucose space, which is in agreement with the previously reported increase in extracellular space. In spite of the changes in glucose distribution there did not appear to be a major change in the rate of glucose metabolism due to altitude acclimation.

SUPPRESSION OF THE LUTEOTROPHIC RESPONSE TO COITUS IN RATS BEARING PITUITARY GRAFTS IN THE HYPOTHALAMUS. R. L. W. Averill, University of Tennessee Medical Units, Memphis, Tennessee.

Mature female Wistar rats received grafts in the anterior hypothalamus of pituitary (PG rats) or cerebral cortical tissue (CG rats) from neonates. Estrus cycle lengths determined from daily vaginal smears were essentially normal in rats with both types of graft and in sham operated controls (SO rats). After introduction of males of proven fertility all control rats conceived, littered and lactated at least once. 81% of 64 matings in CG rats, 78% of 30 matings in SO rats and 82% of 29 matings in colony controls were followed by the birth of litters. By contrast only 3 out of 151 matings (1.98%) in PG rats resulted in litters and none of the 3 does lactated. Mating was proven by presence of spermatozoa in vaginal smears. After 112 matings in PG rats estrus returned after a mean of 4.54 ± 0.09 days *post coitum*. Ovulation and fertilization occurred normally as shown by the presence of penetrated cleaved tubal ova in 12 PG rats, but estrus smears recurred in 4 or 5 days. Both the grafted and *in situ* pituitaries were examined histologically from 16 PG rats using Herlant's tetrachrome stain to distinguish prolactin acidophils. Prolactin cells were more numerous in the grafts than in the *in situ* pituitaries and were significantly larger (mean diam. = 9.8 ± 0.12 μ for 150 graft cells vs. 5.7 ± 0.07 μ for 150 *in situ* cells, $p < 0.001$). Progesterone (2 mg) given daily from mating to 13 PG rats resulted in birth of 4 litters. The luteotrophic response to coitus was blocked by the presence of neonatal pituitary tissue, but not cerebral cortex, grafted into the anterior hypothalamus. The data suggest that prolactin secretion of the *in situ* pituitary was inhibited by prolactin from grafts in the hypothalamus, confirming the likelihood of an internal feedback loop in control of prolactin secretion. Supported by NSF Grant GB 7319.

THE ROLE OF GLUCAGON AND ADENYL CYCLASE IN THYROCALCITONIN RELEASE IN DOGS. Louis V. Avioli, Carole K. Early* & Susan L. Scott,* Dept. of Medicine, Washington University School of Medicine, St. Louis, Missouri.

Previously, it had been demonstrated that the thyroid gland of the dog responds to glucagon perfusion *in situ*, by the release of a hypocalcemic substance presumed to be thyrocalcitonin. To further evaluate this phenomenon, the thyroid glands of adult anesthetized mongrel dogs were perfused *in situ* with varied concentrations of glucagon (5-23μg/ml) and dibutyryl cyclic AMP ($5x10^{-5}$-$2x10^{-4}$M). Changes in thyrocalcitonin secretion rate were deduced from inverse changes in the systemic plasma calcium concentration. Thyroid perfusion with glucagon (23μg/ml) or dibutyryl cyclic AMP ($2x10^{-4}$M) resulted in systemic hypocalcemia. Concentrations of glucagon (5μg/ml) and dibutyryl cyclic AMP ($5x10^{-5}$M) in the thyroid perfusates which did not induce systemic hypocalcemia when perfused individually, resulted in an abrupt and sustained fall in serum calcium when perfused simultaneously. The addition of 5mM theophylline to thyroid perfusates containing glucagon (5μg/ml) caused a sustained hypocalcemia. Similar changes in serum calcium were noted upon the addition of dibutyryl cyclic AMP ($5x10^{-5}$M) to perfusates containing 5mM theophylline. These results support the conclusion that the glucagon-stimulated release of thyrocalcitonin, like hypercalcemia, is mediated via activities of an adenyl cyclase system within the thyroid light cells.

PROPERTIES OF THE LUNG LINING LAYER IN SITU. H. Bachofen*, J. Hildebrandt and M. Bachofen*. Virginia Mason Research Center, Seattle Washington 98101.

The method of Brown (P.S.E.B.M. 95:168, 1957) for the calculation of γ -A curves from P-V curves has been modified and applied to extended data including complete tidal volumes at various FRC's covering a wide range of frequencies. Fresh excised cat, dog or monkey lungs were inflated with air at fixed flow rates in a volume-displacement plethysmograph according to predetermined volume patterns, followed by saline inflation in the same patterns. Pressures were read after 5 sec stops. When the period of a given tidal volume was varied from 70 sec to 2050 sec, the areas of both air and saline P-V loops were found to be almost constant. By implication, the hysteresis of the surface lining is also frequency independent, and accounts for about 3/4 of the total hysteresis of the normal P-V loop. When the volume pattern simulated normal and deep breaths beginning at various FRC's, the γ -A loops derived from P-V curves differed in certain respects from typical surface balance loops. (1) γ fell very rapidly to 5 dynes/cm at 80% of A_{max} and continued to fall below 2 dynes/cm at 60% A_{max}. (2) The re-expansion limbs of the γ -A loops were displaced from the compression limbs, but not widely. The difference in γ between compression and expansion limbs for tidal volumes of 15-20% TLC, near mid-lung volume, was only 2-3 dynes/cm. (3) The area of tidal γ -A loops was roughly proportional to $\Delta\gamma$ between the ends of the loop, thus becoming much larger near TLC. (4) If the deep breath commenced from below 60% of A_{max}, a knee began to appear on the expansion limb, which became more pronounced the lower the FRC. This knee may in part arise from airway closure or alterations in geometry. (Supported in part by the Tuberculosis Association of King County, Washington)

MICROVASCULAR SMOOTH MUSCLE: INTERFERENCE WITH MUSCLE CELL SHORTENING ACTION OF CATECHOLAMINES AND POLYPEPTIDES BY DIBENZYLINE, HISTAMINE AND BETAHISTINE. S. Baez Depts. of Anesth. and Physiol. Albert Einstein Col. of Med. Yeshiva University, Bronx, New York 10461

Following procedures already described (Science, 159:536, 1968) the chemo-mechanical transducing action of selected stimulating and relaxant molecules on single smooth muscle cells have been examined in situ. The changes (in micra and per cent) of muscle cell thickness in the wall of microvessels of the lightly anesthetized rat to the action of the catecholamines, epinephrine and norepinephrine, and the polypeptides, pitressin and angiotensin, were first determined. The modifying effects of topical dibenzyline, histamine, and betahistine, on the action of the above muscle stimulating agents were then assessed. Increases in muscle cell thickness of 57.8% and 47.4% produced, respectively, by epinephrine (aver. 1.7 µg/ml) and norepinephrine (aver. 1.9µg/ml) were completely supressed by a 3 min. exposure of the cells to dibenzyline (0.01µg/ml). The same amount of dibenzyline failed to modify increases in cell thickness (aver. 32.2%) produced by angiotensin (aver. 2.17µg/ml) and rather enhanced increases in cell thickness (aver. 62.4%) produced by pitressin (aver. 0.049p.u./ml). In contrast to this, both topical histamine and betahistine usually abolished the muscle shortening action of the catecholamine and the polypeptides. In light of the findings possible mechanism(s) of such differing actions of the alpha receptor blocker, the autacoid and its synthetic homologue will be discussed.

Supported in parts by NIH Grant #HE-06736-09 and funds from Unimed, Inc.

BLOOD FLOW AND VOLUME DISTRIBUTION WITH ELEVATED VENOUS PRESSURE. Carleton H. Baker. University of Louisville School of Medicine. Louisville, Kentucky 40202.

It has been reported by several authors that with elevated venous pressure there is an increase in total vascular volume, an increase in small vessel resistance and a reduction in filtration coefficient indicating a smaller capillary surface area. Is this increase in vascular volume contained in vessels with actively flowing blood or is it sequestered in closed off vessels? Is there also a redistribution of blood flow between the parallel circuits? Two groups of isolated dog forelimbs were perfused at constant blood flow rate (11 innervated, 8 denervated). Each group of forelimbs was studied at venous pressure levels of 5 mm Hg, 15 mm Hg and 35 mm Hg. There seemed to be no differences between the groups. The filtration coefficient and PS values decreased as the venous pressure was increased to the 15 mm Hg level, but changed little with increase to 35 mm Hg. Total vascular volume (Plethysmograph) increased with each venous pressure elevation. Active vascular volume, as determined by red cells-^{51}Cr and albumin-^{131}I, remained unchanged on the first elevation of venous pressure, but with the final increase in venous pressure the volume increased by an amount approximating the sum of the total vascular volume changes for the two venous pressure increases. Therefore, blood added to the forelimb by the first elevation of venous pressure was trapped in blood vessels not actively flowing. Following the final increase in venous pressure blood flow was redistributed to non-exchange vessels that bypassed capillary vessels and emptied into venules that had been closed (Supported by USPHS Grant 2 RO1 HE 11966.)

VENOUS SHUNTING IN THE NON-CROCODILIAN REPTILE HEART. Lawrence A. Baker* and Fred N. White. Department of Physiology, UCLA School of Medicine, Los Angeles, Calif.

Ventricular output (VO) and venous shunting were determined in the chronically prepared common Iguana (Iguanidae) and Tegu (Teiidae) by modified Fick method under controlled conditions of body heating (average rate of core temperature increase was 0.125°C/min). Determinations for O_2 (ml/100 ml) were made on blood taken from cannulas placed in the right common carotid artery (A_{O2}), sinus venosus (V_{O2}), and femoral artery (F_{O2}); blood flow in the dorsal aorta ($\dot{Q}_{da}$) was measured with an electromagnetic flowmeter; and oxygen consumption rate (OCR) was recorded spirometrically. Calculations were made from the following equation: $VO = [OCR/(A_{O2}-V_{O2})] + [\dot{Q}_{da}(A_{O2}-F_{O2})/(A_{O2}-V_{O2})]$. The first term represents the contribution to VO made by blood returning from the pulmonary circuit, while the second represents shunted venous blood. Shunting of venous blood, bypassing the pulmonary circuit, was between zero and 30% of ventricular systemic output during heating, effective separation of venous and arterial blood taking place during states of thermal equilibrium. The shunting of venous blood past the pulmonary circuit may aid in acquiring heat by reducing heat loss through the lungs due to heat conductance from blood to air. Shunting during body heating may also conserve cardiac energy when increased ventricular output is required to sustain an increase in peripheral blood flow necessary for increasing body thermal conductance. (Supported by USPHS grant HE 5696 and NSF grant GB 8523)

ACTIVITY OF SINGLE NEURONS IN THE SOMESTHETIC CORTEX OF THE AWAKE CAT. M. A. Baker, E. E. Fetz* and A. L. Towe, Dept. of Physiol. & Biophys., Univ. of Wash. Sch. of Med., Seattle, Washington 98105.

The spontaneous and evoked activity of 103 single neurons isolated in somatosensory area I has been studied. The cat was restrained in a hammock, while simultaneous recordings were made of extracellular unit activity, the cortical EEG, and gross behavior. In the awake cat, 37% of the neurons were silent, but could be driven by natural stimulation of the skin or by electrical stimulation of the forearm nerves through implanted electrodes. The remaining 63% showed a resting discharge of low frequency. Of these, the discharge of 41% was apparently produced by gross movements of the animal which stimulated the cutaneous fields of the neurons, whereas the activity of the rest could not be ascribed to such movements. Units were isolated in coronal cortex, lateral to the dimple on posterior sigmoid gyrus; they could be activated by hair deflection or skin touch over small areas of the contralateral forepaw and by electrical stimulation of the median or ulnar nerves. Response to a single 0.05 msec., 0.5-1.0 ma. shock to a nerve usually consisted of a single spike at 5-6 msec. latency; it remained constant over many iterations (100-200) at low rates. Such shocks did not disturb the cat in any way.

Most spontaneously active neurons showed a burst pattern of spikes during slow EEG sleep, resulting in a less regular discharge than seen during waking. Several neurons which were silent during waking showed a similar burst pattern during slow EEG sleep. On the other hand, the response to both natural and electrical stimulation was similar during waking and slow EEG sleep.

(Supported by NINDS research grant NB396, the Bank of America-Giannini Foundation, and NIH training grant NB05082-13.)

MODIFICATION OF STRESS PEPTIC ULCERATION BY DIET. B. E. Baldwin* and Marjorie V. Baldwin*. Loma Linda Univ. Med. Sch., Loma Linda, Calif., 92354

Production of stomach ulcers in rats by restraint stress has been demonstrated by many workers. Cheney and others have shown that histamine induced peptic ulceration of the stomach can be modified by heat labile factor(s) in fresh cabbage. We have examined the dietary manipulation of ulceration of restraint stress. A total of 74 female Fischer weanling rats were put into 3 feeding groups: ground lab chow, ground chow plus fresh cabbage, ground chow plus black pepper. After 6 weeks of feeding, animals were fasted 24 hours, and placed into quantitative volume restraint cages set for 1.42 ml/gm of body weight for 24 hours. After sacrifice, the area of stomach lesions was measured with an ocular micrometer in a Zeiss dissection microscope. Results: average lesion area for the lab chow group, 7.4 mm^2; lab chow plus fresh cabbage, 5.3 mm^2; and for lab chow and black pepper, 10.3 mm^2. We conclude that stress ulceration can be reduced by protective diet and increased by the spice black pepper.

OSMOLAR AND pH SENSITIVITY OF SOME INTESTINAL MUCOSAL RECEPTORS. Marjorie V. Baldwin* and J. Earl Thomas. Loma Linda Univ. Med. Sch., Loma Linda, Calif., 92354

Evaluation of the intrinsic intestinal mucosal reflex of Hukuhara (contraction above and relaxation below a point of mucosal stimulation) (1) requires knowledge of the adequate stimuli. We have previously (2) reported on the effect on distribution of intraluminal pressures of mucosal stimulation with certain food products and digestive secretions in unanesthetized fistula dogs. This report deals with the sensitivity of the mucosal receptors to the pH and osmolar concentrations of aqueous solutions. Phosphate, bicarbonate, and glutamate buffers were used to study pH sensitivity, and distilled H_2O and NaCl solutions for osmolar stimulation. No consistent response was obtained to 1 ml of buffer solution between pH 4.5 and pH 9.5. Bicarbonate buffer at pH 10, and glutamate buffer at pH 3.1 consistently induced the reflex, phosphate buffer at pH 4.5 usually did so. Isotonic Locke-Ringer solution was without effect. Distilled H_2O in 1 ml doses gave only equivocal responses as did 2% NaCl. Five percent NaCl was an effective stimulus. We conclude that, except in the acid pH range, the mucosal receptors involved in this reflex are insensitive to hydrogen and hydroxyl ion activity within the physiological range and relatively insensitive to osmolar activity. (Supported by NIH Grant AM01445).

REFERENCES:

1. Hukuhara, T., Yamagami, M., and Nakayama, S., (1958): Jap. J. Physiology., 8:9-30
2. Baldwin, M.V., and Thomas, J.E., (1969): Fed. Proc., 28:717.

ELECTRON TRANSPORT RELATIONSHIPS IN ENDOTOXIN SHOCK. Basdeo Balkissoon, Leslie C. Costello, and Robert L. Simmons*. Depts. of Surgery and Physiology, Coll. of Med., Howard University, Washington, D.C. 20001

The underlying mechanism and biochemical alteration associated with endotoxin shock has not been elucidated. It has been observed that animals with endotoxin shock develop decreased oxygen consumption. We have studied the involvement of the cytochrome system and lactate and pyruvate changes in blood and tissues of animals given endotoxin shock. Rabbits were injected with E. coli endotoxin 4 mg/kg and were sacrificed 5 hours later. The heart, liver and kidneys were excised and the mitochondria from these tissues and those from normal animals were prepared by differential centrifugation. Cytochrome c oxidase activity was determined spectrophotometrically by tracing the oxidation of reduced cytochrome c. Cytochrome c reductase activity was determined by following the reduction of oxidized cytochrome c with succinate. The results indicate no significant difference in the rates of cytochrome oxidase or cytochrome reductase specific activities as compared to controls in the 3 tissues in 12 animals studied. Therefore it seems that the electron transport system is not inhibited by endotoxin treatment and would not account for the changes in O_2 consumption observed by others. Initial studies show that in the endotoxin animals plasma pyruvate and lactate levels are increased. Pyruvate levels in the 3 tissues are not elevated. Lactate levels in liver and kidneys but not heart are increased. Studies on the effects of the toxin on phosphorylation are in progress. Supported in part by Grant 2ROI AM 12187-02 GMB

OXYGEN TRANSPORT IN THE LLAMA. N. Banchero, J.A. Will* and R.F. Grover. Univ. of Colo. Med. Ctr. Denver, Colo. and Univ. Wisc. Madison, Wisc.

Because llama Hb has high affinity for O_2 cardiac output and in vivo O_2 dissociation curves were determined in male, unmedicated, sea level llamas (A, 5 mo; B, 7 mo; C, 14 mo.) at rest and during hypoxia (P_{IO_2} 72-78 mmHg) while at 260 m. and after 5 and 10 weeks at 3420 m.

		Sea Level			5 wks at 3420			10 wks at 3420		
		A	B	C	A	B	C	A	B	C
REST	Hb g/100 ml	9.5	11.9	10.3	9.4	10.2	9.8	10.5	10.9	14.1
	$\dot{Q}$ ml/min/kg	137.9	112.3	104.9	124.8	128.0	119.3	129.9	145.0	108.3
	A-V ml/L	40.9	48.6	46.0	43.8	41.2	53.2	41.5	44.6	56.2
	O_2T ml/min/kg	17.4	17.9	14.5	15.0	16.1	14.6	17.3	19.5	19.6
	S_a O_2%	97.8	98.7	95.0	93.5	90.2	91.9	93.7	90.7	94.2
	P_a O_2 mmHg	79.2	95.9	86.9	49.2	53.9	51.1	53.2	51.2	53.5
	S_v O_2%	68.0	70.0	63.5	60.0	61.2	52.5	65.0	61.2	65.4
	P_v O_2 mmHg	28.0	30.0	32.0	25.2	28.8	26.0	30.5	28.1	29.3
HYPOXIA	$\dot{Q}$ ml/min/kg	138.8	116.4	122.0	150.9	152.7	136.0	129.9	155.0	104.0
	A-V ml/L	41.4	34.5	31.4	36.7	33.7	33.4	42.6	51.5	54.8
	O_2T ml/min/kg	13.3	12.3	12.0	15.8	15.9	12.3	14.3	18.8	15.9
	S_a O_2%	74.0	70.0	72.4	81.0	76.7	70.2	75.0	77.7	77.7
	P_a O_2 mmHg	27.5	30.0	35.5	33.0	34.8	30.2	30.8	32.0	36.5
	S_v O_2%	42.4	47.2	49.4	52.8	52.1	44.2	46.1	44.8	50.1
	P_v O_2 mmHg	17.2	22.2	26.2	22.0	25.1	21.9	21.0	22.2	24.8

Prolonged hypoxia did not cause a systematic shift in the O_2 dissociation curve. Due to the shape of the O_2 dissociation curve adequate O_2 uptake was maintained at altitude by narrowing the difference between P_aO_2 and P_vO_2, the latter being above 25 mmHg. During acute hypoxia increased $\dot{Q}$ helped maintain an adequate tissue O_2 uptake, while keeping P_vO_2 at about 20 mmHg. (Supported by GRS-108 and Colo. Heart Asso.)

PRECESSION CLEARANCE OF WATER. R.O. Banks* & E.C. Foulkes. Dept. of Env. Health & Physiol., Univ. of Cinti. Col. of Med., Cincinnati, Ohio.

We have reported (A.J.P. 215:574, 1968) that urinary precession of Na^{22} over simultaneously injected inulin, when expressed as precession clearance ($CPR_{Na^{22}}$) approximates medullary plasma flow. Results from 14 kidneys in 7 dogs receiving 10% mannitol and 0.1 mg/min/kg Furosemide establish the close correlation of $CPR_{Na^{22}}$ with arterial blood pressure ($CPR_{Na^{22}}$, ml/min/kg body wt = 0.0026 x B.P., mm Hg - 0.16; r = 0.98, S.E. 0.009) over the range of 70-190 mm Hg. In contrast, RPF and GFR showed the expected autoregulation. Blood pressures below and above normal were attained by means of a balloon catheter in the thoracic aorta or carotid clamps, respectively. Studies in the same dogs with tritiated water (TOH) revealed the same relationship between CPR_{TOH} and blood pressure. In 4 stop-flow studies, where Na^{22} and TOH were injected intra-arterially 20 sec. before release of ureteral clamps, both tracers first appeared in samples of tubular fluid slightly proximal to the distal Na minimum. These similarities suggest that TOH precession, like that of Na^{22}, results from influx of label into Henle's loop. This conclusion further implies that TOH does not suffer appreciable countercurrent delay across vasa recta under our experimental conditions. In support of this view we observed that indeed the 2 tracers appeared in the medulla at the same time (about 15 sec. after start of square-wave perfusion). (Supported by USPH grant HE 10346).

MECHANISMS OF OXYGEN DEBT. R. J. Barnard,* M. L. Foss,* K. M. Baldwin* and C. M. Tipton. Univ. of Iowa, Iowa City, Iowa.

Male mongrel dogs were run on a treadmill at 4 mph with a 20 percent grade. The mean and SEM of the control debt following 19 min of running was 23.66 ± 2.78 liters. When tryptophan and quinolinic acid, inhibitors of gluconeogenesis, were administered to block the removal of lactate by the liver the mean debt was reduced to 10.72 ± .73 liters. We believe that this measure represents the classical concept of an alactacid oxygen debt. Propranolol administration reduced the mean oxygen debt to 14.96 ± 1.62 liters. When propranolol was administered in addition to tryptophan and quinolinic acid the oxygen debt was further reduced to 7.54 ± .44 liters. Thus, it is apparent that lactate, via the process of gluconeogenesis, is involved in oxygen debt. It also appears that catecholamines, acting through β-receptors have an effect on both the lactacid and alactacid components of oxygen debt.

Six weeks of progressive treadmill training resulted in a decrease in the peak arterial lactate and concomitantly a reduction in the oxygen debt. (Supported in part by funds provided by PHS Grant AM-08893-4.)

GUANETHIDINE EFFECTS ON THE METABOLIC RESPONSE OF THE RAT UTERUS TO ESTROGEN. Ayalla Barnea* and Jack Gorski. Dept. of Physiology and Biophysics, Univ. of Illinois, Urbana, Ill.

Guanethidine (G), injected prior to estradiol-17β (E), completely blocked the water imbibition response of the uterus to estradiol in immature adrenalectomized rats (Barnea, 1969). The effect of guanethidine (injected 1.5 hr before E), on other metabolic responses of the uterus, has been studied 5 hr after injection of E. Guanethidine injection was followed by a 2-9 fold increase in the incorporation of ^{3}H-cytidine and ^{14}C-leucine (injected 1 hr prior to killing) into their respective acid-soluble pools. This occurred irrespective of whether the injection of G was followed by E or not. The incorporation of ^{3}H-cytidine into RNA, however, was not affected by the drug: either E or G+E induced an increase of about 70% above the saline controls. In contrast to the ineffectiveness of G on RNA synthesis, the incorporation of ^{14}C-leucine into proteins was markedly reduced by G: compared to saline controls, G or G+E injections reduced the S.A. of proteins by 40-50%, while 5.0μg E alone resulted in an increase of 50%. When uteri from animals treated with G or G+E were incubated for 1 hr with ^{3}H-leucine, the inhibitory effect of G on protein synthesis was no longer observed. Injection of E causes a 3 fold increase in U-^{14}C-glucose conversion to $^{14}CO_2$ by incubated uteri. Treatment with G, prior to E, had no effect on this estrogen response. It is suggested that in the presence of G, E exerted its metabolic effects on the uterus of the immature adrenalectomized rat. Guanethidine might have an effect on transport mechanisms in the uterus, which are either the result of a direct effect of G on this parameter or a consequence of its interaction with the sympathetic nervous system. (USPH grant AM06327)

DISSOCIATION OF SPINAL CORD EFFECTS PRODUCED BY VESTIBULAR VOLLEYS. Charles D.Barnes and Ottavio Pompeiano. Instituto di Fisiologia Umana, Cattedra II, Univ. di Pisa, Pisa, Italy.

In decerebrate cats repetitive stimulation of the VIIIth cranial nerve elicites two effects in the lumbar cord which have the same time course.Tension is developed in extensor muscles of the ipsilateral hindlimb, while DRP is due to PAD in the group I afferents from both extensor and flexor muscles of the ipsilateral hindlimb as well as in cutaneous afferents. Both these phenomena were abolished by complete distruction of the medial (MVN) and lateral vestibular (LVN) nuclei.Selective lesion of the LVN however abolished only tension of the extensor muscles, but not the DRP. The monosynaptic extensor reflex, which was facilitated by stimulation of the ipsilateral VIIIth nerve in the intact preparation was later depressed for the same parameters of VIIIth nerve stimulation after electrolytic lesion of the LVN.It is concluded that the descending vestibular volleys responsible for PAD in the extensor pathway originate from the MVN, while LVN is essential for the facilitatory effect on extensor motoneurons. The contribution of this nucleus to PAD cannot be ruled out as stimulation of LVN in animals submitted to chronic section of the VIIIth nerve and cerebellectomy still produces a measurable DRP. (Supported in part by USPHS, NIH Grants NB 34986 and NB 07685).

RELATION OF CARDIAC FINE STRUCTURE CHANGES AND METABOLIC ACTIVITY AFTER CORONARY INFARCTION. Frank Barrera*, Guido Ascanio, S. J. Phillips*, and M. J. Oppenheimer. Temple Univ. School of Med., Philadelphia, Pa.

Reflexes of an inhibitory or Bezold type are clearly absent after coronary artery occlusion yet are demonstrably present and operative when myocardial cellular damage is produced by selective intracoronary artery injection of Hexachlorotetrafluorobutane (Hexa). In order to provide information which would be useful in understanding this difference the electron microscopy of Hexa cardiac infarction has been studied simultaneously with the metabolism of the heart, including free fatty acids (FFA), lactic (LA) and pyruvic (PA) acids. Coronary blood flow was determined by the I^{131} antipyrine technique. Catheters in a peripheral artery and the coronary sinus provided A-V differences in concentration. After Hexa infarction FFA uptake and extraction is increased. EM samples from the apex of the posterior papillary muscle of the left ventricle demonstrated a selective mitochondrial lestion. Mitochondria of cardiac muscle after Hexa were swollen and vacuolated. In addition mitochondria of neuronal processes and epithelial capillary cells were similarly involved. These lesions may be productive of stimuli eliciting the Bezold type reflexes. Extraction of lactic acid by the heart is decreased in 80% of the cases after Hexa infarction.

THE NATURE OF THE SINGLE PASSAGE PULMONARY ANGIOTENSIN CONVERSION. Jack D. Barrett* and M.P. Sambhi. Univ. Southern California Medical School. Los Angeles, California

Ng and Vane (Nature 216:762,1967) concluded Angiotensin I (Ang I) conversion to Ang II occurs predominately in the pulmonary circulation. The nature of this conversion remains unknown. We have developed an in vitro rat uterus assay method which when coupled with pressor assay is capable of quantitative differentiation of Ang I and II in mixtures of the two peptides. With this method we have studied the in vivo pulmonary conversion of Ang I in the rat. Single pulmonary passage of Ang I resulted in approximately 80% conversion to Ang II. Ang I (350 ng/0.5 ml) was injected as a single dose via the jugular vein. Both carotid arteries were tied and a cannula from the abdominal aorta was opened. All blood was collected immediately in cold ethanol and processed by the method of Boucher. Recovered Ang peptides were assayed on the rat uterus preparation. It was found that 80% (range 75-95) of the recovered Ang was in the form of Ang II. Hippuryl-L-histidyl-L-leucine (HHL) was shown to act as a substrate for semipurified Ang converting enzyme (CE) from dog lung (Cushman and Cheung, Fed Proc. 28:799,1969), it should therefore alter the degree of conversion of Ang I when given in large doses. HHL (950 γ/ml) injected simultaneously with Ang I did not alter the fraction of Ang I converted to Ang II during single pulmonary passage. I.V. injections of Ang I and II were then compared before, during and after continous infusion of HHL (100γ/min/Kg). Neither the pressor response to Ang I nor its relative activity to Ang II changed over the 1 hr infusion period. Single injections of HHL, to 6.0 mg/Kg, did not alter the maintained pressor responses to Ang I infusions (25 ng/min/Kg). This study confirms the observations that Ang I is converted by the pulmonary circulation and shows that HHL does not influence this in vivo conversion in the rat under the above conditions. The hydrolysis of this peptide may proceed in vivo by other processes different than angiotensin conconversion.

POSTNATAL DEVELOPMENT OF THE LUNG. Donald Bartlett, Jr., (intr. by S. M. Tenney). Dartmouth Medical School, Hanover, New Hampshire 03755.

Development of alveoli in mammalian lungs is predominantly a postnatal process. In an effort to identify factors that influence postnatal lung development, the lungs of young rats, maintained for several weeks under various conditions, have been studied using morphometric techniques. Changes in metabolic rate, induced by exercise or alteration of thyroid function, did not influence lung growth relative to body growth. This suggests that the previously observed interspecific proportionality between alveolar surface area and metabolic rate is determined genetically, and that the rate of lung development within a single species is not modified by changes in metabolic demand. Rats exposed to 10.4% O_2 at sea level pressure gained weight less rapidly than control animals, but their lung development relative to body weight was no different from that of controls. Animals exposed to 45.8% O_2 gained weight more rapidly than controls. Lung development in this group was inhibited, not only relative to body weight, but in absolute terms as well. Whether this effect is O_2-specific, and what long-term consequences derive from early interference with lung development by exposure to high O_2 concentrations, are at present unknown. [Work supported by USPHS Grant HE 02888(12).]

THE IMPORTANCE OF UNSTIRRED LAYERS AT BIOLOGICAL MEMBRANES. Peter H. Barry, (intr. by R.S. Eisenberg) Department of Physiology, UCLA School of Medicine, Los Angeles, California 90024.

At most biological membranes, even for reasonable stirring rates, there are unstirred layers which are generally greater than 100 μ. Because of this, measurements of hydraulic, electrical and electro-kinetic parameters will involve both a time independent and a transient component caused by enhancement or depletion of solute at each membrane-solution interface. The giant algal cells have provided a convenient preparation for a detailed investigation of such phenomena. Measurements of hydraulic conductivity, Lp, have shown that the flow decreases with time, so that after about 8 min it is less than about 1% of its initial maximum value. This is caused by local solute concentration changes, resulting from the sweeping-away effect of the volume flow in these unstirred layers, which in turn generates membrane diffusion p.d.'s. Such p.d.'s may then be mistaken for streaming potentials. Similarly, when a current is passed through a membrane, local concentration changes will result because the transport numbers of ions in membranes are generally different from those in adjacent solutions. These will produce (1) a current-induced volume flow and (2) transient changes in p.d. during and after a current pulse. The true electro-osmotic flows, measured as the instantaneous rate of flow at the onset of a current pulse (i.e. within 0.2 sec), were found to comprise about 40% of the maximum rate of flow achieved after 1-2 min. The experimental results, including some actual measurements of local concentrations, agreed well with the theoretical predictions[1] and demonstrate the need for valid measurements particularly of Lp or electro-kinetic parameters to be made instantaneously (i.e. within about 1 sec).

[1]Barry, P.H. and Hope, A.B. (1969), Biophys. J. 9:700, 9:729.

SPLANCHNIC CIRCULATION DURING ACUTE RESPIRATORY ACIDOSIS. F.A. Bashour, A.E. Price*, H.L. Gaspar*. Cardiopulmonary Inst. at Methodist Hosp. and The Univ. of Texas Southwestern Med. Sch. at Dallas, Dallas, Texas.

Splanchnic hemodynamic response to acute hypercapnea was studied in anesthetized mongrel dogs (normal and splenectomized) before and after alpha-blocker. All vascular parameters, mean systemic arterial (FA), hepatic vein (HV) and wedge (HW), hepatic blood flow (HBF) and cardiac output (CO) were determined simultaneously during room air breathing, 8-10% CO_2 breathing and for 30 minutes after phenoxybenzamine (1 mg/Kg). HBF was estimated at 10 min. intervals, and splanchnic blood volume (SBV) 20 min. after single intervention. Hypercapnea decreased FA (2-10%), increased both HV (12-21%) and HW (11-18%). HBF increased to 146 -187% of control and CO to 104-117%. Total Splanchnic Resistance decreased (30%) and Total Systemic Resistance only 10%. Splanchnic blood volume decreased from 29.8% to 17.4% of the total blood volume. During hypercapnea, phenoxybenzamine decreased HBF, which averaged 82%, 91% and 89% of the control in the 1st, 2nd and 3rd 10-min. intervals, respectively. Similarly, the ratio of HBF to CO decreased to 84%, 95% and 92%, respectively. The results would indicate that hypercapnea constricted splanchnic venous, and dilated splanchnic arteriolar, systems. Hepatic blood flow is slightly influenced by sympathetic discharge.

SARCOPLASMIC RETICULUM: PRESENCE OF A MEMBRANE BOUND CREATINE KINASE.
R.J. Baskin and D.W. Deamer*. Department of Zoology, University of California, Davis, California 95616.

Preparations of fragmented sarcoplasmic reticulum (FSR) were obtained from rabbit skeletal muscle and tested for creatine kinase activity, in which phosphate is transferred from creatine phosphate to ADP and ATP is synthesized. ATP was measured spectrphotometically by reaction of ATP with glucose (hexokinase) and subsequent reduction of NADP (glucose-6-phosphate dehydrogenase). Free creatine formation was also measured. 1) A creatine kinase activity could be demonstrated on FSR membranes. The activity was membrane bound since centrifugation resulted in loss of activity in the supernatent. 2) Addition of FDNB, (5mM) which inhibits creatine kinase, immediately stopped ATP production in the FSR reaction mixture. 3) The time course of free creatine formation corresponded to the time course of ATP synthesis. 4) The Michaelis Constants (Km) for the FSR creatine kinase, with CP and ADP as substrates were slightly lower, though in the same range, as the Km's for crystalline creatine kinase.

TRIGEMINAL AND RETICULAR NEURONS CONCERNED WITH SNEEZING.
H.L. Batsel, V.A. Hosp., Long Beach, Calif. 90801 and Dept. of Physiology, UCLA, Los Angeles, Calif. 90024.

Mechanical stimulation of the nasal mucosa in lightly anesthetized cats activated neurons in the ventromedial border of the descending trigeminal nuc. and in the underlying reticular formation. Trigeminal neurons driven exclusively from nasal mucosa were surrounded by neurons which were driven from most of the ipsilateral upper face. "Reticular" neurons responding to nasal mucosa stimulation were also activated by touching laryngeal and tracheal mucosa and by pressure on limbs, trunk and face. About a third of trigeminal neurons responding to stimulation of ipsilateral nasal cavity also respond to contralateral nasal stimulation. Single shock stimulation of the ethmoidal nerve (the sneeze nerve) evoked trigeminal unit responses with latencies ranging from 1.8 to 9 msec ipsilaterally, and from 7.5 to 11 msec contralaterally. A number of trigeminal neurons exhibited long after-discharge to either mechanical stimulation of nasal mucosa or electrical stimulation of the ethmoidal nerve. Repetitive stimulation caused these neurons to accelerate, apparently to a critical frequency for triggering sneeze.

PLASMA RENIN ACTIVITY AND THE RESPONSE TO MINERALOCORTICOID EXCESS IN DOGS WITH CHRONIC LEFT VENTRICULAR OVERLOAD. J.S. Baumber*, J.O. Davis, E.G. Schneider*, and J.A. Johnson*. Dept. of Physiology, University of Missouri School of Medicine, Columbia, Mo.

A method of producing chronic isolated left heart failure by suturing a teflon graft between the aorta and the left atrium has been previously described (Fed. Proc. 28:584, 1969). In 8 dogs this procedure resulted in an average left ventricular end diastolic pressure (LVEDP) of 23 mm Hg. Higher levels of LVEDP were achieved by superimposed aortic constriction. Following aortic constriction plasma renin activity (PRA) was elevated and the animals showed marked sodium retention. Three dogs died in pulmonary edema within 3 days of aortic constriction; the average maximal LVEDP was 45 mm Hg. In the 5 dogs which ran a more chronic course PRA fell progressively following aortic constriction and this was associated with a return to sodium balance within 5 days. However, in some dogs LVEDP increased to levels over 35 mm Hg following recovery from the acute effect of aortic constriction; PRA was elevated, there was sodium retention and, frequently, pulmonary edema resulted. Dogs not retaining sodium were given 15 mg/day of desoxycorticosterone acetate (DOCA) to study the "escape" phenomenon. When LVEDP was 30 mm Hg or less a normal "escape" pattern was observed. However, with a LVEDP over 35 mm Hg "escape" failed to occur and marked sodium retention resulted; a further elevation in LVEDP was observed and pulmonary edema occurred on 3 occasions. PRA was decreased during DOCA administration. The present data indicate that the sodium retention observed in dogs with chronic isolated left heart failure was associated with increased PRA. The failure of dogs with a marked elevation of LVEDP to escape from the sodium-retaining action of DOCA indicates that some other factor in addition to the renin-angiotensin-aldosterone system is involved.

HEAD INJURY EFFECTS ON PULMONARY COMPLIANCE. David L. Beckman*and John W. Bean. Biosciences Division, Highway Safety Research Institute, and Department of Physiology, University of Michigan, Ann Arbor, Michigan.

Previous work (Proc Soc Expl Biol Med, 130:5-9, 1969) has shown that severe pulmonary pathology results from cerebral trauma in rats which can be ameliorated by prior injection of sympatholytic, antiepinephrine or general anesthetic agents (Fed Proc, 28-2:719, 1969). Experiments were carried out in an attempt to determine the functional significance of these pulmonary changes. Quasi-static pressure-volume (P-V) curves using 1) air 2) saline were recorded from 45 rats which had been previously subjected to cerebral trauma by means of a captive bolt mechanism producing immediate unconsciousness or death. The lungs heart and trachea were excised and the trachea cannulated and connected to a P-V apparatus. Air curves were run over a range of 0-10 cm H_2O pressure and to 20 cm in a second series. Maximum volumes attained for curves run from 0-10 for control lungs were .64±.06 ml (17 rats); traumatized .23±.03 ml (18 rats); and for traumatized rats pretreated with Dibenzyline .47±.09 ml (10 rats). For the 0-20 air curves, maximum values for the control lung were 2.9±.29 ml (10 rats); traumatized rats 2.3±.29 ml (18 rats); traumatized Dibenzyline pretreated rats 4.20±.33 ml (10 rats). In an attempt to nullify the possible initial volume errors which might arise from the presence of excess fluid in the lungs, volume changes were calculated for the range from 5-15 cm H_2O pressure (J Appl Physiol 26-6, 1969)and these also indicated a statistically significant decrease for the traumatized as compared with the control values. In summary, it was shown that cerebral trauma in the rat resulted in pulmonary functional changes as exhibited by P-V relationships which apparently may be attributed to alterations in surface tension forces rather than tissue changes per se as shown by saline curves.

TACHYCARDIA ASSOCIATED WITH BREATHING IN TURTLES. Daniel A. Belkin (intr. by A. B. Otis). Dept of Physiol., Univ. of Fla., Gainesville.

The usual respiratory pattern of turtles consists of long periods of apnea interrupted by short periods of breathing. To substantiate a previous observation that an increase in heart rate usually accompanies these breathing periods, electrocardiograms were recorded continuously for periods of from 4 to 8 days from unrestrained turtles at 22°C. More than 100 individuals representing 7 families were tested. From each turtle the following data were obtained: mean, minimum, and maximum heart rates during and between breathing periods while resting on land, and, for aquatic species, during voluntary diving in water; resting heart rate after vagal block with atropine; and heart rate during vigorous exercise. Generally, results were as follows: for both aquatic and terrestrial species at rest, heart rates during periods of apnea were between 3 and 12 beats per minute; mean rates of aquatic and terrestrial species were not significantly different. Aquatic turtles usually had slightly higher heart rates when resting on land than they had when submerged. During breathing periods, heart rate increased strikingly in all species. The degree of tachycardia was roughly proportional to the length of the preceding period of apnea; in aquatic species these periods were relatively long and heart rates during breathing periods sometimes approached the rates seen during exercise: 25 to 45 beats per minute. Within species, resting heart rates were much more variable than maximum (exercise) rates. Atropinized turtles at rest had heart rates similar to those associated with severe exercise; exercise or epinephrine injection did not increase them by more than 10% in most species. I suppose that breathing tachycardia is associated with increased blood flow in the pulmonary vascular circuit, allowing rapid equilibration of lung and blood gas tensions during breathing periods. (Supported by NSF G 6014 and NIH Research Career Development Award K3-GM-31, 779).

ANATOMY OF MAMMALIAN RENAL PELVIS AND ITS RELATIONSHIP TO INTRARENAL PRESSURES, R. D. Bell* and M. J. Keyl, Univ. of Okla. Med. Ctr., Oklahoma City, Oklahoma.

Ludwig demonstrated in 1863 that ureteral obstruction caused dilation of renal lymphatic vessels. Such dilation suggests that renal lymph flow increases secondarily to an elevation of intrarenal pressure. Recent observations of Gottschalk suggest that increases in intrarenal pressure in the dog following elevations in pelvic pressure are mediated by compression of intrarenal veins. In the present investigation, silicone rubber casts of the canine renal pelvis and vein were prepared. In these casts, it was observed that each interlobar vein is partially encircled by protruding portions of the renal pelvis. It is visualized that a significant increment in pelvic pressure would cause these pelvic structures to compress the veins, resulting in a passive venous constriction. Direct measurement of intrarenal venous pressure during elevated pelvic pressure in the dog shows a positive correlation between these two parameters. These pressure data suggest that intrarenal venous pressure elevations observed during increased pelvic pressure result from an increase in venous resistance. The resistance increase appears to occur in those segments partially encircled by portions of the renal pelvis. It is concluded that the interstitial pressure and lymph flow responses to elevated pelvic pressure in the dog are related to the intimate relationship of the renal pelvis and the interlobar veins found in this species. (Supported in part by NIH Grant #HE 10808-02).

OLFACTORY BULB POTENTIALS. M. H. Bennett. Department of Anatomy, Louisiana State University Medical Center, New Orleans, La.

D.C. recordings of olfactory bulb potentials in response to odorous stimulation of the olfactory mucosa and electrical stimulation of the anterior limb of the anterior commissure were obtained in rabbits. With both stimuli, inversion of the surface positive response as well as an increase in amplitude occurred just below the mitral cell layer. Repetitive odorous stimulation at high concentration produced a maintained 7 to 10 mv negative potential shift deep within the bulb. At these levels repetitive commissural stimulation produced up to 15 mv negative potential shifts maintained for the duration of the stimulus (3-5 sec.). With electrical stimulation the peak amplitude of the response and its latency were dependent upon the magnitude and frequency of stimulation. Simultaneous application of both stimuli resulted in an occlusive effect indicating common elements in both stimulus-response paths. Along with evidence from other works, these results are interpreted as reflecting response patterns of those neural elements involved in the central components of olfactory adaptation.

INSULIN SECRETORY DYNAMICS IN THE ISOLATED, BLOOD PERFUSED PANCREAS. R.N. Bergman* and J. Urquhart, Department of Physiology School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania.

Quantitative information about the dependence of insulin secretion rate upon pancreatic arterial glucose concentration is essential for the modeling of glucose homeostasis. Extirpated pancreas-duodenum preparations from immature dogs (2-4 kg) were perfused with arterial blood from anesthetized, overnight fasted intact dogs (20-35 kg) and the pancreatic venous effluent returned to the blood donor. Glucose was added to the arterial supply of the perfused pancreas at controlled rates and the rate of insulin secretion was measured at 1-5 min intervals. We maximized the weight ratio between the large blood donor and the small pancreas donor to minimize the effect of infused glucose or secreted insulin on the blood donor.

We imposed 20-80 mg% stepwise increases in pancreatic arterial glucose concentration above the donor's prevailing arterial glucose concentration (av. 129 mg%). Insulin secretion rate began to rise within 1-2 min, reached a peak value at 2-4 min and then declined to a steady value at 5-10 min after the increase in glucose concentration. The 2-4 min peak value ranged between 124% and 155% of the final steady value. After a stepwise decrease in glucose concentration insulin secretion rate decreased to a new lower value within 10 min. The ratio of changes in insulin secretion rate to changes in glucose concentration is approximately constant at .5 mμg insulin/min/gm pancreas/mg% glucose over the range 110 to 180 mg%, above which the ratio becomes less. Supported by grant GM 14637 from NIGMS.

Intracellular responses of caudate neurons to cortical and mesencephalic stimuli-G.A. Bernardi*, C.D. Hull, L.M. Vernon* and N.A. Buchwald, Dept. of Anatomy, MRI and BRI, UCLA. Sixty neurons were impaled in the caudate nucleus of intact, immobilized cats. The cells were held for periods of 10 min. to 2 hours and their responses to low frequency (< 1pps) anterior cortex and mesencephalic stimuli were observed. In response to cortical stimulation, an EPSP-IPSP sequence most commonly occurred. Latency to onset of the EPSP averaged 8-10 msecs although the spike latency often was more than 20 msecs. IPSP durations were 150 msecs or longer. Brain stem stimulation was effected by an array of electrodes oriented in coronal or saggital planes in the ipsilateral mesencephalon. The array was lowered to the peduncular level. Stimulations were made at this level and in millimeter steps as the electrodes were raised. In general, responses occurred at low thresholds just above the substantia nigra and continued to be elicited up to the tectal region. Three classes of responses were catalogued, pure EPSP's, EPSP-IPSP sequences and pure IPSP's. The first two classes were more common. The latency of EPSP onset to brain stem stimulation was shorter (1-5 msecs) than to cortical stimulation. The cells never followed high stimulation rates and probably were not antidromically activated. When IPSP's occurred they were shorter and sharper than those elicited by cortical stimulation. Very long (up to 10 seconds) hypo- or hyperpolarizations sometimes followed short bursts of high frequency stimuli even if no response to lower frequencies occurred. Lesions of the intralaminar thalamus modified these cellular responses. (Supported by USPHS MH 07097 and H D 02712).

URINARY 17-HYDROXYCORTICOSTEROIDS IN HUMANS SUBJECTED TO PROLONGED CONFINEMENT. E. L. Besch and R. R. Gronwall, Department of Physiological Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas 66502.

In the conduct of experimentation involving prolonged shelter occupancy, pooled, 24-hour urine samples for each person were analyzed for 17-hydroxycorticosteroids (17-OHCS). Two groups of subjects, 16 males in one and 16 females in the other, were each exposed, in series, for a five-day period to a simulated shelter environment at an effective temperature of 82^{o}F. All subjects received the OCD food ration and one quart of water per day. No apparent, consistent, significant changes were seen in the heart rate, blood pressure or oral temperature. The significant decrease in these 17-OHCS values for females ($P<0.01$) and the non-significant increase in males between day 1 and day 2 of the trial may indicate that the former group was more emotionally stressed prior to and including day 1 than the latter group. In addition, a significant decrease in urinary 17-OHCS between day 2 and day 5 was found for both groups (males-$P<0.02$ and females-$P<0.01$).

Supported by OCD Contract DAHC 20-68-C-0173

DIRECT MEASUREMENT OF UPTAKE OF SODIUM AT THE OUTER SURFACE OF THE FROG SKIN. Thomas U. L. Biber and Peter F. Curran. Department of Physiology, Yale University School of Medicine, New Haven, Conn.

A combination of the methods described by Schultz et al. (J. Gen. Physiol. 50: 1241, 1967) and by Ussing and Zerahn (Acta Physiol. Scand. 23: 110, 1951) was used to measure directly the unidirectional uptake of sodium from the outside solution into the frog skin under short-circuit conditions. The sodium uptake was determined at six sodium concentrations ranging from 3.4 to 114 mM. NaCl was replaced by choline chloride in the solutions bathing both sides of the skin. Sodium uptake is not a linear function of sodium concentration but appears to be composed of two components, a saturating one and one that varies linearly with concentration. The sodium uptake is inhibited by the addition of lithium to the outside solution. The effect appears to be primarily on the saturating component and has the characteristics of competitive inhibition. In addition, lithium uptake by the skin is inhibited by sodium. The effects of lithium cannot be ascribed to changes in electrical potential difference. Measurement with microelectrodes indicate that under short-circuit condition there is no change in the intracellular potential when lithium chloride is added in the outside solution. Sodium uptake is furthermore partly inhibited by ouabain and amiloride.

(Supported by Grant-in-Aid 67-729 of the American Heart Association and U.S.P.H.S. Grant No. AM-12028)

BARORECEPTOR CONTROL OF DIAPHRAGM AND ABDOMINAL MUSCLE ACTIVITY IN THE CAT. Beverly Bishop. Dept. Physiology, State Univ. of New York at Buffalo, Buffalo, N. Y.

Strong stimulation of baroreceptors not only inhibits medullary vasomotor neurones but may also depress ventilation. How baroreceptors project to inspiratory and expiratory neurones to cause this ventilatory decrease is not known. This study elucidates baroreceptor projection to respiratory neurones by measuring inspiratory and expiratory responses to changes in baroreceptor firing. Integrated EMG's of diaphragm and abdominal muscle of ten Dial-anesthetized cats are used as indices of inspiratory and expiratory neurone activity. Since abdominal muscles are silent in quiet respiration they cannot reveal expiratory inhibition. Hence, positive pressure breathing was used to excite expiratory abdominal activity. Baroreceptor firing was decreased by common carotid occlusion or hemorrhage and increased by release of carotid occlusion or saline distention of the carotid sinus. Decreased firing caused a rise in blood pressure, augmented diaphragm and abdominal muscle activity, and increased respiratory rate. Increased firing caused a fall in blood pressure, depressed diaphragm and abdominal muscle activity, and alowed respiration. Since changes in receptor firing always altered diaphragm more than abdominal activity, it was concluded that baroreceptors make stronger projections to inspiratory than to expiratory neurones. Furthermore, decreases in firing augmented both muscles, indicating that baroreceptors send inhibitory impulses to both inspiratory and expiratory neurones in spite of their reciprocal innervation.

(Supported in part by U. S. Air Force, Air Force Systems Command, Aero-Space Medical Division.)

RESPONSE IN PLASMA RENIN ACTIVITY TO HEMORRHAGE IN THE ABSENCE OF SODIUM DELIVERY TO THE MACULA DENSA. Edward H. Blaine*, and James O. Davis, Dept. of Physiology, University of Missouri School of Medicine, Columbia, Missouri.

Currently there are two popular hypotheses on the mechanism of renin release. One is that renin is secreted in response to decreased stretch of the afferent glomerular arterioles. The other hypothesis states that the macula densa responds to a decreased Na load or concentration with increased renin release. In this study the macula densa mechanism has been eliminated and the response in plasma renin activity to acute hemorrhage determined. Under sterile conditions the ureters of 6 dogs were ligated and the kidneys subjected to a 2 hour period of total renal ischemia by clamping both renal arteries. The dogs were then maintained by daily periotoneal dialysis and on the 4th day after surgery were bled 20 ml/kg. Plasma renin activity was measured before and 30, 60, and 90 minutes after hemorrhage. The blood was returned and the dogs were anesthetized with pentobarbital (30 mg/kg). The left kidney was exposed and lissamine green dye injected into the aorta above the origin of the renal arteries. The dye was not visualized in the renal tubules in any of the dogs, a finding which demonstrates the absence of glomerular filtration. During all 3 post-hemorrhage periods in the 6 dogs, plasma renin activity was higher than the control values. The mean values ± SEM and P values were: control 5.8 ± 1.4 ng angiotensin/ml; 30 min. after hemorrhage 9.6 ± 2.6, $P < .05$; 60 min. after hemorrhage 10.8 ± 2.3, $P < .01$; 90 min. after hemorrhage 13.0 ± 3.7, $P < .05$. Renin substrate in plasma was measured before and after hemorrhage in all dogs and did not change. It is suggested that renin was released after hemorrhage in the non-filtering dog kidney and that renin release was not associated with a change in Na at the macula densa. (Supported by NIH grant HE 05810).

INCREASE IN EXPIRATORY AIRFLOW BY STINTING THE TRACHEA. N. Blank*, R. Dilley* and J.A. Nadel. Cardiovasc. Res. Inst. and Dept. Medicine, Univ. of Calif. Med. Ctr., San Francisco, California 94122.

We evaluated the role of the trachea as a flow-limiting segment during maximal expiratory airflow by stinting the trachea in 6 isolated dog lungs and in 4 intact dogs. We measured simultaneously airflow and volume change using a volume displacement body plethysmograph. After inflating the lungs to a transpulmonary pressure of 30 cm H_2O, we produced a forced expiration by exposing the lungs to a negative pressure. We increased this driving pressure until no further increase in flow occurred (P_{max}) and used pressures in excess of P_{max} during the experiment. After obtaining control measurements, we inserted a rigid tube to just above the carina and repeated the measurements. When the same driving pressures were used, the flow during stinting increased over approximately the upper half of the vital capacity compared with control values. We compared maximum airflows over the lower 70% of the vital capacity. The largest increases in flow, which occurred at 30-40% of the expired volume, averaged 120% (range, 44-230%) for the isolated dog lungs and 68% (range, 30-93%) for the intact dog lungs. In 4 isolated lungs a catheter was placed in a lower lobar bronchus to measure lateral airway pressure. In the control state, pressure at the catheter tip was 0 during maximal airflow when 30-50% of the vital capacity had been expired. During stinting, the pressure was 0 at the catheter tip during maximal airflow when only 7-15% of the vital capacity had been expired. We ruled out flow limitation at the orifice of the tracheal stint by visual and roentgenographic observation and by measurement of bronchial pressure. These studies indicate that the trachea acts as an important determinant in limiting maximal flow. Supported in part by NIH grant HE06285 and Contract NONR 222(55), (NR 101-323) between Office of Naval Res., Dept. of the Navy, and the Cardiovascular Research Institute.

HYPOXIC REDUCTION OF ENDOTOXIN PYROGENICITY IN GUINEA PIGS. Clark M. Blatteis and Daniel W. Doherty, Jr.* Dept. of Physiol. Biophys., Univ. of Tenn. Med. Units, Memphis, Tenn. 38103

The pyrogenicity of S. enteritidis endotoxin (2 γ/kg iv) was tested in unanesthetized adult guinea pigs breathing air or 9.7% O_2 in N_2 at T_A=25C. Two designs were used: 1) uninterrupted exposure to either gaseous environment during the complete experiment, and 2) abrupt transition from either air or hypoxia, or vice-versa, at 60 min after endotoxin injection. Colonic temperature (T_R) and O_2 consumption ($\dot{V}_{O_2}$) were monitored continuously. In air, T_R characteristically rose 1.4C in two successive maxima at 70-90 and 150-180 min post-endotoxin, respectively. $\dot{V}_{O_2}$ also increased biphasicly, from 8.8 to 14.4 ml/kg/min 45 min, and to 11.7 ml/kg/min 145 min following pyrogen administration. In hypoxia, S. enteritidis endotoxin also induced a significant biphasic rise in both T_R and $\dot{V}_{O_2}$, but the maxima were significantly lower than in air: T_R rose only 0.4C, while $\dot{V}_{O_2}$ was 12.2 and 11.0 ml/kg/min at the two peaks. The sudden induction of hypoxia during the first febrile maximum in air abruptly depressed T_R and abolished its second rise, and significantly reduced the second increase in $\dot{V}_{O_2}$ as compared to this response when the whole experiment was conducted either in air or in hypoxia. By contrast, the induction of air after hypoxia 60 min post-pyrogen produced an immediate, rapid increase in both T_R and $\dot{V}_{O_2}$, so that the second maxima were not different from those obtained in the animals breathing air continuously. These results show that: 1) unanesthetized adult guinea pigs are sensitive to S. enteritidis endotoxin, 2) the pyrexia is due, in part, to increased thermogenesis, 3) acute moderate hypoxia depresses this pyrogenic effect by, in part, reducing the thermogenic response to the endotoxin. These findings are consistent with other observations showing that the increase in $\dot{V}_{O_2}$ produced by cold and catecholamines is especially susceptible to hypoxic depression.

CORRELATION OF PERIPHERAL CORONARY PRESSURE DURING CORONARY ARTERY OCCLUSION IN THE UNANESTHETIZED DOG WITH THE SIZE AND DISTRIBUTION OF INTERCORONARY ANASTOMOSES. C.M. Bloor and F.C. White*. Dept. of Pathology, UCSD School of Medicine, La Jolla, California.

It has been stated that peripheral coronary pressure (PCP) can rise rapidly during 24 hour occlusion of the left circumflex coronary artery (LCCA) in the unanesthetized dog (Pasyk et al: Fed. Proceedings, 28:780, 1969). This suggested that intercoronary collaterals increase in size or number during this time. In the present study PCP changes during LCCA occlusions, ranging from 2 hours to 4 days, were observed in conscious dogs which had pressure tubes implanted in the aorta and LCCA, the latter tube being placed distal to an occlusive cuff and used for PCP measurements. The animals were sacrificed at the end of occlusion and their hearts injected with a modified Schlesinger's gelatin mass and cleared for determination of the size and distribution of intercoronary anastomoses.

During 2-24 hour LCCA occlusions, mean PCP rose progressively to values 80% of central aortic pressure. On repeated 2-24 hour occlusions in the same dog the rate of PCP rise increased. Intercoronary collaterals, greater than 50μ in diameter, were few in number; a pattern similar to that observed in control hearts not subjected to coronary occlusion. When LCCA occlusion was maintained for 4 days, mean PCP rose rapidly during the first 24 hours and then remained stable. Intercoronary collaterals, greater than 100μ in diameter, were frequent in number. Thus a rise in PCP during coronary occlusion occurs prior to an increase in size and number of intercoronary collaterals. The relationship between this early PCP rise and collateral blood flow awaits further examination. (Supported in part by MIRU Contract PH 43-68-1332 and NIH Program Project Grant HE-12373).

PREPARATION OF INTACT CELLS FROM THE UPPER GASTROINTESTINAL TRACT. A. L. Blum*, B. I. Hirschowitz and G. Sachs. University of Alabama Medical Center, Birmingham, Alabama.

The availability of suspensions of isolated intact cell from the upper G-I tract allows a more direct approach to specific cell function than is possible in intact tissues. Necturus gastric and esophageal mucosal cells have been prepared by a method which we have also applied to other species. The mucosa is stripped of external muscle layers, stretched and incubated for 1 hr with vigorous shaking at 22°C in Ca and Mg free solutions, with or without Na, containing 0.15% hyaluronidase. After several washings, the mucosa is incubated at 37°C in nutrient solution containing 0.1% collagenase, 0.2% lysozyme and 0.1% EDTA. The cells float off the tissue within 30 minutes, are centrifuged at 500g, resuspended in enzyme free solution and kept at 0°C until used. The cells appear intact by phase contrast microscopy, with well defined fine structure. They show a characteristic uptake of dansylated pentagastrin and Janus green B and have a negative intracellular PD as determined by direct microelectrode puncture. In addition esophageal preparations show the presence of many ciliated cells which are not found in fundic preparations. It would now appear possible to relate data obtained in the intact tissue to specific cell types. (NIH, NSF support.)

PALMITIC ACID UTILIZATION AT ALTITUDE. F. Duane Blume (intr. by Nello Pace). White Mountain Research Station, Bishop, California and Department of Physiology, University of California, Berkeley.

The incorporation of 14C label from intraperitoneally injected palmitic-1-14C acid into several body tissues and its oxidation to expired CO_2 were measured in adult mice after a 30-day exposure to an altitude of 3,800 meters. Greater amounts of the label appeared as $^{14}CO_2$ at altitude during the 2 hr post-injection period than at sea level. In addition, higher concentrations of label were found in liver, skeletal muscle, and heart at altitude during the same period. The bulk of the label in these tissues was found in the nonglycogen fraction at both elevations. At altitude, the nonglycogen fractions in the heart and liver contained significantly greater amounts of the label than in the respective sea level tissues, while the muscle had only a slight increase of label in this fraction. On the other hand, the glycogen fraction of all three tissues showed an increased degree of labeling in the altitude animals. The percentage of the total tissue 14C content found in the glycogen fraction of each tissue at altitude was greater in the heart and muscle and lower in the liver when compared to sea level values. At altitude, the extracellular 14C content, extrapolated from the plasma 14C content, was double that measured at sea level. The data suggest greater mobilization and utilization of fatty acids at altitude. The increased levels of the label found in the glycogen fractions of liver, muscle and heart indicate an increased rate of gluconeogenesis in the liver. (Supported by Office of Naval Research Contract Nonr-3656(22) and NASA Grant NGR 05-003-018.)

CIRCULATORY RESPONSES TO ACUTE REDUCTION OF SUPERIOR MESENTERIC ARTERIAL FLOW. S.J. Boley,* W. Treiber,* P.R. Winslow,* M.L. Gliedman,* and F.J. Veith. Montefiore Hosp. and Med. Ctr. and the Albert Einstein Coll. of Med., New York, N.Y.

The circulatory responses to 50% diminution in Superior Mesenteric Artery (SMA) flow were investigated in 35 dogs. Cardiac output and flow through the three major intestinal arteries were measured with electromagnetic flowmeters. SMA flow was controlled with an hydraulic occluder distal to the flow probe. Systemic and mesenteric arterial pressures were monitored and pO_2, pCO_2, and pH of systemic arterial and mesenteric venous blood were determined. The pattern of tissue perfusion was visualized with Patent Blue V dye. A 50% reduction in SMA flow caused a 20-65% fall in mesenteric arterial pressure without change in systemic pressure. Cardiac output decreased 11-33% after one hour but celiac flow in 16 of 19 dogs rose 13-300% and inferior mesenteric (IMA) flow rose 5-100%. Intestinal arteriovenous oxygen difference increased and all layers of the small bowel were evenly stained with dye. After 2 hours at 50% SMA flow, the elevated celiac and IMA flows began to fall. When SMA communications with the celiac and IMA were ligated and SMA flow reduced, celiac flow still rose but much less than in animals with intact collaterals. This increase in flow suggests that mechanisms other than low pressure in the mesenteric bed are operative in increasing splanchnic circulation in response to diminished SMA flow.

THE INFLUENCE OF RENIN AND CATECHOLAMINES ON CUTANEOUS VASCULAR RESISTANCE DURING HEMORRHAGIC HYPOTENSION. Robert F. Bond, Gerald F. Lackey, and Janet A. Taxis*. Bowman Gray Sch. Med., Winston-Salem, N.C. 27103

Previous reports from this laboratory have suggested that the cutaneous vascular resistance during hemorrhagic hypotension increases because of a plasma elevation of some vasoconstrictor hormone. The present report attempts to define which hormone (renin or catecholamines) plays the most active role. The cutaneous vasculature was functionally isolated by ligating the femoral artery distal to the saphenous artery (SA) and all branches of the SA that perfused skeletal muscle tissue. An isolation was considered functionally complete when no reactive hyperemia was recorded following a 60 sec occlusion of flow to the saphenous bed. A Harvard, piston-actuated pulsatile blood pump was employed to maintain a constant, yet pulsatile, flow to the saphenous bed. A cannulation type electromagnetic flowmeter probe was placed in the pump circuit to insure that mean flow was constant. Local perfusion pressure (LPP) was recorded distal to the pump; mean aortic pressure (MAP) was recorded through a cannula inserted into the brachial artery. The vascular resistance varied directly with LPP. The animal was bled in a stepwise manner until MAP was approxiamtely 40 mmHg. LPP increased significantly in both the normal and nephrectomized denervated preparations, suggesting that neither renin nor autonomic nerves were responsible for the increased resistance. However, 1 mg/kg i.a. of phenoxybenxamine (a dose sufficient to block a 5 μg i.a. injection of norepinephrine) did eliminate response to acute hemorrhage, suggesting that an increased plasma concentration of catecholamines caused the increased cutaneous vascular resistance. (Supported by USPH, NHI Grants 487, 5392, and North Carolina Heart Association.)

RESPIRATORY EFFECTS OF PULSED DRUG PERFUSION OF THE CEREBROSPINAL FLUID SPACES IN CATS ANESTHETIZED WITH PENTOBARBITAL. H.L. Borison, P.S.R.K. Haranath*† and L.E. McCarthy*. Dartmouth Med. Sch., Hanover, N. H.

Closed system perfusion from the IIIrd ventricle to exit at the cisterna magna was performed with mock CSF at flow rates up to 16 ml/min without producing detectable respiratory or cardiovascular disturbance. No remarkable changes occurred in response to CO_2 bubbled into the perfusate. In most of 12 experiments flow rate was maintained at 5 ml/min. Deadspace between a temperature-controlled valve manifold and the ventricular input orifice was 0.15 ml. Drug perfusion was interjected through the manifold for intervals from 5 sec to 10 min. Ion-free sucrose (300 mM) solution did not provoke any physiological consequences. Active substances employed include nicotine, acetylcholine, procaine, ethanol, and excess potassium. Perfusion duration-drug concentration relationship was established for elicitation of ventilatory effects measured by pneumography and alteration of end-tidal CO_2. Onset of response was evident as early as 6 sec from start of the drug pulse. The effect generally persisted for at least 30 sec during washout. Allowing for deadspace and ventricular transport lags reduces the response latency to 2-4 sec which is consistent with two possibilities of action: (1) surface receptor activation (or inactivation); (2) vascular participation. An attempt was made concurrently with drug presentation in the CSF to interrupt the blood supply to the brain by the use of a fixed vertebral clamp plus timed occlusion of the common carotid arteries after ligation of cervical collaterals and interruption of the carotid sinus nerves. Circulatory arrest for 15 sec appeared to vitiate the respiratory effect of an interposed 5-sec pulse of nicotine. (Supported by NIH Grant NB 04456; †WHO Visiting Scientist from Kurnool, India.)

A DESCRIPTIVE MODEL OF THE CAT SUPERIOR OLIVE S-SEGMENT. James C. Boudreau and Chiyeko Tsuchitani*. Leech Farm Road Veterans Administration Hospital and University of Pittsburgh School of Medicine, Pittsburgh, Pa.

As far as could be determined from our measurements on the response of S-segment neurons to auditory stimulation, almost all cells with characteristic frequencies above about 4.0 kHz displayed similar response properties when examined on equivalent scales. To obtain statistical measures describing the response properties of an average S-segment neuron, cells were grouped according to the response measurements taken and average values were calculated from the neurons to represent the population. Those response properties for which average values were taken included ipsilateral and contralateral threshold functions (i.e., excitatory and inhibitory tuning curves), spikes elicited by CF and nonCF stimuli at different ipsilateral stimulus levels, and the effect of contralateral stimulus level on ipsilateral threshold and maximum discharge levels. These response properties seemed to be sufficient to describe the magnitude of cell discharge under a wide range of monaural and binaural (both tones simultaneously presented) pure tone stimulation. A model S-segment was mathematically constructed with cellular elements having average empirically derived response properties. These elements differed only with respect to CF. Distributions of activity across the population were examined as the response to stimulation with monaural and binaural tones was simulated.

WALL STRESS AND RADII OF CURVATURE IN THE CANINE LEFT VENTRICLE DERIVED FROM HIGH-SPEED BIPLANE CINERADIOGRAPHS. Alfred A. Bove* and Peter R. Lynch. Temple University School of Medicine, Philadelphia, Penna.

A 270 frames per second 16-mm biplane cineradiographic unit was used to study left ventricular (LV) function in the canine heart. With the aid of a digital computer, on-line correction of distortion errors in the ventricular images was provided. Hoop stress was calculated from the formula: $\sigma = (PR_2/t)\left[(2R_1 - R_2)/2R_1\right]$ where P is LV pressure, t is wall thickness, R_1 the meridian and R_2 the hoop radius of curvature. This formula is based on a thin-walled volume of revolution with no specified shape of the meridian. Wall thickness and radii of curvature are measured at multiple points along the free wall of the left ventricle, and LV pressure is recorded directly on the cine film for precise timing with mechanical events. Average peak stress at the largest diameter of the LV in 29 heart cycles from 8 animals was 255 x 10^3 dynes/cm^2, average LV end-diastolic volume was 60.6 cc. End-systolic volume averaged 27.4 cc. Diastolic meridian radius of curvature measured in 4 of 8 animals was 16.1 cm, diastolic hoop radius was 2.15 cm and thickness was .90 cm. Hoop radius and thickness changed significantly from diastole to systole, but meridian radius showed no significant change. These data indicate that a thin-wall model of the LV provides adequate stress information if radii of curvature and wall thickness are measured directly.

This work was supported by NIH, NHI Grant HE 08886. Dr. Bove is a Postdoctoral Fellow in Physiology supported by NIH Fellowship No. 1-F2-GM-37295-02.

CALORIGENIC EFFECTS OF SODIUM SALICYLATE. Pietro O. Bramante and Yi-li Chang.* Dept.of Physiology,Univ.of Illinois Coll.of Med.,Chicago,Ill.

It is postulated that salicylates exert acute calorigenic effects, manifested by elevation of O_2 consumption, following administration to man and experimental animals. The marked variability of results reported in the literature (especially evident in the case of small mammals) prompted this reinvestigation in the rat, utilizing a particularly sensitive automatic apparatus (1) and a technique of determination (2, 3) by which the total $\dot{V}O_2$ of the animal is continuously registered for many hours and can be partitioned into four components: a) basal metabolism; b) caloric expenditure due to gross muscular activity; c) caloric expenditure due to minimal levels of muscular activity ["microactivity" (3)]; d) calorigenic effects of experimental procedures. Values of "Minimal Calculated Metabolic Rate" (MCMR) can thus be derived which represent the true resting metabolism of the animal at any moment of the run.

I.p. introduction of sodium salicylate in adult rats was followed by MCMR increases not exceeding 25 % for doses of 150 mg/Kg and 45 % for doses of 300 mg/Kg. Dilution and/or neutralization of the drug resulted in even less marked changes. Prolonged treatment (100 and 200 mg/Kg per day,s.c. for one month) resulted in slight decreases of $\dot{V}O_2$.

It is concluded that the calorigenic properties of salicylic acid have, in many cases, been overestimated.

Refs. 1. J.Appl.Physiol.14:1063,1959. 2. ibid. 16:982,1961. 3. ibid. 24:11,1968.

Supported in part by grants from the USPHS and the University of Illinois Graduate College.

VASCULAR RESPONSES TO STIMULATION OF MUSCULAR RECEPTORS BY CAPSAICIN. D. Brender*, M. M. Webb-Peploe* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Capsaicin stimulates both sino-aortic and pulmonary artery baroreceptors, causing hypotension, bradycardia, and relaxation of hindlimb resistance vessels and splenic capacity elements. By contrast, injection of capsaicin into one iliac artery causes hypertension, due to a reflex constriction of hindlimb, gut, and renal resistance vessels (constant-flow perfusion of contralateral iliac artery and superior mesenteric and renal arteries), constriction of splenic capacity elements (venous pressure in isovolumetric spleen), and relaxation of cutaneous veins (constant-flow perfusion of saphenous vein). These responses are unaffected by ipsilateral lumbar sympathectomy or skinning of the limb but are abolished by limb deafferentation. Increase in carotid sinus pressure (constant-flow perfusion of vascularly isolated sinus) attenuated the responses of resistance vessels and splenic capacity elements but not of cutaneous veins. These vascular reflexes caused by injections of capsaicin are similar to those produced by vibration of the quadriceps tendon and electric stimulation of skeletal muscle. The receptors in the skeletal muscles that are stimulated by capsaicin may be those normally activated by muscular exercise to cause redistribution of blood flow. (Supported by NIH Grant HE-5883.)

THE VOLUME OF SKELETAL AND CARDIAC SARCOPLASMIC RETICULUM. F. Norman Briggs, E. W. Gertz* and R. John Solaro*. University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15213.

Although the sarcoplasmic reticulum of skeletal and by analogy cardiac muscle is believed to be the sink for calcium during muscular relaxation this cannot be asserted with certainty since the unit capacity of the reticulum for calcium is not known and the amount of reticulum is, with a single exception, unknown. Since a method for quantitatively estimating the amount of reticulum is particularly pressing we have investigated the possibility of using the calcium oxalate capacities of reticulum and of homogenates to measure the volume of the reticulum. The success of the method depends upon finding conditions which will limit calcium uptake to the sarcoplasmic reticulum and will yield a pure preparation of sarcoplasmic reticulum. To limit calcium uptake to the reticulum 5 mM azide and 1.6 mM EGTA were added to the incubation mixture. The extent to which the sarcoplasmic reticulum fraction was contaminated with mitochondrial material was estimated by measurement of succinic dehydrogenase and cytochrome oxidase activity. Evidence was obtained that the conditions necessary for this method to succeed were realized. When this method was applied, we found a volume of reticulum for frog skeletal muscle of 12.4 percent and a volume of 5.4 percent for dog ventricular muscle.

EFFECTS OF HYPOXIA ON FETAL CARDIOPULMONARY HEMODYNAMICS. C. R. Brinkman, III*, T. H. Kirschbaum*, and N. S. Assali, School of Medicine, UCLA, Los Angeles, California.

Effects of acute maternal hypoxia on fetal systemic and pulmonary hemodynamics were studied in 24 near term pregnant ewes and their fetal lambs. Under spinal anesthesia, fetus was marsupialized to maternal abdominal walls to protect umbilical circulation and head covered with saline filled glove to prevent breathing; fetus remained unanesthetized. Pressures (strain gauges) in fetal aorta (P_A), pulmonary artery (P_{PA}) and left atrium (P_{LA}) were monitored simultaneously with flows (electromagnetic) in ascending aorta ($\dot{Q}_A$), main pulmonary artery ($\dot{Q}_{PA}$) and ductus arteriosus ($\dot{Q}_D$) in control, hypoxic and recovery periods. Results show: a) During moderate hypoxia (12% O_2) P_A, P_{PA}, P_{LA} and $\dot{Q}_D$ did not change significantly; $\dot{Q}_A$ and $\dot{Q}_{PA}$ decreased. Fetal effective cardiac output ($\dot{Q}_A + \dot{Q}_D$) and net pulmonary flow ($\dot{Q}_{PA} - \dot{Q}_D$) decreased; systemic and pulmonary vascular resistances increased. b) During severe hypoxia (6% O_2), all blood flows decreased to a greater degree than in moderate hypoxia. Fetal pulmonary vascular resistance rose strikingly because of the marked fall in net pulmonary blood flow. Conclusion: Acute hypoxia decreases fetal left and right ventricular output either through direct effect on myocardium or through decreased venous return; as in adult, pulmonary vascular resistance increases because of active pulmonary vasoconstriction.

LUNG GROWTH IN THE ADULT:ACROMEGALIC PNEUMONOMEGALY. J. S.Brody,* A. B. Fisher,* A. Gocmen,* and A. B. DuBois. Depts. of Medicine and Physiology (DGM), Univ. Penna., and VA Hospital, Phila., Pa.

We studied pulmonary function in 9 acromegalic subjects ranging in age from 43 to 69 years. All were of normal height and all had enlarged chest cages in the AP diameter with normal chest cage mobility. The six acromegalic males had lung volumes which were increased in relation to predicted values based on age and height. Mean vital capacity was 5.99 liters (135% of predicted), functional residual capacity was 5.18 liters (145%), total lung capacity was 9.11 liters (140%), and the residual volume-total lung capacity ratio was 34.5%. Static lung compliance was increased to 0.43 liters/cm H_2O, but lung pressure-volume curves, airway resistance, and anatomic dead space were all within the range predicted for the large lung sizes. Mean pulmonary tissue volume, measured by acetylene uptake, was increased to 1.1 liters. These studies suggest that lung volumes increased because growth hormone stimulated lung growth. There was no evidence that lung elastic properties changed or that the lungs were stretched to fill the enlarged chest cage. Single-breath diffusing capacity (D_L) averaged 29 ml/min/mmHg (98% of predicted on basis of BSA). The normal D_L suggests that lung growth was not accompanied by an increase in the number of gas exchange units. The three acromegalic females had normal lung volumes, anatomic dead space, lung compliance and tissue volumes, suggesting hormonal modification of the growth hormone influence on lung growth. Studies in one female pituitary giant revealed lung growth similar to that in the acromegalic male although lung volumes were normal in relation to the patients large size. This study shows that the lungs of adults are capable of further growth.

A GAMMA-RAY LABELED FATTY ACID FOR FOLLOWING ABSORPTION AND DISTRIBUTION: 12-SELENATRIDECANOIC ACID-^{75}Se. Kenneth R. Brody*, Salvador Treves*, and Richard P. Spencer. Section of Nuclear Medicine, Yale University School of Medicine, New Haven, Connecticut.

While the ^{14}C-analogues can be used to follow fatty acid blood levels and urinary excretion, they can not be employed to detect localization within the body (because of the weak beta emission). Hence we have synthesized and studied a fatty acid which contains a gamma ray emitter (^{75}Se, 120 day physical half-life, 280 kev). The compound is 12-selenatridecanoic acid-^{75}Se, $CH_3.Se^{75}.(CH_2)_{10}.COOH$. The substance was synthesized via a diselenide intermediate. The final product was white in appearance, had the correct elementary analysis, and a sharp melting point. When given orally to dogs, some absorption occurs and the peak value is about 2% of the administered dose per liter of blood. Following injection of the radiolabeled 12-selenatridecanoic acid into the tail vein of mice, animals were sacrificed 24 to 48 hours later. The highest activities (counts/gram tissue) were found in the fat depots, kidneys and liver. All tissues contained some radioactivity. Retention studies and examination of excreta for metabolites, are proceeding. This compound, or its analogues, may have a role to play in following fatty acid uptake, distribution and mobilization.
(Supported by USPHS Grants AM 09429 and CA 06519).

MODES OF DENDRITIC SPIKE GENERATION IN HIPPOCAMPAL NEURONS. G. Broggi* and D.P. Purpura. Albert Einstein College of Med. New York, N.Y. 10461.

A single maximal stimulus to the perforant pathway in the subiculum (Sub) of encéphale isolé cats exhibiting a high degree of responsiveness may elicit, (a) orthodromic spikes that arise from typical EPSPs, (b) fast prepotentials (FPPs) or (c) spikes that arise directly from the baseline. During conditioning fornix (Fx)-evoked IPSPs spikes arising directly from the baseline are not blocked with long Fx-Sub stimulus intervals (20-60 msec) but are eliminated at shorter intervals during the maximal conductance change of the IPSP. Cells exhibiting only FPPs to Sub stimulation develop full spikes with or without multiple components during conditioning Fx stimulation, when the latter produces admixtures of EPSPs-IPSPs. Fx-evoked IPSPs suppress early Sub-evoked EPSPs and increase the latency and decrease the firing level of associated spikes. In several pyramidal neurons Fx-induced antidromic spikes are succeeded by prominent brief negative field responses. During failure of antidromic invasion orthodromic activation occurs via pathways which generate spikes without depolarizing prepotentials. Dendritic spikes may occur in the absence of frequency potentiation at axo-dendritic synapses and may be elicited by interneuronal pathways linked to fornix afferents or pyramidal axon-collaterals. (Supported by N.I.H. Grant NB-07512)

PATTERNS OF VASOCONSTRICTOR OUTFLOW FROM SPINAL CORD TO SPLANCHNIC REGION IN DOG. Gerald A. Brooksby* and David E. Donald, Mayo Clinic, Rochester, Minnesota.

The distribution of the sympathetic vasoconstrictor outflow from the spinal cord to the splanchnic area was determined by electric stimulation (10 V., 10 cps, 3 msec.,) of the isolated anterior spinal nerve roots from T1 through L4. The coeliac and superior mesenteric arteries were cannulated above the diaphragm and perfused independently at constant flow. Increase in perfusion pressure was used as an index of vasoconstriction. The innervation of the coeliac bed arose from the T3 through T13 levels with maximal responses from T4 through T8. The superior mesenteric innervation arose from T3 through L2 levels and was maximal from T10 through T13. The pattern of response was bilaterally symmetrical for both coeliac and mesenteric beds. The paravertebral sympathetic chain was stimulated between successive ganglia from T3 through L3 levels. The pattern of response reflected the outflow from the spinal cord. The major contribution to the coeliac bed had entered the sympathetic chain by T8, but maximal superior mesenteric response was obtained only with stimulation of the splanchnic nerve. A significant vasoconstriction to the superior mesenteric bed was derived from L1 and L2 and thus section of the splanchnic nerves did not eliminate all vasoconstrictor input. Other than the L1 and L2 outflows the cord outflow to the viscera traveled solely in the paravertebral chain and splanchnic nerves. The vasoconstrictive response of each region to splanchnic nerve stimulation was linearly related to frequency up to 30 cps and thus differed from the pattern of sympathetic response in other tissues. (Supported in part by NIH Grants HE 6143 and GM 00089).

THE INFLUENCE OF pH ON THE MEMBRANE RESISTANCE OF A GIANT CELL OF APLYSIA. A. M. Brown, R. B. Sutton*, and P. R. Berman*. Univ. of Utah College of Medicine, Salt Lake City, Utah 84112.

Input resistance (R_M) in the giant cell of the visceral ganglion of Aplysia was measured by recording the changes in membrane potential (E_M) with one intracellular microelectrode while passing constant current pulses through another. Background synaptic activity could be abolished by tetrodotoxin 10^{-5} gm/ml which did not affect the current-voltage curve. R_M varied from 0.6 to 1.0 MΩ, and the resting membrane potential (E_R) from -55 to -65 mV. Decrease in extracellular pH caused an initial hyperpolarization of 2 - 6 mV and a decrease in R_M of 30 - 60%. E_M subsequently returned toward E_R and after 15 - 20 min. exposure the membrane was depolarized. The response was not affected by large alterations of $(Na)_o$, $(Ca)_o$, $(Mg)_o$, or by cooling to 5° C. The initial hyperpolarization was reversed to depolarization when $(Cl)_o$ was reduced to one-half. The null point for the initial hyperpolarization was 5 mV below E_R while E_K as determined by the equilibrium point of the afterpotential was 10 mV below E_R (at 10°C). The null point for the late depolarization was 20 - 30 mV above E_R. The rate of rise and overshoot of the antidromic action potential were unchanged, while the afterpotential and the rate of fall were greatly reduced. Therefore, decreased pH caused an increase in chloride conductance and a decrease in potassium conductance.

(Supported by USPHS Grant HE 10977.)

WHY THIS SKIN? Konrad J. K. Buettner. University of Washington, Seattle, 98105.

Brain and epidermis seem to differ more between man and other mammals than any other body parts. But for certain upper skin qualities regional differences are larger than species differences. We lack a good argumentation fo the cause of these variations. One item, racial color, can be derived from selection via camouflage: the dark tropical jungle lets a dark man be unseen. The winter-white and summer-brown ("white") man is well suited for cool hunting grounds. Vitamin D and sunburn can easily be excluded as controlling factors. The stoppage of sweat by water on the skin (Hertig) and the entrance of water and water vapor into arm, hand and sole may both be related to a pump in the outer sweat duct. Both effects reduce water loss especially in a man clothed or furry. Recently unexpectedly large regional differences of skin areas were discovered in a) skin water loss into a dry capsule, b) heat caused sweating, c) skin water gain from a moist capsule, d) transfer of ethanol and other chemicals through the skin. On a) areola has lowest, scrotum, penis and labia majora show highest losses. The latter 3 regions do not sweat (b) and do not gain water (c). But these regions are very much more permeable (d) to all kinds of harmless and dangerous chemicals. It might be argued that they are closer to mucous membrane than to normal skin.

INHIBITION OF RENIN-RELEASE BY PUROMYCIN. Ruben D. Bunag* and Irvine H. Page. Research Division, Cleveland Clinic, Cleveland, Ohio.

Puromycin is an antibiotic known to inhibit protein synthesis in vitro (Darken, 1964) and, recently, it has been found to lower arterial pressure when infused into the renal circulation of chronic renal hypertensive but not normotensive rats (Macdonald and Blacket, 1967). Since renin is a protein, there is the possibility that the hypotensive effect of Puromycin in renal hypertensive rats is due to inhibition of renin synthesis. Infused into a renal artery of anesthetized dogs, Puromycin (10-125 μg/kg/min for 20 min) consistently reduced renin activity in samples of renal venous blood (measured by bioassay methods described by Pickens et al., 1965 or by Boucher, Menard, and Genest, 1967) when kidneys were perfused at lowered pressures. It did not affect the smaller amounts of renin present in renal venous blood from kidneys perfused at normal pressures. Because of the rapid reduction of renin activity in renal venous blood from some kidneys perfused at lowered pressures, it is considered possible that a mechanism other than inhibition of renin synthesis is involved. However, Puromycin had no effect either on the amount of angiotensin formed when it was added to incubation mixtures containing known amounts of dog renin and its substrate, or on the appearance of renin from isolated slices of dogs' kidney cortex incubated in Kreb's buffer solution in vitro. (Supported in part by Grant HE6835 from the National Heart Institute.)

The Effect of Denervation on the Phospholipids of Skeletal Muscle Membrane

Wilton Bunch, James Berry and Charles Edwards
University of Minnesota Medical School, Minneapolis, Minnesota

Following denervation of a skeletal muscle fiber there is a marked increase in the membrane area sensitive to acetylcholine. In an attempt to find those membrane components whose metabolic rate paralleled the appearance of these receptors, the lipids of normal and denervated muscle membrane were studied. The turnover was increased with denervation in all phospholipids of frog muscle membrane at four weeks. The ratio of denervated to normal was 1.7 for phosphatidyl serine (PS), 5.2 for phosphatidyl inisitol (PI), 1.9 for phosphatidyl choline (PC) and 2.0 for phosphatidyl ethanolamine (PE). There was no change in the quantity of phospholipid except PS which was increased by 25 per cent. When the saritorius muscle was divided into thirds to give endplate rich and poor areas PS was significantly increased in all regions but greater in those areas developing new receptors.
Support from NB-02712.

DOSE RESPONSIVE GASTRIC H^+ SECRETION IN CHRONIC FISTULA CHICKENS USING SUBCUTANEOUS INFUSION OF HISTAMINE. P.G. Burhol*, and B. I. Hirschowitz. Dept. of Med., Div. of Gastroenterology, Univ. of Ala. Medical Center, Birmingham, Alabama.

HCl and pepsinogen are produced by the same gastric cells in birds and lower vertebrates. However, birds differ from other vertebrates in having their specific glands arranged in distinct lobules deep in the mucosa, each with a central collecting cavity which opens on the mucosal surface through a duct. Gastric juice was collected during a subcutaneous infusion of histamine in 2 experiments in each of 5 White Leghorn chickens (1.4-1.8 kg) with implanted gastric cannulae, starting with 50 and doubling the dose every 45 minutes to give, in order, 100, 200, 400, 800 and 1600 μg/kg/hr of histamine base. Volume, H^+ and pepsin were determined in the last 30 min. collection at each dose level. High doses of histamine base, 400 to 1600 μg/kg/hr, were required to give maximal outputs of H^+, (2.29 to 2.59 mEq/30 min.) and of pepsin (40,700 to 131,600 PU/30 min.). As in mammals, plotting of H^+ and pepsin outputs against log doses of histamine base resulted in sigmoid shaped curves, which was linearized with the equation $S/V = aS + b$ where S = dose of stimulant, V = measured response and a and b are calculated constants. Despite this good response to the peripheral stimulus histamine, the chicken is unresponsive to insulin-induced hypoglycemia (J.F. Long, 1967). Since this could be due to a high level of brain hexokinase as in the sheep and goat, 2-Deoxyglucose was given I.V, in doses of 50-400 mg/kg. No stimulation of gastric secretion resulted. This suggests that the chicken brain is not entirely, nor probably even partially dependent on glucose as substrate.

*International Postdoctoral Fellow, NIH.
Supported by NIH Grants 2A-5286, AM 09260

MECHANICAL RESPONSES OF SINGLE FAST AND SLOW TWITCH MOTOR UNITS IN CAT TRICEPS SURAE. R. E. Burke, P. Rudomin* and F. E. Zajac III*. Lab. of Neural Control, NINDS, NIH, Bethesda, Md.

As part of an ongoing study of the input-output relations of cat triceps surae motor units, the mechanical responses of units in the gastrocnemius and soleus muscles have been examined using intracellular stimulation of motoneurons to isolate single motor units definitively. The existence of clearly separable fast twitch (type F; isometric twitch time to peak (T_p) $<$ 35 msec) and slow twitch (type S; T_p $>$ 35 msec) motor unit groups has been confirmed (cf Burke, J. Physiol. 193,141). The isometric tension output curves of F and S units have been compared at different muscle lengths within the physiologic range with particular attention to output during repetitive activation. When a given unit is stimulated twice at relatively short intervals, the area of the resulting tension output curve is considerably greater than the area obtained by the linear addition of two single twitches. This effect apparently results from an increase in the peak tension and duration of the second response and is maximal with stimulus intervals $\leq T_p$. The effect is qualitatively similar in both F and S motor units but the time scales are quite different. The electromyogram of the second component twitch is the same or less than that of the first, suggesting that the effect is produced by a mechanism operating after muscle fiber excitation. Related to this, there is enhancement of tension output during constant low frequency (5-15/sec for type S; 15-25/sec for type F) repetitive activation when a single extra impulse is interposed on the unfused tetanus. These phenomena appear to be related to an optimization of tension output from motor units activated at low repetition rates which are within the firing rates observed for F and S motoneurons activated by natural synaptic input.

EFFECT OF HYPOXIA ON GLYCOLYSIS IN PERFUSED HEARTS FROM RATS AND GOLDEN MANTLED GROUND SQUIRRELS. Roy F. Burlington and Bertwell K. Whitten*
U. S. Army Research Institute of Environmental Medicine, Natick, Mass.

The ground squirrel (Citellus lateralis) exhibits a striking tolerance to severe hypoxia. Previous evidence suggested that cardiac tissue from the squirrel is adapted for function at a relatively low P_{O_2} and that anaerobic glycolysis may be an important factor in this adaptation (Fed. Proc. 48(3):1042, 1969). To test the latter hypothesis, paced hearts (375-385 beats/min) from rats and squirrels were perfused at 35° C with Krebs-Ringer bicarbonate solution containing 20 mM glucose and equilibrated with 95%O_2-5%CO_2 (P_{O_2} = 680 mm Hg). After a 30 minute control period, the hearts were immediately switched to a similar perfusate which had been equilibrated with 95%N_2-5%CO_2 (P_{O_2} = 20 mm Hg). Wollenberger clamps were employed to freeze (-190° C) hearts at intervals during the transition from aerobiosis to anaerobiosis, and tissue levels of adenine nucleotides and selected glycolytic intermediates were measured. During the first minute of hypoxia, left ventricular systolic pressure decreased markedly in hearts from both species. At the same time, coronary flow increased to significantly higher levels in squirrel hearts compared to rat hearts. Hypoxia elicited significant decreases in ATP and creatine phosphate with concomitant increases in ADP, AMP and inorganic phosphate. During the transition to anaerobiosis, the apparent activity of phosphofructokinase (PFK) was significantly increased in hearts from both species. Although the per cent change in PFK activity was greater in the ground squirrel heart, significantly higher total activity was observed in the rat heart. Lactic acid production was also greater in the rat heart. Therefore, the data are not consistent with the hypothesis that ground squirrel myocardial tissue has a greater capacity for anaerobic glycolysis than rat myocardial tissue during hypoxia.

A COMPARISON OF CALCULATED AND DIRECTLY MEASURED LEFT VENTRICULAR WALL STRESS IN THE INTACT CANINE HEART. J. W. Burns*, J. W. Covell, and J. Ross, Jr. Dept. of Medicine, Univ. of Calif., San Diego, School of Medicine, La Jolla, California 92037

Mean left ventricular (LV) wall force was determined using a transmural auxotonic strain gauge in the LV of 8 anesthetized, open-chest dogs. Recorded force was divided by the transmural area acting on the gauge to yield measured mean wall stress (WS). In 3 of the experiments, using right heart bypass, the right ventricle was excised and mean wall force was determined at 2 or more sites on the LV minor equator. WS at these different sites differed by an avg. of 14.4%. In 5 experiments, with the circulation intact, the gauge was oriented in the plane of the minor LV equator, midway between the papillary muscles. LV volume was derived from the passive pressure-volume curve of the arrested heart and calculated mean WS was derived both from spherical and ellipsoidal reference figures for the LV. Control end-diastolic pressure (EDP) averaged 3.7 $\pm$ 1.0 mm Hg (SEM). At this level of EDP measured peak WS averaged 86.8 $\pm$ 13.2 gm/cm^2, whereas calculated peak WS averaged 81.0 $\pm$ 14.7 and 122.7 $\pm$ 19.4 gm/cm^2 for the spherical and ellipsoidal models, respectively. When EDP was increased to 11.3 $\pm$ 2.5 mm Hg, measured peak WS averaged 155.8 $\pm$ 24.9 gm/cm^2, while calculated WS averaged 196.7 $\pm$ 21.5 gm/cm and 272.6 $\pm$ gm/cm^2 in the spherical and ellipsoidal models. These studies indicate that stresses around the minor equator are relatively uniform, supporting the use of single direct force measurements in that equator, and lending validity to the application of geometric models for the calculation of mean WS. At lower EDPs good agreement was found between calculated and measured values of WS, although at higher EDPs WS calculated from the geometric models, particularly the ellipsoidal model, tended to deviate from the measured values. Supported by USPHS Grants HE 12031 and HE 12373.

DECREASED VENTILATORY RESPONSE TO HYPOXIA AND HYPERCAPNIA IN ATHLETES. E. Byrne-Quinn*, J. V. Weil*, I. D. Sodal*, G. F. Filley and R. F. Grover. Dept. of Medicine, Univ. Colorado Med. Center, Denver, Colorado.

Decreased hypoxic ventilatory drive (HVD) has occasionally been observed in otherwise normal low altitude residents. So far no particular group of normal individuals has been described in whom there is a consistent decrease in HVD. Using a technic of progressive hypoxia with isocapnia a continuous curve relating P_AO_2 and $\dot{V}_E$ is obtained. In previously studied normal subjects the curves can be closely approximated by $\dot{V}_E = \dot{V}_E o + A/(P_AO_2 - 32)$, where $\dot{V}_E o$ is the ventilatory asymptote and the parameter A determines curve shape such that an increase in A denotes an increase in HVD. The linear response of $\dot{V}_E$ to hypercapnia is expressed as the slope $S(\Delta \dot{V}_E/\Delta P_ACO_2)$. Maximum oxygen uptake ($\dot{V}_{O2}$ max.ml/min/kg) was obtained by treadmill exercise. Nine sedentary non-athletes were compared with 12 conditioned college athletes:

	n	$\dot{V}O_2$ max	A	S
non-athletes	9	39.2 $\pm$ 2.4 (SEM)	178.3 $\pm$ 15.7	2.03 $\pm$ .21
athletes	12	60.6 $\pm$ 2.2	62.0 $\pm$ 11.6	0.95 $\pm$ .09
	P	$<$ 0.01	$<$ 0.01	$<$ 0.01

For the entire series HVD as measured by A was inversely related to $\dot{V}_{O2}$ max. r=-0.71 (P$<$0.01), similarly CO2 sensitivity S was also inversely related to $\dot{V}_{O2}$ max r=-0.76 (P$<$0.01). Finally there was a linear relationship between A and S, r=0.82 (P$<$0.01). In contrast to this evidence of decreased HVD at rest both groups showed similar increases in $\dot{V}_E$ when F_IO_2 was changed from 100% to 14% during exercise. Hence while these studies show that resting hypoxic and hypercapnic ventilatory drives are substantially decreased in athletes, the relevance to athletic performance is unclear. The question of whether the attenuations of the hypoxic and hypercapnic responses are independent or are causally related through an interactive mechanism remains to be explored.

THE EFFECT OF TEMPERATURE CHANGES ON THE HEART RATE OF DEVELOPING CHICK EMBRYOS. J. R. Cain and V. L. Rogallo. Poultry Department, University of California, Davis, California 95616 and ARC-NASA, Moffett Field, California 94035 (intr. by W. O. Wilson)

This study with a ballistocardiograph has shown that between the twelveth and fourteenth day of embryonic development, the White Leghorn chick embryo changes its response to thermal influences. This time seems to correspond to the change from a state of poikilothermia to one of partial homeothermia in this species. The heart rate of 12 day embryos at 42°C is >410 bpm., whereas that of 14 day embryos is < 300 bpm. Ten day embryos generally exceed 450 bpm. at temperatures above 42°C. Heartbeat frequency at 29°C is 120-140 bpm. for both 12-14 day groups. Older embryos yield a sigmoid temperature-heart rate relationship, whereas younger ones have an essentially linear function.

It was reported over 300 years ago that the heart rate of the avian embryo is a direct function of environmental temperature. However, rapid temperature fluctuations affect the heart rate of all embryos measured differently than do gradual changes from 23 to 48.6°C. The latter yield linear correlations, but the former produce stepwise chronotropic as well as drastic ionotropic changes in the embryonic heart.

RESPIRATORY MOVEMENTS DURING SONG OF THE CANARY. William A. Calder, Jr. Dept. of Biology, Virginia Polytechnic Institute, Blacksburg, Va.

The respiratory system of birds is very important for communication in addition to its primary function of gas exchange. Some small birds produce sustained song of remarkable duration in view of their normally high breathing frequencies and undoubtably limited vital capacities. Little is known about respiration in avian song except that an artificially imposed air flow produces sound only in the expiratory direction.

The respiratory movements of roller and water slager canaries were recorded from impedance pneumograph and microphone simultaneously. Song notes or pulses occurred in 1:1 correspondence with thoracic movements. Trilled notes as frequent as 25/sec appear to be formed by individual, shallow breaths. The dorso-ventral dimension can be maintained almost constant, and may even increase to augment air stores during trills. The song is immediately followed by an expiratory movement. This suggests that song duration would not necessarily be limited by the volume of air taken in before beginning a song, but more likely by the oxygen or carbon dioxide content of the air contained in the system after a period of shallow tachypnea.

EFFECT OF ARTERIAL PRESSURE ON RENAL VASCULAR AND EXTRAVASCULAR VOLUMES. M.H. Caley* and A.M. Scher. Dept. of Physiol. and Biophys., Univ. of Wash., Seattle, Wash.

Kidney volume increases with arterial pressure. To ascertain the role of renal fluid compartments in the expansion of the kidney, changes in renal vascular and extravascular volumes were measured over a pressure range of 50 - 200 mmHg in isolated dog kidneys perfused with blood via a constant pressure perfusion pump. At each arterial pressure and steady-state renal blood flow I^{131}-serum albumin, alone or with Cr^{51}-labeled red blood cells, was injected into the renal artery at constant rate. When venous isotope concentration reached a plateau, isotope injection was stopped and venous blood was collected until isotope washout was complete. Plasma and red cell volumes were determined from the amount of isotope in washout and the plateau isotope concentration. Extravascular volume was determined by subtracting blood volume from the steady-state kidney weight.

As perfusion pressure increased between 100 and 200 mmHg, average kidney weight increased 11%. Vascular volume decreased 20%. Combined interstitial and intratubular volumes were estimated to increase by 40%.

(Supported by Public Health Service Grants AM38224-02 and HE07746-06)

NORMAL AND ABNORMAL GROWTH AND DIFFERENTIATION OF TYPE I AND TYPE II MUSCLE FIBERS IN THE DOG. G. H. Cardinet, III, L. J. Wallace, M. R. Fedde, M. M. Guffy, and J. W. Bardens (intr. by E. L. Besch). Coll. Veterinary Medicine, Dept. Physiol. Sci., Kansas State Univ., Manhattan

The purpose of this investigation was to study the pectineus muscles of dogs since it has been suggested that this muscle restricts abduction of the hip joint in potential hip dysplastic puppies.

Muscle fiber types described herein are based on their reaction for myofibrillar ATPase. At birth, the muscle is composed primarily of Type II muscle fibers. By 9 months of age there are approximately 50% Type I and Type II fibers due to a Type II to Type I transformation. In addition, there is approximately a 30 fold increase in muscle fiber cross-sectional area. Abnormal development of the muscle was observed in German Shepherd and mongrel dogs 37-118 days of age which appeared to be transient. It was characterized by extreme variations in muscle fiber sizes in which Type I fibers were larger than normal and Type II fibers smaller than normal. The extent of involvement within the muscle varied from focal to diffuse. In diffusely affected muscles there was a tendency for gross atrophy of the muscle.

Analysis of the normal growth and differentiation of the muscle suggests that the abnormality consists of Type II fiber hypotrophy with delayed Type II to Type I differentiation and Type I fiber hypertrophy. Experimental evidence suggests that growth and differentiation of muscle fiber types is directed by neuronal trophic factors. The lesions in the pectineus muscle may represent a spontaneous disease where such factors are missing or delayed in their availability to the muscle fibers.

Supported by grants from the Seeing Eye, Inc.; Morris Animal Foundation; Air Force Office of Scientific Research, AFOSR Grant No. 69-1718 and PHS Research Grant No. NB 05786, National Institute of Neurological Diseases and Stroke.

PROPIOCEPTIVE STIMULUS IN THE REGULATION OF PULMONARY VENTILATION IN MAN. David Cardus, Departments of Physiology and Rehabilitation, Baylor College of Medicine, 1333 Moursund Avenue, Houston, Texas 77025

An experiment was carried out to study the relationship between propioceptive activity and pulmonary ventilation during exercise. The study was conducted on 4 healthy men. Each subject was tested with a bicycle ergometer at three different work loads each of which was performed at three different pedaling rates at a constant load. Heart rate, frequency of breathing, pulmonary ventilation, O_2 consumption and CO_2 exhaled were recorded. The frequency of breathing increased with work load and rate of pedaling. The ventilatory equivalent for O_2 did not change with work load or rate of pedaling. It is concluded that if propioceptive activity controls the rate of pulmonary ventilation during exercise this activity must be related to the level of metabolic activity. The existence of a strictly neural factor consisting of receptors exclusively responsive to movement or force determining the quantitative adjustment of pulmonary ventilation to physical work could not be proved in the present experiment.

This study was supported in part by Project RT-4, Social and Rehabilitation Service, Department of Health, Education and Welfare, Washington, D. C. and by grant FR-00254, National Institute of Health, Department of Health, Education and Welfare, Washington, D. C.

RELATIONSHIP OF ENVIRONMENTAL CONDITIONS TO RATES OF INSENSIBLE WATER LOSS THROUGH THE SKIN. W. M. Carleton*, W. J. Sears*, and B. E. Welch. USAF School of Aerospace Medicine Brooks AFB, Texas. (Partial support by NASA PR T-74393(G)

It has long been known that physical variables play an important role in the rate of human perspiration. Arguments have arisen about the influence of humidity, barometric pressure, temperature, and air movement upon the rate of the "diffusional" or non-sweat component of skin water loss (IWL). To resolve these questions 6 subjects were placed in a controlled-environment chamber and subjected to varying combinations of temperature (T_a), water vapor pressure (P_w), total pressure (P_B), air movement (V), and gas mixtures. Water loss was measured on a metabolic balance sensitive to $\pm$1gm while subjects lay semi-nude on a screen platform. Respiratory water was trapped in a mask-drierite system fixed to the scale so that only IWL was recorded. All environmental and subject data (including rectal, skin temps.) were continuously recorded by an automated digitalized system. T_a was varied from 20° to 28° C with a change in rate of IWL of +0.41 gms/m^2/hr/°C. P_w was varied from 4 mm to 14 mm Hg with a change in slope of -0.26 gms/m^2/hr/mm P_w. P_B varied from 258 mm to 700 mm Hg with an IWL change of -0.7 gms/m^2/hr/100 mm P_B. The range of V was from 15 to 90 m/min with a change in slope of +1.4 gms/m^2/hr/30 m V. Varying the gas mixture at 258 mm Hg P_B from 70% O_2: 30% N_2 to 70% O_2:30% He and 100% O_2 resulted in IWL decrease of 24% in the 1st case and an increase of 6% in the 2nd. The influence of each environmental variable was uniform through the range studied; each was additive without evidence of synergism or antagonism. The lowest rates of IWL measured were 7.6 and the highest 14.8 gms/m^2/hr. Rates of IWL were closely correlated with average skin temp. All data support the idea that environmental conditions have a constant and predictable influence on the non-sweat component of skin water loss.

ANGIOTENSIN-PROTEIN BINDING IN PLASMA. O. A. Carretero and J. A. Houle (intr. by H. Sparks). Henry Ford Hospital, Detroit, Mich.

A property of the plasma proteins is their ability to bind a number of molecules of differing chemical structures. In view of this, binding of angiotensin II (ang.) by nephrectomized dog plasma (Nx. Pl.) was investigated. The method of equilibrium dialysis was employed in which a solution within a cellophane bag was dialyzed against a solution containing a known amount of ang. After 18 hrs. of dialysis the concentrations of ang. (ng/ml) in the outside solution (o.s.) and inside solution (i.s.) were measured by bioassay. Observation of a higher concentration of ang. in the i.s. was interpreted as binding. When Nx. Pls. (i.s.) were dialyzed against distilled water (o.s.) the following concentrations were obtained: 1) i.s.= 72, o.s.=16; 2) i.s.=58, o.s.=14; 3) i.s.=58, o.s.=10. When the o.s. was citrate buffer of pH 5, 7 and 8, the respective results were: i.s.=48, o.s.=16; i.s.=56, o.s.=16; i.s.=62, o.s.=16. When Nx. Pl. containing ang. was dialyzed against saline and dextran coated charcoal (which absorbs ang.), the concentrations were i.s.= 64, o.s.=0. In control experiments, when the i.s. was dextran or water and the o.s. was water, similar concentrations were found in i.s. and o.s. (difference less than 12%). It was concluded that Nx. Pl. contains an ang. binding factor. However, fractional precipitation of Nx. Pl. with $(NH_4)_2SO_4$ at 50 and 100% saturation failed to separate as a constituent of the globulin or albumin fraction. This binding factor may be a specific protein but it has not yet been characterized. The physiological implications of this binding is unknown.

MODIFICATION OF NEUROMUSCULAR SENSITIVITY BY RESERPINE. Gerald O. Carrier*, Barbara L. Pegram*, and Oliver Carrier, Jr. The Univ. of Texas Med. School at San Antonio, San Antonio, Texas.

This present study was conducted to investigate reserpine's effect at the neuromuscular junction. This action was apparent by reserpine's interaction with d-tubocurarine. It was found that the dose of d-tubocurarine causing paralysis of the hindlimbs of normal rabbits was 0.176 ± 0.008 mg/kg. However, after the animals were pretreated with various doses of reserpine, the dose of d-tubocurarine needed to elicit the same response increased significantly (ave. 0.209 mg/kg). It was also observed that the lethal dose of d-tubocurarine for control animals was 0.294 ± 0.01 mg/kg, while after reserpine; the lethal dose of d-tubocurarine increased to 0.409 ± 0.03 mg/kg or 0.448 ± 0.02 mg/kg depending on the dose and time regimen for reserpinizing the animals. Since reserpine does not alter neuromuscular transmission, it is possible that reserpine increased the sensitivity of the end-plate; thus a larger dose of d-tubocurarine was needed for hindlimb paralysis and death. This work was supported in part by USPHS Grant HE-09391.

STUDIES ON THE EFFECTS OF TEMPERATURE ACCLIMATION ON THE WHOLE-BODY PROTEIN TURNOVER RATE IN MACACA MULATTA. R.R.J. Chaffee, J.R. Allen*, F.C. Kelley*, J. Love*, J.T. McClintock* and R.H. Rochelle*. Univ. of Calif., Santa Barbara, Calif. 93106.

The whole body turnover rate of Se^{75}-selenomethionine is faster in cold-acclimated rats and mice than in controls (Chaffee et al, Fed. Proc. 27:633, 1968; Yousef & Luick, Can. J. Physiol. Pharmacol. 47:273, 1969) even when the diet is controlled. Similar studies using the same techniques were made on cold- and heat-acclimated and control Macaca mulatta to see if the same response occurs in primates. Monkeys were acclimated, in individual cages, for three months or more at 35°C, 24°C and 5°C with equivalent amounts of dietary protein/gm body weight. The additional caloric requirements of cold-acclimated monkeys were made up by feeding fat and carbohydrate in the form of fresh fruit. These fruits contained insignificant amounts of protein in comparison to the high content of the chow pellets. The results showed that whole body turnover rate (K/day) of Se^{75}-selenomethionine in the cold-acclimated monkey (K/day = 0.0193) was significantly higher than in the control (K/day = 0.0138); the turnover rate of the heat-acclimated animals (K/day = 0.0122) was not significantly different from the control. These studies indicate that protein turnover is increased in the cold-acclimated animal and that any increases in enzyme activity involved are not induced by increased dietary protein, but by cold acclimation. The evidence supports the hypothesis (Chaffee, et al) that there is a more rapid amino acid ⟷ protein recycling in the cold which would result in greater cellular calorigenic output due to a more rapid intracellular ADP production and mitochondrial respiratory release. (Supported by Contract # DADA 17-68-C-8064, from the U. S. Army Medical Research and Development Command.)

RESPIRATORY AND CARDIAC PATTERNS ASSOCIATED WITH CONDITIONED EEG ACTIVITY OF THE SENSORI-MOTOR CORTEX. M. H. Chase and R. M. Harper*. Veterans Administration Hospital, Sepulveda, Department of Anatomy, UCLA, Los Angeles, California.

Five cats were prepared with implanted electrodes to record the EEG of the sensori-motor cortex (anterior and posterior sigmoid gyri), and the respiratory pattern and heart rate. While the animals were freely moving the EEG was passed through a tuned frequency filter and relay system so that activity within a range of 12-14 cps could be reinforced by the contingent presentation of 15 cc of milk. The EEG, filter, and relay activity was compared with the ongoing respiratory pattern and heart rate in each cat. The onset of sensori-motor activity most often occurred in conjunction with inspiration, while the termination usually occurred during expiration. During trains of this EEG activity the heart rate decreased. It has been suggested that the sensori-motor rhythm may be a cortical correlate of internal inhibition. During this conditioned EEG activity, eye and locomotor movements cease, and to this observation we now add that the respiratory pattern and heart rate are regulated. (Supported by the Veterans Administration, USPHS grant #10083, and by the Canadian MRC.)

EARLY TISSUE AND CORONARY VEIN POTASSIUM LEVELS IN EXPERIMENTAL MYOCARDIAL INFARCTION AND ITS RELATIONSHIP TO VENTRICULAR FIBRILLATION (VF). G.W. Cherry and M.B. Myers (intr. by H.S. Mayerson) Touro Research Institute, New Orleans, La.

Tissue K levels were determined on avascular oval infarcts created on the left ventricle of 9 dogs and 3 pigs. All infarcts over 16% of the ventricular mass in dogs and over 6% in pigs led to VF at a $\bar{x}$ of 43 min. Four dogs with infarcts less than the critical size were sacrificed at a $\bar{x}$ of 38 min. Delineation of the avascular myocardium was made with fluorescein dye. In the VF group the $\bar{x}$ infarct wt. was 33.8 gms and the $\bar{x}$ K loss was 0.44 meq. In the non-VF group $\bar{x}$ infarct wt. was 20.3 gms. with a 0.30 meq. K loss. K loss per gram of infarct was the same in both groups; however, the total K loss was greater in those animals that developed VF. In an additional 13 dogs and 5 pigs the anterior descending coronary artery was ligated and the great cardiac vein cannulated for serial K levels. Before coronary ligation, femoral artery and coronary vein K levels were the same ($\bar{x}$ 3.4 meq./L). After ligation the coronary vein K rose in all animals reaching a $\bar{x}$ peak of 4.8 meq./L at a $\bar{x}$ of 4.5 min. declining thereafter. The femoral artery K level remained unchanged during the procedure. No correlation between the K level and maximum ectopic activity was noted in the 11 animals that ended in VF and the 7 that did not. In another 5 dogs, saline was injected into small infarcts followed by KCL. Two dogs developed VF with the saline injections, in the 3 remaining dogs KCL failed to produce VF even though the K level in the coronary vein consistently rose. Thus K loss from ischemic myocardium is not an important factor in the production of VF.

(Supported by a grant from the John A. Hartford Foundation.)

EFFECT OF NEGATIVE ACCELERATION ON RENAL BLOOD FLOW OF UNANESTHETIZED DOGS. J.E. Chimoskey. Present address: Physiology Div., AMRD, Naval Air Dev. Center, Johnsville, Warminster, Pa. 18974, and Dept. of Physiology, Hahnemann Medical College, Philadelphia, Pa. 19102.

Renal blood flow velocity was measured in four trained unanesthetized dogs by a Doppler principle ultrasonic flow meter during exposure to negative centrifugal acceleration ($-G_z$) up to three times the acceleration of gravity ($-3\ G_z$). Renal arterial pressure and renal arterial-venous pressure gradient were measured by indwelling polyvinyl catheters connected to external transducers mounted on the centrifuge at kidney level. The Doppler flow signal was telemetered and the pressure signals were transferred by sliprings from the centrifuge to an ink writing oscillograph. Experiments began about ten days after the operations which were performed under pentobarbital anesthesia, 30 mg/kg. Renal blood flow velocity decreased during $-G_z$; the decrease was proportional to $-G_z$ level. The flow velocity was significantly lower at $-3\ G_z$ than it was at -1 and $-2\ G_z$. By the end of the 27 to 30 second periods of constant $-G_z$, renal blood flow velocity had recovered significantly from the minimum values; the flow velocity did not return to the pre-acceleration control level until after the accelerations were terminated. The lowest mean arterial-venous pressure gradient, 129 ± 7 (S.E.) mm Hg, was recorded during $-3\ G_z$; it did not differ significantly from the pre-acceleration control. Calculated intrarenal resistance to blood flow increased. In each of the four dogs the flow velocity reduction tended to be greater during the first exposure to $-G_z$ than during subsequent exposures to $-G_z$ on any given day. Increased intrarenal resistance to blood flow is part of the response to $-G_z$.

MECHANISM OF EPINEPHRINE INDUCED BLOCKADE OF GANGLIONIC TRANSMISSION IN THE RABBIT SUPERIOR CERVICAL GANGLION. D.D. Christ* and S. Nishi. Loyola University Stritch School of Medicine, Maywood, Illinois 60153.

Epinephrine (Epi) blockade was studied by means of intracellular recordings from the postsynaptic neurons of isolated ganglia. Epi bitartrate (10^{-7}M) depressed the EPSP but had no effect on the direct spike or resting membrane potential. Concentrations as high as 10^{-5}M Epi were required to elicit consistent changes in the resting membrane potential. The blocking action of Epi was abolished by phenoxybenzamine hydrochloride (10^{-5}M), but was not affected by propranolol (3×10^{-5}M). Thus the Epi action involves alpha adrenoceptive sites.

To determine whether the depression of transmission by Epi was due to presynaptic or postsynaptic mechanisms, the effect of Epi on ACh-potentials was observed. Epi (10^{-5}M) produced no change in the ACh-potentials, even when the EPSP was markedly depressed. This observation indicates that Epi blocks ganglionic transmission by depressing the release of transmitter from the presynaptic terminals. This conclusion is supported by the observation that Epi decreased m.e.p.s.p. frequency but was unable to depress m.e.p.s.p. amplitude.
(Supported by NIH Postdoctoral Fellowship 1 F02 NB41370-01, NSF Grant GB-8718 and NIH Grant NB06672-04).

VENTILATORY PATTERNS AFTER SELECTIVE ABLATION OF RESPIRATORY FEEDBACK MECHANISMS. H.D. Christensen*, A.J. Krieger* and S.C. Wang. Columbia University, New York, N.Y.

Thirty midcollicular decerebrate cats were used to assess ventilatory pattern changes after afferent feedback circuits were interrupted. The selective ablation consisted of combinations of bilateral ventrolateral or dorsal cervical cord lesions with either midpontine transection or bilateral vagotomy. The combination of midpontine transection with bilateral vagotomy produces apneustic breathing. Bilateral ventrolateral cord lesions and midpontine transection resulted in a variety of slowed respiratory patterns. In those animals which exhibited patterns similar to apneustic breathing, they differed from classical apneustic respiration in that the inspiratory spasm was not maximal as electrical stimulation of the medullary inspiratory center increased the depth of inspiration further. Apneustic respiration was also produced following bilateral ventrolateral cord lesions and bilateral vagotomy. The combination of bilateral dorsal cord lesions with either bilateral vagotomy or midpontine transection, however, did not alter the respiratory pattern. This study suggests the presence of another afferent feedback pathway in the ventrolateral cervical cord, modulating the apneustic mechanism in the pons.
(Supported by USPHS Grants NB05173, NB05511, and NB00031).

RHEOLOGICAL PROPERTIES OF SOFT EXTENSIBLE ANIMAL TISSUE IN BOTH LIVING AND EXCISED STATES. Billie Chu (Intro. by Harold Wayland), Div. of Engr. & Applied Science, Calif. Inst. of Tech., Pasadena, Calif.

A mechanical characterization of a wide range of response of a particular soft extensible animal tissue, the mesentery, is presented. Certain individual aspects of the mechanical response of living mesenteric membrane per se have been studied and contrasted with (1) membrane strongly influenced by or containing large blood vessels, (2) excised membrane, and (3) membrane after circulatory collapse and accompanying sustained gut contraction.

The tension level in the tissue at the initial configuration length is not unique but can vary significantly according to the activity of the components of the membrane per se as well as the state of the gut and the large blood vessels. The most nearly unique length of the tissue which can be detected by these experimental methods is a relaxed length determined by excising a piece of tissue of known dimensions and measuring the freely floating (in a physiologic solution) dimensions to which the tissue relaxes. There is no marked material anistropy in the plane of the membrane, i.e. the two principal dimensions in the plane of the mesentery do not vary by more than five percent even with wide history variations just prior to excision.

A theoretical characterization that correlates rather well with the data of the loading curves for the various tissues has been proposed. The limitations and assumptions incorporated in this treatment have been discussed and when appropriate additional experimental data are procured, the analytical treatment can likewise be extended to a more adequate characterization.

'AUTOMATIC' CARDIAC VENTRICLES. Leon Churney. Department of Physiology, Louisiana State University Medical Center, New Orleans, La. 70112.

Forty seven out of 50 Amphiuma ventricles and 4 out of 6 Necturus ventricles excised in Ringer's sol'n. beat spont. Mostly the rate of the excised ventricle was that of the whole heart, but in 1 case the rate was 2/3 and in 3 cases twice that of the whole heart. One excised A. ventricle beat at 60/min, which is the limit that one can drive this tissue & still get a 1:1 stimulus-response ratio. In 1 in situ heart, atrium & ventricle beat independently. When the atrial beat was abolished by locally applied mecholyl, the ventricle did not assume spont. activity. Six A. ventricles were split into 2/3 base and 1/3 apex. All basal pieces & 1 apical piece continued to beat spont. The action potentials (APs) recorded from the base of the excised ventricle usually preceded those from the apex, & the APs from the endocardium preceded those from the epicardium (cond. dist. 2.2 cm). Yet at the ends of a 1.7 cm span on the base, the APs arose almost simultaneously. Persistent search for pacemaker-type potentials (PAPs) failed to reveal a focal region of pacemaker potentialities. Ventricles stored at 8 C for several days beat spont. upon rewarming & showed PAPs. Dividing the ventricle into 2 or more parts often left each temporarily inactive. Resumption of spont. activity was associated with the presence of PAPs. Automaticity is initiated in quiescent ventricular strips by K^+—free Ringer's, by adrenalin, by Ba^{++}, & at times by electrical stimuli — even by subthreshold pulses. But not by stretch. Automaticity initiated in ventricular preparations by K^+—free Ringer's was abolished in normal Ringer's. When spont. activity ceased in K^+—free Ringer's, it often resumed in normal Ringer's. Normal pacemaker activity recorded from the excised atrium was abolished in K^+—free Ringer's & restored in normal Ringer's. Adrenalin induced automaticity in (turtle) ventricular strips, but not in atrial strips.

PROLACTIN RESPONSIVE NEURONS IN THE RABBIT HYPOTHALAMUS. J.A. Clemens*, R.V. Gallo*, D.I. Whitmoyer* and C.H. Sawyer. Dept. Anat. and Brain Research Institute, UCLA, Los Angeles, California 90024.

A study has been made of the effects of intravenous injections of small amounts of prolactin on the electrical activity of single hypothalamic neurons in unanesthetized, ovariectomized rabbits recorded by the method of Findlay and Hayward (J. Physiol. 201: 237, 1969). The cortical EEG was monitored simultaneously with single unit activity, and hypothalamic units were recorded continuously on magnetic tape and paper, many for several hours. Unit firing rates that changed in parallel with cortical EEG patterns were analyzed either entirely during sleep or entirely during arousal to prevent nonspecific alterations in brain function from biasing changes in hypothalamic unit firing rates induced specifically by the hormone. Under these conditions intravenous prolactin (NIH-S8, 50 μg) induced changes in firing rates of single neurons in the hypothalamus independent of alterations in EEG. Of 22 units tested with prolactin, the firing rate decreased in 12 and increased in 4, while 6 remained unchanged. Histological verification of recording sites suggested that there may be several sites in the hypothalamus that are responsive to prolactin feedback. Attempts are now being made to more accurately define the hypothalamic loci responsive to prolactin and determine what functional relationships may exist among these areas. (Supported by NB 01162 and the Ford Foundation).

VOLTAGE CLAMP ANALYSIS OF A NEW POTASSIUM CONDUCTANCE MECHANISM AND ITS RELATION TO REPETITIVE FIRING. J.A. Connor* and C.F. Stevens*. Introduction by H.D. Patton. Dept. of Physiol. and Biophysics. Univ. of Wash., Seattle, Washington

Experiments were performed on Nudibranch molluscs. The neural soma was isolated from its axon by means of a silk filament ligature giving a neurite-free structure, the interior of which is approximately isopotential under voltage clamp conditions. Resting potential of such cell bodies ranged between -35 and -50 mV at 5°C, with a spike overshoot of 30 to 40 mV. Two operationally separate sets of potassium channels were investigated: (1) a potassium conductance giving rise to delayed rectification analogous to that described for squid axon and other preparations; (2) a previously undescribed set of channels (early potassium channels). This second set is separable from the delayed rectification channels because (a) they are activated at values of membrane voltage (V_m) more positive than -50 mV and are completely inactivated for V_m more positive than -35 mV. The delayed channels also display activation-inactivation characteristics but the voltage range over which this occurs is approximately 30 mV more positive and the channels do not inactivate completely. (b) The early potassium channels activate and inactivate much faster than the delayed rectification channels. (c) There is a small difference in equilibrium potential (3 to 7 mV) between the two processes: The equilibrium potential for delayed channels was generally more positive. In a cell firing repetitively to constant current stimulation, V_m is controlled largely by part of the interspike interval. After the first part of the interval, the early current, having been activated by the spike undershoot exerts significant control over V_m.

Supported by PHS Grants NB 05934-04 and NB 05082.

EFFECT OF NEAR-VACUUM EXPOSURES ON PULMONARY CIRCULATION IN DOGS. Julian P. Cooke and George F. Gee (intr. by Henry B. Hale). USAF School of Aerospace Med., Brooks AFB, Tex.

Pulmonary circulation was studied during exposure of 8 anesthetized dogs to a near-vacuum pressure of 2 torr by injecting albumin I^{125} into either the pulmonary artery or superior vena cava about 20 seconds after the exposure had begun and later ascertaining the location of the isotope. A slight forward flow was detected in the pulmonary circulation in 50% of the dogs whereas the remaining 50% showed absence of blood flow in either direction. Higher levels of I^{125} in hemorrhagic lung tissue exceeded levels in other tissues. This suggests movement of blood into the damaged areas occurred during the latter part of the exposure or during the recompression.

RELATIVE EFFECTIVENESS OF CALCITONIN FROM HOG THYROID AND SALMON ULTIMOBRANCHIAL. D.H. Copp, C.E. Brooks*, F. Hui* and F.E. Newsome*. Dept. of Physiology, University of B.C., Vancouver, Canada.

The structure of pure salmon calcitonin has recently been established, and resembles that of the hormone obtained from hog thyroids. Both consist of 32 amino acids with a seven membered disulfide ring at the N terminus and proline-amide at the C terminus. However, there are a number of differences in amino acids, and the salmon hormone is 25-100 times as potent. It also has a much more prolonged action when injected into rats, rabbits and monkeys. One explanation for the more prolonged action is the greater stability of the salmon calcitonin when incubated with whole blood. Hog calcitonin was completely inactivated when incubated for 1-2 hours at 37°C in rabbit, human, hog and salmon blood. The loss of activity of salmon calcitonin under similar circumstances was very slow.

Supported by grants from the Medical Research Council of Canada.

MECHANISMS OF CONDITIONAL ANTIDIURESIS. E. O'Leary Corson*, Samuel A. Corson, and Steve Vanecko*. Laboratory of Cerebrovisceral Physiology, Division of Behavioral and Neurobiological Sciences, Department of Psychiatry, Ohio State University College of Medicine, Columbus, Ohio.

Pavlovian conditional motor defense responses were developed in several breeds of dogs by electrocutaneous reinforcement of neutral auditory signals. Some dogs (e.g., many wire-hair fox terriers) developed persistent conditional antidiuretic responses to the conditioning room. Since the urine osmolality was high (1000-2200 mOs/L) and the GFR and RBF did not decrease, we ascribed the antidiuresis to vasopressin release. However, using the ethanolized rat bioassay method (measuring urine flow and conductivity) we failed to detect sufficient vasopressin to account for the intense antidiuresis and high urine osmolality. We are currently trying to improve the vasopressin bioassay method and to utilize also a radioimmunoassay technique. Two other mechanisms may contribute to this antidiuresis: a) increased sensitivity of the renal tubules to vasopressin, and b) participation of aldosterone. Preliminary experiments suggest that these two factors may possibly operate in psychogenic antidiuresis. (Supported in part by research grants MH 12089 of the National Institute of Mental Health, LM 00635 of the National Institutes of Health, and the NIH General Research Support Grant to the Ohio State University College of Medicine.)

PSYCHOGENIC AND CONSTITUTIONAL FACTORS IN ENERGY METABOLISM. Samuel A. Corson, J. Hajek*, M. Hajkova*, V. Kirilcuk*, and E. O'L. Corson*. Laboratory of Cerebrovisceral Physiology, Division of Behavioral and Neurobiological Sciences, Department of Psychiatry, Ohio State University College of Medicine, Columbus, Ohio 43210.

Rectal and skin temperatures (using thermistors) and O_2 consumption and CO_2 production measurements (by means of a Beckman Biomonitor) were made in several breeds of trained, unanesthetized dogs in two different environments: a neutral control room and a room where Pavlovian motor defense responses were developed using electrocutaneous reinforcement to a leg. Two distinct energy metabolism (EM) patterns were observed: dogs with low BMR (mean 2.2 Cal/kg/hr) and dogs with high BMR (mean 3.9 Cal/kg/hr). In the Pavlovian room the low BMR dogs showed little or no change in EM, whereas the high BMR dogs increased the EM (to a mean of 5.28 Cal/kg/hr). The rectal and skin temperatures were higher in the high BMR dogs in the neutral and Pavlovian rooms. The high BMR dogs in the Pavlovian room also exhibited hyperpnea, tachycardia, copious salivation, and antidiuresis, with a high urine osmolality. In spite of intense panting, the rectal temperature remained constant or even increased. (Supported in part by research grants MH 12089 of the National Institute of Mental Health, LM 00635 of the National Institutes of Health, and the NIH General Research Support Grant to the Ohio State University College of Medicine.)

INFLUENCE OF ALTERED RETICULOENDOTHELIAL (RE) FUNCTION ON THE FATE OF ^{51}Cr S. ENTERITIDIS ENDOTOXIN. Clifford G. Crafton * and N.R. Di Luzio, Univ. of Tenn. Med. Units, Memphis, Tenn. and Tulane Univ. Med. Sch., New Orleans, La.

Glucan, methyl palmitate, and heparin, agents which modify RES activity, markedly alter endotoxin lethality in rats. Glucan treatment results in extreme sensitivity to endotoxin; whereas, methyl palmitate and heparin promote endotoxin resistance. To define the mechanism of RES influence on endotoxin lethality, vascular clearance and tissue distribution of ^{51}Cr S. Enteritidis were determined in rats pretreated with either glucan, methyl palmitate, or heparin. Endotoxin clearance was biphasic consisting of an initial, fast (t/2=15.3 min) and a subsequent slow component (t/2=55.3 min). Glucan, a RES stimulating agent, induced an acceleration of both the early and late phases of endotoxin clearance as denoted by a respective 59 and 36% reduction in the half times. The enhanced clearance was due to a 53% increase in hepatic uptake, as splenic and pulmonary localization were unaltered. Methyl palmitate, which induces RES hypofunction, exerted no influence on clearance or hepatic and pulmonary uptake but significantly diminished splenic uptake by 85%. Heparin, a phagocytic stimulant, induced a prolongation of the early phase of endotoxin removal but did not modify the later phase. A 20% reduction in hepatic uptake was also noted. No definitive relationship existed between endotoxin fate and endotoxin lethality; therefore, agents which alter RES function and influence endotoxin lethality, do not exert their activity by altering the vascular clearance or initial tissue localization of endotoxin. These studies implicate an unidentified cellular component as a determinant in the altered endotoxin sensitivity of animals with RES functional modifications.

THE EFFECT OF ANEMIA ON THE RESPONSE OF THE PULMONARY CIRCULATION TO ACUTE HYPOXIA. G.J. Cropp. Univ. Colorado Med. Ctr., Denver.

Nine anesthetized dogs were studied during air and 10% O_2 breathing before, and after they had recovered for several days from having been made anemic by exchange transfusions with plasma. The results are summarized in the table.

	AIR	10% O_2	Δ	AIR	10% O_2	Δ
Hct %	38.2	40.5	+ 2.3	11.7	14.0	+ 2.3
Syst. P_{PA}	20.7	39.1	+18.4	27.3	46.4	+19.1
Diast.P_{PA}	8.7	21.9	+13.2	9.0	22.7	+13.7
Mean P_{PA}	13.2	28.7	+15.5	15.7	31.2	+15.5
C.O./kg	223	297	+74	312	386	+74
T.P.R.	66.0	100.6	+34.6	51.4	84.7	+33.3
$P\bar{v}O_2$	43.6	25.3	-18.3	34.6	20.5	-14.1
PaO_2	67.5	30.1	-37.4	68.8	31.2	-37.6

The P_{PA} rose more quickly during hypoxia in anemic than in normal dogs. The hypoxia-induced increase in hematocrit was attributed to release of RBC's from the spleen. We concluded that the low T.P.R. in anemia during air-breathing was due to passive dilation of vessels by high blood flow and low blood viscocity, that 10% O_2 breathing elicited similar hemodynamic changes in normal and anemic dogs, and that lowering $P\bar{v}O_2$ at constant alveolar and systemic arterial P_{O_2} does not constrict pulmonary resistance vessels.

Supported by U.S.P.H.S. grant-in-aid HE 06895-08.

A COMPARISON OF THE LUNG UPTAKES OF ISOTOPIC TRACER $^{18}O_2$, CO AND C_2H_2 IN THE ANESTHETIZED DOG. C.E. Cross*, D.H. Meyer* and J.R. Gillespie. University of California School of Medicine and Veterinary Medicine, Davis, California.

Trace amounts of $^{18}O_2$, CO, C_2H_2 and Ne were used in the modified, single-breath diffusion capacity technique to estimate the relative importance of pulmonary capillary blood volume and pulmonary capillary blood flow on the uptake of $^{18}O_2$ in the lungs of 7 dogs. Each study was preceded by a brief rebreathing period so as to reduce alveolar $^{16}O_2$ tension to that of mixed venous blood. The inspired test gas $^{16}O_2$ tension was also mixed to approximate that of mixed venous blood. Thus, the alveolar and pulmonary capillary $^{16}O_2$ tensions were approximately equal and constant during the diffusion capacity measurements, thereby negating any diffusion gradient for $^{16}O_2$. Alveolar gas samples were obtained at varying time periods for gas chromatography and mass spectrometry analysis. Simultaneously obtained mixed venous and arterial blood gas samples were analyzed polarographically and with mass spectrometry analysis. We compared maximal and minimal calculated $^{18}O_2$ diffusion capacities to the simultaneously determined CO diffusion capacities and to the simultaneously determined C_2H_2 fractional uptakes. The fractional C_2H_2 uptakes permitted us to estimate the flow-dependent and volume-dependent aspects of the $^{18}O_2$ diffusion capacities. The data indicate that, under the conditions of these experiments, $^{18}O_2$ capacities appear to be dependent on pulmonary capillary perfusion rates whereas CO diffusion capacities are less dependent on perfusion rate and are probably largely volume dependent.

HEAT EXCHANGE CHARACTERISTICS OF LABORATORY-ACCLIMATED AND FIELD GROUND SQUIRRELS, CITELLUS LATERALIS AND C. SPILOSOMA[1]. T. J. Crowley* and M. L. Riedesel, Dept. of Biol., Univ. of New Mexico, Albuquerque, New Mexico 87106.

Conduction, radiation, convection, and evaporation are physical processes of heat transfer between animals and their environment. Thermal homeostasis is achieved by changes in physiological and behavioral mechanisms which in turn alter the extent of heat exchange by physical processes. In the arid Southwest, citellid rodents depend largely on conduction, convection, and radiation to remain in thermal equilibrium. Small body mass and limited access to water preclude the extensive use of evaporative heat loss for body cooling.

Experiments were conducted on laboratory-acclimated and field animals. Heat flux transducers, a wind tunnel surrounded by a water jacket, and a cooled copper plate permitted partitioning of heat exchange pathways. The data demonstrate acclimation and acclimatization can be as important as species differences in determining heat exchange capacities of small rodents.

Elucidation of heat transfer pathways provides an approach to quantitative assessment of the thermal environment impinging on an animal in its natural state. Quantitative description of the environment permits prediction of the animal's tolerance to extreme environments.

1 Supported in part by NSF grant GB 5339

Mean Pulmonary Artery Pressure and Alveolar Oxygen Tension in Man at Different Altitudes. L. Cudkowicz, Cardio-Pulmonary Laboratory, Dalhousie University, Halifax, N.S. Canada.

Actual measurements of mean pulmonary artery pressure (MPAP) and alveolar oxygen tension (pA02) in normal man of 8 altitudes between sea level and 17,100 ft. and predicted values for similar altitudes were compared in a computer program which plotted regression slopes and the constants of linear regression equations. PA02 predictions were derived from the linear regression slope of actual pA02 (y) and altitude (x) ($y = 103 - 0.00365\ x$; $r = 0.995$) MPAP predictions were based on an empirical formula i.e.

$$MPAP = \frac{PI02 \times 10}{\frac{PAB - 47}{713} \times PA02}$$

utilizing inspired oxygen tension (PIO_2) the ratio of ambient and sea level barometric pressures and predicted pA02

There was highly significant positive linear correlation between 1. predicted MPAP (y) and altitude (x) ($y = 13.00 + 0.00115\ x$; $r = 0.967$); 2. predicted (y) and actually measured MPAP (x) ($y = 2.25 + 0.960\ x$; $r = 0.977$) and 3. Actual (y) and predicted PA02 (x) ($y = 0.985 + 0.985\ x$; $r = 0.995$.) The actual MPAP (y) and altitude(x) for both natives and newcomers also showed highly significant positive linear correlation ($y = 11.8 + 0.00112\ x$ $r = 0.928$) and measured mean PA02 and MPAP of both populations fell within 2 SE of the linear regression slopes.

TISSUE CONTENT OF NOREPINEPHRINE IN SALT HYPERTENSIVE AND CHLOROTHIAZIDE TREATED RATS. A. S. Dahr (intr. by F. A. Bashour). Cardiopulmonary Inst. at Methodist Hosp. and The Univ. of Texas Southwestern Med. Sch. at Dallas, Dallas, Texas.

Relationship between sodium intake, blood pressure (BP) and tissue norepinephrine (NE) were studied. Effect of Chlorothiazide (CZ) on tissue NE was also evaluated. Six groups of adult rats were studied: groups A and B were fed 4% and 6% sodium chloride rations, respectively, for 8 months, and group C was control group. Groups D and E were treated with 50 mg and 500 mg CZ/kg body weight per day, respectively, for 3-4 months, and group F served as control for the CZ treated groups. NE content of ventricles and spleen was determined fluorometrically. BP averaged 125 ± 3.0, 127 ± 3.9 and 110 ± 5.3 mm Hg for groups A, B and C, respectively. Ventricular NE content averaged 1.04 ± 0.05, 1.01 ± 0.06 and 0.96 ± 0.06 mcg/g in groups A, B and C, respectively. Splenic NE content averaged 2.30 ± 0.24, 2.69 ± 0.22 and 2.76 ± 0.21 mcg/g in groups A, B and C, respectively. Ventricular NE content averaged 0.82 ± 0.05, 0.81 ± 0.04 and 0.86 ± 0.04 mcg/g in groups D, E and F, respectively. Splenic NE content averaged 2.27 ± 0.08, 2.6 ± 0.12 and 2.54 ± 0.12 mcg/g in groups D, E and F, respectively. These findings indicate that NE content was not altered with salt-induced hypertension or with CZ treatment.

Recording of A-V Nodal Activity in the Intact Dog Heart. Anthony N. Damato*, Sun H. Lau*, Gustavus A. Bobb*, Charles Steiner* and Andrew L. Wit. USPHS Hospital, Staten Island, N.Y.

The electrical activity of the A-V node (N) was recorded in 30 open chested intact dog hearts using close bipolar recording wires. The N potential was recorded as a biphasic wave contiguous with the atrial (A) and His bundle (H) electrograms and during sinus rhythm had a duration of 30-50 msec. The most characteristic feature of the N was the slurring or notching of both limbs. The earliest activity of the N was recorded at the peak of the P wave of the surface electrocardiogram. During A-V conduction delay (increase in the A-H interval) induced by vagal stimulation and/or atrial pacing, the duration of the N increased and the amplitude decreased indicating a decrease in conduction velocity in the A-V node. Retrograde N activity was recorded during His bundle and right ventricular (R.V.) pacing. During R.V. pacing a retrograde H was recorded within the QRS complex. The H-A time during retrograde conduction was always longer than the antegrade A-H time measured at comparable rates. Retrograde 2:1 block, and "reverse Wenckebach" with re-entry were also recorded. During the re-entry phenomenon, the prolonged retrograde P wave was followed by an antegrade H which resulted in premature capture of the ventricles. The presence of a single H deflection and the absence of an N preceding each QRS complex during A-V junctional rhythms suggests that the H and not the N is the pacemaker site in these rhythm disturbances.

EFFECTS OF CENTRALLY ADMINISTERED ANGIOTENSIN II IN THE UNANESTHETIZED RAT. A.E. Daniels*, E. Ogden, and J. Vernikos-Danellis. Environmental Biology Division, Ames Research Center, NASA, Moffett Field, California 94035.

Many systems affected by angiotensin II (ANG) are prominent in the physiological response to stress. However, little is known about its CNS effects, where autonomic and endocrine stress responses originate. ANG elicits centrally mediated effects on the peripheral vasculature. The effects of central administration on the pituitary-adrenal system have been investigated in unanesthetized rats. Under nembutal anesthesia cannulae were implanted in the left lateral ventricles of groups of male Sprague-Dawley rats (5/group). They were kept in individual cages and given food and water ad lib. 24 hrs. later, unrestrained, unanesthetized animals received intraventricularly (IVT) artificial CSF or ANG at various time intervals before decapitation. Plasma and adrenals were assayed fluorometrically for corticosterone. Fifteen, 30, 60, and 120 min. after injection, plasma corticosterone levels in animals given 0.25 µg ANG were 102, 157, 223, and 102 percent, respectively, of those treated with CSF alone. Adrenal corticosterone levels paralleled these changes, showing 122, 145, 250, and 184 percent of control levels at the same respective intervals. No differences were seen in similarly treated groups of animals hypophysectomized 20 days previously. In addition, one min. after receiving 0.25 µg ANG rats in normal water balance drank 3-5 ml water during the next 10 min. Control animals did not drink. These experiments show that in unanesthetized, unrestrained rats, ANG produces marked elevations in plasma and adrenal corticosterone levels as well as stimulation of water consumption.

EFFECT OF WATER TEMPERATURE ON BLOOD AND MUSCLE LACTATE IN SWIMMING RATS. C.A. Dawson*, E.R. Nadel*, and S.M. Horvath. Institute of Environmental Stress, University of California, Santa Barbara, Cal.

Arterial blood and gastrocnemius muscle samples were taken for lactate analysis at rest and after 3 and 15 minutes of swimming in 22 C water and after 3, 15, and 30 minutes of swimming in 37 C water. In 22 C water the rats became exhausted after about 20 minutes of swimming. However, in 37 C water they could swim easily for 30 minutes without signs of exhaustion. In 37 C water blood lactate showed an initial increase from 1.83 mM* to 5.20 mM. After 15 and 30 minutes of swimming the blood lactate had fallen to 3.26 mM and 2.27 mM, respectively. In 37 C water the muscle lactate was essentially the same as the blood: 2.46 mM at rest, 5.18 at 3 minutes, 3.00 at 15 minutes, and 3.25 mM at 30 minutes. In the 22 C swims there was a greater initial increase in blood lactate to 10.50 mM and the lactate level decreased with swimming time to 7.40 mM at 15 minutes. The rate of decrease in blood lactate concentration was similar to that seen in the 37 C swims. In the 22 C swims the muscle lactate tended to be higher than the blood: 14.43 mM at 3 minutes and 10.24 mM at 15 minutes. However, after the initial increase the muscle lactate decreased at about the same rate as the blood lactate. The pattern of muscle and blood lactate seen in the 22 C and 37 C swims was similar to that seen during submaximal exercise in man and indicated that net lactate utilization occurred after the first minutes of swimming performance in 22 C water was probably not the result of a progressive shift towards increasing anaerobic metabolism. The greater discrepancy between blood and muscle lactate seen in the 22 C swims may be related to body cooling and altered circulatory patterns. (*Lactate concentrations are in mMoles/liter of muscle or blood water.)

The Effect of Human Chorioonic Gonadotropin (HCG) and Luteinizing Hormone (LH) Upon the Membrane Potential of Unovulated Frog Oocytes.

John E. Dawson* and John T. Conrad School of Medicine, University of Washington, Seattle, Wash. 98105.

The consensus of opinion (Morrill, Rosenthal and Watson, J. Cell Physiol. 67:375-382,1966) appears to be that the vertebrate egg undergoes a marked change in permeability during ovulation. The exact mechanism responsible for this change has not been investigated, but it would appear that the transient increase in luteinizing hormone produced by the animal at the time of ovulation could be responsible for the permeability changes induced in the egg.

A test of this hypothesis was made on unovulated frog eggs, in vitro, by measuring the membrane potentials, with and without, the addition of HCG and LH. It was found that the majority of oocytes responded to these hormones by depolarization, when the material was added to the normal Ringer's solution surrounding the egg. Not all responses were uniformly depolarizing, however, and both hyperpolarizing and biphasic responses were noted. The threshold dose was about 251U per cc for LH and 451U per cc for HCG.

It is suggested that the membrane potential changes noted here are due to luteinizing hormones. Activation of the egg, during normal ovulation, may be heralded by a membrane potential change mediated by LH.

(Supported in part by the Ford Foundation and NIH Grant 5TOI AM 05428-05)

HEMODYNAMIC AND MYOCARDIAL METABOLIC RESPONSES TO ELECTRICAL PACING IN NORMAL DOGS. Dear, H. D.*, Harman, M. A.*, Jones, W. B.*, Walker, A. A.*, and Reeves, T. J., Univ. of Ala. Med. Center, Birmingham, Alabama.

Anaerobic myocardial metabolism has been documented in coronary insufficiency during induced stress; however, the response to pacing induced "maximal stress" has not been well defined in the presence of a normal coronary circulation. Catheters were placed in the left ventricle, ascending aorta, and coronary sinus in 13 anesthetized dogs. A bipolar pacing electrode was positioned in either the right atrium or right ventricle and following control determinations, heart rate was increased in graded fashion to rates in excess of 300 beats/min. at 10 min. intervals. At each level of pacing, simultaneous paired (arterial and coronary sinus) blood samples for measurement of lactate, pyruvate, potassium, and 0_2 saturation and EKG, LV and aortic pressure measurements were obtained. In 11 dogs, the 0_2 extraction ratio (A-V/A) increased with progressive increases in heart rate (0.79 ± 0.06 to 0.83 ± 0.09); there was a decrease in this ratio (0.71 ± 0.10) 5 min. after pacing. None demonstrated anaerobic myocardial metabolism as indicated by lactate production, although a decrease in the lactate extraction ratio was observed (0.52 ± 0.15 to 0.46 ± 0.10). In 2 dogs at rates exceeding 300/min. lactate production occurred. These animals differed in the marked differences in lactate (0.65 to -0.67) and oxygen (0.84 to 0.97) extraction ratios. In addition a greater decrease in the 0_2 extraction ratio was observed in the post pacing period. These dogs were unable at maximal pacing rates to maintain systolic pressure above 75 mmHg and coronary venous 0_2 saturation fell to levels less than 5%. This study suggests that normal dogs do not produce lactate until the coronary circulation is compromised by a marked decrease in perfusion pressure in the presence of maximal 0_2 extraction.

ACTIVITY OF PALLIDAL NEURONS IN THE MONKEY DURING MOVEMENT AND SLEEP. Mahlon DeLong, M.D. (intr. by E. V. Evarts). NIMH, Bethesda, Md.

The discharge activity of 232 neurons in the globus pallidus was recorded extracellularly in awake monkeys during periods of rest and movement. Movement occurred both spontaneously and was elicited by small food rewards. On the basis of discharge patterns during periods of rest, units could be placed into 4 categories: 1) 58 units exhibited high maintained firing rates (40-100/sec); 2) 103 units exhibited periods of high frequency discharge (50-125/sec) separated by intervals of total inactivity lasting up to several seconds; 3) 21 units exhibited repeated high frequency (300-400/sec) bursts of 5-15 spikes; and 4) 50 units showed more regular discharge at lower frequencies (10-50/sec). During movement most units of each type showed transient increases in discharge rate with resultant increase in mean discharge rate and decrease in modal interspike interval. Slowing of mean discharge rate was less common. Changes in activity were observed both during spontaneous and elicited movements, and were correlated better with contralateral than ipsilateral movement. Ninety-five of these units were also studied during slow wave and REM sleep. During slow wave sleep, mean discharge rate usually declined well below that in the awake state. During REM sleep, however, discharge rate generally increased to levels exceeding those in the awake, moving animal. Histology showed that with rare exception, cells of type 1 were located in the internal segment and cells of types 2 and 3 were in the external segment of the globus pallidus. Type 4 neurons were located along the external and internal medullary laminae. The marked changes in activity observed during movement in the majority of units supports the view that the globus pallidus plays a role in motor behavior.

QUANTITATIVE ANALYSIS OF EXERCISE EFFECTS ON HYPOXIC VENTILATORY RESPONSIVENESS IN MAN. J. A. Dempsey*, H. Forster*, R. Jackson*, E. Vidruk*, L. Chosy* & J. Rankin. Univ. of Wisc. Med. Sch., Madison, Wisc.

The concept of a work-induced potentiation (pot.) of hypoxic ventilatory responsiveness (HVR) has been reported in man & dog. Our support of H + work as a unique V drive was shown in patients with a marked sensitivity to this combination relative to their insensitivity to humoral or work stimuli alone. This study attempts to quantitate the degree of HVR pot. via the working steady-state, from rest over 4 moderate work levels (0.7-1.8 l $\dot{V}O_2$), & across 10 to 14 levels of hypoxia (PaO_2 250-45) at varying degrees of iso-$PaCO_2$ & pHa. HVR pot. was observed in all subjects at 1 or more work levels, & varied in degree among subjects according to their response to each of the stimuli alone. The nature of the pot. was primarily one of decreased H "threshold," the change in response slope being highly variable & pronounced only at the higher work loads. Neither parameter showed a clear step-wise increment with increase in work. The apparent work-H interaction was not secondary to work induced changes in response either to CO_2 alone (PaO_2 250) nor to CO_2-(mild) H interaction. Similarly the work was insufficient to induce significant measurable changes in rectal temp., plasma lactate or catecholamines. Based on assumptions of unchanging CO_2 related sensitivities & of levels of additional humoral stimuli calculations of isolated V drives revealed a contribution to the total H exercise $\dot{V}$(PaO_2, 50-55) of 10-15%($\dot{V}O_2$, 0.7) to 15-40%($\dot{V}O_2$, 1.8) attributable to H-work interaction. The possible contribution to HVR of work induced changes in CO_2-H pot. & in plasma catechol. with more severe H is under study. Supported by NIH Grant HE 07474 & the Wis. Heart Assn.

RELATION OF CATECHOLAMINE STORES TO MYOCARDIAL CONTRACTILITY UNDER VARIOUS CONDITIONS. N. S. Dhalla*, J. A. Moorhouse, K. R. J. Naidu* and K. Christensen*. Dept. of Physiology, Faculty of Med., Univ. of Manitoba, Winnipeg, Canada and Sch. of Med., St. Louis Univ., St. Louis, Mo.

Catecholamine stores in the heart are considered to be important for the maintenance of myocardial function in the failing heart in vivo but relationship between catecholamine content and contractile force in models of heart failure using isolated hearts is not known. To study this relationship the contractile force and catecholamine content (histochemical fluorescence) of isolated rat hearts were measured under different experimental conditions. Hearts perfused for 2 hr with oxygenated Krebs-Henseleit solution exhibited the same level of contractile force as hearts perfused for only 3 min but exhibited a slight decrease in the catecholamine stores. When hearts were perfused with substrate free, oxygenated medium contractile force decreased after 30 min but catecholamines did not decline until after 60 min. An appreciable decline in the endogenous catecholamines was observed when the heart failed to generate contractile force after perfusion with oxygenated substrate-free medium for 2 hr. The dissociation between catecholamine depletion and decrease in contractile force was especially marked in hearts perfused with hypoxic substrate free medium. In this group failure to develop contractile force occurred within 7 min but catecholamine stores were unaffected. Pre-treatment of the animal with reserpine depleted the heart of its catecholamines and increased the force of contraction whereas nialamide increased the intensity of fluorescence due to catecholamines in the heart without any effect on the contractile force. These results do not reveal a direct relationship between catecholamine stores and myocardial contractility.

(Partly supported by the Manitoba Heart Foundation)

INFLUENCE OF SMOOTH MUSCLE ON THE ELASTICITY OF ARTERIES FOLLOWING ISOBARIC AND ISOMETRIC CONTRACTION. P. B. Dobrin. Loyola University, Stritch School of Medicine, Dept. of Physiology, Maywood, Illinois 60153.

Lengths of dog carotid artery were excised, cannulated and restored to in situ length. They were immersed in a Krebs-Ringer solution and inflated with 100% O_2. Radius was continuously monitored with a linear displacement transducer. Vessel behavior was compared after treatment with Norepinephrine (NEpi) and after KCN. ISOBARIC CONTRACTION: vessels were treated with NEpi while holding pressure constant. This caused contraction, and pressure was then lowered to O mm Hg. Subsequent distention in 25 mm Hg non-oscillating pressure steps indicated that elastic modulus (EM) was higher after NEpi than after KCN when EM was plotted vs. strain; but EM was lower after NEpi than after KCN when EM was plotted vs. pressure. The latter occurred because NEpi caused contraction to a smaller, less elastic, radius. ISOMETRIC CONTRACTION: vessels were treated with NEpi but contraction was prevented by elevating pressures just enough to maintain a constant radius. Subsequent distention revealed that EM was slightly lower after NEpi than after KCN over the same range of radii. This occurred because isometrically contracted vessels are at very high pressures.
(Supported by National Institutes of Health Grant HE 08682)

PRODUCTION OF EDEMA IN DOG TONGUE BY SUPERFICIAL APPLICATION OF DILUTE HYDROGEN PEROXIDE. Homer L. Dorman and Robert H. Guentherman* Baylor Univ. Coll. Dent. Dallas, Texas.

Experimental edema has previously been produced by tissue trauma induced by a variety of thermal, mechanical and chemical insults. Equally severe edema can be produced by the most gentle application of dilute (0.3 Molar) hydrogen peroxide solutions. The edema is progressive and reaches a maximum in about 3 hours. The edema is probably of the extracellular variety because trypan blue dye leaks into the edematous tissue along with many neutrophils. Erythrocytes do not usually escape into the extracellular spaces but are largely confined to the capillary vessels. The edematous tongues showed an increase in Na^+ content from 62 MEQ/Kg. to 79MEQ/Kg., but K^+ decreased from 59 MEQ/Kg. to 45 MEQ/Kg. Since sodium is mainly an extracellular ion and potassium is mainly intracellular, these data are interpreted to indicate that the edema results mainly from increased extracellular fluid which could result from leakage of plasma from the vascular system. This method of production allows the tongue tissue to remain essentially atraumatic yet to accumulate fluid and it therefore may be used as a model system for studying the effects of certain treatment techniques directed towards reducing or preventing the edema. Pretreatment of the animals with intravenously injected antihistamine, dextrans, or hydrocortisone did not reduce the severity of the edema and thus far all attempts to prevent the edema have failed.

Supported in part by USPHS HE09049

NATRIURESIS INDUCED BY VENTRICULAR SALINE PERFUSION. Janice Dorn* and John C. Porter. Univ. of Tex. Southwestern Med. Sch., Dallas, Texas.

Much evidence implicates the CNS in the natriuresis which follows isotonic body fluid expansion in the dog or instillation of hypertonic NaCl solution into the third ventricle of the brain of goats. The present work demonstrates that large increases in Na^+ excretion, unaccompanied by changes in urine volume, are seen during perfusion of the third ventricle of anesthetized rats with hypertonic (0.85M) NaCl. The natriuresis was not observed after ventricular infusion of isotonic (0.15M) NaCl or 1.7M glucose, or following intravenous infusion of hypertonic NaCl. Anesthetized male rats were prepared for ventricular cannulation by a parapharyngeal procedure which permits direct visualization of the third ventricle and the surrounding basal diencephalic area. All test solutions were infused through polyethylene tubing at the rate of 0.8 µl/min, and urine was collected at thirty minute intervals from the bladder or ureters. To insure a constant urine flow, 0.15M NaCl was infused continuously into the femoral vein. In most instances, the natriuresis appeared with a latency of 1-1½ hours after the initiation of the hypertonic NaCl infusion, increased over the next few hours, and remained at this elevated level for the duration of the experiment (up to 10 hours). Although K^+ excretion rose in association with that of Na^+, urine volume remained essentially unchanged.

(Supported by NIH Research Grant AM01237.)

EFFECT OF LOW CALCIUM INTAKE ON BLOOD PRESSURE ELEVATION CAUSED BY SALT LOADING. Ben H. Douglas, P. J. Whittington-Coleman*, Herbert G. Langford, and Robert L. Watson*, Dept. of Medicine, Univ. of Mississippi Medical Center, Jackson, Mississippi.

Blood pressure is relatively high in our rural areas and calcium intake is low. This study was designed to determine a possible relationship between the two. Two groups of rats were used. Group I (10 rats) received a standard diet plus 0.9% NaCl as drinking water and Group II (10 rats) received a calcium deficient diet plus 0.9% NaCl as drinking water. The blood pressure of both groups rose to hypertensive levels but those on the low calcium diet took only 48 ml saline/day compared to 79 ml saline/day intake of the rats on the normal diet. There was no significant difference in plasma sodium or calcium levels between the two groups. Two additional groups were used for pair-feeding studies. Ten rats received the low calcium diet and 0.9% NaCl and 10 rats received a normal diet but were limited to the same quantity of 0.9% NaCl/day as those on the low calcium diet. Both groups developed hypertension but the blood pressure of the group on the calcium deficient diet was significantly higher starting at the 9th week. These data suggest that a Na/Ca ratio might modulate hypertension caused by high sodium intake.

DEPENDENCE OF ^{42}K EXTRACTION FRACTION ON TRANSIT TIME IN MYOCARDIUM. H. F. Downey and E. S. Kirk*. Dept. of Vet. Physiol. & Pharm. and Dept. of Physiol. & Biophys., Univ. of Ill., Urbana, Ill. 61801

The left common coronary arteries of anesthetized dogs were perfused in situ with autologous blood. Following pulse injections of mixtures of ^{42}KCl and ^{131}I human serum albumin (RISA) into the arterial tubing, blood from the coronary sinus was continuously withdrawn and collected in a turntable at the rate of 50 samples per min. The ^{42}K and ^{131}I activities of each sample were determined, and the results expressed as the ratio of ^{42}K to RISA, relative to the ratio of these materials in the injectate. In 30 experiments utilizing 7 hearts, we have consistently observed a transient decline in the ratio of ^{42}K to RISA following the first sample. The minimum value of these ratios, as well as their rate of rise after the minimum, is dependent upon the rate of coronary perfusion. In some experiments, extraction of ^{42}K, defined as one minus the relative ratio of ^{42}K to RISA, exceeded 88%. When the time course of the ratios of ^{42}K to RISA is examined along with the distribution of transit times through the coronary circulation, it is apparent that blood-tissue exchange is less effective for blood with the shortest transit time than for blood entering the coronary sinus several seconds later. This is consistent with the direct relationship between transit time and ^{42}K extraction seen in single membrane models of the capillary. However, a strict interpretation of this kind is not possible since the capillaries contribute only a portion of the total dispersion of observed transit times. Moreover, other factors, such as shunt vessels and diffusion shunting, may be involved. In any case, the initial capillary extraction revealed by the ratio of ^{42}K to a vascular-bound marker yields an erroneously low estimate of the average capillary extraction of ^{42}K by the myocardium.

INDUCTION OF SINGLE AND MULTIPLE OVULATION IN THE NON-HUMAN PRIMATE. W. Richard Dukelow. Department of Biochemistry, Univ. Georgia, Athens.

Fifty-two monkeys were studied to develop means of accurate ovulation induction. Ovaries were exposed to determine ovulation time and in some cases ova were flushed from the oviducts. Recycling with progesterone (5 mg daily for 5 days) was followed by: 1) no FSH, 2) 1 mg FSH, 3) HMG equivalent to 75 IU FSH, or 4) 200 IU PMS, each for 4 additional days. Ovulation was induced with either 250 or 500 IU of HCG administered intravenously (IV) or intramuscularly (IM). Four monkeys were subjected to the regime of Bennett (J. Reprod. Fertil. 13:357, 1967) to see if superovulation could be induced. Thirty-seven percent of the animals ovulated. Four double ovulations were noted, the rest were single except in the superovulated animals where an average of 4.8 ovulation points were found. No follicular development occurred in animals which did not receive an exogenous source of FSH. FSH was superior to PMS and HMG in its ability to promote follicular growth. Of animals receiving 250 IU of HCG, 26.7% ovulated compared with 52.1% of those receiving 500 IU. Ovulation was observed in 43.4% of the IV-administered animals, compared with 40.0% with IM injections. Ovulation times varied from less than 6.5 to 11.7 hr with IV injections and from 10.2 to 11.9 hr with IM. Double ovulations were found to vary as much as 2.6 hr between first and second ovulations. Squirrel monkeys of the Brazilian type ovulated 46.4% of the time, compared with 33.3% with Peruvian-type, a non-significant difference. This work was supported by a Biomedical grant from NIH, a grant from the Lalor Foundation and an NIH Research Contract for the Development of New Methods of Contraception.

INCREASED 2,3-DIPHOSPHOGLYCERATE (DPG) IN THE HUMAN RED BLOOD CELL DURING MUSCULAR EXERCISE. John W. Eaton,* John A. Faulkner, and George J. Brewer.* The University of Michigan, Ann Arbor, Michigan, 48104.

Recently, variations in the concentration of red cell DPG have been shown to cause shifts in the oxygen dissociation curve. Several reports indicate that higher concentrations of DPG (which is a phosphorylated intermediate of red cell metabolism) will shift the curve to the right, enhancing oxygen release by the red cell. During altitude acclimatization, an increase in DPG has been found to occur within about 24 hours. We have found significant elevation (18%) of red cell DPG during 60 minutes of vigorous muscular exercise (basketball). A 50 minute bicycle ergometer test was then used to provide a more standardized physiological stress. The bicycle ergometer work load was set to require an energy expenditure of approximately 70% (range 55 to 90%) of the maximum oxygen uptake of each of 10 subjects. During the bicycle ergometer ride, the 30 minute DPG was not different from the resting value. However, the 50 minute DPG change was proportional ($r = +0.74$) to the intensity of the exercise as estimated by the blood lactate concentration. These results indicate that the levels of red cell DPG may change much more rapidly than previously reported. The higher concentration of DPG probably increases the oxygen delivered to the contracting muscles and appears to represent an important adaptive response to prolonged physical exertion.

Supported in part by USPHS training grant T01-GM-0071, USPHS research grant Am-09381, Career Development Award AM 07959 (GJB), NIH grant GM-12554, and in part by Contract DADA17-69-9103 with the U.S. Army and Navy Medical Research and Development Commands.

SELECTIVE AND CONTRASTING EFFECTS OF EXERCISE AND ELECTRICAL STIMULATION ON MUSCLE PHOSPHORYLASE

V. R. Edgerton, R. J. Barnard and J. B. Peter (Introduced by A. J. Brady). Departments of Physical Education and Medicine, University of California, Los Angeles.

Skeletal muscle total phosphorylase, demonstrated histochemically, has been studied in adult guinea pigs immediately following 5 min, 10 min and exhaustive treadmill running (1.6 km/hr) and also immediately after electrical stimulation of the gastrocnemius and plantaris through the tibial nerve of an in situ preparation in which the muscles were contracting 5 times/sec against a 200 g load for 1 hr. With increasing durations of treadmill running increasingly larger proportions of the muscle fibers become phosphorylase negative (negligible phosphorylase activity). Red muscle fiber types are more susceptible to becoming phosphorylase negative than white muscle fibers following treadmill running. Conversely, with electrical stimulation white muscle fibers are more susceptible to phosphorylase negativity than are red fibers. Since muscle glycogen is largely depleted following exhaustive runs, demonstration of phosphorylase negativity in select fiber types may be a manifestation of muscle glycogen depletion rather than phosphorylase inactivation. The relatively greater resistance of white fibers to becoming phosphorylase negative may be due to selective involvement of red fibers during treadmill running. The reason for the opposite effects of running and electrical stimulation is not known, but our data show that inferences must be made with caution when comparing electrical stimulation and normal exercise.

CIRCULATORY REFLEXES FROM STRETCH OF PULMONARY VEIN-ATRIAL JUNCTIONS. A. J. Edis* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The reflex alterations in the systemic circulation caused by stretch of the pulmonary vein-atrial junctions were studied in dogs anesthetized with morphine sulfate (2.5-3.0 mg/kg, intramuscularly) and chloralose (80-100 mg/kg, intravenously). After thoracotomy the left pulmonary artery was ligated and a Silastic balloon, 1.5 cm long and attached to a nylon catheter, was inserted into each of the 3 left pulmonary veins and tied so that the tip lay at the junction of the vein with the left atrium. In 11 dogs (18-23 kg), the influence of the high-pressure baroreceptors was eliminated by denervating both carotid sinuses and selectively denervating the aortic arch. In these dogs 94 inflations of 2-3 balloons with 3-4 ml of saline were made for an average period of 30 sec. Aortic pressure decreased (mean maximum decrease, 31 mm Hg; range, 22-58); hindlimb resistance decreased due to reduced activity of the sympathetic adrenergic fibers (mean maximum decrease in perfusion pressure at constant flow, 40 mm Hg; range, 10-78). Heart rate decreased from a mean of 218 to 208 beats/min ($P<0.001$). Splanchnic capacity vessels relaxed, but cutaneous veins were unaffected. These responses, which were not sustained throughout the period of distension, were abolished or attenuated by vagotomy or vagal cooling. In 6 dogs (19-22 kg) the high-pressure baroreceptors were left intact. Similar changes in the systemic circulation were evoked by the distension. But, in contrast to the denervated group, these animals did not have uniformly fast initial heart rates and it now was found that the initial heart rate determined the direction of heart rate change during distension: slowing occurred with initial rate >160 beats/min and acceleration if it was less. (Supported in part by NIH Grant HE-5883.)

ACTION OF HYPERTONICITY ON TOAD BLADDER PERMEABILITY. Patrick Eggena, Irving L. Schwartz and Roderich Walter. Physiol. Dept., Mt. Sinai Med. and Grad. Schls. of The City Univ. of N.Y., and The Med. Res. Ctr., Bkhvn. Nat'l. Lab., Upton, N. Y., USA.

The permeability to water of the urinary bladder of toad, Bufo marinus, can be increased with certain hypertonic serosal solutions. This response to hypertonicity was found to be similar in several respects to the hydroosmotic response of the bladder following stimulation with vasopressin or cyclic 3',5'-AMP. Relatively impermeant solutes, such as sodium and mannitol, are considerably more effective in promoting net mucosal to serosal water movement whereas highly permeant solutes, such as urea, are ineffective. While vasopressin inhibitors (prostaglandin E_1 and Mn^{++}) do not alter the response of the bladder to hypertonicity, cyclic 3',5'-AMP inhibitors (Zn^{++}, low K^{+}, pH 6.5) drastically reduce this response. It is concluded that there is an osmosensitive compartment, i.e. an osmoreceptor, in the toad bladder epithelium the activation of which triggers a hormone-like increase in the permeability to water of the tissue. It is suggested that this osmoreceptor exerts its effect after the formation of cyclic 3',5'-AMP in the chain of events which characterizes the action of vasopressin. (Supported by USPHS grant No. AM-10080 and Postdoctoral Research Fellowship for P.E.)

CORONARY FLOW CHANGES IN DOGS DURING EXERCISE AND DURING SPONTANEOUS DEEP INSPIRATION CORRELATED WITH CHANGES OF COMPUTED LEFT VENTRICULAR O_2 CONSUMPTION. W. Ehrlich, J.E.O. Newton & J. Tosev*, Johns Hopkins University, Baltimore, Maryland.

Coronary flow (CF) was recorded from the circumflex branch of the left coronary artery. The left ventricular O_2 consumption ($\dot{V}O_2$) was computed from cardiac output, mean aortic pressure, mean right atrial pressure and heart rate using a modification of the equation of J. Beneken, A. Guyton and K. Sagawa (Pflügers Arch. 305, 76, 1969).- From the outset of exercise, $\dot{V}O_2$ increases steeply, levels off transiently between the 4th and 8th seconds, and increases again steeply to its peak after about 12 seconds. Then it decreases to a markedly lower steady state. CF, however, after an initial decrease or latency starts to increase 6 to 8 seconds later than $\dot{V}O_2$. The steep CF increase peaks 4 seconds later than $\dot{V}O_2$. The lower steady state level is reached more slowly than with $\dot{V}O_2$.-With spontaneous deep inspiration the $\dot{V}O_2$ increases only shortly at the height of inspiration. During and after expiration the $\dot{V}O_2$ is lower than the control values. CF, however, is markedly favored by the fall of intrathoracic pressure. The first phase of the coronary reaction to the short increase in sympathetic function is masked and the second phase, the increase in flow, starts from an already enhanced level.-For the incidence of acute coronary insufficiency, it might be crucial whether a sclerotic vessel maintains the capacity to dilatate, in spite of the increase in intramyocardial pressure and the decrease in MAP, quickly and profoundly enough to match the deep increase of $\dot{V}O_2$.

(Supported by USPHS, NIH Grant HE06945).

MODIFIED REBREATHING PROCEDURE FOR MIXED VENOUS GAS TENSIONS. John C. Elliott*, Silvio Finkelstein* and Ulrich C. Luft. Lovelace Foundation, Albuquerque, New Mexico 87108

An estimate of mixed venous PO_2 is obtained if alveolar gas is adjusted to the proper level within recirculation time by rapid rebreathing of CO_2 + N_2 (Cerretelli et al. 1966). The rebreathing volume (VB) is critical for properly adjusting alveolar gas since blood can provide little exchange for equilibration. After recording endtidal O_2 and CO_2 a precisely measured CO_2 + He + N_2 mixture was rebreathed at constant rate for 15 seconds and O_2, CO_2 and He recorded by Mass Spectrometer. Lung volume (VL) was determined from He dilution and a predicted $P'O_2$, unaltered by gas exchange, derived as $P'O_2 = (VL/VL + VB) PAO_2$. Final O_2 levels varied inversely with VB/VL (0.5-3.0) from 40 - 24 mmHg resp. When VB was small final PO_2 was lower than $P'O_2$ and vice versa, indicating diffusion of gas to or from the blood. O_2 plateaus of several seconds duration were obtained over a wide range of VB/VL coincident with a helium plateau at completion of mixing. Changes in PO_2 beyond this point, but before recirculation, call for adjustment of VB to match the venous level. (Supported by NASA 9-7009 and NIH Grant PH 05531.)

A NEW ANIMAL MODEL - MYOCARDIAL INFARCTION. William E. Elzinga, William M. Kaufman, Dennis E. Upright, and Donald Powell (intr. by William D. Collings). Hittman Associates, Inc., Columbia, Maryland.

Coronary thrombi were precipitated in dogs by magnetically removing blood borne microscopic particles (iron, ~4μ mean diameter) at a designated site within the coronary artery. Three groups of animals were studied: an acute feasibility group (two dogs); a control group consisting of sham operated, iron-particle-injected animals (particle controls) (four dogs) and magnet implanted nonparticle injected animals (magnet controls) (four dogs); and a dose response group (12 dogs). In the control group the iron particles increased the white blood cell count (WBC) shortly after injection. No tissue necrosis was found in any organs reviewed. The implanted perivascular magnet caused a local inflammatory response. Doses of 0.2 g/kg, 0.1 g/kg, and 0.025 g/kg (injected five days postsurgery, venipuncture) precipitated iron-positive thrombi beneath the magnet. The average vessel occlusion for each dose level was 79% (four dogs), 38% (four dogs), and 3% (four dogs), respectively. Serial electrocardiogram (ECG) and enzyme (LDH and SGOT) data postparticle injection (PPI) were comparable to data obtained from humans with coronary occlusions.

This research was performed pursuant to Contract No. PII 43-66-90 with the Artificial Heart Program, National Heart Institute, National Institutes of Health, Department of Health, Education, and Welfare.

MODULATION OF THE ACTIVITY OF HYPOTHALAMIC "FEEDING NEURONS" BY STIMULATION OF THE GUSTATORY NUCLEUS OF THE CAT THALAMUS. R. Emmers, Department of Physiology, College of Physicians and Surgeons, Columbia University, New York City.

Neurons of the lateral hypothalamic area were approached stereotactically with tungsten microelectrodes in cats under Nembutal anesthesia. Electrophysiologically isolated neurons were held at the electrode tip for several hours to accumulate extracellular spike activity by a digital computer over 1000 sec periods. Test substances were infused into the circulatory system via the carotid artery and stimulation of the thalamic gustatory nucleus was accomplished by delivering square wave pulses via a double barrel concentric needle electrode positioned in the nucleus. - It was found that most of the neurons in the vicinity of the entopeduncular nucleus decreased their firing frequency after intracarotid infusion of a glucose solution and increased it above the control level after infusion of insulin. With a few neurons, however, this change of spike frequency was reversed. Stimulation of the thalamic gustatory nucleus produced a recurrent innibitory-excitatory pnasing on the activity of those neurons which were sensitive to the infusion of the substances mentioned; no influence was detected on other neurons. The inhibitory-excitatory oscillations lasted for 0.5 to 1 sec following the application of a single pulse to the thalamic gustatory nucleus. This indicates the existence of specific connections between the thalamic gustatory nucleus and the "feeding neurons" of the hypothalamus providing for the influence of taste on feeding behavior. (Aided by grant NB-03266 from NIH)

CANINE SERUM SIALIC ACID ALTERATIONS BY EXOGENOUS STEROIDS. Richard L. Engen. Department of Physiology and Pharmacology, College of Veterinary Medicine, Iowa State University, Ames, Iowa 50010.

Elevated serum sialic acid levels have been observed in pathological conditions such as cancer, leukemia, pneumonia, and infections. Since endogenous steroid hormones increase in stress, the objective of the experiment was to determine the influence of steroids on serum sialic acid levels in dogs. Serum sialic acid concentrations prior to steroid injection were compared to the concentration after daily treatment for 3-4 days. Analyses were conducted manually and by the Auto-Analyzer. In studies conducted with 20 dogs (5 experiments) hydrocortisone (0.5 mg/lbs to 1.5 mg/lbs body wt) increased the serum sialic acid. The pretreatment and post-treatment values averaged 51.4 $\pm$ 5.29 and 70.3 $\pm$ 6.06 mg/100 ml, respectively, ($P < 0.01$). Nine animals receiving Dexamethasone demonstrated a similar, but a more rapid response. The pretreatment and post-treatment values averaged 50.9 $\pm$ 5.15 and 74.6 $\pm$ 8.58 mg/100 ml after two days ($P < 0.01$). (Supported by a General Research Support Grant from USPHS).

CORONARY HEMODYNAMICS IN THE CONSCIOUS DOG DURING HYPOXIA. H. H. Erickson, M. B. Kardon*, E. L. Fitzpatrick*, and H. L. Stone, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas, 78235.

The response to acute hypoxia (5% O_2) before and after beta-adrenergic blockade with propranolol (1 mg/kg) was determined in 6 conscious dogs which were instrumented to measure left circumflex coronary artery, left common carotid artery and ascending aortic blood flow. Heart rate, coronary stroke volume, left ventricular pressure and dp/dt were also determined. The hypoxic atmosphere was administered through a low resistance demand valve connected to an endotracheal tube which could be introduced into a chronic tracheostomy. Isoproterenol (6 μg) was used to test the beta-adrenergic response of the system before hypoxia, during hypoxia, and after beta-adrenergic blockade. Hypoxia resulted in an increase (154%) in coronary flow, while the same level of hypoxia after beta-blockade resulted in only a 120% increase in coronary flow. Isoproterenol given before hypoxia caused a 97% increase in coronary flow, while during hypoxia it resulted in a 69% increase in coronary flow. The increase in coronary flow associated with hypoxia is primarily an increase in coronary stroke volume since the heart rate only increased 24%. The systolic component increased 151%, while the diastolic component only increased 82%. Hypoxia also caused a 43% increase in dp/dt, while after beta-blockade the same level of hypoxia resulted in only a 25% increase in dp/dt. Isoproterenol given initially resulted in a 74% increase in dp/dt while during hypoxia it caused a 55% increase in dp/dt. These results indicate that hypoxia causes an increase in coronary flow which may be mediated through a direct metabolic mechanism and a beta-adrenergic receptor mechanism. The changes in dp/dt and the use of isoproterenol to test the beta-adrenergic receptor response appear to support this hypothesis.

THE EFFECT OF VARIOUS SUBSTANCES ON THE TENSILE STRENGTH OF SOW GRAAFIAN FOLLICLES. L. L. Espey and W. D. McDavid*
Trinity Univ., San Antonio, Texas.

The connective tissue of the Graafian follicle undergoes marked decomposition during ovulation. The active agent in this traumatic process is yet to be determined. A variety of chemicals which could be involved in the normal disruption of follicular connective tissue have been incubated with strips of sow follicles in vitro to determine their effect on the tensile strength of the follicular wall. After 10 hr of incubation in the test substances, the follicular sections were inserted in a special tension-recording apparatus and stretched 10% of their initial length to determine any change in tensile strength. Control tissue normally developed a tension of about 16 g under these conditions. However, strips incubated with enzyme preparations of clostridiopeptidase A, elastase, trypsin, and chymotrypsin developed a tension of only 0, 0.5, 1.6, and 2.3 g respectively. Lysozyme, peptidase, and hyaluronidase had no effect on the tensile strength of the follicle strips. Ascorbic acid and diketogulonic acid reduced the tensile strength to 0 and 7.8 g respectively. (The hydrogen ion and electrolyte concentrations were important in these tests.) The results indicate that a variety of proteolytic enzymes and , at least, one non-enzymic agent (ascorbic acid) have the ability to decompose the follicular connective tissue and effectively reduce the tensile strength of the follicle wall. (Supported in part by NIH Grant HD-02649 and NIH Contract 2126.)

TISSUE HISTAMINE CONTENT AND SYNTHESIS DURING ACID SECRETION IN RATS STIMULATED BY PENTAGASTRIN. D. C. Evans* and T. M. Lin, Lilly Research Laboratories, Indianapolis, Ind.

Young female Carworth rats were given subcutaneously 4μc of C^{14}-histidine and then fed a meal. Forty-eight hours later, the rats received 100 μg/kg of pentagastrin (PG). The total free histamine (TFH) determined fluorometrically and the specific histamine determined as bisulphonyl histamine (BSH) in the glandular stomach were followed at 1½ and 6 hour intervals. PG depleted the TFH content of the glandular stomach by 25% at 1½ hours when the acid secretion was at its peak. Thereafter, the TFH gradually increased and sometimes even exceeded that at control levels long after the acid response to PG had ceased. The preformed C^{14}-histamine participated in the depletion with non-C^{14} histamine as if they were in the same pool at 1½ hours. PG stimulated HCl secretion, depleted TFH and also increased the in vitro histidine decarboxylase activity of the glandular mucosa by 32% at 1½ hours. The ratio of C^{14}-BSH/TFH in the PG-treated stomachs was higher than that in the controls at both 1½ and 6 hour intervals. The DPM in BSH of the PG-treated stomach was almost twice that in the controls at 6 hours indicating enhanced synthesis of nascent histamine. These observations suggest that the secretion of HCl is not related to (1) the TFH level (2) nor to the synthesis of histamine in the glandular stomach. The depletion of TFH which coincided with HCl secretion may be explained on the basis of its availability to the parietal cell or its transformation to an "available" form.

ENVIRONMENTAL CONDITIONS IN THE BURROW OF THE KANGAROO RAT DIPODOMYS MERRIAMI, D. S. Evans* and D. B. Dill, Desert Research Institute, University of Nevada, Boulder City, Nevada.

The kangaroo rat spends the hot sunlight hours in its burrow avoiding the high temperatures of its desert environment. In this study we have observed the temperatures and air composition inside the rats' burrows. A thermocouple lead and a length of polyethylene tubing 1.2 mm id were tied around the rat's neck and it was set free to run into its burrow. When it had run several feet into the burrow and stopped, temperatures were observed and air samples taken. The burrow then was excavated to determine the depth at the rat's location. Burrow temperatures ranged from 8 C in midwinter to 35 C in June when the temperature of the soil surface was 65 C. The percentage of CO_2 was noticably although not critically higher inside the burrow than in outside air, ranging from 0.11 to 0.41%. Similarly, the percentage of O_2 was somewhat lower than in outside air, ranging from 20.89 down to 20.54. Beginning in December 1968 soil temperatures have been observed monthly with thermocouple probes permanently placed at various depths. Minimum soil temperatures in degrees C in February were: 122 cm, 15.2; 92 cm, 12.6; 61 cm, 10.5; 30 cm, 5.7. Temperatures at corresponding depths in early June were: 25.3, 27,3, 30.3, and 40.4. Temperatures observed in the burrows during the 6-month period of observation corresponded closely with soil temperatures interpolated from buried thermocouples.

Supported by NSF Grant GB 7509.

REGULATION OF THE PLACENTAL FRACTION OF FETAL CARDIAC OUTPUT. J. Job Faber. Dept. Physiol., Univ. Oregon Med. Sch., Portland, Ore.

Two considerations appear to restrain steady state fetal placental blood flow: the Frank-Starling mechanism of the fetal heart, approximated by $P^{cv}=K\cdot CO+A$, and the postcapillary resistance of the fetal umbilical circulation, defined by $R_2=(P^{Fc}-P^{cv})/(f\cdot CO)$. (P=pressure, Fc=fetal placental capillary, cv=central venous, CO=cardiac output, f=fraction of CO flowing through umbilical circulation, and A and k are constants). Elimination of P^{cv} yields: $f\cdot CO=(P^{Fc}-A)/(R_2+k/f)$. In the steady state (no net water flow across the placenta from the maternal to the fetal circulation or v.v.), $P^{Fc}=P^{Fc}$; P^{Fc}_o depends only on the maternal capillary blood pressure and the fetal and maternal colloid osmotic pressures. From published values for the new born lamb (Downing et al. Am. J. Physiol. 208: 931, '65), we calculated that for the fetal heart k=ca. 0.003 mm Hg/(ml/min) and A=ca. 4 mm Hg. Our own measurements indicated that R_2=ca. 0.028 mm Hg/(ml/min), and P^{Fc}_o=ca. 24 mm Hg. Comparison of differences in the magnitudes between A^o and P^{Fc}_o and between R_2 and k/f (f=ca. 0.5), indicates that, normally, fetal placental blood flow is already close to its theoretical maximum of P^{Fc}_o/R_2. This means that an increase in cardiac contractility or in heart rate and in fetal systemic arterial pressure cannot, in the steady state, cause a significant increase in fetal placental blood flow.

The author is an Established Investigator of the American Heart Association, supported by the Oregon Heart Association. The experimental work was supported by USPHS HD2313.

FORCE-VELOCITY MEASUREMENTS IN MAN FROM ONE-PLANE CINEANGIOGRAPHY
Herman L. Falsetti*, Robert E. Mates*, David G. Greene and Ivan L. Bunnell, SUNY/B, Buffalo, New York

Left ventricular dimensions (length, breadth and wall thickness) have been measured from one-plane cineangiograms taken in the right anterior oblique projection. Combined with simultaneous left ventricular pressure measurements they permit left ventricular wall stress σ and myocardial velocity of shortening (VCF) to be calculated throughout the cardiac cycle. The 25 patients include 12 with normal left ventricular dynamics, 6 with volume overload, 3 with outflow obstruction and 4 with cardiomyopathy. Circumferental fiber shortening (VCF) equals the sum of contractile element velocity (VCE) and series elastic velocity (VSE). VSE was obtained from $VSE = (1/K\sigma)(d\sigma/dt)$ where σ is equatorial or hoop stress and K was assumed equal to 28.8. VCE was then calculated as the difference between VCF and VSE. During isovolumic contraction, the muscle fibers remain very nearly isometric. The maximum, no-load, velocity for the contractile element (V_{max}) was estimated by linearly extrapolating the curve of VCE vs σ to zero stress. V_{max} was 1.5 to 2.5 end-diastolic lengths/sec in normal ventricles and considerably less in patients with myopathy. There was a direct relationship between V_{max} and ejection fraction. V_{max} was also calculated by assuming VCF=0 during isovolumic contraction (VCE=VSE). Results agreed well for most patients. These studies indicate that V_{max} may be generally obtained from pressure data alone. Some knowledge of ventricular geometry is required, however, since significant errors in V_{max} (usually under estimation) may occur if the ventricular geometry changes during isovolumic contraction.

MESENTERIC VASODILATATION IN RESPONSE TO INTRADUODENAL FAT. J.W. Fara*, E.H. Rubinstein*, and R.R. Sonnenschein. Dept. of Physiology, UCLA School of Medicine, Los Angeles, Calif.

Instillation of 5 ml of milk or 0.5-2.0 ml of corn oil into the duodenum of chronically prepared cats, operated on at least 7-10 days prior to testing, elicited a dose-dependent increase of 50-100 percent in superior mesenteric blood flow (blocked by atropine), with latency of 3-6 min and duration of 30-60 min. This was unaccompanied by change in arterial pressure, heart rate, or iliac blood flow. Ongoing, spontaneous duodenal motility was concomitantly inhibited. Of components of milk other than fat, lactose and water in equivalent amounts were ineffective; the action of casein is uncertain. Intraduodenal fat produced the same vascular and motility effects in chloralose-anesthetized cats, but with longer latency (15-20 min) and duration (60-80 min). In chronically prepared or anesthetized cats, intravenous infusion of cholecystokinin-pancreozymin mimicked the mesenteric vasodilatation while increasing duodenal motility. (Supported by USPHS grants HE-05157 and HE-5696, AMA-ERF, and LACHA 400-C1)

EFFECT OF ALTERATION OF NUTRITIONAL STATUS ON SURFACE ACTIVITY OF LUNGS OF RATS. Edmund E. Faridy. (Intr. by J.A. Moorhouse). Dept. of Physiology, University of Manitoba, Winnipeg, Manitoba.

The effects of deprivation of either food or water alone, or both on the mechanical properties of lungs were studied in albino rats. The results of acute (48-69 hrs) deprivations of food and/or water are shown in the Table. Minimum surface tension of lung extracts (γ min) was significantly lowered in water deprived rats (WD), increased in food deprived rats (FD) and unaffected in rats deprived of both food and water (FWD). Only FD rats had decreased compliance as indicated by a decrease in the percent volume retained at 10 cm H20 transpulmonary pressure during deflation pressure-volume measurements (V%10). Lecithin contents expressed either per unit lung weight or per unit DNA content were significantly increased in WD rats, decreased in FD rats and unchanged in FWD rats.

	γ min	V%10	Lecithin mg/gm wet	Lecithin mg/mg DNA
Control	12.3 ± 1	80.3 ± .9	10.1 ± .4	1.48 ± .1
WD	4.4 ± .6	80.4 ± .8	12.5 ± 1.1	1.64 ± .1
FWD	10.8 ± 1.4	79.7 ± .7	10.3 ± .7	1.46 ± .1
FD	17.0 ± 1.5	75.3 ± .8	9.0 ± .4	1.19 ± .05

The results indicate that the nutritional status of the animal influences the mechanical properties of the lung. It is postulated that the effects are due to an altered balance between production and loss of surface active material.

Supported by the Medical Research Council of Canada.

RECTIFICATION OF OSMOTIC FLOW IN RED CELLS Robert E.L. Farmer* and Robert I. Macey (Department of Physiology, University of California, Berkeley, California)

In a recent paper Rich, Sha'afi, Romualdez and Solomon (J. Gen. Physiol. 52:941,1968) conclude from measurements of the osmotic filtration coefficient of human erythrocytes that 1) the filtration coefficient depends upon solution osmolality and 2) there is no rectification of flow, the inward coefficient being the same as the outward coefficient. Since this interpretation is contrary to our experience with beef cells (Farmer, Univ. of Calif. Dissertation, 1968), we have investigated the problem using small osmotic perturbations (Farmer and Macey, Biophys. Soc. Abst., 1967). We have obtained estimates of L_p for beef and human red cells at many different solution osmolalities ranging from 230 to 480 mOsm/l. Our results for each species indicate that over the entire range of tonicites, the measured filtration coefficients cluster about two distinct values, one value for swelling experiments, the other for shrinking experiments. We conclude that 1) the filtration coefficients are independent of cell size and of solution osmolality and 2) rectification of water flow exists, inward flow being greater than outward flow by about 50%. These two conclusions can also adequately account for the data of Rich et al.

Supported by NSF GB11981 and Bay Area Heart Research Committee

PERIPHERAL VENOUS RENIN ACTIVITY DURING EXPOSURE TO LOWER BODY NEGATIVE PRESSURE (LBNP), Fasola, A.F., Martz, B.L., and Rogge, J. (intr. by K. G. Kohlstaedt). Lilly Laboratory for Clinical Research, Marion County General Hosp., Indianapolis, Ind. Brooks Air Force Base, San Antonio, Texas.

Various types of cardiovascular stress such as supine exercise, sitting exercise, 70° head-up tilt and $+G_z$ acceleration have been accompanied by an increase in peripheral venous renin activity in normotensive subjects. The procedure of applying subatmospheric pressure in the supine position to the lower extremities produces changes in cardiovascular dynamics similar to those observed during $+G_z$ acceleration and head-up tilt. Peripheral venous activity was determined after 30 min. of supine rest (control) and after 30 min. LBNP. Four groups of subjects were subjected to LBNP of -20,-30,-40,-50 mm. Hg. for 30 min. No significant difference was observed in any of the four groups after 30 min. of supine rest. Significant increase in renin activity from control values was observed after all levels of LBNP. Renin activity increased as the level of negative pressure increased. These studies would suggest that some of the changes in cardiovascular dynamics such as increase in peripheral resistance and changes in renal function during LBNP may be mediated via the renin-angiotensin system.

GLYCINE'S REVERSAL OF TETANUS TOXIN INDUCED MYDRIASIS IN RABBITS' EYES. A. A. Fedinec and L. E. King, Jr. (intr. by S. R. Bruesch). Dept. Anat., Univ. Tenn. Med. Units, Memphis, Tennessee 38103

It is recognized that tetanus toxin interferes with the inhibitory neurotransmission in the spinal cord and also interferes with ACh release from cholinergic nerves in the rabbit's iris. It has been shown that in cats the central effects of the toxin are temporarily reversed by glycine iontophoresis onto the affected neurons (Curtis and De Groat, Brain Research, 10: 208, 1968). To determine if glycine could reverse the peripheral effects of toxin on the rabbit's iris mydriasis was produced by injecting purified toxin into the anterior chamber of the rabbit's eye (1000 mouse MLDs/0.05 ml). The mydriasis persisted for at least 6 weeks after toxin injection. Control and toxin treated eyes were injected with 0.05 ml of the following glycine solutions: 0.2M, 0.5M, 1M, 2M, 3M at pH 3, 7, and 9. Pupillary responses to diffuse and bright light were measured with calipers prior to and after all injections. Miosis was produced for 20-30 minutes after glycine injections into the toxin treated eyes. The most effective glycine solution was the 0.5M, pH 3. Lower glycine concentrations (0.2M) were ineffective as reported previously (Fedinec and King, Anat. Rec. 163(2): 184, 1969). Toxin treated and control rabbit eyes were equally responsive to ACh, carbachol, and eserine administered topically or intraocularly. Atropine produced mydriasis in the control eyes and did not alter the sustained mydriasis in toxin treated eyes. The addition of glycine to atropinized control and toxin treated eyes produced a temporary miosis. Therefore, glycine, at the appropriate molarity and pH, appeared to reverse temporarily the sustained mydriasis induced by intraocularly injected tetanus toxin in rabbit eyes. A direct effect of glycine on control or toxin treated atropinized pupillary sphincter was not excluded. (Supported by USPHS, NIH grant AI-08610.)

SYNTHESIS AND TURNOVER OF NOREPINEPHRINE IN BROWN FAT, HEART, AND SPLEEN OF CONTROL AND COLD ACCLIMATED HAMSTERS. D. D. Feist* and W. B. Quay. Dept. of Zoology, Univ. of Calif., Berkeley, Calif. 94720.

The tyrosine hydroxylase inhibitor α-methyltyrosine (αMT) was administered by injection to control and cold acclimated golden hamsters (Mesocricetus auratus) to assess the rate of decline of endogenous norepinephrine (NE) in different tissues. Synthesis and turnover rate of NE in each tissue was calculated from the slope of the decline in NE content following inhibition of synthesis and application of steady-state kinetics. Fluorometry of tyrosine and αMT in tissues after injection showed that αMT was present at inhibitory levels. While NE was found to decline in a simple linear plot in heart and spleen from both control and cold acclimated animals, the initial phase of decline of NE in interscapular brown fat (ISBF) of cold acclimated animals was more rapid and complex. This difference of cold acclimated ISBF merits further study in relation to its possible physiological significance in the metabolic role of ISBF in thermogenesis and arousal. Synthesis and turnover of NE was most rapid in the control hearts and lower in those of cold acclimated animals. The lowest rate was found in spleen of both groups. Experiments to determine the effect of αMT on arousal time and NE turnover in tissues arousing from hibernation are in progress. (Supported in part by USPHS, NIH Grants 1-F1-GM-32,590-03 and NB-06296).

EFFECT OF CONDITIONING SUPERIOR COLLICULAR STIMULATION ON CORTICAL AND GENICULATE PHOTIC EVOKED RESPONSES. A. Fernández-Guardiola. (Intr. by F. Mena). Laboratoire de Neurophysiologie (Equipe de Recherche 35 du CNRS) et Groupe de Recherches de Physiologie Neuro-Végétative (Unité 60 de l'INSERM).

The role of the superior colliculus in visual function has been investigated. Simultaneous recordings of the electroretinogram (ERG), chiasmatic, geniculate and cortical responses to flashes were performed in intact nonanesthetized cats. Flashes of increasing intensity produced which were characterized during the maximal intensity by the appearence of a sharp delayed response with a latency of 60 - 80 ms.

The conditioning stimulation, with "trains" of pulses applied to the superior colliculus during low intensity photic stimulation produces a reduction on the early deflection of the geniculate response and the appearence on the cortical response of the same delayed components provoked by maximal flash intensity.

CARDIAC OUTPUT IN EXPERIMENTAL RENAL HYPERTENSION. Carlos M. Ferrario* and James W. McCubbin. Research Division, Cleveland Clinic, Cleveland, Ohio.

It has been debated whether renal hypertension is initiated, and perhaps maintained, by increase in cardiac output. Refinements in electromagnetic flowmeter technology make possible a re-evaluation of the problem. Flowmeters were implanted chronically around the ascending aorta in dogs, in conjunction with arterial catheters, and measurements made daily while they were resting quietly before and after production of cellophane perinephritis hypertension. Eight to 15 days after wrapping one kidney in cellophane, with the opposite kidney untouched, both stroke volume and cardiac output rose consistently ($P < 0.001$) though there was no change in mean arterial pressure. Heart rate and peripheral resistance both decreased slightly. Three to 7 days after removal of the normal kidney, mean arterial pressure rose progressively in all dogs, reaching a plateau 77 $\pm$8(SE) mm Hg above control after 18 to 23 days. Hypertension was associated initially with further rise in both stroke volume and cardiac output, and peripheral resistance now became elevated. Four weeks after nephrectomy, peripheral resistance became progressively the predominant cause of elevated pressure while cardiac output tended to return to control values. Measurements of plasma volume and mean circulatory pressure suggested that the initial increase in cardiac output that preceded the increase in pressure was due to enhanced venous-return consequent to venoconstriction. Thus, increased cardiac output may have a causative role in the development of renal hypertension, but it is less clear whether an increase in output contributes importantly to maintenance of the chronic phase. (Supported in part by Grant HE-6835 from the National Heart Institute.)

RESPONSE PROPERTIES OF PRECENTRAL NEURONS IN AWAKE MONKEYS. E. E. Fetz* and M. A. Baker, Regnl. Primate Res. Ctr. & Dept. of Physiol. & Biophys., Univ. of Wash. Sch. of Medicine, Seattle, Wash. 98105.

The activity of 233 "spontaneously" firing single neurons in precentral leg cortex of five unanesthetized, chaired M. mulatta was observed under various behavioral and stimulus conditions. The natural stimulus which clearly and repeatably increased the firing of each cell was determined. 189 units (85%) responded to passive movement of one or more joints of the contralateral leg; 148 of these responded only during movement of the joint, 4 fired tonically at rates proportional to the maintained angle of the joint, and 37 showed both tonic and phasic responses. Of the 34 units not affected by joint movement, 18 responded to touching the skin or brushing the hair, often over wide, bilateral areas of the body. No effective peripheral stimulus was found for 16 units. Cells isolated successively in the same track often responded to the same passive joint movements. Units driven by passive extension outnumbered those driven by passive flexion 49:28 for the knee and 65:56 for the ankle. When the cortex was stimulated at a point where cells responded to passive movement of a joint in one direction, the muscles of that joint which had the lowest response threshold were those which opposed that movement. For 20 units, burst patterns of discharge were reinforced by presenting fruit juice to the monkey; this procedure increased the frequency of burst discharges. EMG activity of 2-4 contralateral leg muscles (tib. ant., gastroc., quadr., hamstr.) was recorded simultaneously with the unit activity for periods of hours. The temporal relationship between the EMG activity and individual unit bursts was usually variable; averaging rectified EMG and unit activity over 100 or more bursts showed that all muscles recorded had some increase in average activity broadly coinciding with the average unit burst. (Supported by NIH grants FR 166, PHS 5 T1 NB5082-13, & NB396, & B. of A.-Giannini Fndtn.)

A STUDY OF CHEMORECEPTOR AND BARORECEPTOR A AND C-FIBERS IN THE CAT CAROTID NERVE. S. J. Fidone,* A. Sato* and C. Eyzaguirre. Department of Physiology, University of Utah College of Medicine, Salt Lake City, Utah.

The purpose of this investigation was to compare the relative response characteristics of chemoreceptor and baroreceptor A and C-fibers. Adult cats were anesthetized with sodium pentobarbital and the carotid nerve was prepared for single unit dissection. The ipsilateral thyroid artery was catheterized for the close intra-arterial injections of drugs (NaCN, 1-10 μg; ACh, 1-10 μg) and for the infusion of normal and acidified (pH 2.0) saline. A total of 149 chemoreceptor A-fibers were isolated from the carotid nerve, and their conduction velocity distribution was determined. The velocities ranged from 4 to 53 m/sec, with a median of 16 m/sec. No detailed study of baroreceptor A-fibers was attempted. 52 single-unit C-fiber preparations were obtained, and of these 9 were chemoreceptor fibers, 15 were baroreceptor fibers and 28 failed to respond to any of the chemoreceptor or baroreceptor stimuli employed in this study. Since both the carotid nerve and the ganglioglomerular nerve(s) were routinely cut in all experiments, the absence of 'spontaneous' or induced activity amongst these C-fibers suggests that they may be efferent in origin. The C-fiber conduction velocities varied between 0.5 and 2.0 m/sec. The discharge pattern of chemoreceptor A and C-fibers was characteristically irregular both at rest and during activation. In comparing A and C-fibers, it was found that chemoreceptor and baroreceptor A-fibers had lower thresholds, shorter response latencies, more rapid onset of response and higher discharge frequencies than their C-fiber counterparts (Supported by grants NB 05666, NB 05244 and NB 07938 from the U.S. Public Health Service).

SOMATIC AND VISCERAL RECEPTIVE FIELDS OF SPINAL NEURONS. H.L. Fields,* L.D. Partridge, Jr.* and D.L. Winter. Dept Neurophysiology, Walter Reed Army Inst. Res., Washington, D.C.

The receptive field properties of spinal neurons were examined in unanaesthetized decerebrate cats spinalized at C1. Single units (axons) were recorded primarily from white matter of the second and third lumbar segments. The units were characterized by their responses to mechanical stimulation of both somatic fields and visceral structures and to electrical stimulation of the cervical cord below the level of the transection. Units which could be antidromically activated by cervical stimulation tended to have simple somatic receptive fields and no visceral input. Units which could be orthodromically activated by cervical stimulation had complex somatic fields and often received visceral input. Complex receptive fields could include multiple discrete areas, bilateral and heterosegmental inputs, excitatory and inhibitory effects and multimodal activation. There was a strong tendency however for single units to have inputs of the same modality from bilaterally symmetrical areas. Visceral input could be excitatory or inhibitory and originate from one or more viscera. Neurons receiving input from the urinary bladder tended to be associated with more caudal somatic inputs whereas units effected by gall bladder stimulation tended to have more cephalad somatic inputs. The anatomical location and properties of the units having complex receptive fields indicate that they are propriospinal interneurons.

MECHANICAL PROPERTIES OF THE MUSCLE CELL MEMBRANE. R. W. Fields* and J. J. Faber. Univ. of Oregon Medical School, Portland, Oregon.

The elastic properties of cylindrical segments of sarcolemma were studied in single striated fibers of the frog semitendinosus muscle. All measurements were made on membranes of retraction zones, cell segments from which the sarcoplasm had retracted. Membrane geometry was studied as a function of internal hydrostatic pressure and axial loading to permit calculation of the circumferential and longitudinal tension-strain (T-S) diagrams. The sarcolemma exhibits nonlinear T-S properties concave to the tension axis in both directions. Circumferential T-S slopes (measures of membrane stiffness) ranged from 1500 to greater than 50,000 dynes/cm over the range of deformations investigated, while longitudinal T-S slopes varied from 23,000 to 225,000 dynes/cm. Thus, the membrane is anisotropic being much stiffer in the longitudinal direction. It was also shown that the sarcolemma of intact cells is about four times as wide and two-thirds as long as undeformed membrane. This configuration and the observed mechanical properties are best explained in terms of a helical system of stiff fibril components surrounding the sarcolemma, having some slack in undeformed membrane. The degree of slack and the angle of these fibrils were calculated for all membrane configurations, and the force-extension properties of the elements of the helical system were determined. In the intact cell, the proposed structure is deformed in such a way as to permit the maximum cell volume possible without stretching the helical fibers. (Supported by PHS Grant GM 00538).

INHIBITION OF THE SYMPATHOADRENOMEDULLARY RESPONSE TO COLD BY ANESTHESIA. Vincent Fiorica, P. F. Iampietro, M. J. Burr* and R. Moses*. Physiology Laboratory, Civil Aeromedical Institute, Oklahoma City, Oklahoma.

A number of studies in the literature suggest that cold may not be as effective a stimulus for sympathoadrenomedullary (SAM) activation as is generally believed. The present experiments were conducted to examine the role of anesthesia (pentobarbital) as a factor complicating the interpretation of the SAM responses to acute cold exposure. Unanesthetized and anesthetized dogs were immersed in cold water at 15 C or in 37 C water for control. Heart rate and blood pressure increased markedly in unanesthetized animals immersed in cold water. Anesthetized animals immersed at 15 C had no increase in either measure. Measurements of plasma catecholamines also showed a nearly three-fold increase over control in unanesthetized, cold exposed dogs, but no change from control in anesthetized dogs given a similar exposure. Because the adrenal medulla has been shown to be responsive to appropriate stimulation (hemorrhagic hypotension, hypercapnia, acidemia) in the presence of pentobarbital, our results suggested that the inhibition must involve mechanisms concerned with thermal regulation. Anesthesia may interfere centrally with sympathetically linked thermoregulatory centers, or through its inhibition of shivering, may permit the animal to cool so rapidly that metabolic processes involving synthesis and release of catecholamines are suppressed by cold directly.

DETERMINATION OF ALVEOLAR SURFACE AREA AND SURFACE TENSION AS A FUNCTION OF VOLUME IN THE CAT LUNG FROM IN SITU PRESSURE-VOLUME (PV) MEASUREMENTS. M.J. Fisher*, K.C. Weber* and M.F. Wilson. Department of Physiology and Biophysics, West Virginia University Medical Center, Morgantown, West Virginia 26506.

Cats were anesthetized with Na Pentobarbital and the trachea cannulated with a U shaped glass cannula. The chest was then opened widely and the animal was placed in a whole body plethysmograph and ventilated with oxygen. A differential pressure transducer measured transpulmonary pressure and a spirometer was used to measure volume. Zero volume for both air (O_2) and liquid (saline) was determined by allowing the vascular system to absorb the O_2 in the lung after the trachea was clamped. The rate of inflation and deflation for O_2 was 2.9 cc/sec and for saline it was 1.0 cc/sec. In six cats where the liquid flow rate was changed from 0.5 cc/sec to 5 cc/sec, no difference was found in the PV curves. By comparing liquid and air inflation curves at a volume corresponding to 20 cm H_2O (air inflation) a constant, K, which relates area and volume to the two-thirds power, was determined. In eight such experiments the value of K/kg body wt. = 52.3 $\pm$ 4.4.SEM. From the same relationship, $A = KV^{2/3}$, alveolar surface areas represented by other volumes were determined. At functional residual capacity (assumed to be 90 ml) the alveolar surface area of the cat/kg body wt. = 1.05 $\pm$ 0.09 M^2 SEM. Surface tension (γ) was calculated as a function of the same constant (K), lung volume, and the pressure difference between the liquid and air curves ($\gamma = 3\ PV^{1/3}/2K$). The results show that surface tension approaches zero at low lung volumes and was always lower during deflation than during inflation at a given alveolar surface area.

Supported in part by ALFORD, USPHS, and the Council for Tobacco Research, U.S.A.

Antidiuretic Hormone and Renal Circulation. R. D. Fisher,* J. P. Grunfeld,* and A. C. Barger. Harvard Medical School, Boston, Massachusetts.

The effect of ADH on the permeability of the distal nephron is well established, but the physiological role of this hormone on the renal circulation has not been clarified. We investigated the distribution of renal blood flow (BF) using the ^{85}Kr method in trained, unanesthetized dogs with diabetes insipidus (DI) produced by hypothalamic-hypophysial tract section. The sites of renal vascular changes induced by DI or by ADH were localized by autoradiography and by silicone rubber injection techniques. Renal BF was markedly increased during the initial diuretic phase following tract section, or after withdrawal of systemic or intrarenal Pitressin in dogs with DI. Abundant filling of the renal venous vasculature and glomeruli by the retrograde injection of silicone rubber in the absence of ADH indicated a low efferent vascular resistance. Autoradiography demonstrated that in the absence of ADH outer cortical BF was greater than normal, while juxtamedullary cortical BF was slower. Moreover, outer medullary uptake of ^{85}Kr was decreased during diuresis. Further evidence for a local vascular effect was obtained by infusions of minute amounts of Pitressin into the renal artery of dogs with DI. These results indicate that ADH plays a role in the control of efferent renal vascular tone; in the absence of the hormone outer cortical BF is increased and juxtamedullary cortical BF and outer medullary BF are reduced. Later, during the established diuresis of DI, renal BF varies with the level of dehydration.

THYROID FUNCTION IN PROTEIN-DEPLETED RATS. Warner H. Florsheim, Biruta Suhr* and Albert D. Williams*, Veterans Administration Hospital, Long Beach, Calif.

A number of authors have reported differing effects of protein depletion upon rat thyroid function. The differences in their findings have not been explained, but may be related to the iodine content of the diets employed. Using a commercial protein-depletion diet containing 3.5 mg iodine per kg we find that renal iodide clearance is reduced to 10 % within 2 days and then is maintained at the new level for several weeks. Serum iodide levels build up to concentrations in excess of 150 µg per 100 ml within 3 weeks. The increased serum iodide lowers radioiodine uptake values and is accompanied by a greatly elevated PBI. Thyroxine metabolism as measured with radiothyroxine did not change except for a decrease in the Liver : Serum thyroxine distribution ratio. The BEI was not elevated and it was found that the PBI rose due to the accumulation of iodinated albumin in the circulation. Thyroidal hormone synthesis was depressed by the Wolff-Chaikoff effect. The depression was maximal after 9 days on the depletion diet, but was still significant after 23 days. There was no evidence for an involvement of the pituitary-thyroid system in the effects of protein depletion on the thyroid.

PYRIDINE NUCLEOTIDE CONTENT IN STORED HUMAN ERYTHROCYTES BEFORE AND AFTER IN VITRO INCUBATION. D. L. Ford*, C. B. Scott*, and A. Omachi. Univ. of Illinois at the Med. Center, Chicago, Ill.

Blood collected in acid-citrate-dextrose was centrifuged and extracts were prepared from packed cells. Extracts were also prepared from these erythrocytes after washing and incubation for 2.5 hours in a Tris(pH 7.4)-Ringer's medium at 37° in a Dubnoff shaker. Pyridine nucleotides were measured by procedures previously described (BBA 184: 139, 1969). NAD^+, NADH, $NADP^+$, and NADPH concentrations were 137, 81, 47, and 89 nmoles/gm hemoglobin in freshly collected, nonincubated cells and 133, 74, 40, and 74 nmoles/gm hemoglobin after these cells were incubated. When erythrocytes stored for longer periods were examined, NAD^+ in nonincubated cells appeared to increase slowly with time. On the other hand, if these cells were incubated before being analyzed, a decrease in NAD^+ was observed in cells stored for 2 weeks or longer. NADH rose in both nonincubated and incubated cells during the first few weeks of storage. Since lactate also accumulated, the NADH increase could be associated with this change. Later in the storage, however, NADH seemed to decline toward day zero levels. $NADP^+$ in nonincubated cells appeared to decrease during the first 2 weeks whereas $NADP^+$ in incubated cells showed little change. NADPH was fairly constant in nonincubated cells; in incubated cells, the corresponding values were generally lower during the early phase of storage. It is concluded that (1) pyridine nucleotide concentrations do vary during storage, (2) incubation of red cells at physiological temperatures and pH prior to analysis may reveal changes that are not discernible from direct analysis of cold-stored cells, and (3) these changes may bear some relationship to the development of the storage lesion. (Supported by USPHS grant, GM-11447)

ULTRASTRUCTURAL STUDIES ON OXYNTIC CELLS OF BULLFROG STOMACH USING HEAVY METAL TRACER, SPECIFIC STAIN AND FREEZE-ETCH TECHNIQUES. Trudy Forte* and John C. Forte. Donner Laboratory and Dept. of Physiology, Univ. of Calif., Berkeley, Calif.

Lanthanum, a heavy metal tracer substance, was applied to "in vitro" preparations of secreting and non-secreting bullfrog stomachs. $La(NO_3)_3$ was introduced during the fixation steps and was expected to delineate extracellular space and surface-connected membrane systems. In both the non-secreting and secreting preparations the heavy metal tracer was found in intercellular spaces between adjacent cells; the tracer penetrates the desmosomal region but not the tight junction. The apical surface of non-secreting oxyntic cells is relatively smooth and $La(NO_3)_3$ was often adsorbed to the surface. The tracer was also localized in external spaces of plasma membrane invaginations just beneath the surface. Preparations stimulated to secrete acid revealed that lanthanum frequently penetrated into the cell to the level of the desmosomes via surface-connected tubules, thus further implicating the smooth-surfaced membranes in the secretory process. Replicas of parietal cells obtained by freeze-fracturing and etching definitively show that the smooth-surfaced membrane system is tubular in form,and in the resting state doesn't appear to be connected with the cell surface. Alcian blue, a cationic stain for mucopolysaccharides, stained the inner surface of the tubular cytoplasmic membranes as well as the outer surface of the apical plasma membrane, while silver methenamine, a glycoprotein stain, also stained both these components thus supporting our previous hypothesis on membrane transformations associated with secretion.
Supported by USPHS.

CELLULAR ACTION OF EXOGENOUS PROLACTIN: PROTEIN SYNTHESIS AND SPECIFIC ACTIVITY. Wm. L. FRANTZ, PHYSIOL. DEPT. MSU, E. LANSING, MICH. 48823

Prolactin stimulates amino acid ^{14}C uptake and incorporation into protein. Expressed as T/C ratios significantly greater than 1.0 (paired t test); T=DPM/mg of pigeon crop epithelium 28 hours after intradermal injection of 25 µg prolactin (P-S-8, NIH) and 4 hours after 5 µCi/Kg of leucine ^{14}C IV; C=DPM/mg of sample 28 hours after intradermal injection of 25 µg of fetal calf serum and 4 hours after 5 µCi/Kg of leucine ^{14}C IV. Enhanced uptake is of the order of 43% in the prolactin treated side; enhanced protein specific actively is 140% (table I, treatmentA). Puromycin, Actinomycin D and Ouabain given instead of prolactin inhibit both the uptake and the utilization of ^{14}C amino acids. However, prolactin given 1 hour after puromycin reverses its inhibitory effect. (Table I, treatments B & C). Moreover the total protein content of the prolactin treated samples of crop mucosal epithelium is significantly less than that in the untreated (C) half (Table I, last column).

TABLE I TREATMENT		HOMOGENATE ^{14}C DPM/mg±SD(N)	10% TCA PPT ^{14}C DPM/ng±SD(N)	PROTEIN(LOWRY) ng/mg sample±SD(N)
A	LTH(T)	T/C=1.43±.15	T/C=2.40±.51	T/C=.70±.73
	SERUM(C)	C=5.98±4.06(7)	C=133±101(7)	C=80.98±40.30(7)
B	PURO/LTH(T)	T/C=1.40±.19	T/C=1.65±.29	T/C=.85±.74
	PURO/SERUM(C)	C=9.12±9.42(35)	C=117±88(35)	C=59.42±34.68(20)
C	PURO/LTH(T)	T/C=1.31±.07	T/C=1.65±.16	T/C=.78±.90
	HOH/SERUM(C)	C=5.53±5.12(15)	C=75±65(15)	C=86.57±28.27(15)

In summary, in the intact pigeon crop mucosal epithelium exogenous prolactin 1) causes greater uptake and utilization of ^{14}C amino acids, 2) reverses the inhibitory effect of puromycin, but not actinomycin D or Ouabain and 3) decreases the total protein, but increases the specific ^{14}C activity of newly formed protein.
Support was by NIH GM 39556-02, NSF GB 6024 and GB 8197.

ALVEOLAR GEOMETRY AS A FUNCTION OF LUNG VOLUME. D. G. FRAZER, W. S. ADAMS AND R. A. RHOADES (Intr. by E. Buskirk). Center for Air Environment Studies, Dept. of Electrical Engineering and Laboratory for Human Performance Research, The Pennsylvania State University, University Park, Pennsylvania 16802.

To determine alveolar geometry over a complete volume range, i.e. total collapse to full expansion, volume pressure (v-p) curves were recorded from excised rat lungs. Measurements from each lung included three v-p curves (air-filled, saline-filled, and non-ionic-detergent-rinsed) and a subsequent surface tension-area (γ-A) curve from the alveolar wash. Free energy of the lung lining film may be described by the equation ($\int_{V_o}^{V_1} P dv = \int_{A_o}^{A} \gamma dA$). Since the alveolar lining layer in detergent-rinsed lungs has a constant surface tension, the variation in lung area was estimated by integrating the difference between detergent-rinsed and saline-filled v-p curves ($[A-Ao] = {}^{1}/_{\gamma} \int_{V_o}^{V_1} [P_{detergent} - P_{saline}]\, dv$). Area-volume relationships show that an alveolus 1) is not a segment of a sphere and 2) changes shape as lung volume changes. Using the γ-A curve of alveolar lining layer in air-filled lungs, calculated from [$\gamma = (P_{air} - P_{saline})\ (dv/dA)$], and La-Place's equation, the minimum radius of curvature (R_{min}) of an average alveolus was found using the equation ($R_{min} = \gamma / P_{air} - P_{saline}$). Results show 1) an alveolus can be represented by a segment of an ellipsoid whose major and minor axes and radius of opening are a function of lung inflation and 2) alveolar shape changes as a function of lung volume. (Supported by USPH Grants AP 00022 and ES 00335).

TEMPORAL DISPERSION IN PRIMARY OLFACTORY NERVE IN CAT. Walter J. Freeman, Dept. Physiology-Anatomy, Univ. Calif., Berkeley, California.

Axons to each bulb number about 10^8, with a mean diameter of 0.258 microns and a coefficient of variation $\sigma = 0.19$. They form a sheet on the surface of each bulb 350 microns deep tapering to zero at the posterior edge. The axons run almost horizontally in stereotaxic coordinates from the mucosa across the bulb. The shortest axons are about 2 mm and the longest 15-20 mm in length. Bundles of axons diverge slightly from the holes in the cribriform plate but are straight. The axons are unbranched until within a few hundred microns of the glomeruli where they end. Electrical stimulation of the PON layer with a tungsten microelectrode elicits a triphasic compound action potential, which moves at constant velocity (0.42 ± 0.08 m/sec) in a straight line. The amplitude of the volley, v (t), diminishes rapidly with time of travel, t, from the stimulus at t=0 in seconds according to the equation: $V(t) = V_o \exp [0.5\ (j\omega\sigma t)^2]$ where ω is the peak frequency in radians/second obtained from the Fourier Transform of the action potential recorded 0.2 mm from the stimulating electrode, and σ is the coefficient of variation for axonal diameter. The result implies that conduction velocity varies linearly with axon diameter, and that temporal dispersion acts as a powerful high-frequency cut-off filter. NIH Grant MH 06686.

THE CARDIOVASCULAR SERIAL LITERATURE, 1967--ITS CHARACTERISTICS AND SOURCES. Barbara F. Frick* and John M. Ginski. Univ. of Tenn. College of Basic Medical Sciences, Memphis, Tenn.

The cardiovascular serial literature for 1967 was studied: to detect its particular characteristics, to determine the journals most fruitful for cardiovascular information, and to evaluate the bibliographic coverage of this material. Two groups of journals were identified--the specialty journals devoted to publishing cardiovascular information and the journals used by grantees of the National Heart Institute (NHI) to publish findings. International publication patterns for cardiovascular research were revealed through an analysis of the specialty journals--the growth of the field as shown by the birth of new journals, the world-wide importance of English for communication in this area, and the responsibility national and international scientific societies have assumed for sponsoring cardiovascular journals. The dispersion of NHI grantee papers among various journals shows that a relatively few journals contain a high percentage of papers and that few of these are cardiovascular specialty journals. Better coverage is given by the major indexing and abstracting services (Biological Abstracts, Chemical Abstracts, Excerpta Medica, Index Medicus, and Science Citation Index) to the journals containing a majority of NHI grantee papers than to the specialty journals.

Supported by NIH Trng Grant LN-00102 from the National Library of Medicine.

THE ESOPHAGO-SALIVARY REFLEX. M. H. F. Friedman, Z. Pober,* N. J. Grego,* and A. Janson.* Department of Physiology, Thomas Jefferson University, Philadelphia.

Parotid saliva secretion, respiration, heart rate, intra-esophageal pressure and intragastric pressure were recorded in the dog. Salivation could be evoked by several types of noxious stimuli applied to the esophagus and (infrequently) to the stomach. Increased intrathoracic esophageal pressure by balloon inflation provoked salivary secretion in the resting gland and also augmented low rates of secretion due to pilocarpine. Effects persisted for as long as elevated intraesopheal pressures were maintained. Both rapid and gradual incremental increases in pressure were similarly effective at corresponding pressure thresholds. No esophageal area specially sensitive to inflation could be located. No relationship was demonstrated between stimuli of sub-painful strength and salivary response. Secretion due to noxious stimuli while profuse was never at maximum secretory rates. Esophageal distension to degrees judged by associated respiratory and cardiac effects to be noxious inhibited parotid gland secretion (presumably by glandular arteriolar construction). Esophageal motor paralysis by curare did not influence the response. Afferents for the esophago-salivary reflex were found in the vagus nerve.

STUDIES ON THE PATHOGENESIS OF CADMIUM-INDUCED NERVOUS LESIONS.
Giulio Gabbiani and Dusan Baic*. Inst. Med. Chirurgie exp. Univ. de Montréal, Montreal (Canada).

In the rat, the parenteral administration of $CdCl_2$ produces acute hemorrhagic lesions of the Gasserian and spinal sensory ganglia. Electron microscopic examination of the Gasserian ganglion five hours after treatment reveals increased vacuolisation of endothelial cells of small vessels, edema in the interstitial tissue, slight degenerative changes in satellite and Schwann cells; only exceptionally is there destruction of the endothelium and thrombus formation. Twenty-four hours after $CdCl_2$, hemorrhagic lesions of sensory ganglia are visible at histologic examination. Using the electron microscope, numerous endothelial cells of small vessels appear to be destroyed, osmiophilic bodies (varying in shape) are found in satellite and Schwann cells; many satellite and Schwann cells have disintegrated and a few necrotic neurons are seen. Five days after $CdCl_2$, regeneration of fibers has already begun; after 15 days most of the structures of the ganglion appear to be normal, although degenerated fibers and cells are still present. The ganglionic structures affected by $CdCl_2$ are presumed to be small vessels, satellite and Schwann cells.

(This work was supported by the Ministère de la Santé, Québec, Project 604-7-635.)

CHANGES IN THE FINE STRUCTURE OF CAPILLARIES OF EDEMATOUS DOG TONGUE.
T.W. Gage*, J.G. Bishop and H.L. Dorman. Baylor Univ. Coll. Dent. Dallas, Texas

The basement membranes of normal dog tongue capillaries were observed by means of the electron microscope and found to be uniformily dense and free of perforations and tears. Edema induction by superficial application of 0.3 molar hydrogen peroxide for 1 to 3 hours caused partial destruction of the basement membrane which was sufficient to interrupt its continuity and allow escape of plasma. Pinocytotic vesicles were a prominent feature of the endothelial cell membranes of normal vessels. These structures were much reduced in number in the edematous specimens. Barium sulfate in the form of micropaque emulsion was injected into the lingual artery and a tongue tissue biopsy sample was taken after sufficient barium was injected to replace the blood and to fill the vessels. Barium particles could be seen (electron micrographs) in the widened extracellular fluid spaces between adjacent endothelial cells of edematous tongue but not in normal. Barium was not seen in the pinocytotic vessels. These observations support the assumption that the basement membrane is partly responsible for containment of the circulating plasma. The data may also suggest that the pinocytotic vesicles activity is involved in maintaining the integrity of the basement membrane.

Supported in part by U.S.P.H.S. grants D.E. 21 and in part by DE-32, 493-02.

INFLUENCE OF BRONCHOMOTOR TONE ON MAXIMAL EXPIRATORY FLOW RATES. A. Gardiner*, L. Wood*, P. Gayrard* and P. Macklem, Respiratory Division, Royal Victoria Hospital, Montreal.

We measured maximal expiratory flow volume, MEFV, curves under control conditions, during vagal stimulation and after vagotomy, in dogs. A retrograde catheter was used to locate equal pressure points, EPP, and measure the resistance of peripheral airways, Rp, during the forced deflations. We also measured the resistance of airways upstream from EPP, Rus. The greater the bronchomotor tone, the further upstream were the EPP. During vagal stimulation when Rp increased more than Rus there was a reduction in vital capacity, VC, but the MEFV curve slope was unaffected. When Rus increased but Rp did not, the MEFV curve slope was reduced but VC was unchanged. When both Rus and Rp increased,but the increase in Rus was greater,both the VC and the MEFV curve slope were reduced. We conclude that in dogs,peripheral airway constriction does not change the MEFV curve slope because the increase in Rus is counterbalanced by an increase in elastic recoil pressure, whereas central airway constriction causes a reduction in slope because there is an increase in Rus with no change in elasticity.

Supported by Grants from the D.R.B. of Canada and The John A. Hartford Foundation.

SYMMETRY AND REDUNDANCY OF INTERNEURONAL CONNECTIONS IN THE BUCCAL GANGLION OF APLYSIA. D. Gardner (intr. by E. R. Kandel). Dept. of Physiology, NYU School of Medicine, N. Y., N. Y. 10016

The buccal ganglion of the marine mollusc Aplysia offers the same technical advantages for cellular studies as does the animal's abdominal ganglion (Arvanitaki and Cardot 1941; Strumwasser 1965). In addition it provides an opportunity for studying connections in a bilaterally symmetric neural structure. Ten cells in each half of the buccal ganglion have been identified by electrophysiological and anatomical criteria. Each cell has a symmetric mate in the other hemiganglion. Two of the ten cells are interneurons each of which innervates six identified ipsilateral follower cells.

The connections between hemiganglia and within each hemiganglion were examined. None of the identified cells were found to make direct connections with their symmetric mates in the other hemiganglion. Coordination between identified cells in opposite hemiganglia seems to be effected by common inputs differing in latency and amplitude rather than by direct cross connections. Each hemiganglion contains two identified interneurons which also receive common inputs. Each of these interneurons produces three different types of direct synaptic actions on the same ipsilateral follower cell population: chemical inhibition to several follower cells, chemical excitation to one follower cell, and nonrectifying electrical excitation to the other ipsilateral interneuron. Pharmacological evidence suggests that the chemical excitation and inhibition are cholinergic. There is thus a symmetry of connections in the two hemiganglia and an apparent redundancy of pathways for conveying neural information within each hemiganglion.

THE NORMAL DENDRITIC TREE OF SPINAL NEURONS. S. Gelfan, G. Kao* and D. S. Ruchkin.* New York Med. Col., New York City.

The size of the dendritic tree was determined from the number, length and diameter of primary dendrites and number and length of their branches in 360 unselected neurons from the entire spinal gray of L_7 segment in Golgi preparations. Two general principles emerged from the analyses of the data which provide some order to the complexity and variability of the dendritic tree: The basic dependence of the entire dendritic tree upon the number of primary dendrites per neuron, and the existence of two size levels of such trees among spinal neurons; one for large and another for small neurons. The mean dendritic surface area of the large neurons was 5 times greater than that of small ones. Very little of the variability of the parameters or of the whole tree could be accounted for by the variability of the specific cell body size within each of the two groups of neurons or within the entire sample. This was also reflected by the variability, rather than a constancy, for the ratio of dendrite to cell body surface areas. The morphological distinction is between two classes of neurons. The overwhelming preponderance of the intrinsic system (interneurons), as previously determined in Nissl-stained preparations, corresponds very closely to the normally numerical preponderance of neurons having small perikarya over large ones. In addition to size and functional differences between the two types of neurons, therefore, the synaptic connectivity of one must be, on the average, some 5 times greater than the other. (Supported by NIH grants NB 04417-6 and MH 08579-6)

REFRACTORINESS TO ANGIOTENSIN AFTER SPINAL CORD TRANSECTION. R. G. Geller* and J. E. Kendrick. Department of Physiology, University of Wisconsin, Madison, Wisconsin 53706.

Angiotensin (AN) is reported to have a direct excitatory action on renal vascular smooth muscle and indirect excitatory actions through sympathetic structures. Interruption of renal nerve activity by cervical cord transection or by cutting the renal nerves is reported to reduce or abolish the renal vasoconstrictor response to AN (McGiff and Fasy, J.Clin.Invest.44:1911,1965). We found that destruction of the renal nerves failed to reduce the renal response to AN (Geller and Kendrick, Proc.Soc.129:727,1968). The present studies are concerned with the cause of the refractoriness of the renal vascular bed after cord transection. In dogs anesthetized with morphine-chloralose, the kidneys were perfused at a constant flow rate. The pressure response to AN was studied before and after cutting the spinal cord. Cutting the cord (between C_7-T_1 or T_5-T_6) above the level of the origin of the major renal sympathetic nerves reduced the renal vasoconstrictor response to AN. Cutting the cord between L_4-L_5 did not have this effect. Peripheral denervation of the kidneys by stripping or excision, of itself, did not reduce the renal response to AN. In these denervated kidneys, cervical cord transection still caused reduction of the response. These results suggest that the reduced response to AN after cervical cord transection is not due to the interruption of renal nerve activity. They further suggest that AN exerts a major portion of its excitatory action directly on renal vascular smooth muscle. Since the refractoriness to AN following cord transection is seen in denervated as well as in innervated kidneys, it appears that a humoral substance is involved. This substance antagonizes the response to AN to a greater extent than the response to norepinephrine.
Supported by grants from U.S.P.H.S. and Wisconsin Heart Association.

Body Temperature and Thermal Conductance of the Snowy Owl. James A. Gessaman* and G. Edgar Folk, Jr. Utah State Univ. and Univ. of Iowa.

The body temperature of a snowy owl (Nyctea scandiaca) confined in a large outdoor aviary at Barrow,Alaska was recorded by radio telemetry for 20 consecutive seconds every 2 minutes of twenty-two days in November and December, 1966. The mean 24 hr body temperature for 19 days in December ranged from 40.8°C to 41.1°C. with an average of 41.0°C. There is no significant correlation between mean 24-hr body temperature and mean 24-hr air temperature in the aviary. Each day two to nine body temperature depressions, ranging in amplitude from 0.5°C to 8.4°C and less than 188 minutes in duration, occurred arrhythmically. We estimate that in 12 of 50 depressions the energy expended in rapidly rewarming the body exceeded the energy conserved by the lower metabolic rate at the lowered body temperature. The estimated additional energy expenditure associated with these 12 body temperature depressions ranged from 0.039 to 1.351 kcal/depression. The estimates of the energy conserved by the lower metabolic rate during the other 38 depressions ranged from 0.018 to 2.170 kcal/depression. The average thermal conductance of the owl during each sustained drop of body temperature was calculated from values of the rate of body temperature change and of resting metabolic rate measured in the laboratory at an air temperature and speed comparable to that in the aviary. These values range from 0.07 to 0.50 cal/hr-gm-°C.

This work was supported by a PHS training grant (5T1-AP-16) to the C.I.C. Biometeorology Graduate Program and by the Arctic Institute of North America (ONR-379).

DEXAMETHASONE SUPPRESSION OF CORTICOSTERONE LEVELS: A CIRCADIAN VARIATION IN THE RESPONSE TO ETHER. Finley P. Gibbs, Departments of Anatomy and Physiology, University of Rochester School of Medicine and Dentistry Rochester, New York.

Dexamethasone (5.0ug/100g) was given to female rats at 2400hr and at 1200hr to suppress basal levels of corticosterone ('B') to nearly zero and to provide a partial 'brake' on the adrenocortical system. At 0400 hr and at 1600hr the rats were placed into an ether jar until unconsciousness was obtained. Fifteen minutes later blood was taken from a jugular vein for analysis for 'B' by a fluorometric method. At 0400hr the basal dexamethasone-suppressed levels were 4ug%, and after ether they were 33±3ug% (mean ±S.E.). At 1600hr the basal levels were 4ug%, and after ether they were 50±4ug%. By the't' test the difference between the stimulated 'B' levels was significant at the 0.5% level. The data are consistent with the idea that more corticosterone and, therefore, more ACTH are secreted following a standard stimulus at the peak of the normal adrenocortical circadian rhythm than at the trough. It is further inferred that the neural elements regulating this basal circadian rhythm are interconnected with those causing adrenocortical activation following ACTH-releasing stimuli.

LOCALIZATION OF A SITE OF ANGIOTENSIN VASOPRESSOR ACTIVITY IN THE BRAIN. Philip L. Gildenberg, M.D. Cleveland Clinic, Cleveland, Ohio

There is abundant evidence that angiotensin has a centrally mediated as well as peripheral vasopressor action. We previously had reported that angiotensin infused into the vertebral arteries in very small doses (1-12 ngm/kg/min) resulted in an abrupt and consistent rise in blood pressure in dogs. Infusion of angiotensin at these low doses into the carotid arteries or venous system caused no measurable rise in blood pressure, suggesting that the site of action lay in that portion of the brain stem supplied by the vertebral circulation. To localize more definitely the site within the brain stem that responds to such low doses of angiotensin, various vessels supplying the brain were ligated to vary the distribution of the carotid and vertebral circulation. When a clip was applied to the basilar artery at the mid-pontine level, the hypothalamus, midbrain, and upper brain stem were supplied by the carotid arteries; the vasopressor response still occurred on infusion of small doses of angiotensin into the vertebral (but not the carotid) arteries, which suggests that the site of activity is not above the pons. After ligation of the vertebral arteries low in the neck, the entire brain stem was supplied by the carotid arteries; infusion of low doses of angiotensin into the carotid arteries then resulted in rise in blood pressure. Infusion of angiotensin into the vessels supplying the lower part of the pons and medulla, as verified by angiography, consistently resulted in an increase in blood pressure, suggesting that the central site of angiotensin activity lies in that part of the brain stem.

Erythrocytes and Distribution of Coronary Flow in the Isolated Perfused Guinea Pig Heart.
John M. Ginski and Jan M. Hornbuckle, University of Tennessee, College of Basic Medical Sciences, Memphis, Tennessee

In attempt to establish a criterion for adequate perfusion of the isolated heart, coronary flow and total tissue concentration of sodium, pottassium, calcium and magnesium were studied in response to modification of the composition of the perfusion fluid. The modifications consisted of the addition of: dextran (M.W. 60-90,000) to a concentration of 1.2% and homologous erythrocytes to a maximum of 108 x 10^6 RBC/ml, Erythrocytes significantly increased the coronary flow. In the perfused control the coronary flow was 5 ml/g/min; the addition of erythrocytes even in the smallest increment increased the flow to 10 ml/g/min in dextran and non-dextran containing perfusion fluids. Plotting potassium concentration against the erythrocyte concentration produces a sigmoid-like curve with the inflection points approximately 30 x 10^6 RBC/ml and 53 x 10^6 RBC/ml. This data suggests that fluctuations in potassium concentration may reflect variations in flow distribution patterns induced by the physical presence of erythrocytes within the cardiac microcirculation.

Supported in part by USPHS HE-11208 and Tennessee Heart Association

IMPORTANCE OF THE ARTERIAL BARORECEPTORS IN THE REGULATION OF MYOCARDIAL CONTRACTILITY. Gerald Glick, Baylor Col. Med., Houston, Texas

The question whether the carotid sinus baroreceptor mechanism exerts a modulating influence on myocardial contractility remains controversial. Several studies that have stressed the importance of the baroreceptors have been criticized because the possible role of cerebral ischemia was not eliminated. To reinvestigate this problem, 8 vagotomized dogs, anesthetized with morphine, chloralose and urethane, were studied in which both carotid sinus regions were perfused simultaneously with fully oxygenated blood by means of a peristaltic pump. Blood flow in these isolated carotid segments was kept constant and perfusion pressure (PP) was changed by varying the resistance to outflow. Six of these dogs were placed on total cardiopulmonary bypass, and myocardial contractility was assessed by measuring right ventricular contractile force (RVCF), the pressure developed in a left ventricular isovolumic balloon (LVP) and the rate of change of this pressure, dP/dt. When PP was raised from 38 ± 7.8 (SEM) to 201 ± 6.3 mmHg, LVP fell 23 ± 6.4%, dP/dt fell 34 ± 3.8% and RVCF fell 8 ± 2.8%. Changes in heart rate were small. In the remaining two dogs, the circulation was intact and the variables measured were RVCF, left ventricular dP/dt, left ventricular end-diastolic pressure (LVEDP) and arterial pressure (AP). At comparable LVEDP and AP, decreases in PP produced significant increases in RVCF and dP/dt. Prior adrenalectomy did not influence these results. Since cerebral and coronary perfusion pressures could be kept constant in these preparations, the inverse relation observed between carotid PP and the indices of contractility indicates that the baroreceptors are an important regulatory mechanism in the control of myocardial performance. (Supported by NIH, HE-05435, P.30)

DESQUAMATION RATE OF JEJUNAL MUCOSA DURING STARVATION IN CATS. Dale P. J. Goldsmith, University of Nebraska College of Medicine, Omaha, Nebraska.

The effect of starvation on jejunal desquamation rate was studied in cats. Desquamation rate was determined from the rate of accumulation of DNA in luminal perfusion fluid. (Goldsmith, Autumn Am. Physiol. Soc. Meetings 1966, 1968). A cat starved for 1 to 14 days was anesthetized with sodium pentobarbital. The first 12" of the jejunum was perfused with 0.9% NaCl at the rate of 40 ml/hr. The fluid from five hours of perfusion was assayed for DNA. At the end of the perfusion period the animal was injected with colchicine. It was killed one hour later. The percentage of cells in metaphase was determined in a stained section from the perfused segment. The mucosa was scraped from the remainder of the perfused intestinal segment, homogenized and treated with trichloroacetic acid. The resulting precipitate was dried and weighed. The average amount of DNA appearing per hour in the luminal perfusion fluid per gram of TCA precipitable material in the mucosa of female cats decreased during 11 days of starvation to 20% of normal value. This was accompanied by a reduction in mitotic activity of about the same magnitude. The mucosa hypertrophied slightly during this period. After 14 days of starvation there appeared to be an increase in desquamation rate. The reason for this is not known but it may be related to structural changes in the mucosal membrane. Similar changes were observed in male animals except that the desquamation rate decreased only during 5 to 7 days of starvation and then increased again. This suggests a lesser stability of the mucosal membrane in the male animal.

HEPATIC LACTIC ACID UTILIZATION DURING REDUCED HEPATIC OXYGEN DELIVERY. P. J. Goldstein*, D. P. Tashkin*, and D. H. Simmons. Depts. of Medicine and Ob-Gyn., U.C.L.A., Los Angeles, California.

Fifteen dogs were subjected to partial portal vein occlusion, hepatic artery ligation, or both, and 5 dogs were subjected to graded hypoxemia produced by 15%, 10% or 8% inspired O_2. Portal vein and hepatic artery flows were measured using an electromagnetic flowmeter. Systemic arterial, portal venous and mixed hepatic venous blood were analyzed for O_2 and lactic acid content. Mixed hepatic venous blood was sampled by a special technique. Hepatic O_2 delivery and lactate uptake were calculated. Hepatic artery ligation alone resulted in 32.6±3.9% decrease in total hepatic blood flow, 38.7±2.7% decrease in hepatic O_2 delivery and a significant decrease in lactate uptake (-2.0±0.7 μM/min/kg). Partial portal vein occlusion associated with similar reductions in total hepatic blood flow (-39.1±3.5%) and hepatic O_2 delivery (-42.8±7.6%) produced no significant change in hepatic lactate utilization (0.4±0.6 μM/min/kg). Simultaneous common hepatic artery ligation and partial portal vein occlusion resulted in 84.0±2.3% decrease in total hepatic blood flow, 81.1±5.6% decrease in O_2 delivery and a significant reduction in lactate uptake (-4.0±0.8 μM/min/kg). During 8-15% O_2 breathing, significant decreases in hepatic lactate utilization were observed when hepatic O_2 delivery was reduced as little as 13.1±1.6%, despite associated increases in liver blood flow. These results suggest that hepatic lactic acid utilization is readily impaired by systemic hypoxemia or by abolishing hepatic arterial supply whereas it is unaffected by moderately severe reductions in portal venous flow associated with similar or even greater decreases in total O_2 delivery.

EXPERIMENTAL PATHOLOGY AFTER SPONTANEOUS BREATHING OF FLUOROCARBON FLUIDS. Frank Gollan and Robert M. Clark°. Veterans Administration Hospital and University of Miami School of Medicine, Miami, Florida.

Since fluorocarbon fluids dissolve about 60 volume % of oxygen and about 300 volume % of carbon dioxide at normal atmospheric pressure, animals can breathe such inert organic liquids and survive (Clark, L. C., and Gollan, F. Sci. 152: 1755, 1966). These commercially available fluids (3M Comp.) differ from each other in their densities, solubilities, viscosities and surface tensions, but the greatest differences by far exist in the range of vapor pressures which vary from 0.3 to 260 m Hg at 77°F. This may partially explain the different course of events in the recovery period. After removal of puppies from the fluid the lungs are solidly filled with the liquid. The more volatile the liquid, the more rapid is the development of overinflation of the lungs with dilatation of the alveoli and rupture of capillaries. After several weeks these lesions are repaired in the growing animals. Since this condition does not develop in anesthetized and curarized animals with mechanical ventilation and normal intrathoracic pressures, the volatility of the respiratory liquid cannot be the only cause. If a nonvolatile fluid is inhaled, a slow removal of the oil by foam cells is taking place. However, after half a year the remaining fluid of high density still causes the lungs to sink in water. These lesions do not cause any detectable disturbance in gas exchange and do not retard the normal growth of the animals.

EFFECTS OF TRAINING OF THE LIPOLYTIC RESPONSE OF ISOLATED FAT CELLS TO NOREPINEPHRINE. P. D. Gollnick and C. Williams.* Washington State University, Pullman, Washington 99163.

The lipolytic response of isolated fat cells from trained and untrained rats to various concentrations of norepinephrine (NE) has been investigated. Rats were trained by running in motor-driven wheels for 1 hr daily (5 days/week) at 26.8 m/m. Animals were killed by decapitation and fat cells isolated as described by Rodbell (J. Biol. Chem. 239; 375, 1964). Lipolysis was determined from the production of free fatty acids (FFA) by the fat cells following 1 hr incubation in 4% albumin buffer containing 0.02, 0.1, and 10.0 μg of NE/ml. The effects of beta adrenergic blockade (1 μg propranolol/ml) and phosphodiesterase inhibition (10^{-4} M theophylline) were also studied in the two groups. The release of FFA was significantly ($P < 0.01$) greater from the fat cells of the trained animals at all concentrations of NE tested. Theophylline potentiated the lipolytic response of NE in both groups, however, the responsiveness of the cells from the trained rats was significantly ($P < 0.01$) greater than that of the controls. Propranolol was less effective in blocking FFA production in response to NE in fat cells from trained rats than in the untrained controls. (Supported by USPHS grant HE o8262-06).

EFFECTS OF VARIATIONS OF IONIC STRENGTH ON CONTRACTILE TENSION OF SKINNED MUSCLE FIBERS ACTIVATED BY CALCIUM. A.M. Gordon and R.E. Godt*. Dept. Physiol. Biophys., Univ. Wash., Sch. Med., Seattle, Wash. 98105.

The decreased tetanic tension produced by frog twitch skeletal muscle fibers in hypertonic solutions may be due to a direct effect of elevated internal ionic strength (μ) on contractile proteins per se or due to deficient calcium release and/or elevated calcium requirement for contraction. In an effort to distinguish among these possibilities, the effect of μ on contractile tension of skinned frog twitch muscle fibers was measured. The "normal" bathing medium was KCl 140mM/L, Na_2ATP 5mM/L, $MgCl_2$ 1mM/L, EGTA 3mM/L, Tris buffer 2mM/L, pH 7.0, and $CaCl_2$ to produce the desired ratio of $(EGTA/Ca)_{added}$ (μ=.16). μ was changed by varying the KCl concentration. At each μ used the ratio of $(EGTA/Ca)_{added}$ required to produce maximum tension was determined. (A pCa of 5.5 was sufficient in all cases investigated assuming a binding constant of $10^{6.69}$ at pH 7.) Other constituents of the contracting solution were held constant. The effects of their variation are under investigation. The isometric tension produced by a maximal Ca activation decreased monotonically with increasing μ being about 70% of normal at 1.5 X "normal" μ, 25% at 2 X "normal" μ, 7% at 2.5 X "normal" μ and immeasurably small for μ near 3 X "normal". This tension decrease closely parallels the decrease in tetanic tension seen in intact muscles as the tonicity of the bathing solution is raised. Thus increasing ionic strength decreases tension produced by the contractile proteins per se even with maximal Ca activation. This possibly accounts for much of the decreased muscle tension seen in hypertonic solutions.

(Supported by a grant from USPHS - NB08384.)

WHOLE BODY AUTOREGULATION IN AREFLEXIC DOGS. H. J. Granger*and A. C. Guyton. Dept. Physiology & Biophysics, Univ. Miss. School of Med., Jackson, Miss.

Whole body autoregulation in response to changes in arterial pressure was studied in dogs rendered areflexic by decapitation and destruction of the spinal cord. Following 25-50 mm Hg single step changes in arterial pressure cardiac output, O_2 consumption, A-V O_2 difference and right atrial pressure changed transiently before returning toward control values. The time required to reach a new steady-state averaged 35 minutes. Calculated open-loop gain averaged 3.3 $\pm$ 0.7 (SEM) indicating 75% compensation. Whole body pressure-flow curves over the range of 50 to 150 mm Hg arterial pressure showed significant deviation from the pressure-flow relationship of a rigid vascular bed, giving an open-loop gain of the autoregulatory system of 2 to 3. The return of A-V O_2 difference and O_2 consumption to control values following changes in pressure is consistent with a metabolic mechanism of autoregulation. The absence of significant transcapillary fluid flux in autoregulating preparations as measured by hematocrit changes indicates (1) that the precapillary resistance vessels are the major sites of autoregulatory resistance changes and (2) that autoregulation is an important mechanism in maintaining capillary pressure at a normal level as well as maintaining blood flow at the level required by the tissues. (Supported by Grants-in-aid from National Institutes of Health,HE-11678, HE-08375, and American Heart Assn. 65-G-95)

STUDIES ON THE SPEED OF THE CAROTID CHEMORECEPTOR RESPONSE IN RELATION TO THE KINETICS OF CO_2 HYDRATION. B. A. Gray (intr. by S. M. Tenney), Dartmouth Medical School, Hanover, New Hampshire 03755.

Using the acknowledged reaction mechanism and first order velocity constants, it has been possible to develop a treatment of the kinetics of uncatalyzed CO_2 hydration which predicts a striking dependence of the reaction time course on the buffering capacity. In the absence of non-bicarbonate buffers the predicted T 1/2 for the reaction is 20 m sec., as compared to 30 sec at a buffering capacity equal to that in true plasma (30 mM L^{-1}/pH unit). In view of this, the response of the carotid body of the cat to abrupt increases in $[H^+]$ and P_{CO_2} was studied during perfusion with bicarbonate-Ringer's solution to which a non-bicarbonate buffer and/or a carbonic anhydrase inhibitor were added. The changes in impulse frequency in the presence of 40 mM Tris buffer occur as rapidly as the responses in the absence of buffer, and are too fast to be accounted for by the uncatalyzed hydration of CO_2. Exposure to Acetazolamide (100 mg/L) increases the response T 1/2 by 6-8 sec during perfusion with 40 mM Tris, and by 2-4 sec when no buffer was added. The latter effect is greater than would be expected if the H ion sensory mechanism were located in an extracellular environment whose buffering capacity was that of the perfusate. [Work supported by USPHS Grant HE 02888(12) and the Life Insurance Medical Research Fund.]

TRANSCAPILLARY FLUID FLUXES AND SEGMENTAL VASCULAR RESISTANCES (R) IN COLLATERAL-FREE, INNERVATED, NATURALLY PERFUSED DOG FORELIMBS FOLLOWING 60 PERCENT BLOOD VOLUME DEPLETION. G.J. Grega*, J.M. Schwinghamer*, and F.J. Haddy. Dept. of Physiol., Mich. State Univ., East Lansing, Mich.

In 20 anesthetized, spontaneously breathing dogs, forelimb blood flow was separated into skin (S) and muscle (M) components by measuring brachial (M) and cephalic (S) venous outflows. Large and small artery and vein pressures (P) were measured in M and S. Segmental R (large artery, small vessel, large vein) in M and S were calculated by dividing P gradients by appropriate flows. Changes in intravascular volume and capillary fluid fluxes were evaluated from continuous recordings of forelimb weight. Forelimb weight decreased (↓) rapidly (0-1/2 hr) in response to arterial hemorrhage and continued to decline throughout a 4 hr hypovolemic period. The bleeding stress produced steady-state reductions in all arterial and venous P. Total and segmental R in M and S progressively increased (↑) throughout the hypovolemic period. Arterial and venous R in M and S ↑ proportionately more than small vessel R. Venous R ↑ proportionately more than arterial R in S whereas in M arterial and venous R ↑ almost proportionately (0-3 hr) or proportionately more in arteries than veins (3-4 hr). The rapid phase of weight loss (3.5g/100g forelimb) represented largely a ↓ intravascular volume whereas the slow phase of weight loss (3g/100g forelimb) represented largely a net fluid movement from tissue to blood. This study fails to provide evidence for waning of precapillary resistance and for fluid filtration in irreversible shock. The continuous fluid influx may have resulted from a ↓ capillary hydrostatic P (CHP) subsequent to steady-state reductions in arterial and venous P despite a possible ↓ pre/postcapillary R ratio in S. Without considering other factors, the effect of the ↑ venous R on CHP was negated partially in S and completely in M by an ↑ arterial R.

TRANSMURAL PRESSURES AND SARCOMERE LENGTHS IN THE VENTRICULAR WALL A.F.Grimm. Depts. of Histology and of Physiology, Univ. of Ill., Chicago, Illinois.

Sarcomere lengths were measured in serial sections through the free wall of the left ventricle. In previous work utilizing these histologic technics, a sarcomere length of 2.07 micra was found at the optimum length for tension production in isolated muscle preparations. With K arrest and formalin fixation in situ, in both dog and rat, sarcomere lengths were essentially constant through the ventricular wall and were about 1.96 micra (approximately 95% of the optimum sarcomere length). Similar technics were used in open chest rats where ventricular transmural pressures were controlled. Under these conditions, with ventricular pressures of 0, 3, and 6 cm H_2O, sarcomere lengths were 1.89-1.93 micra at the epicardial surface and progressively decreased to 1.76-1.80 micra at the endocardial surface. With increased transmural pressures, sarcomere lengths at the epicardial surface remained essentially constant though there was a progressive increase in the length of deeper sarcomeres. At 24 cm H_2O, sarcomere lengths were essentially constant through the ventricular wall. At even greater pressures, both epicardial and endocardial sarcomere lengths increased.

It is concluded that, with large diastolic ventricular volumes, sarcomere lengths are uniform through the ventricle. With decreasing volumes, the accompanying sarcomere shortening becomes progressively greater with distance from the epicardial to the endocardial surfaces.

(Partially supported by USPHS Grant DE 02417)

EFFECT OF STARVATION ON BILIRUBIN METABOLISM IN THE HORSE. Ronald R. Gronwall and Abdus S. Mia*. Department of Physiological Sciences, Kansas State University, Manhattan, Kansas.

Plasma unconjugated bilirubin levels increased within 12 hours of last feeding and continued to increase, depending upon the physical condition of the animal, for two to four days to levels as high as eight times the pre-starved values. Infusion of bilirubin resulted in a more rapid rise in plasma unconjugated bilirubin levels in starved horses than in fed horses; also the half time for bilirubin removal after infusion was increased, indicating a decreased removal capacity or clearance. Conjugated bilirubin in plasma increased only slightly during starvation or bilirubin infusion. The plasma disappearance curve for tracer dose of 14C labeled bilirubin injected intravenously was delayed after three days fasting. Based on the disappearance curve for labeled bilirubin there was an apparent decrease in the fractional transfer of unconjugated bilirubin from rapid mixing pool to storage pool during starvation, resulting in retension of a larger fraction of the total unconjugated bilirubin in the rapid mixing pool. This redistribution of bilirubin into the rapid mixing pool, which includes the plasma, and an apparent reduction in the volume of distribution of the rapid mixing pool accounted, in part, for the hyperbilirubinemia.

MEASUREMENT OF GASTROINTESTINAL MOTOR ACTIVITY IN UNANESTHETIZED RATS. William G. Groves and Joan S. Long (intr. by Peter T. Ridley). Smith Kline and French Labs., Philadelphia, Pa.

Gastric and colonic motor activity were recorded continuously for four hours in fasted, unanesthetized, chronic fistula rats. Pressure changes were detected by miniature balloons, and electronically recorded. Individual contractions were classified according to the nomenclature of Code (Amer. J. Med. 13: 328-51, 1952) and counted to determine frequency of each wave type. Average hourly frequencies of Type I, II, and III waves were 50, 28, and 4 for the stomach, and 138, 45, and 19 for the colon, respectively. Total hourly wave frequency of the colon was 2 1/2 times that of the stomach. The colonic motor pattern tended to be very stable and regular while the gastric pattern was cyclical, with alternating 15-20 minute periods of high and low activity. Propantheline, 30 mg/kg, p.o., virtually eliminated gastric type II waves for 3 hours, producing progressive inhibition of colonic type II waves ranging from 50% (1st hour) to 93% (3rd hour). Other wave types were much less affected. Dycylomine, 80 mg/kg, p.o., produced marked, but shorter-lived, inhibition of gastric type II waves and similar but less pronounced inhibition of the colon than propantheline. Colonic motor activity was also quantitated by summing wave durations and expressing this as # seconds per observation period (CT). CT reduction roughly paralleled Type II wave inhibition in the colon with both drugs. The stability of the basal motor pattern and its sensitivity to standard therapeutic agents suggest that this method can be used successfully to evaluate potential spasmolytic agents.

ROULEAUX FORMATION IN VIVO. M. Mason Guest, Ted P. Bond* and Charles H. Wells*. Dept. of Physiology, University of Texas Medical Branch, Galveston, Texas.

The assumption is generally made that erythrocytes form rouleaux within blood vessels whenever plasma fibrinogen concentration is increased. Furthermore, numerous investigators have utilized the concept of rouleaux formation to explain dynamic aspects of apparent viscosity and other variables influencing rheologic characteristics of blood. Our observations of the circulation, in mesenteries of man, dogs, rats and ground-hogs, utilizing cinephotography at both conventional filming rates and rates to 3200 frames per second indicate that in arterial vessels with diameters below 100 μ rouleaux do not occur except when flow is essentially stopped. On the venous side rouleaux also are seen only when flow is very slow or absent. In contrast, with tissue injury, such as following crushing or burning of tissues, three dimensional aggregates of randomly oriented erythrocytes occur. Apparently shear stresses in flowing blood under normal physiologic conditions are sufficient to overcome forces involved in maintaining rouleaux formations but may not be adequate to disrupt a different type of bonding characteristic of aggregates formed during relatively severe tissue injury. These relationships will be demonstrated with photographic evidence supported by simultaneous measurements of fibrinogen concentrations and relative shear rates. (Supported in part by NIH Grant HE 10893.)

CHANGES IN SINGLE UNIT ACTIVITY IN THE PREOPTIC REGION DUE TO TEMPERATURE CHANGES OF THE SPINAL CORD. J. D. Guieu* and J. D. Hardy. John B. Pierce Foundation Laboratory, and Department of Epidemiology and Public Health, Yale Univ. School of Medicine, New Haven, Conn.

Evidence of thermoregulatory responses evoked by spinal cord thermal stimulation has been reported (Jensen et al., Experientia, 24, 694, 1968; Kosaka et al., Am. J. Physiol., 1969). In an attempt to locate a possible integration level of this activity urethanized rabbits were implanted with two steel thermodes in the preoptic region (PO) on one side and a reentrant tube for thermocouple. A "U shaped" steel thermode was inserted in the spinal canal extending from T_6 to C_7. Circulation of warm or cold water through these thermodes permitted independent control of temperature in these regions. Thermocouples were inserted into the preoptic region, spinal canal, rectum and on the ear pinna; respiratory rate was monitored by a thermocouple in the tracheal cannula. 40 units have been studied in the medial PO of which 4 have been influenced by changes in spinal cord temperature 32-44°C. 3 of these units responded to changes in T_{PO} but were sensitive to rubbing the skin and auditory stimuli. 1 unit was inhibited by heating the PO above 38C and was insensitive to cooling; such neurons have been classified as interneurons. This neuron was inhibited by spinal cord heating above 39C and was unaffected by cooling; it was also unaffected by mechanical or auditory stimuli. Both rate of breathing and ear pinna temperature increased with spinal cord and preoptic heating but were unaffected by cooling. It is concluded that neural thermoregulatory pathways link temperature structures of the spinal cord with those in the preoptic-anterior hypothalamus, a probable location for the integration of central and peripheral neural responses to elevated temperature. Supported by NIH Grant No. NBO-4655.

CHARACTERIZATION OF THE MECHANICAL PROPERTIES OF DOG PAPILLARY MUSCLE. J. F. Gunning, A. L. Brown, Jr., and H. N. Coleman (intr. by J. T. Shepherd). Mayo Foundation, Rochester, Minnesota.

Current and past investigations of the mechanics of contraction of the dog ventricle have been based on series elastic constants derived from studies of cat papillary muscle, since studies of the mechanics of contraction of isolated dog papillary muscle are not available. Accordingly, papillary muscles averaging .98±.08 SEM mm^2/cross sectional area were rapidly excised from 21 dogs, mounted in a myograph, and studied at a temperature of 29°C. Electron microscopic examination demonstrated normal appearance and linear arrangement of sarcomeres. The force-velocity-relations were described by a sigmoid curve with an intrinsic velocity of contraction (V_{max}) of 1.10±.08 muscle lengths per second. Isometric length-tension curves were qualitatively similar to those of cat papillary muscle and contraction at the apex of the length tension curve (L_{max}) resulted in a mean developed tension of 5.60±.53 gm/mm^2. Resting tension at L_{max} averaged 1.31±.27 gm/mm^2. Acetylstrophanthidin (2×10^{-7}G/ml) resulted in a 50% increase in V_{max} and a 58% increase in isometric developed tension at L_{max}. Stress strain characteristics for the series elastic component (SEC) were determined by isotonic quick release and corrected for equipment extensibility. The resultant SEC curve was exponential in form with an average extension of 6.2% of muscle length for a preload of .55 gm/mm^2 at a developed tension of 4 gm/mm^2. The results indicate that the SEC of dog myocardium is significantly more extensible than previously reported for cat papillary muscles while the contractile properties are quantitatively similar.

STEADY STATE DIFFERENCES IN WEAK ACID CONCENTRATION ACROSS THE ALVEOLAR CAPILLARY MEMBRANE. Gail H. Gurtner. The Johns Hopkins University, Baltimore, Maryland 21205.

It has previously been reported (Gurtner, Song and Farhi, Physiologist 10:#3 190, 1967; Resp. Physiol. In press) that under conditions of no gas exchange there is a steady state difference between the pCO_2 of the alveolar gas or fluid and the mixed venous blood, alveolar pCO_2 being higher and that the difference is related to the pH and HCO_3^- content of the mixed venous blood. The explanation involved an intracapillary difference in pH due to a negatively charged capillary wall and a coupling of viscous and diffusional flows causing the carbonic acid reactions to be shifted toward CO_2. The postulated mechanism is not specific for CO_2 and other weak acids should also be affected. Furthermore, the hypothesis predicts that the difference in undissociated weak acid in proportion to the venous concentration of the dissociated form ($\Delta HA/A^-$) should be directly proportional to the H^+ ion activity and inversely proportional to the equilibrium constant. To test the hypothesis the distribution of the non-metabolized, C_{14} labelled, weak acids, DMO (pK - 6.12, equilibrium constant .76 X 10^{-7}) and barbital (pK - 7.8, equilibrium constant .158 X 10^{-8}), between mixed venous blood and a fluid-filled lobe was measured in anesthetized dogs after introduction of the isotope into the systemic circulation. When DMO was used, values of ($\Delta HA/A^-$) were approximately the same as for CO_2. When barbital was used the proportional differences in the undissociated form were about 10 times larger at a given pH, and the difference increased as pH decreased in a similar manner to CO_2. Although the proportional differences for barbital are smaller than predicted, the findings are qualitatively consistent with the hypothesis.

Supported by P.H.S. Grant #HE 10342

A VORTEX METHOD OF EXTRACTING GASES FROM FLUID FOR ANALYSIS BY GAS CHROMATOGRAPHY. Jack D. Hackney, Charles E. Spier,* Rancho Los Amigos Hosp., Downey, Calif.

We have developed a practical system for the extraction of gases from small liquid samples. A key element of this system is the efficient gas exchange which results when liquid is whirled by a stirring magnet to produce a vortex which is in contact with a flowing stream of helium carrier gas. The gas exchange chamber is a 1.5 ml disposable glass vial that contains a small stirring magnet and is closed with a rubber stopper and aluminum seal. Carrier gas enters and leaves this chamber through 2 needles that pierce the rubber stopper. The operation sequence is as follows: An auxiliary flow of carrier gas vents to the atmosphere and deaerates the vial and its reagent contents. The sample is then introduced with a precision syringe, mixed and directed into the chromatograph. One sample can be processed about every 6 minutes. Using peak height response, we found reproducibility in the analysis of whole blood to be: O_2, CO_2 ± 1% or less of the absolute value for one standard deviation (0.1 ml samples); CO ± 1% or less (0.4 ml samples); N_2 ± 0.3% or less (0.7 ml samples of blood or urine). For N_2 studies the extraction device was enclosed in a plastic bag that was flushed with 100% O_2 and this overcame the serious problem of atmospheric N_2 contamination. Analysis of blood for CO_2 and O_2 content by this system usually agreed within 2% of the absolute value of comparison measurements with the manometric Van Slyke. Room air was used as the O_2 standard (with argon and STPD corrections) and a known concentration of sodium carbonate was used as the CO_2 standard. The vortex gas exchanger principle works well in this system and may be useful in other gas exchange applications.

INFLUENCE OF MOLECULAR WEIGHT OF DEXTRAN ON THE ANTIHYPERTENSIVE EFFECTS OF INTRAPERITONEALLY INJECTED SOLUTIONS IN RATS WITH DOCA HYPERTENSION. C. E. Hall and O. Hall.* University of Texas Medical Branch, Galveston.

A prior experiment showed that intraperitoneal injections of a 6% dextran solution halted the rise of blood pressure and reduced the polydipsia in rats with desoxycorticosterone acetate (DOCA)-salt hypertension. This experiment was undertaken to evaluate dextrans of different molecular weights. Groups of young female albino rats were implanted with DOCA pellets and given distilled water to drink: hypertension and mild polydipsia developed. Giving 1% saline to drink for a week greatly augmented fluid intake but had no effect on evolution of hypertension. Twice daily intraperitoneal injections of 3 ml/100g body weight of 6% dextran were then begun, using materials of 50,500, 72,000, 113,000 and 142,000 molecular weight. The first reduced fluid intake to levels in effect before water was substituted by saline, as did injections of physiological saline, but neither affected the course of hypertension. The three other polymers all entirely abolished polydipsia. The two medium weight dextrans caused blood pressure to stabilize at levels in effect when they were begun, but the largest caused a marked reduction. The antihypertensive effect thus bears some relationship to the molecular size of the dextran used, but could not be correlated with the serous inflammatory anaphylactoid response which all of the samples caused, with the reduction in saline intake, or with intraperitoneal injections *per se*. All of the dextrans above 50,500 MW caused some hemorrhaging which may have contributed to, but could not be held solely accountable for, the observed effects on blood pressure.

*Supported by a Grant HE-08054 from the USPHS.

THE CIRCULATORY EFFECTS OF MORPHINE SULFATE FOLLOWING MYOCARDIAL INFARCTION. John R. Hamilton*, Brian T. Paaso*, Stephen R. Corday* and Donald C. Harrison, Cardiology Division, Stanford University, Palo Alto, California.

Morphine sulfate (MS) has been known to have prominent cardiovascular (CV) effects for many years. In order to define its CV action following acute myocardial infarction (MI), studies were performed in 14 anesthetized open-chested dogs in which MI was produced by serial ligation of coronary arteries. In 4 control dogs, MS 0.5 mg/kg produced early and transient decreases in LV dp/dt of 18%, in aortic mean pressure (AP) of 20%, and in systemic vascular resistance (SVR) of 20%, without significant changes in other CV parameters. These CV changes persisted for less than 5 minutes. Following MI (average 40% of weight of the left ventricle) MS, 0.5 mg/kg, produced decreases in LV dp/dt of 25%, in AP of 30%, in SVR of 23%, and in left atrial pressure of 15%. In the control animals the return of CV parameters to baseline levels was more rapid and increases in LV dp/dt, LA pressure, and SVR occurred rapidly after the transient depression. After MI, the return of CV changes toward baseline was delayed and only SVR increased. It is known that MS may produce increases in LV dp/dt and SVR indirectly through activation of the adrenergic nervous system. These findings suggest that MS has a depressant effect on myocardium independent of its effect on the adrenergic nervous system, and this depressant effect is greater following MI.

ATRIAL ACTIVATION AND FORM OF P_Y FOR SINUS AND ECTOPIC BEATS. Robert L. Hamlin, David L. Smetzer*, Tetsuo Senta*, and C. Roger Smith. Dept. Vet. Physiol., The Ohio State University, Columbus, Ohio 43210.

P wave of Y axis ECG and electrograms from numerous foci on epicardium of both atria (RA and LA) and RA face of interatrial septum (IAS) were analyzed from 22 horses. Pacemaker could be identified from polarity (- or +) of initial (I) and terminal (II) peaks of P_Y, which could be predicted from the sequence of structures activated (str. act.) and direction (ant. to post., post. to ant., RA to LA) traversed by front of activity.

Site of Pacemaker	P_Y^I			P_Y^{II}		
	polar.	str.act.	direct.	polar.	str.act.	direct.
RAu, aRA S-A node	+	RA	a-p	+	IAS	RA-LA
pRA, cor. sinus	-	RA	p-a	+	IAS	RA-LA
aLA, LAu	+	LA	a-p	-	RA	p-a
pLA	-	LA	p-a	-	RA	p-a

R=right, L=left, a=anterior, p=posterior, A=atrium, AU=auricle

For any RA pacemaker, all foci on LA were activated within 15 msec. of each other (forming no general front of activity), in identical sequence, and after peak of P_Y^{II}. During inscription of P_Y^{II}, activity was registered from only IAS. These findings indicate activity of IAS produces peak P_Y^{II}, and activity of LA is "silent." Pacemaker within ant. RA produced activity of that atrium from ant. to post., followed by activity of IAS from RA to LA but with different form than from post. RA pacemakers; while LA was activated identical with activation for post. RA pacemaker.

THYROID-CATECHOLAMINE INTERACTION: STUDIES ON ISOLATED BROWN FAT CELLS. Rupert P. Hammond* and Milton W. Hamolsky. Division of Biological and Medical Sciences, Brown University, and Division of Medical Research, Rhode Island Hospital, Providence, Rhode Island.

Treatment of rats with thyroxine (T4) causes an increase in the catecholamine (CA)-induced lipolytic response of white adipose tissue and a rapid depletion of triglyceride (TG) from white adipose storage sites. This has been attributed to a T4-stimulated increase in one or more of the components of the adenyl cyclase system for lipase activation. In our experiments, T4 treatment of rats causes an apparent marked inhibition of the CA-induced lipolytic response of isolated brown adipose cells (IBAC) when fatty acid (FA) and glycerol production are expressed as Δ μmoles/mmole TG. However, TG content is increased approximately 2x, as is the TG/DNA ratio, in IBAC from T4 treated animals, so that if the data are expressed per μmole DNA (or per cell) there is clearly no change in the CA-induced lipolytic response. T4 treatment does not alter the lipolytic response of IBAC to small amounts of theophylline; however, theophylline in the incubation medium at levels higher than 10^{-3} M causes artifactual increases in measured FA release in both control and experimental flasks. The lipolytic response of IBAC to dibutyryl cyclic AMP (DCAMP) is not changed by T4 treatment, nor is the rate of disappearance of CA from the incubation medium. Our studies indicate that T4 does not change the CA or DCAMP-induced lipolytic response of IBAC, but causes a marked increase in TG content of the cells. We would suggest that at least a part of the function of T4 might be the selective mobilization of FA from white adipose to brown adipose tissue sites. Preliminary results indicate that potentiation by T4 of the action of insulin on IBAC may be of importance in this mechanism. (Supported in part by USPHS Training Grant #2TI-CA-05007-11 and by the Sergei Zlinkoff Fund for Medical Education, New York)

DIURNAL CHANGES IN BRAIN LEVELS OF ACETYLCHOLINE: RESULTS DEPENDENT UPON METHODOLOGY. I. Hanin*, R. Massarelli*, and E. Costa. Lab. of Preclinical Pharmacology, Natl. Inst. of Mental Health, Saint Elizabeths Hospital, Washington, D.C. 20032.

Male rats were kept in a cycle of 12 hours of light and 12 hours of darkness for at least 8 days prior to each experiment. Brain acetylcholine concentrations were determined at 8 different times within the diurnal 24 hour cycle. Levels of acetylcholine were measured using gas chromatography (Hanin and Jenden: Biochem. Pharmacol. 18: 837-845, 1969). Results depended upon the mode of sacrifice of the animals. When rats were decapitated using a guillotine, the levels of acetylcholine followed a circadian rhythm with a peak at 2 hours of light (32.69 mμmoles/g) and a trough at 8 hours of darkness (17.03 mμmoles/g). When the animals were killed by total immersion in liquid nitrogen, acetylcholine levels were lower and ranged between 9.04 and 12.85 mμmoles/g at all times tested. In these animals, comparable diurnal changes in brain levels of acetylcholine were not observed. Levels of brain acetylcholine in isolated rats were higher than those in the brains of grouped litter mates. This observation was consistent irrespective of the method or time at which the animals were killed.

RESPONSES OF THE GASTROINTESTINAL VASCULATURE TO THE ADMINISTRATION OF VASOPRESSIN (PITRESSIN). K. M. Hanson
Department of Physiology, Ohio State University, College of Medicine, Columbus, Ohio.

In the 15 experiments which have been done thus far, the effects of Pitressin on the blood flow and vascular resistance in the in situ, denervated dog liver preparation have been studied. Pitressin was infused Iv at a rate of 1.5-3.0 U/min. Total dose given was 20-30 U. Systemic and hepatic arterial pressures were increased, while portal pressure was decreased. Heart rate and liver blood flow were also decreased. Portal pressure and flow remained decreased for an hour or longer after infusion was stopped. Hepatic artery flow was initially decreased in most cases; however, after a dose of 10-15 U had been given it usually returned to a value even above that which existed before the infusion was begun. At the same time, as the infusion was continued, heart rate still decreased and the arterial pressure, which was initially increased, began to decline. At a dose of 20 U the mean decrease in portal pressure and flow were 15 and 35%, respectively, resulting in a 45% increase in intrahepatic portal resistance. Of particular interest is the behavior of the hepatic arterial vasculature, the response being similar to that seen during prolonged stimulation of the hepatic nerve truck (auto-regulatory escape). At a dose of 20 U, artery flow showed an average 30% increase.
Supported by grants from the American Heart Association (67-689), Northwestern Ohio Heart Association and Public Health Service(HE-09884).

THE INVESTIGATION OF THE BRADYPNEA RESPONSE IN DOGS FOLLOWING LEFT ATRIAL DISTENTION. E. L. Hardie*, H. P. Mauck, Jr.*, T. N. P. Johns* and J. L. Patterson, Jr. Medical College of Virginia, Richmond, Va.

The observation of marked decrease in respiratory rate after inflation of a balloon in the left atrium of a dog anesthetized with chloralose warranted further study. Respiratory rate, left atrial pressure, and usually tidal volume, femoral and pulmonary arterial pressures were measured in 93 experiments before, during and after atrial balloon inflation in 3 groups: 1) 11 dogs under chloralose, 2) 4 dogs under pentobarbital, and 3) 10 dogs unanesthetized (some mildly sedated). Balloon placement was by retrograde catheterization in the anesthetized, and by surgical implantation in the unanesthetized animals. Marked, moderate or slight bradypnea was observed in 7 of 11 chloralosed dogs, in 4 of 10 unanesthetized dogs but in none of the pentobarbital group. Alternating bradypnea and tachypnea following inflation, and bradypnea on deflation were other common responses observed in all groups. Tachypnea, seen in only 3 experiments of the chloralose group, was predominant in the pentobarbital group and occurred in 50% of experiments without anesthesia. The detailed results suggest that two opposing reflex mechanisms are operating during left atrial distention. Tachypnea may result from sensitization of pulmonary stretch receptors secondary to pulmonary vascular engorgement. The hitherto undescribed bradypnea might be mediated by left atrial receptors. Absence of bradypnea in chloralosed dogs, in which the left atrial appendage and a single pulmonary vein near its atrial junction were distended by implanted balloons indicates either that these regions are not the sites of the postulated receptors or that an insufficient area was stimulated. Marked bradypnea, observed when the inflated balloon slipped from the atrial appendage into the mitral orifice in one dog, suggests that receptors mediating this response might be situated in tissues surrounding the mitral ring.

VOLTAGE-CLAMP OF CARDIAC MUSCLE. Lesley Harrington* and E. A. Johnson. Duke University Medical Center, Durham, North Carolina.

The rise-time (10-90% limits) of the depolarization phase of an action potential of mammalian cardiac muscle is close to 1-2 msec. It would seem to us that a rough criterion of approaching a satisfactory, if not ideal, voltage-clamp of cardiac muscle would be that the surge of inward current during a depolarizing step in clamp potential should have a similar duration. In recent reports of voltage-clamp experiments of cardiac muscle, the time-course of inward membrane currents falls short of this by one if not two orders of magnitude. The reasons for this seem to arise from limitations imposed by (a) the preparation and (b) the method. Of the many preparations that have been examined (Johnson, E. A. and J. R. Sommer, J. Cell Biol., 33, 103 (1967); Sommer, J. R. and E. A. Johnson, J. Cell Biol., 36, 497 (1968); Sommer, J. R. and E. A. Johnson, Z. Zelfforsch., in press), a tiny bundle of electrically interconnected fibers from the ventricles of hearts from animals the size of the cat or rabbit, or smaller, approaches most closely the ideal of a long cylindrical cell. These strands contain fibers which except where they are closely apposed to one another (e.g. forming tight junctions or nexuses) are relatively widely spaced, and since the fibers do not have a transverse tubular system, little, if any, sarcolemma is in series with an appreciable resistance. The sucrose-gap technique was chosen because it avoids a point source of current with its attendant difficulties (Eisenberg, R. S. and E. A. Johnson, Progress in Biophysics, in press). Preliminary experiments with such strands show inward sodium currents which rise and decline within 1-2 msec. (Supported by NIH grant 5 R01 HE 08620 and by a grant from the North Carolina Heart Association.)

INTEGRATED CIRCUIT CAPACITANCE TRANSDUCER SYSTEM. Dean R. Harrison*, Harold Sandler and Grant W. Coon*. NASA-Ames Research Center, Moffett Field, California

A miniature (1.0 mm in diameter) capacitance manometer tipped catheter has been developed which includes improved electronic circuitry design. The capacitance bridge electronics have been incorporated as part of the catheter tipped transducer through the use of integrated circuit techniques. The transducer circuit requires only a single coaxial cable for drive voltage and output signals. The circuit consists of two opposed polarity half-wave rectifiers connected in parallel. The transducer forms the capacitance of one of the rectifier RC filters. By adjusting RC so that it is approximately 1/2f, the average output voltage is very sensitive to changes in transducer capacitance. A system is described which is simple to operate, can accomodate multiple catheters and is entirely battery powered. The .005 mm air gap in the transducer communicates to the outside via the catheter for in vitro or in vivo calibrations by application of known stepwise gradations of vacuum. The system provides 0 to 10 V output for 0 to 200 mm Hg pressure with a resolution of 0.5 mm Hg. Although the transducer is nonlinear, compensating circuits have been employed to provide an overall linearity of approximately 1% in the output. Thermal effects are less than .04%/°C from 20°C to 45°C. Frequency response is 0 to well above 250 Hz. The small size of the unit allows for intravascular introduction of the catheter via a needle or through the lumen of standard catheters. These units have been used to measure right and left sided pressure by these means. The design of this system allows for the use of as many as five catheters from a single carrier-oscillator. This system is presently being qualified for use in man.

THE EFFECT OF ACETYLCHOLINE ON PEAK DYE TRANSIT TIMES THROUGH SURFACE STRUCTURES OF DOG KIDNEY . Rodney B. Harvey. Dept of Physiology, Univ. of Minn., Mpls. Minn.

A filterable dye (FD&C Green #3) can be injected into the aorta of a dog in a dose sufficient to intensely color fluid within the nephrons. The passage of the dye bolus through the surface capillaries as well as the surface convolutions was recorded by color cinemicrography. The dye transit curves were read off of the movie film by placing silicon cells covered with appropriate filters at the projected images. A galvonometer recorder was used to record the silicon cell outputs. Three distinct dye peaks were seen, first the vascular peak produced by dye in the capillaries, second a peak due to dye transit through loops of proximal tubules, and a late third peak due to dye in the distal convolutions. A urine dye peak was also recorded by mounting a transparent white backed uretral catheter in the photographic field. The dead space of the catheter was approximately 30 microliters. It was found that in 11 hydropenic dogs the intra-arterial infusion of Acetylcholine decreased the time between the PCTand DCT dye peaks and decreased the time between DCT and urine peaks. This was associated with diuresis and reduced urine osmolality. Control measurement made 20 minutes after cessation of Ach infusion showed a return to control conditions for dye transit, urine flow, and urine osmolality. The effects of Ach were compared with mannitol diuresis of a similar magnitude in the same dogs. These data permit some further conclusions regarding the site of action of Ach on tubular water reabsorption. A brief film showing the dye passage through surface structures will be shown.

Supported by grants from the USPHS.

HYPOTHALAMIC BLOOD FLOW AND TEMPERATURE DURING VENTRICULAR INJECTION OF MONOAMINES. C.R. Hassler* and R.D. McCook. Loyola University, Stritch School of Medicine, Maywood, Illinois.

Hypothalamic blood flows were measured in the anesthetized cat with heated thermistors. Hypothalamic, rectal, and aortic temperatures and plethysmographic blood flow in the pinna were also measured. Both thermistors, indirectly heated with D.C. current, and newly designed probes, which were directly heated with a high frequency current (10 KHz), were employed. The thermistor flow probes were bilaterally placed in the anterior hypothalamis (A+14.0, L±1.5, H-2.4). One probe was used as a reference while the other was heated. The inverse of the temperature differential between the two thermistors was used as the flow measurement. A cannula was inserted into the third ventricle for the injection of drugs. Following the injection of 200 µg of 5 HT, hypothalamic flow, rectal temperature, and hypothalamic temperature increased. Following epinephrine or norepinephrine (50 µg) hypothalamic flow increased while hypothalamic and rectal temperature decreased. All drugs were given in normal saline. The rectal temperature changes are in agreement with Feldberg (1964) as to the action of the three amines. The recordings often do not show the expected inverse relationship between hypothalamic and rectal temperature, therefore these amines must be in some manner altering this relationship. This might possibly be an alteration of neural transmission or a direct chemical effect. *(Supported by National Institutes of Health Grant HE 08682 and National Institute of General Medical Sciences Grant GM 999.)*

AUDITORY EVOKED POTENTIALS DURING NEGATIVE AND POSITIVE MOTIVATION IN THE SAME ANIMAL. V. Havlicek and K. R. Hughes (intr. by A. Naimark). Dept. of Physiology, University of Manitoba, Winnipeg, Canada.

The same conditioned stimulus was presented to the same rat in a modified Skinner-Box. The rat discriminated a change in the apparatus cues by performing, (a) an avoidance response of lever pressing to avoid shock when a door covering the water source was closed (negatively motivated situation), and (b) lever pressing to obtain water when the door was open (positively motivated situation). In both situations the UCS (shock or water) was presented 10 sec after the onset of the CS (clicks). In this delay period unipolar recordings of evoked potentials were taken. Responses in the auditory cortex, medial geniculate, and hippocampus were averaged with digital computers (Nuclear Data Enhancetron and Intertechnique Didac 800). Comparison of averaged e.p.'s (1000 summations) showed that in all observations (6 rats) the amplitude of the e.p.'s during the negative motivation was 50-150% larger than during the positive. Bipolar EEG recording from the auditory and sensori-motor cortex showed more pronounced activation during negative motivation than during positive. During the positive CR's animals produced more lever presses and more movements than during negative CR's. During the initial period of avoidance learning when our recordings were made, the behavior observed was predominantly conditioned fear accompanied by crouching, defecation and piloerection. During this phase the rat did not press the lever to avoid shock.

(Supported by the Medical Research Council of Canada)

COMPETITIVE INHIBITION OF ATP-INDUCED MUSCULAR CONTRACTIONS. Philip L. Hawley*, Sol Roy Rosenthal, and Anwar A. Hakim*. Department of Preventive Medicine, University of Illinois, College of Medicine, Chicago, Illinois, U.S.A.

A factor (TF) has been extracted and purified from scalded human skin which specifically inhibits the development of tension by glycerinated rabbit psoas muscles (Hakim, et al., Fed. Proc., 28, 712, 1969) apparently by competition for ATP binding sites on actomyosin ATPase. The inhibition of contraction cannot be reversed by Mg++, Ca++, excess ATP, or by a variety of pharmacological agents. Antibodies prepared in rabbits against TF will counteract the inhibitory effects of TF. Antibodies against one preparation of TF are effective against other preparations of TF from skin but not against preparations from normal human serum. The effective binding ratio of antibody to antigen as determined by the checkerboard titration technique is 1:2. Interaction of antigen to antibody was determined by measuring the development of tension in glycerinated muscle. Preliminary studies indicate that there are antibodies in the serum of severely burned human patients which show properties similar to those prepared against TF in rabbits.

HYPOTHALAMIC UNIT RESPONSES TO CENTRAL THERMAL STIMULI IN THE UNANESTHETIZED MONKEY. J.N. Hayward. Dept. Anatomy and Brain Research Institute, UCLA School of Medicine, Los Angeles, Calif. 90024.

Preoptic thermosensitive neurones in the monkey receive a single direct thermal input from the carotid arterial blood. This blood stream carries the integrated sum of bodily heat production (muscular and metabolic) and peripheral heat loss (cutaneous and respiratory). Thermoregulatory adjustments during sleep and waking lead to identical shifts in carotid arterial blood, cerebral arterial blood and hypothalamic temperatures. Hypothalamic single cell discharges related to thermoregulatory or EEG aspects of spontaneous sleep-waking behavior have been reported in the rabbit by Findlay and Hayward (J. Physiol. 201:237, 1969) and in the monkey by Hayward (Anat. Rec. 163:197, 1969). In the present study, in order to examine further the responsiveness of hypothalamic units to induced central thermal stimuli, warm and cool isotonic solutions were remotely injected into a chronic right atrial cannula of sitting, unanesthetized monkeys. When the hypothalamus was warmed or cooled by 0.1-0.5C over 30-60 sec there often resulted a peripheral vasomotor response, a shift in behavior (sleep or arousal) and EEG and a change in the temporal pattern of unit discharge. This approach allows comparison of spike train statistics with other parameters during control periods, during intravenous thermal loading and during the post-infusion period associated with vasomotor and behavioral responses. Abrupt changes in carotid arterial blood temperature induced by intravenous thermal loads produce shifts in hypothalamic temperature within the physiological range, alters hypothalamic unit activity and results in peripheral thermoregulatory and behavioral adjustments. (Supported in part by NIH Grant NB-05638)

AN NMR STUDY OF SKELETAL MUSCLE: CHANGES IN WATER STRUCTURE WITH NORMAL DEVELOPMENT. C. F. Hazlewood and B. L. Nichols*. Department of Pediatrics, Section of Cytocybernetics and Department of Physiology, Baylor College of Medicine, Houston, Texas 77025.

The presence of ordered or adsorbed water in skeletal muscle has been demonstrated[1,2]. These studies were made on muscles from mature rats which characteristically have low sodium concentration and resting potentials of 80 mV. Muscles from newborn rats have a very high concentration of sodium and low resting potentials. It was predicted that the muscle water of very young rats would be more free (less adsorbed or ordered) than mature rat muscle water.

The present studies utilized nuclear magnetic resonance (NMR) spectroscopy to examine the changes in the physical state of water that occur in developing skeletal muscle of the rat. The width of the NMR signal at one-half amplitude is an index of the degree of order to tissue water[3]. It was found that the NMR water signal of normal skeletal muscle increased two fold from birth to 30 days of life, indicating an increase in the order or structure of water. One consequence of this change in the state of water is a reduction in the solubility of sodium. It is suggested that the observed changes in the state of water may explain the changes in sodium solubility and voltage that occur with normal skeletal muscle development.

[1] Cope, F., Biophysical J., 9:303, 1969.
[2] Hazlewood, C. F., B. L. Nichols, and N. F. Chamberlain, Nature, 222: 747, 1969.

This work, with the support of U.S.P.H.S. Grant Nos. FR-5425, FR-00188, FR-00259 and AM-011285, was accomplished.

N,N-DIMETHYLATED INDOLEAMINES IN BLOOD. B. Heller*, N. Narasimhachari* H.E. Himwich and J. Spaide*. State Res. Hosp., Galesburg, Ill. 61401.

In our present studies for the first time on the blood samples of acute schizophrenics, dimethyltryptamine and 5-methoxy-N,N-dimethyltryptamine were identified in all the 4 patients studied while bufotenin was found in one acute case. In 9 chronic schizophrenics and 2 normals and 1 depressive case studied, the dimethylated indoleamines could not be detected in any of the blood samples. The identification was made using both the thin-layer chromatography and gas-liquid chromatography techniques and in one sample the finding was further confirmed by the GLC of a trimethylsylyl derivative.

Cardiac Myosin B: Changes in Biochemical Properties with Age. Lois J. Heller* and William V. Whitehorn. Univ. Illinois at the Medical Center, Chicago, Illinois

Biochemical tests were applied to myosin B extracted from ventricular muscle of rats of different ages. The initial rate of superprecipitation was obtained by monitoring the rate of increase in O. D. upon addition of ATP to a suspension of cardiac myosin B. ATPase activity of myosin B was determined by the rate of P_i liberation measured by the Fiske-Subbarow method. Optimal conditions were determined for both tests with respect to [ATP],[Mg++], [Ca++],[KCl] , and [cardiac myosin B]. Animals were divided into four groups according to age. Identical simultaneous extraction of myosin B from the oldest group and one of the three younger groups of rats allowed relative comparison of the rate phenomena investigated. This reduced the problems of experimental variability. Under standardized testing conditions the cardiac myosin B extracted from young rats had a greater rate of superprecipitation and a greater rate of ATPase activity than did the cardiac myosin B extracted simultaneously from older rats. The conclusion can be drawn that these biochemical rate phenomena are age dependent. The relationship of the biochemical parameters studied to the mechanical properties of papillary muscle preparations from rats of similar age groups is under investigation.
(Partially supported by Grants #HE 01353-16 USPHS and PHS GM 738)

AUDIOGENIC SEIZURES IN INBRED MICE AFTER PRIMING AND TESTING WITH MAXIMAL ACOUSTIC STIMULATION TO ONE, BOTH, OR NEITHER EARS. Kenneth R. Henry* and Robert E. Bowman. University of Wisconsin Regional Primate Research Center, Madison, Wisconsin.

Six hundred forty 16-day old mice of two separate strains were given an exposure (priming) to a loud acoustic stimulus which resulted in their becoming highly susceptible to audiogenic seizures 5 days later. This priming was performed with either one, both, or neither ears flooded with glycerine. Testing at 21 days of age was also performed under one of these same conditions of glycerine flooding, presumably varying the amount of sound received by the subjects during both priming and testing. With both the SJL/J and C57BL/6J strains of mice, the latency to wild running was a direct function of the number of ears filled with glycerine during testing, and both the frequency of clonic seizures and an audiogenic seizure severity score varied as an inverse function of the number of ears filled with glycerine during priming. For the C57BL/6J's, but not for the SJL/J's, the seizure severity scores and frequency of clonic seizures were an inverse function of the number of ears filled with glycerine during testing. Glycerine was observed to be reasonably effective in preventing the effects of priming, but was much less effective in blocking seizures during testing. The data suggest that the number, and not the laterality, of ears exposed is the most important variable, ascribing a CNS, and not a peripheral, mediation to this phenomenon.

NUMERICAL RECORDING OF VERY SMALL OXYGEN CONSUMPTION UNDER STERILE CONDITIONS. A.A. Heusner. Dept. of Physiological Sciences, School of Veterinary Medicine, University of California, Davis, California.

The principle of the microrespirometer consists of Faraday's Law applied to the production of oxygen by electrolysis. A differential manometer detects the volume variation in the respiratory chamber; its manometric liquid, a copper sulfate solution, rises until the solution touches a platinum electrode inside the limb connected to the respiratory chamber. Then a capacitor is discharged through the copper sulfate solution and a constant amount of oxygen is set free by electrolysis. The capacitor is automatically recharged and discharged as long as the liquid remains in contact with the platinum electrode. The discharge of a capacitor through a copper sulfate solution releases a known amount of oxygen. This amount is kept constant (± 0.2%). Thus in replacing quantitatively the consumed oxygen, the number of discharges is proportional to the oxygen consumed. This number is recorded at regular time intervals. The amount of oxygen released may be continuously adjusted from 0.001 to 0.05 µl so that the relative error of a measurement is kept constant (± 2%) over a wide range of oxygen consumptions (0.05 to 50 µlh-1). The oxygen production within the respiratory chamber permits a sterile maintenance of precise partial pressures of oxygen during long-term experiments. This technique has been used to record oxygen consumption during the development of sterile axenic drosophila, from the egg to the imago and during the entire life span of adult flies. Application of this principle to long-term recordings of oxygen consumption in mammalian tissue cultures is presently being developed. (Supported by a Postdoctoral Fellowship from the National Research Council of Canada, a NASA Research Grant NSG 721 and GRS grant 68-118.)

RECEPTIVE FIELDS OF CELLS OF A MARSUPIAL VISUAL CORTEX. Richard M. Hill and Jerry L. Christensen*. Ohio State University, Columbus, Ohio

Analysis of the response characteristics of receptive fields of the cortex of the common marsupial Didelphis virginiana and their comparison with cortical receptive fields of placentals were the purposes of this investigation. Based on more than one hundred cells studied the following was found: 1) that at least three different receptive field geometries are present; 2) that no antagonistic receptive field zones could be demonstrated; 3) that these visual cells responded very well to diffuse light; 4) that little correlation between field diameter and eccentricity from the optic axis was found and 5) that about 40% of these cells responded to stimulation of either retina, a full spectrum of dominancies from ipsilateral to contralateral being present. Although sharing such advanced characteristics as binocularity with the placentals, this primative mammal has, never-the-less, several distinctive features among the response characteristics of it's cortical visual cells, characteristics which may provide further keys to the processing of visual information.

A COMPARISON OF NOREPINEPHRINE TREATMENT AND COLD ACCLIMATIZATION ON THE VASCULAR HUNTING REACTION OF RATS. K. Hirai* and S.M. Horvath. Institute of Environmental Stress, University of California, Santa Barbara, California 93106.

Adult rats were subjected to a series of treatments for four weeks. Two groups were maintained in a warm room (26 C), one injected with saline (1 ml/Kg/day), the other with norepinephrine (300 µg/Kg/day; two other groups were maintained at 2 C, one injected with saline, and the other with reserpine (0.5 mg/Kg/day). The vascular hunting reaction (limb skin temperature during immersion in 0 C water for 30 minutes), resting oxygen consumption (at 26 C), and the rectal temperature response to cold water immersion (30 minutes at 12 C water) were used to determine the altered responsiveness to cold. The cold acclimated rats showed a significant increase in hunting reaction (limb average skin temperature 2.98 C, cf warm adapted rats 1.58 C), resting oxygen consumption (150.4 ml/M^2/min, cf W.A.R. 118.2 ml/M^2/min), and rectal temperature response (27.1 C, cf W.A.R. 23.7 C). Reserpine treatment tended to prevent the increased hunting reaction (L.A.S.T. 1.92 C) and increased oxygen consumption (11.9.7 ml/M^2/min) seen in cold adapted controls, but the resistance to immersion cooling was not effected. Norepinephrine treatment did not increase the effect of cold acclimatization as determined by the hunting reaction (L.A.S.T. 1.92 C), oxygen consumption (109.9 ml/M^2/min), and rectal temperature response (24.8 C). The resting oxygen consumption in the norepinephrine treated rats was actually lower than in the warm adapted controls. These results imply that norepinephrine treated rats did not acquire adaptations normally associated with cold adaptation, and that some characteristics of cold adaptation were inhibited by reserpine treatment.

NONLINEAR EFFECTS OF PRESSURE AND FLOW ON THE TRANSMISSION OF PRESSURE WAVES IN THE CANINE AORTA. M. B. Histand and M. Anliker*. Dept. of Mech. Engr., Colorado State Univ., Fort Collins, Colo. 80521, and Dept. of Aeronautics and Astronautics, Stanford Univ., Stanford, Calif. 94305. (Supported by NASA Grant NGR-05-020-223.)

A method was developed to determine the elastic behavior of large blood vessels in terms of their transmission characteristics for small pressure signals of the form of finite trains of sine waves that are superimposed on the naturally occurring pressure fluctuations.[1] Its application to the thoracic aortas of 18 mature mongrel dogs anesthetized with Nembutal has shown that for frequencies between 40 and 200 Hz the descending aorta behaves in a nonlinear fashion with respect to large pressure fluctuations such as those produced by the heart. This is demonstrated by significant variations in the transmission characteristics of wave trains generated at different instants of the cardiac cycle. The change in wave speed due to pressure in the absence of a mean flow, $\partial c/\partial p$, is usually between 3 and 6 cm/sec per mm Hg. $\partial c/\partial p$ is essentially constant within the range of normal arterial pressures. Simultaneous measurements of the wave speed in the up- and downstream directions in a single aortic segment indicate that pressure waves are convected by the blood flow. The mean flow velocity determined from the speed difference between down- and upstream waves compares favorably with that measured with catheter-tip flowmeters. Due to the viscoelastic nature of the vessel wall, the waves are strongly attenuated and exhibit a logarithmic decrement of .7 to 1.0 in the downstream direction and 1.2 to 1.6 in the upstream direction. The discrepancy in these values is attributed to the taper of the vessel, and the actual value of the logarithmic decrement for a vessel with uniform cross section would be of the order of 1.0 to 1.2.

1) Anliker, M., et al., Dispersion and Attenuation of Small Artificial Pressure Waves in the Canine Aorta, Circulation Research, 23:539-551, Oct. 1968.

ENHANCEMENT OF SUBSTRATES ON HORMONE-STIMULATED FFA RELEASE FROM FAT CELLS. R. J. Ho and H. C. Meng, Dept of Physiol. Vanderbilt Univ., School of Med., Nashville, Tenn. 37203

The effect of added substrate on hormone stimulated lipolysis was studied in the incubated free fat cells in vitro. Fat cells were prepared from the epididymal fat pad of rats fasted for 48 hours, in Krebs-Ringer bicarbonate buffer containing defatted serum albumin of pH 7.4. Glycerol and FFA were measured by conventional methods. Some of the FFA samples were measured by a radiochemical assay which was developed in our laboratory. It was found that in addition to an inhibitory effect on FFA release by 20 mM glucose, the release of FFA stimulated by epinephrine (3.4×10^{-7} M) and ACTH (20 mU/ml) was significantly enhanced by 0.5 mM glucose. This effect of glucose was shown to be inhibited by its non-metabolizable analoge, 3-0-methyl-D-glucose (5.0 mM) and 2-deoxy-D-glucose (7.5 mM) by 53 and 80% respectively. It is clear that this effect of glucose cannot be explained by the traditional theory, that glucose enhanced lipolysis is a result of a removal of FFA inhibition. Furthermore, the enhancement of epinephrine-stimulated lipolysis by other substrates, such as pyruvate (0.5 mM), L-glutamate (5.0 mM) and L-aspartate (5.0 mM) can also be demonstrated. It is possible that all these substrates tested were utilized by fat cells as the source of energy, namely ATP. The present finding suggests that the activation of lipolysis required the added substrate if the endogenous energy supply is inadequate. (Supported by grant from USHPS HE-04372 and AM-07462).

RELATION OF INTERNAL ORGANS TO BASAL METABOLIC RATE (BMR) IN HUMANS DURING GROWTH. Malcolm A. Holliday. Univ. of Calif. San Francisco Medical Center and San Francisco General Hospital, San Francisco, Calif.

It is well known that organ metabolic rate (OMR), kcal/kg organ weight, of the major internal organs (brain, liver, heart, and kidney) in adult humans is 10-20 x the basal metabolic rate per kgm (BMR/kg) of the body as a whole. These 4 organs together account for 70% of BMR, although they comprise but 7% of total body weight. Infants and children have a higher BMR/kg than adults. We have shown (Ped. Res. 1, 185, 1967) the pattern of increase in BMR to body weight to be very similar to the pattern of increase of the sum of the weights of these 4 organs (ΣOW) to body weight. We have inferred that the latter relation is directly responsible for the former and neither conforms closely to surface area, weight, or to any single power function of weight. However, BMR is related to ΣOW by the equation: $BMR=a(\Sigma OW)^{1.0}$. We have also inferred that OMR/kg of each organ is relatively constant during growth. This is supported from direct studies of brain and kidney during growth. We have recently constructed a model which predicts the relative contribution of each organ system to total metabolic rate. Brain accounts for a major share of heat production in infancy. Such a model can be applied to people of unusual body composition usefully. The BMR of the fetus during the last trimester of gestation (data from Sinclair et al., Pediatrics 39, 724, 1967) increases at a more rapid rate than body weight ($BMR=aBW^{1.2}$) and at an even more rapid rate than ΣOW ($BMR=a\Sigma OW^{1.3}$). During fetal growth and maturation, metabolic capacity of the organ increases in relation to its weight. BMR overall during growth is largely a function of the product of organ size and OMR.

TENSION DEPENDENT AND TENSION INDEPENDENT HEAT PRODUCTION BY THE SEMITENDINOSUS MUSCLE OF RANA PIPIENS. E. Homsher and N. V. Ricchiuti (intr. by W. F. H. M. Mommaerts). Dept. of Physiology, Univ. of Calif. at Los Angeles, Calif.

Unlike the sartorius muscle (SART), the dorsal head of the semitendinosus muscle (SEMI) of Rana pipiens, can be reversibly stretched to lengths at which there is no detectible twitch tension and the tetanus tension is less than 0.05 P_o. Since this property should be useful in studies of the energetics of excitation-contraction coupling (ECC), heat measurements, using thermopiles, were made to compare the thermal behavior of the SEMI to that of the SART and to examine the heat production of the SEMI at long muscle lengths. Comparative studies revealed that the SEMI is quantitatively similar to the SART with respect to isometric twitch heat (3.40 mcal/g), the tetanic heat production (see below), the Fenn effect (max. isotonic twitch mechanical efficiency = 36%), and shortening heat ($\frac{S}{P}$ = 0.13 at P = 0). When the SEMI was stretched so that no twitch tension was recorded, a tension-independent heat of 1.03 mcal/g was produced. When the SEMI was stretched so that little or no tetanus tension could be developed, the stable maintenance heat (SMH) was about 0.55 mcal/g/sec as opposed to 1.85 mcal/g/sec at L_o. The SMH of the SART at L_o was 2.10 mcal/g/sec. These results indicate that the energy liberation by a contracting semitendinosus muscle is essentially identical to that of the sartorius muscle as formulated by Hill (1964). Furthermore, it appears that about 30% of the initial heat liberated in a twitch or tetanus is associated with ECC processes.

BROWN FAT: EFFECT OF NOREPINEPHRINE ON INTRACELLULAR-POTENTIALS AND Na^+/K^+ ATPASE ACTIVITY. B. A. Horwitz, P. A. Herd*, J. M. Horowitz, Jr.* and R. Em. Smith. Depts. Physiol. Sci. and Animal Physiol., Univ. California, Davis, Calif.

Previous work in vivo has shown that the membrane potential of brown fat cells in cold-acclimated rats (4^oC for 3-4 weeks) is depolarized following administration of norepinephrine (NE) or electrical stimulation of the mixed nerves to the tissue. In the present study, i.v. injection of the β-adrenergic antagonist, propranolol (0.5 to 1.0 mg/kg), substantially diminished the magnitude of this depolarization and abolished the NE-induced temperature increase of the tissue. This result and the observation that a thermogenic dose of theophylline (325 μm/kg) does not depolarize the membrane suggest that the NE-induced depolarization is associated, in part, with the biochemical pathway terminating in the activation of adenyl cyclase. However, administration of the α-adrenergic blocker, phentolamine (10 mg/kg), also antagonized the depolarization, thus implying that the membrane phenomenon may be partially associated with events other than those involved in the adenyl cyclase activation. That the activity of the Na^+/K^+ pump may have also been involved in the NE response was examined. The specific activity of the Na^+/K^+ ATPase {(ATPase in presence of added $Mg^{++} + Na^+ + K^+$) minus (ATPase in presence of added Mg^{++})} of the defatted and mitochondria-free homogenate and the 14,000 x g supernatant was significantly enhanced by addition of NE. This finding as well as the effects of α- and β-adrenergic blocking agents is consistent with our previous suggestion that the thermogenic effect of NE on brown fat initially reflects an increased availability of substrate and is associated with an increased requirement for ATP. (Supported in part by NASA NGR 05-004-035; USPHS HD-03268; USPHS Predoctoral Fellowship 1-GM-33,505-03.)

THE RENIN-ANGIOTENSIN MEDIATION OF HYPOTENSIVE DRINKING. Katherine A. Houpt* and Alan N. Epstein, Dept. of Biology, Univ. of Pa., Phila., Pa.

Hypotension induced by beta-adrenergic activation provokes short latency, copious drinking in rats (Lehr et al., J. Pharm. Exp. Ther. 158, 150). Given Lehr's most effective dose (0.33 mg/kg, sc) 5 adult rats drank 14.6 ml (Range: 13-17) in 3 hr after the administration of isoproterenol, 9.4 ml in the first hour. The drinking is abolished by nephrectomy (N=21, 2.7 ml average intake vs. 2.1 ml by nephrectomized, saline-injected rats, N=10); but survives sham nephrectomy (N=5, 12.6 ml) and ureteric ligation (N=8, 11.5 ml in 3 hr) implicating a renal dipsogen. Systemic renin and intracranial angiotensin II restore drinking to the nephrectomized, hypotensive rat. Six such animals given 2U hog renin/100 g, ip, 1 hr after isoproterenol, drank 10.8 ml in the succeeding 2 hr. Three with unilateral, lateral preoptic cannulas that did not drink for 1 hr after nephrectomy and isoproterenol, drank an average of 16.8 ml (average latency 120 sec) after injection of 2 ug angiotensin II (Hypertensin, 1 mg/ml in water) into the preoptic area. Lastly, drinking induced by cell dehydration is unaffected by prior nephrectomy and hypotension (N=5, 24.2 ml in 3 hr after 2 ml/100 g of 1M NaCl, ip, in nephrectomized animals treated with isoproterenol 45 min before cell dehydration). Hypotension like hypovolemia is a potent releaser of renin-angiotensin. The drinking provoked by both intravascular states depends on the kidney as endocrine organ and is reproduced in the absence of the kidney by systemic renin-angiotensin (Fitzsimons & Simons, J. Physiol. 196, 39 P) and by intracranial angiotensin (Epstein, Fitzsimons & Simons, J. Physiol. 200, 98 P). These results extend the significance of renin-angiotensin as a hormonal basis for thirst, operating by peripheral release of the renal dipsogen and its direct action on the brain. (USPHS NB 03469)

COMPARATIVE ASPECTS OF HEMODYNAMIC CHANGES INDUCED BY PREGNANCY. Arthur S. Hoversland* and James Metcalfe. Heart Research Laboratory, University of Oregon Medical School, Portland, Oregon.

Data on pregnant ungulates (Pygmy goats and sheep) are compared with data for pregnant women. Blood volume increases 10% in ungulates with its peak at term, and 43% in humans peaking at 34 wks. Plasma volume increases more (ungulates +11% vs women +37%) than red cell mass (+5% vs +22%); the result is an insignificant change in hemoglobin concentration in sheep and goats but a significant decrease in women (-17%). Cardiac output (CO) in ungulates peaks at term (+39%) whereas the human CO peaks between 26-30 wks (+39%). In ungulates, heart rate is elevated more than stroke volume (+31% and +10%) but the reverse is true in pregnant humans (+21% and +27%). Peripheral vascular resistance shows a marked decrease (-45%) at the time of maximum CO. O_2 consumption increases to a lesser degree (+25%) than CO (+39%), resulting in a narrower A-V O_2 difference at the time of peak CO. Hemoglobin flow (product of CO in L/min and hemoglobin concentration in gm/L) was highest at peak blood flow (+42% vs +25%). The tissues of the pregnant ungulate enjoy adequate oxygenation as indicated by an elevated hemoglobin flow, decreased A-V O_2 difference, increased mixed venous Po_2, and decreased coefficient of O_2 utilization. The same is true in women at the time of peak flow, but in late pregnancy CO has been reported to decline near term when O_2 requirements are the greatest. This decline in blood flow near term in women studied in the supine position is due to vena caval compression by the pregnant uterus. Cardiodynamic adjustments in ungulates during pregnancy exceed the requirements of the maternal organism and the developing fetus, but in pregnant humans these adjustments are interfered with at term in the supine position. (Supported by NIH and Oregon Heart Association.)

GRAVITATIONAL FORCES AS A DETERMINANT OF THE DISTRIBUTION OF DIFFUSING CAPACITY TO BLOOD FLOW ($D_L/\dot{Q}_c$) IN THE LUNG. R. W. HYDE, A. B. FISHER*, M. MARIN*, and J. SONNEMANN*. University of Penna., Philadelphia, Pa.

Studies in normal, sitting man have shown that one-half of the pulmonary blood flow ($\dot{Q}_c$) is distributed to about 85% of the total diffusing capacity (D_L). Although gravitational forces are known to influence the distribution of $\dot{Q}_c$, its relation to uneven $D_L/\dot{Q}_c$ has not been defined. After the insertion of a tracheal divider, D_L and $\dot{Q}_c$ of each lung of 4 dogs were measured with breathholding methods in both lateral positions. When a lung was moved from the lower to the upper lateral position, D_L decreased 20% ($0.10 > P > 0.05$) and $\dot{Q}_c$ decreased 63% ($P < 0.001$). The $D_L/\dot{Q}_c$ ratio increased from 0.0064 mm Hg^{-1} in the lower lung to 0.011 mm Hg^{-1} ($P < 0.01$) in the upper lung. In these dogs about one-half of the upper lung was in Zone I (pulmonary artery pressure(P_a) < alveolar pressure (P_A)) during breathholding. In 3 additional dogs both P_a and left atrial pressure (P_{LA}) were monitored. During breathholding all of the lower lung remained in Zone III ($P_a > P_{LA} > P_A$); the upper lung was divided about equally between Zone II ($P_a > P_A > P_{LA}$) and Zone III. Uneven $D_L/\dot{Q}_c$ within each lung was appraised by comparing the rate of uptake of 0.4% CO ($D_{LO.4\%}$) to the rate of uptake of 5% CO ($D_{L5\%}$) in the right lateral position during breathholding. The presence of stagnant blood or other forms of uneven $D_L/\dot{Q}_c$ would cause $D_{L5\%}$ to be less than $D_{LO.4\%}$. The difference between $D_{LO.4\%}$ and $D_{L5\%}$ was 32% in the upper lung and 12% in the lower lung. These data are compatible with an "effective" stagnant capillary volume of 31% of the upper lung's capillary blood volume and 11% of the lower lung's capillary blood volume. These experiments indicate that pulmonary capillary transit times are longer in the upper parts of the chest. The finding of uneven $D_L/\dot{Q}_c$ even when the lung is entirely within Zone III suggests that gravitational forces are not the only factors that result in uneven $D_L/\dot{Q}_c$.

PRESSOR RESPONSE TO CHEMORECEPTOR STIMULATION. M. Ikeda*, E.H. Rubinstein*, and R.R. Sonnenschein. Department of Physiology, UCLA School of Medicine, Los Angeles, Calif.

Administration of gas mixtures of low oxygen content to artificially ventilated, chloralose-anesthetized or decerebrate cats, with pneumothorax, induced initially (within 7-12 sec) an increase of systemic arterial pressure, associated with gradual decrease in hind limb blood flow, bradycardia (in decerebrate animals), and initial increase and subsequent decrease in mesenteric blood flow. Division of the carotid sinus nerve prolonged (up to 30-40 sec) the latency of the pressor response, while bilateral vagotomy had little effect. On the other hand, a response similar to that induced initially by hypoxia was elicited by stimulation of the carotid sinus nerve. The threshold for the pressor response was determined both by perfusion of the carotid bodies, via the common carotid arteries, with varying mixtures of the animal's own arterial and venous blood, and by administration of gas mixtures of graded content of O_2 and CO_2. By either method, the absolute threshold was at P_{A-O2} of 75-80 mm Hg, below which, changes of 5-10 mm Hg P_{A-O2} elicited further pressor responses. The dependency of the threshold on P_{A-CO2} was limited. (Supported by USPHS grant HE-05157 and LACHA 400-C1)

PERIPHERAL CIRCULATORY RESPONSES TO CENTRAL THERMAL STIMULI IN THE ANAESTHETIZED PIG. Douglas L. Ingram* and Robert El. Smith. University of California School of Medicine, Davis, California.

Pigs 9 to 12 weeks in age were anaesthetized with various agents. Carotid blood was circulated through an extracorporeal heat exchanger and returned to the head while brain temperature was recorded in the region of the hypothalamus. Peripheral blood flow was measured by a mercury-in-rubber strain gauge placed around the carpal region. Skin, rectal and air temperatures, as well as peripheral heat flow, were also monitored. Under Fluothane anaesthesia peripheral blood flow remained high even at rectal and brain temperatures of 36°C and an ambient temperature of 25°C. In other experiments, injection of Pentabarbitone produced a transitory increase in blood flow. In contrast, under Metafane or Urethane anaesthesia, a wide range of peripheral flows were obtained in response to the imposed brain temperatures. The relationship between these variables was a curvilinear one represented equally well by either a quadratic or an exponential equation, but in either case no clearcut set point was observed. Under these anaesthetics, peripheral blood flow was never completely suppressed by lowering brain temperature, for even at a brain temperature of 36°C and an ambient temperature of 25°C a measurable blood flow was observed. This flow was then suppressed to an undetectable level by the injection of adrenaline. Finally, the influence of both direction and rate of change of brain temperature, in a range between 36°C and 42°C, was studied at ambient temperatures of 25°C and 35°C.

SPINAL AND BRAINSTEM REFLEX ACTIVITY DURING PARADOXICAL SLEEP IN BRAIN TRANSECTED CATS. Y. Iwamura*, M.B. Sterman and D.J. McGinty*. V.A. Hospital, Sepulveda, Calif. and Dept. of Anatomy, U.C.L.A., Calif.

Spinal and brainstem reflex activity was studied in brain transected cats: diencephalic, mesencephalic and pontine. The brain rostral to the transection level was removed by aspiration, leaving a small hypothalamic island for levels below the diencephalon. Monosynaptic and polysynaptic reflexes, in both hindlimb and jaw muscles, were recorded using techniques previously developed for the intact cat. The recording of these reflexes together with other polygraphic variables was initiated on the second post-operative day and continued periodically in surviving animals for up to two months. In pontine preparations reflexes were consistently depressed during the atonic phase, in a manner analogous to the reflex depression reported during paradoxical sleep in the intact cat. In mesencephalic and diencephalic preparations, a sustained facilitation of mono- or polysynaptic reflexes, or both, was observed during the atonic phase. The critical transection level for this facilitation differed for hindlimb and brainstem reflexes. Thus, the dominant supraspinal influence on a particular reflex depended upon the level of transection. This suggests the existence of a systematic hierarchal modulation of reflex activity, which may provide a basis for the various phasic changes in motor activity observed during paradoxical sleep in the intact cat, such as periodic facilitation of reflex pathways and twitch movements. The tonic reflex inhibition normally observed during paradoxical sleep may depend, in part, upon control of these facilitatory influences by forebrain structures. (Supported by the Veterans Administration and NSF grant # GF-262.)

CENTER-SURROUND INTERACTION IN GENICULATE RECEPTIVE FIELDS. G. H. Jacobs and R. L. Yolton*. Dept. of Psychology, Univ. of California, Santa Barbara.

There is wide variability in the relative prominence of the responses produced by center and by surround stimulation in the receptive fields of cells in the visual system. We have investigated this interaction by examining the center-surround balance in receptive fields of cells in the lateral geniculate nucleus of the squirrel monkey. A set of standard stimulus conditions that allow a measure of center-surround balance have been defined and applied to a substantial sample of cells. The results of this survey include the following features: (a) many cells (55%) require the presence of a contrast spot imaged on the center of the receptive field before a response to illumination of the surround can be obtained; (b) under a wide range of stimulus conditions, a surprisingly large proportion (18%) of geniculate cells show no direct response to surround stimulation and, thus, respond optimally to diffuse-light stimulation; (c) a small percentage (2%) of the cells surveyed show a surround-dominated response; (d) there are differences in the relative distributions of center-surround balance between those cells having excitatory and those having inhibitory centers; (e) there is, at best, only a weak relationship between the diameter of the receptive field center and the center-surround balance; (f) for approximately one-third of the cells, center-surround balance can be altered by raising the background light level--the alteration may result in either an increase or a decrease in the dominance of the center component. (Supported by NSF Grant GB-7970.)

EFFECTS OF PROSTAGLANDIN E_1 ON VENOUS RETURN AND PERIPHERAL RESISTANCE IN THE DOG. G.W. Jelks*, R.M. Daugherty, Jr. and T.E. Emerson, Jr. Depts. of Physiol. and Med., Mich. State Univ., East Lansing, Michigan.

Transient and steady-state effects of a 10 min Prostaglandin E_1 (PGE_1) infusion (12.3 µg/min) on venous return (VR), arterial blood (ABP), pulmonary artery (PAP) and left atrial (LAP) pressures were studied in dogs anesthetized with Nembutal. VR was measured with a cylinder and stopwatch from the cannulated venae cavae and returned to the right atrium with a Sigmamotor pump. Cardiac inflow was a) adjusted continually with the inflow pump to equal VR (N=10) or b) maintained constant (N=8). When cardiac inflow was variable, PGE_1 infusion caused a slight, transient increase in VR which then returned to near control level. ABP and total peripheral resistance (TPR) decreased markedly and remained below control throughout the infusion period. PAP decreased but LAP was unaltered, reflecting a decrease in pulmonary vascular pressure gradient. Pulmonary vascular resistance decreased on the average. Heart rate did not change. When cardiac inflow was held constant, VR, ABP, and TPR changes were similar to those of the natural flow experiments. Heart rate did not change. These data indicate that the predominant effect of PGE_1 in this preparation is a marked fall in TPR apparently resulting from active vasodilation. However, unlike other potent vasodilators studied in this preparation, i.e. acetylcholine and bradykinin, PGE_1 produces only a slight transient increase in VR. The latter observation may be due in part to peripheral pooling due to venous dilation (Proc. Cen. Soc. Clin. Res. 41:35, 1968). (Supported by NIH Grant HE-10899)

RETICULOCYTOGENIC AGENT IN THE VOLATILE FRACTION OF PLASMA OBTAINED FROM ANAEMIC DOGS. Donald B. Jennings and Duncan G. Sinclair*, Dept. of Physiology, Queen's University, Kingston, Ontario, Canada.

Previous studies (Can. J. Physiol. Pharm. 42: 719, 1964) demonstrated that plasma obtained from dogs 4 days after the rapid production of anaemia by a dextran-for-blood exchange contained maximal erythropoietic stimulating activity as compared to control plasma. Subsequent studies of the solid fraction of 4 day plasma obtained by lyophilization were suggestive that erythropoietic activity was diminished after freeze-drying. Therefore, the volatile fluid component of plasma was separated from the solids by lyophilization and was collected by condensation in a cold trap. Aliquots of both control and 4 day whole plasma from 6 dogs together with their solid and volatile fractions were assayed in starved rats. The volatile fraction of 4 day plasma as well as the solid fraction and the whole plasma stimulated reticulocytosis in starved rats. The active volatile fraction also stimulated reticulocytosis in polycythaemic mice with little effect on ^{59}Fe uptake. We therefore conclude that a reticulocytogenic volatile factor occurs in the plasma of anaemic dogs and that this factor has little effect on haemoglobin synthesis. The results of these experiments also raise the interesting possibility that highly volatile organic substances, that hitherto have been inadvertantly lost or overlooked, play important roles in other metabolic and endocrine systems. Supported by the Medical Research Council of Canada.

AVERAGED VOLUME-CONDUCTED POTENTIALS TO AUDITORY STIMULI IN THE CAT. Don L. Jewett. Univ. of Calif. Medical School, San Francisco, Calif.

In deeply anesthetized cats, potentials in various brain locations were averaged (up to 1500 times) relative to the tongue using an auditory "click" stimulus. Recording equipment included a Tektronix 2A61 in a 565 scope and a Mnemotron 400A averager. Four positive waves (P_1,P_2, etc.) were recorded from rostral (non-auditory) brain areas and from the scalp. P_1, which usually had a magnitude of 1-4 microvolts and a latency from the click to the start of the wave of 1.1 to 1.8 msec, occurred simultaneously with N_1 recorded at the round window and is probably generated by VIII. Other waves are larger than P_1 and are probably composites of both fast and slow wave activity, but each shows increased amplitude and/or inversion of polarity in the area of classical auditory pathways: P_2 near the cochlear nucleus, P_3 near the superior olive, P_4 in, above, and below the inferior colliculus. A P_5 wave was seen in association with the inferior colliculus, although there were no evoked potentials recorded from the medial geniculate or auditory cortex. Since averaging can allow widely spaced electrodes to detect neuronal activity at distances of 30 mm or more, one cannot assume that the potential generator is near the electrode and additional evidence is needed to localize the generator. However, the technique can be used to record auditory system responses with an electrode placed outside of the system.

(Work done partly at Yale University under NSF G-23584 and USPHS Fellowship NB-13,852.)

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM AND SODIUM EXCRETION DURING PREGNANCY IN THE DOG. J. Alan Johnson*, James O. Davis, Charles A. Robb*, John S. Baumber*, Edward H. Blaine*, and Edward G. Schneider*, Dept. of Physiology, University of Missouri School of Medicine, Columbia, Mo.

Studies of plasma renin in pregnant women have yielded variable results and the mechanisms regulating Na excretion have not been defined. The present observations were conducted in 37 dogs to allow extensive studies to be made. Daily Na balances revealed that about 40% of ingested Na was retained during the last half of pregnancy. For the entire group of pregnant dogs, plasma renin activity and aldosterone secretion were significantly higher than normal; however, some animals repeatedly showed normal values. GFR was significantly higher than normal by midpregnancy and decreased to postpartum levels during the last half of pregnancy. Desoxycorticosterone acetate (DOCA) administration to dogs in advanced pregnancy produced marked Na retention, but "escape" to the pre-DOCA Na excretion rate occurred. The data indicate that although increased activity of the renin-angiotensin-aldosterone system is sometimes present during pregnancy, the normal rates of aldosterone secretion in some dogs and the DOCA "escape" in pregnancy point to other sodium-retaining mechanisms. (Supported in part by NIH Grant HE-05810)

THE CHOLERETIC EFFECTS OF CHOLECYSTOKININ (CCK), GASTRIN II, AND CAERULEIN IN THE DOG. Rayford S. Jones* and Morton I. Grossman. V. A. Center and UCLA School of Medicine, Los Angeles, Calif.

Three mongrel dogs weighing 20 to 23 kg were prepared by cholecystectomy, ligation of the lesser pancreatic duct, insertion of a Thomas cannula into the duodenum opposite the opening of the common bile duct, and insertion of another Thomas cannula into the stomach. The common bile duct was cannulated through the duodenal cannula and the flow and composition of hepatic bile was observed during intravenous infusion of NaCl and sodium taurocholate solution with and without CCK, caerulein, or gastrin II. The gastric fistulas remained open during all experiments. Each of the peptides produced increased bile flow and bicarbonate concentration. CCK and caerulein produced increased bile chloride concentration. The slopes and positions of the lines relating bile flow to bicarbonate concentration and bile flow to chloride concentration during CCK and caerulein infusion were not different. Therefore CCK and caerulein produce similar bicarbonate as well as chloride concentrations at the same bile flow rates. Caerulein was 19.5 times more potent than CCK on a weight basis and 6.8 times more potent on a molar basis. Comparing data from a previous experiment, secretin was about 56 times more potent than CCK on a weight basis and about 44 times more potent on a molar basis. Gastrin II was the weakest choleretic of the peptides studied.

SUCCUS ENTERICUS COLLECTED FROM INTERVILLOUS BASINS OF GUINEA PIG JEJUNUM. Jin Soon Ju* and E. S. Nasset. University of California, Berkeley.

In the anesthetized (Dial-urethane) guinea pig a loop of upper jejunum was brought out intact and hung over a support just outside the belly wall. A 1-2 cm longitudinal slit opposite the mesentery exposed the mucosa, which was washed 2-3 times with warm isotonic galactose solution. Tissue dehydration was minimized by application of neutral mineral oil saturated with water, and normal body temperature was maintained. With the aid of dissecting microscope and micromanipulators a few villi were spread apart enough to reveal openings of 2-3 crypts of Lieberkühn lying in the intervillous basin. A glass micropipet was placed with its tip at the crypt openings. There was little or no observable resting secretion, but when an extract of dog gut mucosa was injected intramuscularly a fluid appeared in the intervillous basin. Several portions (0.1-0.2 µl) were collected and pooled for qualitative enzyme tests. Peptidase, sucrase and enterokinase were demonstrated. Pending quantitative enzyme assays and DNA determinations, we conclude that secretion of intestinal enzymes may be increased without a paralled increase in the shedding of mucosal cells from villous tips.
(Supported by NIH research grant AM 11108.)

DIFFERENTIAL VISUALLY RESPONDING UNITS IN THE SUPERIOR COLLICULUS OF THE SQUIRREL MONKEY. S. Kadoya*, L. R. Wolin* and L. C. Massopust, Jr. Cleveland Psychiatric Institute, Cleveland, Ohio.

To clarify the function of the superior colliculus in a primate (squirrel monkey), single neuronal responses to visual stimuli including color were investigated. Using tungsten microelectrodes, a total of 282 visual sensitive units in 74 tracks were analyzed. The monkeys were anesthetized with urethane-Nembutal and paralyzed by Flaxedil. Disc and fovea position were projected to the screen at a distance of 1.5 m. (A) All units in the superior colliculus had well organized laminar and columnar organization with retinotopic projection. 1. In the uppermost layer of the colliculus (stratum griseum superficiale [S.G.S.]) units responded to diffuse light throughout the entire visual field (57 units). 2. It was shown that a fair number of simple cells were located in the S.G.S. They consisted of 'on' (74) and 'off' (28) units, which were surrounded by an antagonistic peripheral field. Seventeen units had an 'on-off' center response with inhibitory "surround". 3. Below this layer including the stratum opticum, units tended to respond vigorously to movement rather than stationary stimuli and about half of these were directionally selective (56 units). (B) Forty-one units, 14.5% of the total number of responding cells, showed color coded responses for monochromatic stimuli of equal photopic luminosity. 1. Twenty-nine out of 41 units showed an 'on' response exclusively for long-wavelength stimuli with a surrounding inhibitory area. No spectrally opponent firing could be found even under selective chromatic adaptation. A few also showed blue 'on' or green 'on'. 2. Eight spectrally opponent units were found, six were red-green sensitive and two green-blue sensitive. (Supported by grant FR-05563 from N.I.H.)

IN VITRO STUDIES OF POTASSIUM EXCRETION BY THE TOAD BLADDER. F. T. Kallus*, J. C. Vanatta, W. H. Burke*, and E. A. Hetherington*. Physiol. Dept., Univ. of Tex. Southwestern Med. Sch. and Mobil Research and Development Corp., Field Research Laboratory. Dallas, Texas 75235

We have previously reported (Tex. Rep. Biol. Med. 27(2), 1969) in vivo studies showing that the urinary bladder per se of Bufo marinus excretes K. This is a report of in vitro studies which confirm the net excretion of K by the toad bladder. Simultaneous bi-directional fluxes of K were determined on the same bladder mounted between plastic chambers. Using K-42 labeled plasma and standard techniques, the S→M flux was determined, and 3% enriched K-40 in matched Ringer solution was used for measurement of the reverse flux with K-40 being determined by mass spectroscopy. All 7 pairs of fluxes from 4 bladders of K loaded toads showed a net S→M flux which averaged 36.1 ± 10.6 (± SEM) nanoeq/100mg/min ($P<0.01$). All 8 pairs of fluxes from 4 bladders of non-K loaded toads showed a net S→M flux which averaged 3.3 ± 0.7 nanoeq/100mg/min ($P<0.01$). Results in the K loaded group are significantly greater than in the non-K loaded group ($P=0.005$). These experiments were done with the bladder in the open-circuited condition. Similiar experiments (not to be reported) are planned to be done with the bladder in the short-circuited state to determine if this net excretory movement of K is against an electrochemical gradient.
(Supported by NIH grants HE 01574-14 and GM 34243-03)

EFFECT OF HYPOTHALAMIC DEAFFERENTATION AND ESTROGEN TREATMENT ON FSH RELEASE IN IMMATURE FEMALE PARABIOTIC RATS. S.P. Kalra*, M.E. Velasco* and C.H. Sawyer. University of California, Los Angeles, Calif. 90024.

Frontal deafferentations of the hypothalamus at two different levels were made with a Halász knife in 23-day old female rats. The anterior frontal cut (AFC) along the caudal border of the optic chiasma, severed the rostro-dorsal connections of the hypothalamus but left intact the anatomical links of the anterior hypothalamic area (AHA) with more posterior hypothalamic structures. The posterior frontal cut (PFC) was made behind AHA interrupting its posterior connections with the remaining hypothalamus. These animals were ovariectomized on day 24 and joined in parabiosis with intact female rats of same age on day 28. Daily estrogen or oil injections to operated animals were started immediately following parabiosis and continued until autopsy on day 34. FSH activity was assessed by ovarian augmentation produced by injecting 20 IU HCG/day to intact partners during the last three days of the experiment. A significant decrease in ovarian weight was found in PFC group when compared to sham operated controls; however no difference was observed in AFC group. Small doses of estrogen (0.5 μg/day) resulted in a significant decrease in ovarian weight in AFC group; same treatment was ineffective in sham controls. Higher doses of estrogen (1 μg/day) however, were equally effective in reducing ovarian weight in sham operated controls and in AFC pairs. These results suggest that the separation of AHA from its posterior connections prevents the postcastration rise of FSH release whereas interruption of rostro-dorsal connections of AHA allows normal postcastration increase of FSH. Furthermore, anterior deafferentation of the hypothalamus appears to result in increased sensitivity to estrogen. (Supported by NB 01162 and the Ford Foundation).

THIOCYANATE CONCENTRATION GRADIENT IN RABBIT BRAIN. Ralph J. Kaplan* and Michael Pollay. Division of Neurosurgery, Univ. of New Mexico School of Medicine, Albuquerque, New Mexico. 87106

The purpose of this study was to determine the thiocyanate concentration gradients in rabbit brain at low and high plasma thiocyanate (CNS^-) concentration levels. The effect of intraventricular DNP (.05 mM), ouabain (.01mM), and intravenous sodium iodide (NaI) on the concentration of CNS in brain was also studied. After establishing a constant concentration of CNS^- in plasma and cerebrospinal fluid (CSF), a core of brain tissue was taken from the wall of the lateral ventricle (ependymal to pial surface) and floor of fourth ventricle. The tissue was sectioned at intervals of .5 mm and analyzed for $CN^{35}S$ activity and blood volume (activity of ^{131}I-albumin). The results revealed a significant drop of ^{35}S activity (corrected for blood content) at both the ependymal and pial surfaces of the brain stem when the concentration of CNS^- in blood was less than 1.0mM. This was also found in the pial surface slice from the cerebrum, but not the ventricular surface slice where there was an apparent accumulation of CNS^-. It is tentatively proposed that a CNS^- pump is operating across the brain-CSF barrier (ventricular ependyma?) and CSF-blood barrier (choroidal ependyma) which serves to clear CNS^- and possibly other substances from brain tissue and CSF. Therefore, the rising concentration of CNS^- in brain at high plasma CNS^- level and in the presence of metabolic and competitive inhibitors is due to the accumulation of this ion in CSF and lessening of the sink effect between brain and CSF as well as the decreased effectiveness of the CNS^- pump operating between brain and CSF.

CARDIOVASCULAR EFFECTS OF SOME COMMON VASOACTIVE DRUGS. M. B. Kardon,* H. L. Stone, and E. J. Engelken,* USAF School of Aerospace Medicine, Brooks Air Force Base, Texas, 78235.

In an attempt to clarify the relationship of some of the more commonly used vasoactive drugs in the intact cardiovascular system, cardiac output and its distribution were measured in 10 mongrel dogs weighing an average of 28 Kg. Each was instrumented as follows: Doppler ultrasonic flow probes were placed around the ascending aorta, left circumflex coronary artery and left common carotid artery. Miniature semiconductor pressure cells were placed within the left ventricle and descending aorta. In addition, in 4 of the above dogs Doppler flow probes were placed around the left renal artery and superior mesenteric artery. The following drugs and doses were used: isoproterenol 1, 2, and 4 μg; levarterenol 2, 4, and 6 μg; and metaraminol 123, 247, and 494 μg/min; all injected intravenously in the conscious animal. Listed below are the values for average control blood flows, aortic pressure, heart rate and left ventricular max. dP/dt, % change from that control level for each parameter at the highest dose level of each drug used.

Parameter	Control	Isoproterenol	Levarterenol	Metaraminol
Aortic Flow	3443 ml/min	+24%	- 5%	-16%
Coronary Flow	52 ml/min	+83	+36	+ 8
Carotid Flow	178 ml/min	+27	-14	-15
Renal Flow	366 ml/min	-15	-30	--
Mesen. Flow	625 ml/min	+21	-40	--
Aortic Press.	96 mm Hg	-14	+27	+64
Heart Rate	96 BPM	+52	-10	-25
LV max. dP/dt	2797 mm Hg/sec	+40	+29	0

In terms of vascular resistance, isoproterenol decreased coronary resistance 53% and carotid resistance 33% while metaraminol increased coronary resistance 56% and carotid resistance 94%.

A DESCRIPTIVE CLASSIFICATION SYSTEM FOR UTERI OF PREPUBERTAL RATS. Barbara A. Kasprow (intr. by Joseph Thomas Velardo). Loyola University of Chicago-Stritch School of Medicine, Maywood, Ill

Utilizing sexually immature, Sprague-Dawley derived, albino rats of ages 23 - 42 days, it has been possible to characterize the several cytophysiological parameters of the uterus during its actively growing states. Such studies revealed that five distinctive classes of uteri could be so characterized.

The description of these comparative classes is as follows: uteri possessing low columnar luminal epithelium (CLE) up to a mean height of 20μ with mitotic figures absent or rare in CLE, stroma and circular muscle have been designated as class I uteri; uteri possessing CLE as described in I, above, but showing substantial mitotic activity in one, two or all three of the areas designated in class I, above, as class II uteri; uteri possessing CLE of mean height 20-30μ which does not exhibit vacuolar degeneration as class III uteri; uteri possessing CLE of mean height greater than 30μ and exhibiting either no vacuolar degeneration or only small vacuoles in a small minority of cells as class IV uteri; and uteri possessing CLE exhibiting moderate or extensive vacuolar degeneration irrespective of height as class V uteri.

Of notable interest, the cytological manifestations of uteri of the class I designation were quite parallel to those noted in uteri of ovariectomized rats; those of class III were in the main closely related to patterns observed in uteri of diestrous rats; and those of classes IV and V were reminiscent of the stages proestrus through metestrus of adult, cycling rats. (Supported by USPHS grant HD 03487-01 to Prof. J. T. Velardo)

FUNCTIONAL DEVELOPMENT OF THE TACTILE PAD RECEPTOR SYSTEM. H. Kasprzak* & D.N. Tapper. Dept. Physical Biol. & Sect. Neurobiology and Behavior, Cornell University, Ithaca, N.Y. 14850

Development of the structure and function of the tactile pad sensory unit of the cat was studied during the first seven weeks after birth. The epidermal pads are found in greatest density($400\pm32/cm^2$) at birth. The number of pads per primary afferent(1-4) is similar to that observed in the adult. The number of afferents and spatial distribution in the adult appear to be fixed at birth; as the animal grows, no significant change in the number of pads per anatomical region is observed. Pad diameters are small at birth($120\pm7\ \mu$) and approach the adult size ($210\pm10\ \mu$) by the 3rd week. Histological examination of pads reveals none or few Merkel cell-neurite complexes at birth, followed by a gradual increase during the first three weeks. Responses recorded from the primary afferent demonstrate that at birth the receptor is selectively sensitive to short duration mechanical pulses(4 msec) at the low displacements seen in the adult($5-20\ \mu$). The capacity for sustained response(1 sec,1:1 at 200Hz) is lowest at birth. An improvement in this capacity appears to be correlated with the occurrence of Merkel cells rather than with increase in fiber conduction velocity. In contrast to the evidence from regeneration studies(Iggo, 1963), these data suggest that Merkel cells are not important for selective sensitivity but contribute to sustained response. (Supported by USPHS, NIH Grant NB-07505-02).

THE DYNAMIC RELATION BETWEEN HYPOTHALAMIC TEMPERATURE AND PERIPHERAL BLOOD FLOW. K. G. Kastella* and A. C. Brown. Dept. of Physiology and Biophysics and Regional Primate Research Center, University of Washington, Seattle, Washington.

The purpose of this study was to determine the dynamic relationship between hypothalamic temperature and peripheral blood flow measured at the terminal portion of the descending aorta in the unanesthetized baboon (Papio anubis). Hypothalamic temperature was varied sinusoidally using a water-perfused thermode; the water temperature was controlled by a feedback control circuit. Brain temperature was monitored by two thermocouples, one located at the tip of the thermode and the other located in the hypothalamus 2 mm. from the thermode tip. A chronically implanted electromagnetic flow-transducer was used to measure blood flow. In some animals, arterial pressure was monitored using a chronic catheter, the tip of which was located in the ascending aorta. Blood flow is influenced markedly by hypothalamic temperature changes; an increase in hypothalamic temperature resulted in an increase in blood flow with the flow response lagging the change in hypothalamic temperature. An increase in blood flow can result from either an increase in arterial pressure or a decrease in peripheral resistance. Simultaneous measurements of pressure and flow indicate that flow changes did not result from pressure changes; hence flow changes were a result of a change in peripheral resistance. The relationship between thermode tip temperature and blood flow was approximated by a second order transfer function characterized by long time constants and a time delay. Changes in environmental temperature affect the value of the time constants but not the form of the transfer function.

EFFECTS OF DOSE LEVEL AND FREQUENCY OF D-PENICILLAMINE TREATMENT ON RETENTION OF ^{203}Hg-NEOHYDRIN IN RATS. Bergene Kawin and Edward E. Winters*, VA Hosp., Washington, D. C.

Early administration of d-penicillamine (P) is known to effectively decrease kidney retention of ^{203}Hg labeled neohydrin (HgN) in rats. In order to quantize the relation between dose level of P and HgN kidney retention and to measure the effectivities of multiple doses of P, 9 combinations of from 50 to 100 μmoles of P/kg bw administered intraperitoneally from 2 to 6 hr after intravenous injection of HgN were compared. The data obtained were treated statistically as a 3^2 factorial experiment. Analysis of the results showed that the linear component of dose level was significant, with $P \leq .01$. Interactions between dose level and frequency of treatment were not statistically significant. The estimated mean kidney retention of HgN corresponding to the combination of factor levels used was 22.9%. As calculated from this value and the factorial effect coefficients, the theoretical maximum response of kidney retention to P treatment was evaluated as 12.6% of the administered dose of HgN, and was located at a dose level of P of nearly 200 μmoles/kg bw. The optimum dose frequency was a single dose of P administered at 110 min after HgN injection. The use of 2 or 3 single doses increased the retention of HgN by kidney, but the HgN concentrations were less sensitive to changes in dose level of P. Supported by VA.

PARACARDIAC AUTONOMIC NERVE PATHWAYS. Michael P. Kaye*, John M. Geesbreght* and Walter C. Randall. Depts. of Physiology and Surgery Loyola University Medical Center and V.A.H., Hines, Illinois.

To delineate the pathways of autonomic fibers in the immediate paracardiac regions, experiments were performed on dogs placed on total cardio-pulmonary bypass. While recording myocardial contractile force (MCF) from both ventricles, the pulmonary artery, venae cavae and pulmonary veins and ventrolateral cervical cardiac nerve (VLCCN) were successively but randomly severed. Prior to and following each surgical intervention, both stellate ganglia and vagosympathetic trunks were electrically stimulated. Following transection of the pulmonary artery augmentation of MCF of the right ventricle did not occur during stellate stimulation. After severing both the pulmonary artery and (VLCCN), stellate stimulation caused no augmentation of MCF of either ventricle. The chronotropic effect of stellate stimulation was not significantly changed by this procedure and response to vagal stimulation remained almost identical to that during control stimulation. When the pulmonary veins and venae cavae were severed as the first procedure, vagal stimulation caused no change in heart rate or MCF. The effect of stellate stimulation on MCF was not significantly changed. These data indicate that fibers which effect positive inotropic influence on the ventricles travel primarily through peripulmonary tissues and the VLCCN. Sympathetic fibers exerting positive chronotropic influence travel to the sinus node mainly along the great veins although some chronotropic sympathetics are also found in the peripulmonary area. A large preponderance of parasympathetic fibers enter the atria along the superior vena cava and superior pulmonary veins.

(Supported by grants HE 08682 and O.S.A. Sprague Memorial Inst.)

CHARACTERISTICS OF MONOAMINE OXIDASE IN BRAIN AND LIVER OF A REPTILE. Tad D. Kelley* and Wilbur B. Quay. Dept. of Zoology, Univ. of Calif., Berkeley, Calif. 94720.

Little is known about the nature of monoamine oxidase (MAO) in vertebrates other than mammalian species. Subcellular distribution, pH optima, thermostability, and effects of monoamine oxidase inhibitors were determined for MAO in brain and liver of a lizard, Anolis carolinensis. As in mammals, MAO in this reptilian species was found to be associated primarily with the mitochondria, with a smaller, but definite percentage also in the microsomal fraction. Optimal pH for MAO in homogenates and mitochondrial and microsomal fractions of brain and liver was similar, about pH 10 with 5-hydroxytryptamine as the substrate. Differences in thermostability between brain and liver suggest that these tissues may possess different isozymal complements. The effects of two inhibitors of MAO, iproniazid and M&B 9302, on brain and liver MAO were studied in vitro. Inhibition curves for iproniazid were similar for brain and liver, but curves for inhibition by different concentrations of M&B 9302 suggested the possible presence of isozymes of MAO in these two tissues. (Supported in part by a NSF Science Faculty Fellowship and USPHS, NIH Grant NB-06296).

THE CANINE GASTRIC PACEMAKER. Keith A. Kelly* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The objective of this experiment was to determine if the canine gastric pacesetter potential (PP) originates on the greater or on the lesser curvature of the proximal stomach. In 6 dogs, the stomach was completely separated into greater-curvature (GC) and lesser-curvature (LC) halves by a longitudinal, orad-caudad, gastric bisection from the apex of the fundus to and through the pylorus. The bisection was immediately resutured, and 4 Ag-AgCl electrodes were implanted serially on each side of it. After recovery, the PP on the GC was found to arise in the orad corpus. Its rhythm was regular; its frequency was the same at all recording sites along the GC and was similar to that found in dogs with intact stomachs (mean, 5.2 cycles/min). The cycles were propagated aborally. The PP on the LC did not have a fixed site of origin, was often of irregular rhythm, and was not coupled to that of the GC. Its frequency (mean, 3.2 cycles/min) differed among LC recording sites and was always slower than that on the GC. The frequency of the LC-PP gradually increased after bisection and, by 14 days later, the rhythm was regular and was coupled to that on the GC in all dogs. However, the velocity of PP propagation remained slower on the LC (1.1 cm/sec) than on the GC (3.0 cm/sec). After the rhythms were again coupled, insulin-induced hypoglycemia increased the mean incidence of bursts of spikes superimposed on cycles of PP, on both GC and LC, from 25% to 90%. The data indicate that normally the dominant gastric pacemaker is located on the greater curvature of the orad corpus. Bisection caused only temporary interference with coupling. The mechanism of recovery is unknown. (Supported by NIH Grant AM-2015.)

THE REGRESSION AND REAPPEARANCE OF CORONARY COLLATERALS. Edward M. Khouri and Donald E. Gregg. Dept of Cardiorespiratory Diseases, Walter Reed Army Institute of Research, Washington, D. C.

The regression of coronary collaterals after release of an occlusion and their ability to reopen following reocclusion was studied in two groups of unanesthetized dogs. In one group, the circumflex occlusion was abrupt, with massive myocardial infarction; in the other group, the circumflex occlusion was gradual with only transient myocardial ischemia. Aortic blood pressure (ABP), left circumflex coronary artery branch flow (LCF), and ECG were monitored. Collateral development was evaluated by the increase in flow in the unoccluded descending branch of the left coronary artery (LDF) and in the peripheral coronary pressure (PCP), i.e., the pressure beyond the point of coronary artery occlusion. In both groups, following the initial occlusion, collateral flow indices increased gradually, and on the third day, LDF rose at least 50%, and PCP reached 50-60 mm Hg from a control range of 8-20 mm Hg. The occlusion was then released; LDF and PCP returned to control in 3 or 4 days. Following circumflex reocclusion, LDF and PCP began to rise immediately and in less than one hour had reached the values obtained on the third to fifth day after initial occlusion. The results suggest that coronary collaterals, once stimulated to open, become nonfunctional when the need is removed but may remain available and ready to supply the myocardium should a subsequent coronary insufficiency occur.

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council.

ELECTROPHYSIOLOGY OF THE ACOUSTIC REFLEX. M.I. Kitzes* and J.S. Buchwald. Dept. of Physiology and Brain Research Institute, UCLA, Los Angeles, Calif.

Contraction of the middle ear muscles to a sound stimulus, the acoustic reflex, is known to occur within 5 to 10 msec of the initiating sound stimulus. These contractions may be sustained for varying periods of time but repeated sound stimuli result in increasingly weak activation. As the central pathway of this reflex has not been studied electrophysiologically, it was the purpose of this study to describe the nuclei involved and their responses to procedures of single and repeated auditory stimulation. In acutely decerebrated or urethane anesthetized cats, extracellular recordings were carried out in the cochlear nucleus, trapezoid body, superior olivary complex, and motor nuclei of the middle ear muscles, i.e., the trigeminal motor nucleus innervating the tensor typmpani and the facial motor nucleus innervating the stapedius muscle. In response to click or 100 msec tones delivered through microphones attached to the stereotaxic ear bars, very fast evoked potentials were found in the trigeminal nucleus with latencies of 3-4 msec; the most prominent responses were elicited by contralateral stimulation. Similarly rapid evoked responses were recorded in the facial nucleus at latencies of 3 msec. As the cochlear nucleus responses to such auditory stimuli occur at approximately 2 msec, these data suggest mono- or pauci-synaptic relays between input and output stages of the acoustic reflex pathway. Attempts to identify intermediate synaptic relays are presently underway. In both motor nuclei progressive changes during acoustic habituation procedures are also currently undergoing investigation.

(Supported by USPHS Grants NB-05437 and NB-21935)

SEX HORMONE EFFECTS ON MEMORY CONSOLIDATION. W. R. Klemm. Department of Biology, Texas A&M University, College Station, Texas. 77843.

Memory consolidation was studied in both sexes of rats with conventional passive avoidance methods. Rats received a foot shock after stepping off an insulated platform, and then electroconvulsive shock was given in an attempt to cause amnesia. Retention testing occurred 24 hours later; retention was indicated by a rat staying on the platform to avoid foot shock.

Under certain conditions, females in estrus demonstrated better retention of the avoidance response than did females in diestrus. Retention was better in males than in females, even when the males were castrated as adults. Males that were castrated at weaning, however, performed very poorly, when they were trained and tested as adults. The amnesia in castrated weanlings was retrograde, as indicated by the decrease in amnesia with increasing foot shock-electroconvulsive shock intervals. No general activity differences were indicated by no-foot-shock controls or by the step-off latencies prior to initial foot shock.

The data are collectively interpreted to indicate that sex hormones are necessary for normal memory consolidation and that important ontogenetic influences exist.

ORTHODROMIC, ANTIDROMIC EXCITATION AND INTERACTIONS BETWEEN NEUROENDOCRINE CELLS OF THE HYPOTHALAMUS. K. Koizumi and H. Yamashita*. State University of New York, Downstate Medical Center, Brooklyn, N.Y.

In cats anesthetized with α-chloralose (70 mg/kg) or with Nembutal (40 mg/kg) recordings were made from supraoptic (SO) and paraventricular (PV) nuclei neurons in hypothalamus with glass capillary electrodes. In both SO and PV nuclei some cells were activated by stimulation of the neurohypophysis or stalk. Latencies of these action potentials were 10-20 msec. for SO neurons and 15-25 msec. for PV cells. When two stimuli were given within 5-10 msec. intervals, response to the second stimulus was blocked and only a small spike, the initial segment spike, was seen. Repetitive stimulation of the neurohypophysis at a rate of 100/sec. still evoked neuron firing in SO and PV nuclei. These and other evidence indicate that these hypothalamic neurons were antidromically excited by impulses set up in nerve fibers in stalk or neurohypophysis; thus they were identified as neuroendocrine cells. Some neuroendocrine cells show spontaneous activity. Stimulation of the ipsilateral septal area and the anterior commissure evoked excitation of certain neuroendocrine cells in both SO and PV nuclei. On a few occasions these stimuli inhibited antidromic firing and spontaneous discharge of neuroendocrine cells for 100-250 msec. Interaction between neuroendocrine cells in SO and PV nuclei was also observed. Cells in the SO nuclei were excited by stimulation of PV nuclei or vice versa with latencies longer than that of antidromic potentials. In certain cases these orthodromically evoked potentials in neuroendocrine cells exerted an inhibitory influence on their excitation by antidromic stimuli for 100 msec. Evidence was found indicating existence of recurrent collaterals in neuroendocrine cells.

(Supported byUSPHS grant NB-6537-03 and NB-847-14)

GASTRIC SECRETION INHIBITION IN CHICKENS. Eszter Kokas and W. D. Brunson, Jr.* Dept. of Physiol., Univ. of North Carolina, School of Med., Chapel Hill, N. C.

In acute experiments in chickens it was shown that slight duodenal distension with air, saline or 0.4% HCl inhibited basal, histamine- and gastrin- (pentagastrin) stimulated gastric secretion. By distension with procaine this inhibitory effect was abolished. Hexamethonium blocked basal gastric secretion and the stimulatory effect of histamine and gastrin. By chronic double vagotomy of the proventriculus the inhibitory effect of duodenal distension was greatly diminished. Enterogastrone (3-74T, #1) and secretin inhibited gastric secretion similarly to duodenal distension, except their action was shorter-lasting. Cholecystokinin-pancreozymin and serotonin inhibited basal gastric secretion, but did not influence the stimulatoty effect of histamine and gastrin. The results suggested that gastric inhibition following duodenal distension is regulated partly by neural and partly by hormonal mechanisms. Supported by USPHS Grant No. AM04675.

Effects of Phloretin and Phlorizin on the Uptake of D-Xylose in Isolated, Perfused, Contracting Rat Diaphragm. Ralph C. Kolbeck* and H. Mead Cavert. Univ. of Minnesota Medical School, Minneapolis, Minnesota.

The effects of phloretin and phlorizin on the uptake of a non-metabolized sugar have been studied in the isolated, perfused, intact rat diaphragm muscle. During perfusion for 30 minutes with Krebs solution containing 7.3 mM D-xylose -1-C^{14}, the muscle was maintained at rest or was stimulated to contract 2.5, 5.0, or 7.5 times per second, with or without the addition of 1.0 mU/ml insulin. In the non-insulinized system, the ratio of intracellular to extracellular concentration of D-xylose, expressed as a percentage (f), increased progressively as the rate of repetitive muscle contraction was elevated. In resting muscle, without added insulin, f decreased in the presence of either phloretin or phlorizin. On a molar basis, phloretin exerted a stronger inhibitory effect than phlorizin. For example, 1.0 mM phlorizin was required to produce the same degree of inhibition, 82% less than the control value of f at rest, as that obtained with 0.2 mM phloretin. In resting diaphragm, both phlorizin and phloretin reduced the insulin-insensitive component of sugar transport, but the two inhibitors appeared to act differently on the insulin-stimulated carrier system. When the inhibitor was added in a concentration previously shown to produce maximal inhibition of D-xylose uptake at rest, either phlorizin or phloretin reduced by about 70% the stimulatory effect of repetitive muscle contraction (at 7.5 per second). Differential inhibitory effects evoked by phlorizin and phloretin suggest that insulin and contractile activity may involve different pathways in modifying D-xylose transport in perfused rat diaphragm muscle. (Supported by USPHS, NIH grants GM 07305 and HE 10956).

HORMONAL EFFECTS ON THE CONTRACTILE AND SERIES ELASTIC COMPONENTS OF RAT MYOCARDIUM. B. Korecky, R. Minelli* Department of Physiology, University of Ottawa, Canada.

It was shown in our unpublished experiments that in rats after hypophysectomy (Hx) the maximum developed isometric tension (MT) of isolated papillary muscle decreased. The maximum (dT/dt) and mean ($\Delta T/\Delta t$) rates of tension development, were also decreased and the time to maximum tension (TMT) was prolonged. Growth hormone (GH) administered after Hx had little effect on the above described parameters, while thyroxine (T4) restored them to normal. Since after Hx the decrease in dT/dt and $\Delta T/\Delta t$ was larger than that in MT it was felt, that the velocity rather than the force of contraction was impaired. To prove this the force-velocity (FV) relationship of isotonically contracting papillary muscle was determined in five groups of animals: 1) normal, 2) hypophysectomised (Hx), 3) Hx subsequently treated with GH, 4) Hx subsequently treated with T4, 5) Hx subsequently treated with GH+T4 simultanecusly. After hypophysectomy the maximum velocity of shortening (Vmax) was more depressed than the maximum developed tension (Po) and the slope of the FV curve was changed. GH had no effect but T4 restored both Vmax and Po to normal. T4 and GH administered simultaneously had the same effect as T4 alone. It seems that T4 is the missing hormone which after Hx restores the function of the contractile element to normal. Since the decrease of Vmax after Hx was larger than that of dT/dt, a change in series elasticity (dp/dl) was postulated. dp/dl calculated from isotonic afterloaded contractions, was found to be significantly higher after Hx and was returned to normal after T4 treatment.

Supported by the Medical Research Council of Canada and Ontario Heart Foundation.

INHIBITION OF PURKINJE CELLS IN THE FROG CEREBELLAR CORTEX

Henri Korn and Donald S. Faber (intr. by J. C. Eccles) SUNYAB Buffalo, New York

Experiments were performed on decerebrate bullfrogs (Rana Catesbiana) which were curarized and artificially respirated. Bipolar stimulating electrodes and glass micropipettes were used. When recording at the level of the Purkinje cells (PC), white matter (WM) stimulation produces a short latency negative field potential which is generated by antidromic invasion of the PC. This field is inverted in the molecular layer. A conditioning parallel fiber (Loc) stimulus reduces the amplitude of these antidromic fields for up to 300 to 400 msec, indicating a diminished antidromic invasion. That this decrease in responsiveness of the PC is not simply due to a post-activation depression of these cells is shown by the observation that after a conditioning antidromic invasion there is full recovery in 40 to 50 msec. This corresponds to the total duration of the depression reported by Llinas and Bloedel (Science 1967 155 601-603) who did not observe the later inhibitory depression. Investigations of discharge patterns of single PC (identified antidromically and/or by typical climbing fiber responses) have provided additional evidence for the long duration inhibition. Post-stimulus time histograms have revealed a complete suppression of all spontaneous discharges for periods up to 100 to 250 msec after a parallel fiber volley, with total recovery often requiring 350 msec. This evidence for inhibition in the frog cerebellar cortex is consistent with the presence of stellate cells in the molecular layer as suggested by Cajal (1911) and recently confirmed by C. Sotelo (personal communication) these neurons being inhibitory in the cat (Eccles, Ito, and Szentagothai, The Cerebellum as a Neuronal Machine, Springer, (1967).

EFFECTS OF HOMEOSTATIC ACTIVATION ON A PSYCHOPHYSIOLOGICAL RESPONSE, B. Korol*, G.J. Yaffe* and K.M. Kleinman* (Sponsor: P. Nathan), Cochran V.A. Hosp., St. Louis Univ. Med. Sch., and Univ. of Mo., St. Louis, Mo.

In humans, homeostatic tone is presumed to be maximal in the upright and minimal in the supine position. This study examined the effects of homeostatic activation, accomplished by body positional change from horizontal (H) to 10° from vertical (V) on the basal level and response amplitudes of the galvanic skin response (GSR) to an innocuous repetitive stimulus. The subjects (Ss) were 18 caucasian males 17 to 30 years old. Nine Ss initiated in the H position received 2-sec. 1000 Hz, 70 db tones through earphones every 20 sec. for 29 trials, followed by positional change (over 1-min) to V, and after 5 min rest the tones were again repeated for 29 trials. The other 9 Ss were treated in a reciprocal positional order. Mean H basal GSR level was significantly higher than the mean V basal level. Over the first 7 trials, the tone-induced GSR responses were of a significantly greater amplitude in the H position. Although the rates of diminished response amplitudes to the repetitive tones were not different, the number of trials to habituation occurred later in the H position. Further analysis revealed that Ss in V position showed greater frequency in responding over trials, although response amplitude was reduced. The results illustrate that the interoceptive stimulus of change in body position influences both the basal GSR level as well as GSR responsivity to an exteroceptive stimulus. Thus, homeostasis and its physiological implications should be considered in the evaluation of psychophysiological phenomena.

(Supported in part by NSF Grant GB-14531)

A FUNCTIONAL RELATIONSHIP BETWEEN THE PARS INTERMEDIA AND ACTH SECRETION IN THE RAT. J. Kraicer, J. L. Gosbee*, A. J. Kastin and A. V. Schally, Department of Physiology, Queen's University, Kingston, Ontario, and Veterans Administration Hospital and Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana.

Uncertainty still exists as to the cellular site of ACTH production in the rat adenohypophysis. The incorporation of thymidine-H^3 into the various cell types of the adenohypophysis has been studied autoradiographically one month following adrenalectomy, when ACTH secretion is greatly increased and one month following the daily administration of cortisol, when ACTH secretion is suppressed. Using a dual microscope system with a comparison tube, sections stained with Herlant's tetrachrome or Alcian blue-PAS-Orange G were superimposed on adjacent sections processed for autoradiography. Only one cell type, restricted to the pars intermedia, demonstrated an increase in label index following adrenalectomy and a decrease in label index following cortisol administration. Following adrenalectomy, the volume of only the pars intermedia was increased. Histological changes were restricted to the pars intermedia. These changes do not simply reflect alterations in MSH secretion since no changes in plasma or hypophysial MSH content were found. We conclude that there is a functional relationship between the pars intermedia and ACTH secretion.

INTRAPULMONARY ARTERY BALLOON PUMPING (ASSIST TO THE RIGHT VENTRICLE). A. Kralios*, C.S. Kwan-Gett*, Risto Collan*, S.D. Moulopoulos*, and W.J. Kolff. Div. of Artif. Organs, University of Utah, Salt Lake City, Utah.

Knowing the high compliance of the pulmonary arterial vascular bed, some investigators predicted that application of the concept of intra-aortic balloon pumping in the pulmonary artery would have no hemodynamic effect. We have demonstrated that it does have effect. In ten sheep, diffuse massive pulmonary embolism was caused by injection of a suspension of corn starch or homologous small thrombi in a peripheral vein, until signs of acute pulmonary hypertension and right ventricular failure (high atrial pressure, low left atrial and aortic pressure, and low cardiac output) appeared. An especially made balloon was introduced via the right jugular vein in the trunk and one of the main branches of the pulmonary artery. Diastolic pumping was accomplished by proper timing and duration of the inflation of the balloon by means of an R-wave detector and programmer, driving a three way solenoid valve. Within a few minutes, the effect of the balloon pumping appeared as a decrease of the right atrial pressure and increase of the cardiac output. Increase of the right ventricular peak systolic, left atrial and aortic pressure were also noticed. The oxygenation of the arterial blood remained normal throughout the procedure and the venous blood oxygenation which had decreased after the pulmonary embolization returned to normal. A few premature atrial extrasystoles seem to be caused by the presence of the connecting tube in the right cardiac chambers rather than the balloon itself. The procedure could probably be of help in cases of acute diffuse pulmonary embolism. Its effect on chronic pulmonary hypertension (cor pulmonale) is to be studied.

CORRELATION OF UREA CYCLE ENZYME ACTIVITY AND UREA SYNTHESIS. J.W. Kramer* and R.A. Freedland. Department of Physiological Sciences, School of Veterinary Medicine, University of California, Davis, Calif.

Rates of urea synthesis from NH_4Cl, in the absence and presence of added ornithine, were obtained from perfused rat livers. In order to alter urea cycle enzyme activity donor rats were fed diets containing different levels of protein (0, 25, 90 percent) and some groups were treated with thyroxine (1 mg/day for 5 days) or cortisol acetate (5 mg/day for 5 days). There was good correlation between NH_3 disappearance and urea synthesis at low rates of urea synthesis. Levels of urea cycle enzyme activity correlated well with rates of urea synthesis in the absence of exogenous ornithine. However, when faster rates of urea synthesis were obtained in the presence of exogenous ornithine there was less correlation. The addition of exogenous ornithine increased rates of urea synthesis considerably when compared to rates with NH_4Cl alone with livers having lower enzyme activity. However rates were only moderately increased by addition of exogenous ornithine with livers having high enzyme activity. In livers with normal enzyme activity, from rats fed a 25% protein diet, and high enzyme activity, from rats fed a 25% protein diet and treated with cortisol, rates of urea synthesis with exogenous ornithine are similar. Therefore, it appears that a factor or factors in addition to ornithine concentration or enzyme activity may be rate limiting for maximal urea synthesis.

EFFECT OF INTERMITTENT EXPOSURE TO SEVERE COLD ON METABOLIC RESPONSE TO NOREPINEPHRINE (NE) IN RATS. M. B. Kreider (Intro. by James A. Vogel), U. S. Army Research Institute of Environmental Medicine, Natick, Mass.

Brief daily exposures (1-4 hrs) of clipped rats to -10 C resulted in an increase of up to 220 per cent by day 4 in the time required for rectal temperature (T_r) to drop from a normal to a hypothermic level (32 C). The purpose of the study reported here was to compare this adaptive phenomenon, as measured by increased metabolic sensitivity to exogenous NE, with the response to a standard acclimating temperature. Four groups of 11 male Sprague Dawley rats weighing 124 ± 2.1 gm (S.E.) were exposed to either: (1) control ambient temperatures (25 C); (2) 3 C continuously for 5 days; (3) 3 C continuously for 14 days; (4) -10 C daily for 5 days, clipped, until T_r = 32 C (1 to 4 hrs). On the day following the end of the exposure periods, differences in $\dot{V}_{O_2}$ before and after the injection of NE (0.3 mg/kg., subcut.) under anesthetization with 250 mg/kg (i.p.) of Na barbital was determined to be 10.8 ± 1.5, 14.8 ± 1.5, 17.5 ± 1.0 and 19.7 ± 1.7 ml/min/kg for Groups 1 to 4. By analysis of variance, Groups 3 and 4 were significantly different from Group 1 ($P<.01$) but not from each other. Group 2 was not significantly different from Groups 3 or 4. Daily exposures of Group 4 averaged 111 ± 10, 125 ± 11, 144 ± 13, 188 ± 17, and 197 ± 22 minutes on days 1 to 5 for a total of 765 minutes which is less than 0.2 of the time required to produce the same response in Group 3. Thus rats exposed for several hours daily to severe cold for 5 days developed the same response to NE which required 5 to 14 days at a standard acclimating temperature.

OVERDRIVE SUPPRESSION OF IDIOVENTRICULAR PACEMAKERS IN ISOLATED CANINE HEARTS. **Daniel J. Krellenstein*, Michael B. Pliam*, Mario Vassalle and Chandler McC. Brooks. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York, U.S.A.**

Driving idioventricular pacemakers at a rate higher than their intrinsic rate causes a temporary suppression of pacemaker activity when the drive is discontinued. The characteristics and mechanism of this phenomenon were investigated in 50 puppy hearts perfused with Tyrode's solution using a modified Langendorff preparation. The relationship of overdrive suppression to overdrive rate was sigmoidal between driving rates of 30 to 240/min. With increasing duration of overdrive, there was a maximum inhibition at 3 minutes of overdrive, followed by a slight decline and plateau. The relationship between idioventricular rate and pause duration was linear. During overdrive at 240/min for 1 minute there was a net loss of myocardial K^+ (10.8 ± 1.8 μEq) which was followed by a gain of K^+ during the post-drive period. When the drive was continued for 5 minutes, the coronary sinus $[K^+]$ returned toward control but a small loss of K^+ continued. On cessation of the 5-minute overdrive, the $[K^+]_{CS}$ still fell well below control. The pH of the coronary sinus effluent decreased during the overdrive period and slowly returned toward control after the drive was stopped. In conclusion, overdrive suppression of idioventricular pacemakers has been shown to be determined by: 1) overdrive rate; 2) overdrive duration; and 3) intrinsic automaticity. Also, ionic shifts with overdriving are likely to participate in the mechanism of the suppression and subsequent restoration of pacemaker activity. **(Supported by NIH Grant HE 10070)**

VENTILATORY RESPONSE TO 5% CO_2 AFTER SELECTIVE ABLATION OF RESPIRATORY FEEDBACK MECHANISMS. A.J. Krieger*, H.D. Christensen* and S.C. Wang, Columbia University, New York, N.Y.

The ventilatory response to 5% CO_2 in oxygen was assessed in 58 midcollicular decerebrate cats after selective ablation of various feedback circuits: bilateral vagotomy, midpontine transection, and bilateral ventrolateral or partial dorsal cervical cord lesions. Bilateral vagotomy and ventrolateral cord lesions abolished the rate increase in response to CO_2, whereas midpontine transection and lesions in the dorsal cord showed the same percentage response as control. The tidal volume response to CO_2 varied with each preparation. With bilateral vagotomy the increase was 140% over the control, with midpontine transection 35%, with ventrolateral cord lesions 80%, and with dorsal cord lesions 100%. The slope of the CO_2 ventilation response curve ($\Delta V_E / \Delta P_{aCO_2}$) showed no alteration compared to control values following bilateral vagotomy, midpontine transection or dorsal cord lesions, and a 62.5% decrease with a marked shift to the right following bilateral ventrolateral cord lesions. Small discrete bilateral ventrolateral cord lesions which had little effect on spontaneous respiration had profound changes on rate regulation, as well as pH and P_{aCO_2} in response to CO_2 inhalation. This study suggests that another afferent pathway exists in the ventrolateral cervical cord for the regulation of normal respiration. Its mechanism of action has some features in common with both the known pneumotaxic and vagal mechanisms. (Supported by USPHS Grants NB05511, NB05173 and NB00031).

CARDIOVASCULAR RESPONSES TO HEMORRHAGE UNDER PULSATILE AND NONPULSATILE FORCINGS OF THE CAROTID SINUS. M. Kumada*, R.M. Schmidt*, K.S. Tan*, and K. Sagawa. Departments of Biomedical Engineering and Surgery, Case Western Reserve University, Cleveland, Ohio.

To evaluate the quantitative importance of the rate sensitivity of the carotid sinus reflex following hemorrhage, anesthetized dogs were subjected to rapid 20% blood loss under one of two separate forcings of the sinus: (A) the animal's own pulsatile arterial pressure or (B) a nonpulsatile pressure which followed the animal's mean pressure through servocontrol. Mean arterial pressure (MAP) and cardiac output per kilogram (CO) were studied and mean values 8 to 14 minutes after hemorrhage are presented as percent change from control; standard errors have been calculated.

	CONTROL VALUE		% CHANGE AFTER HEMORRHAGE	
	MAP (mmHg)	CO (cc/min/kg)	MAP (%)	CO (%)
Vagi Intact				
Normal	130±5	92±9	-11±2	-33±9
Depulsated	135±4	98±5	- 7±3	-25±5
Vagi Severed				
Normal	128±2	94±11	-16±2	-36±11
Depulsated	134±5	104±12	- 9±5	-34±12

A significantly greater fall in MAP occurred under the normal, pulsatile condition ($P<0.05$, paired t-test). Thus, in the anesthetized dog, the pulsatile component of intra sinus pressure does not appear to contribute positively to the carotid sinus reflex compensation of MAP and CO following a 20% hemorrhage. (Supported by PHS-NIH - HE 12389)

VOLTAGE CLAMPING OF SMOOTH MUSCLE. M. Kumamoto* and L. Horn. New Jersey College of Medicine and Dentistry, Jersey City, N.J.

A sucrose-gap voltage clamping technique, modified from Narahashi and Anderson, has been used with smooth muscle preparations from the superior mesenteric vein and taenia coli of the guinea pig. The electrical activities of both preparations are quite unaffected by tetrodotoxin (TTX) in concentrations of 10^{-6} g/ml, which is known to inhibit the voltage dependent increase in specific sodium conductance in the squid giant axon and skeletal muscle. Manganese in concentrations of $5 \cdot 10^{-4}$M has been shown to drastically reduce the calcium permeability and also to render our smooth muscle preparations inexcitable. Our clamping experiments on taenia coli show that Mn^{++} inhibits the early transient current, but has little or no effect on the steady state current, suggesting the possibility that calcium plays a role as a current carrying ion during the early transient phase. Experiments with TTX are underway. The compatibility of our voltage clamp data with the conventional current carrying mechanisms during the action potential will be discussed. (This research was supported by a grant from the New Jersey Heart Association and Contract DADA 17-68-C-8058 with the U. S. Army Medical Research and Development Command).

EFFECTS OF DESFERRIOXAMINE ON SERUM IRON, IRON-BINDING CAPACITY, HEMOGLOBIN, ERYTHROCYTE NUMBER, PACKED CELL VOLUME, AND URINARY IRON EXCRETION OF THE PIG. Jerry P. Kunesh* and Melvin J. Swenson, Department of Physiology and Pharmacology, Iowa State University, Ames, Iowa 50010.

Eight pigs having iron-deficiency anemia and eight pigs which were not iron deficient were given I.M. injections of 200 mg. of desferrioxamine for 18 consecutive days starting at 18 days of age. By 35 days of age significant differences between non-anemic, desferrioxamine-treated pigs and non-anemic controls could be demonstrated in R.B.C., P.C.V., hemoglobin levels, serum iron, and iron binding capacity. No significant differences could be demonstrated between anemic, iron-deficient, desferrioxamine-treated pigs and anemic, iron-deficient controls except that serum iron levels were significantly lowered after 17 days of desferrioxamine treatment. Average urinary iron excretion was determined on 3 iron-deficient and 3 iron-treated pigs. Average urine iron loss was shown to be 7 µg per day in iron-deficient pigs while urine of iron-treated pigs contained 18 µg per day. The effects of desferrioxamine on urinary iron excretion were studied on 8 non-anemic, iron-treated pigs. Urinary iron excretion increased to 10.5 times the preinjection levels on the first day following desferrioxamine treatment and gradually decreased to 2 times by the 18th day. The greatest excretion occurred during the 10-hour period following treatment. Postmortem examination of 6 pigs treated with desferrioxamine revealed no pathologic changes except those associated with anemia. The results indicate that desferrioxamine is an effective iron-chelating agent in the pig.

(Supported in part by N.I.H. Grant HE-05228 and by CIBA Pharmaceutical Company.)

ALPHA HELIX AND HALOTHANE. L.H. Laasberg* and J. Hedley-Whyte. Dept. of Anesthesia, Beth Israel Hospital and Harvard Med. School, Boston, Mass.

Solubility of halothane in blood varies in a complex manner with Hct and plasma protein con. To test our hypothesis that a major determinant of halothane-protein interaction is α-helical content we investigated the solubility of halothane in aqueous solutions of amino acids, polypeptides and proteins with G.L.C. Four g of these compounds/100 ml Krebs Henseleit solution and/or 0.2 M NaCl were equilibrated with halothane in air (29.7 mg/100 ml). The pH of protein solutions was kept at 7.37-7.44. Correlation coefficient (r) between λ-halothane and the α-helical content of human serum albumin, β-lactoglobulin, γ-globulin, fibrinogen, hemoglobin, lysozyme, ribonuclease and myoglobin was +0.59 at 25 C, +0.65 at 30 C and +0.53 at 37 C. At pH 11.5 poly-l-lysine has an α-helical conformation, at pH 1.8 it is random coil; at pH 11.5 poly-l-glutamic acid is random coil, at pH 4.5 it is α-helix. The λ-Hal ± SEM for poly-l-glutamic acid was 0.83 ± 0.02 (R.C.) v. 1.29 ± 0.02 (αH) at 20 C, 0.67 ± 0.01 (R.C.) v. 1.02 ± 0.02 (αH) at 25 C, 0.59 ± 0.01 (R.C.) v. 0.75 ± 0.01 (αH) at 30 C and 0.42 ± 0.01 (R.C.) v. 0.52 ± 0.01 (αH) at 37 C. For polylysine the corresponding values were 1.51 ± 0.01 (R.C.) v. 3.05 ± 0.01 (αH) at 20 C, 1.15 ± 0.01 (R.C.) v. 2.34 ± 0.02 (αH) at 25 C, 1.03 ± 0.01 (R.C.) v. 1.59 ± 0.01 (αH) at 30 C and 0.91 ± 0.01 (R.C.) v. 1.23 ± 0.01 (αH) at 37 C.

		λ-Halothane for Monomers			
Amino acid	pH	20 C	25 C	30 C	37 C
L- glutamic	4.5	0.97 ± 0.01	0.82 ± 0.02	0.62 ± 0.01	0.42 ± 0.01
L- glutamic	11.5	0.93 ± 0.02	0.61 ± 0.01	0.53 ± 0.01	0.43 ± 0.01
L- lysine	1.8	1.32 ± 0.02	1.10 ± 0.01	0.88 ± 0.01	0.58 ± 0.01
L- lysine	11.5	1.15 ± 0.01	0.90 ± 0.01	0.75 ± 0.01	0.53 ± 0.01

We conclude that the α-helical pitch of 5.44 Å allows halothane to fit between two nonpolar amino acid residues. Supported by USPHS GM 15904.

URETERAL PERISTALSIS DURING CONVULSIONS. P. Labay, ° R. H. Wilkinson, Jr., ° S. Boyarsky, and M. J. Short. ° Duke Univ. School of Med., Durham, N. C.

Convulsions were induced electrically 53 times in 11 dogs with 170 volts AC to the frontal regions for 1 sec. Ureteral function was monitored by the catheter-transducer-electronic recorder technique in dogs after bladder explantation. Urine flow was monitored by a suction collector. A typical grand mal seizure lasted 1 min. and was followed by hyperventilation for 2-5 min. Return of consciousness seemed to be complete in 1 hour. At the start of the convulsion, peristaltic rate accelerated 3 times and the ureteral intraluminal pressure rose. This was followed by slowing, cessation, or intermittency for several minutes. Recovery was complete in 30 min. Ureteral and renographic effects were dissociated. The ureters responded asymmetrically and the manifestations of a convulsion varied on repetition but were basically consistent. Ureteral response was not significantly altered by Propranolol 5 mgm/kg IV (7 convulsions), Phenoxybenzamine 5 mgm/kg IV (7 convulsions), Atropine 1 mgm/kg IV (6 convulsions). Blocking drugs were anticholinergic, anti-alpha-adrenergic, and anti-beta-adrenergic. Sympathico-adrenal discharge during physiologic crisis lowers renal blood flow, urinary secretion, and alters the renogram and the intravenous urogram. Ureteral response seems to travel a parallel nervous pathway susceptible to the same origins. Incontinence associated with seizures is due to bladder contraction, whereas the diuresis observed in these animals represented a return of urinary secretion.

EXPERIMENTAL VARIATIONS IN THE CHARACTERISTIC IMPEDANCE OF DOG FEMORAL ARTERY. Gerald F. Lackey, Robert F. Bond, and Janet A. Taxis*. Bowman Gray Sch. Med., Winston-Salem, N. C.

A technique has been previously described for the separation of incident and reflected components of pressure in rubber tube model systems (The Physiologist, 9: 225, Aug. 1966). The technique requires knowledge of the characteristic impedance (Z_o) of the vessel at the point of pressure and flow measurement. The Z_o was measured by calculating the complex ratio of pulsatile pressure to flow under reflection-free conditions. In the model system this was accomplished by studying single isolated pulses that were manually generated. In the dog femoral artery the Z_o was determined from pressure and flow data taken during the first portion of the pulses before appreciable reflections could return from the periphery to the point of measurement, the femoral artery. Experimental procedures designed to alter the peripheral vascular impedance, and thus the amount of reflections, also affected the Z_o. These procedures were a) bilateral carotid occlusion, b) methacholine (5 μgm i.a.), c) norepinephrine (6 μgm i.a.), and d) intra-arterial air embolism (5 cc). It is postulated that these effects are either 1) direct pharmacological or neural effects on the femoral artery, or 2) indirect effects on vessel geometry and wall tension due to changes in the mean blood pressure. (Supported by NIH grants HE-5392 and HE-487.)

INHIBITION BY DEXAMETHASONE OF CRF-INDUCED ACTH RELEASE FOLLOWING INTRAPITUITARY INJECTIONS OF CRF IN CONSCIOUS DOGS. M. L'age*, A. Gonzales-Luque* and F. E. Yates, Dept. of Physiology, Stanford Univ., California.

Male mongrel dogs (approx. 24 kg BW) were prepared with a modified Hume-Nelson snare and cannula for collection of adrenal venous blood. In addition, an indwelling cannula (No. 30 needle, with bevel) was placed into the anterior pituitary from the ventral surface, and fixed to the basisphenoid bone. The cannula was connected to PE tubing No. 10, which was led through the lateral wall of the nasopharynx, then subcutaneously to the vertex of the skull. It was brought through the skin at that point. Crude ovine CRF prepared by A. P. S. Dhariwal was injected into the pituitary in a volume of 42 μl, over 25 minutes. The doses used were ineffective intravenously. Sharp rises in cortisol secretion from the adrenal occurred almost immediately. This CRF response was totally inhibited 3-6 hours after a 4 mg/dog subcutaneous dose of Dexamethasone phosphate (Dex). The inhibition was gone 15-24 hours after the Dex. Apparently the anterior pituitary may be a corticosteroid feedback point in the hypothalamic-pituitary-adrenal system. (Supported by USPHS Grant AM 04612, and a Grant from Deutsche Forschungsgemeinschaft, Germany to M. L'age)

THE RUBRO-OLIVO-CEREBELLO-RUBRAL LOOP AND POSTURAL TREMOR IN THE MONKEY. Louis Larochelle*, Paul Bédard* and Louis J. Poirier. Lab. Neuropsychiatrie exp., Dépt Physiologie, Université Laval, Québec.

Ventromedial tegmental lesions simultaneously involving the corresponding rubral and tegmental descending pathways, cerebellofugal ascending fibers and ascending monoaminergic pathways are associated with sustained parkinsonian tremor of the contralateral limbs in the monkey. Under such circumstances, harmaline greatly exaggerates tremor. Harmaline does not induce tremor in monkeys with isolated lesions of the ascending dopaminergic and serotoninergic fibers ending in the striatum. Tremor of the contralateral limbs may be induced by harmaline in monkeys with unilateral lesions involving either the small-celled red nucleus, its descending efferent fibers in the central tegmental tract or their area of termination in the ventrolateral area of the principal olivary nucleus. Harmaline may evoke tremor in the ipsilateral limbs of monkeys with unilateral lesions involving either the olivocerebellar fibers (contralaterally to their origin) and/or the cerebellar lateral nuclei or the superior cerebellar peduncle. Under such conditions, alpha-methyl-dopa also induces tremor. In the light of the above data, postural tremor appears to result from the combined involvement of ascending monoaminergic pathways ending in the striatum (which apparently are pharmacologically interrupted by harmaline and possibly by alpha-methyl-dopa) and of the rubro-olivo-cerebello-rubral loop and related pathways.

(Supported by grants from the Medical Research Council of Canada).

EFFECT OF ACUTE HYPOXIA ON LUNG DIFFUSING CAPACITY FOR CO (D_{CO}) AND PULMONARY CAPILLARY BLOOD FLOW ($\dot{Q}_C$). W.H. Lawson Jr. SUNY, Brooklyn, New York.

Simultaneous measurements of D_{CO} and $\dot{Q}_C$, C_2H_2, were made with the 10 sec. breathholding method in 6 normal seated humans breathing 8.5% O_2 for 3 to 10 min. Hypoxia will increase D_{CO}, apart from any effect it has on the pulmonary circulation, by increasing the rate that CO reacts with erythrocytes; and we attempted to eliminate this variable by measuring control D_{CO} at similar mean capillary PO_2 as estimated from average alveolar PO_2. This was accomplished during air breathing by inspiring the single breath gas mixture containing 2-3% O_2; control PO_2 in the breathholding alveolar sample was 43$\pm$ S.D. 3 mm Hg compared to 50+4 for quasi steady state hypoxia. Mean control D_{CO} and $\dot{Q}_C$ were 38$\pm$9.9 ml/min/mm Hg and 7.1$\pm$2.8L/min, and increased to 41.7$\pm$12.3 and 8.7$\pm$3.2 during steady state hypoxia, $p < .01$. There was a linear relationship between D_{CO} per L of total lung capacity and cardiac index; $D_{CO}/TLC = 5.62 + .62\ \dot{Q}_C/BSA \pm 1.27$, $r = .73$, $n = 41$, $p < .001$. This regression slope is significantly greater ($p < .001$) than that obtained from increasing resting cardiac index by adrenalin infusion, hyperventilation, or releasing a Valsalva in these same 6 subjects; $D_{CO}/TLC = 4.01 + .44\ \dot{Q}_C/BSA$, $r = .76$ (Clin. Res. 16:562, '69). These results suggest that the pulmonary capillary bed expands during acute hypoxia, and that this expansion may be only partially accounted for by that increase in transmural vascular pressure produced by an increase in $\dot{Q}_C$.

Circadian Patterns of LH Secretion in Intact and Chronically Gonadectomized Rats. Irene E.Lawton and Stuart W.Smith*. Loyola Univ.Sch.Med.,Dept.Physiology,Maywood,Illinois.

A 24-hour periodicity exists in the neural mechanism regulating release of the cyclic ovulatory surge of LH in adult female rats; plasma LH at proestrus peaks between 2PM and 4PM. This cyclic release of LH for ovulation is abolished if females are treated with androgens neonatally. To determine whether a circadian rhythm exists in the system controlling basal LH secretion,pituitary and plasma LH levels were determined over a 24-hour period in chronically gonadectomized female and male rats housed under controlled lighting(lights on 5AM-7PM). Autopsies were performed five months after gonadectomy at $6AM_1$,10AM,2PM,6PM,10PM,2AM, and $6AM_2$. In the ovariectomized females, pituitary LH content did not vary with time of day,but plasma LH fluctuated significantly($p<.005$),reaching peak levels at 2PM as in the cyclic proestrous rats. Thus there is a 24-hour rhythm in the basal LH secretory system and it is independent of cyclical ovarian activity. This circadian periodicity is most probably inherited, with the environmental light-dark cycle subsequently determining the exact timing of the peaks and troughs. In contrast to the females, no change was seen in pituitary or plasma LH over the 24-hour period in the castrated male rats;LH in the plasma of intact males also failed to show the 2PM peak. This sex difference suggests that the cyclical nature of basal LH secretion,as well as of the surge of LH for ovulation, may be suppressed by neonatal exposure to androgens. (Supported by NSF grant GB 8726.)

A COMPARATIVE STUDY OF PROTEIN METABOLISM AMONG LOBES OF THE RAT LIVER. A.V. LeBouton* and T.H. Hoffman* (intr. by James N. Hayward). Dept. of Anatomy, Univ. of California, Los Angeles, Calif.

Streamlined portal blood flow resulting in specific liver lobes being perfused by blood from certain viscera has been described. Assuming these various blood streams to be of different composition the possibility exists that the several liver lobes might differ in their metabolism. Therefore rats were injected with leucine-H^3 via the external jugular vein. At times thereafter the radioactivity was estimated in trichloroacetic acid soluble and insoluble fractions from 15,000 g supernatant fluids of homogenates from each liver lobe. The results indicated that all liver lobes metabolize protein at similar rates when the radioisotope is injected in the peripheral circulation. also an almost perfect positive correlation was demonstrated between lobe weight and total lobar radioactivity. However when the label was injected into the spleen the right lobes contained more radioactivity. Conversely when leucine-H^3 was injected into the jejunum it was lobes of the left side which were most radioactive. This was interpreted as evidence for a streamlined flow of blood in the rat portal vein which is exactly opposite to the situation in humans. This streamlining is considered as a "crossing-over" of splenic and superior mesenteric blood flows due to the angle at which the splenic vein joins the superior mesenteric vein which in the case of the rat is very close to a right angle. Supported by NSF Grant GB 8306.

ETHACRYNIC ACID AND DIRECT INHIBITION OF SODIUM-POTASSIUM TRANSPORT IN CELL MEMBRANES: POSSIBLE ACTION ON MYOCARDIAL PUMP AND SIGNIFICANCE OF THERAPEUTIC DOSES ON DIGITALIS TOXICITY. Garrett Lee*, Robert Zelis*, Carroll E. Cross*, James F. Spann, Jr., and Dean T. Mason. Univ. Calif. at Davis School of Medicine, Davis, Calif.

It has been reported that there are two distinct human red blood cell (RBC) membrane pumps which actively transport sodium (Na^+) out of and potassium (K^+) into the cell: one is inhibited by digitalis (D) and the other by ethacrynic acid (ECA). Since it has been postulated that D-induced tachyarrhythmias are due to inhibition of the myocardial Na^+-K^+ coupled pump, thereby accentuating diastolic depolarization, in this study the possibility was considered that ECA might alter the myocardial Na^+-K^+ pump as well and thereby diminish the threshold toxic dose of digitalis required to produce arrhythmias. Fifteen experimental and seven control dogs were investigated; the renal arteries were ligated in both groups to exclude the diuretic effect of ECA. Ouabain (OU) was infused into all dogs at a rate of 1 µg/kg/min until the appearance of tachyarrhythmic toxicity, which occurred after the infusion of 44.3 $\pm$ 3.7 (SEM) µg/kg OU in the control group. In eight animals the clinical dose of ECA (1 mg/kg) was injected prior to OU. The accumulated OU dose which produced D-toxicity in these animals was 45.5 $\pm$ 6.3 ($p>.5$). In seven animals the dose of ECA injected prior to the infusion of OU was increased to 10 mg/kg which approximated the in vitro dose of ECA necessary for inhibition of RBC pump cation transport; these animals died after receiving a total dose of 42.7 $\pm$ 4.8 µg/kg OU ($p>.5$). In four additional animals ECA alone (10 mg/kg) did not produce arrhythmias. It is concluded that extrarenal effects of ECA therapy do not enhance D-toxicity. This suggests absence of an ECA inhibitable myocardial pump or that the inhibition of Na^+-K^+ exchange across myocardial cell membrane does not underlie D-induced toxicity.

ELECTROPHYSIOLOGICAL CHARACTERISTICS OF CAT DORSAL ROOT GANGLION CELLS. W. D. Letbetter* and W. D. Willis, Jr. Department of Anatomy, University of Texas Southwestern Medical School at Dallas, Texas.

Dorsal root ganglion cells of the seventh lumbar segment in anesthetized cats have been investigated by intracellular recording with glass microelectrodes. The connective tissue capsule of the ganglion was either incised or treated with collagenase to allow electrode penetration. The electrolyte was generally a sodium solution to prevent leakage of potassium when electrodes were broken. Confirmation that the records were made from ganglion cell bodies was obtained by intracellular marking with methyl blue. It was found that, contrary to an earlier report (Sato & Austin, J. Neurophysiol., 24: 569, 1961), the spike potential exhibits an inflection point on its rising phase similar to that of motoneuron spikes. A block could be produced, although the two components of the spike appeared to be more closely coupled than in motoneurons. The after-hyperpolarization was associated with the later component of the spike. The amplitude of the after-hyperpolarization varied in response to current pulses in the manner expected if it tended to approach a potassium equilibrium potential. With repetitive activation, the after-hyperpolarization following the second and later spikes generally reached a smaller absolute level of membrane potential than that reached by the first spike; this contrasted with the summation typical of motoneuronal after-hyperpolarizations (Ito & Oshima, Nature, 195: 910, 1962). A possible interpretation would be that potassium accumulates in the extracellular space around dorsal root ganglion cells and changes the potassium equilibrium potential following activation.

(Supported by USPHS grant NB 04779.)

RETENTION OF INSPIRED FOREIGN GASES. Benjamin M. Lewis, Wayne State University School of Medicine, Detroit, Michigan

Retention of an inspired insoluble foreign gas in the lung after full expiration is related to size of the residual volume, variations in the ratio of ventilation to residual volume within the lung and diffusion equilibration between the inspired gas and alveolar air. This retention has been quantified by inspiring a gas bolus of known size and measuring the volume of the subsequent expiration and the concentration of test gas in this expiration. When the residual volume is independently measured, the amount retained can be compared with retention that would obtain if the bolus were evenly and instantaneously distributed in the total lung volume. Preliminary data in normal subjects show retention of the test gas is about 95% of expected when the bolus is inspired at FRC and followed by 1 liter of air. Inspiration of the bolus 1 liter below VC (again followed by 1 liter of air) increases the percentage of actual retention in relation to expected retention.

DEVELOPMENT OF ATPase AND K^+-STIMULATED PHOSPHATASE IN MICROSOMES ISOLATED FROM METAMORPHOSING BULLFROG TADPOLE STOMACH. L. Limlomwongse*, D. K. Kasbekar* and J. G. Forte. Dept. of Physiology, Univ. of Calif., Berkeley, California.

The capacity to secrete gastric HCl appears relatively late in bullfrog tadpole metamorphosis, at stage XXIV where tail reabsorption is almost complete (stages according to Taylor and Kollros, Anat. Rec. 94:7 1946). Appearance of HCl secretion was coordinated in time with developmental changes of at least two enzymes, ATPase and K^+-stimulated phosphatase, in microsomes isolated from tadpole gastric mucosae at various stages. Not only does total ATPase activity increase, but the SCN^- sensitive ATPase also markedly increases at stages where HCl secretion is present. For the K^+-stimulated phosphatase there is a bimodal distribution with respect to various developmental stages: a small, but reproducible activation at earlier larval stages which disappears during stages XX to XXII as the metamorphic process commences, and reappears at stage XXIV and increases sharply from this stage to full-grown adult. The larval and the adult K^+-stimulated phosphatase have several similar characteristics, e.g.: same pH optimum (7.5) and a Mg^{++} requirement for optimal activity; phospholipase C reduces, and acetone-extraction abolishes, K^+-activation (whereas an acid phosphatase retains activity in the acetone powder). One possibly significant difference between larval and adult forms of K^+-stimulated phosphatase is the sensitivity to cardiac glycosides, i.e. an effective inhibition of the larval enzyme activity, whereas fully metamorphosed gastric microsomes were not affected up to 10^{-3}M ouabain. The precise role of SCN^--sensitive ATPase and K^+-stimulated phosphatase (both are ouabain insensitive) in the mechanism of HCl secretion is still speculative; however, the present studies add further weight to the circumstantial evidence that the enzymes are involved in the gastric secretory process. Support by USPHS.

INHIBITION OF PERIPHERAL GLUCOSE UTILIZATION BY BEDREST. R. Lipman*, F. Ulvedal, E. Bradley*, and F. Lecocq*. USAF School of Aerospace Medicine and Wilford Hall USAF Hospital, San Antonio, Texas.

Although many investigators have reported impaired glucose tolerance as a consequence of bedrest (B), there are no published data which permits a physiologic interpretation of this defect. The current study details the effects of 2 weeks of B on forearm arterial-venous glucose difference (A-V) with simultaneous forearm blood flows (F) in 10 normal subjects fed a 380 gm carbohydrate diet. A constant 180 minute intravenous infusion of glucose solution was administered twice during a 2-week control (C), on the 14th day of B and on the 7th day of recovery (R). Venous glucose from the contralateral arm was recorded continuously and arterial glucose, serum insulin and forearm F were measured every 10 minutes. Glucose loads were varied during B and R to match venous glucose levels achieved during C. Whereas fasting A-V and F were similar during C, B and R, significant differences were obtained in mean glucose loads, A-V and (A-V) x F during glucose infusions comparing C to B and C to R.

	GLUCOSE LOAD (gms)		A-V (mgm%)		(A-V) x F (mgm/min)	
	$\bar{X}$	±SEM	$\bar{X}$	±SEM	$\bar{X}$	±SEM
C	165.3	9.2	50.6	4.0	0.92	0.09
B	84.3	10.1	19.1	2.1	0.53	0.06
R	106.5	11.2	26.8	2.5	0.51	0.05

In conclusion, the reported glucose intolerance of bedrest is in large part the result of inhibition of peripheral glucose utilization. It is suggested that this is due to local changes rather than hormonal or circulatory adaptation to bedrest.

REDISTRIBUTION OF PULMONARY BLOOD FLOW DURING SUBMERSION. M. Litman*, P. Cerretelli*, A. Chinet*, J. P. Farber*, L. E. Farhi, and D. W. Rennie. Depts. of Physiology, Univ. of Milan, Italy, and State Univ. of New York at Buffalo, Buffalo, N. Y.

Cardiogenic oscillations of O_2 and CO_2 normally found on the alveolar air plateau have been observed by Cerretelli and Rennie to disappear during head-out immersion in water. Since these oscillations are commonly thought to reflect heterogeneous distribution of $\dot{V}_A/\dot{Q}$, their disappearance may indicate changes in distribution of $\dot{V}_A$, $\dot{Q}$, or both. However, a change in distribution of $\dot{V}_A$ has been ruled out since cardiogenic oscillations of an inert, poorly soluble tracer (argon, single breath) are not altered by submersion. A breath taken in air followed by expiration after immersion still shows O_2 and CO_2 oscillations. Negative pressure breathing in air slightly diminishes oscillations and positive pressure breathing in water may partially restore them. Gradual submersion leads to progressive disappearance of the oscillations, except in unusually tall subjects, but not when venous tourniquets have been placed around the upper portion of the extremities before submersion. We suggest that disappearance of the cardiogenic oscillations is due to a redistribution of pulmonary blood flow probably caused by increased venous return and/or increase in pulmonary blood volume during immersion.
(Supported in part by grants from the National Institutes of Health, Office of Naval Research, and U. S. Air Force.)

FROG CEREBELLAR ACTIVITY EVOKED BY CONSTANT ANGULAR ACCELERATION.
R. Llinás and W. Precht.* Institute for Biomedical Research, AMA/ERF, Chicago, Ill 60610.

The electrical activity of Purkinje cells was recorded extracellularly during physiological stimulation of the horizontal semicircular canal in Rana catesbeiana, paralyzed with d-tubocurarine Four different types of Purkinje cell responses could be recorded from the vestibular cerebellum. Type I Purkinje cells located in the auricular lobe continuously increased their discharge frequencies to ipsilateral angular acceleration and decreased their firing to contralateral acceleration. The increase of discharge frequencies was close to linear with respect to the angular acceleration rate. Type II units showed the opposite response, that is, increase by contralateral and decrease by ipsilateral rotation. Type III Purkinje cells were found along the vestibular commissure of the cerebellum and their firing increased during both ipsi- and contralateral rotation. Type IV Purkinje cells responded with decreased spike activity during both ipsilateral and contralateral rotation. Since no evidence for a direct inhibitory action on Purkinje cells has been found, it is concluded that the reduction of the spontaneous activity observed in Purkinje cells of Type I, II and IV is brought about by disfacilitation. Direct evidence for this mechanism will be presented. The results will be discussed with respect to the general organization of the neuronal circuits of the frog cerebellum.

EFFECTS OF OLIVE OIL AND MEDIUM CHAIN TRIGLYCERIDES (MCT) ON ACID OUTPUT IN DOGS WITH VAGALLY INNERVATED AND VAGALLY DENERVATED POUCHES.
James F. Long, Albany Medical College, Albany, New York.

Four dose levels of olive oil and MCT were infused via a duodenal fistula over a 1 hr period starting 30 min after a meat meal in 4 dogs with vagally innervated gastric pouches. Gastric collections were made at 15 min intervals for 30 min before and 4 hr after feeding and acid outputs determined on each sample. During the period 45-90 min after feeding, significant inhibition of gastric acid output occurred with 1.0, 0.5, and 0.25 ml of olive oil/kg body wt with ave values of 15, 26, and 49 per cent of control feeding acid outputs, respectively. During the 150-240 min period the outputs were 166, 96, and 86 per cent of control. MCT infused at 1.0, 0.5, and 0.25 ml/kg body wt given similarly to the olive oil, yielded acid outputs of 21, 32, and 59 per cent of control during the 45-90 min period and 66, 83, and 96 percent at 150-240 min. Identical experiments were performed on 4 dogs with vagally denervated gastric pouches. Olive oil infused at 1 ml/kg body wt resulted in a significant inhibition of gastric acid output during the period 45-90 min after feeding with an ave value of 60 percent of control feeding. The period 150-240 min was 133 percent of control. The lower doses of olive oil and MCT, at all dose levels, did not result in significant inhibition. The results of these studies indicate that vagal innervation is essential for optimal inhibition of gastric secretion with olive oil and is necessary for inhibition following MCT. Also, the acid output is elevated above control in late stages of the experimental period when 1.0 ml olive oil/kg is employed but not with MCT or lower doses of olive oil either in vagally innervated or vagally denervated pouch preparations.
This study was supported by NIH Grant 09559.

THE PLACENTAL EXCHANGE OF CO_2 FOLLOWING THE INHIBITION OF FETAL CARBONIC ANHYDRASE. Lawrence D. Longo*, Maria Delivoria-Papadopoulos* and Robert E. Forster, Dept. Physiol., Loma Linda Univ. Sch. of Med., Loma Linda, Calif., and Dept. Physiol. Div. of Graduate Med., Univ. of Pa., Phila., Pa.

In order to determine the rate limiting factors for the transplacental movements of CO_2 and bicarbonate, we have measured their exchange following inhibition of fetal carbonic anhydrase. In 7 ewes and their fetuses mean control values of P_{CO_2} were: uterine art. 32mmHg; uterine vein 40mmHg; umbilical vein 46mmHg; umbilical art. 52mmHg. Following intravenous administration of acetazolamide (25 mg/kg) to the fetal lamb, the values of P_{CO_2} gradually changed over a 60 min. period until at the new steady state they were: ut. art. 32mmHg; ut. vein 42mmHg; umb. vein 60mmHg; and umb. art. 72mmHg. During the control period, of the total fetal CO_2 output, 82% represented a change in blood [HCO_3^-] + carbaminohemoglobin, and the remaining 18% a change in blood dissolved [CO_2]. Following the administration of acetazolamide, approximately 57% of the total CO_2 output represented a change in blood dissolved [CO_2] and only 43% a change in [HCO_3^-] + carbaminohemoglobin. In further studies in which THAM was given to 5 fetal lambs, there was a net movement of CO_2 from mother to fetus, against a considerable [HCO_3^-] gradient. From a consideration of the CO_2 hydration and intracellular hemoglobin reaction rates, we conclude that the major species of CO_2 crossing the placenta is dissolved CO_2 rather than bicarbonate. Furthermore, we calculate that the placental CO_2 diffusing capacity is about 18 ml/(min x mm Hg x kg fet. wt.), and that P_{CO_2} equilibrates between maternal and fetal placental blood during the course of a single capillary transit. (Supported by USPHS 01860 and 03807)

ARTERIO-VENOUS SHUNTING IN EXTREMITIES. Vincent Lopez-Majano and Buck A. Rhodes (intr. by P. Caldini). V. A. Hospital and The Johns Hopkins Medical Institutions, Baltimore, Maryland.

Radioactive particles ranging between 20 and 40 microns in diameter were injected into each femoral artery of 16 dogs. The distribution of this radioactivity in the hindlegs was studied by external radiation detection. The radioactivity in the lungs was also determined externally after both intra-arterial and a comparable intravenous injection of the same radioisotope. The radioactivity in the lungs following the intra-arterial injection was evidence of arterio-venous anastomosis in the hindlegs of the dogs, because the particle size was greater than the size of the capillaries. Shunts were observed in most of the dogs. The amount of shunting ranged from zero to nearly 60% and it was calculated according to the following formula:

$$\frac{\text{Net counts per minute per millicurie injected intra-arterially}}{\text{Net counts per minute per millicurie injected intravenously}}$$

Two of the particles used, macroaggregates and microspheres of human serum albumin, are innocuous in human beings; thus, they can be used in the clinic for the detection of vascular shunts.

(Supported in part by U.S.P.H.S. Grant GM-10548)

RESPONSES TO ACh OF DEPOLARIZED DENERVATED MUSCLES AT LOW IONIC STRENGTH. H. Lorković. Depts. of Neurol. and Physiol., Univ. of Iowa Med. School, Iowa City, Iowa 52240.

Denervated skeletal muscles of rats and frogs depolarized by high K respond to ACh by weak contractures or not at all (Jenkinson and Nicholls, 1961, Frank, 1963). Muscles bathed in sucrose solutions respond to ACh by strong contractures; changes in membrane potential are small or absent (Lorković and Edwards, Fed. Proc. 27, 443). To determine whether the responsiveness was enhanced by the normal membrane potential or by the low ionic strength, chronically denervated toe muscles or thin muscle bundles of rats and frogs were soaked for 10-200 min in a Tris-Cl solution made hypertonic by addition of 100 mM KCl. Following 1 min wash in sucrose solution (SS) the membrane potential was +25 to +50 mv and dropped rapidly and transiently to about -60 mv on application of 55 μM ACh. Contracture tension was up to 70% of control responses in SS of nonloaded muscles provided the solution contained Ca. At constant $[Ca]_o$ decreasing responses were obtained by gradually replacing sucrose by Tris-CH_3SO_3 or KCH_3SO_3. With $[C^+]^2/[Ca^{++}] = 200$, $Tris^+$ or K^+ being used as C^+, the sizes of responses to ACh were about one half of the responses provoked in the absence of monovalent cations. It was concluded that contracture activation by ACh in depolarized denervated muscles may involve a step in which competition of Ca and monovalent ions for some sites in the membrane determines the size of the mechanical responses.
(Supported by USPHS, NIH Grant NB-3354).

HYPOTHALAMIC STIMULATION AND PLASMA CORTICOSTERONE LEVELS IN X-IRRADIATED RATS. James R. Lott and Joe Burks* Dept. Biology Sciences, North Texas State University, Denton, Tex.

The aim of this study was to study the effect of electrical stimulation of the posterior hypothalamus on the adrenal response before and during X-irradiation. Rats were stimulated via implanted electrodes (3V/25imp./sec.) at 5 sec. intervals for 5 mins. X-irradiation (940R) was delivered at 188R/min. (120KVP, 5ma) for 5 min. Blood samples were taken from guillotined animals at 6, 12, and 24 hrs. post-irradiation. Pre-radiation samples were taken from cannulated juglar veins. Plasma corticosterone was determined using the fluorometric method. Eosinophil counts and adrenal weights were also determined. Electrical stimulation of the hypothalamus produced a significant increase in corticosterone and eosinopenia at the 6 hr. post-radiation. X-irradiation alone produced a significant and sustained increase in corticosterone concomitant with an eosinopenia. X-irradiation following stimulation failed to produce an additive corticosterone response, however, a distinct and sustained eosinopenia was noted. X-irradiation and stimulation applied simultaneously produced an additive corticosterone response. The data indicate that the hypothalamus may contain radio-sensitive areas that may account in part for the adrenal response in irradiated animals.

RELATIONSHIP BETWEEN GFR AND BLOOD PRESSURE IN NEWBORN PUPPIES. R.J. Lubbe and L.I. Kleinman. (Intr. by D.L. Kline) Dept. of Physiol., Env. Health and Pediatrics, Univ. of Cinti. Col. of Med., Cincinnati, Ohio 45219.

Glomerular filtration rate (GFR) and renal plasma flow (RPF) were measured as functions of age and mean arterial blood pressure (B.P.) in 36 puppies aged 1 to 36 days and in 6 adult dogs. GFR/gm kidney wt increased from 21% of adult value at birth to 53% at 30 days. B.P. in newborn puppies was low (40 mm Hg). Correlation of B.P. with age during the first month was fair ($r = .38$, $p<.025$) but was much better with GFR ($r = .81$, $p<.001$). The increase of GFR with age (determined by partial regression analysis) could be largely attributed to change of GFR with B.P. Acute changes in B.P. were then obtained by carotid occlusion, hemorrhage or spontaneously. In puppies fractional change in GFR correlated with fractional change in B.P. ($r = .64$, $p<.001$). In adults, no such relationship existed. RPF also varied with B.P. in puppies and not in adults. This lack of autoregulation of GFR and RPF over the low B.P. range found in early life further supports the conclusion that GFR in puppies is low primarily because B.P. is low and that GFR increases with age as B.P. rises. (Supported by USPH ES-00159 and HD-42230.)

AIRWAY RESISTANCE INFLUENCED BY SUGGESTION. Harold A. Lyons, E.R. McFadden Jr.*, Eugene Bleecker* and Thomas Luparello*. The State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, New York. Supported by U.S.P.H.S. Grant # 5R01 HE 11932-02.

Airway resistance is an important physiological determinant and changes of airway resistance are used to explain responses to pharmacologic agents and biological effectors. Nineteen asthmatic subjects were studied in a symptom-free state. Each subject was administered a sham allergen by nebulizer. Twelve subjects developed an acute asthmatic attack. Ga/TGV decreased to 0.10 L/sec/cm H20/L. Alleviation of the attack followed the administration of a sham bronchodilator. In both instances the sham agents were normal saline. Normals and patients did not react. Further investigation demonstrated that atropine blocked the reaction. The results imply that caution must be used for the interpretation of bronchomotor responses, such responses must be evaluated in terms of reactivity of the airways of each individual.

RELATIVE MAGNITUDE OF MEMBRANE FRICTIONAL COEFFICIENTS IN BEEF ERYTHROCYTES. Robert I. Macey and Robert E.L. Farmer*
University of California, Berkeley, California 94720

Volume perturbation experiments with beef erythrocytes have been designed to measure membrane transport parameters L_p, σ, and ω in the presence of a penetrating non-electrolyte (Farmer and Macey, Biophys. J. 7 Abs:6, 1967). Following Kedem and Katchalsky (J.G.P. 45:143, 1961) these parameters can be written in terms of frictional coefficients between solute and water (f_{sw}), solute and membrane (f_{sm}) and water and membrane (f_{wm}). Theoretically, L_p depends on $\bar{c}_s$, a weighted-mean concentration of penetrating solute in the membrane. Experiments with glycerol and ethylene glycol equilibrated across the membrane at concentrations up to 1.2 M show that L_p is essentially independent of $\bar{c}_s$. Using this result and measured values of L_p, σ, and ω together with the functional dependence of L_p and σ on frictional coefficients, it can be shown that f_{sm} is considerably smaller than f_{sw}. This implies that ω can be expressed as $\omega \approx K/(\Delta x\, f_{sw})$, where the primary frictional force is with water rather than with the membrane itself. These results can be interpreted in terms of small water-filled channels. (Supported by NSF GB 11981 and Bay Area Heart Research Committee.)

The Mechanism of the Phase Lag of Respiratory Blood Pressure Waves in Chickens. M. Magno* and P. D. Sturkie, Dept. of Physiology, Albany Medical College, Albany, N. Y. and Dept. of Animal Sciences, Rutgers University, New Brunswick, N. J.

Respiratory blood pressure waves are known to be at least partially caused by the effect of respiratory mechanics on blood flow. However, these waves are not always in phase with respiration. This experiment was conducted to determine if the phase relationship was dependent upon respiratory frequency. Blood Pressure was measured directly and respiration was recorded with a pneumotachograph in seven spontaneously breathing chickens. No significant correlation was found between the phase lag and respiratory frequency. However, there is an inverse relationship between the relative phase lag and the ratio of heart rate to respiratory frequency which can be described the the equation $\theta = 173 - 6.29(HR/f)$ where θ is the phase lag in degrees with 360° equal to one cycle and HR/f is the ratio of heart rate to respiratory frequency. While the correlation coefficient (-0.726) is not significant at the 0.05 level, this equation is able to predict the phase lag seen in previously reported records of blood pressure and respiration from chickens. This relationship reflects the fact that right heart output does not increase until after the first heart beat following an increase in venous return and that left heart output does not increase at least until after the second beat. Therefore, the more beats per breath, the earlier in the respiratory cycle the increase in blood flow will appear.
Supported By USPH HE 10502

THE STRUCTURE OF AVIAN INTRAFUSAL FIBERS. Alfred Maier* and Earl Eldred. Department of Anatomy, University of California at Los Angeles.

The question of whether intrafusal (IF) fibers in muscle spindles in birds are separable into one or more types has been studied from Von Gieson-stained serial sections and camera lucida reconstructions. Spindles of the sartorius, a flexor, and the adductor, an antigravity muscle of the hindleg, were examined. Both muscles in the chicken had 3 to 8, usually 5 or 6 IF fibers; pigeon and canary spindles generally contained 4 or 5 fibers. The IF fibers did not show the pronounced central aggregation of nuclei characteristic of mammalian IF fibers, although the midlength region was occupied by centrally located nuclei and occasionally 2 or 3 of these might be seen on a single cross-section. In the polar regions most nuclei were peripherally located. The cross-sectional area of a fiber was minimal at a juxta-equatorial level and usually largest in the polar region. No prominent differences were observed in length of fibers within a spindle, most fibers terminating within the extent of the fibrous portion of the capsule. Comparisons on the basis of nuclear configuration, fiber size and length of fiber did not suggest the presence of two distinct fiber types.

RECOVERY OF THE CONTRACTILE RESPONSE IN RAT PAPILLARY MUSCLE FOLLOWING A PREVIOUS CONTRACTION. G.W. Mainwood and S.L. Lee (Intr by K. Kako) Department of Physiology, University of Ottawa, Ottawa, Ontario.

In rat papillary muscle, action potentials are relatively short (20-30 msec). Fibres can thus be re-excited electrically after 35-50 msec giving action potentials of normal amplitude after 80-100 msec. The mechanical response to the second of two pulses is difficult to detect at stimulus intervals of less than 80 msec but a small hump appears in the derivative of the contraction curve at about this time which grows progressively as the stimulus interval increases. If this is used as an index of recovery of the contractile mechanism, recovery is seen to be much slower when the external calcium concentration is reduced. The recovery rate increases progressively for about 90 min after the muscle has been removed from the ventricle and this is correlated with an increase in the mean resting potential of the fibres. It is tentatively proposed that a releasable calcium fraction is completely discharged by a single action potential and is recharged at a rate depending on the external calcium concentration and the resting membrane potential.

Supported by the Medical Research Council of Canada

CORONARY ADRENERGIC RECEPTORS. George S. Malindzak, Jr., Russell D. Miller* and Harold D. Green. Bowman Gray Sch. Med., Winston-Salem, N. C.

Propranolol, a β-adrenergic blocking agent was given in combination with nitroglycerin, papaverine, aminophylline, isoproterenol and phenylephrine while recording mean coronary blood flow with an electromagnetic flowmeter, mean aortic pressure and heart rate in anesthetized mongrel dogs. Propranolol alone produced a 34% increase in mean coronary arterial resistance, probably due to stimulation of α receptors by circulating catecholamines or to autoregulation as myocardial O_2 was reduced. Nitroglycerine, papaverine and aminophylline all transiently decreased coronary peripheral resistance (57%, 54% and 39%, respectively, probably through non-specific relaxation of arteriolar smooth muscle because this effect was not blocked by propranolol. Isoproterenol caused a 5-fold increase in coronary blood flow and concomitant decrease in coronary resistance which was blocked by propranolol, suggesting the presence of β receptors in the coronary vasculature. Phenylephrine administration transiently decreased coronary resistance (40%) and increased flow (> 3-fold). However, when given after β-adrenergic blockade, coronary resistance increased (39%), perhaps due to activation of α constrictor receptors. Conclusion: (a) Isoproterenol probably increased coronary flow by activating β dilator receptors or by increasing myocardial metabolism, (b) α constrictor receptors can be unmasked by β blockade. (Supported in part by USPHS, NIH grants HE-487, 5392, 344 and North Carolina Heart Association.)

REVERSAL POTENTIALS FOR IONTOPHORETIC POTENTIALS PRODUCED BY SEVERAL CHOLINOMIMETICS. R. S. Manalis* and R. Werman. Dept. Anat. & Physiol., Ind. Univ., Bloomington, Ind., Inst. Psych. Res., Ind. Univ. Med. Ctr., Indianapolis, Ind., and Dept. Zool., Hebrew Univ., Jerusalem, Israel.

Do each of a group of strong and weak cholinomimetics depolarize the frog endplate via similar or dissimilar ionic mechanisms? Since the reversal potential is a measure of the ionic mechanism underlying a postsynaptic potential (PSP), the reversal potentials for each of the iontophoretic potentials produced by carbachol, nicotine, succinylcholine, edrophonium (weak), and heptyl-trimethylammonium (weak) were measured and compared to that for the acetylcholine (ACh) iontophoretic potential; each comparison was performed on a single endplate from a muscle sartorius. A PSP reversal potential was determined by interpolating the relationship between the height of the PSP and the experimentally varied membrane potential. The use of glycerol-treated muscle (Howell, J. N. and Jenden, D. L., Fed. Proc., 26: 553, 1967) permitted the successive depolarization of a given endplate membrane to be performed in contraction-free conditions. No large differences were observed between the reversal potentials for each of the various cholinomimetic drug potentials and the ACh potential: Ratios of the driving force (PSP reversal potential minus the resting potential) for a cholinomimetic to that for ACh ranged from 0.95 (edrophonium) to 1.02 (succinylcholine). The mean ±S.D. value of the reversal potential for the ACh potential was -1.2 ±5.5 mV (16 fibers). PSP reversal potentials were shown to be independent of dose and of desensitization. The data strongly indicate that the endplate receptor is activated in an all-or-none fashion and that, therefore, differences among the intrinsic activities of the weak and strong depolarizers may be due to differences in the probabilities that the various drug-receptor complexes will be active. (Supported by USPHS grant NB07307.)

INITIATION AND SUPPRESSION OF FEEDING BEHAVIOR BY ADRENERGIC RECEPTORS IN RAT BRAIN. D.L. Margules, Wyeth Labs., Inc.,Phila., Pa.

Direct application of low doses of l-norepinephrine (l-NE) to lateral hypothalamus initiates intake of dry food. In the present study, application of higher doses suppressed milk intake. This suppressant effect was localized to the perifornical region of the medial forebrain bundle (pMFB). It was specific to the biologically active l isomer rather than the d isomer. It was reduced by 24 hr of chow deprivation which indicates that normally induced hunger minimizes the suppression. These results suggest that feeding behavior is both initiated and suppressed by adrenergic receptors in the brain. Such receptors could also be responsible for the suppression of feeding which occurs after systemic administration of l-NE and d-amphetamine. Support for an adrenergic satiety theory was obtained with direct application of an alpha adrenergic blocker, phentolamine, which caused overeating of milk or mash. This effect was localized to the pMFB and was specific to alpha rather than beta blockade. Overeating caused by phentolamine was reduced by pre-feeding milk, which indicates that normally induced satiety minimizes this effect. When milk was adulterated with quinine, phentolamine caused finickiness. Blockade of alpha adrenergic receptors in the pMFB appears to cause the same effects as ventromedial hypothalamic lesions: overeating and finickiness. Low concentrations of l-NE in pMFB initiate feeding; higher concentrations suppress feeding. Adrenergic receptors present in pMFB may mediate both effects. Histological evidence suggests that the cells of origin of these terminals are located in classical ventromedial satiety region of the hypothalamus, an area with well known initiatory and suppressant effects on feeding.

IONIC AND METABOLIC COMPONENTS OF A NEURONAL MEMBRANE POTENTIAL. M. F. Marmor and A. L. F. Gorman (intr. by G. C. Salmoiraghi). Nat'l. Inst. Mental Health, St. Elizabeths Hosp., Washington, D. C.

The ionic hypothesis, that the resting potential is generated by ionic concentration gradients across the selectively permeable neuronal membrane, fails to predict the potential of many molluscan neurons. The ionic hypothesis might apply to these cells if other processes that contribute to potential could be experimentally eliminated. Experiments were performed on a giant neuron from the marine mollusc, Anisodoris nobilis (MacFarland). The membrane potential was recorded while varying the temperature and the external ionic concentrations. At 4°C the membrane potential varied with external K in good agreement with a theoretical curve derived from the Goldman equation, as predicted by the ionic hypothesis. At 11° and 17°, however, there was progressively greater deviation from the theoretical curves. At 17° the cell was markedly hyperpolarized in normal K, and it depolarized in response to lowering external K. In the presence of ouabain, or after depletion of internal Na, the resting potential was described by the Goldman equation regardless of temperature. Thus, the resting potential of the giant neuron can be divided into two components: one which is predicted by the ionic hypothesis and a second which is sensitive to temperature and external K and probably depends upon an electrogenic Na pump.

DEPLETION OF PLASMA ASPARAGINE IN THE DOG USING L-ASPARAGINASE IN A HEMODIALYSIS SYSTEM. Larry Martel*, Michael T. Snider*, and Pierre M. Galletti. Brown Univ., Providence, R.I.

A study was conducted to determine the usefulness of artificial kidneys as extracorporeal chemical reactors for the purpose of removing a specific plasma constituent. In the first series of experiments, hemodialysis was carried out for 16 hours using a Klung dialyzer, 2 m^2 of cuprophane membrane, a blood flow of 200 ml/min, and a non-recirculating dialysate flow of 400 ml/min. In the second series of experiments, 10^5 units of L-asparaginase were added to 1.3 l of recirculating dialysate under the same flow conditions. The recycling dialysate was submitted to continuous ultrafiltration in a second artificial kidney equipped with 2 m^2 of cuprophane. The ultrafiltrate (about 600 ml/hr) was returned to the venous system ("cascade dialysis"). In this system plasma asparagine (mw 133) passed quite freely into the dialysate, was split by the enzyme (mw 136,000) into aspartic acid and ammonia, and the degradation products were returned to the vascular system. With conventional hemodialysis without enzyme, the plasma asparagine levels did not fall significantly below the control level of 30±10 nm/ml although the quantity of asparagine removed approximated 14 times the total plasma content under control conditions. With "cascade dialysis" using L-asparaginase, plasma levels fell below 2 nm/ml within 4 hours and remained at that level for the duration of the procedure. Hemodialysis against enzyme containing solutions permits depletion of a specific plasma component without introducing the enzyme itself in the blood stream. It may be of value when the enzyme is either rare, toxic, or contaminated, and when the development of antibodies must be prevented.

RENAL ELECTROLYTE EXCRETION PATTERNS IN THYMECTOMIZED AND THYMECTOMIZED-ADRENALECTOMIZED MALE HOODED RATS. Constance R. Martin. Dept. Biol. Sci., Hunter College, C.U.N.Y., New York, N.Y.

It was previously reported that thymectomized male rats given Purina chow and either 1% sodium bicarbonate or 1% sodium chloride ad lib. had smaller urine volumes and excreted less sodium and potassium than did sham thymectomized or unoperated controls. Thymectomized-adrenalectomized rats drinking sodium chloride also excreted less sodium, potassium and water than did sham thymectomized-adrenalectomized or adrenalectomized controls. Chloride output is also reduced in thymectomized and thymectomized-adrenalectomized animals given sodium chloride, but the inorganic phosphate content of the urine is increased. Injection of ammonium heparin increases urinary excretion of water, sodium, potassium and chloride in thymectomized rats drinking water or salt solutions and in thymectomized-adrenalectomized rats on sodium chloride. Heparin also increases electrolyte excretion in salt loaded sham operated animals but not in sham thymectomized or unoperated rats drinking water. Urinary excretion of inorganic phosphate was not influenced by heparin injection in any of the experimental groups. A marked seasonal variation in sodium excretion was observed in all groups. The effects of thymectomy and of heparin injection were greatest during periods of low sodium output. No seasonal variation in phosphate excretion was observed.

THE ELEVATION GRADIENTS OF THE COMPONENTS OF LUNG DENSITY.
F. Martorano*, D.H. Bristow*, B. Groome*, and J.L. Patterson, Jr.
Medical College of Virginia, Richmond, Va.

Following the report by Altobelli et al. in 1966, which showed an apex-to-base increase in lung density in anesthetized animals placed in the vertical head-up position, the purpose of this project was to establish the relative contributions of blood, tissue and gas to the composite density at each elevation in the lung. The elevation gradients of these components of lung density were measured on 19 anesthetized dogs. Ten were placed in a vertical head-up position, and nine in an inverted head-down position. The method previously used was followed, consisting of electrical fibrillation of the heart, temporary tracheal clamping, and immersion of the lungs, still held vertically, in liquid nitrogen. Small cubes were cut from the lungs at various distances between the apex and base. These cubes were measured on each edge, weighed and ground in a colloid mill. Hemoglobin from this ground lung tissue was measured after conversion to cyanmethemoglobin. From the rough data blood volume, tissue volume, and gas volume was calculated for each piece. These values were expressed as percentages of total (i.e. composite) volume and plotted against vertical distance. In the vertical head-up animals there was a significant increase in blood and tissue volume and decrease in gas volume from apex to base. The percentages of each component (blood, tissue, gas) of the composite volume were, respectively: apex - 4, 10, 86 percent; base - 12, 15, 73 percent. The inverted dogs showed no significant gradient of any of these three components. The findings in the head-up dogs suggest the existence of large differences in the actual volumes of alveolar gas and pulmonary capillary blood in apex versus base.Lack of volume gradients in the inverted dogs suggests that factors in addition to gravity affect density.

QUANTITATIVE ANALYSIS OF CARDIAC CONTRACTILITY BETWEEN PATIENTS WITH NORMAL, HYPERTROPHIED, AND FAILING HEARTS USING TWO INDICES: 1) MAXIMUM VELOCITY OF CONTRACTILE ELEMENT SHORTENING and 2) VENTRICULAR PRESSURE AND ITS RATE OF RISE CORRECTED FOR LOADING. Dean T. Mason, James F. Spann, Jr., and Robert Zelis*. U. Calif. Davis, Davis, Calif.

Since velocity of shortening of contractile elements and rate of elongation of series elastic are equal in the intact heart during isovolumic contraction, and isovolumic tension is related by a constant to isovolumic systolic pressure (IP), maximum velocity of contractile element shortening (Vmax) was determined by extrapolation to zero load of the curve derived from the relation: IP divided into the function: instantaneous rate of pressure rise (dp/dt) divided by the product of IP and series elastic constant. In 29 patients, Vmax averaged 1.53 muscle lengths/sec in normal patients, 0.87 with cardiac hypertrophy, and 0.61 with congestive heart failure (CHF). Determination of instantaneous dp/dt at IP of 50 mm Hg and its relations to left ventricular end-diastolic volume (LVEDV) provided another inotropic index independent of variations in ventricular preload and afterload. In the same patients the ratio, dp/dt at 50 mm Hg divided by this common IP/LVEDV averaged 0.34 in normal patients, 0.15 with hypertrophy, and 0.12 with CHF. The two contractile indices correlated positively ($r=.95$, $p<.01$) and the differences between the groups were significant ($p<.05$). It is concluded that determination of Vmax from IP and its dp/dt, and the ratio of dp/dt at common IP related to IP/LVEDV provide simple and valid means of quantifying contractility between patients. Further, CHF in patients is associated with profound quantitative abnormalities of contractility per unit of heart muscle. Ventricular hypertrophy even in absence of CHF is also associated with depression of contractile state per unit of myocardium, but of a lesser magnitude, while increase in total muscle mass maintains compensation.

FACILITATION AND INHIBITION OF ACTH RELEASE WITH AMYGDALOID STIMULATION IN CONSCIOUS CATS. G. Keith Matheson*, B. J. Branch* and A. Newman Taylor. Dept. of Anatomy, Univ. of California, Los Angeles, Calif. 90024

While the amygdala is considered to facilitate ACTH release, it was of interest to study whether all its nuclei participate in the response. The effects of amygdaloid stimulation (0.03-0.1 mA, 10-100 cps, 0.1-0.75 ms/pulse; 15 sec on-15 sec off, 30 min) on ACTH release in 6 chronically implanted cats were determined. Blood samples (1.5 ml) were collected 30 min prior, at onset, termination and 30 min after stimulation from an indwelling venous catheter. Cortisol (F) and corticosterone (B) were extracted from plasma (0.2 ml), separated by thin-layer chromatography and quantified fluorometrically. Stimulation at these parameters produced neither behavioral nor electrocortical changes.

STIM. SITE	RESPONSE	PRESTIMULATION F (μg/100 ml)	PRESTIMULATION B (μg/100 ml)	CHANGE, FINAL-INITIAL F (μg/100 ml)	CHANGE, FINAL-INITIAL B (μg/100 ml)
Basal	Increase	2.00±0.99(SE,5)	0.35±0.13(3)	3.70±2.15	0.61±0.08
	No change	2.41±0.53(11)	0.91±0.19(9)	0.45±0.36	0.01±0.13
	Decrease	-----	1.52±0.79(4)	-----	1.50±0.81
Cortical	Increase	1.38±0.67(3)	0.52±0.26(3)	2.07±0.62	0.61±0.16
	No change	2.15±0.29(4)	1.49±0.36(6)	0.18±0.65	0.36±0.21
	Decrease	4.48±0.59(7)	1.60±0.25(5)	2.92±0.45	1.20±0.35

Whereas stimulation of the basal amygdala produced an F increase in 5/16 cases, mixed effects were observed with cortical stimulation. The direction of response in the cortical group may be related to prestimulation steroid levels since both F and B in the "decreases" were significantly higher ($P<.05$) than prestimulation levels of the "increases". In 70% of the cases B either followed the F change or was unaltered. The overall prestimulation F/B ratio was 3.0±0.36(SE). These results indicate that various amygdaloid nuclei have differential effects on ACTH release. (Supported by NIH grants NB 07884 and AM 08468.)

Direct Potentiometric Determination of Potassium and Sodium in Blood and Serum. George Matsuyama*, Ernest Carlsen*, and Weldon B. Jolley. Beckman Instruments, Inc., Fullerton, Calif. and Loma Linda University Surgical Research Laboratory, Loma Linda, Calif.

A flow cell incorporating a potassium ion-sensitive electrode, a sodium ion-sensitive glass electrode and a saturated calomel electrode has been developed. The potassium electrode has a selectivity of approximately 100:1 for potassium over sodium and of approximately 4:1 for ammonium over potassium. The sodium electrode is a lithium aluminum silicate glass electrode having a selectivity of approximately 1000:1 for sodium over potassium. The cell has been used on aqueous solutions, blood, and serum samples. When calibrated on aqueous solutions, essentially equivalent results are obtained for sodium and potassium determinations on blood and the corresponding serum or plasma. Results also agree with those obtained with a flame photometer. The electrodes require approximately two minutes to equilibrate to each new sample. Repeatability of determinations is about ±0.3 meq/l for potassium and ±3 meq/l for sodium in the normal physiological range.

EEG POWER SPECTRAL CHANGES IN RHESUS MONKEYS DURING GRADED INCREASE IN ENVIRONMENTAL CO_2. J. L. Mattsson* and J. M. Stinson. 6571st Aeromedical Research Laboratory, Holloman Air Force Base, New Mexico.

Narcosis induced by abrupt exposure to high levels of inspired CO_2 is accompanied by distinctive changes in the electroencephalogram (EEG). The EEG changes produced by graded increases of 7.5, 15 and 30% CO_2/hr at ground level barometric pressure (660 mm Hg or 4300 ft) were studied in six unanesthetized rhesus monkeys chronically implanted with stainless steel cortical electrodes. Maximum CO_2 levels ranged up to 60%; O_2 was maintained at 20.94%. In an effort to quantitatively examine the gradual changes in the electrical activity of the brain, the EEG was recorded on analog tape for power spectral analysis on a TD-100. Results indicate that there are distinctive EEG power spectral changes as animals pass from the conscious to unconscious state, and that these changes are similar in all animals regardless of the rate of CO_2 increase. More specifically, there appears to be a band of frequencies (10-25 Hz) which shows a power decrease that is well correlated with loss of motor function and responsiveness to sound. This decrease in power could be a useful tool in the detection of CO_2 narcosis.

DOES Na^+ OUTFLUX CONTRIBUTE TO SHORT CIRCUIT CURRENT IN ISOLATED FROG SKIN? **R.D. McAFEE, VA Hospital and Tulane University, New Orleans, La.**

Short circuit current (I_{sc}) is often equated with sodium ion influx (Na_I^+) and outflux (Na_o^+), both being measured with radioisotopes of Na: $I_{sc} = Na_I^+ - Na_o^+$ (1). This implies actual ion fluxes that contribute algebraically to I_{sc}. However, isotope exchange may inflate flux measurements (2,3). We examine this further. If an exchange reaction inflated the Na_I^+, calculated from radioisotope measurement, it would inflate Na_o^+ an equal amount since an exchange reaction results in no net transfer of substance. Possibly, I_{sc} would actually equal Na_I^+, and Na_o^+ would be negligible. To test this, we placed living frogs injected with 22 Na in deionized water. The daily loss of 22 Na to the medium was much less than that expected on the basis of Na_o^+ experiments on isolated frog skin. Addition of NaCl to the deionized water produced over a hundredfold increase in 22 Na outflux - reversed upon return of the frogs to deionized water. To determine if the loss of Na from living frogs is actually so minute, frogs were placed in a container which periodically filled with deionized water and flushed every 40 minutes. These frogs showed no significant change in total body Na after 30-60 days of washing. These observations suggest that an exchange reaction may inflate values for Na_I^+ and Na_o^+ in isolated frog skin and mislead one to think of Na_o^+ as actually contributing to the I_{sc}.

(1) H.H. Ussing and K. Zerahn, Acta Physiol. Scand., 23:110, 1951.
(2) H.H. Ussing, Nature, 160:262, 1947.
(3) H.H. Ussing, Acta Physiol. Scand., 17:1, 1948.

ENVIRONMENTAL STIMULATION AND SLEEP. D. J. McGinty* (intr. by M. H. Chase). Veterans Administration Hospital, Sepulveda, Calif.

In a previous study, cats reared in an impoverished environment exhibited less than normal amounts of sleep, while following their placement in an enriched environment, sleep was facilitated. These observations suggested that exposure to novel stimulation produces one of the drives for sleep. To test this hypothesis, the amount of sleep was measured following periods of exposure to a novel stimulating environment. Four isolation-reared cats (for whom the environment was novel) and four normal cats were each exposed to three conditions: (1) 270 min. in an enriched environment, (2) 270 min. of sleep deprivation (to control for sleep loss during stimulation), or (3) a combination of enrichment and sleep deprivation (90-180 minutes). Sleep was measured in the subsequent 18 hours. In isolated cats exposure to the enriched environment increased sleep significantly, the greatest increase following maximal stimulation. The sleep of normal cats was increased no more by stimulation than by sleep deprivation. Other controls suggest that fatigue or stress did not produce the sleep facilitation. This experiment demonstrates that exposure to novel stimulation facilitates sleep, and provides support for the concept that sleep is a restorative process following physiological information processing. (Supported by the Veterans Administration and by USPHS grant MH-10083)

LOOP GAIN OF THE STRETCH REFLEX. T. McKean, W. Roberts*, P. Rosenthal*, and C. A. Terzuolo. Laboratory of Neurophysiology, University of Minnesota Medical School, Minneapolis, Minnesota.

It will be shown that for the special case in which the myotatic reflex is perturbed by sinusoidally stretching the gastrocnemius muscle of decerebrated cats, the gain provided by the reflex can be computed in dimensionless units. The gain is defined as the ratio of the peak to peak active tension developed by the muscle during sinusoidal stretching to the peak to peak passive tension developed at that same mean muscle length and muscle tension in the absence of the reflex. The latter measurements were made, after sectioning the motor nerve, by applying a steady stimulus to the distal end of the cut nerves. Active tension was computed as the vector difference between the sinusoidal tensions observed in the presence and in the absence of the reflex. The phase of the computed active tension closely agreed with the phase measured by recording the integrated EMG and the discharge of single motor units.

Values for the loop gain in the stated condition varied in different experiments from 0.2 to 2.5. These values were dependent upon the mean muscle tension with the gain decreasing with increasing mean tension and modulation frequency.

EFFECTS OF Na^+ CONCENTRATION ON MICROELECTRODE VOLTAGE MEASUREMENTS WITH RAT INTESTINE MUCOSA. J. R. McKenney, Dept. Physiol., Med. Col. Ga., Augusta, Ga, U.S.A.

The objective of this study was to determine the effects of Na^+ concentration on the P.D. across single cells of intestinal mucosa. Glass microelectrodes were used with everted segments of rat ileum. Incubation media (30-37C) contained fructose as substrate. Microelectrodes were driven towards the mucosal border using a hydraulic microdrive. With normal Na^+ concentration (145 mM) the P.D. across the mucosal membrane was about -25 mV as compared to -45 mV when the concentration of Na^+ was reduced to 50 mM. Results obtained suggest that both the mucosal and basal borders of the absorbing cells are about 20 per cent as permeable to Na^+ as K^+ with fructose as substrate. The relationship between transport activity and the net $[Na^+]$ dependent P.D. across the intestine may result from the concentrations of Na^+ and K^+ established in the extracellular space adjacent to the basement membrane relative to their concentrations in the incubation medium. This could result in a difference between the diffusion potentials across the mucosal and basal borders of the cells of the same magnitude and time course as the net P.D. observed upon altering $[Na^+]$ in the incubation medium. Work supported by U.S. A.E.C. Contract No. AT-(40-1) 3882.

CONCENTRATIONS OF FIBRINOGEN AND OTHER PLASMA PROTEINS IN RATS FED CARBOHYDRATE. Jess M. McKenzie, Patsy R. Fowler* and Noal D. May*. Physiology Laboratory, Civil Aeromedical Institute, Oklahoma City, 73125.

Male rats, fasted for one day and then refed pure carbohydrate (CHO) for an additional day, had fibrinogen levels which were 70-80% of those refed the regular laboratory ration; in rats fasted the entire two day period, fibrinogen concentrations were 95% of the ration refed group. Fasting enhanced the CHO effect, but was not necessary for a qualitative response; changing the diet abruptly from regular ration to CHO lowered fibrinogen concentrations within one day to 82% of those in normally fed rats. The mechanism of CHO-induced hypofibrinogenemia is not likely to involve dilution; the 5-minute albumin space, measured with I^{131}-albumin, was reduced to 80% of control values after 24 hours of CHO-refeeding. Diffuse thrombosis or generalized protein leakage were not considered as probable mechanisms; total protein, albumin and plasma cholinesterase were reduced by CHO refeeding, but prothrombin levels (1-stage method) were not affected. Reports that CHO refeeding induces increased synthesis of certain hepatic enzymes, suggest an interesting possibility: if the machinery and substituent amino acids were sufficiently limited, the induction of large amounts of enzyme-specific mRNA might result in depressed synthesis of plasma proteins via some competitive process.

UNIT RESPONSES IN THE DENTATE NUCLEUS OF THE CAT. D. McLeod* and T.T. Kennedy. Dept. of Physiology and Biophysics, Univ. of Washington School of Medicine, Seattle, Wash. 98105

Units in the dentate nucleus of cats anesthetized with α-chloralose were recorded extracellularly and their responses to a variety of peripheral, brain stem and cerebral cortical electrical stimuli were studied. Units were identified by antidromic stimulation from brachium conjunctivum and/or histological localization of electrode tracks or iontophoretically deposited fast green dye. Unit activity was recorded on film and/or analog tape. Filmed data were analyzed for latencies and preliminary determination and classification of firing patterns. Data on analog tape were digitalized and analyzed by computer for a more detailed characterization of firing patterns over time. Three-fourths of the units were spontaneously firing, either continually at a low, varying frequency or, more often, in higher frequency bursts of several hundred milliseconds duration. Over 95% of the units responded to stimulation of more than one stimulus site, many responded to as many as ten stimuli. For a given unit, the pattern of firing was remarkably similar for all stimulus sites. Firing patterns of at least 1 second duration were characterized by 1) presence or absence of early firing, 2) silent period and 3) presence or absence of late firing. When early firing was present, it appeared as a short, high frequency burst. Silent periods were varied in duration, sometimes over 500 msec. Late firing most frequently appeared as one or more bursts of long duration whose frequency was less than the early firing, but higher than the spontaneous rate. The firing pattern tended to be more related to the individual unit than to the site of stimulation. Little topographical organization was seen in the nucleus.
(Supported by PHS 5T1-NU-05004, PHS NB 05136, PHS 1PO7 00374-02 and PHS 5T1 NB5082-13)

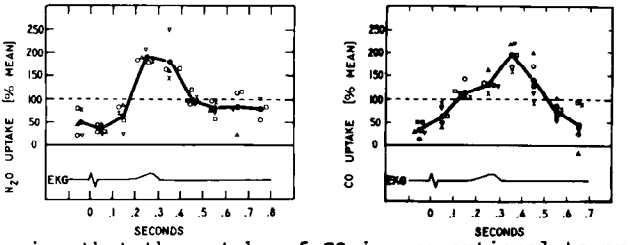
EFFECT OF LARGE DOSES OF OXYTOCIN ON MILK SECRETION IN INTACT AND SPINAL CORD TRANSECTED RATS. F. Mena and C. Beyer+ Inst. Invest. Biomed. U.N.A.M. and Dpto. Investigación Científica, I.M.S.S. Mexico, City.

The mechanism of the inhibitory action of large doses of oxytocin on milk secretion in the rat (1), was investigated. Lactating rats of the Wistar strain with litters of 6 pups and with the 6 anterior pair of mammary glands thelectomized had their litters removed on postpartum days 12 or 16-18 for 8 hrs and then suckled for 30 minutes (first suckling). After this, the pups were separated again for 16 hrs and the amount of milk reaccumulated was determined by another suckling period of 30 min. (second suckling). Oxytocin (400 mU) was injected s.c. to the mothers before each suckling period. It was found that 75 to 90% of milk was reaccumulated by control rats on either day of lactation. Four I.U. of oxytocin (Syntocinon, Sandoz) injected either 1 hr before or immediately after the initial suckling inhibited 80 to 95% milk reaccumulation on either day of lactation. Two units of oxytocin induced an inhibition of 60 to 70% and 1 unit had no significative effect. The inhibitory effect of 4 units of oxytocin was blocked completely on days 16-18 by spinal cord transection (T-9 - T-11). The results indicate the existence of an inhibitory mechanism for milk secretion of mammary origin which is probably activated by the injection of large doses of oxytocin and whose influence is removed by spinal cord transection.

1. Kuhn, E. Program of the 1969 meeting of the Endocrine Society. Abstract 113.

PULSATILE CO AND N_2O UPTAKE IN THE HUMAN LUNG. Harold A. Menkes*, Kazuaki Sera*, Robert M. Rogers*, Richard W.Hyde , Robert E. Forster,II, and Arthur B. DuBois. Dept. of Physiology, D.G.M., Univ. of Pa., Philadelphia, Pa.

Although it is known that the flow of blood into the pulmonary capillaries is pulsatile during the cardiac cycle, the relation between this flow and capillary volume change is not known. Using a water-filled body plethysmograph, we measured the rate of uptake of CO in the lungs of five normal men and compared this to the rate of uptake of N_2O.



Assuming that the uptake of CO is proportional to pulmonary capillary volume, our data suggest that during the heart cycle, blood volume in the lung capillaries fluctuates between 0.4 and 2.0 times the mean volume. We conclude that the lung capillaries are not rigid. Subtracting capillary volume change from the integrated inflow curve one finds a pulmonary capillary outflow which is at least as pulsatile as the inflow.

BILIRUBIN-^{14}C STUDIES IN MUTANT SOUTHDOWN SHEEP WITH CONGENITAL HYPERBILIRUBINEMIA: Abdus S. Mia*, Ronald F. Gronwall and Charles E. Cornelius, Department of Physiological Sciences, Kansas State University, Manhattan, Kansas.

Bilirubin-^{14}C was injected intravenously into mutant and normal Southdown sheep. Intercompartmental rate constants and pool sizes of unconjugated bilirubin was calculated from the plasma disappearance curves. The "rapidly mixing pool" (M.P.) of unconjugated bilirubin averaged 56 μg/Kg in normal sheep and 217 μg/Kg in mutants. The "storage or hepatic pool" (S.P.) was approximately 400 μg/Kg in both groups. The excretion of bilirubin was proportional to the total pool in both groups, indicating that no defect exists in the removal of unconjugated bilirubin from the total pool in mutant sheep. The fractional transfer of unconjugated bilirubin from the M.P. to the S.P. in mutant sheep was one-half that of normal sheep. The fractional transfer of unconjugated bilirubin from the S.P. to the M.P. was 5 times greater in mutant sheep. The net hepatic uptake of unconjugated bilirubin was found to be on average 1.4% of the M.P. in mutants as compared to 4.4% in normal sheep. The hyperbilirubinemia observed in mutant Southdown sheep appears, therefore, to be due to a defect in the uptake of bilirubin by hepatic cells and resembles Gilbert's syndrome in man.

IODINE KINETICS IN THE DOG.* Sol M. Michaelson and William J. Quinlan, Jr.* Univ. of Rochester, School of Medicine and Dentistry, Rochester, N.Y.

Although the dog is commonly used in biomedical investigations, there is a paucity of information on thyroid physiology in this species. Thyroid function studies have been performed in Beagles ranging in age from 2 months to 14 years of age. Analysis of parameters of iodine kinetics reveals essential similarities and differences between the dog and man, as well as other species. Thyroid uptake of ^{131}I reaches a peak 3-5 days after intravenous injection of the isotope. At the end of 7 days, 25% of the injected activity is still retained in the gland. Thyroxine is bound to albumin, α_1, and α_2 globulin fractions and to a lesser extent to the beta globulin fraction; the serum content of protein bound iodine (PBI) is 2.1 ± 0.5 µg/100ml serum (mean ± s.d.); and free thyroxine is 2.2 ± 0.6 mµg/100ml serum. The relative binding affinity for triiodothyronine (T3) is almost comparable to that of thyroxine (T4) as indicated by resin sponge uptake of 51.0% (T3) and 42% (T4) in contrast to that of the human, 30.1% (T3) and 11.7% (T4) suggesting greater saturation of T4 binding proteins in man. The disappearance curve of T4 from the serum is triphasic represented by a rapid initial component attributed to a distribution phase; followed by a second component which describes a half-life of 9.1 ± 0.06 hours and a slower third component characterizing a half-life of 32.0 ± 0.11 hours. The disappearance rate of T3 is similar. These data provide a basis for comparative analysis of iodine kinetics in the dog in relation to man and other species.

*This paper is based on work performed under contract with the U.S. Atomic Energy Commission at the University of Rochester Atomic Energy Project and has been assigned publication No. UR-49-1120.

MYOCARDIAL GLUCOSE AND FREE FATTY ACID METABOLISM IN UNANESTHETIZED DOGS. Harvey I Miller, Keuk Yong Yum * and Beatrice C. Durham * Lankenau Hospital, Division of Research, Philadelphia, Pa. 19151

In studying myocardial FFA metabolism in the unanesthetized dog, it was found that the arterio-venous glucose difference across the heart was so small that precise uptake of this substrate was not possible. It was felt that the use of tracer quantities of ^{14}C glucose (UL) infused into unanesthetized dogs fitted with coronary sinus and carotid artery catheters could measure the exact degree of participation of this substrate in heart muscle metabolism. Coronary blood flow was measured so that uptake could be calculated. Mongrel dogs of either sex trained to rest quietly or run on a treadmill were infused continuously for 2 hours with ^{14}C glucose after an initial primer dose. Under similar conditions, we have shown that FFA contributed 25% to 100% of energy needed for the myocardium. In the present study, 7% of myocardial O_2 consumption was utilized for glucose oxidation during rest while 34% of O_2 was needed for FFA. When FFA levels and myocardial uptake were decreased with a glucose infusion, the percent oxygen for FFA utilization was lowered to 25% while that for glucose rose to 22%. Norepinephrine which raised the FFA myocardial oxygen consumption to 80% lowered that for glucose to 2%. During work of trained dogs, the O_2 used for glucose utilization in the heart did not change but O_2 FFA percent rose to 80%. The sum of the FFA and glucose oxidized plus glycerol, lactate and pyruvate taken up by the heart provide more energy than the heart utilized. Since we have shown that virtually all the FFA taken up is oxidized, it is felt that the myocardium is storing some carbohydrate in the form of glycogen. Glucose is a minor contributor of immediate energy to the heart and only under severe conditions does this substrate provide a considerable amount of energy.

(Supported in part by USPHS, NIH Grants FR-5585 & HE 12636)

PROSTAGLANDIN E_1 AND LSD INDUCED CHANGES OF THE PLASMA PHOSPHOLIPIDS WHICH VARY WITH PHYSICAL AND PSYCHIC STRESS. R.P. Miller, B.D. Polis, A.M. Pakoskey, E. Polis, H.P. Schwarz, and L. Dreisbach. Aerospace Medical Research Dept., NADC, Johnsville, Warminster, Pa. 18974, and Phila. Gen. Hosp., Philadelphia, Pa. 19104 (Intr. by R. Squires)

Humans and animals subjected to different types of stress exhibit elevations in plasma phosphatidyl glycerol. These changes and the variable changes in the other plasma phospholipids permitted statistical differentiation of the stressed populations (Biochem. Med. 2:286, 1969). To study the controlling mechanisms of the observed changes, 3, 10 and 30 µg of prostaglandin E_1 were injected into normal rats and 5, 10 and 20 µg into hypophysectomized rats. A separate series of rats received 500 µg of lysergic acid diethylamide (L.S.D.). Control animals were injected with saline. After 45 minutes the animals were sacrificed, and the plasma and brains analyzed for phospholipids. The normal rat injected with PGE_1 showed a straight line log dose response both in the elevation of plasma phosphatidyl glycerol and in the decrease in lecithin, as well as a non linear increase in phosphatidyl ethanolamine. Injection of 500 µg LSD into normal rats duplicated the rise in plasma phosphatidyl glycerol and phosphatidyl ethanolamine as well as the decrease in plasma lecithin. Hypophysectomized rats failed to significantly alter the plasma phospholipid pattern. The brains of the normal rats injected with either PGE_1 or LSD showed elevations in phosphatidyl glycerol and the brains of hypophysectomized rats showed a rise in phosphatidyl glycerol of lesser magnitude. The changes in phospholipid patterns mimic those previously reported (ibid, above). The data indicate that the plasma phospholipid changes found in stress reflect energetic control mechanisms mobilized by brain excitation which are mediated by prostaglandin and pituitary hormones.

CALCIUM-45 UPTAKE AND POTASSIUM-INDUCED RELEASE OF ACTH FROM THE ADENOHYPOPHYSIS. J. V. Milligan* and J. Kraicer, Department of Physiology, Queen's University, Kingston, Ontario, Canada.

According to the "stimulus-secretion coupling" hypothesis, the release of hormone is initiated by a depolarization of the plasma membrane which is followed by an increased entry of Ca^{++} into the cells. Exposure of rat adenohypophyses, in vitro, to increased concentrations of K^+ provokes the release of several of the adenohypophysial hormones, including ACTH, presumably as a result of depolarization. Experiments have been performed to see if the increased release of hormone initiated by the high-K^+ medium is indeed accompanied by a movement of Ca^{++} into the cells. We have measured simultaneously the H-3 mannitol and Ca-45 spaces in rat adenohypophyses incubated in Krebs-Ringer bicarbonate (KRB) which contains 5.9 mM K^+, or KRB containing 29 mM K^+ (5K). We have found that the Ca-45 space is almost doubled in the 5K medium while the H-3 mannitol space remains unchanged. The addition of corticosterone (1 µg/ml), which prevents the augmented release of ACTH in 5K, does not prevent the increase in the Ca-45 space. Conclusions: (1) There is a flux of Ca^{++} into the cells of the adenohypophysis associated with the augmented release of adenohypophysial hormones in 5K. This is consistent with the "stimulus-secretion coupling" hypothesis. (2) Corticosterone, which acts on the adenohypophysis to inhibit the 5K-induced increase in ACTH release, does not act simply by preventing the entry of Ca^{++} into the cells.

PYRIDINE NUCLEOTIDE CONTENT IN STORED HUMAN ERYTHROCYTES SUBJECTED TO METABOLIC INHIBITION IN VITRO. M. S. Millman*, C. B. Scott*, and A. Omachi. Univ. of Illinois at the Med. Center, Chicago, Ill.

Erythrocytes collected in acid-citrate-dextrose were washed and incubated for 2.5 hours in a Tris(pH 7.4)-Ringer's medium at 37° in a Dubnoff shaker. Extracts were prepared from packed cells and pyridine nucleotide concentrations (in nmoles/ml of erythrocyte) were determined. As observed previously (BBA 184: 139, 1969), NADH and NADPH decreased and $NADP^+$ increased when medium glucose was omitted. In the present study, these changes were noted in cells stored briefly (0-2 days) as well as in cells stored for 2 weeks. In contrast, no change in NAD^+ was observed in briefly stored cells whereas an increase in this nucleotide was found in cells stored for 2 weeks. Similarly, NAD^+ did not vary when freshly drawn cells were incubated in the presence of 0.5 mM iodoacetate but did increase when cells preserved for longer periods were tested. In the presence of 5 mM fluoride (F^-), NADH increased and NAD^+ decreased in briefly stored cells; after 2 weeks of storage, NADH did not change but NAD^+ decreased so that the sum of these nucleotides was lowered. If F^- were added to a glucose-free medium, the decline in NADH observed in the absence of substrate was not as great in either fresh or 2 week-old cells; the NAD^+ level after 2 weeks was lower in the presence of F^- but no change was observed in fresh cells, in contrast to all other cases in which this inhibitor was added. Alterations in $NADP^+$ and in NADPH in the presence of either iodoacetate or F^- were minor. The variations seen in this study, notably in NAD^+, suggest that the regulation of erythrocyte metabolism involving pyridine nucleotides appears to be modified during the first few weeks of storage.

(Supported by USPHS grant, GM-11430.)

Effect of hypoxia with constant arterial $[HCO_3^-]$, $[H^+]$, and PCO_2 on cerebrospinal fluid (csf) $[HCO_3^-]$ and lactate concentration $[La^-]$. A.H. Mines and S.C. Sørensen (Intr. by R.H. Kellogg). Dept. of Physiol. and Cardiovasc. Res. Inst., Univ. Calif. Med. Ctr., San Francisco, Calif. 94122

Ventilatory acclimatization to chronic hypoxia is mediated by a fall in $[HCO_3^-]$ in csf and presumably in brain extracellular fluid. We proposed that this fall is largely due to the hypoxic brain's enhanced lactic acid production. A hypoxic mammal hyperventilates, however, raising pH_a and reducing $[HCO_3^-]_a$. This will tend to reduce $[HCO_3^-]_{csf}$ in 2 ways: 1) Reducing $[HCO_3^-]_a$ lowers the concentration gradient $[HCO_3^-]_a$ minus $[HCO_3^-]_{csf}$. 2) Raising pH_a reduces the potential (csf minus blood) and thus reduces the electrical potential gradient (blood minus csf) for $[HCO_3^-]$. This might explain why, in chronic hypoxia, $[HCO_3^-]_{csf}$ falls more than $[La^-]_{csf}$ rises. These experiments examined the changes of $[HCO_3^-]_{csf}$ and $[La^-]_{csf}$ in 8 anesthetized paralyzed dogs during 6 hr of hypoxia (P_aO_2=28 mm Hg) when pH_a and $[HCO_3^-]_a$ were held at control values.

Mean±S.E.M. at	Control	1 hr hypoxia	3 hr hypoxia	6 hr hypoxia
pH_a	7.396±0.004	7.400±0.003	7.391±0.005	7.394±0.003
$[HCO_3^-]_a$ (mEq/l)	24.9±0.3	25.4±0.3	25.1±0.2	25.1±0.2
pH_{csf}	7.313±0.009	7.311±0.006	7.304±0.007	7.292±0.009
$[La^-]_{csf}$ (mEq/l)	1.68±0.10	1.96±0.15	2.27±0.18	2.32±0.17
$[HCO_3^-]_{csf}$ (mEq/l)	25.2±0.4	24.3±0.4	23.4±0.5	23.1±0.3

We conclude that in hypoxia the fall in $[HCO_3^-]_{csf}$ is greater than the rise in $[La^-]_{csf}$ even when pH_a and $[HCO_3^-]_a$ are held constant. The results are consistent with this hypothesis: H^+ ions from brain production of HLa titrate HCO_3^- out of csf. The La^- ions then move out of csf more rapidly than HCO_3^- ions move back in, causing more fall in $[HCO_3^-]_{csf}$ than rise in $[La^-]_{csf}$. (Supported by NIH grants GM-09262 and HE-06285.)

CURRENT ELICITED REPETITIVE FIRING IN CAT FAST AND SLOW TWITCH MOTOR UNITS. David J. Mishelevich[1]. Laboratory of Neural Control, National Institute of Neurological Diseases and Stroke, Bethesda, Md. 20014.

Spinal cord motoneurons innervating fast and slow twitch muscle units in the lateral and medial gastrocnemius, soleus and plantaris muscles of the cat were investigated with regard to repetitive firing behavior with intracellular stimulation. Approximately two-thirds of the motor units had fast twitch muscle units and one-third had slow twitch units. Slightly more than half the fast twitch and all the slow twitch motoneurons fired repetitively to the intracellular injection of a current step. In the fast twitch groups, the cells that did and did not repetitively fire could not be separated on the basis of resting membrane potential, antidromic action potential, twitch time to peak amplitude of the single twitch or peak amplitude of the single twitch. There was, however, a significantly higher rheobase in the fast twitch cells that did not repetitively fire. The proportion of cells falling into the three groups: fast twitch-repetitively firing, fast twitch-nonrepetitively firing, and slow twitch-repetitively firing did not significantly change when the cells were chosen on the basis of minimum antidromic action potential between 65 and 85 mv. All underwent rapid adaptation in the first few interspike intervals. Nonlinear addition of single muscle twitches during repetitive firing suggests a possible mechanism at the level of the single motor unit which may contribute to the initiation of movement.

[1]Present address: Subdepartment of Biomedical Engineering, Traylor Building, Johns Hopkins University School of Medicine, Baltimore, Md. 21205

SEASONAL CHANGES IN HEART RATE-CORE TEMPERATURE RELATIONSHIPS. Sherwin Mizell and L. Craig Miller*. Indiana University, Bloomington, Indiana.

Our investigations have been focused on the separate and collective roles of the thyroid gland and the autonomic nervous system in regulating the heart rate-core temperature relationship in Rana pipens. Using a unique data acquisition system we have tested intact, unrestrained and unanesthetized frogs throughout the year over a core temperature range of 15-32°C. During the summer (June, July, August) animals tested over this temperature range exhibited a linear response of heart rate to increasing and decreasing core temperature. The slope of the best fit line was 4.52. During the winter (December, January, February) animals exhibit a linear response which is reduced and contains two statistically different components. From 15-24°C the slope is 2.91. At a core temperature of 24°C the heart rate response line flattens out and the slope from 24-32°C is 1.61. Spring and fall animals exhibit intermediate, transitional responses. Atropinized animals tested during fall, winter and spring exhibit the summer pattern of response but with decreased slopes. Reserpine and dichloroisoproterenol decrease the slope of the response. Thyroxine and propylthiouracil did not cause a deviation from untreated controls. The autonomic nervous system seems to act as the mediator or intermediary in regulating heart rate response to changing core temperature. Apparently in the intact animal the functional level of the thyroid is not involved in this phenomenon.
(Supported by grant no. GB-6937 from the National Science Foundation, Indiana Heart Association and by Air Force Office of Scientific Research, contract no. F44620-68-C-0014.)

EFFECT OF SYNTHETIC SURFACTANTS ON INTESTINAL ABSORPTION OF GLUCOSE IN HAMSTERS. Jack D. Moore*, M.L. Zatzman* and D.K. Meyer. University of Missouri School of Medicine, Dept. of Physiology, Columbia, Mo.

Two anionic (alkylbenzene sodium sulfonate, ABS and linear alkylate sulfonate, LAS), a cationic (cetyltrimethylammonium bromide, CTMB) and a nonionic (triton x-100) synthetic surfactant were examined for their effects in varying concentrations (10 to 1000 ppm) on the intestinal absorption of glucose *in vivo* through the use of an infusion-autoanalysis system. Each surfactant was found to decrease glucose absorption in a dose-related manner. These effects were reversible for the anionic and cationic agents at levels of 250 ppm and less. The nonionic surfactant effect was reversible at levels as high as 1000 ppm. The effect of these agents on intestinal permeability to glucose as a possible mechanism responsible for decreased glucose absorption was examined in an *in vitro* everted, phlorizinized preparation. Permeability to glucose was increased in a dose-related manner by each surfactant. Histologic preparations revealed irregularity of the striated border at 250 ppm for ABS and CTMB and at 100 ppm for LAS, whereas no abnormalities were observed for Triton at levels as high as 1000 ppm. The demonstration of decreased glucose absorption *in vivo* at levels which did not increase intestinal permeability to glucose, and was reversible suggested that their mechanism of action at low levels was not secondary to gross cytolysis, inhibition of metabolic pathways or due solely to increased permeability to glucose. Supported in part by USPH Environmental Sciences R01 ES00302.

NATURE OF HEAT INDUCED CUTANEOUS VASCULAR RESPONSE IN *IGUANA IGUANA* Kenneth R. Morgareidge* and Fred N. White. Department of Physiology, UCLA School of Medicine, Los Angeles, Calif.

Iguanid, varanid, and agamid lizards are known to heat more rapidly than they cool. We have previously associated this with increases in cutaneous blood flow during heating as determined by the clearance rate of Xe^{133} (Nature, in press). *Iguana iguana* was used to determine whether changes in cutaneous flow were under central nervous or local control. A small amount of Xe^{133} dissolved in saline was injected subcutaneously into the dewlap, neck, flank, tail, back, or leg. The selected area was heated with an infrared lamp. A decrease in the Xe^{133} half-time indicating an increase in blood flow was observed in any heated area. On cooling, the half-time returned to near the control value. Clearance rate did not change when the injection site was heat shielded and the rest of the animal was heated. Systemic infusion of pentolinium in doses known to cause ganglionic blockade in *Iguana* had no measurable effect on blood flow or on the cutaneous vascular response to heating. Neither control flow nor heating response of the dewlap changed significantly when lidocaine was infiltrated along its base. Local injection of vasodilators (papavarine, acetylcholine) caused an increase in blood flow. We conclude that the cutaneous vascular response to heating is not controlled by a general or segmental reflex, but is most probably a direct effect of heat on vascular smooth muscle. (Supported by NSF grant GB-8523 and USPHS grant HE 5696)

COMPARISON OF IN VITRO AND IN VIVO EFFECTS OF PANCREOZYMIN (PZ), URECHOLINE (U), AND DIBUTYRYL CYCLIC AMP (DCAMP) ON SECRETION AND SYNTHESIS BY RAT PANCREAS. J. Morisset* and P.D. Webster. V.A. Hosp. and Med. Coll. of Ga., Augusta, Ga.

Confusion exists in the literature concerning effects of PZ and U on pancreatic zymogen secretion and synthesis. Observations made using in vitro models report that PZ and U are associated with increases in rates of secretion without an effect on synthesis; observations made using in vivo models report increases in rates of both secretion and synthesis. In an attempt to clarify this problem, studies were performed in rats using both in vivo and in vitro models. In vitro addition of PZ (0.45 units/ml.), U (10^{-3} molar) and DCAMP ($1.16 \cdot 10^{-3}$ molar) initiate secretory responses as measured by increases in protein and amylase in supporting media. Neither PZ, U nor DCAMP in vitro were associated with increases above control levels in L-phenylalanine-C^{14} incorporation into protein. In vivo PZ and U were associated with prompt increases in rates of both amylase secretion and incorporation of L-phenylalanine-C^{14} into protein. These studies show administration of PZ, U, and DCAMP in vitro are associated only with secretion; in vivo they are associated with increases in both synthesis and secretion. These studies resolve differences in the literature based on observations derived from different experimental models.

A NEW TOOL FOR NEUROPHYSIOLOGICAL RESEARCH: PARADOXICAL SLEEP WITHOUT ATONIA, Adrian R. Morrison and Kerstin Henley (intr. by J. M. Sprague). Depts. of Animal Biology and Psychology and Institute of Neurological Sciences, University of Pennsylvania, Philadelphia, Pennsylvania.

Bilateral lesions of the dorsolateral pontine tegmentum in four cats eliminated the normal atonia of paradoxical sleep (PS) and released elaborate behavior during this state as early as two days postoperatively. Episodes of PS without atonia occurred after synchronized sleep and with the same frequency as normal PS. The episodes began with elevation of the head and various movements of the limbs. The animal righted itself and moved its head forward ataxically. Several attempts at standing followed. Movements became increasingly violent. The episodes terminated as the cats convulsed while recumbent or actually stood and leaped. Licking, chewing, and signs of rage appeared occasionally. The EEG showed desynchronization. The pupils were miotic, and the nictitating membranes relaxed. Intense light or tactile stimulation did not awake the animals although low-intensity sound did. PS without atonia remained unchanged in one animal until sacrificed six months postoperatively. One cat appeared normal during wakefulness except for slight stumbling. The others showed varying degrees of cerebellar ataxia. The movements released during PS resembled those obtained by electrical stimulation of the medullary reticular formation and fastigial nuclei. This preparation provides a tool for the investigation of structures controlling movements during PS and wakefulness. Our results confirm Jouvet and Delorme's demonstration that the atonia of PS can be eliminated by pontine lesions but do not support the reports that pontine lesions selectively abolish PS. (Supported by NIH Grants NB-08377O1 and 5 TO1 GM-1036).

PARTITION OF ENERGY EXPENDITURE BETWEEN HOST AND TUMOR. S. D. Morrison. Lab. Physiol., NCI, NIH, Bethesda, Md. 20014.

The constancy of the 24 hr energy compartment expended by normal rats on spontaneous motor activity (Morrison, S. D., J. Physiol. 197: 305, 1968) suggested a new approach to the problem of partition of energy expenditure between host and tumor. As the tumor cannot generate motor activity the total activity compartment of energy expenditure of the whole organism would be expected to decline during tumor growth by an amount determined by the energy metabolism of the tumor in vivo. The activity compartment of energy does decline during growth of a Walker tumor (Morrison, S. D., Fed. Proc. 28: 786, 1969). The amount of decline leads to an estimate of tumor metabolism about 3 times greater than either the estimate derived from in vitro metabolism of the tumor or that derived from the expected metabolism of the host. All of the depression of activity vanishes within 24 hr of excision of the tumor. These results can describe three definable energy compartments of the tumor bearer: (a) the endogenous energy expenditure of the tumor; (b) the effective energy expenditure of the host which is lower than would be expected from its body mass and food intake and which is defined as that part of the host's metabolism that is capable of generating spontaneous activity; and (c) a compartment that is imposed on or induced in the host by the tumor, but that is unable to support or generate motor activity. Compartment (c) is quantitatively equal to the energy equivalent of the lactic acid produced by the Walker tumor in vivo (Gullino, Grantham and Courtney, Cancer Res. 27: 1031, 1967). This equality and the lability of the load compartment suggests that the lactate output of the tumor is a non-utilizable metabolic load on the host.

EFFECT OF GRAVITATIONAL STRESS ON CEREBRAL BLOOD FLOW. P. J. Moser, F.E. Williams, and W. K. Brown (intr. by R. W. Bancroft). Biodynamics Branch, USAF School of Aerospace Medicine, Brooks AFB, Texas.

Although techniques for the determination of cerebral blood flow are available, there has been little application of these methods to the determination of flow during gravitational stress. In the present study five normal mongrel dogs were prepared by surgical ligation of all extracranial branches of the carotid artery. Following extracranial placement of a scintillation detection probe, Xenon-133 dissolved in saline was injected into the internal carotid artery and the clearance curve plotted on a standard XY plotter under the following conditions: pre-run control, $+2G_z$, $+3G_z$, and $+4G_z$. Mean cerebral blood flow was calculated by the least squares method as described by Bergner. Resting flow rates were also calculated using two-compartment analysis and correlation with the least squares method was obtained. The curves were corrected for background and recirculation. Cerebral blood flow during control conditions ranged from 15-28 ml/100g/min. The means of cerebral blood flow for the five animals were 17.8, 5.3, 3.0, and 0.5 at 1, 2, 3, and 4 G respectively (values given in ml/100g/min.). Cerebral flow appears to decrease as expected with increasing G levels ($p<.001$). Although the mean values in this laboratory are lower than those reported by Howard, the animals in question in this study were deeply anesthetized (Nembutal) and had surgical ligation of the extracranial carotid branches. No difficulty was encountered in maintaining constant probe-animal geometry under G. The technique used appears to give consistently reproducible results and should prove valuable in the study of the mechanics of cerebral blood flow during acceleration stress.

SELECTIVE ACTIVATION OF Ia VOLLEYS BY TRANSIENT MUSCLE STRETCH. Carter G. Mosher*, Douglas G. Stuart, Rebecca L. Gerlach*, & Robert M. Reinking*. Dept. of Physiology, College of Medicine, Univ. of Arizona, Tucson, Ariz.

Studies on the central connections of muscular afferents have often employed electrical stimulation of peripheral nerves to generate a group I volley. The ratio of Ia to Ib contribution to such volleys remains uncertain. This report extends our own work (Fed.Proc.28:783,1969) and that of Lundberg and Winsbury (Acta Physiol. Scand. 49: 155-164,1960) in emphasizing the usefulness of brief mechanical stretches for selective activation of a Ia volley. "Square" stretches, 20 msec in duration, were applied to de-efferented cat soleus muscles maintained at comparable degrees of initial tension by setting length to give a peak of active tension during an isometric twitch. An averaging computer was used to summate soleus nerve volleys recorded simultaneously at nerve-muscle and spinal cord-dorsal root (L_7 or S_1) levels. A stretch of 5μ amplitude was sufficient to generate a clearly defined group I volley. As stretch amplitude was raised by 5μ increments to 60μ, the volley grew progressively in size, decreased in duration (5 msec to 1.5 msec) and displayed a 4 msec reduction in time from stretch onset to volley peak. These changes were accompanied by the less predictable appearance of a second volley (peak 1.5 msec after the first). Our data on isolated afferents suggest that the first volley is of Ia origin while the second volley represents double firing of some Ia afferents plus a group II input. Significant Ib contribution is excluded since only 4 of 127 Ib fibers responded within this stretch range and then at latencies beyond formation of either volley. (Supported in part by USPHS, NIH Grant NB 07888).

ALTERATIONS IN DRINKING FOLLOWING ISOPROTERENOL STIMULATION OF HIPPOCAMPUS. Damon Mountford (intr. by F. E. Samson, Jr.). Department of Psychology, The University of Kansas, Lawrence, Kan.

Subcutaneous injections of small amounts of isoproterenol are known to increase drinking in albino rats. The purpose of this study was to find a site in the central nervous system where isoproterenol would elicit drinking. Double cannulae were permanently implanted, using stereotaxic procedures, in the hippocampus or medial septal area of albino rats. This allowed direct application of 1-5 micrograms of isoproterenol or other drugs directly to the central nervous system. Histological examination of the brains on termination of the experiment confirmed the intended implant sites. Direct application of either isoproterenol or carbachol to hippocampus significantly increased drinking. Direct application of carbachol to medial septal area significantly increased drinking, but applications of isoproterenol had no effect on drinking. Applications of atropine to hippocampus 5 minutes before applying either carbachol or isoproterenol significantly reduced the drinking elicited by carbachol but had no effect on the drinking elicited by isoproterenol. It appears that peripheral injections of isoproterenol may alter drinking by acting in the hippocampus of the brain. Isoproterenol does not seem to act by stimulating a cholinergic system since atropine fails to block its effects on drinking. The hippocampus may contain a β-adrenergic system of fibers involved in the regulation of drinking.

EVIDENCE FOR BRAIN SODIUM RECEPTORS CONTROLLING RENAL SODIUM EXCRETION AND PLASMA RENIN ACTIVITY. David R. Mouw* and Arthur J. Vander. Department of Physiology, Univ. of Michigan, Ann Arbor, Mich.

Ventriculo-cisternal perfusion was employed in pentobarbital-anesthetized dogs. All solutions perfused through the ventricles closely resembled the electrolyte composition of normal cerebrospinal fluid, except with regard to sodium chloride. The hypo-osmotic low-sodium solution was identical to the control (normal-sodium) solution minus 25 mM/L NaCl. The iso-osmotic low-sodium solution also contained 25 mM/L less NaCl, but contained 50 mM/L mannitol. Renal function was studied during alternating 50-minute periods of control and low sodium perfusions. The hypo-osmotic low-sodium perfusion caused decreases in sodium excretion (48.2%) and potassium excretion (17.3%) and a 121% increase in arterial plasma renin activity. The changes were reversed during the recovery period (control perfusion). The effects of the iso-osmotic low-sodium perfusion were qualitatively similar. Changes in hematocrit, pulse pressure, GFR, RPF, and filtration fraction were minor and inconstant; nor did they correlate with the changes in electrolyte excretion. Similar changes in electrolyte excretion were observed during low-sodium perfusion after acute renal denervation. It is concluded that there exists a brain receptor near the ventricles which is sensitive to sodium and which can initiate hormonal mechanisms controlling renal electrolyte excretion and renin secretion.

IMMEDIATE AND DELAYED EFFECTS OF ACUTE DEHYDRATION ON PLASMA VOLUME IN MAN. Loren G. Myhre* and Sid Robinson. Indiana Univ., Bloomington, Indiana 47401.

Four unacclimitized young men were rapidly dehydrated by walking for two or more hours on a treadmill at 5.6 km/hr up a 2½ grade in a hot environment (50°C dry bulb, 26° wet bulb). Blood volume by carbon monoxide, serum electrolyte concentrations, plasma osmolality, and plasma protein concentration by refractive index were determined prior to and at various intervals following the work in the heat. Salt and water balances were determined for a 24 hour period beginning with the initial exposure to the heat. Acute dehydration averaging 4.2% of body weight was accompanied by an average plasma volume decrease of 17% and no change in total circulating red cell volume. Refractive index increased an average of 23% while changes of less than 2% were observed in serum electrolyte concentrations and plasma osmolality as a result of the dehydration. Following the work in the heat the subjects were kept dehydrated and resting in a cool room (25°C) for several hours. Blood volume measurements were repeated in this resting recovery at 5 hours post exercise at which time dehydration had progressed, largely by insensible water loss, to an average of 4.5% of control body weight. In spite of this continued loss of body water, the plasma had regained an average of 45% of the loss observed immediately following the acute dehydration. Food and water intake were controlled to maintain the subjects state of dehydration until they returned to the laboratory the next morning. At this time little or no change was observed in any of the parameters studied at 5 hours post exercise the evening before. It is apparent that within 5 hours following acute dehydration plasma volume losses are partially replaced by shifts from other body fluid compartments. (Supported by U S-AMRDC Contract MD-2449).

INHIBITION OF ADENOSINE DEAMINASE ACTIVITY IN HUMAN SERUM. N.E. Naftchi, S. Jonas*, E.W. Lowman* and M. Demeny*. Dept. Pharmacol. and Inst. of Rehab. Med., N.Y.U. Med. Ctr., N.Y. 10016.

Adenosine deaminase (AD, adenosine amino hydrolase, EC 3544) has a general distribution in blood and tissue fluids. Serum AD activity has been used for the diagnosis of various diseases especially leukemia and liver disease. Saturating levels of substrate adenosine (5.5 μmolar) were incubated with 0.01, .025, 0.05, 0.1 and 0.2 ml of human serum for 60 minutes at 37° C. AD activity increased linearly with increasing amounts of serum (.01 to 0.05 ml). Despite using adenosine concentrations in excess of 5.5 μmolar and keeping the ratio of serum to substrate constant, AD activity decreased when 0.05 to 0.2 ml of serum were used in the reaction mixture. The inhibition was significantly decreased when sera were dialyzed against distilled water from 16 to 72 hrs. The activity of AD in fresh serum was inhibited by heat denatured serum (15 minutes intermittently at 90° C). These experiments indicate the presence of an inhibitor in human serum which inhibits AD activity when concentration of serum in the reaction mixture exceeds 0.5 ml. The inhibitor cannot be 5'-adenylic acid deaminase (5'-AD) which precipitates during dialysis, since heat denaturation of serum destroys 5'-AD activity. Furthermore, 10 to 150 old units of 5'-AD isolated from rabbit muscle incubated with 0.05 ml of human serum produced no inhibition of AD activity. The nature of the inhibitor (s) remains obscure until further work with metalic ions, purines, 5'-AD and AD isoenzymes is completed. It follows from the above that elevated serum AD activity in certain diseases may be due to diminished amounts of inhibitor, increased enzyme production, or to both.

EFFECTS OF TEMPERATURE ON THE VASCULAR RESPONSES OF THE RABBIT EAR. T. Nagasaka* and L. D. Carlson. Dept. of Human Physiol., School of Medicine, Univ. of Calif., Davis, Calif.

Responses of the auricular vessels to various peripheral and central temperatures were studied in 48 male white rabbits. After anesthetization with urethane (0.75g/Kg) and chloralose (40mg/Kg), the ear was perfused with the femoral arterial blood by means of a peristaltic pump. The ratio of perfusion pressure to perfused flow is a measure of vascular resistance of the ear. Temperature of the blood was kept at 40, 30, 20 and 10°C for 20 minutes at each temperature, and each stepwise change followed a Latin square sequence beginning with blood temperature of 40°C. Changing blood temperature from 40 to 10°C caused a steady increase in vascular resistance in both isolated and phenoxybenzamine perfused ears. In these ears, the change in vascular resistance among other factors could be explained by change in viscosity of the blood with temperature. In the innervated normal ears, reduction in blood temperature from 40 to 20°C caused a marked increase of vascular resistance; whereas, cooling of the blood to 10°C caused a decrease of the resistance. Thus, cold induced vasodilatation was observed only when the vasoconstrictor fibers were intact during cold blood perfusion. Vascular resistance was highest in the innervated ears and lowest in the ears perfused with phenoxybenzamine at any given blood temperature. Constrictor response of the vessels to noradrenaline (0.14μg/ml blood perfused) was maximum with blood temperature between 40 and 20°C, but it was reduced greatly at 10°C. Body temperature fell during the perfusion sequences and average resistance for a given blood temperature in the innervated ears was influenced by change in body temperature.

FACTORS AFFECTING VENTRICULOAURICULAR (V-A) CONDUCTION IN MAN, Onkar S. Narula, Benjamin J. Scherlag, Frank J. Hildner, Lawrence S. Cohen and Philip Samet, Mount Sinai Hospital, Miami Beach, Florida

In 35 patients with 1:1 atrioventricular (A-V) conduction and 15 with complete heart block (CHB) antegrade and retrograde conduction were studied during atrial and ventricular pacing (VP), respectively. All patients, except 3, had bundle branch block or intraventricular conduction defects. Bundle of His (BH) recordings were used to measure atrial to BH activation (A-H) and BH to ventricular activation (H-V) time. A-H approximates conduction time through the A-V node and H-V represents conduction time through the His-Purkinje System. Of the 35 patients with 1:1 A-V conduction 14 showed V-A conduction during VP. In these 14, mean A-H and H-V times were 75 $\pm$16 msec and 44 $\pm$6 msec, respectively. The remaining 21 patients had no V-A conduction during VP. The average value for A-H and H-V time in this group was 137 $\pm$70 and 55 $\pm$13 msec, respectively. There was a significant difference in A-H ($p < .02$) as well as H-V ($P < .05$) times of the patients with and without retrograde conduction during VP. In the 15 patients with CHB 5 had V-A conduction during VP. In these 5, the antegrade block was distal to the BH deflection and the average A-H time was 69 $\pm$16 msec. Of the 10 patients in CHB without VA conduction, 8 had antegrade block distal to the BH deflection with an average A-H time of 104 $\pm$17 msec, which is significantly higher ($p < .02$) than in the 5 with V-A conduction. The remaining 2 patients without V-A conduction had block in the A-V nodal region. Our data indicate that the presence of functionally intact antegrade conduction (A-V node and His-Purkinje System) increases the probability of V-A conduction. Even in patients with complete heart block distal to the BH deflection the presence of normal antegrade conduction through the A-V node (A-H) significantly increases the chances of retrograde conduction. This study suggests that there is generally a single functional pathway for both A-V and V-A conduction.

RENIN RELEASE: FURTHER EVIDENCE FOR THE ROLE OF A TUBULAR NATRIASTAT. Franklin D. Nash. Department of Physiology and Cardiovascular Research and Training Center, Indiana University Medical Center, Indianapolis.

These experiments were designed to determine whether renin release (RR) by the canine kidney is controlled by a preglomerular barostat or by a tubular natriastat. A Starling resistance was used to produce controlled elevations in ureteral pressure (UP) without cessation of urine flow. The resultant decrease in the vascular transmural pressure gradient would stimulate a barostat while the decrease in GFR and tubular sodium delivery would stimulate a natriastat. Renal arterial infusion of NaCl, superimposed upon UP elevation, would then increase tubular sodium delivery, decreasing the stimulus to a natriastat while the stimulus to a barostat would be maintained. The following values were obtained; RR is expressed as ng angiotensin-II/min·g (mean $\pm$ SE).

Control	0.74 $\pm$ 0.13
UP 25-30 mm Hg, normonatremia	4.28 $\pm$ 0.93
UP 25-30 mm Hg, hypernatremia	1.35 $\pm$ 0.35
Recovery	0.87 $\pm$ 0.15
UP 50-60 mm Hg, normonatremia	13.0 $\pm$ 1.51
UP 50-60 mm Hg, hypernatremia	5.77 $\pm$ 0.75
Recovery	0.75 $\pm$ 0.18

These data provide further evidence that RR by the canine kidney is regulated by a tubular natriastat rather than by a vascular barostat.
(Supported by USPHS Grants HE 08055, HE 09339, HE 05625, and H 06308.)

N-METHYLATION OF HISTAMINE DURING GASTRIC SECRETION. Henri Navert,* Eunice V. Flock, Gertrude M. Tyce and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

In a previous study (The Physiologist 10:261, 1967) we found methylated histamine but little histamine (H) in gastric juice and mucosa during gastric secretion stimulated by H-^{14}C in dogs with gastric pouches. In the present study under similar steady state conditions, samples of gastric mucosa and plasma were collected after 140 minutes of infusion of H-(2-ring-^{14}C) diHCl, 10.05 mg/kg/min. Urine and gastric juice were collected continuously during the infusion. Improvements in the methods of analysis by TLC and TLE permitted characterization of the methylated metabolites of H. The percentage distribution of total ^{14}C of the amine fraction at steady state in the various samples was

		Corpus mucosa	Pouch mucosa	Juice	Aortic plasma	Portal plasma	Urine
I	Histamine	4.0	4.8	1.4	9.0	5.6	1.5
II	N-Methylhistamine	3.9	5.4	4.3	2.0	2.0	6.4
III	N-Dimethylhistamine	2.7	9.5	48.6	6.0	5.2	2.1
IV	1,4-Methylhistamine	43.6	36.4	21.1	6.0	6.0	8.7

The observation by Lin, T. M. et al. (Ann. N.Y. Acad. Sci. 99:30, 1962) that II and III are more potent secretagogues than H has also been confirmed. The identification of circulating II and III and the accumulation of III in the juice suggest that III may be the preferred specific metabolite of I for stimulation of HCl secretion. (Supported by NIH Grants NB-4004 and AM-2827.)

ASSESSMENT OF CONTRACTILE STATE OF THE HEART UTILIZING THE MAXIMUM VALUE OF (dP/dt)/P. N. S. Nejad, M. D. Klein, I. Mirsky and B. Lown (introduced by M. G. Herrera). Harvard School of Public Health and Harvard Medical School, Boston, Mass.

The ratio of rate of change in left ventricular pressure to instantaneous pressure [(dP/dt)/P] provides a sensitive method for evaluating myocardial function during isovolumic systole. Changes in peak (dP/dt)/P were evaluated in Starling canine heart-lung preparations (HLP) and in intact dogs. Some animals had selective occlusions of the left anterior descending coronary artery (LAD) with injection of 0.1 ml of mercury. Left ventricular pressure was recorded with a fiberoptic pressure catheter. dP/dt was derived electronically and the ratio (dP/dt)/P plotted every five msec during isovolumic systole. In the HLP those variables known to influence contractility were examined separately. Increasing end-diastolic pressure (EDP) from 4-10 mmHg by varying preload did not significantly change peak (dP/dt)/P (52-59 sec^{-1}). With selective variations in afterload (EDP 4-14 mmHg), peak (dP/dt)/P remained essentially constant (47-51 sec^{-1}). With sustained elevation of EDP greater than 16 mmHg, peak (dP/dt)/P was depressed by an average of 47%. Isoproterenol (0.1 μgm/min) restored it to control value. In intact dogs isoproterenol infusion (5 μgm/min) increased the peak (dP/dt)/P approximately two fold. Following LAD occlusion in intact dogs decreases in peak (dP/dt)/P paralleled increases in EDP but did not necessarily correlate with changes in cardiac output. These results indicate that peak (dP/dt)/P can be utilized as a reliable index of the state of myocardial contractility.

MATERNAL PROTECTION OF THE FETUS AT HIGH ALTITUDE. Marita L. Nelson (intr. by P. S. Timiras). Dept. of Physiology-Anatomy, University of California, Berkeley, California.

Previous studies have demonstrated marked impairment of postnatal growth in rats developing at high altitude. The present investigation was designed to assess the same parameters during late gestation and the early neonatal period. Adult Long-Evans rats were taken from the Berkeley animal colony (250 ft) to Barcroft Laboratory, White Mountain Research Station (12,470 ft), allowed time for acclimatization, and bred. The females were autopsied either at late gestation or at term. A group of rats were maintained at Berkeley as sea level controls. Fetal and neonatal body weights, lengths, hematocrits, heart and adrenal weights were recorded, as well as placental weights. Body length and weight were identical in both high altitude and sea level animals and no significant differences were found in heart weights, or adrenal weights between the two groups. The hematocrits of the high altitude pups were slightly lower than those of the controls. Placental weight was significantly greater in high altitude rats suggesting that the maternal organism is capable of compensating for the reduction in ambient oxygen tension by an increase in placental size, thus affording normal fetal development in utero.

(Supported by Grants USPHS GM 09267 and NSF GB 3171).

EFFECT OF PANTOTHENIC ACID DEFICIENCY ON TRANSPORT OF WATER AND SODIUM IN CANINE DUODENUM. Ralph A. Nelson and Bertram Fleshler*. Mayo Clinic and Mayo Foundation, Rochester, Minnesota, and Western Reserve University, Cleveland, Ohio.

Sorption of water and sodium was studied before, during, and after pantothenic acid deficiency in dogs. Tyrode's solution with added ^{24}Na was instilled into a chronic Thiry-Vella intestinal loop for 5 minutes. Net water transport and insorption, exsorption, and net sodium transport were determined. A total of 136 tests were performed in three dogs through two courses of pantothenic acid deficiency. Insorption of sodium steadily decreased and was least when deficiency was most severe. Exsorption did not change until halfway through the deficiency period, when it increased not only significantly but to a level exceeding that of insorption. Exsorption remained increased until treatment began. After therapy, insorption increased and exsorption decreased, thus reverting to their usual relationship and approaching control values in rates of transport. As a result of changes in unidirectional flux, enterosorption of sodium occurred during the latter half of the deficiency period and reverted to absorption after treatment. Enterosorption of water occurred concurrently with that of sodium and it too was converted to absorption after treatment. It was concluded that pantothenic acid deficiency produced a loss of body water and sodium into the gut lumen during transport. These changes occurred early in deficiency. Sodium loss was caused by two factors: a decrease in insorption and an increase in exsorption. (Supported by NIH Grant AM-12069.)

INDICATION OF A DIRECT STIMULATORY ACTION OF TYRAMINE ON RABBIT AORTIC STRIPS. Thomas E. Nelson, Jr. Department of Physiology Pharmacology, University of Texas Dental Branch, Houston, Texas.

Displacement of stored norepinephrine (NE), from sympathetic nerve terminals is generally accepted as the major, if not only mechanism by which tyramine produces a sympathetic response. However, this mechanism, originally presented by Burn and Rand (J. Physiol. 1958), and elaborated by Furchgott et al., (J.P.E.T., 1963) has not gone entirely without question (Fawaz, Ann. Rev. Pharmacol. 1963)and this author and co-workers later suggested that tyramine acts on its own but requires the presence of a small amount of NE at the receptor sites to elicit the sympathomimetic response. In experiments using pulsed rabbit aortic strips and rapid oxidation of added NE in the bath the response to NE can be separated from the tyramine response in a manner similar to differentiating the NE and serotonin or histamine contractions. Another suggestion of an action independent of NE is the fact that repeated dose response curves show a progressively decreased sensitivity at lower doses of tyramine but with similar maxima while in the presence of cocaine the maxima are raised significantly above those of controls. These observations suggest one of three possibilities: (1) tyramine acts by a mechanism other than NE, (2) the endogenous NE released by tyramine is protected from removal or (3) the NE released by tyramine is acting on different receptors. (Supported by N.I.H. Grant HE 10124.)

PULSE WAVE VELOCITY IN THE ASCENDING AORTA OF THE DOG. W. W. Nichols*, J. E. Webster* and D. A. McDonald, Department of Physiology and Biophysics, University of Alabama, Birmingham, Alabama 35233.

It is necessary to know the wave velocities or alternatively pulse wave velocity or the elastic properties of the ascending aorta to evaluate methods of deriving stroke output from the ventral aortic pressure. We have used two methods. Apparent phase velocities (c') in the ascending aorta were calculated from simultaneous measurements of pressure at two sites in 10 anesthetized, open-chest dogs, at heart rates ranging from 0.5 to 3.2 beats/sec. The pressures were measured using catheter tip manometers with very high resonant frequencies. Harmonic analysis of both pressure curves was performed by a digital computer (PDP-7) and the apparent phase velocity was calculated from the measured phase shift between the two pressures. The values of c' were fairly constant for frequencies above 2 Hz, in the range of 3.4 - 4.4 m/sec (mean pressure 80-130 mm Hg). Below 2 Hz c' increased sharply due to reflections. The high frequency values were assumed to be dominated by the wall elasticity. Comparisons were made with the "wave-front velocity" (McDonald, J. Appl. Physiol. 24: 73-78, 1968) which is not affected by reflections. The values here were 3.3 - 4.7 m/sec. From previous wall thickness estimations these velocities imply an elastic modulus of $1.46 - 2.45 \times 10^6$ dyn/cm^2. The dependance of the wave velocity upon mean arterial pressure was also studied. The pressure was varied by the infusion of vasoactive drugs and hemorrhage. Work supported by PHS Grant HE-11310.

SYMPATHETIC NERVE ACTIVITY IN UNANESTHETIZED CATS. I. Ninomiya*, W. V. Judy*, W. M. Caldwell*, and M. F. Wilson. Department of Physiology and Biophysics, West Virginia University Medical Center, Morgantown, West Virginia 26506

Sympathetic nerve activity (SNA) to kidney was recorded in 5 unanesthetized cats. In one of these cats, the SNA in the cervical nerve was recorded simultaneously with renal SNA. Under aseptic conditions, the left renal nerve was separated 1-3 cm from the surrounding tissues. Electrodes were looped around the central cut end of the nerve, and then both the electrodes and nerve were isolated from the surrounding tissues by silicon rubber material. Cervical sympathetic nerve was separated from the left vago-depressor-sympathetic trunk in the neck and the electrodes were looped around the intact nerve. In all cats, other electrodes were implanted for the measurements of electrocardiogram (ECG) and electromyograms (EMG). All electrodes were chronically implanted. In unanesthetized cats, SNA changed significantly in association with the EMG and body movements. In these cases, the noise signals (e.g., EMG and mechanical artifacts) and the SNA have not yet been discriminated. Even when the cats lay down quietly and no EMG was detected in ECG traces, the SNA was not always constant. Therefore, the average SNA synchronous to heart rate was computed from 200 cardiac cycles by using a CAT. QRS spikes were used as a trigger signal for this device. In 4 cats the grouped SNA synchronous to heart rate was recorded 2-4 days after surgery, and in 1 cat it was recorded 10 days after surgery. The maximum amplitude and the time interval between QRS spikes and the grouped SNA varied with heart rate. The changes in renal and cervical SNA were not always identical under spontaneous conditions, but both SNA increased simultaneously to sound stimuli.
Supported in part by NASA Grant NGL 49-001-001 and NIH Grant HE 10234-04.

ASSESSMENT OF THE SYNERGISTIC RELATIONSHIP BETWEEN SERUM CALCIUM AND DIGITALIS. Gaeton T. Nola*, Steven Pope* and Donald C. Harrison, Cardiology Division, Stanford University School of Medicine, Palo Alto, California.

A controlled, quantitative study to evaluate the relationship between elevated levels of serum calcium and enhanced sensitivity to the toxic arrhythmic effects of digitalis glycosides was performed in 21 anesthetized dogs. The amounts of acetylstrophanthidin (AS) necessary to produce ventricular tachycardia (VT) in dogs with normal serum calcium were compared to the toxic doses of AS in these same animals, but with either moderately high (less than 15 mEq/L) or extremely high (greater than 15 mEq/L) serum calcium levels. The changes in serum calcium were produced by infusions at various rates. Blood gases, pH values, and serum K+ were maintained within normal limits. The amounts of AS necessary to produce VT were 871 ± 82 μg in normals and 945 ± 49 μg in animals with moderately high serum calcium. The toxic amount of AS was significantly less, 774 ± 137 μg, in animals with extremely high serum calcium. The increase in arterial pressure produced by AS was significantly greater in hypercalcemic animals, but duration of toxicity and increases in serum K+ were not. Thus it appears that the inotropic and/or peripheral vasoconstrictor responses to AS were not altered by elevations in serum calcium. It is concluded from these studies that extremely high levels of serum calcium do enhance the development of toxic arrhythmias produced by AS. However, these high levels of serum calcium are seldom observed in patients with disease states producing hypercalcemia.

REINNERVATION OF RAT TONGUE: EVIDENCE THAT TASTE NEURONS HAVE UNIQUE TROPHIC FUNCTIONS. Bruce Oakley. Dept. of Zoology, Univ. of Michigan, Ann Arbor, Mich. 48104.

When denervated, mammalian taste buds degenerate completely, although they will reappear if the nerve fibers regenerate into the tongue. Mixed non-taste nerves, foreign to the tongue, (e.g. auriculo-temporal, mylohyoid) can be made to innervate the posterior part of the tongue by crossing to the distal stump of the IXth nerve. Thus, touch or gentle pressure (especially on the papillae where taste buds are normally found) or cooling of the tongue will elicit action potentials in these cross-regenerated nerves. However, unlike nerves containing taste fibers, the foreign nerves lack trophic abilities vis-a-vis taste buds in that they can neither reform nor structurally maintain existing taste buds. It is postulated that taste nerve fibers contain a trophic agent(s) which is necessary both for the formation and maintenance of taste buds, and this agent is unique to taste neurons.
Supported, in part, by PHS Grant NB-07072.

GENERALIZED SWEAT RESPONSIVENESS TO PERIODIC CUTANEOUS HEATING -- WITH SPECIAL REFERENCE TO ITS RELATIONSHIP TO HEAT TOLERANCE. Tokuo Ogawa* (intr. by R. W. Bullard), Niigata Univ. Sch. of Med., Niigata, Japan and Indiana University, Bloomington, Indiana.

Periodic infrared irradiation was given to the back of the trunk, and the sweat rate of non-irradiated regions was recorded continuously by means of resistance hygrometry. Sweat rate fluctuated in response to the cyclic change of the skin temperature of the irradiated area, depending on the length of the irradiation period. This sweat responsiveness varied with individuals, and the individuality was found most distinct with repetitive irradiation of two-minute periods, i.e., one min on and one min off. The majority of subjects native to warm regions and only few of those native to cool environments showed good sweat responsiveness. Athletic and physical labor careers apparently improved sweat responsiveness, while ageing, seasons, sleep and the background level of sweat rate failed to show effects on the latter. This type of sweat response is considered to be mediated through neural pathways originating from the cutaneous thermoreceptors, involving the central thermoregulatory mechanism, and ending up at the secretory cells of the sweat glands. Improvement in sweat responsiveness may result from an increase in sensitivity or activity somewhere along these pathways, which may be acquired only by long-term heat acclimatization.

PHYSIOLOGIC ACTIVITY OF THE CANINE VENA CAVA in vivo. E. Ogden, W. Yates* and M. Anliker*. Environmental Biology Div., NASA, Ames Research Center, Moffett Field, Calif. 94035, and Dept. of Physiology and Dept. of Aeronautics and Astronautics, Stanford Univ., Stanford, Calif. 94305.

To investigate the part played by the inferior vena cava in the venous reservoir system, we have studied the properties of this vein in nembutalized dogs in terms of the speed and attenuation of small sinusoidal pressure waves, and measured the intraluminal pressure and diameter (Pieper gauge) using catheter tip gauges. The wave speed and the effective Young's modulus usually increased with transmural pressure. In order to certify the transmural pressure and to ensure that the cross section of the vein approximates a circle, we have opened the abdomen and displaced the viscera. This procedure produced no consistent change in wave speed. We have changed the transmural pressure by: massive infusions, tilt, balloon occlusion, vagus stimulation, and intravenous injection of lethal doses of various substances. Electrical excitation of the distal end of the cut greater splanchnic nerve also increased the wave speed; in this case, the diameter diminished with increased pressure. Whereas the increases in wave speed were usually accompanied by an increase in pressure, and therefore might be ascribed to passive effects of distension, the response to splanchnic stimulation clearly must involve an active, physiologically produced change in the properties of the vein, since the diameter increased while the pressure rose. Similar effects were noted with large doses (20 μg/kg) of epinephrine. This additional evidence that the vena cava in vivo can show an active change which could help to adapt its capacity to diminished blood volume (Franklin, 1936, 1937) again raises the question as to how far this capability aids the reservoir function.

STUDY OF THE SOURCES AND SINKS OF THE ERG OF THE BIRD. Thomas E. Ogden, Depts. of Neurology and Physiology, University of Utah College of Medicine, Salt Lake City, Utah.

The location of sources and sinks of current in a biological volume conductor can be closely approximated by determination of the second spatial derivative of the resultant field potential. Because of its radial symmetry, retina, when uniformly illuminated, is essentially isopotential in the tangential plane,

i.e., $\frac{\partial^2 V}{\partial x^2} = \frac{\partial^2 V}{\partial y^2} = 0$. A plot of $-\frac{1}{R_z}\frac{\partial^2 V}{\partial z^2}$ against z provides a convenient display of source and sink position (R_z = specific retinal resistance at depth z) From an application of these considerations to the ERG of the bird, it is suggested that the source of PIII, in this form, is uniformly distributed over the outer receptor segment.

(Supported by USPHS Grant NB-04135)

PHYSIOLOGICAL REACTIONS OF MEN PERFORMING MONOTONOUS WORK. James F. O'Hanlon Jr.* and Steven M. Horvath. Inst. Environ. Stress, UCSB, Santa Barbara, Calif.

The blood concentrations of adrenaline (A), noradrenaline (NA), free fatty acids (FFA) and glucose (G), and the heart rate (HR), respiratory rate (RR), palmar skin conductance (C) and neck muscle tension (EMG) were studied in 11 men under basal conditions and in each of three different experimental conditions. The latter were two monotonous (vigilance) tasks that differed in difficulty, and a control task requiring relaxed attention. In experimental conditions the subject sat within a special chamber which permitted him to perform the task while blood samples could be taken and electrophysiological recordings made without alerting him to the fact. [A] and [NA] were analyzed by a new, uniquely sensitive assay. Comparing both vigilance tasks to the control the results were: [A] was higher at onset but no different later; [G] was no different; HR was higher but HR variability was much less; RR was higher; and C was greater but C variability was much less. [NA] increased in all tasks in a manner related to [FFA] and EMG. [A], HR variability, RR, C and EMG were related to vigilance performance. Conclusion: monotonous "mental" work evokes widespread physiological reactions, some of which parallel performance.

EFFECTS OF LITHIUM IONS ON THE EXCITATORY AND INHIBITORY SYNAPTIC PROCESSES OF APLYSIA GANGLION CELLS. Hirohisa Ono*, Makoto Sato, Division of Neurosurgery, University of Oregon Medical School, Portland, Oregon

1.) Effects on the resting membrane: The resting potential is slightly hyperpolarized (1-4mV) during the initial 20 min. of Li^+-Ringer perfusion, then depolarized progressively beyond the original resting level. Depolarization reaches 2-4mV after one hour of Li^+-Ringer perfusion. (2.) Effects on the excitatory synapses: The acetylcholine (ACh)-induced depolarizing response, particularly the increase in membrane conductance is markedly depressed during Li^+-Ringer perfusion, from 90-44% of the control at 60 min. and 22-15% at 300 min. Cholinergic EPSP's activated by afferent stimulation are also depressed by Li^+-Ringer but more markedly so than the same cell's response to directly applied ACh. On the contrary, non-cholinergic EPSP's are slightly enhanced by Li^+-Ringer perfusion, suggesting that a different ionic mechanism underlies these EPSP's. (3.) Effects on the inhibitory synapses: The ACh-induced hyperpolarizing response is significantly augmented by Li^+-Ringer perfusion; the normal membrane conductance increase during the response is further enhanced & reaches a maximum of 122-198% of the control value in 40 min. of Li^+-Ringer perfusion. The enhancement of these inhibitory synaptic responses is abolished by treatment with Eserin, thus suggesting a change in cholinesterase activity resulting from Li^+-Ringer perfusion. (4.) After-effect of Li^+-Ringer perfusion: Depression of the excitatory ACh-induced response resulting from Li^+-perfusion is followed by a super-normal increase in the response (300% control), when perfusion is returned to normal Ringer. The super-normal enhancement is not abolished even after treatment with anti-cholinesterase. In conclusion, the blocking action of Li^+ on synaptic transmission is specific to the Na^+-dependent, excitatory synaptic process.

Supported by U.S. PHS Grant No. NBO 1687-11

FORELIMB VASCULAR RESPONSES TO LOCAL CHANGES IN PLASMA OSMOLARITY IN RENAL HYPERTENSIVE DOGS. H.W. Overbeck. Depts. of Physiology and Medicine, Michigan State Univ., E. Lansing, Mich.

We have presented evidence suggesting decreased forelimb vascular responses to local changes in plasma concentrations of several vasoactive agents in renal hypertensive dogs (Physiologist 10:270, 1967; XXIV Internat. Congr. of Physiol. Sciences 7:333, 1968). We now report the effect of experimental renal hypertension on the forelimb vascular response to local changes in plasma tonicity. Hypotonic (150 mOsm/l) NaCl solution or hypertonic (2700 mOsm/l) dextrose solution were infused at 8 and 1.5 ml/min., respectively, into the pump-perfused (100 ml/min.) brachial arteries of 50 male mongrel dogs. In 27 of these dogs (Hypertensive Group) sustained hypertension was created by unilateral nephrectomy and cellophane perinephritis. The remaining 23 dogs (Control Group) underwent only unilateral nephrectomy. Approximately nine weeks later vascular responses to local changes in plasma tonicity were studied again in the opposite forelimb. Responses within each group before and after nephrectomy were compared by the paired Student's t test. Mean P_A in the Hypertensive Group had increased from 124 to 164 mm Hg; mean P_A in the Control Group remained unchanged at 124 mm Hg. In normotensive dogs there was a significant linear correlation ($P<.01$) between magnitude of response to each solution tested and initial level of limb vascular resistance. Considering this covariance relationship, there was a significantly decreased response ($P<.02$) to both hypo- and hypertonic solutions within the Hypertensive Group. In contrast, there was no significant change ($P>.5$) in response within the Control Group. The results suggest that similar to most other vasoactive agents tested, limb vascular responses to local changes in plasma osmolarity are decreased in renal hypertensive dogs.

EXPERIMENTAL PULMONARY GAS EMBOLISM. Yohtaro Oyama* and Merrill P. Spencer. Tonan Hospital, Sapporo, Japan and Virginia Mason Research Center, Seattle, Washington.

Nine sheep with chronically implanted ultrasonic Doppler flow probes on pulmonary and brachiocephalic arteries were subjected to experimental intravenous injections of oxygen, nitrogen and carbon dioxide. Three different rates of injection (0.03 cc/Kg/min., 0.09 cc/Kg/min. and 0.15 cc/Kg/min.) were used for 30 minutes. Findings included transient and moderate elevation of right ventricular pressure, decrease in pulmonary blood flow and diminished arterial Po_2. The degree of these cardio-pulmonary changes was dependent on the kind and dosage of the gas used, as listed on the table, showing the maximum changes in systolic right ventricular pressure (SRVP) and Pa_{O2} in each experiment by the percentage of the control value. In the amounts of the gases tested, no bubble signals were detected by the probe on the brachiocephalic artery, but at the terminal experiments, using lethal dose of air, many distinct bubble signals were observed on this systemic artery, indicating the passage of the gas through the pulmonary vasculature.

	SRVP (% of Control)			Pa_{O2} (% of Control)		
	N_2	O_2	CO_2	N_2	O_2	CO_2
0.03 cc/Kg/min	123.3	122.5	100.0	85.3	90.8	100.0
0.09 cc/Kg/min	176.8	155.8	100.0	76.4	77.3	91.6
0.15 cc/Kg/min	199.7	171.3	100.0	67.7	73.7	88.3

Supported by Boeing UGN & USPHS grants HE 09131 & FR 05588.

ROLE OF THE CAROTID BODY IN THE INTERACTION BETWEEN ARTERIAL PO2 AND PCO2 IN THE INITIATION OF BREATHING. R.D. Pagtakhan*, E.E. Faridy*, and V. Chernick. Depts. of Physiology and Pediatrics, University of Manitoba, Winnipeg, Canada.

We have previously reported an interaction between arterial PO2 and PCO2 during the initiation of breathing in exteriorized fetal lambs (Fed.Proc. 28: 439, 1969). Fetal sheep were cross-circulated with newborn lambs and during cord occlusion could be maintained in the apneic fetal state for up to 30 minutes. In order to initiate respiration fetal blood gases were altered by adjusting the ventilation and composition of the inspired gas of the newborn donor. Liquid ventilation was monitored by a plethysmograph and fetal femoral arterial blood sampled at the time of the first breath. These experiments have been repeated in 7 fetuses following bilateral carotid sinus nerve transection. Mean (range) arterial PO2 (mmHg) at various ranges of PCO2 (mmHg) before and after denervation are shown below:

PCO2	PO2 (Before)	PO2 (After)
<40	4.0 (2-5)	11.1 (6-15)
40-100	8.9 (6-14)	8.4 (6-15)
>100	19.2 (17-20)	8.9 (5-13)

In the presence of the carotid body an increase in PCO2 is associated with an increase in PO2 at the time of the first breath. Following carotid body denervation, hypoxemia will still initiate respiration but the PO2 at the time of the first breath is independent of the arterial PCO2. The results suggest that the fetal carotid body responds to hypercapnia. Central chemoreceptors appear to be insensitive to hypercapnia at the time of the first breath. (Supported by the Medical Research Council of Canada).

RELATIONSHIP BETWEEN ARTERIAL INFUSION OF ATP, ADP; THEIR Ca^{++} CHELATION PROPERTIES AND VASODILATION. W.N. Palmer and D.L. Jones (intr. by L.A. Toth). Dept. of Physiology, LSU Med. Ctr., New Orleans, Louisiana.

The relationship between vasodilation caused by ATP and ADP and chelation of the vasoconstrictive calcium ion by these agents has been investigated. The isolated forelimb of the dog was perfused at constant flow with femoral arterial blood via an extracorporeal roller pump. Solutions of ATP or ADP were introduced into the circuit between the femoral artery and the pump. The vasodilator response of the forelimb to such infusions was recorded from the brachial artery, a small artery in the foot pad, a small vein in the dorsum of the paw and a branch of the brachial vein. When the vasodilator response to each of these agents reached its maximal steady-state value the Ca^{++} activity of the arterial blood perfusate was determined by use of a calcium ion flow-thru electrode system (Orion Research ionalyzer). A T-tube with a three-way stopcock bonded into the side arm was interposed into the perfusion system between the pump and the brachial artery of the perfused forelimb. Arterial blood samples were taken from the T-tube side arm immediately prior to, during, and after infusion of ATP or ADP. The calcium ion activity of these blood samples was determined immediately by use of the calcium ion electrode. Certain infusions of ATP or ADP into the perfusate caused a fall of the calcium ion level which was attended by a vasodilator response of the forelimb vascular bed. Incremental increases of the rate of ATP or ADP infusion caused an incremental decrease of the blood calcium ion level and increased the vasodilator response. Cessation of drug infusion was followed promptly by return of the various pressures of the forelimb to their control values and restoration of the calcium ion level to its control value.

Supported by a Grant-in-Aid from the Louisiana Heart Association.

MECHANISM OF SODIUM INACTIVATION IN THE SQUID GIANT AXON

Y.Palti* and W.J.Adelman,Jr. Univ. of Maryland, Baltimore and Marine Biol. Lab., Woods Hole, Mass.

It has been shown (Adelman and Palti, 1969, J. Gen. Physiol. 53:685) that elevating external potassium conc. inactivates the initial transient sodium current in the squid axon. Giant axons were voltage clamped in ASW and in Na-free ASW. Membrane potential, E_m, was held at resting potential, stepped to some depolarizing value, E_{pulse}, and then after various delays, t_{pulse}, stepped instantaneously to a post-pulse potential value, E_{post}. The amplitude of the transient tail current initiated upon stepping membrane potential from E_{pulse} = 0 to a variety of E_{post} values indicated a linear relationship between the transient tail current and E_m. The reversal potential, E_r, for the delayed potassium current was shown to be a function of t_{pulse}. The locus of change of E_r with t_{pulse} was similar to that of both the sodium inactivation parameter h and K conductance parameter n. The changes in [K] external to the axon membrane calculated from the above data provide values which are sufficient to attenuate g_{Na} as potassium conductance turns on in agreement with the kinetics of sodium inactivation. Thus sodium inactivation is the result of accumulation of K ions at the external axon membrane surface.

EFFECTS OF UNILATERAL RENAL ISCHEMIA ON SALT AND WATER METABOLISM IN SHEEP MEASURED BY SPLIT FUNCTION TECHNIQUES. Harold R. Parker, Dept. of Physiological Sciences, University of California, Davis, California 95616.

Constriction of one renal artery sufficiently to reduce blood flow by 40-50% consistently produced hypertension in sheep. During early hypertension plasma expanded transiently then contracted to a normal or subnormal volume. 24-hour urinary aldosterone was elevated during initial increases in blood pressure but did not remain at the higher level despite persistence of hypertension. Plasma renin activity increased in a manner parallel to blood pressure. Accompanying hypertension was a marked salt hyperphagia which was associated with polydipsia and polyuria. Salt ingestion sometimes reached five times normal daily intake. In most experiments the unoperated kidney developed severe natriuresis which was augmented by intramuscular injection of ADH. Salt restriction did not lower blood pressure, but lessened sensitivity to ADH. Withholding salt resulted in negative $T^C_{H_2O}$ in the unclamped kidney which returned to normal when salt was given. Nephrectomy of the clamped kidney in one ewe resulted in prompt cessation of salt hyperphagia, disappearance of natriuresis of the remaining unclamped kidney and return to normal of blood pressure and plasma renin activity. Results suggest that an intrarenal mechanism influencing salt ingestion is stimulated to supranormal activity by renal ischemia, but operates independently of blood pressure. (Supported in part by U.S. Public Health Grant No. FR-05457).

CAUSE OF ABOLITION OF CAFFEINE CONTRACTURE OF FROG SKELETAL MUSCLE IN CALCIUM FREE SOLUTIONS. David J. Parry* and George B. Frank. Dept. of Pharmacology, University of Alberta, Edmonton, Canada.

Two possible explanations have been given for the disappearance of the caffeine-induced contracture of frog skeletal muscle in Ca^{++}-free solutions. Frank (J.Physiol. 163: 254, 1962) suggested that it resulted from depletion of a bound, intracellular store of Ca^{++}, whereas Luttgau and Oetliker (J.Physiol. 194: 51, 1968) considered it to be due to a block of excitation-contraction coupling. To differentiate between these hypotheses, the amount of Ca^{++} remaining in the muscle, at the time when no further contracture occurred in response to 5 mM. caffeine, was determined in a number of muscles. Toe muscles of Rana pipiens were exposed to Ringer's solution containing ^{45}Ca (20 μ c/ml.) overnight at 4°C. The muscles were then set up in a bath through which Ca^{++}-free Ringer flowed at a constant rate. After 180 mins. of perfusion the muscles were exposed to 5 mM. caffeine Ringer without Ca^{++} for various lengths of time. Radioactivity in the effluent was determined and an efflux curve for Ca^{45} constructed. When no further contracture could be elicited the muscle was removed and the amount of Ca^{45} remaining determined. This fraction was expressed as a proportion of the Ca^{45} originally present in the slow-efflux compartment. When pairs of muscles from the same frog were treated identically the proportion of ^{45}Ca remaining in each at the time when contractures failed was similar. However, when one muscle was exposed to caffeine more frequently than the other, the residual Ca^{++} in the two muscles varied markedly in an unpredictable manner. This suggests that a simple depletion of an intracellular site is not an adequate explanation of the phenomenon.

Supported by the Muscular Dystrophy Association of Canada.

EFFECTS OF CATIONS ON PROLACTIN (PL) AND GROWTH HORMONE (GH) SECRETION BY RAT ADENOHYPOPHYSES (AP) IN VITRO. J. A. Parsons* and C. S. Nicoll. Dept. of Physiology-Anatomy, Univ. of California, Berkeley.

Rat AP explants were incubated in medium 199 or in 199 with different Ca^{++}, Mg^{++}, Na^{+}, and K^{+} concentrations for 4 to 6 hr. at 37 C in 95% O_2 and 5% CO_2 atmosphere. The amounts of Pl and GH secreted into the medium were estimated by disc electrophoresis and densitometry. Low Ca^{++} inhibited Pl secretion by 40-60%. Low Mg^{++} showed no effect on Pl secretion. Slightly elevated (5x) Mg^{++} (4.1 mM) was without effect, but 10 mM and 20 mM Mg^{++} inhibited Pl secretion by 50 and 70%, respectively. Inhibition of Pl secretion by low Ca^{++} or high Mg^{++} was reversible. Low Na^{+} and K^{+} had no effect on Pl secretion. Elevated K^{+} (54 mM) produced slight but significant stimulation of Pl secretion by male AP, but had no effect on female AP. In 1.8 mM Ca^{++} GH secretion by male and female AP was markedly stimulated by 54 mM K^{+}, but was not affected by K^{+} in low Ca^{++}. Secretion of Pl and GH by rat AP in vitro is dependent upon Ca^{++}, but only GH secretion is markedly influenced by elevated K^{+}. The possible involvement of these ions in mediating the effects of hypothalamic factors which regulate Pl and GH secretion is being investigated.

Supported by N.I.H. Grant AM-11161

INACTIVATION OF MUSCLE POSTJUNCTIONAL RECEPTORS: THE EFFECT OF MAGNESIUM
R. L. Parsons* and W. L. Nastuk, Dept. of Physiol. and Biophys., Univ. of Vt., Burlington, Vt. and Dept. of Physiol., Columbia Univ., N. Y., N. Y.

Calcium has been shown to increase the rate of "desensitization" of the postjunctional membrane (PJM) receptors. To elucidate the mode of action of calcium in this process, the influence of magnesium on the rate of PJM receptor desensitization has been studied "in vitro" on the sartorius muscle of the frog, Rana pipiens, bathed in Ringer's solution made hypertonic by addition of sucrose to avoid muscle twitching. Desensitization of PJM receptors, produced by sustained application of 0.27 mM carbamylcholine (CARB) was estimated by measuring the rate at which the PJM effective membrane resistance (EMR) rises to control values after its initial reduction. Substitution of magnesium for calcium in the extracellular fluid reduced the rate and extent of receptor desensitization. The half-time of recovery of the EMR was 52 ± 10 seconds (12 fibers) from 6 muscles equilibrated in the hypertonic 1.8 mM calcium Ringer solution. In contrast, the half-time of recovery of the EMR in 4 fibers from 3 muscles equilibrated in the hypertonic calcium-free 2 mM magnesium Ringer solution was 201 ± 34 seconds. In the presence of 1.8 mM calcium the addition of magnesium (up to 12 mM) decreased the rate of desensitization. The inhibitory influence of 12 mM magnesium on the rate of inactivation was lessened as the calcium concentration was increased from 1.8 to 10 mM. The results indicate that the influence of calcium in PJM "inactivation" is not simply explained by calcium's ability to act as a membrane "stabilizing agent", but that this ion has some more specific action which is not comparably shared by magnesium ions. (Supported by NIH Grants: NB-04988 and Postdoctoral Fellowship 2F2-NB-21,225.)

EFFECTS OF THYROXINE AND COLD-ACCLIMATION ON LIVER MITOCHONDRIAL FATTY ACIDS.
J.F. Patton* and W.S. Platner. University of Missouri School of Medicine, Dept. of Physiology, Columbia, Missouri.

In cold-acclimation, changes in the fatty acid composition of hamster liver mitochondria occur (Chaffee, et al, 1967). In the present study relative concentrations of fatty acids from whole liver and liver mitochondria of rats cold-acclimated for 6 to 7 weeks were analyzed by gas chromatography. A Barber-Colman gas chromotograph equipped with dual hydrogen flame detectors was used to separate and identify the spectrum of fatty acids from C14:0 to C22:6. The columns were packed with 20% ethylene glycol succinate and all analyses were carried out isothermically at 190°C using helium as the carrier gas. Involvement of the thyroid gland was studied by the administration of propylthiouracil or L-thyroxine for 10 days to both warm- and cold-acclimated animals. Comparisons between various treatment means were statistically analyzed by the Tukey procedure. Cold-acclimation resulted in no change in total unsaturation of whole liver fatty acids but produced a significant decrease in total unsaturation of mitochondrial fatty acids. Injection of warm-acclimated rats with thyroxine also resulted in a significant decrease in unsaturation of mitochondrial fatty acids but no change occurred in whole liver. Treatment of cold-acclimated rats with propylthiouracil prevented the decrease in total unsaturation of mitochondrial fatty acids. Individual fatty acid changes were similar in mitochondria from cold-acclimated rats and warm-acclimated thyroxine-treated animals. The data suggest that cold-acclimation induces changes in mitochondrial structure which appear analogous to the effects of thyroxine. Supported by the University of Missouri Space Science Research Center and USPH - Nutrition Section of Arthritis and Metabolic Diseases. AM-12437-01.

TURNOVER AND OXIDATION OF PLASMA GLYCEROL IN LEAN AND OBESE HUMANS

Pavle Paul, Walter M. Bortz and Agnes C. Haff. (Intr. by H.I. Miller)
From the Division of Research, Lankenau Hospital, Philadelphia

Following a priming dose, Glycerol $^{14}C(u)$ was infused i.v. at a constant rate for 7.5 hours into human non-obese (65-82 kg) and obese (77-165 kg) subjects with indwelling arterial and venous catheters. O_2 uptake, CO_2 output, specific activity of CO_2, plasma glycerol, and plasma glucose were determined. Glycerol turnover and oxidation were calculated from the specific activities and the infusion rate of radioactive glycerol. Incorporation of glycerol into glucose was also calculated. There was straight line correlation between FFA concentration and plasma glycerol level; glycerol concentration and glycerol turnover; and glycerol turnover and per cent CO_2 from plasma glycerol. Positive correlation was found between the logarithms of glycerol turnover and the amount of glycerol oxidized. Positive log-log correlation was found between FFA concentration and glycerol turnover; also between glycerol turnover and % glucose derived from glycerol. After overnight fasting (11 subjects), the average glycerol level was 0.089 μmole/ml and the glycerol turnover was 73.5 μmole/min or 9.7 gms/24 hr. Some 30% of the glycerol turnover was converted to glucose and this represented only 2.3% of the total glucose turnover. After long starvation (21 or 35 days), the glycerol level was 0.404 μmole/ml and the turnover rate rose to 347.0 μmole/min or 46 gms/24 hr. Some 70-90% of the glycerol turnover was converted to glucose which was then in turn oxidized to CO_2. During long starvation glycerol turnover could account for 30% of the total glucose turnover and 70% of the glucose oxidized.

Supported by Grant No. AM-08887 and FR-5585

PHYSICAL PROPERTIES OF THE PERICARDIUM. Barbara L. Pegram* and Vernon S. Bishop. The Univ. of Texas Med. School at San Antonio, San Antonio, Texas.

Pericardial membranes for these studies were obtained from white albino rabbits weighing 1.4 to 2.4 kg and from mongrel dogs weighing 10 to 14 kg. The filtration coefficient for the pericardium was determined using a modification of the method described by J.M. Diamond. It was found to be $3.04 \times 10^{-4} \pm 0.42$ gm/cm^3-min and $3.04 \times 10^{-4} \pm 0.43$ gm/cm^3-min for the rabbit pericardium and the dog pericardium respectively. Pressure-volume experiments indicated that the relationship between pressure and change in radius could best be described as a curve which is concave to the y-axis and rises steeply with increasing pressure. With small pressure gradients molecules such as Evan's blue and albumin were found to penetrate the membrane. Supported in part by the Texas Heart Association and Air Force Contract F 41609-69-C-0022.

PATTERNS OF INTERACTION IN LATERAL GENICULATE CELLS. J. H. Penaloza* and G. P. Moore. Biomedical Engineering Lab., Univ. Southern California, Los Angeles, Calif.

Multiple neuronal spike trains have been recorded in the lateral geniculate nucleus of the cat thalamus under pentobarbitol anesthesia. Recordings were made with paired stainless steel microelectrodes whose tip separations were less than 1 mm. Under this anesthetic and with ambient light conditions many geniculate cells show burst activity randomly distributed in time. Spikes from each pair of cells recorded were fed into a computing system which was programmed to display autocorrelation histograms for each cell and the cross correlation histogram for each simultaneously recorded pair. A significant fraction of the cell pairs observed show correlated patterns of firing which we attribute to direct or shared excitatory synaptic connections. Hypotheses about the connections between these pairs, which can be inferred from analysis of the cross correlation, have been tested successfully by subsequent digital computer simulations. The cross correlation histogram, although derived from purely extracellular pulse train timings, can also yield details about the intracellular synaptic potentials generated in these cells, and inferences drawn from our records are quite consistent with previously published examples from intracellular records.

This work was supported by National Institutes of Health Grants NB 08207 and GM 16437.

EFFECT OF HYPERCAPNIA OR PROPRANOLOL ON COOLING RATE AND OXYGEN UPTAKE OF THE DOG. W. E. Pepelko, Ph.D* and S. M. Cain, Ph.D., Respiratory Physiology Branch, Physiology Division, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

Five groups of 8 dogs each were cooled in a water bath, 3 groups at 32°C and 2 at 34° C. The dogs were anesthetized with pentobarbital, paralyzed with a succinylcholine infusion, and respired with a Harvard respiration pump. Of the 3 groups at 32° C, 1 group breathed room air, 1 breathed 10% CO_2, and the third breathed room air and received 0.5 mg/kg/30 min of beta-adrenergic blocking agent, propranolol. Only the room air and 10% CO_2 groups were cooled at 34° C. At 32° C, the rectal temperature of the room air group decreased 1.6° in 2 hrs while the CO_2 group declined 3.0° and the beta-blocked group, 3.2°. At 34° C rectal temperature of air breathing dogs dropped 0.8° in 2 hrs compared with a 1.7° drop while breathing 10% CO_2. Oxygen consumption of control dogs at 32°C declined from 6.99 to 6.88 ml/kg/min STPD compared with a decline from 6.84 to 5.90 ml/kg/min during CO_2 exposure and 6.33 to 4.94 ml/kg/min during propranolol treatment. At 34° C, V_{O_2} increased from 6.28 to 6.77 ml/kg/min in controls while declining from 6.57 to 5.54 ml/kg/min during CO_2 exposure. It is suggested that the effect of hypercapnia is upon the beta-adrenergic receptors mediating nonshivering thermogenesis.

EFFECT OF VAGAL BLOCKADE ON VENTILATION IN CONSCIOUS, EXERCISING DOGS. E.A. Phillipson*, R.F. Hickey*, J.A. Nadel. Cardiovasc. Res. Inst., Depts. of Med. and Anesth., U.C. Med. Ctr., San Francisco, California.

We studied the influence of the vagus nerves on ventilation in conscious, trained, tracheostomized dogs at rest, during treadmill exercise, during inhalation of CO_2, and during body heating. At rest with the vagi intact, the duration of apnea produced by the Hering-Breuer inflation reflex (HBIR) varied directly with the inflating pressure. Inflating the lungs with airway pressures of 5-25 cm H_2O resulted in apnea of 20-40 sec duration. During exercise, the duration of apnea produced by HBIR decreased with increasing oxygen consumption; during inhalation of CO_2, the duration of apnea decreased as arterial pCO_2 increased. Heating the dogs decreased the duration of apnea; when panting occurred, no HBIR could be elicited. Bilateral vagal blockade with local anesthesia abolished HBIR, decreased resting respiratory frequency, increased tidal volume, but arterial pCO_2 was unchanged. During exercise ($\dot{V}O_2$ 20-30 ml/min per kg) with intact vagi, the respiratory rate increased to a maximum of 32 (± 4) breaths/min; during similar exercise and vagal blockade, respiratory rate remained fixed at 10-15/min. With the vagi intact, breathing various concentrations of CO_2 for 8 min (producing arterial pCO_2 ranging from 40 to 56 mm Hg) resulted in respiratory rates of 21 to 42 per min and increased ventilation (3.0-4.0 L/min per mm Hg CO_2); vagal blockade fixed the respiratory rate at 10-14/min and decreased the ventilatory response (0.5-1.5 L/min per mm Hg CO_2). In response to body heating with vagi blocked, panting still occurred. We conclude that afferent vagal stimuli, probably from pulmonary inflation receptors, are required for normal ventilatory control in the dog. These stimuli interact with the respiratory stimulation produced by exercise and CO_2 inhalation. Thermal panting is uninfluenced by this vagal information. (Supported in part by NIH Grant HE 06285 from National Heart Institute.)

RELATION OF DIRECT CORTICAL RESPONSES TO SOMAL FIRING IN THE CEREBRAL CORTEX. J. W. Phillis* and S. Ochs. Indiana University Medical Center, Indianapolis, Indiana.

Interaction of N wave DCR responses of apical dendrites in the cerebral cortex has shown an occlusive-like phenomenon indicative of a long-lasting active response [Ochs, in Frontiers Physiol. Psychol. (Ed.) R. Russell, 1966]. Our present studies of single cell responses in cat cerebral cortex, recorded from the central barrel of a multiple-barrel micropipette which contained Na glutamate and gamma-aminobutyric acid in the other barrels, were compared with surface responses evoked from either of a pair of surface stimulating electrodes. A third stimulating electrode was placed on the ipsilateral medullary pyramidal tract for some studies. Results were obtained from 172 cortical neurones, including 42 Betz cells, distributed at depths between 200 and 2000 microns. Surface stimuli which generated an N wave DCR evoked action potentials in 24 of the cells. A subthreshold excitant action of surface stimulation on a further 125 neurones was revealed by a simultaneous application of glutamate. Interaction of paired surface stimuli was manifested by occlusion of the second DCR and a failure of the response of cortical neurones to the second shock over a 10-20 msec period. A failure of the unit response to surface stimulation also occurred when it was preceded by the invasion of an antidromic spike. Inhibitory phenomena were not pronounced with the restricted surface stimulation employed in these experiments. Our results can best be explained by the hypothesis that the response of apical dendrites is an active one having a duration of 10-20 msec accompanied by an absolute and then a relative refractory period with a total duration of approximately 20-40 msec.

Supported by NIH Grant #R01 NB 01993-10.

THE CURRENT-VOLTAGE RELATIONSHIP OF FROG SKIN AND ITS ALTERATION BY OUABAIN. Gordon L. Pierpont* and Warren H. Dennis. Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Abdominal skin of Rana pipiens is mounted in a four electrode chamber containing a modified Ringer's solution. The current-voltage relationship is studied by sending a low frequency triangular wave of current through the skin via one pair of electrodes while recording the potential across the skin with the second pair. The slope of the I-V plot defines the dynamic resistance. The typical pattern during hyperpolarization showed a linear resistance at low current followed by a non-linear increase in the dynamic resistance until a "breakdown" point was reached. At this time the resistance fell rapidly to very low values and remained low until the current was reversed. The potential at which this "breakdown" phenomenon occurred was shown to be a function of current density, and not of total charge delivered. This breakdown phenomenon was also correlated with occurrence of a prolonged PD response upon cessation of current. The hysteresis and non-symmetry of the I-V plot indicated the existence of rectification in the skin. Addition of ouabain resulted in disappearance of the distinctive breakdown pattern. In some experiments ouabain addition resulted in a transient rise in the "breakdown" resistance and a diphasic response in the low current resistance. The PD response to high current was attenuated even before the PD had fallen to zero. (Supported in part by P.H.S. predoctoral fellowship.)

SYNTHESIS OF SERINE IN RAT KIDNEY IN VIVO AND IN VITRO. Robert F. Pitts, August Damian* and Martha MacLeod*. Cornell University Medical College, New York, N.Y.

Serine is synthetized in the kidneys of man, dog and rat and added in net amounts to renal venous blood. The probable precursor of renal serine has been identified as glycine by infusion of ^{14}C - labeled compounds into one renal artery of the rat for 40 min., removing the kidney, homogenizing it in picric acid, chromatographing the filtrate and measuring amino acid concentrations and radioactivity automatically in the column eluate. Infusion of ^{14}C - glycerol and ^{14}C - glucose did not result in labeling of kidney serine; accordingly, the pathway from 3 - phosphoglycerate, to phosphoserine to serine is not significant. ^{14}C - sarcosine is rapidly transformed to serine, but since sarcosine is present in blood or kidney of the rat only in trace amounts, it cannot be the precursor of the considerable amounts of serine formed. Rate of synthesis of serine in vivo has been measured by pulse labeling of kidney glycine and freezing the kidney in liquid nitrogen after 10, 20 or 30 sec. Since the reaction is reversible, the rate of conversion of serine to glycine has also been measured in vivo by the same procedure. Net rates in vivo are roughly comparable to those measured in vitro in homogenates of kidney. Both in vivo and in vitro rates are of the same order of magnitude as the rates of addition of serine to renal venous blood by the functioning kidney of the rat. Supported by research grants from the National Heart Institute and the Life Insurance Medical Research Fund.

EFFECT OF DORSAL RHIZOTOMY ON POSTURAL TREMOR IN THE MONKEY. Louis J. Poirier, Chihiro Ohye* and Rémi Bouchard*. Lab. Neuropsychiatrie exp., Dépt Physiologie, Université Laval, Québec.

A unilateral rhizotomy involving the dorsal roots between C2-4 and T1-2 was made in six monkeys that presented spontaneous and/or harmaline-induced tremor following brain stem and/or cerebellar lesions. Tremor was recorded (cinematographically and electromyographically) before and after the rhizotomy. Section of the cervical dorsal roots resulted in complete anaesthesia and akinesia of the corresponding limb which displayed only unpurposeful movements and posture. The rate and rhythm of the tremor and the reciprocity of the bursts in opposite muscles were not affected by the rhizotomy; the amplitude of the bursts, however, was less regular in the deafferented limb. The incidence of tremor episodes was greater and was still influenced by the posture of the limb in some animals. Faster bursts (12-13/sec) were also noted on the EMG and alternated with the more frequently encountered slower rhythm (5-8/sec) in response to harmaline in monkeys with cerebellar lesions. These findings suggest that the spinal dorsal roots do not play an important role in iniating postural tremor although they apparently exert a stabilizing effect on the amplitude of the bursts. Moreover the rate and rhythm of tremor are apparently integrated centrally and do not involve a peripheral reflex arc.
(Supported by grants from the Medical Research Council of Canada).

MOLECULAR AND KINETIC PARAMETERS OF SUGAR PERMEATION ACROSS THE FROG CHOROID PLEXUS. John W. Prather* and Ernest M. Wright. Department of Physiology, UCLA School of Medicine, Los Angeles, California 90024.

Sugars appear to employ a carrier mechanism for transport through the "blood-cerebrospinal fluid barrier" although the rate of permeation of most nonelectrolytes is directly related to their lipid solubility. Using an *in vitro* preparation of the frog posterior choroid plexus, we have investigated and characterized the nature of this transport process. The permeability of the epithelium to 37 sugars was measured by a rapid osmotic procedure and by tracer fluxes. Sugar transport across the membrane was found to be stereo-specific, inhibited by 1,5-difluoro-2,4-dinitrobenzene, insensitive to anoxia, and independent of the external alkali cation composition. Transport occurred equally well from the ventricular or from the serosal surface of the tissue. Formally, the rate of transport can be described by Michaelis-Menten kinetics. The mutual inhibition of transport between sugars was found to be noncompetitive which indicated that there were at least two binding sites available on the carrier. A good correlation between the apparent Km and the molecular conformation was observed. Sugars having two or more hydroxyl groups in the equatorial plane had the lowest Km while sugars possessing a majority of axially orientated hydroxyls had the highest Km. On the basis of these results, we conclude that the carrier for the facilitated transport system has a broad specificity in that it will transport many sugars but at different rates.

Supported by grants from the Los Angeles County Heart Association and the NIH.

HEPATIC CLEARANCE OF THYROXINE IN THYROGLOBULIN IMMUNITY.
B. N. Premachandra and Stanley Lang, V.A. Hospital, Jefferson Barracks, and Washington Univ., St. Louis, Missouri.

In studies on metabolism of thyroxine in active thyroid immunity, biliary clearance of radioiodine was determined in control and thyroglobulin immune rats. Thyroglobulin immunity was produced by 3 weekly injections of bovine thyroglobulin (10 mg/rat) as previously reported. Seven to ten days after final injection, 10 μc of ^{131}I-T_4 were injected IP. Eighteen hours later the bile ducts were cannulated and bile samples collected each hour for 4 hours. Blood was drawn halfway between each bile collection. Organic and inorganic radioactivity in plasma and bile was determined and the bile radioactivity was subjected to thin-layer chromatography. A 4-fold decrease in biliary clearance of radioiodine was noted in the immune animals. $T\frac{1}{2}$ of radio-thyroxine was prolonged by about 4 times over controls as measured by whole body counting. In other experiments, injection of thyroglobulin immune sera into normal rats reduced biliary clearance of thyroxine derived radioactivity by 50%. In contrast, a single injection of thyroglobulin and radiothyroxine led to a 3-fold increase in biliary clearance of radioiodine.
(Supported in part by NIH grant AM07676).

MECHANISMS OF RADIO-PROTECTION BY SYMPATHOMIMETICS.
Russell Prewitt* and X.J. Musacchia. Dept. Physiol. and Space Sciences Research Center, Univ. Mo., Columbia, Mo.

The concept that the radio-protection by epinephrine is due to tissue hypoxia mediated through the alpha receptors has not been satisfactorily demonstrated by adequate experimentation. Mechanisms of radio-protection by catecholamines were investigated in a pharmacological study involving alpha and beta blockers. 1.5 mg/kg of epinephrine, norepinephrine, and isoproterenol were administered i.p. to male hamsters 15 minutes before exposure to 1000 rads of ^{60}Co radiation. Effective doses of phenoxybenzamine, propronalol, or both were given to identify the receptor mediating the radio-protection. Animals were observed every 12 hours for 30 days after irradiation and the time of death (percent survival) and weights of the animals were recorded. The survivals were 30% for norepinephrine, 45% for epinephrine, and 80% for isoproterenol. Propranolol lowered the radio-protection of isoproterenol to control levels of 10%, and phenoxybenzamine only slightly decreased the radio-protection of epinephrine. Beta stimulation seems to give stronger radio-protection than alpha stimulation and the concept that catecholamines work through a simple tissue hypoxia mechanism is subject to question. (Supported by Grants: PHS 1 F01 GM41410-01 and NASA NGR 26-004-021-S3 and S4.)

A PHYSIOLOGICAL METHOD FOR CALIBRATION OF LARGE VESSEL NON-CANNULATING ELECTROMAGNETIC FLOW PROBES. L. L. Priano, * R.D. Wilson* and D.L. Traber. Depts. Physiol. and Anesthesiol. U. of Texas Med. Br. and Shriners Burns Institute, Galveston, Texas.

Current methods used for the determination of calibration factors for large electromagnetic flow probes involve the use of extracorporeal pumps and often employ synthetic materials in the place of normal blood vessels. These unphysiological aspects can be eliminated. A standard Starling heart-lung preparation is established in an anesthetized, open chest dog. The tubing emerging from the peripheral resistance portion of the circuit is divided into two routes with a plastic Y fitting. One of these channels (B) goes directly to the venous reservoir. To the other channel (A) is attached a plastic two-way fitting onto which a two-three inch section of dog aorta is tied. The opposite end of this vessel section is tied to another plastic fitting which then continues on to the venous reservoir. The flow probe is then fitted on to this section of aorta. Pieces of aorta taken at different distances from the heart can be used to accommodate various size probes. By clamping off channel (B) flow is diverted through channel (A) and the vessel. Zero flow can be established by clamping the tubing on either side of the vessel while channel (B) is reopened to allow flow to continue. Hematocrit can be varied at will by adding several hundred ml. of Ringer's Solution to the venous reservoir. Known flows, for calculating probe factors, are measured with a graduated cylinder and stop watch. These flows can be adjusted to any desired level, within the limits of the animal, by manipulating the venous return clamp. Data obtained with this method will also be presented to establish its usefulness.

COMPARISON OF EXPIRATORY NEURON DISCHARGE IN RESISTANCE TO EXPIRATION AND IN SNEEZE. W.M. Price* and H.L. Batsel, Dept. of Physiology, UCLA, Los Angeles, Calif. 90024 and V.A. Hosp., Long Beach, Calif. 90801.

In cats, lightly anesthetized with sodium pentobarbital, expiration against resistances of 1 to 6 cm. H_2O pressure (H_2O R) resulted in a graded increase in the frequency and duration of the discharge from expiratory neurons and in the activation of the external oblique muscle (E.O.M.). An increase in the discharge frequency of approximately 30% has been noted when the intrapleural pressure becomes positive during the forced (active) expirations. Probing of the nasal mucosa may elicit a sneeze with activation of the E.O.M. While the duration of the expiratory neuron discharge with sneeze is shorter (.2 sec.) than during forced expirations caused by H_2O R ($>$ .5 sec.), the peak discharge frequency is the same or greater. For any given expiratory neuron under observation it seems to be the relative increase in discharge frequency rather than the total number of spikes or the burst duration which is the greater determinant in the production of active expiration. Trigeminal input seems more likely to recruit previously silent expiratory units than H_2O R. Sneezes are more likely to occur during the normal expiratory phase but can occur at any time in the respiratory cycle. A unit recruited by H_2O R is more likely to be a late expiratory unit than an early one. Facilitation of units discharging late in the expiratory cycle to fire earlier in the cycle (phase-shifting) occurs readily with nasal probing but less frequently with H_2O R.

EFFECTS OF DC POLARIZATION ON CELLULAR AND EEG ACTIVITIES IN CORTICAL EPILEPTOGENIC FOCI. D. A. Prince, K. J. Futamachi*, W. Logan*, and M. Gutnick*, Stanford University, School of Medicine, Stanford, Calif.

In order to investigate the relationships between EEG interictal paroxysmal discharges (PDs) and the associated depolarization shifts (DSs) which occur in neurons of epileptiform foci, we studied the effects of DC cortical polarization on surface EEG and intracellular activities in acute penicillin foci of cat pericruciate cortex. Weak polarizing currents had pronounced effects on PDs so that surface anodal polarization enhanced surface negativities and cathodal polarization reduced or even caused apparent inversion of negative waves. These gross changes in PDs with polarization were not associated with significant alterations in DS or spike generation in deeper lying neurons. With more intense polarizing currents, changes in cellular activities occurred; cathodal current increased DS amplitude and spike height and anodal current did the reverse. These changes were small compared to the alterations in the PD. The rise time and peak latency of triggered PDs were shortened during surface anodal polarization and intracellular records showed parallel increases in the slope of the depolarizing limb of the DS. The findings suggest that the potentials recorded in deeper lying neurons, although time locked to certain surface events, are not crucial for generating those events. The effects of surface polarization are complex and probably reflect alterations in transmitter release from terminals as well as changes in membrane potential of subsynaptic membrane. (Supported by USPHS, NIH Grant NB-06477.)

THE MECHANICAL ACTIVITY OF THE CANINE MITRAL VALVE IN SITU. Donald V. Priola, John Moorehouse*, Carol Fellows* and J. Steven Schwarting*. University of New Mexico, Albuquerque, New Mexico.

Recently it was shown that the muscular elements in the canine mitral valve leaflet behave in vitro like typical cardiac muscle and that they contain releasable stores of catecholamines. Other work has demonstrated in situ electrical activity of the valve muscle. In the present experiments, we attempted to record the mechanical activity of the mitral valve leaflet to determine if it does actively contract during the cardiac cycle. 20 dogs were placed on total cardiopulmonary bypass and both ventricles were continuously drained of blood by suction. The left atrium was opened and a miniature semiconductor strain gauge sutured to the atrial surface of the septal mitral valve leaflet. The mechanical and electrical activity of the leaflet were measured along with the left ventricular (LV) pressure and ECG. A potential was recorded which preceded or was simultaneous with the initial deflection of the QRS complex. In the empty heart, this was followed rapidly by displacement of the leaflet toward the ventricular lumen. This displacement would be consistent with a contraction of the valve muscle on the atrial surface. When normal circulation was restored or the LV drain tube clamped, the major direction of leaflet displacement was reversed, being directed primarily toward the atrium. This would be expected if the leaflet were to move passively according to the ventriculo-atrial gradient generated by ventricular systole. Application of 35% phenol to the leaflet surface increased the leaflet displacement toward the atrium at any level of LV pressure. It is concluded that the data provide a basis for further consideration of an active role for the valve muscle in the dynamics of valvular movement. Supported by Grant #HE-10869 from the NIH

EXPERIMENTAL CORONARY INSUFFICIENCY(CI)EFFECTS OF NOREPINEPHRINE (NE) AND ISOPROTERENOL (ISOP). Pritpal S. Puri* and Richard J. Bing. Wayne State University Dept. of Medicine, Detroit, Michigan.

Coronary insufficiency without myocardial infarction was induced in dogs by application of ameroid constrictors around the main coronary arteries. Coronary artery constriction (CAC) resulted in a significant fall of stroke volume (SV) stroke work (SW) and stroke power; due to compensatory tachycardia, however, cardiac output (CO) and minute left ventricular work (CW) remained relatively normal. NE and Isop. augmented LV performance before and ten days after CAC. The tachycardia of CI prevented reflex slowing of heart rate by NE; this lead to significantly greater increase in CO and CW induced by NE after CAC than before CAC. The increase in mean arterial pressure resulting from NE was also greater after CAC than before. Isop. resulted in a marked tachycardia before CAC; after CAC, however, the compensatory tachycardia prevented further significant increase of heart rate by Isop. Consequently, after CAC, despite a greater increase in SV and SW, the increase in CO and CW induced by Isop. was significantly less marked than before CAC. In conclusion, CAC resulted in a decline of LV function and compensatory tachycardia. CI did not impair positive inotropic effects of the drugs. The tachycardia of CI enhanced the effects of NE and impaired those of Isop.

ELECTRICAL ACTIVITY OF THE TURTLE CEREBRUM, PSEUDEMIS SCRIPTA ELEGANS. S. J. Putnam, R. H. Wadle* and K. M. Chapman*. Division of Biological and Medical Sciences, Brown University, Providence, R. I., 02912.

Because the primitive generalized turtle brain has evolved the first "patch" of general pallium it is well suited for a study of the organization and function of neocortex. Following cold anesthetization, the right brachial vein was cannulated and the trachea intubated. Flaxedil was administered and the animal was artificially respired. The cerebrum was exposed and covered by a pool of mineral oil. Spontaneous activity and evoked potentials were recorded monopolarly. A concentric bipolar electrode was used for cortical stimulation and light flashes for visual stimuli. In all experiments, recording was done at one millimeter intervals. Spontaneous activity was recorded in both cerebral hemispheres. The activity seen over most of the cortex ranged in frequency from 35-60 cps and in amplitude from 30-60μV. All attempts to evoke transhemispheric responses were unsuccessful. No homotopic or heterotopic responses could be elicited. Attention was then turned to mapping cortical visual responses to light stimulation. The evoked response was characterized by a series of biphasic waves. The initial deflection was a surface negative wave with a duration of 50 msecs. The responses elicited ranged in amplitude from 100-500 μV. The initial peak latencies were 100msec and the duration of the entire complex varied from 80-200 msec. The areas where visual responses could be elicited were in that part of the cerebrum which is the general pallium.

QUANTITATIVE EXAMINATIONS OF HUMAN SEMINAL PLASMA PROTEINS. W. Leslie G. Quinlivan. Univ. of Calif. at Irvine Med. College, Irvine, Calif.

The proteins in 20 samples of human seminal plasma were examined by means of cellulose acetate electrophoresis, disc electrophoresis, and Kjeldahl's microdetermination of nitrogen. After staining the cellulose acetate electrophoresis strips and the disc electrophoresis polyacrylamide columns, optical density measurements were made by means of densitometers. The micro-Kjeldahl measurements showed that the average amount of protein in human seminal plasma was 58 milligrams per ml. The percentage of individual proteins present as shown by cellulose acetate electrophoresis was: albumin 14, alpha globulin 48, beta globulin 28, and immunoglobulin 10. Disc electrophoresis provided greater resolution which permitted the quantitation of more proteins. Optical density readings of the polyacrylamide columns gave the following percentages: prealbumin 13, albumin 14, alpha 1 globulin 36, alpha 2 globulin 15, beta 1 globulin 8, beta 2 globulin 6, and immunoglobulin 7. Seminal plasma from semen with spermatozoa counts below 20,000,000 per ml. contained more prealbumin and beta 1 globulin, and less albumin than average, while seminal plasma from semen with spermatozoa counts of over 130,000,000 per ml. contained less prealbumin and beta 1 globulin, and more albumin than average. The quantitative results obtained from densitometry measurements of polyacrylamide columns following disc electrophoresis of human seminal plasma were more detailed than those obtained by cellulose acetate electrophoresis, and may prove of value in the examination of infertile men.

EFFECT OF UREA ON URINARY NON-UREA SOLUTE CONCENTRATION. L. Rabinowitz, A.B. Thompson*, and R.B. Wagman*, University of California Medical School, Davis, California.

The effect of acute i.v. administration of urea on urinary osmolality and non-urea solute concentration was studied in thirsted, anesthetized dogs maintained on normal protein diets. Urea was given after an estimate of basal concentrating ability was obtained during a prior mannitol diuresis. On administration of urea, urine osmolality always increased (mean change $\pm$ SD: 489 $\pm$ 282 mosM), urine non-urea solute concentration either increased or decreased (mean change $\pm$ SD: 48 $\pm$ 179 mosM), and mean Unus/Uosm decreased from .69 during mannitol infusion to .51 during urea infusion. These changes were independent of changes in solute excretion rate and plasma osmolality, but were associated with small increases in glomerular filtration rate and small increases in total body water estimated from fluid balance data. It is proposed on the basis of these results and other considerations that acute administration of urea to dogs on normal protein diets leads to an increase in the concentration of sodium chloride in the renal papillary interstitial fluid as well as an increase in the concentration of urea and that both of these changes in medullary composition lead to the increase in urine osmolality commonly observed during urea administration.

THE ROLE OF PLASMA OSMOLARITY, [K^+], AND [Mg^{++}] IN ACTIVE (AH) AND REACTIVE HYPEREMIA (RH) OF THE COLLATERAL-FREE CANINE GRACILIS MUSCLE. D.P. Radawski*, J.B. Scott and F.J. Haddy. Department of Physiology, Michigan State University, East Lansing, Michigan.

To more clearly define the role of osmolarity in local regulation of blood flow, changes in resistance (R, mm Hg/ml/min/100g) and venous plasma osmolarity (O) were observed in the gracilis muscle during AH and RH. These changes were compared to those seen in the resting muscle during intra-arterial infusion of hypertonic NaCl and dextrose solutions. [K^+] and [Mg^{++}] in the venous plasma were also measured during local regulation. The collateral-free gracilis muscle was perfused at either constant pressure or constant flow. AH and active dilation (AD) were produced by faradic stimulation of the gracilis nerve. RH and reactive dilation (RD) were produced by a five minute period of no flow.

	Active Hyperemia				Active Dilation			
	Control	10 sec	1 min	5 min	Control	10 sec	3 min	5 min
R	10.8		1.7*	1.5*	10.2	5.9*	5.2*	4.7*
O (mOsm/L)	294	296	303*	296	292	297*	318*	313*
K^+(mEq/L)	3.6	4.8*	4.8*	4.2*	3.6	4.8*	6.2*	5.7*
Mg^{++}(mEq/L)	1.91	1.98**	1.96**	1.93	1.88	1.91**	2.10*	2.07*

* $P < 0.01$ relative to control. ** $P < 0.05$ relative to control.

Comparable increases in O, produced by infusion, caused a much smaller fall in resistance. Osmolarity, [K^+], and [Mg^{++}] did not change in RH. However, [K^+] rose 0.3 mEq/L in RD. It appears that O, [K^+] and [Mg^{++}] participate in the genesis of AH but not RH. The studies are consistent with previous investigations from our laboratories which indicate that no one vasoactive substance can account for AH and thus reinforce the concept that a number of substances participate (Physiol. Rev. 48:688, 1968).

THE MECHANISMS OF HYPOTENSION PRODUCED BY CORAL SNAKE (MICRURUS F. FULVIUS) VENOM. **H. W. Ramsey, S. S. Sbar, I. Boruchow, and W. J. Taylor (intr. by Sidney Cassin). University of Florida College of Medicine, Gainesville, Florida.**

Investigation into the physiological mechanisms responsible for the sustained hypotension occurring with coral snake envenomation was accomplished by administration of a predetermined lethal dose of venom (.25 mg/kg) intravenously into 15 mongrel dogs. Respiration was maintained by a Harvard respirator. Data was obtained sequentially after venom injection until all animals expired. Death invariably occurred within 55 to 60 minutes. All animals demonstrated profound hypotension within 30 seconds of venom administration with mean arterial pressures averaging 39 mm. Hg. Systemic vascular resistance decreased slightly (10-15 per cent) initially but returned to normal within three minutes. Cardiac output fell to levels approximating 35 per cent of control values. Mean pulmonary arterial pressures increased 20 per cent with pulmonary vascular resistance increasing threefold. Right and left atrial pressures decreased to near zero levels. Right ventricular and left ventricular end-diastolic pressures were unchanged or decreased slightly. Myocardial contractility increased 50 per cent immediately after injection. This increase in contractility was sustained for five to six minutes. After this period of time, contractility progressively decreased with eventual systolic arrest. It is concluded that peripheral venous sequestration with a reduction in cardiac venous return and impaired myocardial contractility are responsible for the severe hypotension observed with coral snake envenomation.

THE MACROSCOPIC DISTRIBUTION OF BLOOD FLOW IN THE SHEEP PLACENTA. John H.G. Rankin,* E. Makowski,* F.C. Battaglia* and G. Meschia. Dept. of Physiology, Univ. of Colo. Medical Center, Denver, Colo.

Regional variations of ventilation perfusion ratios within the lung are primarily a consequence of the lung being an air-filled organ of finite height. One would not expect to encounter analogous variations of maternal to fetal flow ratios in the placenta which is a fluid filled organ. Gross variations in maternal to fetal flow ratios throughout the sheep placenta have been reported in the acute preparation (Powers et.al. J. Clin. Inv. 46:2053, 1967.) In 12 near term sheep we tested the applicability of this finding to the chronic preparation by injecting 25μ Cr^{51} labelled microspheres into the maternal abdominal aorta and 15μ Yb^{169} or Ce^{141} labelled microspheres into the fetal inferior vena cava. The whole cotyledonary mass was recovered, cut into 100-300 segments and counted for radioactivity. The data were analyzed graphically and then pooled by calculating the % decrease that these distributions would cause in the clearance of an infinitely diffusible substance at a flow ratio of 1 in a concurrent exchanger. This figure was found to be approximately 1%. The flow ratios were not randomly distributed throughout the placenta. Occluding the umbilical arterial flow to 20% to 30% of the placenta did not cause the flows or their ratios to be more evenly distributed over the remainder of the placenta. We conclude that the macroscopic distribution of uterine and umbilical blood flows as observed in the chronic near term sheep has very little effect on the transfer of materials across the placenta and cannot explain the uterine venous to umbilical venous differences found in this species. (Supported by grants UCP R-196-68C; USPH-HD-00781-06; and AEC-AT (11-1)-1762).

RESPONSES OF SMALL PIAL ARTERIES AND ARTERIOLES TO CARBON DIOXIDE A.J. Raper,* H.A. Kontos, and J.L. Patterson, Jr. Dept. of Medicine, Medical College of Virginia, Richmond.

Available studies describe only the large pial arteries' response to carbon dioxide (CO_2), and are limited in number and in methods. Cats anesthetized with pentobarbital and paralyzed with decamethonium were fitted with a small (12 mm) glass skull window (modified after Forbes), permitting reflected light photomicrography at 138 X. A special clamp apparatus immobilized the head on the stage of a Leitz Ultrapak microscope. An electrically driven 35 mm still camera recorded vessel diameter 2 - 20 times per minute. $PaCO_2$, pH and PaO_2 were measured with electrodes, and expired air PCO_2 was monitored continuously with a CO_2 analyzer. A tracheal T-tube was connected to a respirator. Arterial pressure was recorded from a Statham transducer attached to a femoral artery catheter. Diameter was measured from projected frames of uncut filmstrips using a blind technique. For calibration a stage micrometer was photographed and projected using the same optics and projection distance. The projected image was undistorted and linear within the error of measurement (S.E. = 0.3μ, N = 25). Hypercapnia caused increased mean arterial pressure in 25 of 37 cats studied. In the remaining 12, no significant pressure change occurred; all 12 showed significant arterial and arteriolar dilation. The increase in internal diameter was greater (+45%) than previously reported for larger arteries. The increase was discernible at 60 seconds and was of significant magnitude at 90 seconds. Small cerebral arteries and arterioles dilate actively in response to arterial hypercapnia. The reaction is large and rapid.

Plasma Catacholamines and Lactic Dehydrogenase Isozymes Following Exhaustive Exercise. Peter B. Raven* and Eugene Evonuk. Center of Research for Human Performance, U. of Oregon, Eugene, Oregon.

The purpose of this study was to investigate the changes due to exhaustive exercise in trained and untrained rats on plasma catacholamine and lactic dehydrogenase (LDH) isozyme levels. The training consisted of swimming adult male rats 2 hours every second day for six weeks. Blood was obtained by cardiac puncture from both the trained and untrained animals 2 weeks prior to, and immediately following swimming to exhaustion. Plasma LDH isozyme separation was made by cellulose-acetate paper electrophoresis and densitometrically evaluated. Plasma catacholamines were determined by the trihydroxyindole method and evaluated fluorometrically. Following exhaustive exercise, a rise in plasma catacholamines, particularly norepinephrine, occurred in both trained and untrained animals. A change in cell membrane permeability of the skeletal muscle and liver was indicated by an elevation of both LDH isozymes IV and V. The trained animals showed a smaller increase in plasma LDH IV and V isozymes and a reduced resting level of circulating catacholamines. These findings suggest that the release of catacholamines during exercise may be the reason for the increased cell permeability.

THERMOREGULATORY RESPONSES TO INTRA-ABDOMINAL HEATING IN SHEEP. Robert O. Rawson. John B. Pierce Foundation Laboratory, New Haven, Conn.

Four flat electrical heaters measuring 2x6 inches implanted intra-abdominally against the body wall in sheep were heated to 40-43°C to dissipate 20-22 watts within the animal. In a neutral environment, respiratory frequency (RF) increased twofold over its basal rate of 20-25 breaths per minute, with a concomitant doubling of respiratory water loss (He). Hypothalamic temperature usually declined precipitously as much as 0.5°C, while metabolic rate (MR) remained unchanged. Heating the skin over the site of the internal heaters elicited none of these responses. With cessation of internal heating, parameters returned to basal levels. In a progressively colder environment to 0°C, these responses disappeared, being replaced by a rapid decline in MR. In hotter environments, internal heating elicited correspondingly greater responses of He and RF until a maximum of 240 breaths per minute was reached in 40°C air. At 45°C, there was rapid onset of hyperthermia. Responses appeared to be in some proportion to the level of heating and the ambient temperature, and are believed to be due to stimulation of deep body thermoreceptors having a thermoregulatory function. This work was supported by grant #HE12038 from the National Heart Institute.

A RESPIRATORY INHIBITION REFLEX ORIGINATING IN MUSCLE SPINDLES OF INTERCOSTAL MUSCLES. J. E. Remmers and S. M. Tenney, Dartmouth Medical School, Hanover, New Hampshire 03755.

Mechanical manipulation of the thorax inhibits phrenic motoneuron discharge in spontaneously breathing, anesthetized cats and dogs. The phrenic burst can be either transiently interrupted or completely arrested. Three independent findings indicate that intercostal muscle spindles initiate the reflex, namely: 1) the inhibitory effectiveness of chest compression is potentiated by succinylcholine and abolished by mid-thoracic deafferentation, 2) inhibition by intercostal muscle stretch is stretch-rate dependent, and 3) rib vibration with small displacements at high frequencies evokes inhibition. Because phrenic inhibition is associated with a decrease in respiratory rate and, in the case of muscle stretch, a similar inhibition of inspiratory intercostal muscle discharge, the reflex traverses a central pathway. Two findings suggest that central factors influence inhibitory effectiveness: effectiveness increases late in inspiration and decreases with chemical stimulation. Chest wall afferents account for the decrease in phrenic discharge with tracheal occlusion in vagotomized animals; the inhibition persists after bilateral phrenic section but is eliminated by thoracic dorsal rhizotomy. While segmental reflexes of intercostal spindle afferents promote muscle activation related to load, central reflexes of these same afferents might modulate muscle activation as load increases, thereby tending to increase mechanical efficiency. This respiratory inhibition reflex might also cause disproportionate recruitment of chest wall versus diaphragmatic motor units. [Work supported by USPHS Grant HE 02888(12).]

EFFECT OF INHALED CARBON ON BIOPHYSICAL PROPERTIES OF LUNG SURFACTANT. R. A. RHOADES AND D. GODISH (Intro. by W. Dunson). Center for Air Environment Studies and Laboratory for Human Performance Research, The Pennsylvania State University, University Park, Pennsylvania 16802.

Previous studies have indicated inhaled particles alter lung mechanics via loss of pulmonary surfactant. To determine the effect of inhaled carbon on biophysical properties of the surfactant material, Long Evans Hooded male rats (N=10) were chronically exposed to 4,102 $\mu g/M^3 \pm 854$ (S.D.) of carbon for 16 days. Control animals (N=10) received filtered air. Surfactant material was removed by a modification of Bondurant and Miller's method wherein physiological saline was pumped into the lungs via the pulmonary artery and surfactant material was collected by suction. Determinations made on the alveolar wash included surface tension-area curves, total phospholipid and phosphatidyl choline content. Maximum and minimum surface tensions for carbon-exposed animals were 44.0 dynes/cm $\pm$ 0.83 (S.E.) and 1.3 dynes/cm $\pm$ 0.40 (S.E.), respectively. Stability ratio ($\bar{S}$) was 1.89 $\pm$ 0.003 (S.E.). Surface compressibility (K) for the compression limb of the surface tension-area curve was 0.015 $\pm$ 0.002 (.SE.) at 95% trough area, 0.058 $\pm$ 0.014 (S.E.) at 55% area, and 0.189 $\pm$ 0.034 (S.E.) at 25% area. Maximum and minimum surface tension, $\bar{S}$, and $\bar{K}$ did not differ significantly from controls. Total phospholipid and phosphatidyl choline expressed per μg lipid/mg dry lung showed significant 26% and 32% increases, respectively. It is concluded that chronic exposure to carbon does not destroy surfactant properties, and appears to stimulate secretion of surfactant. The results do not support the hypothesis that inhaled particulates alter lung mechanics via loss of pulmonary surfactant. (Supported by U.S.P.H.S., N.I.H. Grant ES 00335.)

LEFT VENTRICULAR FUNCTION IN GOATS DURING EXERCISE. E. A. Rhode* and J. P. Holt. Univ. of Calif., Sch. of Vet. Med., Davis and Heart Research Lab., Div. Exp. Med., Dept. Med., Univ. of Louisville, Louisville, Ky.

Measurements were made of left ventricular end-diastolic (EDV), end-systolic (ESV) and stroke volumes (S) using an indicator dilution method and of left ventricular end-systolic (ESP) and aortic pressures on goats standing at rest and during treadmill exercise. Ventricular wall forces and stress-length relationships on the contracted left ventricle were calculated using methods described earlier by us. Results in eight goats whose average body weight was 49.6 Kg were EDV, 131 ml rest, 112 ml exercise; ESV, 80 ml rest, 58 ml exercise; S, 51 ml rest, 54 ml exercise; residual fraction (ESV/EDV) 57% rest, 51% exercise; ESP 132 mm Hg rest, 134 mm Hg exercise; heart rate 108 beats/min. rest, 170 beats/min. exercise and cardiac output 5.6 liters/min. and 9.2 liters/min. exercise. The stress-length relationship shifted towards the stress axis. The stress, F/A, force per unit area, averaged 225 Gm/cm^2 and the length, R_m, radius of the chamber containing the internal volume plus one-half the wall volume, averaged 3.21 cm at rest and during exercise, 207 Gm/cm^2 and 3.08 cm respectively. Comparing the stresses at equivalent length, R_m=3.08 cm, the calculated F/A at rest is 181 Gm/cm^2 compared to that obtained during exercise, 207 Gm/cm^2 an increase of 14.2% during exercise. The ventricular wall thickness associated with a particular ESV was generally greater during exercise than at rest. (Supported by USPHS Grant HE 5622.)

EFFECTS OF NOREPINEPHRINE INFUSION ON ERYTHROCYTE VELOCITY IN MESENTERIC CAPILLARIES. Daniel R. Richardson* and Paul C. Johnson. Department of Physiology, University of Arizona College of Medicine, Tucson, Arizona.

The effects of intra-arterial infusion of norepinephrine on mesenteric capillary blood flow were analyzed from continuous photometric recording of erythrocyte velocity in single capillaries, and compared with simultaneously recorded total intestinal blood flow. In 53 percent of the experiments, total flow initially decreased then recovered during the infusion to a steady state level usually somewhat below control flow -- a phenomenon known as autoregulatory escape. Erythrocyte velocity showed similar changes in 35 percent of the experiments. However these variations did not closely parallel total flow and occasionally occurred in the absence of escape in total flow. In other capillaries erythrocyte velocity increased during infusion, and in some cyclic variations in velocity were observed. The fact that escape patterns were evident in single capillaries of the mesentery suggests that special shunts are not necessary for escape to occur. These findings are consistent with the hypothesis that the phenomenon of autoregulatory escape results from secondary relaxation of vascular elements regulating capillary flow. Supported by a grant-in-aid from the American Heart Association and NIH grant AM 12065. Work done during tenure of NIH predoctoral fellowship 5-F1-GM-28,651.

THE TRANSPLANTED MOUSE HEART: A MODEL FOR STUDYING CHOLINERGIC STIMULATION ON VENTRICULAR MYOCARDIUM. J. D. Ridges*, D. K. Hunter*, W. A. Clark* and D. C. Harrison, Cardiology and Immunology Divisions, Stanford University School of Medicine, Palo Alto, California.

Although it is generally stated that parasympathetic innervation of the heart via the vagus nerve is isolated to the atria and coronary arteries without functional effect on ventricular tissue, recent reports have shown a negative inotropic effect of vagal stimulation on ventricular function. A model for testing the pharmacological responses of denervated cardiac muscle and the effect of cholinergic stimulation on ventricular myocardium has been developed in the mouse. Syngeneic and allogeneic ventricular muscle grafts were placed in a pouch in the ear of C57 B10 mice. Simultaneous host EKG and graft electrical activity were measured following graft placement. Response of the grafted tissue to the intravenous and intraperitoneal injection of acetylcholine (ACh) was then measured serially in 18 mice. Significant slowing of the host heart rate (HR) in response to acetylcholine always occurred. The slowing ranged from 100 to 400 beats/min and occurred within 2 seconds of IV injection of ACh. The transplanted syngeneic tissue HR responded in a similar manner in 16 of the 18 mice. The slowing occurred later and was more sustained. These findings suggest that the transplanted denervated ventricular myocardium has the capacity to respond to cholinergic stimulation. Preliminary data on the response of rejecting allogeneic grafts to ACh suggest that the capability to respond to ACh is modified.

ACID SECRETORY RESPONSES TO INSULIN AND 2-DEOXY-D-GLUCOSE IN ANESTHETIZED AND UNANESTHETIZED RATS. P. T. Ridley, J. H. Schlosser*, and W. G. Groves*. Smith Kline and French Labs., Philadelphia, Pa.

Insulin and 2-deoxy-D-glucose (2-DG) were compared for their ability to increase gastric acid secretion in both anesthetized and unanesthetized rats. In rats anesthetized with urethane, the perfused stomach technique (Ghosh and Schild, Br. J. Pharm. 13: 54, 1958) was used to measure titratable acid output at 10 minute intervals for 3 hours following various doses of crystalline insulin (0.4-3.2 U/kg) or 2-DG (50-1600 mg/kg). In experiments on unanesthetized rats with gastric fistulas, the volume, titratable acid concentration, and titratable acid output of the gastric contents were determined at hourly intervals for 4 hours following doses of insulin (0.125-1.0 U/kg) or 2-DG (25-200 mg/kg). In anesthetized rats, the greatest hourly titratable acid output occurred with 1.6 U/kg of insulin. Doubling the dose resulted in depressed secretion and/or lethality. At doses up to 1600 mg/kg, 2-DG seldom increased acid secretion. In unanesthetized rats, the greatest hourly increase in volume occurred with 0.5 U/kg of insulin and with 50 mg/kg of 2-DG. Peak responses in titratable acid concentration and output were found with 0.25 U/kg of insulin and with 200 mg/kg of 2-DG. 2-DG produced a significantly greater peak hourly titratable acid concentration than insulin. This was the only significant difference in the responses to these two agents. The maximal acid output responses to insulin in anesthetized and unanesthetized rats were similar, although a 6-fold greater dose was required in anesthetized rats. This result and the lack of responsiveness of anesthetized rats to 2-DG are attributed to the hyperglycemia produced by urethane.

CIRCADIAN PATTERNS OF OXYGEN CONSUMPTION IN THE DEER MOUSE (PEROMYSCUS MANICULATUS SONORIENSIS. J.C. Roberts*, A.A. Heusner and R.Em. Smith, Depts. of Biological Sciences, UC Santa Barbara; Physiological Sciences, UC Davis, California.

In nocturnal animals oxygen consumption is higher during the night than in the day. These periodic changes in the level of oxygen uptake are manifestations of circadian rhythms. Indeed, circadian rhythm in oxygen consumption is a composite phenomenon, involving the rhythms of activity, body temperature, feeding behavior and possibly the rhythm in basal metabolism. These rhythms are not necessarily synchronous. The pattern of the rhythm of oxygen consumption reflects the phase relationships of these rhythms. Long-term recordings of oxygen consumptions (2 weeks) in deer mice put in constant dark and temperature, but previously subjected to a 12:12 hour dark-light cycle, show that 1) a male deer mouse has a tendency to display a daily pattern which is replicated every day; 2) this pattern may vary among individual males put in identical environments. With respect to the duration and shape of the transitory phases -- passage from high level to low level of oxygen uptake and vice versa -- four basic patterns can be distinguished in males. In females the circadian pattern is partially masked by the superimposed oestrous cycle. Handling of the animal, at the beginning of the experiments, disturbs the pattern during the first day. A constant pattern could be interpreted as a tendency of an animal to keep a constant phase relationship, whereas various patterns in different animals would demonstrate that different phase relationships tend to be maintained in different mice even if kept under identical ambient conditions. A constant circadian pattern in a mouse suggests that the coupling of the various circadian rhythms is rigid. (Supported by a NASA Research Grant NSG 721 and GRS grant 68-118).

MECHANICAL PROPERTIES OF A PERMEABLE FLEXIBLE "CAPILLARY." Simon Rodbard. City of Hope Medical Center, Duarte, California.

Previous studies have shown that flexible "capillaries" enclosed with fluid in a capsule (an arrangement we have called a "capillaron") exhibit autoregulation, reactive and compression hyperemias, and other phenomena usually attributed to vital action at the arteriole. The present study examines properties of capillaries in which permeability is distributed along the entire length of the "capillary," rather than being lumped at its upstream and downstream ends. With the onset of flow and filtration into the extracapillary spaces, extravascular pressure rises and partially collapses the downstream end of the capillary. Conductance falls to about 15% of its maximum value, simulating "basal tone." Extracapsular pressure and basal conductance are functions of capillary permeability/capillary length. When flow from an arterial source is distributed among two or more capillarons in parallel, the intravascular and extravascular pressure are reduced. Closure of one capillaron is associated with immediate opening of the capillarons in parallel with it, simulating the reciprocal changes in conductance usually attributed to reflex regulations. Exchange of extravascular fluid is facilitated by such intermittence of flow. These findings indicate the remarkable similarities of the capillaron system to behavior of vascular beds and suggest that some of the vascular effects usually attributed to arteriolar intervention may be accounted for adequately by purely mechanical arrangements.

EFFECTS OF NEPHRECTOMY AND THE READMINISTRATION OF RENOMEDULLARY EXTRACTS OF THE VASCULAR RESPONSE TO RENIN AND THE KINETICS OF THE RENIN-ANGIOTENSINOGEN REACTION

Juan Romero*, Jeffrey Lazar*, Mary Elkins*, and Sibley Hoobler.
Univ. of Michigan, Ann Arbor

It is well known that nephrectomy (Nx) results in enhancement of the vascular response to renin as well as an increased plasma renin substrate concentration. In addition, we have observed that the initial velocity of the hog renin-rat substrate reaction is markedly increased. However, when nephrectomy is followed by the IP injection of a renomedullary (M) homogenate, these changes are suppressed. With the renin-depleted renal cortex, no such prevention is seen. It appears that one renal medulla contains an active principle which alters renin kinetics in vitro. This idea is supported by a study of the kinetics in normal rats, in rats 8 hours after Nx, and in rats 8 hours after Nx plus M: Km and Vmax values in these three groups were 119, 192 and 125 ng/ml and 35, 62 and 41 ng/ml/4 min., respectively.

Distensibility Changes Induced in Follicular Tissue in vitro.
Paul Rondell, Sandra Harvey*and Duncan Munroe.* Dept. Physiology. Univ. Michigan Medical School, Ann Arbor, Michigan 48104.

The fact that the intrafollicular hydrostatic pressure does not rise at ovulation (AJP 205: 1067, 1963) indicates that the preovulatory increase in distensibility demonstrated in vivo (AJP 207:590, 1964) and in vitro (AJP 212: 1397, 1967) is the physical basis of rupture. An enzyme has been extracted from the follicular wall which has some collagenase-like properties (AJP 214:326, 1968), but it has not been determined if this enzyme has an effect on follicular distensibility. In the work to be reported, thin strips of mature sow follicle wall were incubated for up to 24 hours in either 1) buffered salt solution 2) bacterial collagenase solution or 3) extracts of theca interna of mature follicles. After incubation they were suspended in a muscle chamber arranged so that tension could be recorded while the tissues were stretched fixed amounts (10% or 25% of rest length) at a slow, steady rate. When stretched 10% of rest length, tissues incubated in buffered salt solution developed 650 ± 20 mg tension; those incubated in bacterial collagenase 249 ± 20 mg & those in follicular extract 330 ± 21 mg. The permanent deformation (slippage of structural elements) induced by the stretch averaged 40 ± 1.0% of the original stretch in the control tissues, 67 ± 3.4% in those incubated in bacterial collagenase and 58 ± 1.8% in tissues incubated in follicular extract. Tissues stretched by 25% of their original length showed similar effects of treatment. It is concluded that follicular tissue contains a factor capable of increasing the distensibility of its connective tissue framework.

Supported by NIH Grant HD 0470.

MODIFICATION OF THE CELL SURFACE AND THE MUSCULAR TRIAD IN THE HEART OF A HIBERNATOR. T.H. Rosenquist* and M.L. Zimny. Louisiana State University Medical Center, New Orleans, Louisiana.

Cardiac muscle samples were obtained from eight ground squirrels, Citellus tridecemlineatus, that had hibernated at an ambient temperature of 3-5° C, and from six controls. Tissue for electron microscopy was stained with ruthenium red before embeddment in Maraglas or was stained after sectioning with uranyl acetate-lead citrate. For light microscopy, Alcian blue and periodic acid-Schiff's reagent were applied to undigested sections and sections digested with diastase and hyaluronidase. Electron microscopic evidence indicates that the cell coat thickness increased significantly during hibernation, from an average of 250 Å to 350 Å. The sarcoplasmic reticulum is more abundant during hibernation, and the terminal cisternae or lateral sacs of the myocardial triad are more electron opaque than those of controls. The transverse tubules increase significantly in diameter near the cell periphery, those nearer the center part of the cell do not increase. These morphological changes indicate an increase in ion transport to maintain electrophysiological activity of the heart during hibernation.

EFFECTS OF ACUTE HYPOKALEMIA ON RESISTANCE TO BLOOD FLOW THROUGH THE GRACILIS MUSCLE IN THE DOG. S.A. Roth*, D.K. Anderson*, D.P. Radawski*, J.B. Scott, and F.J. Haddy. Departments of Physiology and Chemical Engineering, Michigan State University, East Lansing, Michigan.

We have previously reported that local hypokalemia, produced by a dilutional method, raises the resistance to blood flow through the vascular beds of the dog forelimb and kidney (Am. J. Physiol. 204:202, 1963). We now report the effect of acute local hypokalemia, produced by a non-dilutional method, on resistance to blood flow through a pure skeletal muscle vascular bed in the dog. In 19 experiments, a miniature dialyzer was interposed in the arterial supply of the collateral-free gracilis muscle. Blood flow was held constant while measuring perfusion pressure. During the control period, the blood was dialyzed against Ringers solution. In the experimental phase, the blood was dialyzed against Ringers solution lacking potassium ion, producing arterial plasma potassium ion concentrations ranging from 2.6 to 0.2 mEq/L. Perfusion pressure quickly increased in each experiment and, when dialysis against Ringers solution was re-instituted after four to five minutes, perfusion pressure promptly fell approximately to the control level. The relationship between percent change in potassium ion concentration and percent change in perfusion pressure appeared to be linear, perfusion pressure increasing 12% for a 50% decrease in potassium ion concentration. Prolonged hypokalemia produced an irreversible increase in perfusion pressure and a decreased responsiveness to close arterial injection of levarterenol. These studies suggest that this skeletal muscle vascular bed constricts in response to a low plasma potassium ion concentration.

GRADED CARDIOVASCULAR CHANGES DURING WAKING AND SLEEP IN THE CAT. E.H. Rubinstein* and R.R. Sonnenschein, Dept. of Physiology, UCLA School of Medicine, Los Angeles, Calif.

Cats were prepared for recording arterial pressure, heart rate, gastric and duodenal motility, sup. mesenteric and iliac blood flow, EEG, eye movements, neck and limb EMG. Spontaneous associated behavioral and autonomic changes were followed from 1-2 weeks after surgery to 3-5 months later. Several patterns were observed during this period: 1) Habituation: After 3-5 sessions, the daily initial elevated pressure and heart rate declined more rapidly to a steady level, together with a gradual decrease in somatic activity. 2) Awake attentive: Frequent episodes of tachycardia, transient hypotension and atropine-blocked iliac vasodilatation. 3) Awake relaxed: Frequently observed short lasting tachycardia associated with EEG desynchronization, or bradycardia and transient apnea. 4) Slow wave sleep (SW): Marked sinus arrhythmia, regular breathing pattern, and a 3/min cycle of mesenteric vasoconstriction, heart rate acceleration and rise in arterial pressure. 5) Rapid eye movement sleep (REM): The transition from SW sleep to REM sleep was marked by a gradual drop in arterial pressure, increase in respiratory rate, disappearance of the sinus arrhythmia, mesenteric vasodilatation and iliac vasoconstriction. Also, sympathetic chronotropic activity seemed to gradually decrease. Episodes of tachypnea, arterial pressure rise, cardioacceleration (blocked by propranolol) mesenteric vasoconstriction and iliac blood flow increase were recorded at variable intervals. 6) Active: Increased arterial pressure, tachycardia and a varying degree of mesenteric vasoconstriction and iliac vasodilatation; the two latter changes were minimal during sitting, moderate during standing and maximal during walking. (Supported by USPHS HE-05157, AMA-ERF, and LACHA 400-C1)

CORRELATION OF POLYAMINE SYNTHESIS WITH RAPID GROWTH PHENOMENA. Diane H. Russell, Janice L. Gregory, Vicente J. Medina, and Solomon H. Snyder. (Intr. by Edith D. Hendley). Departments of Pharmacology and Experimental Therapeutics and Psychiatry. The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.

The polyamines spermidine and spermine, and their precursor putrescine, appear to play early roles in rapid tissue growth. Polyamine concentrations and the activity of ornithine decarboxylase, the putrescine synthesizing enzyme which may be the rate-limiting enzyme in spermidine synthesis, increase markedly in chick embryo, mouse and rat fetuses, regenerating rat liver, certain tumors, and increase in Xenopus laevis embryos after gastrulation in parallel with initiation of rRNA synthesis. Ornithine decarboxylase activity in regenerating rat liver correlates with enhanced RNA synthesis and precedes increases in DNA synthesis and mitotic index. Ornithine decarboxylase can be induced in normal rat liver by growth hormone and heparin. The temporal pattern of polyamine synthesis found in fetal tissues and in regenerating rat liver suggests that liver regeneration closely resembles the pattern of changes in early developing embryonic systems. (Supported by USPHS Grants RO1-NB-07275, KO3-MH-33128, and GM-1183).

INOTROPIC EFFECT OF STROPHANTHIDIN ON FROG VENTRICLE AND ITS RELATION TO BLOCKAGE OF THE MEMBRANE SODIUM PUMP. J. M. Russell* and A. M. Brown. Depts. of Pharmacology and Physiology, Univ. of Utah, Salt Lake City, Utah, 84112.

We have investigated the proposition that the inotropic effect of the cardiac glycosides is due to blockage of the sodium pump, increase in $(Na)_i$ and an associated increase in $(Ca)_i$ (Baker et al., J. Physiol. 200, 431). Intracellular cardiac action potentials and isometric tension were measured in strips of frog ventricle at different $(Na)_o$, $(Na)_i$ or in the presence of strophanthidin 10^{-4} to 3×10^{-6} M. The maximum rate of rise of the action potential (dV/dt) max. had a linear relationship with the $(Na)_o/(Na)_i$. When $(Na)_o$ was reduced by 25%, dV/dt max. fell by 40% and tension increased by 79% as predicted by the new $(Ca)_o/(Na)_o^2$ (Niedergerke and Luttgau, Nature, 179, 1066). Strophanthidin 3×10^{-6}M provoked a 4-fold increase in tension which could also be produced either by quadrupling $(Ca)_o$ or halving $(Na)_o$. $(Na)_i$ would have to be doubled to produce a similar increase in $(Ca)_i$ and an equivalent rise in tension. Therefore, a 25 - 65% reduction in dV/dt max. was anticipated; however, no change was observed. It is concluded that the inotropic effect of strophanthidin cannot be explained by an increase of $(Na)_i$ accompanied by an increase of $(Ca)_i$.

(Supported by USPHS Grant HE 10977.)

COMPUTER ANALYSIS OF PULMONARY CAPILLARY BLOOD FLOW CURVES. M.A. Sackner and N. David Culver. Mt. Sinai Hosp., Miami Beach, Fla. and Agrippa-Ord Corp., Carlisle, Mass.

Lee and DuBois in 1955 found that the rate of N_2O uptake by the lungs could be measured from pressure changes within a body plethysmograph. A record during breath holding on air was necessary to subtract mechanical oscillations in the airway from the tracing during breath holding on N_2O before calculating instantaneous pulmonary capillary blood flow ($\dot{Q}c$). Wasserman and Comroe in 1962 demonstrated that the voluntary relaxed thorax was analogous to a body plethysmograph and showed that air and N_2O oscillations could be detected by a spirometer connected to the airway. Although these technics comprise a bloodless procedure for measurement of beat by beat cardiac output, they have not received widespread application because of difficulties encountered in teaching breathing maneuvers to untrained subjects and to the tedium involved in subtracting the air control from the N_2O test tracing. We have used a modified spirometric method in anesthetized paralyzed subjects and developed a program for the LINC 8 digital computer. The latter converts flow tracings from a spirometer or pneumotachograph to digital form using the R-R interval of the electrocardiogram to distinguish individual pulses. Data are transferred from core to digital tape and stored for examination. Individual pulses can be recalled and displayed on an oscilloscope (CRO). Each pulse is displayed along with the breath and beat number and the R-R interval. One or multiple beats can be selected, averaged and displayed. Upon command, the air tracing is subtracted from the N_2O tracing and $\dot{Q}c$ computed and displayed on the CRO. Further optional manipulations on $\dot{Q}c$ include 1) a smoothing routine, 2) an extrapolation routine to eliminate artifacts in late diastole, 3) integration of the flow curve between two indicated time intervals, 4) Fourier analysis and 5) storage on digital tape for future reference.

THE INHIBITION OF ENDOGENOUS GROWTH HORMONE SECRETION BY EXOGENOUS GROWTH HORMONE INFUSION IN THE RHESUS MONKEY. M. Sakuma* and E. Knobil. Dept. of Physiol., University of Pittsburgh Schl. of Med., Pittsburgh, Pa.

The acute release of growth hormone in response to the injection of pitressin or to insulin hypoglycemia is a quantitatively reproducible phenomenon in monkeys maintained in a controlled environment. Animals were subjected to 2 stimuli, the first during a control period when plasma growth hormone concentrations ranged between 0 and 9.4 mμg/ml and the second during an infusion of human growth hormone (0.92-1.75 μg/min.) which elevated plasma growth hormone concentrations to 38-78 mμg/ml, within the physiological range. The second stimulus was given 2 hrs. after the beginning of the infusion. In all instances, the abrupt rise in plasma growth hormone concentration occasioned by the intravenous injection of 0.3 U/kg pitressin (8 experiments) or 0.1 U/kg insulin (5 experiments) was markedly reduced or abolished by the growth hormone infusion. The infusion of cortisol (0.5 to 1.0 mg/minute) had no such effect, tending to enhance the response to the stimuli. It is concluded that growth hormone can inhibit its own secretion in response to acute stimuli and that this effect may be of physiological significance.

HORMONAL INFLUENCES UPON THE MATURATION OF THE RAT BRAIN'S RESPONSIVENESS TO SENSORY STIMULI. Manuel Salas*, Instituto de Investigaciones Biomedicas, UNAM, Mexico City, Mexico; and Shawn Schapiro, V. A. Hospital, San Fernando, Calif. and Department of Psychiatry, UCLA, Calif.

The effects of the neonatal administration of cortisol or thyroxine upon the maturation of electrocortical responses to sensory stimuli were studied in the rat. Evoked potentials were recorded from control and hormone treated animals. Records were obtained from animals 6 days old to adults. Thyroxine injection on postnatal days 2, 3 and 4, accelerated by approximately 2-3 days the maturation of evoked responses to visual, auditory and sciatic nerve stimulation. Cortisol administration on postnatal day 1 retarded development of the evoked response to these same sensory stimuli. These effects were more marked in the visual cortex. Our results agree with previous reports that these hormones cause a chronological displacement of various biochemical, behavioral and neurophysiological parameters of development and suggests that the hormonal climate bathing the growing neurone may be one factor in the internal environment which plays a role in determining the rate of development of the Central Nervous System.

This research partially supported by USPHS Grant #AM-06603.

INHIBITION OF INTESTINAL AMINO ACID TRANSPORT BY HEAVY METALS. V.Sallee (intr. by A.Despopoulos). Univ. of New Mexico Sch. of Med., Albuquerque, N.M.

Effects of mercury and cadmium on net transfer of branched chain amino acids (isoleucine and valine), hydroxy amino acids (serine and threonine), and glucose from mucosal to serosal fluid was determined in everted sacs of rat intestine. Increasing doses of mercury ($HgCl_2$) or cadmium (Cd Acetate) produced logarithmic decreases in transport of all amino acids. A linear regression of the data was calculated by the method of least-squares. The following table summarizes the inhibition of each function by 1 x 10^{-4}M dose of each metal.

	Mercury	Cadmium
threonine transport	95%	63%
valine transport	77%	42%
glucose transport	78%	36%
glucose metabolism	38%	18%
oxygen utilization	18%	1%

The slopes of the regression lines for the effect of mercury on serine and threonine transport were significantly different ($P<.001$) than the slopes of the lines for valine and isoleucine transport. The dose of mercuric chloride at which transport of the substance was half of control was 2.3 x 10^{-5}M for threonine and serine and was 4.1 x 10^{-5}M, 4.6 x 10^{-5}M, and 4.7 x 10^{-5}M for isoleucine, glucose and valine respectively. These data demonstrate that the intestinal transport of the hydroxy amino acids serine and threonine is more sensitive to heavy metal inhibition than the transport of the branched chain amino acids valine and isoleucine or the transport of glucose.

(Supported by grants from NIH, AM 08719 and HE 05633.)

EFFECTS OF CHANGES IN IONIC COMPOSITION OF EXTERNAL FLUIDS ON SECRETORY MEMBRANE OF FROG GASTRIC MUCOSA. S. S. Sanders* and W. S. Rehm, Dept. of Physiology and Biophysics, University of Alabama in Birmingham, The Medical Center, Birmingham, Alabama.

Using an in vitro technique, we measured the response of the potential difference (PD) to changes in ionic composition of the bathing media as a means of assessing the relative conductances of the two limiting membranes to various ions. Previously we found that the conductance of the nutrient membrane is equal to the sum of the K^+ and Cl^- conductances, i.e., $\Delta PD/\Delta 10K^+ + \Delta PD/\Delta 10Cl^- \doteq 58$ mv. The PD's do not respond stepwise to a change in conc. because of the presence of diffusion barriers on each side. The time constant for the diffusion of ions across the nutrient barrier is about 1 min and less than 1 min for the secretory membrane; hence the PD responses after periods equal to 5 time constants are assumed to be due to changes in the parameters of the system. Changes in $[K^+]$ (K^+ for Na^+) in the secretory fluid resulted in an increase in PD (positivity of nutrient increased) with a peak at about 2 min followed by a gradual fall over 20 min to a level slightly below control. Using the peak value, the $\Delta PD/\Delta 10K^+$ was 7 mv $\pm$ 3.2. Replacing Na^+ with choline [or with Ca^{++} or Mg^{++} (sucrose used for osmotic deficit)] results in ΔPD of about 2 mv. Replacing total Cl^- with $SO_4^=$ (+ sucrose) gave ΔPD of 10 mv $\pm$ 1. Substituting H^+ for Na^+ results in ΔPD of 7.8 mv $\pm$ 2.5. The sum of all PD changes per 10X is much less than 58 mv. Composition of fluid at border of outer surface cells is essentially the same as in secretory fluid. We think this is not so for the tubular cells where a 10X change of Cl^- or H^+ of the secretory fluid results in a smaller change in the luminal fluid of the tubules. Therefore this method does not yield reliable partial ionic conductances for the secretory membrane. (NIH and NSF support.)

NEUROENDOCRINE ADAPTATION TO THE STRESS OF GROUP CAGING IN M. MULATTA. E.N. Sassenrath (intr. by L.F. Chapman). University of California School of Medicine, Davis.

Subadult Macaca mulatta housed in small established cage groups show varying degrees of behavioral and physiological adaptation to the chronic social stress of the home cage. Experimentally induced competitive interaction was utilized to assess the relative levels of aggressive stimulation received by each group member and the individual behavioral responses to this stimulation. In the groups studied, female cagemates showed exceptionally high frequencies of anxiety-fear behaviors concurrent with three to tenfold increases in adrenocortical response to exogenous ACTH (measured as urinary Porter-Silber chromogens). These elevated ACTH-responses were lowered toward basal levels several weeks after transfer to individual caging, removal of the dominant alpha-male from the home cage, or consort-pair formation with the alpha-male. After removal from the home cage to metabolism cages, female cagemates also showed excretion levels of metanephrine and normetanephrine which were consistently higher than male cagemates, whether or not ACTH response levels were greatly elevated. Mean 5-hydroxyindole acetic acid excretion levels tended to correlate with behavioral and adrenocortical measures of stress response, but individual differences were much less marked. The data are discussed in terms of hormonal interrelationships during adaptation to sustained social stress.

MITOCHONDRIAL RESPIRATION AT VARIOUS LEVELS OF RAT SMALL INTESTINE. M.M. Sayeed, C. D. Bucana* and A. E. Baue, Jewish Hospital and Washington Univ. School of Medicine, St. Louis, Mo.

Studies with everted sacs of mammalian small intestines have demonstrated differences in the absorptive capacities and oxygen utilization along its length. Factors that may be related to oxygen consumption differences were examined in this study. Oxygen consumption by mucosal cell mitochondria and whole epithelial cells was followed by means of polarographic oxygen monitoring system (YSI). The reaction medium consisted of 15 mM sucrose, 20 mM $MgCl_2$, 40 mM KCl, 20 mM potassium phosphate buffer (pH 7.3) and 16 mM succinate. Effect of addition of 0.8 μM cytochrome c, .16 mM ADP and 45 mM mannitol was studied. The mitochondrial oxidation of succinate decreased aborally. Mean oxygen values $\pm$ SEM in μM O_2 change per mg protein per minute for duodenal, mid-jejunal and ileal samples were 6.85 $\pm$ 0.51, 4.74 $\pm$ 0.47, and 1.84 $\pm$ 0.18 respectively. A similar decline in oxygen consumption along the intestinal length was observed with whole epithelial cells. The addition of cytochrome c enhanced the rate of mitochondrial O_2 utilization. The extent of this enhancement in ileum was significantly higher than in duodenum and mid-jejunum. Mean oxygen values in the presence of cytochrome c with units as above were: 7.89 $\pm$ .84 for duodenum, 7.11 $\pm$ .45 for mid-jejunum, and 6.36 $\pm$ .62 for ileum. The ratios of O_2 change in the presence of cytochrome c over the change in its absence were 1.61 $\pm$ .05 in duodenum, 1.74 $\pm$ .03 in mid-jejunum and 3.61 $\pm$ .38 in ileum. No significant changes in O_2 consumption were observed with ADP and mannitol. (Supported in part by NIH Grant No. AM 13780-01.)

EFFECTS OF DIABETES ON INTESTINAL GROWTH AND HEXOSE TRANSPORT IN THE RAT. H. P. Schedl and H. D. Wilson*. Univ. of Iowa College of Med., Iowa City, Ia.

Small intestinal growth and hexose transport were compared between controls (C) and rats 5, 8, and 44-70 days following induction of diabetes (D) with alloxan. After 5 days the total wet weight of intestine was significantly greater in D rats. D dry weights were usually not significantly greater for the whole gut, but mean dry weight as g/cm length of proximal segment was significantly greater at 44 days and thereafter. The dry weight of villi (g/cm length) was significantly greater in D at 8 days and thereafter. Transport was measured with everted sacs prepared from mid segments using 1.0 mM 3-O-methyl-D-glucose (3-O-MG) in mucosal (M) and serosal (S) solutions. Net transport of 3-O-MG (μmoles/hr/g wet weight) into the serosal fluid was significantly greater in D rats at 5-8 days, but not at 55 or 70 days. Based on dry weight, the increase was significant at 5-8 and 55 days, but not at 70 days. S/M concentration ratios were also increased significantly at 5-8 and 55 days. Transport expressed as uptake from M (μmoles/hr/g dry weight of sac) and as concentration in mucosal tissue water (μmoles/ml) was significantly greater in diabetic animals at all time intervals. The accelerated growth of D intestine was progressive, but the transport increase was significant by all criteria only at 5-8 days. Transport into the serosal fluid requires penetration of all layers of the intestine and would be depressed by increased wall thickness of D rats at the later stages of growth. Thus, uptake from M and mucosal tissue concentration of 3-O-MG may be the most valid indexes of transport by sacs: the maximal transport increase was at 5-8 days, but transport per unit of D intestine was increased at all time intervals.

DIURETIC AND NATRIURETIC EFFECT OF HYPOTONIC EXTRACELLULAR FLUID (ECF) VOLUME EXPANSION IN THE PRESENCE OF EXOGENOUS VASOPRESSIN AND MINERALOCORTICOID. G.H. Schmitt, M.U. Tsao and J. Tjen (intr. by Robert El. Smith). Departments of Pharmacology and Surgery, Univ. of Calif. School of Medicine, Davis, Calif.

During prolonged administration of mineralocorticoids to mammals, the kidneys "escape" from the sodium-retaining effect. We showed previously that following this "escape" intravenous infusions of hypertonic NaCl solutions or of isotonic NaCl solutions plus exogenous vasopressin cause marked diuresis and natriuresis in chronically deoxycorticosterone acetate (DOCA) treated dogs. A hypotonic solution of 0.09% NaCl and 1.5% glucose was infused intravenously in 5 dogs at rates of 0.2 ml or 0.25 ml/Kg/min. for 3 hours with 0.04 units vasopressin (Pitressin). The dogs had received 0.8 mg DOCA in oil (Ciba) intramuscularly daily for one week before the experiments. In 4 dogs marked diuresis and natriuresis (negative Na balance) ensued. In two of these dogs the infusion was continued for longer periods. After the initial rise in urine flow and $U_{Na}V$, antidiuresis occurred in one dog after 3 1/2 hrs. and in the second after 3 3/4 hrs. of infusion. When the infusion was continued further but without the exogenous vasopressin, water diuresis with increasing free water clearance was seen. This latter response represents appropriate renal response to the dilutional hyponatremia. The initial diuresis and natriuresis followed by antidiuresis may represent the result of competition between the ECF volume control system and the osmo-control system. Infusion of a similar hypotonic solution, but without exogenous vasopressin into chronically DOCA treated dogs resulted in water diuresis after about one hour of infusion.

LACK OF EVIDENCE FOR AN HEPATIC OSMORECEPTOR MECHANISM IN CONSCIOUS DOGS. E.G. Schneider*, J.O. Davis, C.A. Robb*, J.S. Baumber*, J.A. Johnson*, and F.S. Wright*. Dept. of Physiology, University of Missouri School of Medicine, Columbia, Mo.

The possible role of the liver in osmoregulation was investigated in 28 trained conscious dogs with chronic indwelling catheters in the portal vein and inferior vena cava. The effects of sterile distilled water infusions of 0.25 ml/min per Kg, 0.50 ml/min per Kg, or 0.70 ml/min per Kg into either the portal vein or vena cava on urine flow and on either sodium excretion or urine osmolality were studied. The renal responses following the portal vein infusion were not detectably different from those observed after vena cava infusion. There was a significant increase in both urine flow and free water clearance following the 0.50 ml/min per Kg and 0.70 ml/min per Kg infusions with no change in osmolal clearance. To keep the osmolality of plasma perfusing the hypothalamic osmoreceptors constant, in a fourth experiment an isotonic infusion was given partly as 0.50 ml/min per Kg distilled water into one catheter and partly as 0.11 ml/min per Kg of a 5% sodium chloride solution into the other catheter; a marked diuresis with a large increase in osmolal clearance and little change in free water clearance occurred. The response was the same whether the portal vein received distilled water or 5% sodium chloride while the inferior vena cava received the complementary solution. The data failed to provide evidence for an osmoreceptor mechanism in the liver of the dog. (Supported by NIH grant HE 10612).

INTRAVENTRICULAR MONO- OR INDOLAMINES AND LH-RELEASE IN THE RAT. H.P.G. Schneider* and S.M. McCann. Dept. Physiol., Univ. Tex. Southwestern Med. Sch., Dallas, Texas 75235.

Blood samples were drawn by cardiac puncture in ether-anesthetized animals bearing chronic cannulae in the 3rd ventricle (V) directly before and 15 min after intraventricular inj. ($4\mu g/2\mu l$). In the interim between removal of the two blood samples the rats recovered from anesthesia. Plasma LH was measured by radioimmunoassay. Serotonin (5-HT) did not significantly alter plasma LH levels at any stage of 4-day estrous cycles. Nor-epinephrine (NE) also did not produce overall significant changes in plasma LH although there were some positive responses. Dopamine (DA) raised LH levels to 8 or 10 fold above controls ($P<.01$) in rats on the 2nd day of diestrus (D2) or in proestrus (P). DA proved to be less effective in D1 or estrus (E). In normal males DA raised plasma LH in 5 out of 10 animals, whereas NE was ineffective. The DA effect in D2 and P rats could be blocked by simultaneous 3rd V. inj. of $30\mu g$ phenoxybenzamine, but remained unaltered after the same dose of pronethalol. In spayed females NE or DA produced variable results independent of baseline LH levels; however, 5-HT significantly ($P<.01$) decreased LH release in these animals. Estrogen progesterone-blocked, castrated female rats responded with up to 10 fold increases ($P<.01$) in plasma LH following 3rd V. inj. of DA, whereas NE produced only slight increases in 5 out of 9 rats. Monitoring an individual rat of this type by drawing blood from a carotid artery catheter at 3-7 min intervals revealed an 8 fold increase of plasma LH 7 min after intraventricular inj. of DA. Saline (0.9%) did not produce an effect on LH release under any of the described conditions. The results provide *in vivo* evidence for the role of DA in LH release, probably as transmitter for the release of LRF as shown by the authors in earlier *in vitro* experiments. A possible inhibitory role of 5-HT is also suggested. (Supported by NIH and Ford Found.)

CENTRALLY EVOKED SYMPATHETIC VASODILATION IN SQUIRREL MONKEY. L. P. Schramm*, C. R. Honig, and K. E. Bignall. Univ. of Rochester, Rochester, N. Y. 14627.

Sympathetic vasodilation (SVD) has been sought unsuccessfully in subhuman primates. Recent studies in this laboratory provide new criteria for SVD which may clarify this apparent species difference. Ten squirrel monkeys were anesthetized with chloralose and vagotomized. Femoral flow, exclusive of paw flow, was measured with an electromagnetic meter. Close arterial injections and blood pressure measurements were made via the other femoral artery. Vasodilations were evoked by constant current stimulation at 70 Hz, 2 ms duration 0.15 ma in areas of hypothalamus and mesencephalon homologous to areas from which atropine-sensitive SVD can be evoked in cat and dog. Responses peaked within 14 sec. They were not blocked by up to 0.5 mg/kg atropine IA and hence would not have been regarded as SVD by others. However, small ipsilateral lesions in bulbar lateral spinothalamic tract did block them. Similar lesions block only atropine-sensitive vasodilation (SVD) in cats. Also as in cats, responses were not blocked by large electrolytic lesions in medial or lateral bulbar regions mediating decreased vasoconstrictor tone. Vasodilations in squirrel monkey were reversibly blocked by 7.5 mg/kg propranolol. In dogs, comparable doses block responses acceptable as SVD by the classical criterion of atropine sensitivity. We conclude that a system analogous to SVD appears to exist in squirrel monkey and that anatomical rather than pharmacological criteria more clearly define SVD.

PRESERVATION OF FUNCTIONAL AND STRUCTURAL CHARACTERISTICS OF ANIMAL AND HUMAN HEART MITOCHONDRIA. A. Schwartz, L.A. Sordahl*, S. Harigaya*, E.B. Diethrich*, J.E. Liddicoat* and M.E. DeBakey*. Div. of Myocardial Biol. and Dept. of Surgery, Baylor Col. Med., Houston, Texas.

Mitochondria, isolated from 5 normal human hearts which were maintained for protracted periods (18-36 hrs.) in a Portable Preservation Chamber (PPC), retain their oxidative phosphorylation capacities for a week or more. NADH-linked respiration declines slightly but can be restored by the addition of Mg^{++} to the assay medium. Succinate-linked respiration remains unaffected. Isolated heart mitochondria from beef, dog and all rodent species always exhibit complete deterioration of NADH-linked respiratory activity after 3 days storage. Swelling-contraction studies of human heart mitochondria (HHM) indicate quantitatively greater changes than those of animal heart mitochondria similarly prepared. These HHM also retain capacity for rapid Ca^{++} uptake as measured by dual-beam spectroscopy. Electron micrographs of HHM, in various biochemical states, are consistent with the biochemical results. The various agents added to the PPC (insulin, K^+, glucose) somehow effect this unusual preservation of mitochondrial activity.

(Supported by USPHS grants: HE-05435-09, P.8, HE-07906-07 and K_3 HE 11,875-05).

INFLUENCE OF THYROID HORMONE ON MYOCARDIAL ENERGY UTILIZATION. Shirley C. Seagren*, C. Lynn Skelton*, Peter E. Pool, and Eugene Braunwald. Cardiology Branch, NHI, Bethesda, Md. and Dept. Medicine, U.C.S.D., La Jolla, Cal.

The purpose of this investigation was to determine the influence of thyroid hormone on the process of energy utilization in the myocardium under conditions where energy production (mitochondrial function) was not a contributing factor. Energy utilization was determined from the progressive decline with time of high energy phosphate stores, ATP and creatine phosphate (CP), in the isolated cat papillary muscle treated with iodoacetic acid and nitrogen in amounts sufficient to inhibit completely energy production. Papillary muscles were isolated from 45 cats made hyperthyroid (L-thyroxine 0.75 mg/Kg/day, I.P., 10-17 days), 16 cats made hypothyroid (^{131}I, 1 mC/Kg, I.P., 3-6 months prior to sacrifice) and 86 euthyroid cats. Energy stores were determined in groups of muscles rapidly frozen at the onset of complete inhibition of energy production and after 3, 7, and 10 minute periods of inhibition. Initial energy stores (CP + ATP) in papillary muscles from euthyroid and hyperthyroid cats were similar (16.6 $\pm$ 0.7 vs. 16.4 $\pm$ 0.6 μ moles/g) while stores from hypothyroid cats were lower (14.2 $\pm$ 0.6 μ moles/g) ($.10 > P > .05$). A regression analysis of total energy stores with time indicated that the basal rate of energy utilization was increased in muscles from hyperthyroid animals (1.00 μ moles/g/min) compared to that from euthyroid animals (0.78 μ moles/g/min)($P < .10$) while the rate was decreased in muscles from hypothyroid animals (0.23 μ moles/g/min)($P < .05$). It is concluded that thyroid hormone directly influences the process of energy utilization and that at least a portion of the effect of thyroid hormone on basal energy metabolism is mediated at this level.

The effect of norepinephrine on ^{45}Ca exchange and total tissue Ca content in rabbit aorta. C.L. Seidel* & David F. Bohr, Univ.of Michigan, Ann Arbor.
There is evidence that ^{45}Ca flux in squid axon, red blood cell and guinea pig atria is via a mediated transport system. We have explored the possibility that vasoactive agents may influence contraction of vascular smooth muscle by their effect on the handling of Ca by such a system. The effects of norepinephrine (NE) on ^{45}Ca exchange and total tissue Ca were determined in rabbit thoracic aorta. The exchange of ^{45}Ca for intracellular Ca was determined by measuring the activity of strips exposed to ^{45}Ca for 30 min in the presence or absence of NE (10^{-7} g/ml). From the specific activity of the incubation medium and the activity of the muscle an "estimated" intracellular Ca concentration was determined. The "actual" Ca concentration was also measured on the same muscle strip by atomic absorption spectrophotometry. In six muscle strips NE increased the "estimated" Ca concentration from 2.48$\pm$0.33 mM/kg wet wt to 2.92$\pm$0.42 and the "actual" from 2.85$\pm$0.08 to 3.33$\pm$0.39. The washout of ^{45}Ca from previously loaded muscle strips into a zero Ca medium was also followed. In 5 out of 8 experiments NE had no effect, but in three experiments, washout was reduced. Since NE causes an increase in "estimated" and "actual" Ca concentration without increasing ^{45}Ca washout, it would appear that the increase in Ca mobility is unidirectional and therefore not due to a simple increase in membrane permeability. These observations suggest that NE is influencing a mediated Ca transport system. Supported by USPHS Grant HE-03756.

EFFECT OF SATURATED AND UNSATURATED DIETARY FAT ON LIPOGENESIS IN THE ISOLATED PERFUSED GERBIL LIVER. M.W. Seiler*, M.A. Hamilton* and M.G. Herrera. Harvard School of Public Health, Boston, Massachusetts

Groups of male gerbils were fed three purified diets 1) "CHO": casein 15%, dextrose 75%, 2) "COC": casein 15%, dextrose 60%, coconut oil 15%, 3) "SAF": casein 15%, dextrose 60%, safflower oil 15%. 10% of all diets was a mixture of Celluflour, minerals and vitamins. After two months during which weight gain was similar in all groups high KM hepatic glucokinase (GK) was significantly higher in the CHO and COC groups than in the SAF animals. Parallel differences in serum cholesterol were observed. The livers of similarly fed animals were perfused in a Miller Apparatus with a cell free medium consisting of KRB, 3% bovine albumin, 25% rat serum and 20mM glucose-U-C^{14}. Net glucose utilization was: CHO: 204 $\pm$ 28, COC: 153 $\pm$ 10, SAF: 98 $\pm$ 22. Glucose carbon incorporation into liver lipids was: CHO: 26.7 $\pm$ 1.8, COC: 17.2 $\pm$ 2.0, SAF: 9.2 $\pm$ 1.6 and into perfusate lipoprotein lipids: CHO: 9.6 $\pm$ 1.1, COC: 6.8 $\pm$ 1.2, SAF: 2.6 $\pm$ .4. Units are uM/gm/2hr and figures represent means of six (CHO) or seven (COC and SAF) observations $\pm$ S.E.M. Net glucose utilization was significantly higher in the CHO and COC groups than in the SAF group - $P < .05$. Significant differences in glucose carbon incorporation into tissue and perfusate lipoprotein lipids were also observed: CHO vs. SAF, $P < .001$, COC vs. SAF, $P < .01$. Calculated GK activity required to phosphorylate the glucose which was metabolized falls in the range of observed values in similarly fed animals. Preliminary experiments show that liver mitochondrial supernates from CHO and COC animals incorporate more acetate-1-C^{14} into lipid than SAF animals. It is concluded that unsaturated fat feeding diminishes hepatic lipogenesis and that this effect may be mediated in part by a reduction of hepatic GK.

EFFECTS OF CIGUATOXIN ON NA TRANSPORT ACROSS THE FROG SKIN. James A. Setliff, Martin D. Rayner and Suk Ki Hong (intr. by T. A. Rogers) University of Hawaii, Honolulu, Hawaii.

The effect of Ciguatoxin (CT) on Na transport across isolated frog skin (R. pipiens) was studied by measuring the electrical potential difference (PD) and the short-circuit current (SCC). When chloride Ringer was used, CT (5 to 10 mg %) added to the outside bathing medium induced a substantial reduction in PD and a slight reduction in SCC, indicating a reduction in resistance to Na movement. Moreover, the recovery was extremely slow and incomplete. The CT effect was much less pronounced and more variable when it was added to the inside bathing medium. When sulfate Ringer was used, the reduction in PD was smaller than that of SCC. The presence of ADH in the inside medium did not alter the response of the skin to CT. Similarly, the presence of CT in the outside medium did not affect the response of the skin to ADH. However, the action of CT was not evident in the presence of 10 mM calcium in the outside bathing medium. These results suggest that CT primarily alters the permeability of the outer barrier to Na, although an effect on the Na pump cannot be ruled out completely. (This work is supported in part by PHS grant UI-00216.)

CARDIOVASCULAR EFFECTS OF DOPAMINE IN ENDOTOXIN SHOCK. Linda L. Shanbour* and Lerner B. Hinshaw. V.A. Hospital and Univ. of Okla. Med. Center, Oklahoma City, Oklahoma.

This study was designed to characterize the cardiovascular effects of dopamine (3-4 Dihydroxyphenylethylamine) in dogs administered an LD_{80} of E. coli endotoxin. In order to separate peripheral from cardiac effects, a venous return preparation was used in which cardiac inflow was held constant. Dopamine infusion started 10 minutes prior to an LD_{80} of endotoxin and continued for 60 minutes post-endotoxin markedly prevented pooling until the infusion was stopped. Ten minutes after cessation of dopamine infusion, pooling rates were not significantly different from those of the untreated, shocked animals. Dopamine infusion begun ten minutes after endotoxin injection resulted in tachycardia and decreased left atrial pressure in the presence of a steady cardiac input and relatively constant systemic vascular resistance. Right atrial pressure and pulmonary vascular resistance were maintained above pre-endotoxin values during dopamine infusion, while portal vein pressure fell and venous return progressively increased. The primary action of dopamine (maximum 38 μg/kg/min) appears to be on the liver vasculature. With an isolated, perfused liver preparation, dopamine increased hepatic arterial resistance and decreased liver blood volume; both factors contributed to an increase in venous return. Increased venous return augmented cardiovascular output and supported arterial pressure. Results from survival studies, in correlation with the above findings, suggest beneficial effects of dopamine on both the left ventricle and peripheral vasculature in maintaining an adequate circulating blood volume in endotoxin shock. (Supported in part by U.S. Navy Contract N00014-68-A-0496.)

RESTORATION OF THE VISUAL PROJECTION FROM THE RETINA TO THE ROTATED TECTAL REIMPLANTS IN ADULT GOLDFISH. S. C. Sharma* (Intr. by H. Davis). Biology Department, Washington University, St. Louis, Mo.

The retinotectal projection has been studied in young adult goldfish following excision and reimplantation with 90° clockwise rotation of the right optic tectum. After preliminary operation, the animals were allowed to survive for 3 or more months and the retinotectal projection was then mapped electrophysiologically. In six successful experiments the restitution of the visual projection with approximately rotated maps has been observed. The optic fascicles at the site of the lesion are deflected from their original pathways at the angles of 90° or less. The extent of the tectal graft was determined by reconstruction of serial sections. Grossly abnormal structure of the tectum was observed within the graft. Although there were abundant nerve fibers present in the graft, it lacked the normal layering. The sequence of the visual responses throughout the depth of the tectum was not restored. (Supported by USPHS Grant NB-0571 to Dr. V. Hamburger.)

PULMONARY RESPONSES TO UNILATERAL PULMONARY ARTERIAL BALLOON OCCLUSION (UPAO) AND UNILATERAL THROMBOEMBOLISM (UPAT).
J. W. Shepard Jr.*, T. Hirose*, T. Yasutake*, A. A. Tarabeih*, and M. Stein.
Brown University Providence, Rhode Island.

Bronchospirometry was performed in twelve anesthetized, spontaneously breathing dogs to monitor total lung flow resistance (R_{TL}) and dynamic lung compliance (C_L) of each lung independently. UPAO of five minutes duration in eight dogs resulted in statistically significant increases in R_{TL} and decreases in C_L in both the occluded and the unoccluded lungs. Ventilation of the occluded lung with 5.0% CO_2 in air prevented changes in R_{TL} and C_L in both lungs, suggesting that hypocapnea on the occluded side was the major cause of airway constriction. Following bilateral section of the cervical vagosympathetic trunks, UPAO failed to produce changes in R_{TL} and C_L in the non-occluded lung. However, on the occluded side, C_L dropped significantly without change in R_{TL}. These findings suggest a role for vagal activity in mediating the changes in R_{TL} and C_L in the non-occluded as well as R_{TL} in the occluded lung. Autologous thrombi were released to one lung during transient occlusion of the main stem pulmonary artery of the opposite lung. In each of four dogs confirmed by necropsy to be unilaterally embolized, a marked rise in R_{TL} and fall in C_L was observed only on the embolized side. Although the alterations in R_{TL} and C_L during UPAO and UPAT are similar, the mechanisms appear to be different. As shown previously, UPAT induces changes by release of a humoral substance, UPAO by hypocapnea and vagal reflexes. (Supported by USPHS, NIH Grant HE-10017)

GAS-LIQUID CHROMATOGRAPHY OF VOLATILE RETICULOCYTOGENIC CONSTITUENTS OF PLASMA CONDENSATES. Duncan G. Sinclair* and Donald B. Jennings.
Department of Physiology, Queen's University, Kingston, Ontario.

The volatile fraction obtained by lyophilization of plasma from anaemic dogs stimulates reticulocytosis in starved rats and polycythemic mice when compared to control condensates obtained from the same animals prior to the production of anaemia by dextran-for-blood exchange; neither control nor 4-day anaemic condensates affect 59Fe uptake. Analytical gas-liquid chromatography (GLC) indicates the presence of unique peaks as well as organic constituents in greater concentration in anaemic plasma condensates than in control condensates. These compounds are comparable on GLC to the glycerol ethers and are similar in polarity and boiling point to compounds present in the condensates of urine from some anaemic patients which also exhibit reticulocytogenic activity. Reticulocytosis is shown to be stimulated by lipid-soluble, volatile, heat-labile compounds in plasma which do not stimulate the uptake of 59Fe into erythrocytes.
Supported by the Medical Research Council of Canada.

ELECTRICAL EFFECTS OF MUCOSAL ANIONS IN THE TOAD URINARY BLADDER. Irwin Singer. Mass. Gen. Hosp. and Harvard Med. Sch., Boston, Mass.

The hypotheses (a) that the transepithelial electrical potential difference arises from separation of sodium and chloride movements across the apical membrane, and (b) that the slower chloride ion is one rate-limiting factor for "active" sodium transport, were tested by comparing the electrical effects of 13 different sodium salt substitutions in the mucosal medium. The spontaneous transepithelial potential and short-circuit current were measured intermittently in paired quarter-bladders. It was found that the electrical effects of anionic substitution were relatively small. For the sodium halides, which produced almost the entire range of anion effects, the range of differences in these electrical properties was < 50% of the initial values in NaCl. Those differences found were not simply related to either anion size or mobility in aqueous media. Little difference (< 13%) was observed between chloride and propionate, anions of relatively different size and mobility, whereas larger differences (> 25%) were observed between chloride and iodide, anions of more similar size and mobility. When the 13 anions are ranked according to their ability to increase the transepithelial potential and short-circuit current, they follow the rough sequence: $SCN > I > NO_3 > Br > Cl >$ propionate > acetate > citrate, tartrate > $SO_4 > HPO_4 > F$, azide, where thiocyanate produced the largest values. This order follows a typical lyotropic sequence for a macromolecular system. These data suggest that the transepithelial potential is not a simple function of anion size or mobility in aqueous media, and that anion movement across the apical membrane is restricted non-specifically. The small differences in the electrical properties of toad urinary bladder in the presence of these different anions may be related to interactions with membrane macromolecules.

CORRECTION FOR MECHANICAL DEAD SPACE IN THE CALCULATION OF PHYSIOLOGICAL DEAD SPACE. G. J. Singleton*, R. L. Smith*, R.L. Trager*, and C. R. Olsen. V.A. Center, L.A., and UCLA School of Medicine.

Suwa and Bendixen (J. Appl. Physiol. 24: 556, 1968) showed that subtraction of apparatus dead space (V_{Dm}) leads to underestimation of physiological dead space (V_{Dp}) when Enghoff's modification of the Bohr equation is applied for patients having $P_{ACO_2}/P_{aCO_2} < 1$. Asmundsson et.al. (Fed. Proc. 28: 653, 1969) completely recovered added V_{Dm} in their measurements with 3 of 5 healthy subjects. We added varying V_{Dm}'s to 6 patients having obstructive and/or embolic pulmonary disease. Recovery of added V_{Dm} tended to be more complete as P_{ACO_2}/P_{aCO_2} approached unity. In every case when we subtracted V_{Dm} the ratio V_{Dp}/V_T decreased in a non-linear manner with increasing V_{Dm}. We propose two formulas which underestimate V_{Dp} much less than does the complete subtraction of V_{Dm}.

1) $$V_{D_p} = \frac{P_{aCO_2} - P_{ECO_2}}{P_{aCO_2}} \cdot V_T - \frac{P_{ACO_2}}{P_{aCO_2}} \cdot V_{D_m}$$

2) $$V_{D_p} = \frac{P_{aCO_2} - P_{ECO_2}}{P_{aCO_2}} \cdot V_T - \frac{P_{ECO_2} \cdot V_T}{P_{aCO_2}\,(V_T - V_{Dan} - V_{Dm})} \cdot V_{D_m}$$

When end-tidal CO_2 (P_{ACO_2}) is assumed to be the same as mixed expired alveolar CO_2 the two formulas are equivalent. Formula 2 uses either measured or estimated anatomical dead space (V_{Dan}) and gives results in agreement with formula 1. A more correct formula can be applied only with a second measurement of P_{ACO_2}, $PaCO_2$, and V_T with no V_{Dm}. Despite the underestimation of V_{Dp} with large V_{Dm}'s, both operational formulas hold the ratio V_{Dp}/V_T more nearly constant than the conventional subtraction of V_{Dm}.

Individualities in effects of Ca among vascular muscles. M.D. Sitrin* and David F. Bohr, Univ. of Michigan, Ann Arbor. Helical strips of rabbit aorta, renal, skeletal muscle and mesenteric arteries (500u od) were studied in terms of their ability to utilize extracellular and cellularly bound Ca for activating contraction. The aorta, mesenteric and renal arteries contracted moderately (10-20% of maximum) in response to 25-50 mM $CaCl_2$ in the bath, but skeletal muscle artery failed to contract in high [Ca], although it responded well to epinephrine. Mesenteric artery incubated 30 min in high [Ca] and subsequently transferred to Ca-free physiological salt solution (PSS) relaxed immediately; aorta and renal vessels contracted transiently; skeletal muscle artery showed no change in tension. The contrasting effects of a Ca-free environment on these arteries indicate individualities among vascular smooth muscle in their ability to store Ca or subsequently release it in a Ca-free medium. In Na-free PSS all arteries showed enhanced response to high [Ca]. The transient contraction of the renal artery and aorta in the Ca-free medium was also potentiated in Na-free PSS, but under these conditions the mesenteric artery only relaxed. Enhancement of the response to high [Ca] by a Na-free environment is consistent with a postulated pump in the smooth muscle cell which links Ca influx with Na efflux (Baker et al, J. Physiol. 200:431,69); enhancement of the response to a Ca-free solution in a Na-free environment suggests that vascular smooth muscle contraction is also regulated by a link between Ca efflux and Na influx (Reuter & Seitz, J. Physiol. 195:451,68). Supported by USPHS Grant HE-05682.

THE EFFECT OF NOREPINEPHRINE ON FREE FATTY ACID CONCENTRATION OF SLICES OF RAT HYPOTHALAMUS AND CORTEX IN VITRO. A. Sklenovsky and V. Havlicek (intr. by V. Chernick). Palacky's Univ., Olomouc, Czechoslovakia and Dept. of Physiology, Univ. of Manitoba, Winnipeg, Canada.

The concentration of free fatty acids (FFA) in hypothalamus and cortex slices was studied in the presence of 10, 100 or 1000 µg norepinephrine (NE) per ml Krebs-Ringer solution (pH 7.4, 100% O_2, 37°C). After 90 min incubation of the hypothalamic slices FFA in the slices increased significantly ($p<0.01$) from 22.6 ± 1.7 µEq/g to 24.0 ± 1.4, 26.3 ± 1.6 and 31 ± 2.7 with increasing concentrations of NE. Similarly, 90 min incubation of cortical slices was associated with a significant rise in FFA of the tissue from 12.3 ± 0.8 µEq/g to 13.1 ± 0.6, 14.5 ± 1.2 and 14.8 ± 1.0 with increasing concentrations of NE. However, the increase in FFA in brain cortex was significantly less than in hypothalamic slices. We have previously shown that NE liberates glutamic acid from hypothalamic slices into the incubation medium (Activ. Nerv. Super. (Praha) 9:190, 1967). Furthermore the presence of oleic acid in the medium enhanced the liberation of glutamic acid significantly. It is suggested that regional variations of the effect of NE on lipolysis may account for regional variations in the release of the excitatory transmitter, glutamic acid.

(Supported by the Medical Research Council of Canada and the Research Fund, Winnipeg Children's Hospital)

A VENOUS WATERFALL IN OPEN CHESTED DOGS. H.C. Smith* and J. Butler. Dept. of Medicine, Univ. of Wash., Seattle, Wash.

Evidence has been obtained that a pulmonary venous waterfall exists in the living dog in addition to the well recognized alveolar vascular waterfall. The demonstration of a venous waterfall in excised dog lungs has been criticized because perivascular cuffs of edema may form if the lymphatic and bronchial circulations are interrupted. Open chested dogs anesthetized with nembutal and morphine were used. The left lower lobe vein was cut. Small catheters were passed up it in a retrograde manner into the intra-pulmonary veins. They pierced the venous walls and were then pulled out through the surface of the lung until their bell shaped inner ends wedged in small side branches of the veins. This allowed upstream venous pressures to be measured without occlusion. The pulmonary lymphatics and bronchial circulation were untouched. A catheter was tied into the extra pulmonary portion of the vein and then attached to a reservoir so that downstream extra-pulmonary venous pressures could be raised and lowered without altering atrial pressures and hemodynamics of the remainder of the lung. The upstream venous pressures were measured as extra-pulmonary vein pressure was varied at constant alveolar pressures. We found that upstream venous pressures did not respond to extra-pulmonary vein pressures below about 5 cms. H_2O. This pressure (below which the venous waterfall was present) was always less than but varied with alveolar pressure. The waterfall was found to occur in the larger veins inside the lungs within a few mms. of the lung surface. The presence and location of this venous waterfall suggest that the intra-pulmonary perivascular pressure in the living animal is less than alveolar, but greater than extra-pulmonary pressure. (Supported in part by MRC (Canada) and Washington Tuberculosis Association).

CUTANEOUS WATER LOSS AS A SIGNIFICANT CONTRIBUTION TO TEMPERATURE REGULATION IN HEAT STRESSED PIGEONS. Richard M. Smith* and Roderick Suthers. Indiana University, Bloomington, Indiana 47401

It has long been assumed that birds do not lose a significant amount of water through the skin because of an absence of sweat glands and the protective layer of feathers. The experimental testing of this assumption is the purpose of this paper. Evaporated water was collected from three groups of pigeons. Under ether anesthesia, subcutaneous and deep body thermocouples were inserted and the cloacas were infiltrated with procaine HCl, and sealed with surgical clips, waterproof glue and tape. Birds in the first (free) group were placed in an air tight chamber (15 cm x 36 cm x 38 cm) through which dry, gradually warmed air was blown at a rate of 30 l/min. In addition, these birds were directly exposed to a 12 km/hr breeze from a fan in the chamber. Pigeons in the second group were sealed in a whole body plethysmograph (WBP) before being exposed to the same conditions as the free group. The WBP allowed the measurement of respiratory volumes and prevented any evaporative water loss from the skin. The free birds lost significantly more water at all body temperatures (40-47°C) than did the birds in the WBP. This difference in evaporation was enough to give the free birds a 10°C advantage in the highest ambient temperature tolerated. Water loss in birds in the WBP was a linear function of minute volume. In the third group of pigeons, the head was excluded from the water collection system, allowing direct measurement of body cutaneous water loss. We found that cutaneous water loss was greatly influenced by air velocity and postural adjustments and was of sufficient quantity to explain the above results. We believe cutaneous water loss could play a major role in the temperature regulation of pigeons, especially during flight. (Supported by USPHS, ES 0075-03 and NSF GB 5821.)

Temperature Dependent Processes in Limulus Photoreceptors
T.G.Smith, W.K.Stell, G.C.Murray*, LNP,NINDS,NIH,Bethesda, Md.

In cells whose steady-state membrane potential (V) is determined only by ionic concentration gradients and described by the Goldman equation, the V dependence on temperature is 0.2-0.3mV/^{o}C. Recently a number of excitable cells have been found to have an electrogenic sodium pump, which contributes directly to V. In such cells the temperature dependence of V significantly exceeds 0.3mV/^{o}C, since cooling inhibits the pump and removes its contribution to V. Also, treatment of such cells with cardiac glycosides, like ouabain, which inhibit the pump, alters the temperature dependence of V. In Limulus ventral eye photoreceptors, the membrane hyperpolarizes with warming by >1mV/^{o}C over the range 0-12^{o}C. In steady, bright light or after treatment with 1mM ouabain, warming initially hyperpolarizes (0-5^{o}C) then depolarizes (>5^{o}C) the membrane. Cooling below 2^{o}C also abolishes the generator potential and alters the current-voltage curve from multi- to singly rectifying, as does bright light or treatment with ouabain. These observations suggest the following interpretations: 1) Limulus ventral eye cells have an electrogenic pump which contributes directly to V (20mV at 20^{o}C), 2) light and ouabain reduce the electrogenic action of the pump, 3) the passive membrane properties (permeabilities, E.M.F.'s) are dependent on temperature and 4) the electrogenicity of the pump is potential dependent. Specifically, it appears that when steady-state V is inside negative the electrogenic pump contributes a steady outward current proportional to V. The pump is electroneural near zero V, but generates a steady inward current when the V is inside positive.

Sequential events in radiothyroidectomy. J.G.Snedecor and M.H.Koch.*
Zoology Department, University of Massachusetts, Amherst.

The thyroidectomizing effect of ^{131}I is well established in the literature. In these experiments the sequential histological and physiological effects of a large dose of ^{131}I were studied in chicks. The chicks to be radiothyroidectomized ($\overline{RT}$) were given 2 mCi ^{131}I/100 g body weight at age 5 days after being fasted 18 hours. A tracer dose was given to an equal number of chicks. The chicks were returned to normal diet and groups of six chicks of each dosage level were autopsied at intervals from 2 to 288 hours after injection. The effects of the ^{131}I on liver glycogen, serum cholesterol, iodine conversion ratio, residual thyroid radioactivity, and histology of the thyroid were studied. Beginning at 120 hours after injection the following changes were noted in the $\overline{RT}$ chicks: a marked reduction in the thyroidal retention of iodine, a concurrent increase in the amount of liver glycogen, and an increase in liver weight above that of the tracer-dose chicks. The iodine conversion ratios for both $\overline{RT}$ and tracer-dose chicks steadily increased up to about 75% by the 90th hour after injection and this value was retained throughout the remainder of the experiment. Two hundred sixteen hours after ^{131}I injection, the serum cholesterol values of the $\overline{RT}$ chicks had risen significantly above those of the tracer-dose chicks. The histological changes occurred in the following sequence: as early as the 96th hour many follicles showed an absence of colloid and were reduced in size as compared to the tracer-dose chicks; 120 hours after injection, follicles lost their spherical architecture; and by 216 hours hemorrhagic areas had appeared and fibrous tissue had begun to replace follicular cells. These effects were most marked in the center of the gland while the follicles on the perimeter showed damage later. USPHS AM 01266

ENHANCED RNA SYNTHESIS IN HYPERTROPHIED RAT SKELETAL MUSCLE. Burton E. Sobel and Seymour Kaufman (intr. by Colin M. Bloor). University of California at San Diego, School of Medicine, Department of Medicine, La Jolla, California, and the National Institute of Mental Health, Bethesda, Maryland.

Skeletal muscle undergoing compensatory hypertrophy contains increased amounts of microsomal RNA. Since the tissue's capacity for compensatory hypertrophy may depend in part on increased RNA, the mechanism responsible for the increase is of considerable interest. Accordingly, compensatory hypertrophy was produced in rat solei by tenotomy of synergist muscles. Solei from contralateral sham operated limbs served as controls. RNA polymerase, a nuclear enzyme known to regulate RNA synthesis, was studied in nuclei isolated by differential centrifugation from tissue from 50 rats in each of seven experiments. Enzyme activity was determined by the rate of incorporation of ^{14}C-UTP into acid precipitable product under conventional assay conditions with and without $(NH_4)_2SO_4$ and/or exogenous DNA in the medium. Activity increased 180% [from 360 $\pm$ 23 (mean $\pm$ S.E.) to 817 $\pm$ 83 picomoles/mg DNA/15 minutes] in hypertrophied muscle. No increase was observed until after 48 hours following tenotomy. On the other hand, RNA synthesis in vivo increased 24 hours earlier as evidenced by increased incorporation of ^{14}C-orotic acid (1 μc/g i.p. three hours prior to study) into RNA without any significant change in nucleotide precursor pool site. Thus, compensatory hypertrophy of skeletal muscle is characterized by a prompt increase in RNA synthesis in vivo and by a subsequent and probably secondary increase in RNA polymerase activity in isolated nuclei.

BLOOD VOLUME EXPANSION AND PROXIMAL SODIUM REABSORPTION IN SALT-LOADED AND SALT-DEPRIVED RATS. H. Sonnenberg, Dept. of Physiol., Univ. of Tor., Faculty of Med., Toronto, Canada.

The natriuretic response to blood volume expansion is enhanced by pretreatment with DOCA and salt, and reduced by salt deprivation (Pearce et al, Can.J.Physiol.47:377, 1969). To determine whether this difference in response could be explained by changes in proximal reabsorption, sections of proximal tubules of both salt-loaded and salt-deprived rats were perfused in vivo at a rate of 22 nl/min. Active sodium transport was measured in control rats and in others following an infusion (33% of estimated blood volume) of 4.5% bovine albumin in Ringer's. In the latter experiments urine was reinfused to maintain intravascular expansion. In control animals there was no difference in proximal sodium transport, whether the rats had been on a high or low salt intake. Despite a large natriuresis in response to sustained blood volume increase in high-salt animals, proximal sodium transport remained unchanged. Similarly, the smaller renal response in low-salt rats was not associated with changes in active transport of sodium in perfused tubules. The results therefore indicate that the differences in basal sodium excretion, as well as differences in the magnitude of natriuresis of blood volume expansion, are not dependent on changes in proximal transport capacity. Supported by AHA grant #67-663.

INTERACTION BETWEEN ADRENERGIC VASOCONSTRICTION AND CHOLINERGIC VASODILATATION IN SKELETAL MUSCLE. R.R. Sonnenschein and E.H. Rubinstein*, Dept. of Physiology, UCLA School of Medicine, Los Angeles, Calif.

Folkow et al. (Angiologica 1:197, 1964) reported a marked reduction in cholinergic dilatation by reflex or direct activation of adrenergic constrictor nerves, while Bolme et al. (Acta Physiol. Scand. 71:323, 1967) suggested that such inhibition occurs only during abnormally intense vasoconstriction. To elucidate this further, graded vasoconstriction was induced in a skinned hind limb of chloralose-urethane anesthetized cats either by direct stimulation of the sympathetic chain, or reflexly by carotid occlusion or partial obstruction of the inferior vena cava. While the initial conductance (C_1) was held at each of several points within a 5-10 fold range, cholinergic dilatation (conductance at peak response = C_2) was elicited by a standard electrical stimulation of the hypothalamic "alarm area". Generally, the lower C_1, the less the absolute amount of dilatation. However, over the major part of the range of C_1, the relative change in conductance, during dilator activation (C_2/C_1) was fairly constant. At very low and very high C_1 relative dilatation was diminished (C_2/C_1 was low). Results were essentially the same whether change in C_1 was accomplished reflexly or by direct sympathetic stimulation. Thus 1) essentially all interaction is at ganglionic or neuroeffector levels; 2) except at lowest constrictor activity, interaction of some sort occurs; 3) the significance of this must be tested in intact, awake animals. (Supported by USPHS HE-05157, AMA-ERF, LACHA 400-C1)

CORONARY SINUS PERFUSION WITH OXYGENATED BLOOD AT SYSTEMIC PRESSURE IN EXPERIMENTAL CORONARY ARTERY LIGATION: A NEW THERAPEUTIC CONCEPT IN THE TREATMENT OF PUMP FAILURE DUE TO ACUTE CARDIAC ISCHEMIA. James F. Spann, Jr., Dean T. Mason, and Robert Zelis*. Univ. of Calif., Davis, Calif.

The mortality with pump failure in myocardial infarction shock is 85%; thus development of new modalities of therapy is essential. Since the coronary sinus (CS) offers access to cardiac capillaries just as do coronary arteries, it is proposed in this study that the heart can be supported by retrograde perfusion of the CS with oxygenated blood at systemic pressure by a pump (CSP). In 12 dogs both left coronary arteries were totally occluded (CAO) with and without CSP with aortic blood via an occlusive balloon catheter inserted retrograde into the CS. With CSP, cardiac contractility was not depressed by CAO: maximum velocity of left ventricular contractile element shortening (Vmax) averaged 1.52 ± 0.16 lengths/sec (SEM) before and 1.53 ± 0.22 after CAO. In contrast, in the same dogs with CAO without CSP, Vmax fell 25% from a control (C) of 1.68 ± 0.28 to 1.28 ± 0.25 ($p<0.001$). Further, with CSP and CAO, mean aortic pressure decreased an average of 12 mm Hg (C=94); without CSP this fall averaged 24 (C=96). With CSP, ventricular fibrillation (VF) did not occur with CAO but, without CSP, VF occurred in four animals. It is concluded that coronary sinus perfusion with oxygenated blood at systemic pressure improves ventricular contractility, blood pressure and cardiac rhythm in experimental coronary occlusion and that this new technique merits clinical trial.

FACTORS AFFECTING UPPER AIRWAY RESISTANCE IN CONSCIOUS MAN. R.W. Spann,* and R.E. Hyatt. Mayo Clinic and Mayo Fdn., Rochester, Minn.

Upper airway resistance (subglottic area to airway opening) (Ru) accounts for approximately 50% of total pulmonary resistance during quiet breathing in normal man. However, little is known about factors affecting Ru. Rattenborg (Fed. Proc. 19:378, 1960) has suggested that during expiration the larynx alters its resistance in response to changes in external resistance to maintain constant total resistance. In 5 normal males we investigated this observation by measuring resistance from lung surface (esophageal balloon) to oral pharynx at constant lung inflation before and after adding external loads (2 to 12 cms. $H_2O/l/sec.$). No decrease in resistance from lung to oral pharynx occurred with loading. In later studies we measured lateral subglottic pressure with a needle, and lateral pressure just above the larynx via a catheter. This provided laryngeal resistance (Rlx). In 3 subjects the addition of external loads did not alter Rlx but was associated with a definite decrease in resistance mouthward. There was no change in resistance below the larynx. Rlx averaged 0.37 cms. $H_2O/l/sec.$ or 48% of Ru without added load and 66% of Ru during loading. Effect of lung inflation on Ru was studied. Increasing lung volume 2.5 l. was associated with a 12% fall in Ru during quiet breathing (QB) but no fall during panting-type respiration (P). Effect of head position was evaluated. Head flexion caused a 170% increase in Ru during QB and 120% during P. Hyperextension of the neck was associated with increases of 30 and 50% in Ru during QB and P, respectively. Inhalation of 6-7% CO_2 led to only a 7% decrease in Ru when lung inflation and breathing rate were carefully controlled. (Supported by PHS Grant HE 12229-07.)

ABSORPTION OF CALCIUM IN HYPERTHYROIDISM AND HYPOTHYROIDISM. Herta Spencer and Joseph Samachson*. Metabolic Research Unit, Veterans Administration Hospital, Hines, Illinois.

The absorption and excretion of calcium was studied under controlled dietary conditions in patients during different phases of thyroid function. Radioisotope studies, using ^{45}Ca and ^{85}Sr as tracers and balances of calcium, phosphorus and nitrogen as well as calcium tolerance tests were performed in the hyper-, hypo- and euthyroid states. Marked changes in calcium metabolism were noted in the different phases of thyroid function. During hyperthyroidism and during hypermetabolism induced by desiccated thyroid extract, the intestinal absorption of calcium was lower than in the euthyroid or hypothyroid state. The most striking change was the marked increase in intestinal absorption of calcium in the euthyroid or hypothyroid state following the correction of the hyperthyroid or hypermetabolic state as was indicated by the very low fecal excretion of calcium, of ^{45}Ca and ^{85}Sr, and by a marked increase in the plasma levels of the radioisotopes following the oral administration of ^{45}Ca and of ^{85}Sr. The endogenous fecal calcium also decreased in the hypothyroid and euthyroid state and the fecal calcium consisted practically of endogenous fecal calcium following the correction of the hyperthyroid and hypermetabolic state. The calcium tolerance test performed in hyperthyroid patients with hypercalcemia was similar to the test in patients with hyperparathyroidism. After the correction of the hyperthyroidism the test returned toward normal in the euthyroid state. Supported by U.S. Public Health Service Grant A-5572.

OXIDATION OF β-HYDROXYBUTYRATE INFUSED INTO THE CORTICAL SUBARACHNOID SPACE. John J. Spitzer, Judy A. Spitzer* and Theodore Matulewicz*. Hahnemann Med. Col., Philadelphia, Pa.

In order to determine whether β-hydroxybutyrate (BOHB) undergoes oxidation from the cerebrospinal fluid, a constant infusion of Na DL-3-hydroxybutyrate-3-^{14}C was administered directly into the cortical subarachnoid space of anesthetized dogs. Simultaneous samples of cortical subarachnoid fluid, and arterial as well as sagittal sinus blood were removed during and following the infusion. The samples were analysed for $^{14}CO_2$, CO_2 and ^{14}C-BOHB. Infusion of the labeled compound resulted in the appearance of $^{14}CO_2$ in the cortical subarachnoid fluid. A gradient in $^{14}CO_2$ concentration was observed from the cortical fluid to the sagittal sinus, and from the sagittal sinus to arterial blood. During infusion, ^{14}C-BOHB concentration also became higher in sagittal sinus than in arterial blood. These results suggest that BOHB present in cerebrospinal fluid may undergo oxidation by neighboring tissues. The CO_2 resulting from this oxidative metabolism is removed via the venous outflow from the brain. While under physiological conditions ketone oxidation may assume only a minor role in the total energy metabolism of the brain, under non-physiological circumstances it may gain much greater importance.

OXYGEN UPTAKE FOR ISOMETRIC TETANIC CONTRACTIONS OF DOG SKELETAL MUSCLE IN SITU. W. N. Stainsby and J. T. Fales, Univ. of Fla. Coll. of Med., Gainesville, Fla., and the School of Hygiene and Public Health, The Johns Hopkins Univ., Baltimore, Md.

The venous outflow from the gastrocnemius-plantaris muscle group was isolated and measured. Oxygen uptake was calculated from the blood flow and arterial and venous oxygen differences. The tendon in the muscle group was connected to an isometric myograph for measurement of developed tension. Tetanic contractions were produced by 55 cps square pulses of 10 to 20 volts and 0.5 msec. duration applied to the sciatic nerve. The contractions were graded by changing the preload and hence the developed tension and by varying duration of the contraction from 0.5 to 11 seconds. Oxygen uptake was measured during and after each contraction until recovery was complete, and was then integrated with respect to time. Tension-time, $\int$Pdt, was calculated for each contraction. The total oxygen uptake for each contraction was not related to $\int$Pdt but was well correlated with the duration of stimulation. Statistically the data fit well the traditional two component model of energy for maintenance of tension plus extra energy for the development of tension. The data fit equally well another model in which energy exchange varied with time according to the equation $Y = B \log (1 + X)$ without regard for tension development. Since oxygen uptake was unrelated to $\int$Pdt we favor the second model. (Supported by NIH Grant GM 06264).

WHOLE BODY CO_2 DISSOCIATION CURVE OF DOG, AND ITS RELATION TO THE DYNAMICS OF CO_2 STORES. I. Staw,* C. Poyart* and G. G. Nahas. Columbia Univ., Coll. of P & S, New York, N. Y. 10032

The concentration of CO_2 in various parts of the body is not uniform and is determined locally by a variety of physiologic factors such as the rate of perfusion, CO_2 production, and the CO_2 titration curve at any given point. A thorough investigation of the distribution of CO_2 in any of its chemical forms in the body and of the mechanism by which the CO_2 stores are changed (e.g. hyperventilation) requires the use of complicated multicompartment mathematical models of the biological system involved. The conclusions drawn from such a study depend upon the values assigned to the various parameters used in the mathematical simulation. One very important yet questionable parameter is the CO_2 dissociation curve slope of soft tissues (S_T). Most published estimates for the average S_T are of the order of 1-2 cc CO_2/kg tissue/mm Hg. The present experiments yielded much higher values for S_T. Nine dogs were anesthetized, paralyzed and mechanically ventilated, first for one hour with 30% O_2 in N_2 and then up to two hours with 2% CO_2 and 30% O_2 in N_2. $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, $paCO_2$, $pvCO_2$, $pACO_2$, paO_2 were measured. The calculated S_T averaged 6.5 cc/kg with a range of 4-9. Using a model recently developed by one of us (I. S.) for the dynamics of CO_2 stores, these results imply that the cellular membrane represents a substantial barrier to the diffusion of CO_2 from its sites of production into the blood.

PHYSICAL PROPERTIES OF SERIES ELASTIC COMPONENT OF TRACHEAL SMOOTH MUSCLE. N. L. Stephens* and A. Naimark. Department of Physiology, University of Manitoba, Winnipeg, Canada.

A complete description of the nature of active tension development by tracheal smooth muscle (TSM) requires characterization of the physical properties of both its contractile element (CE) and its series elastic component (SEC). We present here the results of 19 experiments describing the physical properties of the SEC of TSM in terms of its dynamic stiffness (dP/dL, where P = load or tension and L = muscle length) at various loads, and of its length-tension (L-T) relationships. The length of the TSM was 1.08 cm + 0.03 (SE) and its weight was 0.011 g + 0.001 (SE). The length chosen was the pre-determined optimal (L_{max}). Over a suitable range of loads, simultaneous measurements were made of maximum velocity of shortening (dL/dt in cm/sec, and dP/dt in g/sec), under pre- and after-loaded isotonic conditions at 37°C. These observations were made at the instant when isometric contraction became isotonic. Dynamic stiffness was obtained by multiplying dP/dt by dt/dL. The resultant dP/dL was plotted against P and the following linear regression equation obtained: dP/dL = 1.82 + 13.50 P. Integration of this equation yielded the L-T curve of the SEC. This displayed a logarithmic configuration. Calculation also revealed that under the mean maximum isometric tetanic tension (P_o) developed by the TSM (1.050 Kg/cm^2 + 0.112 (SE)) the extension of the SEC was 7.5 % + 0.59 (SE) of L_{max}. The compliance of TSM at P_o thus proved to be intermediate between voluntary and cardiac muscle.

(Supported by the Medical Research Council of Canada and the Canadian Tuberculosis Association)

PRESENTATION OF A GENERAL THEORY TO ENCOMPASS THE MULTIPLE CAUSES OF OBESITY. Joseph W. Still. 11401 E. Valley Blvd., El Monte, Calif.

The theoretical presentation will be supported by data collected during the course of treating 600 obese patients in my office. The basic point of the paper is to demonstrate that obesity can result from the action of any of several causative agents or from the combined action of two or more. Because of this we should stop discussing obesity as if it was a single physiological or pathological entity when in fact it is merely a symptom that can have a number of causes. One can only treat it rationally if he analyzes and treats each of the several causes according to its importance as a causative agent in each specific case.

PERIPHERAL SEQUESTRATION OF PLASMA PRODUCED BY A REDUCTION IN BODY TEMPERATURE. John T. Stitt* and Robert E. Semple, Department of Physiology, Queen's University, Kingston, Ontario, Canada.

Hypothermia in mammals has been shown to produce a reduction in circulating plasma volume (CPV)(1). Recently, we have observed a similar phenomenon in reptiles when body temperature was lowered acutely. Unanaesthetized turtles were cooled from 20°C to 5°C within 2 hours; CPV, measured with RISA, was reduced from 94 to 73 ml/kg. The change in CPV was reversible with warming to 20°C in the same period of time. The nature of the CPV changes was investigated using I-125 and I-131 RISA in the same animals at both temperatures and by measuring extracellular fluid volume (ECFV) with inulin-C-14. Since the reduction in CPV of warm animals caused by cooling failed to produce a concentration of RISA, while the increase in CPV of cold animals produced by warming caused a dilution of RISA, and since measured ECFV reduced from 232 to 135 ml/kg when body temperature was lowered, it was deduced that the CPV changes produced by changes in body temperature were due to sequestration of plasma within the vascular bed. Tissue 'RISA spaces' were determined in the same animal at both temperatures using the 2 types of RISA. Skin, shell, muscle, kidney and gut all had reduced circulating RISA spaces in the cold, while liver and lung RISA spaces were unchanged. Investigation into the cause of sequestration showed that CPV and mean arterial pressure (MAP) of turtles at 20°C were reduced by cervical cordotomy, whereas cervical cordotomy at 5°C prevented the increase in CPV and MAP normally associated with increasing body temperature. Changes in CPV accompanying changes in body temperature may be due to the changes in MAP which are produced by the effect of temperature on the total peripheral resistance and cardiac output of the animal.

(1) Rodbard et al., Am. J. Physiol., 167:485, 1951.

(Supported by the National Research Council of Canada.)

SPECTRAL SENSITIVITY OF THE BARNACLE. Wilford P. Stratten* and Thomas E. Ogden. Depts. of Neurology and Physiology, University of Utah College of Medicine, Salt Lake City, Utah.

The electroretinogram of the isolated eye was used as an indicator of the sensitivity of the animal to monochromatic lights. The ERG was recorded between the eye-cup and the optic nerve, using an air gap technique. Maximum chromatic sensitivity of the animal, as determined by two methods (equal quanta stimuli and criterion response), was 535 ± 5 nm. Relative sensitivity was greater than 10 percent from 350 to 630 nm. Chromatic adaptation studies indicate that a single pigment mediates the animal's light sensitivity. Data describing the transmission and fluorescence of the ocular media will also be presented. (Supported by USPHS Grants NB-04135 and NB-05244)

EFFECT OF PULSATILE AND NONPULSATILE FLOW ON PULMONARY VENOUS RESISTANCE. Christian J. Streck and George R. Daicoff. (intr. by E. R. Woodward). University of Florida College of Medicine, Gainesville, Florida.

The pulmonary veins are assumed to be the capacitance vessels of the pulmonary circulation and to contribute little to the vascular resistance of the lungs. We have measured pulmonary vein pressure (PVP) directly in anesthetized open-chested dogs and found that the pulmonary vein-left atrial pressure difference to be a significant portion of the total pulmonary artery-left atrial pressure difference. In 12 dogs the right pulmonary artery was occluded diverting the entire cardiac output to the lung. Pulmonary artery pressure (PAP) increased from 19.8 mmHg to 34.8 mmHg; PVP increased form 14.3 mmHg to 20.7 mmHg; and left atrial pressure (LAP) increased from 3.0 mmHg to 4.3 mmHg. The basal pulmonary vascular resistance of the left lung was 0.380 units. Increased flow reduced the vascular resistance to 0.256 units. The venous segment of the resistance accounted for 64 % of the pulmonary vascular resistance at basal blood flow and 55 % at increased blood flow. In 5 dogs the left lung was perfused with an extra-corporeal pump delivering venous blood and pressure/flow relationships were observed. Doubling the blood flow produced the following changes: PAP increased from 22.2 mmHg to 34.2 mmHg, PVP increased from 18.5 mmHg to 23.8 mmHg, LAP increased from 7.0 mmHg to 9.6 mmHg, total pulmonary vascular resistance decreased from 0.326 units to 0.261 units, and the venous contribution was 61 % to 59 % of the total pulmonary vascular resistance. The pulmonary venous resistance contributed significantly to the total vascular resistance both at basal and increased flow rates delivered by pulsatile and nonpulsatile methods.

EXPERIMENTAL STUDIES OF A NEURON WITH AN ENDOGENOUS OSCILLATOR AND A QUANTITATIVE MODEL OF ITS MECHANISM. F.Strumwasser & M.Kim*. CIT, Calif.

The parabolic burster (PB) is a neurosecretory neuron in the PVG of Aplysia that produces impulse bursts at somewhat regular intervals (microcycles) and has been shown to possess a circadian rhythm of impulse activity. When isolated PVGs are perfused with Ca-free artificial sea water and TTX, all spike electrogenesis is abolished in the ganglion as judged by intracellular and extracellular recordings from cell bodies and nerves. Under such conditions intracellular recordings from PB reveal cyclic variations of V_m with amplitude of ∿30mV and period of ∿1.5 min. at 14°C. Applied hyperpolarizing current increases the amplitude and decreases the frequency of such endogenous oscillations while applied depolarizing current has the opposite effect. These oscillations are abolished by any of the following procedures: Cl is substituted with acetate or propionate; Na is substituted with Li; Na is reduced to 60% by substitution with Tris; or by addition of ouabain. These and earlier findings indicate that the hyperpolarizing phase of the oscillation is probably due to an electrogenic Na pump coupled with Cl extrusion. TEA does not abolish oscillations although the waveform is influenced. A mathematical model to account for endogenous oscillations and their manipulation by applied currents has been constructed and studied. The model has three components: 1) a standard nerve membrane with g_{Na} and g_K fixed but adjusted to give a V_m of -30mV; 2) the rate of a Na-Cl hyperpolarizing electrogenic pump is a function of [Na] at the inner membrane surface (im) with counterclockwise asymmetrical hysteresis and first-order kinetics; 3) $[Na]_{im}$ was calculated from considerations of diffusion and its dynamics was approximated by a fourth order ordinary D.E. According to the model the existence of oscillations is critically dependent on the slope of the hysteresis curves and the amplitude and frequency of the oscillations are a function of the hysteresis interval.

GOLGI TENDON ORGAN RESPONSES TO MUSCLE STRETCH AND CONTRACTION. Douglas G. Stuart, George E. Goslow*, Carter G. Mosher*, Rebecca L. Gerlach* and Robert M. Reinking*. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona.

Golgi tendon organs (GTOs) have received comparatively little attention since their functional identification by Matthews (J. Physiol. 78: 1, 1933). This report is concerned with the properties displayed by the GTOs of de-efferented soleus muscles under the following conditions: A, threshold responses to twitch contraction with initial muscle length set to give zero tension, maximum active tension during twitch contraction (T_{opt}), and the tension associated with right angle ankle position (T_{ra}); B, threshold response to static stretch; and, C threshold and suprathreshold responses to variable frequency triangular wave stretches with initial length set to give T_{opt} for a 2.5 mm stretch and, for a 5 mm stretch, to bring peak length to give T_{ra}. Our initial data (40 Ib afferents from 6 cats) suggest that: 1) while some soleus GTOs provide no information about static muscle length many others could signal length-tension information associated with the extremes of dorsiflexion; 2) many GTOs fire within the physiological range of dynamic stretch including some not signaling static stretch; and, 3) responses to static and dynamic stretch cannot be predicted from conduction velocity, response to twitch contraction or position of the receptor within the muscle. There are approximately 90 GTOs in the cat soleus muscle and its tendon. In view of the wide range of static and dynamic sensitivities displayed by GTOs it is obvious that substantial sampling will be necessary before the transducing properties of these receptors can be firmly established. (Supported in part by USPHS, NIH Grant NB 07888).

DISTRIBUTION OF RADIOACTIVITY IN HIPPOCAMPUS AND AMYGDALA AFTER INJECTION OF ^{3}H ESTRADIOL BY DRY-MOUNT AUTORADIOGRAPHY. Walter E. Stumpf and Madhabananda Sar (intr. by D. J. Ingle)Dept. of Pharmacology,University of Chicago,Chicago, Ill.

Two 24-day old female rats were injected subcutaneously, each with 0.1 µg of 6,7-^{3}H estradiol-17β, specific activity 208 µc/µg, dissolved in isotonic saline, and killed after one hour. 2 µ freeze-dried serial sections were prepared for dry-mount autoradiography as described (Stumpf,W.E.,Science 162, 1001 (1968)). The autoradiograms showed concentration of radioactivity in nuclei of neurons in distinct areas of the amygdaloid complex while neurons of the hippocampus, the putamen and the claustrum remained unlabeled. In the amygdala extensive radioactive labeling of neurons existed in the medial portion with the highest labeling index in the nucleus medialis. Neuronal concentration of radioactivity was also found in a cortical portion of the nucleus corticalis; the nucleus centralis; the nucleus lateralis,pars anterior; and the nucleus basalis, pars medialis. The distribution of labeled neurons followed classical neuroanatomical patterns to a limited degree. The autoradiographic findings suggest a genomic effect of estradiol on certain amygdaloid neurons,which may be involved in the production of releasing factors or other messengers, and support the concept of an amygdaloid-diencephalic-hypophysial-gonadal interrelationship.

THE MECHANICAL PROPERTIES OF PULMONARY TISSUE IN MAN. T. Sugihara* and C. J. Martin. Institute of Respiratory Physiology, Virginia Mason Research Center and Firland Sanatorium, Seattle, Washington.

The properties of tissue in the air-lung interface determine the pressure-volume (P-V) characteristics of lung. Tissue properties are usually inferred from the P-V curves of liquid-filled lung. Direct measurements of the length-tension (L/T) relationships of individual alveolar walls in man are reported here. Suspended in a saline bath between length and force transducers the wall was stretched to obtain the stress-strain relationships as reported previously (J. Appl. Physiol. 25: 689, 1968). Eulerian stress was calculated at several extensions and the maximum extension (λ max) was predicted from the equation $\sigma = \frac{\lambda^2 - 1}{\lambda} f(\lambda)$ (Biophysics J., in press). Normal alveolar walls in man have L/T properties qualitatively similar to those of the cat. The stress-strain relationships were not uniform in normal man and varied considerably in pathological states. λ max correlated well with age ($r = -0.71$) and less well with peak expiratory flow ($r = 0.47$). λ max varied from 2.2 in lungs of an 18 year old male to 1.7 in an 88 year old man. In patients with an irreversible diffuse obstructive pulmonary syndrome ($DOPS_I$) λ max was 1.65 or below. Females tended to have a lower λ max than males. The stretch-release pathway in those with $DOPS_I$ showed a rapid decay in wall tension while older subjects with similar values maintained a wall tension throughout the shortening. The effect of such changes upon lung compliance, elastic recoil and lung volume will be discussed.

Supported in part by grant NE 12596 (NIH).

STEREOSPECIFIC BINDING OF ALDOSTERONE TO CHROMATIN OF RAT KIDNEY NUCLEI. G. E. Swaneck*, L. H. Chu*, and I. S. Edelman. Cardiovascular Research Institute, University of California School of Medicine, San Francisco.

In earlier studies, 73% of total binding of ^{3}H-aldosterone to renal nuclear macromolecules was to nuclear proteins extractable with 0.1M tris-3 mM $CaCl_2$, pH = 8. By modifications in the methods used to prepare nuclear fractions, we succeeded in reducing the proportion of ^{3}H-aldosterone bound to tris-extractable proteins and have studied the role of chromatin in the binding to the non-extractable material. Adrenalectomized rats were injected with 2.6×10^{-10} moles of ^{3}H-aldosterone, the kidneys were removed 30 min. later and homogenized gently in 0.25 M sucrose-3 mM $MgCl_2$, pH = 8. The homogenate was filtered through nylon mesh and centrifuged in 0.88 M sucrose and 2.1 M sucrose in succession. The labile component of nuclear binding was removed by extracting the intact nuclei with 0.1 M tris-3 mM $CaCl_2$. The nuclei retained 78% of the initially bound ^{3}H-aldosterone. Most of the retained steroid was recovered in the chromatin fraction. The steroid was bound to nucleoproteins as judged by G-50 Sephadex chromatography of the sheared chromatin. The aldosterone-nucleoprotein complex was stable for 24 hrs. at 0°C but dissociated completely on heating to 37°C. The relative affinities of competing steroids, d-aldosterone, 9α-fluorocortisol, 17α-isoaldosterone and 17β-estradiol for the ^{3}H-aldosterone binding sites indicate that these sites are both stereo- and mineralocorticoid-specific. Specific binding of aldosterone to chromatin may be related to previous findings that the hormone acts through induction of RNA synthesis. The interrelationship between binding of the steroid and induction is under study. (Supported by N.I.H. Grants Nos. HE-06285 and HE-05725 from the National Heart Institute.)

EFFECTS OF ADENOSINE DERIVATIVES ON RENAL FUNCTION AND RENIN SECRETION. Hitoshi Tagawa* and Arthur J. Vander. Dept. of Physiology, Univ. of Michigan, Ann Arbor, Michigan.

Single injections of adenosine and AMP have been reported to induce renal vasoconstriction, whereas ATP produced vasodilation. The present study employed continuous infusion of these agents directly into a renal artery of chronically salt-depleted anesthetized dogs. Total renal blood flow (electromagnetic flowmeter) decreased transiently (1-2 min) at the start of adenosine (20-500 μg/min) infusion, but was unchanged or slightly increased during steady-state. Statistically significant decreases occurred in GFR (34.7%), filtration fraction (38.4%), urine flow (28.2%), sodium excretion (61.6%), and renal venous renin activity (40.4%). ATP (50-500 μg/min), AMP (200 μg/min), and cyclic AMP (1-5 mg/min) induced changes qualitatively similar to those of adenosine during steady-state. However, they induced no or only slight initial transient reduction in blood flow. Smaller doses of adenosine (5 μg/min), AMP (20-50 μg/min), and cyclic AMP (50-200 μg/min) produced either no effects or inconstant ones. Inosine (200 μg/min) and IMP (50-200 μg/min) produced no detectable effects. The data suggest that, during continuous infusion, adenosine and its nucleotides induce afferent arteriolar constriction and efferent dilation. The inhibition of renin secretion is difficult to explain by previously postulated theories and may indicate a direct effect of those agents on the JG apparatus, perhaps as normal intermediates of the metabolic pathways regulating renin secretion.

Effects of Glycogen on Molecular Size of Amylase in Normal and Macroamylasemic Serum. S. Take*, L. Fridhandler, and J.E. Berk*. Col. Med., U. of Calif., Irvine, Calif. 92664.

Macroamylasemia is characterized by the presence in serum of a macroamylase whose large size precludes its excretion in the urine. The continued circulation of this macromolecule appears to be responsible in some cases for persistent hyperamylasemia. Evidence has been advanced indicating that the macroamylase may be a complex of normal serum amylase bound to a protein. Other possibilities regarding origin of the macroamylase are polymerization of normal serum amylase or binding of the latter by a large non-protein molecule. Glycogen and glycogen-limit dextrins are known to form complexes with amylase (Loyter and Schramm, J. Biol. Chem. 241:2611, 1966). We found that after incubation of normal serum with glycogen from shellfish or rabbit liver, the molecular size of the amylase increased to approximately that of the 19S proteins as judged from its elution position after passage through Sepharose. Glycogen was also incubated with human macroamylasemic serum. This substance increased the molecular size of the macroamylase from approximately that of the 7S proteins to one even greater than the 19S proteins. Incubation of serum with other polysaccharides, such as Dextran 80 and heparin, did not change the BioGel P-300 elution pattern of normal serum amylase. The action of glycogen on amylase appeared to be determined in part by the concentration of glycogen, especially in relationship to the degree of amylase activity. Thus, 2 ml of 1% or higher concentrations of glycogen when added to 1 ml of normal serum resulted in formation of a macroamylase, whereas concentrations less than 1% (0.1 and 0.5%) did not.
(Supported by USPHS Grant GM-11897)

^{32}P-LABELED INTERMEDIATE OF MICROSOMAL ATPase FROM RABBIT GASTRIC MUCOSA. Alan S. Tanisawa*, D. K. Kasbekar* and J. G. Forte. Dept. of Physiology, Univ. of California, Berkeley, Calif.

An active ATPase has been reported in microsomes isolated from gastric mucosa. Several characteristic properties of this enzyme have led to the suggestion that it may play a role in gastric H^+ secretion. Gamma-labeled ATP^{32} was used to study intermediate reactions of the light microsomal ATPase (17,000-155,000 x g x hr). A ^{32}P-intermediate was found in the perchloric acid precipitate which was not extractable with lipid solvents. ^{14}C-ATP was used to exclude the possible binding of ATP itself as studies revealed $< 10\%$ of the total binding as the ^{14}C-adenine moiety. The formation and turnover of the ^{32}P-labeled intermediate was very rapid and optimum incorporation requires Mg^{++}. The intermediate was stable in acidic solutions and labile in neutral to alkaline solutions. This coupled with the release of $^{32}P_i$ by hydroxylamine suggests the possibility of an acyl phosphate linkage, which has also been suggested for the Na^+-K^+ stimulated ATPase. However, Na^+ and/or ouabain did not modify its formation which distinguishes it from the ATPase found in tissues which primarily transports Na^+ and K^+. Thiocyanate, a potent inhibitor of gastric H^+ secretion, reduced the ATPase activity and the labeled protein was increased; whereas, potassium ion, which has been found necessary for acid secretion, slightly but consistently stimulated ATPase activity while the labeled protein was decreased. Additional washings of the microsomal preparation resulted in a greater K^+ response. Perhaps SCN^- and K^+ act by either diminishing or accelerating, respectively, the ultimate dephosphorylation of the intermediate. (Supported by USPHS).

EFFECTS OF MANGANESE AND TETRODOTOXIN ON TWO INWARD CURRENTS IN CARDIAC MUSCLE. M. Tarr*, H. G. Haas* and J. Trank. Dept. of Physiol., University of Kansas Medical Center, Kansas City, Kansas and Physiologisches Institut, Heidelberg, Germany.

Two inward currents (a Na^{+}-current and a Ca^{++}-current) contribute to the cardiac action potential. The effects of manganese ions (considered to be a suppressing agent of Ca^{++}-currents) and tetrodotoxin (known to block the transient inward current in nerve) on the membrane currents in frog atria were studied by the double sucrose-gap voltage clamp technique. In Ringer solution, two transient inward currents can be easily distinguished under the conditions of a step depolarizing voltage clamp; 1) a fast inward current with a "time to peak" of 5 to 10 msec; and 2) a slow inward current with a "time to peak" of 50 to 100 msec. In Ca^{++}-free Ringer solution, the slow inward current is absent, whereas, the fast inward current is present. Tetrodotoxin (100nM) blocks the fast inward current without affecting the slow inward current, whereas, manganese ions (10mM) block both the fast and slow inward currents. The data show that tetrodotoxin selectively blocks the fast transient membrane conductance change in cardiac muscle, whereas, manganese ions nonselectively block both the fast and slow transient membrane conductance changes. (Supported by grants from Kansas Heart Association and USPHS.)

ADRENAL STEROIDS AND A RENAL-PRESSOR SYSTEM IN THE CHICKEN. Addison A. Taylor* and James O. Davis, Dept. of Physiology, University of Missouri School of Medicine, Columbia, Missouri.

The concentrations of aldosterone (A) and corticosterone (B) in adrenal vein plasma were measured by the double isotope derivative assay in intact cockerels and in cockerels following hypophysectomy, infusion of ACTH, infusion of chicken kidney extracts, or sodium depletion. In sodium-depleted cockerels, renal renin content, index of juxtaglomerular granularity (JGI) and the width of the peripheral zones of the adrenals were also examined. The adrenal vein plasma levels of B and A in intact "surgically stressed" cockerels were 6.58 ± 1.47 (SEM) and 0.21 ± 0.06 µg/100 ml, respectively. Infusion of ACTH produced a significant increase in B but no increase in A. Concentrations of both B and A were significantly decreased by hypophysectomy while neither sodium depletion nor infusion of chicken kidney extracts produced a detectable change in adrenal vein levels of these steroids. Sodium-depleted cockerels showed a significant increase in JGI. Kidney extracts from sodium-depleted cockerels, when incubated with chicken plasma, produced a significantly greater blood pressure increase in a rat than did kidney extracts from sodium-repleted cockerels. The peripheral zones of adrenals from sodium-depleted birds were larger than those of control birds. It is concluded that the pituitary plays a role in maintaining adrenal secretion of A as well as B in cockerels. A renal-pressor system was found to be present in the cockerel and could be stimulated by sodium depletion although no steroidogenic action of this system was demonstrable.

ENERGETIC COST OF RUNNING. C. Richard Taylor and Knut Schmidt-Nielsen. Dept. of Zoology, Duke University, Durham, N. C.

Desert rodents live in an environment where the food density is low and they presumably must move over considerable distances to obtain food. The energetic cost of locomotion therefore is important. Oxygen consumption, determined on a treadmill, increased almost linearly with running speed. In three species the oxygen consumption (M in ml O_2/g hr) relative to running velocity (V, in km/hr) could be expressed by linear equations (least squares method) as follows:

Kangaroo rat (Dipodomys spectabilis)	M = 1.01 V + 1.89
Ground squirrel (Citellus tereticaudus)	M = 0.63 V + 1.40
White rat (Rattus norvegicus)	M = 0.93 V + 1.79

Although all points are close to the straight lines, the Y-intercept (extrapolated zero running velocity) is well above the resting oxygen consumption. Therefore, the net cost of running (i.e. running - resting oxygen consumption) decreases with increasing speed. The most economical runner is the ground squirrel. The higher cost of running in the kangaroo rat could be due to a predominatly bipedal animal being forced to run on all four legs, but the equally high cost of running for the white rat does not support this argument. Additional species are necessary for evaluation of possible differences in the cost of various types of locomotion. (Supported by NIH Research Career Award 1-K6-GM-21,522 (KSN) and NIH Research Grant HE-02228.)

HYDROGEN ION POTENTIATION OF THYROXINE ACTION IN TADPOLES. R. E. Taylor, Jr. and S. B. Barker. Dept. of Physiology and Biophysics, The Medical Center, University of Alabama in Birmingham.

Rosen (Proc. Soc. Exp. Biol. Med. 38:171, 1938) reported that low pH potentiated the metamorphosis-accelerating action of thyroxine (T_4) administered to tadpoles by the immersion technique. Marzulli (J. Gen. Physiology 25:623, 1941) attributed this to elevation by H^+ of metabolic rate with consequent greater uptake of T_4 by the gills. We have confirmed the effect of low pH on relative T_4 potency; premetamorphic Rana catesbeiana tadpoles exposed to 25 ng T_4/ml aquarium water buffered at pH's between 5.5 and 8.0 with Tris and 2-(N-Morpholino)-Ethanesulfonic Acid, had 87% faster rates of hind limb growth at pH 5.5 than at 8.0. However, we propose an alternative mechanism of effect which is based on pH dependent changes in the relative abundance of the zwitterion (Z) having a net charge of zero and the phenolate (P) having a net charge of -1 as the phenolic hydroxyl (pKa = 6.73) dissociates. With the basic assumptions that T_4 enters the tadpole primarily by passive diffusion, that permeability of Z >>> P and that at equilibrium [Z] in aquarium water equals [Z] in extracellular fluid, it can be predicted with the Henderson-Hasselbalch equation that as aquarium water pH's fall below that assumed for tadpole extracellular fluid (7.4) the ratio of [T_4] tadpole/[T_4] aquarium water will increase. At pH 5.5 the ratio is calculated to be 18X greater than the ratio at pH 8.0 and may thus account for the observed apparent increase in biological potency. Additionally, since the pH range of this phenomenon is dependent on the pKa of the phenolic hydroxyl, this must be considered when comparing potency by the immersion technique of T_4 analogs having different pKa's. (Supported in part by NIH Grant AM-10436.)

DIURNAL VARIATION IN THE EFFECTS OF PROGESTERONE ON MULTIPLE UNIT ACTIVITY IN THE RAT HYPOTHALAMUS. Ei Terasawa* and Charles H. Sawyer, UCLA.

Exogenous progesterone exerts either a facilitatory or an inhibitory effect on ovulation in the rat depending on the time of injection. The release of pituitary ovulating hormone is controlled by the hypothalamus, and the present study seeks electrical correlates of hypothalamic activation and inhibition by the steroid. With large microelectrodes (25μ) recordings were made of integrated multiple unit activity in the arcuate nucleus-median eminence (ME) and the preoptic region in ovariectomized estrogen primed "proestrous" rats under light urethane anesthesia. Cortical EEG, EKG and respiratory rate were also monitored. With lights on 14 h daily (5:00-19:00) artificial proestrus (nucleated vaginal smears) was achieved with injections of 5 μg estradiol benzoate at 17:00 on the two preceding days. On the day of proestrus injection of progesterone (2.5 mg, sc) induced a "sleepy" EEG within an hour regardless of time of administration. However, afternoon (14:30) injections induced a depression in ME multiunit activity followed by several hours of elevated activity starting around 17:00, while injections at 11:00 evoked a rise in activity preceding the phases of depression and secondary elevation (a triphasic effect). In natural proestrus progesterone at 11:00 activates release of pituitary ovulating hormone ("advances the critical period"), and the initial elevation in multiunit activity may represent a neural correlate of this process. The secondary rise in activity occurs at about the time of onset of behavioral estrus. Anterior deafferentation of the hypothalamus eliminates the diurnal variation in responsiveness to progesterone, and injection of the steroid is followed by a slow rise in multiunit activity regardless of time of day. (Supported by NB 01162 and the Ford Foundation.)

RENAL CLEARANCE OF L-PROLYL L-HYDROXYPROLINE. George B. Theil, Polly S. McMurtry*, Lynn R. Willis* Depts. of Med. and Pharm. and the Cardiovascular Research Section Univ. Iowa School of Med., Iowa City, Iowa.

The dipeptide, l-prolyl l-hydroxyproline (HP), was infused into 4 dogs and the renal clearance of HP, free hydroxyproline (FH) and total nonprotein hydroxyproline (TH) were measured before and after the sustaining infusion of HP. Simultaneous inulin clearances (IC) were done. Preinfusion HP clearances averaged 57.6 ml. per minute ± 2.2 (S.E.M.) compared to IC 72.2 ± 6.7. FH decreased from 1.11 to 0.57; TH clearances were unchanged (21.20 vs. 20.78). During HP infusion the mean HP clearance was 124.7 ± 4.9 whereas the mean IC was 70.8 ± 3.1. HP/IC clearance ratios were 0.83 in the control period (range 0.56-1.11) and 1.80 (range 1.36-2.31) after HP infusion. Although a pure dipeptide was used the average plasma concentration of FH increased almost 5 fold while the HP increased by a factor of 1.8. Therefore at least two mechanisms were influencing the HP plasma concentration: 1) rapid renal clearance at a greater rate than could be accounted for by the IC and 2) conversion of a significant fraction of the plasma HP to FH. Dog plasma samples were assayed for HP peptidase activity. Plasma containing added HP in a concentration of 110 μM per liter was incubated at 31° C for 40 minutes. Results showed a 50% decrease in HP and an increase of 50% in FH concentration. Dog plasma had 20-30 times the activity of human plasma which also was assayed. To determine if a non-hydroxyproline dipeptide might compete with HP we infused two dogs with l-glycyl l-tyrosine. This maneuver had no significant effect on the clearance of HP. Conclusions 1) These results support the original however less direct and less precise studies in human subjects (Clin. Res. 12:247, 1964) with respect to HP clearances, 2) A HP peptidase, whose specificity has not been determined, is described in dog and human plasma.

POTENTIATION OF THE CARDIOACCELERATOR RESPONSE TO SYMPATHETIC NERVE STIMULATION IN THE ISOLATED RABBIT HEART DURING ANGIOTENSIN INFUSIONS. J. L. Thompson (intr. by W. B. Youmans). Department of Physiology, University of Wisconsin, Madison, Wisconsin.

The hearts of Dutch rabbits were perfused by the Langendorff method at a constant rate with a modified Tyrode solution containing atropine (2 µg/ml). The sympathetic nerves to the heart were stimulated for 30 sec at a frequency of 2/sec at 5 min intervals before and during angiotensin infusions (0.005 µg/ml). A gradual decrease in the magnitudes of the responses to sympathetic nerve stimulation occurred with consecutive stimulations before beginning infusions of angiotensin. The peak chronotropic responses to sympathetic nerve stimulation in 10 of 12 preparations were greater on the initial stimulation during angiotensin than the responses immediately before angiotensin infusions. In the other two preparations no significant changes in the magnitudes of the accelerator responses during angiotensin were observed. The average response to sympathetic nerve stimulation before angiotensin was 51±6.4 beats/min, while that during angiotensin was 63±7.9 beats/min. This was a significant increase in response ($p<0.005$). The hearts were not sensitized to the actions of norepinephrine during angiotensin, since the chronotropic responses to norepinephrine injections before and during angiotensin were similar. It has been reported that the responses of smooth muscle in some sites to sympathetic nerve stimulation are potentiated in the presence of angiotensin, and that these increased responses may be due in part to facilitated release or prevention of the reuptake of the neurotransmitter. This potentiating effect of angiotensin on the chronotropic responses to sympathetic nerve stimulation in the heart has not been previously described. (Supported in part by a NSF Graduate Fellowship.)

A COMPARISON OF THE CHOLERETIC EFFECTS OF SECRETIN AND INSULIN-HYPOGLYCEMIA IN CONSCIOUS CHOLECYSTECTOMIZED DOGS. D. B. Thornton*, R. D. Soloway*, J. R. Senior and F. P. Brooks. Depts. of Physiology and Medicine, School of Medicine, Univ. of Pennsylvania, Phila., Pa.

Bile was collected by transduodenal catheterization as described by Zaterka and Grossman through a Thomas duodenal cannula in four mongrel dogs. The effects of secretin iv 2 u/kg/hr, 1.5 u/kg of insulin and both given simultaneously were determined with and without restoration of the enterohepatic circulation by iv taurocholate. There was an increase in bile flow of 4.0 ml/30 min, and 4.7 ml/30 min when secretin was given with and without iv taurocholate. Comparable values for insulin were 3.0 and 3.1 ml/30 min. When insulin was given during a secretin infusion, bile flow increased 1.5 ml/30 min. The only significant qualitative difference was a greater bicarbonate concentration (21 and 25 mEq/liter with and without taurocholate) during secretin than after insulin (16 and 18 mEq/liter). When insulin was given during secretin infusion bicarbonate concentration remained unchanged or fell. Acetazolamide produced a choleresis which could not be augmented by secretin but insulin led to an increase in bile flow of 1.5 ml/30 min. Under these circumstances bicarbonate concentration was 13 mEq/liter. There was no greater output of bile salts after insulin than during secretin. The choleretic action of secretin differs from that of insulin hypoglycemia primarily by an increased output of bicarbonate. (Supported by USPHS Grants RCDA K3-AM02983, 5 T01-AM05415 and 5 T01 GM-00205-10.)

Bone Salt Maturity and Its Influence on the Response to PTE in Tissue Culture. Paul A. Thornton, VA Hospital and the University of Kentucky, Lexington, Kentucky.*

Parathyroid hormone is believed to act on the more mature bone salts or those which are not readily exchangeable. This study was an assessment of the relative effect of PTE on ^{45}Ca mobilization from bone in which the isotope had been deposited for varying periods of time. Chicken eggs were injected with ^{45}Ca after 12 days of embryonic development. Bone tissue (calvarium) was harvested on days 13, 14, 15 and 16. The calvarium was equally divided at the saggital suture, providing a means for individual comparisons, and cultured for 48 hours in a chemically defined medium. Bone calcification within the egg, as shown by calcium and ^{45}Ca accumulation, was rapid during the 12-16-day interim. Movement of ^{45}Ca from bone to the medium (in vitro) decreased rapidly and linearly as time of the isotope's incorporation in the bone increased. These results indicate that calcium exchangeability decreased as the bone salt crystals matured. Addition of PTE increased the medium ^{45}Ca activity, both absolutely and relatively, in all groups. The relative difference between control and PTE-treated groups widened with time and supported the idea that PTH acts on bone salts which are not in immediate contact with the surrounding media. No changes in total bone calcium were observed; however, in a similar study with bone taken at 16 days and cultured for 96 hours, PTE caused a 10% decrease in bone calcium and a significant increase in bone ^{45}Ca specific activity. These data illustrate a need for longer culturing periods to demonstrate total bone loss. Further, they show that PTE acted preferentially on stable calcium. This implies that the hormone mobilized bone calcium deposited prior to the isotope injection. *Supported by VA Funds.

EFFECTS OF X-RADIATION ON THE DEVELOPMENT OF THE EVOKED TRANSCALLOSAL RESPONSE IN THE RAT. P.S. Timiras and N. Hatotani*. Dept. of Physiology-Anatomy, University of California, Berkeley, California.

The developmental sequence of the transcallosal response has been determined at various ages from birth to adulthood in terms of latency, wave duration, amplitude, and threshold, and the progressive changes observed have been generally interpreted to reflect stages of cortical maturation. Previous studies have shown that neonatal X-radiation influences the development of gross brain electrical activity, as measured by electroconvulsive responses. The present study was undertaken to investigate the effects of X-radiation on the development of a specific, cortical monosynaptic system. Two-day old rats received a single dose of 500 R whole-body X-radiation and the transcallosal response was measured at 15, 30 and 60 days of age and compared with that of non-irradiated controls. At 15 days the irradiated animals showed a lower amplitude and higher threshold, latency and wave duration than controls; at 30 and 60 days, the amplitude was higher while the other parameters were lower or similar to those of controls. The changes observed at 15 days suggest that X-radiation retards neuronal development. The high amplitude and low threshold at 30 and 60 days of age are in agreement with previous findings of increased convulsibility, as reported for the whole brain after similar doses of X-radiation, and may reflect alterations in myelination and/or neurotransmission.

Supported by USAEC AT (11-1)-34, Project No. 82.

THE INFLUENCE OF ATROPINE ON THE HEART RATE RESPONSES OF NONTRAINED, TRAINED AND DETRAINED ANIMALS. C.M. Tipton, Exercise Physiol. Lab., U. of Iowa, Iowa City, Iowa.

Previous findings with exercised male rats have indicated that trained (T) animals will exhibit less cardiac acceleration than nontrained controls (NT) after an injection of atropine sulfate (1 mg/kg). To determine whether this difference was a consequence of training, additional studies were initiated that involved more than 80 rats. Unanesthetized rats were injected with atropine before, during and at the end of an 11 week experimental period (exercise 1 hr/day; 1 mile/hr). The difference between T and NT began to appear 30-40 days later and became manifested at 70-80 days. When animals were trained and then detrained (DT) for 6 weeks, DT animals had the same type of response to atropine as NT animals. Minute resting heart rates paralleled these findings. Isolated heart rates were measured from NT and DT rats using a modified Langendorff preparation. Using a Krebs-Henseleit solution containing 0.1 μg/ml of atropine, [flow rate 8 ml/minute, 30 mmHg pressure, 95% O_2 + 5% CO_2] no heart rate differences existed between NT and DT animals. When atropine in dosages of 0.5 mg/kg, 2.0 mg/kg, and 3.0 mg/kg were injected into intact T and NT rats, consistent differences between the groups occurred with the 0.5 mg/kg level. However, this effect did not occur at the higher dosages. These results support the concept that in the resting state, trained animals are cholinergically different than nontrained or detrained animals. (Supported by funds provided by the Iowa Heart Assoc.)

[H+] EFFECTS ON OXYGEN CONSUMPTION AND PRODUCTION OF LACTATE AND PYRUVATE BY LIVER SLICES. Richard B. Tobin, M.D. VA Hospital and Univ. of Nebr. Col. of Med., Omaha, Nebr. 68105.

It was shown by Tobin (Am. J. Physiol. 207:601, 1964) that L/P ratios in blood of acidotic and alkalotic cats did not follow theoretical predictions. Circulatory and metabolic explanations were postulated. The present in-vitro study extends previous in-vivo work. Liver slices cut free hand were incubated in Krebbs-Ringers' phosphate media with either 10 mM glucose or 10 mM pyruvate added. pH of media was adjusted after adding all components. Flasks were gassed with O_2, and O_2 consumption measured at 37°C. After one hour, flasks were placed on ice and sampled for lactate and pyruvate, assays being by enzymatic technique. With both substrates, the L/P ratio was proportional to pH of media. This is similar to in-vivo results and is not what is predicted by dissociation or oxidation-potential equations for the LDH reaction. Since circulation is not a factor in these in-vitro studies, we can assume it was not the cause of in-vivo rise in L/P ratio during alkalosis. With glucose, $\dot{Q}_{O_2}$ was maximal at pH 8.0, decreased 40% at pH 6.0 and 15% at pH 9.0. Using pyruvate as substrate, $\dot{Q}_{O_2}$ at 6.0 was 34% less than that at pH 7.4. These results are similar to those of Canzanelli et al (Am. J. Physiol. 127:290, 1939) but very different from results with rat liver mitochondria (Tobin Fed. Proc. 28:335 Mar-Apr. 1969). Mitochondria showed no [H+] effect on state 3 or state 4 respiration with pyruvate as substrate. [H+] effects on respiration and redox state of liver slices are similar to results found in-vivo rather than those found with mitochondria. The observed increase in L/P ratio of liver slices in alkaline media is not yet explained. (VA supported).

Intrahypothalamic infusion of biogenic amines: effect on temperature regulation and neuroendocrine function in baboons. P. Toivola*, C. C. Gale, J. Werrbach*, and C. J. Goodner*. Departments of Physiology and Biophysics and Medicine, Regional Primate Research Center, University of Washington, Seattle, Washington.

The hypothesis that norepinephrine and serotonin are hypothalamic neurotransmitters mediating heat loss and heat gain was tested in 7 adolescent baboons adapted to primate chairs. Amines were infused via cannulae implanted permanently in the anterior hypothalamus or the third brain ventricle. Norepinephrine infusion, 1 μg/min for 15 min, evoked cutaneous vasodilatation and a 1.2 ± 0.2° C (SEM) fall in mid-brain temperature within 1 hour ($P < 0.005$). Baboons shivered and vaso-constricted within 1.5 hours and restored core temperature within 3.5 hours. Plasma glycerol and glucose levels rose significantly during temperature restoration, but plasma cortisol and growth hormone levels did not change. Urinary excretion of free epinephrine rose during this interval. In contrast to this evidence for norepinephrine as a mediator of heat loss reactions, no support was obtained for serotonin as a mediator of heat gain. Intrahypothalamic infusion of serotonin, 1 μg/min for 15 min. ($n = 6$), did not alter core temperature. To elucidate central adrenergic mechanisms, an alpha adrenergic blocking agent, phentolamine (Regitine) was infused intrahypothalamically at 2 μg/min for 30 min. Serum growth hormone fell from control level of 9 ± 2 ng/ml to 3 ± 1 ng/ml ($P < 0.025$) ($n = 4$) within 40 min. These data suggest that hypothalamic adrenergic receptors influence secretion of pituitary growth hormone in baboons. Seemingly, central alpha adrenergic receptors stimulate growth hormone secretion.

Supported by N. I. H. grants FR00166 and NB 06622.

THE REGULATION OF UTERINE CONTRACTIONS BY CATECHOLAMINES.
L. Triner,* N. I. A. Overweg,* R. B. Hiatt,* and G. G. Nahas. College of Physicians and Surgeons, Columbia University, New York, N. Y. 10032

The stimulating and relaxing effect of physiologically active substances on the isolated nonspontaneously contracting rat uterus were studied. The rats were pre-treated with diethylstilbestrol (120 μg) for two days. The first dose of epinephrine (3×10^{-7}M) always produced contraction, but the response to subsequent doses was completely inhibited. Oxytocin and acetylcholine contractions were inhibited by 3×10^{-7}M epinephrine: cumulative dose response curves of both drugs were shifted to the right with lower maximum responses. The inhibition caused by one dose of epinephrine was reversible, lasting at least seven to ten minutes. Norepinephrine (3×10^{-6} M) had a similar but weaker effect than epinephrine. Isoproterenol (3×10^{-7} M) did not cause contraction when first added to the bath and always inhibited response to oxytocin and acetylcholine. Its inhibitory effect was stronger than that of epinephrine. The inhibition of oxytocin and acetylcholine contractions by catecholamines was completely prevented by a beta blocking agent (Propranolol, 1 μg/ml). A similar inhibition was simulated by dibutyryl cyclic 3', 5'-AMP. All three catecholamines used increased adenyl cyclase activity in estrogen pre-treated uteri. These data suggest that cyclic 3', 5'-AMP plays an important role in the regulation of uterine contractility and motility.

CHEMICAL AND ULTRASTRUCTURAL STUDIES ON EXPERIMENTAL CALCIFICATION. B. Tuchweber and G. Gabbiani. Inst. Med. Chirurgie exp. Univ. de Montréal, Montreal (Canada).

We studied the initial stages of cutaneous calciphylaxis in rats sensitized with dihydrotachysterol (DHT) and injected topically with $FeCl_2$. Five minutes after the injection of $FeCl_2$ alone, the calcium and phosphorus content of the skins increased significantly as compared to control values. Only the calcium concentration continued to increase until 3 hrs after treatment. These changes were followed by a decrease in the level of both electrolytes which returned to normal values on the 13th day. At electron microscope examination, 5 min after treatment, a granular material was deposited almost exclusively in collagen bundles at the surface of well-formed collagen fibrils. At later intervals, some of these granules were gradually transferred to macrophages and sometimes fibroblasts. Cellular components of connective tissue exhibited some damage which disappeared by the 5th day. Electron and X-ray diffraction analysis did not show the presence of crystalline material at any time. Following DHT treatment, the initial changes in calcium and phosphorus at site of $FeCl_2$ were similar to those observed after $FeCl_2$ alone. 24 to 48 hrs after treatment, the calcium and phosphorus greatly increased attaining a maximum on the 5th day. Electron microscopic examination initially showed changes similar to those described after $FeCl_2$ alone. Apatite crystals were visible 24 to 48 hrs after injection and consisted of thin rodlets appearing on the surface of collagen fibrils. Thus, $FeCl_2$ alone increases the calcium and phosphorus content of the skin; however, apatite formation only occurs when the animal is pretreated with DHT.

(This work was supported by the Ministère de la Santé, Québec, and the Medical Research Council of Canada, Block Term Grant MT-1829.)

PULMONARY HYPERTENSION IN THE GOAT AT HIGH ALTITUDE. C.E. Tucker,* J.A. Will,* and R.F. Grover. Univ. of Colorado School of Medicine, Denver, Colo. and Univ. of Wisconsin, Madison, Wisconsin.

High altitude exposure may produce pulmonary hypertension but the response varies between species and among individuals in the same species. It would be useful to have an animal model with a reactivity similar to man. The response of the goat has not been reported previously. Ten domestic goats were initially studied at 1600 m, their native altitude. Individual animals were then exposed to 3400, 4300 or 4850 m for 2-5 weeks in a controlled environment. Animals were studied awake and in the normal standing position. Mean pulmonary artery pressure ($\overline{PAP}$ mmHg) was measured using a catheter inserted percutaneously through the jugular vein. Cardiac output ($\dot{Q}$ L/min) was measured using chronically implanted electromagnetic flow transducers. Total pulmonary resistance corrected for body size was calculated ($\overline{PAP}/\dot{Q}$/Kg).

Altitude	n	P_aO_2	$\overline{PAP}$	$\dot{Q}$/Kg.	TPR/Kg.
1600m	7	67	19	.194	98
3400m	3	57	25	.168	149
4300m	3	43	32	.139	230
4850m	4	36	44	.190	232

For the entire group of animals the regression line relating $\overline{PAP}$ to P_aO_2 was: $\overline{PAP} = 63.1 - 0.64\ P_aO_2$ ($r = -0.87$, $p < .0005$). Acute oxygen administration at 4850 m significantly reduced $\overline{PAP}$ but did not decrease TPR to 1600 m values. These data suggest that in the goat the pulmonary vascular response to chronic hypoxia is similar to that observed in man.

Supported by the Colorado Heart Association and U.S. Army Contract DADA17-68-C-8013.

DEPENDENCY OF VAGAL BRADYCARDIA ON TIMING OF THE VAGAL STIMULUS WITH RESPECT TO THE HEART CYCLE. Robert Tuckett*, and Homer R. Warner

One or more vagal stimulus placed early in the cardiac cycle may produce as much as twice the slowing of heart rate that the same stimulus placed late in the heart cycle would produce. For example, in a dog in whom both vagal nerves have been cut in the mid neck region and sympathetic nerves to the heart have been severed bilaterally, stimulation of the distal end of the cut right vagas nerve with a 10 volt pulse, 2 ms long and repeated 4 times 5 ms apart may slow the heart from a rate of 125 per minute to a rate of 60 per minute if the train of stimuli is begun 100 ms after the QRS complex. This response is immediate and occurs by prolonging the heart cycle in which the stimulus occurred. A similar train of stimuli would slow the heart rate to only 85 beats per minute if placed 400 ms after the QRS complex. When stimulus occurs early in the heart cycle and is placed only in every other cycle, recovery to a heart rate of 85 will occur on the second beat following the stimulus. However, if the stimulus occurs late in the heart cycle this rapid immediate recovery is not seen. As the delay between the QRS complex and the onset of stimulation is progressively increased, a point is reached at about 200 ms where the immediate heart rate response is abolished. Further increase in the delay beyond 300 ms brings about a gradual partial return of this response, but now the slowing is in the cycle following the stimulus.

DETERMINATION OF MINIMAL GRADIENT REQUIREMENTS FOR EXCITATION OF MOTONEURONS DURING POST-TETANIC POTENTIATION. Junji Ushiyama and Chandler McC. Brooks. Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York, U.S.A.

The rheobase and minimal gradient requirements for excitation of spinal motoneurons in cats anesthetized with nembutal were determined by intracellular recording and stimulation techniques. Post-tetanic potentiation of reflex action was produced by stimulations (1000/sec. for 200 msec. at 5 second intervals) of peripheral nerves (the tibial posterior or gastrocnemius nerves). The test stimulations were applied about 300 msec. after the end of each tetanic stimulation. It was found that there was no significant change in motoneuron rheobase as a result of post-tetanic conditioning. However, the minimal gradient requirement, as determined by application of linearly rising current, was markedly decreased (more slowly rising current could excite the cells) during post-tetanic potentiation. It is suggested that post-tetanic potentiation of spinal reflexes is due, in part at least, to this change in minimal gradient requirement brought about by an intense bombardment of the motoneurons by impulses arriving through presynaptic fiber terminals. (Supported by USPHS, Grant NB 847-14)

EFFECT OF TEMPERATURE ON REACTIVITY OF DIFFERENT VEINS OF THE DOG. P. M. Vanhoutte* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The contraction of cutaneous veins of the dog caused by sympathetic nerve stimulation or by drugs is potentiated by cooling and inhibited by warming. To determine if this effect was specific for cutaneous veins, the thermosensitivity of spiral strips of saphenous and femoral veins and of longitudinal strips of mesenteric veins of the dog was investigated in an organ bath. Changes in isometric tension of the preparations were recorded. The different preparations relaxed slightly when the bath temperature was decreased (to 25 C) and contracted when it was increased (to 43 C). In addition, warming augmented the spontaneous activity exhibited by the mesenteric veins, while cooling had opposite effects. Electric stimulation caused saphenous and mesenteric vein strips to contract. In both types of veins the contraction was augmented by cooling and attenuated by warming. The femoral veins reacted only weakly to electric stimulation; this reaction, as well as the contraction caused by norepinephrine and 5-hydroxytryptamine, was attenuated by cooling and enhanced by warming. The data suggest differences in thermosensitivity between different parts of the venous system. However, the potentiating effect of cooling, when imposed during active contraction, is not specific for cutaneous veins. (Supported by NIH Grant HE-5883.)

TISSUE GAS TENSIONS DURING HISTOTOXIC HYPOXIA CAUSED BY COBALT. Hugh D. Van Liew. Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, N. Y.

The day after a high dose of cobalt chloride ($CoCl_2$), pO_2 was increased and pCO_2 decreased in artificially-formed gas pockets in unanesthetized rats. The effects were greater the larger the amount of cobalt injected, even to dosages as high as the LD_{50} dose (35 mg/kg), and the effects were partly reversed when the rats breathed pure oxygen. These findings are interpreted to mean that in response to cobalt's interference with enzyme systems in all tissues, there is vasodilatation of capillary beds leading to increased tissue perfusion (up to four times normal) and stimulation of chemosensitive tissues leading to increased respiratory ventilation (up to 1.5 times normal). The stability and long duration of the histotoxic hypoxia caused by cobalt suggest that its administration could be a useful experimental technique for altering energy availability and blood perfusion rate in intact animals.
(Supported in part by ONR Contract No. N00014-68-A-0216.)

EFFECT OF DRUGS WHICH ALTER CATECHOLAMINE METABOLISM ON THE INHIBITION OF STRESS-INDUCED ACTH SECRETION PRODUCED BY L-DOPA. G.R. Van Loon* and W.F. Ganong. Dept. of Physiology, School of Medicine, University of California, San Francisco Medical Center, San Francisco, Ca. 94122.

We have previously reported that L-dopa in a dose of 50 mg/kg IV inhibits stress-induced ACTH secretion in pentobarbital-anesthetized dogs, and that this inhibition is not affected by phenoxybenzamine in doses that abolish the pressor response to the L-dopa (Van Loon et al., Fed. Proc. 28:438, 1969). In further studies in pentobarbital-anesthetized surgically stressed dogs, adrenal venous blood was collected before and 30 minutes after administration of L-dopa intravenously and after 1 IU of ACTH. It was found that 10 mg/kg of L-dopa IV did not inhibit ACTH secretion; mean adrenal venous 17-hydroxycorticosteroid secretion rates before and after injection of L-dopa and after ACTH were 8.9 ± 1.5, 8.6 ± 1.7 and 9.0 ± 1.6 μg/min (n=5). However, in dogs given the monoamine oxidase inhibitor, pargyline, 25 mg/kg IP 43 and 20 hours previously, the mean 17OHCS outputs before and after 10 mg/kg of L-dopa and after ACTH were 9.2 ± 1.8, 2.7 ± 0.9 and 9.6 ± 1.3 μg/min (n=6). On the other hand, in dogs treated with the tyrosine hydroxylase inhibitor, α-methyl-p-tyrosine, 100 mg/kg IV 20 hours previously, the mean adrenal venous 17OHCS outputs before and after 50 mg/kg of L-dopa and after ACTH were 8.2 ± 1.4, 7.7 ± 1.2 and 9.0 ± 2.9 μg/min (n=4). The corresponding values before and after 100 mg/kg of L-dopa and after ACTH were 8.2 ± 0.5, 2.3 ± 1.1 and 7.3 ± 0.8 μg/min (n=5). Thus, the minimum effective dose of L-dopa that inhibits ACTH secretion is decreased by a drug that inhibits catecholamine catabolism and increased by a drug that inhibits catecholamine synthesis. The results support the hypothesis that there is an adrenergic neural system that inhibits ACTH secretion in the dog.
(Supported by USPHS Grant AM06704 and Bay Area Heart Research Committee)

NOREPINEPHRINE AND POTASSIUM FLUXES IN CARDIAC PURKINJE FIBERS. Mario Vassalle and Ottavio Barnabei*. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

The transmembrane potentials and the radioactivity of canine Purkinje fibers loaded with K-42 were measured in vitro in the presence and in the absence of norepinephrine. Potassium influx was measured by the increase in tissue radioactivity after a period of exposure to radioactive potassium. At $[K]_o$=2.7 and 5.4 mM and with the preparation driven at a relatively low rate, norepinephrine enhanced potassium uptake over the control value. At higher $[K]_o$, norepinephrine was without effect on potassium uptake. Also, the same lack of effect was found when the preparations were stimulated at 75/min or faster, even at the usual $[K]_o$. Changes in potassium efflux caused by norepinephrine were determined by the changes in rate constant of tissue radioactivity loss in preparations preloaded with K-42. In quiescent preparations, norepinephrine provoked both the onset of spontaneous activity and an increased potassium efflux. When the fibers were stimulated at a constant rate throughout the experiment, norepinephrine still caused a potassium loss, but this time the loss was smaller. The results suggest that norepinephrine under certain conditions stimulates the uptake of K^+, probably by acting on the Na^+-K^+ pump. This stimulatory action was not found when the pump is presumably already stimulated as with fast driving rates or in high $[K]_o$. Norepinephrine causes enhancement of K^+ efflux, in part through a direct action and in part through the onset of spontaneous activity. Since norepinephrine can induce spontaneous activity without necessarily increasing K^+ influx, its chronotropic action may be independent of an action on the pump.
(Supported by a grant from NIH-HE 10097)

Effects of Variations in the Level of Consciousness on the Response to Carotid Sinus Nerve Stimulation (CSNS). Stephen F. Vatner*, Dean Franklin, Robert L. Van Citters & Eugene Braunwald; Univ. of Cal., San Diego, and Univ. of Wash., Seattle.

In order to determine how variations in the level of consciousness and arousal alter the cardiovascular response to CSNS, the effects of a 30 sec. period of CSNS on aortic blood pressure (BP), heart rate (HR), and regional vascular resistances were studied in 5 healthy dogs at rest, asleep, during exercise, and under anesthesia. Doppler or pulsed ultrasonic flow probes were implanted on the left circumflex coronary, mesenteric, renal, and iliac arteries and a pressure gage placed in the central aorta. Electrodes were implanted on both carotid sinus nerves and a radiofrequency pacemaker used for stimulation. Frequency and voltage for CSNS were constant for each animal under all conditions. In resting conscious dogs 2-6 weeks after recovery, CSNS produced a decrease in BP (34% from control), which returned to control levels generally within 30 secs. after CSNS ceased. HR decreased slightly (10%) and only during the first 5 secs. of CSNS. Vasodilatation occurred in the coronary, mesenteric, renal and iliac vascular beds but was greatest in the iliac bed where resistance declined by an average of 67%. During exercise baseline levels of flows, pressure, and HR differed from resting values but the response to CSNS was quite similar. During sleep, CSNS again produced similar changes in BP and vascular resistances but the initial decrease in HR was more marked. Under pentobarbital anesthesia (20 mg/kg) the response to CSNS was characterized by less vasodilatation, e.g., iliac resistance decreased by only 19% from control, the decrease in HR was maintained throughout the period of stimulation, and recovery of HR and vascular resistance after CSNS was prolonged. Thus, these results suggest that higher centers in the central nervous system modify the magnitude and duration of the response of the cardiovascular system to CSNS.

INFLUENCE OF EXTERNAL POTASSIUM AND STRETCH ON THE OXYGEN CONSUMPTION OF FROG'S SARTORIUS MUSCLE. R. A. Venosa*, and P. Horowicz. University of Rochester, Rochester, N. Y.

An increase in external K^+ to levels which do not produce contractures stimulates the O_2 uptake in frog sartorius muscle. At present, the mechanism for this well-known response is not fully understood. To further study this effect the O_2 uptake of sartorius muscles isolated from R. pipiens was measured in a constant flow respirometer using an oxygen cathode to measure the oxygen tension. Strophanthidin, an inhibitor of active sodium transport, at a concentration of 3×10^{-5}M does not detectably affect either the resting or potassium stimulated ($[K^+]_o$=12.5mM) O_2 uptake. Curare is also added to stop twitching which develops after prolonged application of the aglycone. When applied alone, curare has no detectable effect on the O_2 uptake. The effects of a 25% stretch were studied in order to test whether the degree of overlap between actin and myosin filaments influences the K^+ stimulated O_2 uptake. Taking the resting O_2 uptake at slack length as 100, the O_2 uptake increases to 128 for a 25% stretch with $[K^+]_o$=2.5mM. With the muscles unstretched the O_2 uptake increases to 146 with $[K^+]_o$=10mM and 246 with $[K^+]_o$=12.5mM. When the muscles are stretched the O_2 uptake rises to 316 with $[K^+]_o$=10mM and 402 with $[K^+]_o$=12.5mM. Thus there is an increase in the response to stretch when the $[K^+]_o$ is increased. Tetrodotoxin does not influence these effects. Procaine, at a concentration of 1mM, inhibits the stimulated O_2 uptake by K^+ alone but not the stretch response.

TREATMENT OF HEMORRHAGIC SHOCK WITH WR-2823; A NEW ALPHA ADRENERGIC BLOCKING AGENT. J.Vick, M.Heiffer, W.Webster, and D.Jacobus (intr. by C. C. Hassett). Walter Reed Army Institute of Research, Wash, D. C. 20012

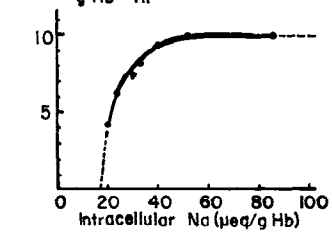
The treatment of hemorrhagic hypotension with S-2-(5-aminopentylamino)ethyl phosphorothioic acid,WR-2823,has been evaluated in 22 adult mongrel dogs and 14 Rhesus monkeys which were anesthetized with pentobarbital sodium (30 mg/kg) and continuously monitored for changes in arterial and venous blood pressures, EKG, heart rate, and determination of pH, O_2, and CO_2 content (Vol %). All animals were bled to a mean arterial pressure of 50 mmHg and maintained at that level for 8 hrs. During this period of time animals were allowed to recover shed blood from the shock reservoir as dictated by the tone of their cardiovascular system. Three hours after initial hemorrhage, paired animals were divided at random into either a control or a treatment group. Control animals received no therapy while the treated group was given 50 mg/kg WR-2823, I.V. The average shock animal showed a progressive decrease in arterial pH from a control of 7.42±.03 to 7.30±.08 during the first 3 hrs. The O_2 content of the venous blood fell from 15.6±2.1 to 8.7±3.8 while arterial CO_2 decreased from 42.0±4.1 to 25.3±4.4. Heart rate increased from 140 to 204. Control animals continued to deteriorate and at 8 hrs had universally taken back more shed blood. Venous O_2 was 6.0± 2.0, arterial CO_2 was 18.0±3.0, and pH was 7.24±.08. Heart rate increased to 240. In contrast treated animals showed slow but progressive recovery of these parameters to pre-hemorrhage levels. At 8 hrs, pH stabilized at 7.45±.03, venous O_2 at 15.5±2.3, and arterial CO_2 at 44.8±5.1. Heart rate decreased from 204 to 120. Seven of 11 dogs and 7 of 7 monkeys treated with WR-2823 survived while none of the control animals were alive at 24 hrs. Results indicate that WR-2823 appears to effectively prevent the onset of irreversible hemorrhagic shock in both the dog and the monkey.

EFFECT OF ACUTE HYPOXIA UPON FEMORAL A-V OXYGEN DIFFERENCE DURING EXERCISE IN MAN. J. A. Vogel, L. H. Hartley* and M. Landowne. U. S. Army Research Institute of Environmental Medicine, Natick, Mass. 01760

During exercise the cardiac output ($\dot{Q}$) response required for increased oxygen delivery is minimized by redistribution of blood flow towards the active muscles and increased oxygen extraction by these tissues. When this delivery is further compromised by working in a hypoxic environment, it is unclear whether the additional requirement is met by enhanced cardiac output, additional redistribution of blood flow or further tissue extraction. Femoral and systemic arterial-venous oxygen differences ($a\text{-}v\dot{O}_2\Delta$) were compared in 6 men exercising upright on a bicycle ergometer submaximally and maximally in a hypobaric chamber at sea level (SL) and at a pressure of 465 mmHg (4,000 M simulated altitude). Oxygen uptake ($\dot{V}O_2$) (Douglas bag) and $\dot{Q}$ (dye dilution) were measured. $\dot{V}O_2$ for a given work load was the same for the two conditions. $\dot{Q}$ at the same submaximal work load (750 Kg-M) was 23% higher at 4,000 M than SL ($P<.01$), 15.53 vs 12.64 L/min, respectively. At this same work load, femoral $a\text{-}v\dot{O}_2\Delta$ was less ($P<.01$) at altitude, 12.6 vs 14.5 vol. % at 4,000 M and SL, respectively. The difference in systemic $a\text{-}v\dot{O}_2\Delta$ between altitudes was of similar magnitude. Since systemic $\dot{V}O_2$ for a given work load was not different between altitudes, and assuming no change in $\dot{V}O_2$ of the tissues drained by the femoral bed, the smaller femoral $a\text{-}v\dot{O}_2\Delta$ at 4,000 M therefore indicates a greater femoral blood flow at that altitude. Though systemic and femoral $a\text{-}v\dot{O}_2\Delta$ change similarly from SL to 4,000 M, evidence is insufficient to conclude whether there is a fractional shift in distribution of flow to the legs during exercise after acute exposure to 4,000 M.

EFFECT OF 6° C STORAGE IN ACD PLASMA ON THE ACTIVE SODIUM TRANSPORT CAPACITY OF HUMAN RED BLOOD CELLS. Roger W. Voight* and Robert E. Taylor, Jr., Department of Physiology and Biophysics, University of Alabama Medical Center, Birmingham, Alabama.

Freshly drawn blood, to which $^{22}NaCl$ was added, was stored for up to 35 days. Fifty ml aliquots were sterilely withdrawn, washed 3X with 15 vol. of ice cold bicarbonate Ringer's equilibrated with $5\%CO_2$-$95\%O_2$ and containing 10 mM glucose, and resuspended in sufficient fresh Ringer's to give a hematocrit of 8-17%. After a 30-min. equilibration period at 37°C, samples withdrawn over a 2-hr. period were analyzed for electrolytes and ^{22}Na. The equation $dC = -k(C-C_f)dt$** describes our data quite well for $t \leq 2$ hrs ($0.990 \leq r \leq 0.998$). We have found that if the sodium pump is functioning, k is apparently dependent on the length of time (T) since collection: $k = -0.00021T + 0.321$; however, if the pump has been suppressed by $5x10^{-5}$ M ouabain, k may be constant at 0.055 hr^{-1}. The figure shows the effect of storage-induced increase in intracellular Na conc ($(Na)_I$) on the rate of active Na transport; active Na transport is low when $(Na)_I$ is less than 20 (normal in fresh cells: 17.6±0.2) and rises to a maximum of 10. μeq/g.Hb-Hr as $(Na)_I$ rises during storage; however, the lower k associated with stored cells suggests a higher maximal pumping rate in freshly drawn cells.



* Supported in part by NIH predoctoral fellowship # GM-37185-01.

** $C=(^{22}Na)_I$, cpm/g. Hb; C_f=C at equilibrium; t=time; k=time coefficient.

BLOOD GASES IN GROUND SQUIRRELS AND HAMSTERS AT REDUCED BODY TEMPERATURES. Wynn Volkert* and X.J. Musacchia. Space Sciences Research Center and Dept. of Physiology, Univ. Mo., Columbia, Mo.

Blood gas parameters were examined in the hibernating and active ground squirrel (Citellus tridecemlineatus) and in the hamster (Mesocricetus auratus) at several body temperatures (38, 26, 18, 10 and 6°C). Blood pH values indicated that acid-base balance was maintained at a nearly constant level at the various body temperatures. Hemoglobin-oxygen dissociation curves for whole blood from the squirrel and hamster at 6°C and 38°C were constructed in order to determine the O_2 affinity temperature coefficient (0.0210 for hamster Hb and 0.0215 for squirrel Hb). Experiments demonstrated that arterial blood in the animals at a reduced body temperature was sufficiently oxygenated to saturate the hemoglobin to capacity. At a body temperature of 6°C, the various oxygen tensions were greatly reduced (6.0 mm Hg in the squirrel and 9.1 mm Hg in the hamster). With the parameters measured, estimates of the free oxygen content in the blood at various temperatures were made. Apparently, less oxygen is available to the tissues from the blood of animals at reduced body temperatures which was judged to be due to the altered position of the Hb-O_2 saturation curve at different temperatures. (Supported by funds from NASA Grant, NGR-26-004-021-S3 and S4.)

CONNECTIONS OF MEMBRANE-LIKE STRUCTURES WITHIN THE SARCOPLASMIC RETICULUM OF DOG CARDIAC MUSCLE FIBERS. Sheppard M. Walker, G. Randolph Schrodt* and Maxine B. Edge*. University of Louisville School of Medicine, Louisville, Kentucky 40202.

The part of the sarcoplasmic reticulum (SR) apposed at the T system and at the sarcolemma was selected for electron microscope study because it contains abundant membrane-like structures and provides a favorable structural arrangement for serial thin sections. The serial thin sections of papillary muscle fibers show that the membrane-like structures are indeed within the limiting membranes of apposed SR. The structures within SR are designated as membrane-like because they show a density pattern that resembles the density pattern in membranes (Nature, 206: 150, 1965). The main feature of the density pattern is a triple-layered structure composed of two dense layers separated by a less dense layer. The two dense layers are not uniform in thickness. Thick segments of these layers with about 40 Å center to center distance alternate with thin segments. The center to center distance from a thick segment in one dense layer to a thick segment in the other dense layer is also about 40 Å. One membrane-like structure is midway between and parallel to the limiting membranes of SR. The other membrane-like structures form numerous perpendicular connections between the midway structure and the limiting membranes of SR. It is concluded that the membrane-like structures within SR are developed from and continuous with the limiting membranes of SR.
(Supported in part by grants from the American Heart Association and the Kentucky Heart Association.)

DIFFUSIVE PERMEABILITY OF EGG SHELL TO GASES.
O. Douglas Wangensteen*, Donald Wilson*, and Hermann Rahn. Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, N. Y.

In the developing chick embryo the pCO_2 increases from about 5 mm Hg after the egg is laid to about 40 mm Hg before hatching. Concomitantly the pO_2 decreases from 140 to 100 mm Hg. These changes might be explained by a diffusion limitation of the egg shell which becomes apparent as metabolism increases. To test this we studied the shell's diffusive permeability to oxygen. After removing the shell's contents the blunt end was mounted on a block containing an O_2 electrode. The enclosed volume was flushed with N_2 and the O_2 influx was then monitored. The permeability was calculated from these data. Shells with the inner membrane removed had an average permeability of 3×10^{-6} $cm^3/sec/cm^2/mm$ Hg, which showed a slight tendency to increase with incubation age. From this value the permeabilities to CO_2 and water vapor were calculated to be 2×10^{-6} and 4×10^{-6} $cm^3/sec/cm^2/mm$ Hg, respectively (molecular weight basis). These values and convective transport results in the literature allow us to predict that gas transport across the shell occurs through pores having an average effective diameter of about 8 μ and a total area of about 2 mm^2. Our results are consistent with the permeability required to account for the rates of gas exchange and water loss reported in the literature. Our pore diameter also agrees with observed values. These results indicate that the diffusion barrier provided by the shell can account for both the observed gas tension changes and the weight changes due to water loss.
(Supported in part by ONR Contract No. N00014-68-A-0216.)

RATE OF INTESTINAL EXCRETION OF ^{47}Ca DURING FEEDING AND FASTING IN RATS. Janet M. Warren* and Herta Spencer. Metabolic Section, Veterans Administration Hospital, Hines, Illinois 60141.

Male Sprague-Dawley rats weighing 250 grams received ^{47}Ca intravenously during both feeding and fasting and were sacrificed at ½, 1, 2, 4 and 24 hours later. The ^{47}Ca content in 6 intestinal segments (stomach, duodenum, jejunum, ileum, cecum and colon) and blood levels and bone concentrations were determined. During feeding, the secretion of ^{47}Ca into the intestinal tract reached equilibrium at ½ hour; the amounts of ^{47}Ca in the intestine ranged from 5.1 to 5.7% of the dose between ½ to 4 hours with relatively no passage into the feces by 4 hours. At 24 hours 8.6% was secreted into the intestine, of which only 1.0% was recovered in the intestine while 7.6% were passed in feces. During fasting, the secretion of ^{47}Ca into the intestine was lower, but equilibrium was also reached by ½ hour, the dose secreted ranging from 3.8% to 4.3% between ½ to 4 hours. However, the total amount of ^{47}Ca secreted into the intestine in 24 hours was only 2.4%, corresponding to about ¼ of the ^{47}Ca excretion in 24 hours during feeding. ^{47}Ca bone uptake was appreciable at ½ hour and increased only slightly from 1 to 24 hours. The uptake of ^{47}Ca in %dose/gm bone was similar during feeding and fasting, however, the ^{47}Ca content of the carcass, which contained the skeleton, was higher in the fasting rats, 93.8% vs. 82.7% in the feeding rats.

PHYSIOLOGICAL THERMOREGULATION IN THE DESERT IGUANA. Wesley W. Weathers (Intr. by Fred N. White). Dept. of Zoology and Dept. of Physiology, University of California, Los Angeles, California.

The purpose of this study was to determine if desert iguanas, Dipsosaurus dorsalis, (20-90 g) possess physiological responses for altering rates of heat exchange with the environment similar to those shown by larger lizards. When live iguanas were heated and cooled between 20°C and 40°C the instantaneous rate of temperature change, when body temperature was 30°C, was as much as 27% greater during heating than during cooling. Dead animals did not heat faster than they cooled. This represents a capacity for controlling heat transfer greater than that shown by a 300 g skink, Tiliqua scincoides, (Bartholomew et al., 1965. Copeia 169-173). Fast heating and slow cooling in Dipsosaurus is partially dependent upon changes in the rate of blood flow between the core and periphery. Cutaneous blood flow was estimated in 16 animals, during heating and cooling, from the rate of clearance of small quantities (0.05 mc in 0.03 ml 0.9% saline) of the isotope Xenon-133 from the subcutaneous space. Heating resulted in a significant increase in blood flow while cooling resulted in a significant decrease in blood flow. Changes in blood flow in response to heating or cooling occurred locally and were independent of body temperature and heart rate. The possession by Dipsosaurus of physiological responses for increasing the rate of heat gain and decreasing the rate of heat loss should enhance the precision with which body temperature is regulated and attenuate the time-space restrictions of behavioral thermoregulation. (Supported by USPHS grant HE 5166-11 and NSF grant GB-8523)

CALORIMETRY DURING TREADMILL EXERCISE

Paul Webb, Webb Associates, Yellow Springs, Ohio

Continuous direct and indirect calorimetry during rest, treadmill work, and other activities has defined the time courses of heat production and heat loss. Heat production was computed indirectly from a continuous oxygen consumption monitor, while heat dissipation was monitored from a water cooling garment under automatic control to keep the subject thermally neutral, i.e. on the warm end of vasomotor regulation, during all activities. Observations have been made over periods of from 3 to 16 hours continuously. Heat balances have been accurate to between 5 and 10% in recent experiments. At the same time we measured skin, rectal, and muscle temperatures to define heat flows and heat storage in major body compartments. The cooled man stored relatively little heat, and his muscle temperatures returned to resting levels 10-15 minutes after work stopped.

HEMODYNAMIC EFFECTS OF IMBALANCING RIGHT AND LEFT HEART OUTPUTS. K.C. Weber*, P. Chevalier*, J. Engle*, D. Gerasch*, & I.J. Fox, Dept. of Physiology, Univ. of Minnesota Medical School, Minneapolis, Minnesota.

At surgery electromagnetic flowmeter probes were implanted at the roots of both pulmonary artery (P.A.) and aorta and a sealed polyethylene tube was implanted into the left atrium (L.A.) of dogs. 1-3 weeks later, under Nembutal anesthesia, catheters for pressure measurement were advanced into the right atrium and P.A. via a juglar vein, into L.A. via the implanted tube and into the aorta via a carotid artery. In 3 dogs 14 head-up and head-down tilts (45° for 20 sec) and in 2 dogs 7 "Valsalva-like" maneuvers (40 mm. Hg positive pressure) were performed to study the effects of imbalancing the right and left heart (R.H. and L.H.) outputs. Such double-probe animals permit study of changes in pulmonary blood volume (P.B.V.) in non-steady-state conditions. During head-up tilts R.H. and L.H. outputs decreased to mean values of 72 ± 4.3% and 57 ± 3.6% of their control values respectively while P.B.V. increased 120 ± 46 ml over the 20 sec test period. In head-down tilts R.H. and L.H. outputs and P.B.V. were virtually unchanged. In the "Valsalva-like" maneuvers R.H. and L.H. outputs decreased to mean values of 23 ± 3.9% and 38 ± 3.9% of their control values respectively while the P.B.V. decreased 135 ± 48 ml over the 20 sec test period. These studies support a significant role for the P.B.V. in buffering differences in outputs of the R.H. and L.H. Supported by Grant HE08873 and A.L.F.O.R.D. USPHS.

LOCALIZATION OF STIMULATORY FEEDBACK EFFECT OF ESTRADIOL BENZOATE (EB) ON OVULATION. Richard F. Weick* and Julian M. Davidson. Physiology Department, Stanford University Medical School, Stanford, Calif.

To localize the effects of ovarian steroids in advancing ovulation, crystalline EB or progesterone (P) was implanted in various brain areas or in the pituitary of four or five day cycling Long-Evans rats. The findings of Everett and others that ovulation could be advanced one day by administering systemically (A) EB on day 2 (5-day cycle) or (B) P on day 3 (5-day cycle) or (C) EB on day 1 + P on day 2 (4-day cycle) were first confirmed. To avoid disruption of the cycle by surgical trauma and anesthesia, an outer intracranial cannula was first implanted, and vaginal smears were taken until regular cycles were established. An inner cannula bearing the steroid at its tip was then introduced without anesthesia. With all 3 experimental paradigms, EB or P in the anterior hypothalamus-preoptic area or median eminence had no effect on ovulation by comparison with cholesterol-implanted controls. With schedules (B) and (C), intrapituitary implants were also without effect on ovulation. However, intrapituitary implants of EB on day 2 (schedule A) advanced ovulation 1 day in 10 of 12 five-day cyclers. Mean ova count was 8.4 $\pm$ 0.9. None of 7 animals similarly implanted with cholesterol in the pituitary ovulated. P on day 1 converted 4-day cyclers to a 5-day cycle. Ovulation was advanced by 1 day in these animals when EB was implanted in the pituitary on day 2. The advancement of ovulation in both experimental situations was prevented by injection of nembutal before 2 P.M. on day 3, i.e. the day before projected ovulation. This study provides evidence that the stimulatory feedback effect of estrogen in advancing ovulation is mediated by a direct effect of estrogen on the pituitary gland. We hypothesize that EB acts by increasing the sensitivity of the pituitary to endogenous LRF.
(Supported by NIH grant HD-00778)

IONIC REGULATION IN THE CNS OF THE HERBIVOROUS INSECT, CARAUSIUS MOROSUS. D.J. Weidler* and F.P.J. Diecke, Dept. of Physiol. & Biophysics, Univ. of Iowa, Iowa City, Iowa.

The physiological mechanism providing for normal neural functioning was investigated in Carausius whose hemolymph contains (in mM): Na, 9; K, 28; Ca, 8; Mg, 73. Electrophysiological studies on totally desheathed nerve cords revealed that excitability is maintained only in solutions containing a high sodium and a low potassium concentration. Viability studies of the nerve cord perfused with solutions containing low sodium concentrations indicate that an active transport mechanism probably is located in the outer fat-body sheath and that this mechanism maintains a high extracellular sodium concentration (150-180 mM) in the nerve cord. The data also indicate that the underlying fibrous and cellular sheath (neural lamella and perineurium) forms a diffusion barrier which is only slightly permeable to the common cations. Radioisotopic studies demonstrated that the uptake of Na-22 by nerve cords with intact sheaths is blocked in the presence of 5 mM azide. But the uptake of Na-22 by nerve cords with the fat-body sheath removed is not blocked in the presence of azide. The following model is proposed for ionic regulation in Carausius CNS. A high extracellular sodium concentration is maintained by active transport across the fat-body sheath, producing a potential difference of 15-20 mV with the inner surface positive. Ions other than sodium distribute according to this electrical gradient resulting in a suitable ionic environment around neurons.

LACTATE AND PYRUVATE AS INDICATORS OF THE SEVERITY OF ACUTE CIRCULATORY FAILURE (SHOCK). Max Harry Weil and Abdelmonem A. Afifi*. USC School of Medicine and UCLA School of Public Health, Los Angeles.

Lactate (L) alone serves as a reliable indicator but neither the measurement of pyruvate (P) nor the computation of the lactate pyruvate ratio (L/P) or excess lactate (XL) were shown to improve either the reliability of L as a measure of cumulative oxygen debt or its value as a prognosticator of survival during shock states.

A standardized method for production of hemorrhagic shock in the Wistar rat was employed. During a 4 hour bleeding period, oxygen consumption of the rat was reduced to approximately 40% of control value, pH was reduced from 7.39 to 7.08 and a concurrent increase in L from 0.80 to 6.06 mM and in P from .07 to 0.18 mM were observed. Cumulative oxygen debt correlated with log L ($r = 0.50$; $p < .0005$) and both were significantly related to survival. Correlation of cumulative oxygen debt and survival, both with P and with computed values of the L/P and XL were of lower magnitude. Partial correlation analysis demonstrated that neither P, L/P nor XL improved predictability.

In 142 patients who presented with clinical manifestations of circulatory shock and of whom 62 survived and 80 died, the best empirical discrimination between survivors and fatal cases was provided by measurement of L, which failed only 11% of the time. This was confirmed by discriminant function analysis in which the percent probability of misclassification based on L was 12% whereas this probability increased to 21% with L/P and 19% with XL. In this series of patients, L served as a sensitive predictor; as L increased from 2.1 to 8.0 mM, the estimated probability of survival decreased from 90 to 10%.

Supported by United States Public Health Service grant HE 05570.

PRIMARY AFFERENT DEPOLARIZATION EVOKED IN THE CAROTID SINUS NERVE BY SUPRAMEDULLARY STIMULATION. Gerald K. Weiss* and Wayne E. Crill. Univ. of Washington School of Medicine, Seattle, Washington

Presynaptic inhibition is one way supramedullary regions could regulate cardiovascular reflexes mediated through the brainstem. Primary afferent depolarization (PAD) measured by an increased excitability of afferent fibers to antidromic excitation[1] is accepted as an indirect indication of presynaptic inhibition. This report shows that PAD is present in the carotid sinus nerve (CSN) following a conditioning stimulus applied in the posterior hypothalamus.

In cats anesthetized with either chlorolose or sodium pentobarbital the CSN was isolated and placed in a suction electrode for recording the antidromic response in CSN evoked by stimulation through a concentric electrode in the ipsilateral solitary tract. The posterior hypothalamus was systematically explored with a concentric electrode for stimulation points that produced PAD in the CSN. The increased excitability of the antidromic response in the CSN occurred 10-20 msec after the supramedullary conditioning stimulus; it reached a maximum at 25-45 msec and lasted 120-150 msec. Loci in the posterior hypothalamus with the lowest threshold for evoking PAD in the CSN were consistently found in the region of the fields of Forel.

Supported by PHS Grants NB 07987 and NB 05082

[1]Wall, P.D. J. Physiol. 142:1, 1958.

QUANTITATION OF BONE MARROW RECOVERY FOLLOWING SUBLETHAL IRRADIATION IN BEAGLES. J.E. West*†, F.D. Wilson*, M. Goldman*, and L. K. Bustad. University of California, Davis.

Sublethal radiation dose rate effects (240R ± 6%, ^{60}CoY) were compared and quantitated on the hematopoietic system of Beagles exposed to either a 24-hr simulated solar flare radiation pattern protracted, low dose rate (LDR) or as a high dose rate, brief exposure (HDR) over 0.5 hr. Nucleated marrow precursor cells showed a similar depopulation to 98% and 99% of pre-irradiation value within 5 days after LDR and HDR exposures, respectively. By 4 mos post-irradiation, recovery was at 70% of pre-irradiation values in both groups although differences in recovery pattern were noted. Dose rate effects were noted in peripheral blood recovery pattern of PCV, Hgb, and thrombocytes. Two of the four dogs from each of the LDR, HDR, and control groups were used to determine total cellularity using ^{59}Fe labeling in bone marrow, myeloid: erythroid ratios, and absolute nucleated marrow precursors. No dose-rate effects were noted in the mean percent ^{59}Fe activity distribution (%) in bone marrow of LDR, HDR, and control animals, respectively: axial skeleton, 79, 80, 77; appendicular skeleton, 21, 23, 22; upper body, 63, 66, 67; lower body, 37, 34, 32. Skeletal ^{59}Fe content in ashed bone compartments and absolute nucleated marrow cell count/mm^3 of marrow from each of 2 LDR and HDR and 1 control dogs were calculated, respectively, at 16, 7; 29, 12; and 13 x 10^9 cells/kg. Quantitative hematologic and erythrocytic ^{59}Fe distribution studies suggested that LDR exposure may cause somewhat less extensive sublethal injury to hematopoietic stem cells but demonstrate a slower and evantually comparable recovery 4 mos after irradiation, relative to the HDR exposure pattern. (Work supported by US AEC.)

† Armed Forces Radiobiol. Res. Inst., Bethesda, Md.

PO_2 OF CAT CEREBRAL CORTEX: EFFECTS OF BREATHING O_2 AND O_2 + CO_2. W. J. Whalen, R. Ganfield*, and P. Nair*. St. Vincent Charity Hosp., and Case-Western Reserve Univ., Cleveland, Ohio.

Previous measurements with a micro O_2 electrode in skeletal muscle in situ have shown that the PO_2 fluctuates, often rhythmically, with a mean level of 4-6 mm Hg; and breathing pure O_2 results in no, or only a slight increase in tissue PO_2, whereas 95% O_2-5% CO_2 causes a decrease. In the present study the PO_2 was similarly measured in 569 locations in the outer 1.7 mm of the cat brain in situ. The electrode was introduced through a small hole in the skull, and lowered into the brain in steps of about 125μ. The brain surface was bathed in oxygen-free physiological solution at 35°C. Arterial pressure was monitored continuously. Rectal temperature of the eleven cats was usually maintained between 36 and 39°C. There was considerable variation in PO_2 from one location to another and from animal to animal. Individual values for PO_2 ranged from 0 to 90 mm Hg with a mean of 25. There was significant downward trend in PO_2 from the surface layers inward. When the electrode was left in one location for several minutes the PO_2 was seen to fluctuate, though not often rhythmically. Breathing pure O_2 or 95% O_2-5% CO_2 (N=41 and 33 respectively) caused an equal (50%) increase in PO_2. These studies show that the PO_2 in brain cortex is much higher than in skeletal muscle and indicate that regulation of blood flow in the two tissues differs markedly. (This work was supported in part by PHS grant HE 11906)

ENDOTOXIN RESPONSE IN CONSCIOUS DOGS FOLLOWING DEPLETION OF HISTAMINE, SEROTONIN, CATECHOLAMINES, AND KININS. Howard Whigham and Richard J. Hahn (intr. by I. J. Pincus). Dept. of Medicine, Univ. of So. Calif., School of Medicine, Los Angeles, California.

Circulatory collapse following the intravenous injection of bacterial endotoxins has been reported to be mediated and or potentiated by release of vasoactive amines and peptides. Dogs weighing from 18 to 24 kg. were prepared with indwelling catheters in the aorta, portal vein, iliac vein and right atrium, and secured in a specially designed holder, for pressure monitoring and blood sampling. Following a 1 week recovery period animals were divided into 4 groups and given the following depleting or inhibiting agents in a conscious state on 4 successive days: Group I reserpine 0.1 mg/kg, Group II compound 48/80 0.5 mg/kg, Group III trysalol 200 u/kg, Group IV saline. All drugs were adjusted to a final volume of 15 ml and infused into the right atrium. On the 5th day animals received E. coli endotoxin 5 mg/kg. Arterial, portal, and iliac venous pressures were continuously recorded. Histamine, serotonin, catecholamines, kinins, pH, and hematocrit, were measured at frequent intervals before, during and after treatment. Following endotoxin, control animals released significant amounts of the three vasoactive substances within 5 minutes, while only small amounts were measured in treated animals. (Hist. $P > 0.01$, catechol. $P < 0.001$, kinins, $P > 0.01$). No significant improvement in the clinical course or in survival was observed in the treated groups. Death in all groups occurred within 8 - 12 hours. This investigation demonstrates that the release of these vasoactive substances, while contributing factors, are the result and not the cause, of the lethal course of endotoxins. (Supported by USPHS Grant AM 01992-11).

OXYGEN DEFICIT-OXYGEN DEBT RELATIONSHIPS DURING EXERCISE. B.J. Whipp*, C. Seard* and K. Wasserman. Harbor General Hospital, Torrance, California and UCLA School of Medicine, Los Angeles, California.

To determine the relationship between O_2 debt and O_2 deficit in steady state and non-steady state phases of exercise, three healthy male subjects were exercised at 685 Kg-M/Min. for each of 1,2,3,4,5 and 6 minute periods on a cycle ergometer. The studies were performed in random order on non-consecutive days. Exercise for 10 minutes was also performed by each subject to determine his steady state O_2 requirement for this work rate. The O_2 cost of each test was computed by summing the exercise and the recovery O_2 consumptions above the requirement of unloaded pedaling. The O_2 deficit was determined by subtracting the O_2 consumption ($\dot{V}O_2$) of each exercise period from the steady state $\dot{V}O_2$. The O_2 deficit increased with time to a plateau value at approximately 4 minutes. In contrast, the O_2 debt increased to a peak value during the second or third minute of exercise and then decreased to a constant level which approximated the O_2 deficit plateau. The total amount of O_2 consumed (O_2 debt + exercise O_2 consumption) was linearly related to the work done except during the early exercise period when O_2 debt exceeded O_2 deficit. It is concluded that 1) O_2 deficit and O_2 debt are equal provided the measurements are made after the exercise $\dot{V}O_2$ has reached a steady state, 2) O_2 debt exceeds O_2 deficit only during the first few minutes of exercise, and 3) O_2 debt does not increase after $\dot{V}O_2$ reaches a steady state. (Supported by NIH grant HE - 11907)

REFLEX CARDIOVASCULAR RESPONSE TO NOXIOUS GASEOUS STIMULI IN UNANAESTHETIZED RABBITS. Saxon White* and Dean Franklin, Univ. of Cal. at San Diego School of Med. and Scripps Clinic and Research Foundation, La Jolla, Cal.

There is little detailed knowledge on how somatic afferent and special sensory information can effect circulatory control mechanisms. In the unanaesthetized rabbit, exposure to noxious gaseous stimuli is known to affect respiration and circulation. In order to study the central and regional circulatory changes in this response, seven unanaesthetized unrestrained rabbits with chronically implanted Doppler ultrasonic flowmeters on the aortic root, terminal aorta, mesenteric and renal arteries were exposed briefly to tobacco smoke, formalin and ammonia vapour, and the phasic flow responses observed. Graded presentation of the stimuli resulted in progressively more intense effects until at maximal levels of stimulation, flow in the splanchnic, renal and hind-limb beds fell close to zero and cardiac output to 25% of control. There appeared little quantitative difference in the regional vasoconstrictor effects in the different regional beds. Atropine (1.0 mg/kg I.V.) essentially abolished the bradycardia but the generalized increase in resistance to flow still occurred. Denervation of one kidney abolished the constrictor effects in that organ. The results suggest that in the unanaesthetized rabbit excitation of receptors in the naso-pharyngeal region evokes a uniformly generalized vasoconstrictor pattern on the beds studied similar to that seen with intense chemoreceptor stimulation in the same species.

Supported by grants from the Life Ins. Med. Res. Fund of Aust. & N.Z., NIH HE08337, HE12373 and NASA, NGR 05-042.

PROPRANOLOL INHIBITION OF CHOLESTEROL INDUCED FAT DEPOSITS IN RABBIT AORTAE. P.J. Whittington-Coleman* and B. H. Douglas, Depts. of Med. and Pharm., Univ. of Miss. Med. Ctr., Jackson, Miss.

The effect of the β-adrenergic blocking agent propranolol on cholesterol induced atherosclerosis was studied. Twenty rabbits weighing 1-2 kg were fed a 2% cholesterol diet for ten weeks. Ten of these rabbits were given daily injections of propranolol (5 mg/kg/day). Ten rabbits weighing 1-2 kg were fed a normal diet while ten rabbits were fed a normal diet and additionally treated with propranolol (5 mg/kg/day). At the beginning of the experiment there was no significant difference in the systolic blood pressure of any of the groups. The cholesterol plus propranolol group as well as the group which received propranolol and a normal diet had a significant drop in blood pressure the fifth week of the experiment. The blood pressure remained lower until the experiment was terminated. The calcium content of the aortae of rabbits which received the cholesterol diet was 9.58 $\pm$ 0.8 mEq Ca++/kg fat free dry wt. This was significantly higher than that of rabbits which received the cholesterol and propranolol (7.55 $\pm$ 0.3 mEq Ca++/kg fat free dry wt.), of normal rabbit aortae (7.91 $\pm$ 0.7 mEq Ca++/kg fat free dry wt.) as well as rabbits on a normal diet plus propranolol (7.67 $\pm$ 0.4 mEq Ca++/kg fat free dry wt.). Histological results showed large deposits of fat within the intimal layer of the aortae of the cholesterol group. Propranolol plus cholesterol treated rabbits had less fat deposition along the intimal layer of the aortae than the cholesterol group. Rabbits receiving the normal diet or the normal diet plus propranolol had no lesions. These results indicate that propranolol has a vascular action in vivo affecting atherosclerosis.

Supported by NIH GM 39063.

STUDIES OF THE ORIGIN OF THE COLON SLOW WAVE. Martin Wienbeck* and James Christensen. Gastrointestinal Res. Lab., University of Iowa College of Medicine, Iowa City, Iowa.

In cat colon the circular muscle layer shows constant regular rhythmic depolarizations (slow waves, SW). To study the genesis of the colonic SW, isolated strips of circular muscle from the pelvic colon (about 30 x 1 mm) were put in a sucrose gap. The muscle strip was fixed at one end and tied to a force-displacement transducer to record contractions. All solutions were preheated to 38° C and aerated with 95% O_2 - 5% CO_2. In fresh strips mean resting potential (RP) was 53.48 ± 1.12 (SE) mv. Resting potential was interrupted periodically by spontaneous depolarizations (SW). Mean amplitude of SW (SWA) was 7.69 ± 0.67 (SE) mv, mean duration of SW (SWD) was 4.79 ± 0.16 (SE) sec, and mean SW rate (SWR) was 5.61 ± 0.08 (SE)/min. Single spikes occasionally occurred at the maximum depolarization. After more than 30 min of hypoxia (from aerating with 95% N_2 - 5% CO_2), SWR diminished 10%, RP diminished about 30%, but SWA and SWD did not change. After complete replacement of Na^+, SWA did not change, but SW became slow and irregular and finally stopped. $[Ca^{++}]$ from 10 to 0 mM had little effect on SWR; $[Ca^{++}]$ 0.6 mM or less reduced SWA progressively and slightly diminished RP. $[Mn^{++}]$ from 0.25 to 1.25 mM had effects similar to Ca^{++} deprivation. Tetrodotoxin (≧ 0.05 µM) increased spike activity and amplitude of contractions and slightly reduced SWR. The slow waves of the colon are maintained by anaerobic metabolism; they appear to be Na-dependent in frequency and Ca-dependent in amplitude. The effect of tetrodotoxin indicates that they are not dependent on functioning nerves. They closely resemble SW of longitudinal muscle of small bowel.

PERMEABILITY OF THE PROXIMAL TUBULE AND THE LOOP OF HENLE TO ^{14}C-UREA AND ^{22}Na. T. W. Wilczewski*, H. Sonnenberg and G. Carrasquer. University of Louisville School of Medicine, Louisville, Ky. and University of Toronto School of Medicine, Toronto, Ontario.

The purpose of this project was to study the relative permeability of the proximal convoluted tubule and the loop of Henle to ^{14}C-urea and ^{22}Na. The microperfusion technique of Sonnenberg and Deetjen (Pfluger's Arch. 278: 669, 1964) has been used for the proximal tubule and a technique similar to that of Schnermann (Pfluger's Arch.300: 255, 1968) for the loop. The percentage recovery of ^{3}H-inulin, ^{14}C-urea and ^{22}Na for proximal tubules was plotted against the length of the perfused tubule. The concentration of ^{3}H-inulin did not change significantly. The concentrations of ^{14}C-urea and ^{22}Na decreased by 11.4% and 24.4% per mm length of the perfused tubule respectively ($p < 0.05$). The concentrations of the fluid collected in the early distal convolution were 145 ±6 percent for ^{3}H-inulin, 46 ±4 percent for ^{14}C-urea and 8 ±1 percent for ^{22}Na with respect to the concentrations in the perfusate. The average length of the perfused loops was approximately 8 mm. The permeability of the tubule to a given substance can be estimated from the slope of the line which results from the semilogarythmic plot of the percentage recovery versus the length of the perfused tubule (Sonnenberg et al. Pfluger's Arch. 286: 171, 1965). Without taking into account the difference in diameter between the loop of Henle and the proximal tubule, the permeability of the loop to ^{14}C-urea was 66% of that in the proximal tubule, and the permeability of the loop to ^{22}Na (including active transport) was 32% of that in the proximal tubule. If the difference in diameter were included in the calculation the difference in permeability between the proximal tubule and loop would be magnified. (Supported by USPHS and AHA)

ALTERATION OF THE EVOKED RESPONSE FROM PREPYRIFORM CORTEX FOLLOWING PROLONGED ELECTRICAL STIMULATION OF THE LATERAL OLFACTORY TRACT. T. Joe Willey* and Walter J. Freeman, Dept. Physiology-Anatomy, Univ. Calif. Berkeley, Calif.

The lateral olfactory tract (LOT) in the cat was activated by electrical pulses at low intensity and almost continuously at rates near 40 pulses/sec for up to six months. During this time averaged evoked responses from the olfactory bulb and prepyriform cortex were evaluated for alterations. After three days, persisting thereafter unchanged, the cortical waveforms, obtained by single-shock stimulation, were altered, whereas the bulbar waveforms were essentially unchanged. The cortical alteration was a reduction in amplitude and duration of the first surface negative wave of the oscillatory evoked potential without equivalent reduction in subsequent waves of the evoked response. LOT axons carrying the repeated input to the cortex were inferred to be undamaged by the experimental procedure, because the orthodromic triphasic action potential preceding the cortical response and the antidromic bulbar response were unaltered. The alteration was localized to a population of neurons receiving long-term stimulation. From experiments attempting to further characterize the response alteration it was postulated that orthodromic excitation of cortical pyramidal cells was blocked after three days of continuous stimulation, and that the remaining altered response represented olfactory bulb dis-excitation of the cortex following antidromic invasion of mitral cell axons. NIH Grant MH 06686.

NEUROPHARMACOLOGICAL PROPERTIES OF 1,4-BUTANEDIOL: EFFECTS ON CENTRAL NERVOUS SYSTEM AND CARDIAC FUNCTION. C. R. Wilpizeski*, M. H. F. Friedman and L. K. McGinley*, Department of Physiology, Thomas Jefferson University, Philadelphia.

Young adult Hartley strain guinea pigs were prepared with permanent monopolar recording electrodes placed on the frontal and occipital cerebral cortex, surface of the cerebellum, and in the vicinities of the internal capsule and brain stem reticular formation. Additional pairs of electrodes were fastened subdermally to the chest wall and neck musculature. Following control EEG, ECG, and EMG in the awake, unrestrained state, animals were injected with 1,4-butanediol 125 to 1,000 mg/kg I.P. Electrical activity was monitored for up to 6 hours thereafter. The predominant CNS effects ranged from tranquilization to coma accompanied by synchronization and high amplitude slow wave EEG activity. With higher dose levels, epileptic-type patterns appeared, and spike discharges occured at relatively regular, widely spaced intervals. During intermediate stages afferent hypersensitivity was evident by the presence of auditory, visual and tactile evoked responses of high amplitude. Additional groups of guinea pigs trained to make a turning response in a water-filled T maze showed impairment when required to learn a reversal response following 125 and 250 mg/kg of 1,4-BD. At profound depths of coma, several types of cardiac arrhythmias were detected, especially sinus bradycardia, reversible heart blocks and episodic alternations in waveform polarity.

AChE ISOENZYMES IN DENERVATED CHICK MUSCLE. B. W. Wilson (intr. by I. H. Wagman). Dept. of Poultry Husbandry, Univ. of Calif., Davis, Cal.

Several isoenzymes associated with acetylcholinesterase (AChE) activity in muscle fiber sarcoplasm are found in normal chick embryo muscle and white-fibered muscle of adult chickens with inherited muscular dystrophy (Wilson et al., 1968 PSEBM, 129, 199). The hypothesis that neural activity represses the activity of these embryo AChE forms in muscles from normal but not dystrophic chicks was tested by a series of denervation experiments. The median nerve was severed in one wing of 2 day to one month old chicks and the AChE activity of the biceps muscles was examined using spectrophotometric, histochemical and electrophoretic methods at periods up to one month following surgery. The results showed that embryo AChE forms were present in denervated normal biceps muscles and lacking in the innervated controls. Total AChE activity in the atrophied denervated muscles averaged more than 3 times that of the controls. Results with dystrophic chicks indicated that embryo AChE forms were present in both denervated and control muscles; total AChE activity in denervated dystrophic muscles was always less than that of control dystrophic muscles. Embryo AChE forms could be detected in month old normal muscle 48-60 hours after denervation. The results, in toto, indicate that innervation represses activity of embryo AChE isoenzymes in white-fibered muscles of normal but not genetically dystrophic chicks. (Supported in part by USPHS-ES 00202 and NIH-NB 07359.)

Activation of Membrane-bound Cholinesterase by Helium and other Inert Gases including some conventional Anesthetics.
Kenneth M. Wilson*, Margaret G. Filbert* and John A. Clements. Johns Hopkins Med. Sch., Baltimore 21205, Medical Rsch. Labty. Edgewood Arsensal 21010 and Cardiovascular Rsch. Inst. San Francisco 94920.

It has been shown that iso-narcotic partial-pressures of inert gases (1) correlate with the pressures decreasing the interfacial tension between lipoprotein and water by 0.39 dynes/cm. (2). We have now compared the action of several inert gases on membrane bound cholinesterase of "synaptosomes" and microsomes from rat brain. Using a special high-pressure apparatus (3) and a very precise assay method (4) we find that Helium at 2400 psig, Methane at 40 psig, N_2O at 0 psig (100%) and Fluothane (3% in O_2) all activate hydrolysis of Acetylcholine (20-30%); Butyrylcholine (40-60%) and Mecholyl (20-40%) by membrane bound cholinesterase. Conversely, soluble electric eel cholinesterase free from toluene extractable lipids is not activated. Hydrostatic pressure alone does not account for the Helium effect which occurs at 160 Ats., i.e. close to the value predicted by extrapolation of the data in ref's 1) and 2). There is some evidence that a change from zero-order towards first-order kinetics may occur during inert gas activation and we suggest that sorption of He etc. at a lipoprotein-water interface could change its energy state and so promote a conformational change in the bound enzyme.

1) Carpenter, "Underwater Physiology" N.A.S.-N.R.C. Publication 377, 1955. 2) Clements and Wilson, Proc. N.A.S. 48, 1008, 1962. 3) Wilson, (to be published). 4) Filbert, Hester and Siakotos, Fed. Proc. 28, No. 180, 1969.

INTERACTION OF POSTERIOR HYPOTHALAMIC STIMULATION AND BAROCEPTOR REFLEXES ON RENAL NERVE ACTIVITY. M. F. Wilson, I. Ninomiya*, W. V. Judy*, and G. N. Franz*. Department of Physiology and Biophysics, West Virginia University Medical Center, Morgantown, West Virginia 26506.

Interaction between posterior hypothalamic stimulation frequency (HS) and baroceptor reflexes on mean renal nerve activity (MRNA) was studied in 10 anesthetized cats. The hypothalamus was stimulated through coaxial electrodes with negative current pulses of 400-500 μA and 0.5 msec pulse duration at frequencies from 10 to 150 Hz. Baroceptor activity was modified by cutting the four major baroceptor nerves, i.e., zero baroceptor input, by manipulating mean aortic pressure (MAP) with epinephrine injection or by clamping MAP with the aid of descending aortic occlusion and an external pressure reservoir. MAP served as an index of baroceptor activity. The original renal neurograms were electronically rectified and then averaged over periods of 5 seconds for quantitative analysis. With the four major baroceptor nerves cut and HS = 0, MRNA remained constant (e.g., 80 μV) at different MAP levels. For HS = 0 and MAP = P_o (baroceptor threshold pressure, 70-90 mm Hg), MRNA = $MRNA_o$ (e.g., 80 μV). For MAP > P_o and HS = 0, MRNA decreased linearly as MAP rose, reaching the noise level at about 155 mm Hg. During hypothalamic stimulation (HS = 10-100 Hz) and for given MAP levels, MRNA increased proportionally with HS. For example, with HS = 50 Hz and MAP = P_o, MRNA = 130 μV ($MRNA_o$ + 50 μV); and for MAP > P_o, MRNA decreased again linearly until the noise level was reached at about 200 mm Hg. Using piece-wise linearization of the MRNA characteristics as a function of HS and MAP, the additive interaction of hypothalamic and baroceptor reflex activity can be expressed by the equation MRNA = a(HS) + $MRNA_o$ - b(MAP - P_o), where a and b are constants, MAP ≥ P_o, and MRNA ≥ 0. Supported in part by NASA Grant NGL 49-001-001 and NIH Grant HE 10234-04.

CAT MEDIAL VESTIBULAR NEURONS INHIBIT NECK MOTONEURONS MONOSYNAPTICALLY. V.J. Wilson and M. Yoshida*, Rockefeller University, New York, N.Y. 10021.

In cats anesthetized by pentobarbital the effect of electrical stimulation of the brain stem on C2-C3 neck motoneurons was tested by means of intracellular recording. Motoneurons sampled consisted of those innervating splenius and other muscles that elevate the head. Single shocks produced in many cells IPSPs with a latency ranging from 0.9-1.5 msec. From comparison of this latency with that of monosynaptic EPSPs produced in the same cell population by brain stimulation (0.8-1.5 msec) and from segmental delay (distributed about a peak at 0.6-0.7 msec) it is concluded that the IPSPs are monosynaptic. In several experiments as many as 13 electrodes were inserted at various depths into the medulla and pons, and the IPSP thresholds at different locations were compared. Low threshold points were absent from the reticular formation and from the lateral and descending vestibular nuclei. The lowest threshold points were in the medial vestibular nucleus and medial longitudinal fasciculus. Therefore IPSPs are produced by long inhibitory fibers that originate in the medial vestibular nucleus and reach the upper cervical segments via the MLF. Electrical stimulation of the ipsilateral labyrinth with single shocks often evokes disynaptic IPSPs in neck motoneurons, very probably with a relay in the medial nucleus. This inhibitory pathway, together with an excitatory pathway relaying in Deiters' nucleus, provides some of the pathways utilized by the labyrinth in regulation of head position. Supported by NIH grant 5R01 NB02619.

MATERNAL-FETAL RELATIONSHIP IN DIURNAL RHYTHMS. C.M. Winget, G.H. Bond*, J. Ishizaki*, and C.W. DeRoshia*. Environmental Biology Division, Ames Research Center, NASA, Moffett Field, Calif. 94035 and Department of Physiologic Sciences, University of California, Davis, Calif. 95616.

In order to quantitate the development of rhythmic processes and to establish the phase relationships of synchronized embryonic rhythms, unrestrained pregnant sheep were maintained in a controlled environment. Deep body temperature data (DBT) and heart rate data (HR) were obtained from the fetus and ewe with miniature radiotransmitters implanted surgically 34 days before parturition. Hourly values were pooled over the course of the experiment (20 days pre-parturition) to obtain hourly means, and to reveal biologic trends in the data. The comparison of the mean hourly data with those of the day of birth also provided a measure of trends. Wave form analyses were accomplished by fitting to the Voltera Integro Differential Equation (VIDE) and by level crossing analysis. The ewe HR showed the most stable wave form and the ewe and fetal HR exhibited stronger diurnal oscillations than DBT. Fetal HR daily means exhibited a decreasing trend as expected, since HR is inversely proportional to a function of body weight. Both fetus and ewe showed a large overshoot in HR as well as DBT at parturition. The ewe HR cycle was out of phase with the fetus and had a greater slope than that of the fetus. The maxima and minima of ewe and fetus HR were significantly different in time. Hysteresis diagrams indicate a phase difference of 90° to 150°. The VIDE model readily fits the data and therefore suggests physiological mechanisms common to other mature homeotherms. However, the rhythm generating mechanisms in the fetus differ from those of the ewe in that the ewe and fetus maintain different phase angles to the Zeitgeber (12L:12D).

EFFECT OF ALTITUDE ACCLIMATIZATION ON ACTIVITY OF MICE RETURNED TO SEA LEVEL. John Winkert, Cheryl Birchette* and Leslie Giddings*. Meharry Med. Col. Nashville, Tenn.

In the course of studying the erythropoietic effects of dibutyryl - cyclic AMP upon Swiss Webster mice it was noted that altitude chamber assay mice appeared to be more active than normal mice. To verify this impression 28 to 32 gram female mice were exposed to increasingly higher altitudes of from 18,000 ft. to 23,500 ft. over a 30 day period for a total exposure of 190 hours. Eight hours after returning to sea level the activity of the mice was compared with that of control mice which were kept in the altitude chamber at sea level. The mean activity of the control mice was 1.1 ± 0.1 epochs per minute while that of the altitude acclimatized mice was 2.0 ± 0.2 epochs per minute which was significantly greater than the controls (P value less than 0.01). Supported by NIH grants 5R01CA02080 and 5S01FR05422.

ELECTRICAL ACTIVITY FROM SINGLE NEURONS IN AUERBACH'S PLEXUS OF CAT INTESTINE. J. D. Wood* and C. L. Prosser. Dept. of Physiology and Biophysics, Univ. of Ill., Urbana, Ill. 61801.

Microelectrode recordings from intrinsic ganglion cells revealed three types of neurons with respect to pattern of electrical discharge: (1) Burst units fire spontaneously in bursts containing 5-25 spikes at intervals of 2-25 sec; approximately 77% of these (1a) were unaffected by cholinergic agents or biogenic amines, whereas, 23% (1b) were blocked by atropine or nicotine and excited by ACh; interburst intervals did not correlate with frequency of electrical slow waves. (2) Stretch receptor units were excited by mechanical stimulation to give trains of spikes of up to 30 sec duration. (3) Continuous units gave single spontaneous spikes at random intervals of 1/2-1 sec. When burst units were prevalent, the circular muscle was electrically and mechanically quiescent. Local anesthetics blocked all nervous activity and released electrical and mechanical activity in the circular muscle. Atropine increased activity in the circular muscle. Transmural electrical stimulation did not inhibit circular muscle motility in the presence of nerve-blocking drugs, but did inhibit it in the presence of atropine only. Circular muscle was relatively inexcitable when the neurons were active and showed increased irritability after nervous blockade. Electrical slow waves from longitudinal muscle did not trigger circular spikes when the enteric plexus was functional; after ganglionic blockade, circular spikes were elicited by the slow waves. The evidence suggests a tonically active inhibitory system to circular muscle. Burst units (1a) appear to be drivers which are linked in series with follower units (1b) by an atropine sensitive, cholinergic synapse; units (1b) release an unknown inhibitory transmitter which modulates the response of the circular muscle to the pacemaker activity of slow waves from the longitudinal muscle.

INFLUENCE OF AIR DENSITY ON THE DISTRIBUTION OF VENTILATION. L.D.H.Wood*, F.Ruff*, A.C. Bryan and J.Milic-Emili. Institute of Environmental Medicine, Toronto and Joint Cardio-Respiratory Service, Royal Victoria Hospital, Montreal.

The influence of air density on the distribution of inspired gas has been studied using Xenon^{133}. Subjects breathed air or oxygen/sulphur hexafluoride mixtures at 1, 1.5 and 2.0 ATA in a hyperbaric chamber, giving a range of equivalent air densities up to 9 ATA. The distribution per alveolus of tidal volumes was studied. In addition, the regional distribution of Xenon^{133} boluses and their concentration in the subsequent expiration were measured. As shown previously, the ventilation distribution of air at 1.0 ATA is determined by the regional elastic properties. It is uninfluenced by regional airway resistance as the distribution is not significantly affected by inspiratory flow rate. However, when breathing a dense gas the regional resistances increase considerably and our results show that this does alter ventilation distribution. At low inspiratory flow rates the distribution is unchanged, but as the flow rates increase the ventilation distribution becomes more uniform. Ventilation per alveolus becomes uniform breathing SF_6 at 1 ATA at about 2.5 l/sec; breathing SF_6 at 2 ATA uniformity is achieved at 1.5 l/sec. At higher flow rates the distribution remained uniform and reversed ventilation distribution was never observed. This suggests that while regional resistances become significant in the distribution of dense gases, the regional resistances are equal.

OXYGEN TRANSPORT IN LOW CARDIAC OUTPUT HYPOXIA. R.D. Woodson*, J.D. Torrance*, and C. Lenfant. Depts. of Medicine and of Physiology and Biophysics, Univ. of Wash., Seattle, Wash.

A decrease in hemoglobin oxygen affinity, probably mediated by erythrocyte 2,3-diphosphoglycerate (2,3-DPG) level has been noted to be a prominent component of the physiological adaptation of man to high altitude hypoxia. Decreased cardiac output represents another circumstance in which oxygen supply to tissue is altered.

Forty-four patients with variable degrees of impairment of cardiac output due to cardiac disease were studied. The erythrocyte 2,3-DPG concentration and the position of the oxy-hemoglobin dissociation curve (P50 [7.4]) were determined and compared with multiple hemodynamic parameters measured during diagnostic cardiac catheterization. A statistically significant inverse correlation of P50 with cardiac index was found, which is described by the equation P50 = -0.99 (CI) + 31.5. A highly significant inverse relation between mixed venous oxygen content and P50 was also found. Additionally, as in high altitude hypoxia, 2,3-DPG and P50 correlated directly.

The decreased hemoglobin oxygen affinity noted in patients with limited cardiac output appears to be a significant physiologic adaptation leading to improved tissue oxygenation. The data suggest that the venous oxygen content is an important regulator of the erythrocyte 2,3-DPG level and the position of the oxy-hemoglobin dissociation curve. The data also confirm that the erythrocyte 2,3-DPG concentration is intimately related to the oxygen binding affinity of hemoglobin in vivo.

(Supported by U.S.P.H.S. Research Fellowship HE-40188, Training Grant AM-5130, and Research Grants - HE-06242 and HE-12174.)

A POSSIBLE ROLE FOR BIOGENIC AMINES IN PRESYNAPTIC INHIBITION. D. F. Wooley (intr. by E. Eidelberg). Barrow Neurological Institute, Phoenix, Arizona.

We studied the effects of changes in tissue levels of 5-hydroxytryptamine (5-HT) dopamine (DA) and norepinephrine (NE) on presynaptic inhibition in the cat lumbar cord. Presynaptic inhibition was measured as a reduction in amplitude of an S_1 monosynaptic reflex caused by an antecedent volley to L_7 dorsal root and as changes in primary afferent excitability recorded antidromically in the gastrocnemius-soleus (G-S) nerve. 5-HT level was increased by injection of 5-HTP, NE by injection of L-DOPA and DA by blocking dopamine-β-hydroxylase with diethyldithiocarbamate. 5-HTP increased the monosynaptic reflex, decreased presynaptic inhibition and reduced or abolished the G-S antidromic response. L-DOPA also increased the monosynaptic reflex and decreased presynaptic inhibition. Diethyldithiocarbamate decreased the monosynaptic reflex, increased presynaptic inhibition and had a bimodal effect on primary afferent excitability, first decreasing and then increasing it. The data indicate that 5-HT has a dual effect: 1) it directly excites motoneurons and 2) it either hyperpolarizes or decreases tonic depolarization of primary afferent fibers. NE stimulates or inhibits interneurons; DA affects interneurons or primary afferent fibers, or both. It may depolarize these fibers and be the presynaptic inhibitory transmitter.

DISTRIBUTION OF RADIOACTIVITY AFTER ^{3}H-TESTOSTERONE ADMINISTRATION IN 4-DAY-OLD FEMALE RATS. Dorothy Woolley, Gloria Talens and Margaret Saari. Depts. of Animal Physiol. and Environ. Toxicol., Univ. of Calif., Davis.

The sterilizing effects of testosterone administration in neonatal female rats and the blockage of these effects by pentobarbital and reserpine pretreatment are well known. The present study was undertaken to determine if testosterone distributes differentially within the CNS of the immature rat and if pentobarbital or reserpine pretreatment block uptake in target neural areas. ^{3}H-testosterone (44,000 mCi/mM) was injected (16 µg/kg, subcu) and tissues were collected 3 hrs later. Radioactivity was extracted with toluene and was about 85% ^{3}H-testosterone in the CNS. Radioactivity distributed differentially in various CNS areas, from high to low activity, as follows: olfactory bulbs, lower spinal cord, posterior hypothalamus, anterior hypothalamus, upper spinal cord, cerebral cortex and remaining brain. Uptake in non-neural areas was higher than in CNS and was as follows, from high to low activity: fat, uterus and liver, plasma, kidneys and pituitary. Treatment with pentobarbital (20 mg/kg subcu) 1 hr before ^{3}H-testosterone administration significantly decreased the radioactivity in the uterus, but did not change uptake in other tissues. On the other hand, reserpine (100 µg/rat subcu) 3 hrs before ^{3}H-testosterone administration increased radioactivity in all tissues. The sterilizing effects of early postnatal androgen administration are believed to be due to actions on the CNS. The present findings show that the 2 drugs do not block these effects by preventing uptake of testosterone by the CNS. The significance of the changes in distribution produced by the drugs remain to be determined. (Aided by NIH grant ES-00163.)

RELATIONSHIPS OF BLOOD FLOW, MYOGLOBIN, CAPILLARY DENSITY AND TWITCH TIME IN RED AND WHITE MUSCLE OF CAT IN DIFFERENT BEHAVIOR. G.F. Wooten*, D. Moorhead* & D.J. Reis. Cornell Univ. Med. College, New York, N.Y. 10021

The relationship between blood flow distribution and myoglobin concentration, capillary density, and contraction times have been determined in different skeletal muscles of the limb and trunk of cats during quiet alertness, excitement, and the rapid eye movement phase of sleep. Blood flow to skeletal muscles was measured by the isotope dilution technique of Sapirstein with ^{86} Rb and ranged from 7.7 to 39 ml/100 gm/min. in quiet alertness being highest in red and lowest in white limb muscles with trunk muscle flow between. Myoglobin concentration ranged from 0.96 mg/gm in white to 3.9 mg/gm in red muscles. Muscle alkaline phosphatase, localized in capillary endothelium in muscle and therefore used as an indicator of capillary density, was highest and twitch times longest in red muscle. There was a direct relationship, highly correlated, between blood flow when measured in this behavior and the other physiological characteristics of skeletal muscle which were measured. In excitement or sleep these relationships were lost. On the assumption that blood flow is matched to the preponderant type of metabolism characteristic of red or white muscle the results suggest that metabolism of individual skeletal muscles is adapted to the activity of each muscle in quiet alert behavior rather than in sleep or excitement. (NIH grant NB-04876)

SWEAT RESPONSES TO UNILATERAL LEG COOLING. Robert D. Wurster and Robert D. McCook. Loyola University, Stritch School of Medicine, Maywood, Illinois.

Changes in sweating were measured during the cooling of one leg of a previously heated subject. All sampled cutaneous areas showed immediate inhibition of sweating upon cooling of the leg. However, upon decrease rate of change of leg temperature, sweating returned to control levels on all areas except on the cooled leg where sweating remained depressed but elevated above the level attained during the rapid cooling period. Upon returning the leg to a warm environment, sweating throughout the body immediately increased above the control levels. Central body temperatures, tympanic membrane and oral temperatures slowly elevated throughout the duration of the experiment. In addition to CNS variables, it was concluded that thermoregulatory sweat responses consist of two peripheral factors: a multisegmental bilateral thermal receptor reflex with marked rate of change temperature sensitivity and a unilateral local temperature effect which may be due to an ipsilateral, ipsisegmental thermal afferent reflex and/or the direct influence of temperature upon the sweat gland. *(Supported by National Institutes of Health Grant HE 08682)*

PROJECTIONS FROM THE INFERIOR DENTAL NERVE TO THE DIEN- AND MESENCEPHALIC AREAS RELATED TO FEEDING. W. Wyrwicka* and M.H. Chase. Depts. of Anatomy and Physiology, UCLA and the Sepulveda VA Hospital, Los Angeles, California.

Ten cats were surgically prepared for acute experimentation under light Brevital anesthesia and then curarized and artificially ventilated. Two jeweler's screws placed into the mandibular canal served as a bipolar electrode for stimulation of the inferior dental nerve. Evoked potentials were recorded in the diencephalon and mesencephalon via bipolar strut electrodes. Single pulse stimulation of the inferior dental nerve initiated activity in various brain stem sites including the medial part of the VPM, which is known to be the thalamic relay for taste. Responses were also detected in areas such as the lateral hypothalamus, the preoptic area and the ventral tegmentum, from which stimulus-bound feeding had been previously obtained by various investigators (Hess, W.R., Diencephalon, 1954; Robinson, B.W. and M. Mishkin, Exper. Brain Res. 4:330, 1968; Wyrwicka, W., EEG clin. Neurophysiol. 17:164, 1964; Wyrwicka, W. and R.W. Doty, Exper. Brain Res. 1:152, 1966). The results suggest that projections from the buccal cavity may influence brain stem areas related to feeding behavior. (Supported by the Veterans Administration and by USPHS grants # MH 10083 and # MH 13958.)

THE DIABETIC SYNDROME IN THE db MOUSE. B. M. Wyse* and W. E. Dulin. Diabetes Research, The Upjohn Company, Kalamazoo, Michigan.

The mutant mouse, C57BL/KsJdb, develops spontaneous diabetes with symptoms similar to those observed in the diabetic human. Food intake, body weight, and plasma insulin in the db mouse are increased by 4 weeks of age and blood sugar by 7 weeks. The blood sugar continues to increase with age but by 3 months plasma insulin, pancreatic insulin, and body weight are decreasing despite continued elevated food intake. Blood sugar and plasma insulin can be stabilized and pancreatic insulin increased if young diabetics are kept on a limited diet. Baseline glucose oxidation by adipose tissue in vitro is elevated in weanling db mice but depressed in older diabetics. The response to insulin of adipose tissue from older db mice is markedly reduced. These observations suggest that diabetes in the db mouse results from the eventual inability of the pancreas to control a continual, abnormally increased supply of glucose. In the very young diabetics, elevated plasma insulin and increased glucose oxidation by the tissues (adipose tissue) maintain the glucose concentration at a normal level. In the older db's, the elevated food intake plus the depressed glucose utilization produce a constant, severe stress on the beta cells, resulting eventually in beta cell exhaustion and in the development of a lethal diabetes.

INTRACRANIAL PRESSURE DURING CARDIAC ARREST AND RESUSCITATION. David Yashon*, Franklin C. Wagner Jr.* and Robert J. White. Department of Neurosurgery, Metro. Gen. Hosp., Case-Western Reserve Univ., Cleveland.

Ten large anesthetized, curarized, ventilated dogs had epidural placement of the Numoto pressure switch for direct, absolute measurement of intracranial pressure (ICP). Ventricular fibrillation was initiated by direct myocardial application 10v alternating current. In three animals circulatory arrest alone resulted in a rise of ICP above control values of 2-8 cm. H_2O to 2-4 times the latter within 60-120 seconds paralleling a rise in central venous pressure (CVP) from control 4-5 cm. H_2O to 16-20 cm. H_2O. A gradual descent to control ICP or below followed the fall in CVP. Intrathoracic venesection was followed by a fall in ICP and CVP to 0. In five animals open manual cardiac massage was maintained for one hour with systolic BP of 60-125 mm. Hg. ICP was supported at 5-12 cm. H_2O for the entire period. A rise in ICP as in animals fibrillated only did not occur nor was hypoxic brain swelling reflected in an unusual rise in ICP. Cessation of intermittent manual cardiac compression resulted in a fall of ICP to control values or lower. In two dogs cardiac massage as above was initiated followed by spontaneous resumption of sinus rhythm at 5 and 8 minutes. B.P. rose to 200-300 mm. Hg. systolic. ICP followed by rising to 47 and 52 cm. H_2O. A gradual fall in ICP to control paralleled systolic B.P. Intracranial pressure, compatible with cerebral viability is maintained by manual cardiac compression and ICP closely parallels systolic BP and CVP during cardiac arrest and resuscitation.

THE MECHANISM OF TETRODOTOXIN ON THE IN SITU ACETYLCHOLINESTERASE IN THE VAGAL HEART SYSTEM. Wei Young. Bio-Medical Div., Lawrence Radiation Laboratory, University of California, Livermore, California.

Our demonstration of the in situ acetylcholinesterase (AChE) kinetics (Biochim. Biophysica Acta, 64:60-64, 1962; Physiologist, 7:292, 1964; 9:324, 1966; 10:354, 1967) may have contributed to a better understanding of some aspects of cholinergic mechanism. The central role of acetylcholinesterase played in synaptic transmission prompted us to investigate the most powerful neurotoxin, namely tetrodotoxin, on the vagal heart system. At a concentration as low as 10^{-10} gm/ml, tetrodotoxin effectively inhibits the AChE activity up to 50% and 70%. Kinetic studies were accomplished by introducing microquantities of substrate (acetylcholine) into the contracting system by either direct injection of acetylcholine or by electrical stimulation of the vagus nerve. Double reciprocal plot indicates that TTX is a competitive inhibitor in contrast to some other noncompetitive metal ions. At low concentration (10^{-10} gm/ml) there was no interference with either the inotropic or chronotropic contraction of the heart. At higher concentration (10^{-8} gm/ml or higher) TTX inhibited the contracting system. The mechanism of inhibition of TTX on AChE activity will be compared with respect to physostigmine and diisopropylfluorophosphate in this biological system. This work was performed under the auspices of the U.S. Atomic Energy Commission.

RESPONSES OF THE KANGAROO-RAT, DIPODOMYS MERRIAMI, TO COLD, M. K. Yousef and D. B. Dill. Desert Research Institute, University of Nevada, Boulder City, Nevada.

The water balance, habitats and behavioral adaptations of the kangaroo rat have been investigated (Schmidt-Nielsen K., Desert Animals, Oxford University Press, 1964). The objectives of this report were to study the effect of 1-week and 4-week exposure to 5C on this rodent. Three groups of rats were used, group A served as control, group B was exposed for 1 week and group C for 4 weeks. Metabolic rate, total solids, body fat, Hct, Hb and plasma protein increased significantly in group C. However, organ weights (liver, kidney, heart, lungs, ovaries, pituitary, adrenal and thyroid) did not change; weight of testes increased. One week exposure to 5C (group B) caused an increase in metabolic rate, total solids, body fat, and adrenal weights. Metabolic rate of rats exposed to 5C returned to normal when measured at 30C in group B and remained about 40% higher in group C. This different response between groups B and C suggests more than one mechanism responsible for the normal metabolic rate at 5C. Perhaps, the reestablishment of normal metabolic rate in group B is due to inactivation of sympathetic activity upon return to 30C. In conclusion the known hypertrophy of the viscera and reduced body fat during cold acclimation of white rats and mice do not occur in the kangaroo rat. Thus, the kangaroo rat has different metabolic pathways leading to the same capacity for heat production seen in other laboratory mammals exposed to cold.

Supported by NSF Grant GB 7509.

THE EFFECTS OF INTRA-ARTERIAL NOREPINEPHRINE ON SKIN AND MUSCLE CAPACITANCE VESSELS IN MAN. Robert Zelis*, Dean T. Mason and James F. Spann, Jr. University of California, Davis, School of Medicine, Davis, California.

Since it has been recently demonstrated that the veins of the muscle bed in man do not participate in venomotor reflexes, it was considered that these veins might be less responsive to exogenously administered norepinephrine (NEP) than the corresponding veins of the skin. Venous volume at a congesting pressure of 30 mm Hg (VV[30]) was determined in nine subjects simultaneously in both elevated forearms with a mercury-in-rubber strain gauge plethysmograph. The skin circulation was suppressed in one arm by the technique of epinephrine iontophoresis thereby allowing separate estimation of muscle VV[30] and skin VV[30] before and after the intra-arterial infusion of norepinephrine at .02 to .5 μg/min into both arms. The actual dose of NEP reaching the tissues was calculated by dividing the infusion rate by the instantaneous blood flow measured during each of the 43 NEP infusions. Before NEP, VV[30] of the veins of the intact forearm was 2.30, of muscle 1.25 and skin 1.05 cc/100 cc. During NEP the muscle VV[30] was not significantly decreased (slope= -.111, r=.242, $p>.05$), whereas VV[30] in the intact arm (slope= -.370, r=.600, $p<.01$), and skin VV[30] (slope= -.243, r=.487, $p<.01$) were both significantly reduced. It is concluded that the muscle veins of the human forearm are considerably less responsive to exogenously administered sympathetic neurotransmitter NEP than the corresponding skin veins, further demonstrating the non-homogenecity of response of forearm veins.

NITROGLYCERIN AMELIORATION OF CARDIAC NECROSIS IN THE RAT. L. Zitowitz, C. Tozzi and F.E. Roth (intr. by R. Neri). Dept. of Pharmacology, Schering Corp., Bloomfield, New Jersey.

Isoproterenol (ISU) has been used by many investigators to produce gross as well as microscopic cardiac lesions in the rat heart as a model for evaluating the protective effect of potential anti-angina agents. Not all clinically useful drugs, however, have been effective in preventing the induced necrosis. Beta adrenergic blocking agents or hydrazine-type MAO inhibitors have been shown to decrease the degree of necrosis. No reference has been found, however, for the protective action of nitroglycerin (NG) in this model, whether administered parenterally, orally or as a solution applied directly to the mucous membranes of the mouth in a manner analogous to the sublingual route used by the angina patient. With the latter approach, we have shown that doses of 250 μg/kg of NG (0.5%), given in a sequence of 5, 30, 60 and 90 minutes after ISU, considerably reduce the severity of the cardiac lesions. Moreover, decreased tissue transaminase levels are returned to normal in the drug-treated animals. The NG-treated rats appear and act normal as compared to the untreated control animals which often are prostrate and cyanotic with rapid, shallow respiration. The ability to demonstrate the efficacy of a recognized clinical reference standard in animals enhances the value of this method as a valid screening procedure for drugs of potential use in the treatment of angina pectoris.