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ABSTRACTS OF PAPERS

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

Effect of Temperature on Aspects of Renal Function in Sickle Cell Disease in the Tropics. Kojo Addae (intr. by A.B. Craig, Jr.)

Little information exists on the renal handling of electrolytes in sickle cell disease (hemoglobin SS and SC). This and other renal functions were studied in the SS, SC and normal Ghanaians (Hemoglobin AA) under usual room conditions (Day, 28-29°C, Rel. Humidity 75%; Night, 25°C, R.H. 80%) and also during acute exposure to 20°C (R.H. 85%) and 40°C (R.H. 55%). The acute exposure studies bear relevance to the seasonal variation here in the incidence of symptoms and crises in sicklers. Under normal room conditions, in absence of induced diuresis, excretion of urine (V), solute (Uosm.V) and sodium (UNa.V) were greater in normals than in sicklers day and night. Diurnal rhythm of these excretion parameters and of potassium was as to be expected in the controls but was either absent or reversed in the sicklers. Urinary Na/K ratio was 2-3 times greater in controls than in sicklers and was considerably less than unity in several sicklers. At 20° under combined water and osmotic diuresis, ERPF, GFR, V, Uosm.V, UNa.V, UK.V and $UHCO_3$.V were greater in sicklers with indication of relative impairment of reabsorption of sodium. At 40° these values decreased in all groups but more greatly in patients. The data strongly suggest greater mineralocorticoid activity in sicklers at usual room conditions and at 40°C. In terms of the parameters studied, renal function appeared less defective in the SC than in the SS particularly at 40° at which temperature it tended to approach that of normals. (This work was supported by grant from Rockefeller Foundation).

THE EFFECT OF ETHER-STRESS AND NEMBUTAL ON LH, FSH AND PROLACTIN LEVELS IN PLASMA OF CHRONIC OVARIECTOMIZED RATS. Katsuya Ajika*, S.P. Kalra*, L. Krulich*, C.P. Fawcett* and S. M. McCann. Dept. of Physiol., Univ. of Tex., Sw. Med. Sch., Dallas, Tex.

In non-stressed rats housed in single cages, decapitation revealed fairly low "resting" levels of plasma LH, FSH and prolactin as measured by radioimmunoassay. When blood was collected from etherized animals, plasma LH, FSH and prolactin were significantly elevated above the resting level. Decapitation performed 1 and 2 hrs after bleeding revealed that plasma LH and prolactin but not FSH levels had returned to the resting value. In another group of animals bled while etherized, Nembutal injected i.p.(30mg/kg)caused significant reductions in plasma LH and prolactin levels at 1, 3 and 5 hrs after its injection. Twenty-four hrs later both LH and prolactin levels had recovered to control preinjection levels. No significant change in plasma FSH level was observed in Nembutalized-etherized rats. It appears that Nembutal eliminates the discharge of LH and prolactin caused by stress without affecting the resting level of these hormones. Moreover, since crude and partially purified hypothalamic extract caused a dramatic increase within a few minutes in plasma LH in Nembutalized rats, the blocking effect of Nembutal is thought to be on the hypothalamus rather than on the anterior pituitary gland.

EVIDENCE FOR EXTENSIVE BLOOD SHUNTING IN HIBERNATED AND NON-HIBERNATED WOODCHUCKS (MARMOTA MONAX) DURING ARTIFICIALLY INDUCED HYPOTHERMIA. Thomas F. Albert* and J. A. Panuska. Dept. of Biology, Georgetown Univ., Washington, D.C. 20007

Hibernated woodchucks (T_A, 6°C) within 24 hours after an evoked arousal and non-hibernated woodchucks (T_A, 25°C) were anesthetized with Nembutal, implanted with multiple thermocouples, cannulated for carotid blood pressure recording, and rendered hypothermic by exposure to cold air. During body cooling the average maximum differences which occurred between the temperature of the carotid (CA) and intraperitoneal fat (IPF), colon (C), hind leg muscle (HLM), and front leg muscle (FLM) in hibernators (n=10) were: CA and C, 8.2°C; CA and IPF, 10.2°C; CA and HLM, 18.3°C; CA and FLM, 18.4°C. In non-hibernators (n=7) the gradients were less: CA and C, 1.5°C; CA and IPF, 4.2°C; CA and HLM, 9.5°C; CA and FLM, 9.4°C. Required cooling time was significantly greater in the hibernators. Under these conditions brown fat appeared to be a major site of heat production, especially in the hibernators. In some cases, as the brown fat temperature fell, the carotid temperature rose. These changes were accompanied by a transient fall in carotid blood pressure, probably reflecting the opening of the brown fat capillary bed. The observed temperature gradients and blood pressure changes associated with temperature shifts suggest extensive blood shunting during hypothermia. Previous hibernation significantly increases this activity.

CLEARANCE OF RIHSA AND ^{22}Na FROM CEREBROSPINAL FLUID IN THE CHICKEN. D.K. Anderson* and S.R. Heisey. Department of Physiology, Michigan State University, East Lansing, Michigan 48823.

Brains of anesthetized (Na phenobarbital; 170 mg/kg; I.V.) chickens were perfused from the left lateral ventricle to the cisterna magna with an artificial cerebrospinal fluid (CSF) containing trace quantities of radio-iodinated human serum albumin (RIHSA) and ^{22}Na. Inflow (V_i) and outflow (V_o) rates and concentrations of RIHSA and ^{22}Na were measured. The steady state clearances of RIHSA (C_{RIHSA}) and ^{22}Na (C_{Na}) from the perfusate were calculated at various ventricular hydrostatic pressures. C_{RIHSA} increased and (V_o-V_i) decreased linearly (with equal but opposite slopes) with increasing intraventricular pressures, suggesting C_{RIHSA} as a measure of bulk absorption of CSF ($\dot{V}_a$). CSF formation rate ($\dot{V}_f$) calculated as the algebraic sum of C_{RIHSA} and ($\dot{V}_o$-$\dot{V}_i$), was approximately 1.4 µl/min., and was independent of intraventricular pressure. Resistance to $\dot{V}_a$ (4545 cm·min/ml) was 12 - 350 X that reported for mammals and 2.5 X that reported for turtles. This high resistance may indicate either a lack of valve-like channels in the arachnoid villi (as described for mammals) or high resistance pathways in the arachnoid membrane. C_{Na} was always greater than C_{RIHSA} and increased linearly with increasing intraventricular pressure. C_{Na} reflects the effects of 2 pressure dependent components, one related to $\dot{V}_a$ and another associated with perfusion time (i.e. preparation deterioration). Evaluation of the latter factor permitted the calculation of an outflux coefficient for ^{22}Na which was independent of intraventricular pressure and representative of a passively diffusing molecule.

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INVESTIGATIONS OF METABOLIC LIMITATIONS IN SURVIVAL OF HYPOTHERMIC HAMSTERS. G.L. Anderson*, R.L. Prewitt*, and X.J. Musacchia. Space Sci. Res. Cntr. and Depts. Physiol. and Radiol., Univ. Mo., Columbia, Mo.

Exposure to He:O_2 (80:20) and low temperature induces hypothermia in hamsters (Mesocricetus auratus). Exposure to heat or cold prior to the induction of hypothermia effects induction time and survival time in hypothermia. In the experiments reported here an attempt is made to elicudate the role of induction time per se as a determinate of survival time in the hypothermic state. Shaven hamsters have reduced induction times (3-4 hrs) similar to those of warm acclimated hamsters (2-3 hrs), and significantly longer survival times ($p<.01$) than unshaven controls. In addition, shaven animals have significantly higher plasma glucose, 73.5 ± 14.7 SE mg%, and liver glycogen 10.6 ±2.1 SE mg/g (wet wt) immediately following induction than do unshaven controls, 31.3 ±6.8 SE mg% and 0.42 ±0.11 SE mg/g (wet wt) respectively. The plasma glucose level during the terminal stages of hypothermia is not significantly different in the two groups. These experiments indicate that there is an inverse relationship between time required to induce deep hypothermia (r.t.=7 C) and survival time in the hypothermic state, and that the relationship probably depends upon the effect of induction time upon severity of plasma glucose and liver glycogen depletion. At the systemic level these effects may account for failure of spontaneous respiration seen in the hypothermic hamster. Supported by NASA Grant NGR 26-004-021 S5 and USPH Grant 5-F01-GM-41418-03.

COMPUTER SIMULATION OF THE DOUBLE SUCROSE-GAP VOLTAGE-CLAMP. Departments of Physiology and Pharmacology and Obstetrics and Gynocology, Duke Univ. Med. Center, Durham, N. C. Nels C. Anderson, Jr., Fidel Ramon* and J. W. Moore.

In an effort to better understand and interpret voltage-clamp data obtained on smooth muscle with the double sucrose-gap, we have initiated computer simulation of such experiments. The first step was to evaluate the simulation method by comparison with the more extensively studied voltage-clamp for the squid axon (Moore et. al. J. Gen. Physiol. 48, 279 (1964). We have solved the partial differential equations for a one dimension cable model, using the Hodgkin-Huxley equations to describe the membrane on a PDP-15 Digital computer. Implicit methods of numerical integration were used (From program supplied by F. Dodge and J. W. Cooley). A typical "artificial node" 500μ in diameter and 200μ long was simulated by 21 segments (of equal length). The voltage could be changed to a new stable level within 40 μsecs. The maximum longitudinal voltage gradient during a 4 msec step of 50mV depolarization was 2-3% of the command pulse. For a nodal length equal to 15 diameters, the potential at the current injection end differs from the 50mv step at the potential end by more than 30mv. There was a double peak of inward current at the current injection end. However, the total nodal current remains relatively smooth because of the relatively small contribution from the poorly controlled segments. Studies with a similar model modified for smooth muscle are in progress. Supported by NICHD grant HD-02742, NINS grant NS03437, NIGMS GM16718.

GLUCOSE FLUX IN THE HORSE. M. Sawkat Anwer*, T. E. Chapman*, and R. R. Gronwall. Dept. Physiological Sci., Kansas State Univ., Manhattan.

Glucose flux and pool sizes were measured using a single injection technique and a primed infusion technique in horses weighing from 100 to 200 Kg. A mixture of glucose labeled uniformly with ^{14}C and glucose labeled with ^{3}H in the 6 position (6-T-glucose) was used for single injection studies on 3 horses--fed and fasted 72 hours. Approximately 200μCi of ^{14}C glucose and 600μCi of 6-T-glucose were injected and the specific activity of periodic samples of plasma glucose was followed for 7 hours. In the primed infusion studies on 4 fed horses, 50μCi of 6-T-glucose was injected as priming dose, followed by continuous infusion of 0.5μCi/min of 6-T-glucose for 3 hours. The plasma glucose specific activity-time relationship from both types of studies was fit to a multi-exponential equation using a least-squares method on a digital computer. Based on the single injection studies the net transfer rate (glucose flux, mg/min/kg) in fed horses (1.291 ± 0.057) was significantly higher than in fasted horses (0.787 ± 0.188) while there was no significant change in the size of the body glucose pool. The ratio of specific activity of ^{3}H to specific activity of ^{14}C ($^{3}H/^{14}C$) in plasma glucose, which is an index of recycling of glucose carbon relative to hydrogen, did not change in fed horses while the ratio decreased in the fasted horses. The recycling of glucose carbon was calculated to be 13.6% in the fasted horses. The net transfer rate (mg/min/kg) calculated from primed infusion studies (1.63 ± 0.11) was significantly higher than that calculated from single injection studies (1.184 ± 0.073).

METABOLIC ABNORMALITIES IN LIVER AND ISLETS OF LANGERHANS IN A DIABETIC MOUSE. Michael C. Appel*, A. Y. Chang*, and W. E. Dulin. Biology Department, Western Michigan University, Kalamazoo, Mich., and Diabetes Research, The Upjohn Company, Kalamazoo, Mich. 49001.

Hyperglycemia and hyperinsulinism have been reported in the diabetic KK mouse. A hybrid cross (KK x C57BL/6J) designated as Toronto-KK also displays this syndrome. Studies were conducted to determine the etiological factors responsible for the hyperglycemia and hyperinsulinism in the diabetic Toronto-KK mouse. Abnormalities in livers and isolated islets of Langerhans were found in six-month old diabetic mice. Livers of these animals showed marked fat deposition, were approximately two times heavier, and contained significantly less glycogen and total protein per tissue unit weight than C57BL/6J mice. Activities of six hepatic "regulatory" enzymes were assayed. Activity of gluconeogenic enzymes (phosphoenolpyruvate carboxykinase, glucose-6-phosphatase, and fructose-1,6-diphosphatase) were significantly elevated in Toronto-KK mice but the glycolytic enzymes (pyruvate kinase, hexokinase, and glucokinase) were normal. A perifusion system was developed to investigate the dynamic aspects of insulin secretion from islets of Langerhans. The patterns of glucose-dependent insulin release were similar in both diabetic and control mice; however, cumulative insulin release after ninety minutes of perifusion was from three to six times greater by diabetic islets than by controls. The data suggest that hyperinsulinism in the Toronto-KK mouse may be due to excessive insulin output in response to glucose stimulation. In addition, the marked elevation in plasma insulin does not affect hepatic enzymes in the expected manner since insulin has been shown to induce liver glycolytic enzymes and suppress liver gluconeogenic enzymes in alloxan-diabetic rats. Hyperglycemia in the Toronto-KK mouse may result from the failure of insulin to control hepatic glucose metabolism.

HEMOLYMPH pH, ENVIRONMENTAL pH, AND RESPIRATION IN A CLAM SHRIMP. Amos Ar and Abel Schejter (intr. by L.E. Farhi). Depts. of Zool. and Biochem., Tel-Aviv Univ., Tel-Aviv, Israel.

Only little is known about the pH regulation of the body fluids of the lower crustaceans. Conchostracs of the species Cyzicus cf. hierosolymitanus (200 to 300 mg) were exposed in buffers to different pH values. Groups of 5 animals were placed for 24 hours in aerated containers with 500 ml of 0.01 M solutions of sodium-phosphate (pH from 4.4 to 9.2), tris-HCl (pH from 7.7 to 9.5) and cacodilate-HCl (pH from 3.5 to 7.0), at 22 $\pm$ 1°C. In another set of experiments at pH of 5.5, the number of animals varied from 0 to 8. The pH of the buffers was monitored periodically. After 24 hours, blood samples (60 to 70 µl), were analyzed with a pH micro electrode. Within the range of pH used for the phosphate buffers, the hemolymph pH was maintained between 7.1 and 8.1 with a slope of 0.166 ΔpH hemolymph/ΔpH medium. It was also found that the clam shrimps partially neutralized their media by a change of up to 1.6 pH units. The degree of neutralization is dependent on the duration of exposure, the density of the animals, and the properties of the buffers. In order to determine whether metabolism is involved, oxygen consumption was measured on groups of 21 animals kept in thermostated, pH-statted, closed containers. Sterilized, filtered pond water, brought to 5 different pH values from 4.8 to 8.4 was used as media. Minimum oxygen consumption of 99 µl O_2 $gr^{-1}hr^{-1}$ was found near neutrality. There was an increase of up to 40 per cent in oxygen consumption at the extreme acid or alkali pH values used. Therefore, besides maintaining their internal pH within a certain range, a process linked to changes in metabolic rate, these animals may influence the pH of their outside environment.

BIOSYNTHESIS AND PROCESSING OF A NEUROHORMONE IN APLYSIA CALIFORNICA. S. ARCH (intr. by F. Strumwasser) Division of Biology, Calif. Inst. of Technology, Pasadena, Ca. 91109

The bag cells (BC) of the parieto-visceral ganglion (PVG) synthesize and secrete a polypeptide (6000 daltons) which induces egg laying in mature animals (Toevs, 1970; Kupfermann, 1970; Arch, 1971). As part of a biochemical study of these neurosecretory cells, the biosynthesis and processing, prior to release, of the egg-laying hormone (ELH) was examined. PVGs were removed from animals and incubated in ^{3}H-leucine containing medium for 30 minutes and then rinsed in a chase medium for variable times at 14°C. After rinsing, BC somata were isolated and prepared for analysis on SDS-polyacrylamide gels. For about 30 minutes after the end of incubation no ELH could be detected in the electrophoretic gels. Instead, a prominent peak of radioactivity at 25000 daltons was found. Between 30 and 50 minutes of rinse the 25000 dalton peak disappeared and simultaneously an ELH peak appeared. Subsequently the ELH peak persisted but gradually grew smaller. This apparent conversion of a 25000 dalton precursor into ELH was quantitative in terms of total radioactivity. It could be prevented for up to 90 minutes by rinsing at 4°C. Inhibition of protein synthesis during the rinse with anisomycin (18 μM) had no effect on the conversion. These data and the results of additional studies employing subcellular fractionation are interpreted to indicate: 1) that ELH is synthesized as a larger molecule and then broken down into 6000 dalton units, 2) that the 30 minute latency between synthesis and conversion is an expression of a transport process within the cell body, and 3) that the slow decrease in ELH in the BC somata after conversion is the result of export of the hormone to the sites of release. This research was supported by an NIGMS postdoctoral fellowship and grants from NINDS and NASA.

CONTROL OF SPIKE GENERATION IN PYRAMIDAL TRACT CELLS OF THE CEREBRAL CORTEX. T. Arikuni* and S. Ochs., Department of Physiology, Indiana University Medical Center., Indianapolis, Indiana, 46202.

Upon electrically stimulating the cortex with a brief pulse direct cortical responses (DCR's) are recorded a short distance away. It had been shown that axons in the molecular layer are excited which synapse on apical dendrites to generate the response. Spatiotemporal interaction studies have suggested that the responses in the distal apical dendrites decrement down to the spike generating region in the axon. A relatively long-lasting period of occlusive-like unresponsiveness lasting up to about 20 msec was shown for extracellular responses of cells in the cortex and in some intracellularly recorded cells non-summating depolarizing potentials were found (Phillis and Ochs, J. Neurophysiol. 34; 374, 1971). In the present study identified pyramidal tract (PT) cells were investigated with microelectrodes for their intracellular responses to antidromic and surface cortical stimulation. A slow depolarizing potential (SDP) was found in the somas which was graded in amplitude depending on the strength of stimulation of the cortex or of the pyramidal tract. This gave rise to single spikes or in some cases a series of spikes at higher stimulation strengths. The SDP did not show summation in spatiotemporal interaction studies using two cortical sites. The occlusive period lasted up to about 20 msec. These SDP's appear to be generated in the dendrites as shown by a spatiotemporal interaction of antidromic and orthodromic stimulated responses. An early antidromic spike with fixed latency was elicited by antidromic stimulation with a later spike having a variable latency identified as an orthodromic response in the cell, possibly arising from the soma or nearby dendrites.

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LOCAL INFLUENCES OF AUTONOMIC IMBALANCE ON CARDIAC FUNCTION. J.A.Armour, D.B. Lippincott* and W.C. Randall. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Stimulation of sympathetic efferent cardiac nerves is known to augment heart rate and regional cardiac force in the atria and ventricles. Stimulation of the ventrolateral cardiac nerve (VLCN) near the middle cervical ganglion augments particularly the posteriolateral left ventricle with little influence on HR. However, stimulation of the anatomic extension of this same nerve at the pericardial level often elicits bradycardia and even decreased contractile force in some myocardial segments, demonstrating the presence of vagal efferent fibers at this level. At the mid pericardial level of the VLCN, stimulation results in marked arrhythmias which may be supraventricular in origin, which are atropine sensitive, and which can drive the heart rate to over 300 beats per minute. Stimulation of the VLCN after it passes onto the ventricle augments the posteriolateral force of contraction with minimal influence on heart rate. The dysrhythmias and tachycardias induced by stimulation of the middle pericardial portion of the VLCN may be attenuated by vagotomy and/or stellatectomy; afferent stimulation of the severed pericardial VLCN will elicit a modified dysrhythmia. Autonomic neuronal regional imbalance which may incorporate central and/or peripheral mechanisms, appear to play an important role in the determination of cardiac rhythms and contractility.
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NEURONAL INTERACTIONS IN OPTIC NERVE IMPULSE PRODUCTION IN APLYSIA. Gerald Audesirk (intr. by Felix Strumwasser), California Institute of Technology, Pasadena, California 91109.

Compound action potentials, recorded by suction electrode from the optic nerve, occur spontaneously in the dark and can be elicited by illumination of the eye (Jacklet, 1969). The response to illimunation consists of an initial burst, followed by a slower rate of spikes which gradually changes into a pattern similar to, but at a higher rate than, the dark pattern. All spikes, in light and in dark, have much the same appearance, and little gradation of size is evident, except for some grading up in size during the "light on" burst. La^{+++}, which inhibits transmitter release in frog N-M junction (Miledi et al., 1966) and the inward Ca^{++} current in squid giant synapse (Miledi, 1971), blocks both the bursts which occur in the dark and those which are a slow effect of light, when applied in 0.1-4.5 mM concentration. Mg^{++}, in concentrations 2.5-3.5 normal, acts similarly to La^{+++}. Replacement of external chloride with acetate or propionate, which uncouples electrical junctions in the crayfish septate axon (Bennett et al., 1967), eliminates all spike activity for moderate periods, while leaving the ERG intact. The data suggest that all spikes observed are due to the action of a single population of axons in the optic nerve, those of electrically coupled secondary neurons. The primary photoreceptors would seem to be electrically coupled to these secondary neurons. The optic nerve population receives excitatory input via chemical synapses from a cell or group of cells which spontaneously discharge in the absence of external input, and which may also be photosensitive themselves. Supported by a predoctoral fellowship from NSF and by NIH Grant NS07071.

EFFECT OF FOOT PAD OCCLUSION ON FORELIMB BLOOD FLOW DISTRIBUTION. Carleton H. Baker. University of South Florida College of Medicine, Tampa, Florida, 33620.

A significant proportion of dog forelimb blood flow is believed to pass through A-V shunts in the foot pads. An attempt to ascertain the amount of flow through the pads and the vascular volume of the pads was made. Ten isolated dog forelimbs were perfused under conditions of controlled flow. Measurements were made during 1) a control period with blood flow at 51 ± 5 ml/min and perfusion pressure at 101 ± 6 mm Hg; 2) occlusion of the footpads; 3) reduction of flow so the perfusion pressure was at the control level. Occlusion of the footpads caused a 17% increase in resistance, markedly increased capillary filtration, increased RBC-^{51}Cr and albumin-^{125}I vascular volumes and reduction of PS (from ^{86}Rb extraction) and filtration coefficient (K) to 24% and 71% respectively of control. Following reduction of flow during the occlusion the resistance was 37% above control, net capillary filtration was near control levels and vascular volumes reduced. PS decreased to 58% of control while K increased to 123% of control. The data indicate that foot pad occlusion causes blood normally flowing through the A-V shunts of the pads to be redistributed to a vascular area having a greater capacity than the pads. The data would also suggest a markedly elevated capillary pressure. Lowering the limb blood flow to control perfusion pressure levels indicated that approximately 22% of the total limb flow passed through the pads. The vascular capacity of the pads was an extremely small part of the total limb capacity. (Supported by USPHS Grant HE - 11966.)

MICROVASCULAR HYPERSENSITIVITY - HYPERREACTIVITY IN ESSENTIAL HYPERTENSION. T.A. Balourdas, Howard Univ. Medical School, Washington, D.C.

The puzzling pathogenesis of Essential Hypertension is an unsolved scientific and social problem of prime medical interest. The present investigations undertaken to elucidate this problem are pertinent to hypersensitivity-hyperreactivity of the mesoappendiceal and retinal microvessels of the spontaneously hypertensive rats (NIH breed of Japanese origin); the direct biomicroscopy and the retinal fundus ophthalmoscopy were used for direct visualization of the capillary vessels and their reactivity. Results. The capillary pattern was excellent without any structural lesion in all in vivo 12 experiments. No microangiopathy, no retinopathy was observed. The microvascular hypersensitivity evidenced by the Epinephrine threshold test on the arteriolar-precapillary sphincters was found very high from the average normal $1{:}4 \times 10^{-6}$ up to $1{:}Q2 \times 10^{-9}$ and $1{:}0.1 \times 10^{-9}$ Epinephrine Threshold Concentration. The retinal hypersensitivity was found lower. The findings are indicative of vascular hypersensitivity. The hypersensitive microvessels become hyperreactive to endogenous or exogenous vasoactive angiotropic agents as catecholamines, steroids, polypeptides, etc. Hence, permanent generalized vasoconstriction, increased peripheral resistance and hypertension. The results indicate that the multi-causal vascular hypersensitivity-hyperreactivity (hereditary, acquired) might be the pathogenetic aetiology of essential hypertension and the common denominator of all forms of hypertension (cf. References: T.A. Balourdas, (1) Fed. Proc. 28:682, 1967, (2) Proc. IV Internat. Congress on Pharmacology, July, 1969, Basel, Switzerland, (3) Circulation, XLII :III - 133, 1970, (4) Proc. XXV Intern. Congress of Physiological Sciences, July, 1971, Munich, Germany).

COMPARATIVE EVALUATION OF METHODS FOR ESTIMATING PULMONARY EXTRAVASCULAR FLUID VOLUME. N. Banchero, P.D. Miller*, M.H. Gee* and M. Pomerantz*. University of Colorado School of Medicine, Denver, Colorado.

The volume of pulmonary extravascular fluid (PEFV) estimated using thermodilution is larger (Fed. Proceed. 30:379, 1971) than the PEFV estimated by others using tritiated water (THO). In this study PEFV was estimated in a group of 8 dogs using cold saline--negative heat--(T°) and THO as diffusible indicators and Cardiogreen^{R} (CG) as the non-diffusible indicator. In 4 dogs transthoracic electrical impedance was measured throughout the experiment (Minnesota Impedance Cardiograph). Changes in blood temperature (thermistor) and changes in CG concentration in whole blood (Waters densitometer) were recorded continuously after appropriate analog computer correction for sampling distortion. PEFV was calculated from the difference in mean transit times ($\bar{t}$) of the two indicators multiplied by cardiac output ($\dot{Q}$). A rotating turntable was used to obtain serial blood samples in which total THO counts were measured and plasma CG concentrations analyzed spectrophotometrically. The average PEFV estimated by T°--CG was 4.73 ml/kg (range 2.96 to 7.08) as compared to 3.56 ml/kg (range 1.76 to 6.99) estimated by THO--CG. The difference in PEFV appears to be due to a smaller pulmonary fluid volume (PFV) estimated by THO associated with a larger "PBV". When measured simultaneously the average $\dot{Q}$ obtained spectrophotometrically (111.7 ml/min/kg) was significantly higher ($p<.001$) than the $\dot{Q}$ obtained densitometrically (95.7 ml/min/kg). Transthoracic electrical impedance (Zo) was inversely related to body weight. Zo was not related to PBV or PFV but smaller values of Zo were measured in dogs with greater PEFV.

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FACTORS DETERMINING HEPATIC CLEARANCE OF BILIRUBIN. J. L. Barnhart*, R. R. Gronwall, and R. Clarenburg*. Dept. of Physiological Sciences, Kansas State University, Manhattan, Kansas.

Hepatic clearance of bilirubin was investigated in isolated perfused rat livers. Media containing red blood cells, physiological buffer and 0.75, 1.5 or 3.0% bovine serum albumin were perfused at equal flow rates. After a priming period, bilirubin was continuously infused into media for 70 minutes at rates of 10, 35, 70 or 90 µg/min/100 g body wt. During the final 50 minutes, constant (submaximal) biliary excretion rates were established. At a given albumin concentration, bilirubin levels in the media were linearly proportional to infusion rates. A log-log relationship was found between albumin and bilirubin levels in the m dia, independent of infusion rate. All kinetics obeyed a single linear relationship between hepatic clearance and level of unbound bilirubin (found by ultracentrifugal analysis of media); a clearance constant was defined. Salicylate, added to perfusion media to compete with bilirubin for albumin binding, changed the unbound bilirubin level and hepatic clearance without affecting the clearance constant. Values of the hepatic clearance constant depend on specific conditions: rats of the same strain (Sprague-Dawley) obtained from different suppliers had significantly different clearance constants. (Supported in part by NIH Grant AM11384.)

MESENTERIC HEMODYNAMICS OF HEMORRHAGIC SHOCK IN THE BABOON. R. W. Barton*, D. G. Reynolds*, and K. G. Swan. Walter Reed Army Institute of Research, Washington, D. C. 20012

In a previous study (Gastroenterology 60: 805, 1971) we have shown that endotoxin shock in baboons is associated with hypotension, an unaltered mesenteric artery blood flow (MBF), decreased mesenteric vascular resistance (R), and a normal intestinal appearance despite significantly elevated plasma catecholamines. These findings contrast the canine shock model and, thus, challenge the target organ theory. To further assess this theory hemorrhagic shock was studied in baboons in which the development of hypotension was controlled to parallel that of endotoxin shock. MBF was measured electromagnetically: arterial (AP) and portal (PP) pressures were recorded. R was calculated from these parameters. Plasma catecholamines were measured fluorometrically. AP fell gradually from 122 $\pm$ 3 (S.E.) to 47 $\pm$ 3 mm Hg ($p < 0.005$) within two hours. MBF fell in parallel with AP from 186 $\pm$ 24 to 38 $\pm$ 14 ml min^{-1} ($p < 0.005$) within two hours. Portal pressure declined gradually from 7.3 $\pm$ 0.5 to 6.0 $\pm$ 0.7 mm Hg ($p < 0.01$). Thus, R increased from 0.62 to 1.14 PRU. Norepinephrine increased from 0.66 $\pm$ 0.34 to 2.77 $\pm$ 1.22 μg L^{-1}. Epinephrine increased from 0.26 $\pm$ 0.10 to 5.83 $\pm$ 2.70 μg L^{-1}. Following reinfusion of the shed blood all parameters returned to control levels within 90 minutes. Although hypovolemia induced mesenteric ischemia and a distinct increase in catecholamine concentrations, no gross pathological changes were observed in the splanchnic viscera and 80% of the shocked animals survived. Consequently,the validity of the gut being a "target organ" in irreversible shock is further questioned.

EARLY AND LATE EFFECTS OF GLUCAGON ON THE HEPATIC ARTERIAL AND VENOUS BEDS. F. A. Bashour, Aida Geumei, and A. G. Nafrawi. Cardiopulmonary Institute at Methodist Hospital and Univ. of Texas at Dallas, Texas.

Effects of intraportal (IP), intra-arterial (IA), and intravenous (IV) administrations of glucagon (GLU) on hepatic arterial (HA) and venous (PV) inflows were studied in anesthetized dogs using non-cannulating electromagnetic flow probes. Flow and pressures (portal vein, hepatic wedge and systemic arterial) were measured simultaneously, and vascular resistances calculated.

15 sec. after IA, GLU increased HA flow and decreased its resistance. This direct (early) effect was not affected by prior denervation or by Propranolol. GLU has no direct effect on PV flow or resistance, when given IP. The late (5 min.) effect of GLU on PV flow was secondary to its vasodilator effect on mesenteric vascular bed. 5 min. after 10γ/kg IV administration, HA and PV flows increased to 154% and 175% respectively (control=100%). This effect was more evident in constricted vessels.

Glucagon possesses a direct effect on HA bed. The hormone may be useful in conditions where potential danger of diminished hepatic blood flow exists.

ISOLATED ADRENAL CELLS: STEROIDOGENESIS AND CYCLIC AMP ACCUMULATION AFTER EXPOSURE TO VARIOUS DOSES OF ACTH. Robert J. Beall* and George Sayers, School of Medicine, Case Western Reserve University, Cleveland, Ohio, 44106

Cyclic AMP has been determined by a competitive protein binding method (Gilman, PNAS 67, 305, 1970) and by incorporation of adenine-8-^{14}C (Kuo and DeRenzo, JBC 244, 2252, 1969). Alterations in concentration of cAMP and of B in the cell suspensions exposed to various doses of ACTH may be described as follows: 1) low doses of ACTH (5 to 25 μU) added to suspensions of isolated adrenal cells stimulate steroidogenesis without detectable changes in the concentration of cyclic AMP; 2) intermediate doses (50 to 250 μU) induce increases in cyclic AMP and B accumulation; 3) large doses (250 to 10,000 μU) result in additional increases in cyclic AMP accumulation without further increase in B accumulation. Theophylline added in combination with low doses of ACTH did not enhance steroidogenesis nor result in significant cyclic AMP accumulation. The results at intermediate and large doses of ACTH are in line with the "second messenger" role for cyclic AMP. The results at low doses do not exclude the intervention of cyclic AMP. Increases in cyclic AMP, too small to be detected by the analytical methods employed, may stimulate steroidogenesis. Kuo and DeRenzo (JBC 244, 2252, 1969) suggest that only a small fraction of cellular cyclic AMP, localized in a specialized compartment, is actually involved in mediating hormone action. On the other hand, ACTH may have two modes of action, one on adenyl cyclase, the other on Ca^{2+} movement into the cell. This would correspond to the situation in skeletal muscle where low doses of isoproterenol stimulate phosphorylase a formation without an associated increase in cyclic AMP; relatively large doses stimulate phosphorylase a formation and increase cyclic AMP accumulation (Stull and Mayer, Fed. Proc. 1971 Abst. 142).
NSF GB 27426

INTRARENAL VASCULAR DISTRIBUTION AND CONSTRICTOR REFLEX MECHANISMS. O. Beaty*, C. H. Sloop*, G. S. Malindzak, Jr., and H. E. Schmid, Jr. Bowman Gray School of Medicine, Winston-Salem, N. C., 27103.

Studies designed to investigate the existence of renal vascular connections between parts of the same kidney and possible intrarenal reflex constrictor mechanisms were carried out in anesthetized dogs possessing two separate renal arteries to a single kidney. Blood flow (BF) was measured in each renal artery supplying the single kidney preparation with a dual channel electromagnetic flowmeter. Each artery had a needle inserted distal to probes. Injection of 0.1 cc of air into either of the two arteries produced a reduction of BF to zero lasting about 30 secs, which slowly returned to pre-injection control levels in about 4 mins. BF through the non-injected artery during this time remained unchanged. Alpha adrenergic blockade (dibenzyline) failed to prevent the cessation of BF following intra-arterial injection of air. A slight overshoot was observed in BF during the recovery phase. The injection of 0.2 and 0.4 mg nitroglycerin into either artery increased BF in only the artery in which nitroglycerin was injected. Angiotensin (250 - 500 ng) reduced BF in only the injected artery. In a single experiment in an animal with known chronic renal disease, some intrarenal cross circulation was observed, suggesting that collateral circulation may be present in the diseased kidney secondary to circulatory abnormalities.

Conclusion: These experiments appear (a) to support the evidence against intrarenal vascular coupling in the normal kidney and (b) to disprove the existence of an intrarenal reflex constrictor mechanism. (Supported by NIH grants H-487, HT-344, HT-5392 and North Carolina Heart Association.)

A STUDY OF PATHWAY FOR THE POSTPRANDIAL COORDINATION BETWEEN ELECTRIC ACTIVITIES OF ANTRUM AND DUODENUM. B. S. Bedi* and C. F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Allen et al (Am. J. Physiol., 207:906, 1964) showed, in dogs, a relationship between antral pacesetter potentials and the duodenal action potentials after feeding. The purpose of our study was to investigate the pathway of this coordination. Three mongrel dogs were used. Monopolar silver-silver chloride electrodes were implanted on the serosal surface of the stomach and duodenum. The electric activities were recorded simultaneously from the antral and duodenal electrodes in fully conscious dogs. After a control study, the gastroduodenal junction was divided and the continuity reestablished by end-to-end anastomosis of the mucosa only. A method of cross-correlation was applied to the electric recordings obtained before and after the transection of gastroduodenal junction to define duodenal-antral relationship. The relationship between antral and duodenal electric activities found by Allen et al, and confirmed by our data, was lost after transection of the gastroduodenal junction. Radiographic and gastric emptying time studies showed no obstruction at the area of transection. The results of our experiments show that the coordination of the electric activities in the antrum and duodenum is accomplished by messages transmitted via neural or muscular elements in the wall of the gastroduodenal junction. (Supported in part by NIH Grant AM-2015.)

RADIOIMMUNOASSAY OF PROSTAGLANDINS. Harold R. Behrman * (intr. by A.C. Barger). Harvard Med. School, Boston, Mass.

A radioimmunoassay has been developed which permits measurement of picogram amounts of prostaglandins (PG) F, E, A and B. $PGF_{2\alpha}$, PGE_1 and PGB_1 were conjugated to fatty acid free-bovine serum albumin with 1-ethyl-3(3-dimethyl-aminopropyl)-carbodiimide HCl and administered separately to 3 New Zealand white rabbits. About 0.5 mg of conjugated PG mixed with equal parts of complete Freund's adjuvant was injected (s.c.) weekly for 4 consecutive weeks and every 1-2 months thereafter. Blood was collected from the ear artery (50-60 cc) every 2-4 weeks, the serum (A/S) isolated, lyophilized and tested for cross-reactivity. A/S raised to $PGF_{2\alpha}$ did not bind PGE_1, PGE_2, PGA_1, PGB_1, arachidonic acid, estradiol-17β, cholesterol or a mixture of phospholipids but bound $F_{2\alpha}$ and $F_{1\alpha}$ equally well at equivalent concentrations. A/S raised to PGE_1 had a 3-fold greater affinity for PGA_1 than PGE_1, but did not bind $PGF_{1\alpha}$. A/S diluted with phosphate buffer (0.01M; pH 7.4) containing 0.1% gelatin, 10^{-3}M EDTA and .01% thimerosol (PBG) was added to tubes containing PG standards and incubated at room temp. for 30 min. High specific activity ^{3}H-PG dissolved in PBG was added and the samples incubated for 2-24 hours at 4°C. Following addition of PB containing 0.5% gel, a solution of charcoal-dextran (.25-.025%) in PB was added, centrifuged and the supernatant fraction counted. Duplicates varied less than 5%, ether and silica gel blanks were 10 and 25 pg, respectively when the standard curve ranged from 0-200 pg. (Supported by NIH Grant 69-2214 and The Ford Foundation.)

EFFECTS OF HEART RATE AND LEFT ATRIAL PRESSURE ON THE STROKE VOLUME IN THE CONSCIOUS DOG. Vernon S. Bishop and Lawrence D. Horwitz*. The Univ. of Texas Med. School at San Antonio, San Antonio, Texas.

The effects of tachycardia on the maximum stroke volume at the plateau of the ventricular output curve were studied in five chronically instrumented dogs. Tachycardia, produced by acute vagal blockage, increased the heart rate to an average of 199 ± 16 (SE) beats/min from an average resting rate of 97 ± 12 beats/min. Resting ventricular output increased from an average of 103 ± 12 to 128 ± 28 ml/min per kg, whereas the stroke volume decreased as a linear function of the increase in heart rate. The plateau of the ventricular output curve increased from an average control level of 217 ± 25 to an average of 297 ± 35 ml/min per kg with the tachycardia produced by vagal blockage (P 0.001). The average peak stroke-volume response at the peak of the ventricular output curve during acute vagal blockage was not significantly different from the average peak stroke-volume response attained during control ventricular output curves. The maximum stroke volume attained by acute loading was not influenced by the changes in heart rate encountered in this study. (Supported in part by PHS, NIH Grant 5 R01 HE 12415-03 and Air Force Grant AFOSR-71-2074.)

THE BARNACLE MUSCLE FIBER AS A MODEL FOR INVESTIGATING THE MECHANISM OF ACTION OF DILANTIN. E. Edward Bittar, Bo G. Danielson,* Edmund Tong* and Stephen Chen,* Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Earlier experiments based on the microinjection technique showed that the efflux of radiosodium is greatly reduced by 10^{-4} M ouabain and that lowering the external pH following inactivation of the ouabain-sensitive component results in a marked rise in Na* loss. In contradistinction to ouabain, 10^{-4} M dilantin produces a smaller inhibiting effect which seems to be limited to the ouabain-insensitive Na efflux. Like ouabain, however, internally applied dilantin is without effect on the Na efflux. Additional experiments were done to determine whether dilantin acts on the proton-sensitive component of the pump. 10^{-4} M dilantin is found to prevent the Na efflux from rising following acidification of the bathing medium. When applied externally following stimulation of the Na efflux by adding protons to the external medium, 10^{-4} M dilantin causes a large reduction in Na loss. Subsequent addition of hydroxyl ions results in a further small reduction in the Na efflux, indicating that the blocking action of dilantin is not complete. The provisional conclusion from this work is that ouabain and dilantin do not act at the same site and that dilantin has the ability to reverse the stimulating action of protons (or pCO_2) on the Na pump.

(Supported in part by grants from the Graduate School Research Committee, the Wisconsin Heart Association, the Office of Naval Research and the Swedish Medical Research Council.)

COMPARATIVE STUDIES OF GLUCOCORTICOID EXCRETION IN LABORATORY RATS AND GUINEA PIGS EXPOSED TO HIGH ENVIRONMENTAL PRESSURES. R.A. Bitter and T.W. Nielsen (intr. by H.E. Ederstrom). Dept. of Physiology and Pharmacology, School of Medicine, U. of N. Dak., Grand Forks, N. Dak. 58201

Urinary excretion of adrenal cortical hormones was used as an index of stress in laboratory rats and guinea pigs. Experiments were conducted on two strains of adult male rats (Sprague-Dawley, and Holtzman, 250-400 gm) and English short hair guinea pigs (400-600 gm). Twenty-four hour urine samples were collected during control periods in room air (1 ATA) and during exposure to He-O_2 (80-20% at 1 ATA). The animals were then exposed to He-O_2 mixtures at 5, 10, 20, and 30 ATA for 14 hours and were then staged decompressed. The partial pressure of O_2 was kept between 150-275 mmHg during experimental periods. Food and water were available ad lib, and chamber temperature was maintained within the He-O_2 comfort zone (29-30° C, 1 ATA). Unconjugated urinary corticosterone or cortisol, expressed as μg/24 hr. sample was analyzed fluorometrically. Increase pressure showed increased glucocorticoid excretion in both rats and guinea pigs. Excretion values of corticosterone obtained from rats were 1.64 ± 0.25; 2.25 ± 0.48; 1.87 ± 0.31; and 2.71 ± 0.31 at 5, 10, 20 and 30 ATA, He-O_2. Increases in cortisol excretion of 21, 24, 48, and 54%, respectively, were obtained from guinea pigs. Statistically significant differences were found between N_2-O_2 and He-O_2 control samples in rats but not in guinea pigs. Six hour guinea pig samples taken throughout the 24 hour cycle indicated that the greatest excretion was during the decompression phase. Supported in part by ONR Contract No. N00014-68-A-0499.

BEHAVIORAL EVIDENCE FOR EXTRAOPTIC ENTRAINMENT IN APLYSIA. Gene D. Block, (intr. by M. E. Lickey). University of Oregon, Eugene, Oregon 97402

Locomotor activity in Aplysia is predominantly diurnal (Kupfermann, Physiol. Behav., 1968). I have found that Aplysia with their eyes surgically removed will remain diurnal and will successfully phase shift to a new light schedule. This behavioral evidence of extraoptic entrainment is consistent with the findings of Lickey et al. (Fed. Proc., 29, 70, 325Abs) who demonstrated extraoptic entrainment of a circadian rhythm in a single neuron of the isolated abdominal ganglion. The eyes of six adult Aplysia were removed and the time of dawn advanced from 2:30 A.M. to 10:30 A.M. (Light:Dark, 12 hr.:12hr.). Locomotor activity was detected by means of plastic rods suspended in individual 15 gallon aquaria and activity records were generated on an Esterline-Angus event recorder. Temperature was constant at 14.5±0.25°C. Eyeless Aplysia, like normals, will shift the onset of locomotor activity by 8 hrs. in response to an 8 hr. shift of light onset. Comparison of preoperative and postoperative activity records revealed two differences: (1) there was a decrease in total locomotor activity after eye removal and, (2), an increase in occasional nocturnal activity. Both of these phenomena, however, have been observed to occur "spontaneously" in intact animals maintained for similar extended periods, and may not distinguish between normal and eyeless animals. Electrophysiological recordings from the isolated nervous systems of these same eyeless Aplysia indicated an off response to light in the posterior pedal nerves that serve the foot. This suggests that photoreceptors in the ganglia may be sufficient for behavioral entrainment. (Supported by NS 07458).

CHANGES IN ANTIDIURETIC HORMONE CONCENTRATION INDUCED BY VERATRIDINE. Gary C. Bond,* and Kenneth L. Goetz. St. Luke's Hosp. and St. Luke's Fndn. for Med. Educ. and Res., Kansas City, Mo. 64111.

The diuresis produced by the intravenous injection of veratridine may be caused by a reflex decrease in antidiuretic hormone (ADH) levels elicited from cardiac receptors. (Thomas, S. Quart. J. exp. Physiol. 52: 313, 1967). To evaluate this possibility, we studied the effect of veratridine (~6μg/kg, iv) on plasma ADH levels and renal function in anesthetized dogs. Blood for ADH determination was withdrawn 5 min prior to veratridine administration and 5, 20, and 60 min after injection of the drug. Urine was collected at 10 min intervals. Results: Veratridine injection produced transient hypotension and bradycardia in all experiments. Plasma ADH levels were elevated 5 min after veratridine administration. The 20 and 60 min values did not differ from control levels. Urine flow, after an initial slight decrease, gradually rose to a peak at 40 and 50 min and then decreased slightly. Sodium excretion increased continuously throughout the experiment. The increase was due, at least in part, to the continuous saline infusion the animals received. Glomerular filtration rate declined during the first 10 min after veratridine injection but by 20 min was elevated above control. During the remaining 40 min, glomerular filtration rate decreased toward control values. The results of this study demonstrate that plasma ADH values are not decreased by the intravenous administration of veratridine. Consequently the modest increase in urine flow observed in these experiments cannot be attributed to alterations in the plasma concentration of ADH. (Supported by USPHS grant HE 13623).

PEAK AORTIC POWER OUTPUT IN RELATION TO MYOCARDIAL CONTRACTILITY, M. N. Boone*, M. G. Gerin* and D. A. McDonald, University of Alabama in Birmingham, Alabama 35233.

It would be desirable to have an index of the functional state of the myocardium that does not necessitate invading the ventricle. The use of on-line computers allows the continuous monitoring of power output from measures of aortic pressure and flow. In a series of anesthetized (morphine-chloralose) open-chest dogs we have studied the changes in peak power throughout variations of ventricular function without changes in contractility. Aortic flow was recorded electromagnetically (Medicon meter); aortic and left ventricular pressures (also end-diastolic pressure at higher gain) were recorded with Statham gauges and in some animals the intraventricular diameter was monitored with a mechanical (Pieper) gauge; the EKG was recorded from intracutaneous electrodes. Records were stored on magnetic tape and analyzed with a digital (PDP-7) computer which also calculated external power and work and the rate of change of L.V.P. (dP/dt) (and when recorded ventricular diameter was converted to volume, assuming a spherical cavity). Heart rate was stabliized by bilateral vagotomy and stellectomy and in some cases controlled by infusions of ACh or physostigmine into the sinus node artery. The maximum ventricular dP/dt was used as a qualitative index of myocardial contractility. At steady heart rates it was found to be constant with changes of after-load unless the initial aortic pressure was low. With the infusion of inotropic agents it showed appropriate increase which was apralleled by the peak power. The effects of changing pre-load (volume infusions) and heart rate as independent factors have also been studied. (Supported by NIH grant HE-11310-03-04 and International Fellowship to M. G. Gerin 5-F05-TW-1506).

EFFECT OF CHRONIC IMMOBILIZATION UPON GLYCOGEN CONTENT AND METABOLIC CAPACITY OF RAT SKELETAL MUSCLE, Frank W. Booth (intro. by Henry B. Hale), Environmental Systems Branch, USAF School of Aerospace Medicine, Brooks AFB, Texas.

Differences in the changes in skeletal muscle resulting from denervation or from disuse (with the nerve intact) have been emphasized by Gutmann (Rev Canad Biol 21:352, 1962 and Physiol Bohemoslov 18:177, 1969). Because of these reported differences, the following information was collected from rats treated with plaster casts on both hind limbs to limit usage of ankle, knee and hip joints.

Male albino rats weighing about 300g were placed into a control (CON) group or a casted (CAS) group for a period of 4 weeks. Terminally, the weights of the plantaris, soleus and gastrocnemius muscles of CAS each amounted to about 50% of those of the corresponding muscles from CON ($P < 0.001$) while the rectus femoris of CAS was about 70% of CON ($P < 0.001$). Despite pair-feeding CAS lost 36g and CON gained 53g during the 4 week study. Adrenal weights did not differ significantly between CAS and CON. The glycogen concentration in the soleus was twice as high in CAS as in CON ($P < 0.05$), although nonfasting serum glucose concentrations were not significantly different. O_2 uptake of gastrocnemius muscle mitochondria in a solution containing excess ADP and glutamate was about 50% lower for CAS (58 µl O_2/mg mitochondrial protein/hr) than for CON (102 µl O_2/mg mitochondrial protein/hr) ($P < 0.05$).

These findings in muscle atrophied through disuse by immobilization are similar to those reported for atrophy occurring in skeletal muscle after denervation.

CHANGES IN LEFT VENTRICULAR FUNCTION DURING INJECTION OF OPAQUE CONTRAST MEDIUM. A. A. Bove, R. E. Sturm*, H. C. Smith*, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

Left ventricular volume and dimensions were measured using a video-computer image processing system to analyze biplane x-ray images of the left ventricle (LV) opacified with opaque contrast material by injections of renovist made over 4-5 heart cycles at a rate of 5.77 ml/second and volume of 0.834 ml/kg. In four dogs studied, end-diastolic and end-systolic volume increased during contrast injection. Values for stroke work and stroke power increased during the injection, and before the remaining contrast was washed out of the LV. A rise in LV systolic and end-diastolic and aortic systolic and diastolic pressures occurred during the injection and a fall in aortic pressure was noted beginning at the 4th and 5th beat after end of injection. The rise in aortic systolic pressure was probably due to a 9% increase in stroke volume (SV) during contrast injection even though this change in SV was below the significance level statistically. ST-T changes were noted in the ECG beginning at the 4th to 5th beat post injection. A contrast media which did not produce ST-T changes or hypotension causes the same volume related changes in LV function. Evaluation of LV function from angiograms must take into account changes due to the added volume load on the LV in addition to the effects of contrast material on the myocardium and peripheral circulation which have been noted previously by others.
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RESPONSE CHARACTERISTICS OF SKIN MECHANORECEPTORS IN CATFISH. A.C. Brown, M.A. Biedenbach, and C.F. Stevens*, Department of Physiology and Biophysics, University of Washington, Seattle, Washington 98105.

The somatosensory system in catfish (Ictal. nebul.), in addition to its usual functions, is essential for survival since this species finds food not by sight but by direct contact. First order afferent input is relatively easy to record from intracranial ganglion cells, obviating microdissection of single axons. In anesthetized fish, unit potentials were recorded from the ganglion of n.5 and n.7, which supply the head region and the barbels. Response properties of mechanosensitive neurons to mechanical stimulation with step, sine wave, and ramp functions were determined. The receptor population was divided into 3 groups. In the first group, "position" neurons were excited by displacement of a barbel from resting position. Firing frequency was, within limits, proportional to amplitude of displacement. For a given maintained displacement, the initial firing level decreased to a slightly lower tonic level. These neurons "followed" sine wave stimulation from low frequencies ($<$ .1 Hz) to approximately 15 Hz. The remaining two groups had small receptive fields on the skin, one rapidly, the other slowly adapting to maintained mechanical displacement. Rapidly adapting neurons depended for excitation on minimal rate of skin displacement; observed threshold rates ranged from 1-15 u/msec. They followed sine wave stimulation from approximately 2-100 Hz. A maximal number of unit potentials per cycle occurred usually at an intermediate frequency. Slowly adapting units displayed transient and tonic properties and followed sine waves from low frequencies ($<$ .1 Hz) to approximately 100 Hz.

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CHARACTERISTICS AND EXPERIMENTAL MODIFICATION OF BRAIN TRYPSIN-LIKE ENZYME ACTIVITY. George F. Buletza, Jr.*, and W. B. Quay. Department of Zoology, University of California, Berkeley, California.

Trypsin-like proteinase activity and an inhibitor of this activity are demonstrable in homogenates of mammalian brain regions, and are being investigated by means of microfluorimetry (Buletza, G. F., Jr. and W. B. Quay, Trans. Am. Soc. Neurochem. 1, 29 (1970)). Stabilization of even low concentrations of standard (bovine) trypsin solutions is obtained by heating for 3 min at 45° C in .05 M Tris (pH 7.8) in 20% tert-butanol containing 10% acetonitrile (= TBA). Synthetic substrate, N$^{\alpha}$-carbobenzoxydiglycyl-l-arginyl-2-naphthylamide (= GGANA), is dissolved also in TBA at 45° and has excellent stability at room temperature. The use of TBA abolishes the action of trypsin inhibitor in rat brain homogenates and with substrate concentrations as low as 50% of optimal. A doubled rate of hydrolysis of GGANA by rat brain homogenates at pH 7.4 and 45° occurs with TBA. Addition of Ca++ results in reduction in the rate of hydrolysis, with or without TBA, for all brain regions studied. Rat brain trypsin-like activity is stable at room temperature in supernatant fractions of homogenates in TBA for at least three weeks. Particulate fractions of rat brain homogenates do not hydrolyze GGANA after extraction with 20% TBA. Vascular perfusion with isotonic NaCl before autopsy did not lead to any detectable change in trypsin-like activity of homogenates from six brain regions. Therefore, blood content of the homogenates is believed to be insignificant as a possible source of the enzyme activity. Preliminary results from rabbit brain regions show a trypsin-like activity twice that of rat brain regions, but the relative activities according to brain region are the same: caudate nucleus>occipital cerebral cortex=optic tectum=cerebellar hemisphere>hypothalamus=medulla.

HYPOCALCEMIC AND NATRIURETIC RESPONSE TO SALMON AND PORCINE CALCITONIN IN BABOONS. R.J. Burnett*, R. Osborne*, H.D. Copp, and C.C. Gale. Dept. of Physiol. Biophys., Reg. Prim. Research Ctr., Univ. of Wash., Seattle, Wash., and Dept. of Physiol., Univ. of Brit. Col., Vancouver, B.C.

Calcitonin, the hypocalcemic hormone, was discovered by Copp in 1962. Recent evidence indicates that calcitonin may exhibit species potency variation, and, further, may cause natriuresis. The present experiments were undertaken to study the hypocalcemic and natriuretic action of salmon (SCT) vs porcine (PCT) calcitonin in conscious baboons. SCT and PCT was injected i.v. in doses of 0.1, 1.0, and 5.0 MRC units/kg in male adolescent baboons via indwelling catheters. In certain experiments glomerular filtration rate (GFR) and renal plasma flow (RPF) were determined by inulin and PAH clearance. The hypocalcemic response to SCT described a log dose response curve with maximum declines of 0.6, 1.5, and 2.4 mg% in serum calcium within 1 to 4 hrs after injection. In contrast, PCT did not produce a log dose response; at all 3 dose levels, serum calcium fell 1.0 mg%. The natriuretic action of SCT and PCT was studied at 1 and 5 MRC units/kg. At both dose levels, SCT produced a marked sodium diuresis. Urine excretion rose from control level of 32 ± 7 μEq/min to 87 ± 17 μEq/min for 2 hours post-injection. At the higher SCT dose, the natriuresis persisted for an additional 2 hrs. PCT administered at 5 MRC units/kg caused a comparable natriuresis for 30 min post-injection, but then declined. 1 MRC unit/kg of PCT caused a smaller response. The natriuresis following SCT was accompanied by slight rises in GFR, from 32 to 35 mls/min, and in RPF, from 183 to 195 mls/min. These data establish a greater hypocalcemic and natriuretic potency for SCT, as compared to PCT, in baboons, and further suggest a direct effect on the renal tubule. NIH grants NB 06626, FR 00166

CEREBRAL TISSUE GAS TENSIONS B. Burns* and G. Gurtner Dept. Env. Med. Johns Hopkins Univ., Baltimore, Md. 21205

Tissue gas tensions (P_tCO_2 and P_tO_2) in cats were obtained by inserting into the cortex a small diameter (300 μ), membrane-tipped probe connected to a mass spectrometer. The half-time for response of the system was 6 seconds. Tensions of CO_2, O_2 and the inert gases (Argon, N_2O and N_2) were measured after long equilibration with inert gas - O_2 mixtures. Tissue tensions of the inert gases were similar to blood; O_2 tensions ranged from 2 to 40 mm Hg; tissue pCO_2, however exceeded what would have been predicted on the basis of the metabolic rate and diffusivity of CO_2 in brain tissue. Cortical P_tCO_2 at a depth of 2-3 mm averaged 90 mm Hg in the normocapnic subject. The magnitude of the difference between tissue and arterial CO_2 tension (ΔPCO_2) was proportional to both arterial $[H^+]$ and P_aCO_2, with ΔPCO_2 decreasing from a maximum of 100 mm Hg to approximately 10 mm Hg at the lower arterial $[H^+]$ and CO_2 tensions. The observed values of P_tCO_2 would lead to a predicted tissue pH of 6.89 in the normocapnic subject. A hypothetical mechanism capable of transporting CO_2 against an apparent concentration gradient has been proposed which postulates that the CO_2 difference can be explained by a rapid movement of H^+ ion from plasma proteins toward a negatively charged capillary wall and a slower repulsion of HCO_3^- resulting in transient production of CO_2 in the wall phase of capillary plasma which acts as a back-pressure to the free diffusion of CO_2 out of the tissue (Gurtner, et al., Resp. Physiol., 7:173-187, 1969). Regulation of the magnitude of ΔPCO_2 may be a physiologically important mechanism for maintaining a relatively constant brain P_tCO_2 during fluctations in blood acid-base conditions.

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EFFECT OF GASTRIN ON INTESTINAL ABSORPTION OF GLUCOSE. Louis J. Bussjaeger*, Gilbert A. Castro* and Leonard R. Johnson. Univ. of Okla. Med. Ctr., Oklahoma City, Okla.

An *in vitro* tissue accumulation method was used to investigate the effects of gastrin on the transport of glucose by strips of hamster intestine. Small intestinal strips prepared from fasted hamsters were incubated in Krebs-Ringer Bicarbonate buffer containing glucose (2.8 mM) with or without pentagastrin (1.0 µg/ml). The amount of substrate removed from the incubation medium and the amount accumulated by the tissue were measured. Gut tissue incubated in the presence of gastrin accumulated glucose to a significantly lesser degree than untreated controls (20% less glucose) in the middle segments of the intestine. Experiments using galactose are in progress to determine whether this effect of gastrin is due to an inhibition of transport processes *per se* or to enhanced catabolism of intracellular glucose.

Supported by NIH Grant #R01 AM14392 and NIH Training Grant AM 05179 and PHS Research Grant #A109348 from NIH (NIAID)

TRANSIENT SURGES OF LH RELEASE IN OVARIECTOMIZED SHEEP. W. R. Butler*, D. J. Bolt*, and P. V. Malven. Purdue University, Lafayette, Indiana.

Levels of LH were measured by radioimmunoassay in jugular venous (V) and carotid arterial (A) plasma samples collected from indwelling cannulae pre- and postovariectomy in ewes. Blood was collected from both cannulae every 15 minutes for periods of at least 3 hr on several days. LH concentrations in "A" samples reflected the body pool concentration while that in "V" samples was the net result of the "A" concentration *plus* LH release by the pituitary *minus* cranial uptake of the hormone *plus* influx of LH from the extravascular spaces of the head. Cranial output (CO) was defined as "V" minus "A" levels in ng LH/ml and reflected both pituitary release and equilibration between arterial LH levels and the extravascular spaces of the head. Ewes ovariectomized at least 3 weeks usually exhibited transient surges of LH release at about hourly intervals (range of 45 to 75 min) which caused "A" levels to fluctuate widely (5 to 35 ng/ml). The LH surges were usually reflected as large CO values, but on occasion an increased CO was absent when "A" levels were sharply increased. It was concluded that LH release by the pituitary occurred in transient surges of such short duration that a surge could occur and the large CO be undetected in the 15 minute interval between samples. The largest CO observed was 56 ng/ml. Two ewes were sampled before ovariectomy. One ewe with anovulatory ovaries exhibited surges of LH in "A" occurring at 2 hour intervals (0.6 to 3.3 ng/ml). One week after ovariectomy the surges occurred hourly and "A" levels of LH were elevated (1.2 to 5.3 ng/ml). One ewe with a midcycle CL showed a low and stable LH level (0.3 to 1.6 ng/ml) which after ovariectomy changed to hourly surges and elevated levels (2.6 to 6.0 ng/ml). It is concluded that LH in ovariectomized ewes is released in large transient surges lasting less than 15 min and occurring at about hourly intervals.

RADIOIMMUNOASSAY OF PLASMA CORTICOTROPHIN IN NORMAL MALES AND FEMALES. Bonnalie O. Campbell, Carolyn Leach* and Harry S. Lipscomb. Departments of Biochemistry and Physiology, Baylor College of Medicine, Houston, Texas.

Immunoreactive adrenocorticotrophic hormone (ACTH) in human venous plasma was measured directly using the method described by Donald (J. Clin. Endocrinol. Metab. 32,223, 1971). Two ml duplicate samples of plasma and standards (Lerner human ACTH) were extracted and assayed. Rabbit anti-human ACTH serum (The Wellcome Research Laboratories) was used at a final dilution of 1:30,000. The ^{125}I human ACTH, S.A. 300-500 μCi/μg, was repurified prior to use. Plasma ACTH levels were determined for 62 healthy employed males, ages 24-61, and 25 females, ages 16-45. Samples from male subjects were obtained during routine physical examination at 7:45-8:40 a.m. Samples from 13 women were taken at 8:10-8:55 under identical conditions. Random samples from 12 employed women and students, ages 23-37, were obtained from 8:30-11:10. The mean immunoreactive level of plasma ACTH for the entire group of 87 subjects was 19.8 ± 1.73 pg/ml. The mean level of ACTH in the male subjects was 20.74 ± 2.31 pg/ml (range 0-120 pg/ml). The mean for all female subjects was 17.48 ± 1.92 pg/ml (range 6-40 pg/ml). When separated, the 8:10-8:55 female group showed a mean ACTH level of 20.46 ± 2.71 pg/ml (range 10-40 pg/ml) and the 8:30-11:10 random samples had a mean level of 14.3 ± 2.39 pg/ml (range 6-35 pg/ml). Samples obtained from the male group and the comparable female group (8:10-8:55) showed no significant differences. On the other hand, a significant difference existed between the 8:10-8:55 and 8:30-11:10 female groups ($t = 1.697$) perhaps reflecting a mid-morning decrease in ACTH secretion. Supported by USPHS Grant AM-04122 and NASA Contract NAS 9-10537.

MECHANISM OF PROPAGATION OF THE INTESTINAL INTERDIGESTIVE MYOELECTRIC COMPLEX. G. M. Carlson,* B. S. Bedi* and C. F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

A cyclically recurring myoelectric complex which migrates caudad in the canine small intestine during the interdigestive state has been described previously by Szurszewski (Am. J. Physiol., 217:1757, 1969). Our study was done to illuminate the mechanism of propagation of the complex by determining the effects on its migration of separation of a loop of bowel. A 30-cm segment of jejunum was prepared as a Thiry-Vella fistula in 7 dogs with continuity of the bowel restored by end-to-end anastomosis. Monopolar Ag-AgCl electrodes were sutured to the serosal surface of the loop and to the remaining bowel proximal and distal to the anastomosis. Postprandial 24-hour recording sessions, 4 to 6 hours in duration, were started 7 days after operation. The animals rested quietly in a supporting sling during the sessions. Migrating myoelectric complexes were recorded regularly in 4 of the 8 dogs. In these 4 animals, all phases of the complex were propagated distally along the segment orad to the anastomosis, then passed distally to and along the loop and, finally, in sequence to the portion of the bowel distal to the anastomosis. The temporal relationships of the different components were similar to those of intact bowel except that action potential activity tended to persist for longer periods in the separated loop. The results indicate that neither the continuity of the bowel wall nor the movement of contents is essential for the coordination of the interdigestive myoelectric complex. We propose that extrinsic neural systems are responsible for propagation and coordination of the interdigestive myoelectric complex. (Supported in part by NIH Grants AM-2015 and GM-28067.)

EFFECTS OF NOREPINEPHRINE ON THE COUPLING RATIO OF THE IONIC PUMP IN PURKINJE FIBERS. Robert Carpentier* and Mario Vassalle. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York 11203.

The action of norepinephrine (NE) on membrane potentials was studied in sheep Purkinje fibers in which the ionic pump was either electroneutral or electrogenic. When the pump was electroneutral, i. e. in quiescent fibers and in preparations driven at a slow constant rate, 8.8×10^{-7} M NE produced a decrease in resting potential and in maximum diastolic potential (E_{max}), respectively. On the contrary, when the pump was made electrogenic, i. e. in fibers driven at 120/min for two minutes, the hyperpolarization induced by the overdrive was enhanced by NE. The latter effect was reduced or abolished by agents which interfere with the function of the pump: Mg^{++}-free solutions, 2-deoxy-d-glucose and strophanthidin. It was also absent when the pump was previously maximally activated by prolonged overdrive. It is concluded that the effect of NE on E_{max} depends on the state of the ionic pump. When the pump is electroneutral, NE does not modify its coupling ratio; the effect of the amine on potassium conductance (g_K) becomes then apparent and E_{max} diminishes. On the contrary, when the pump is made electrogenic, its activation by norepinephrine leads to a hyperpolarization of the fiber, due to the shift in the steady-state Na^+ curve.

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INFLUENCE OF HISTAMINE ON TRANSPORT OF MACROMOLECULES ACROSS THE BLOOD-LYMPH BARRIER. R. D. Carter* and E. M. Renkin. Dept. of Physiol. & Pharmacol., Duke Univ. Med. Cntr., Durham, N.C.

To determine the mechanisms by which molecules larger than serum albumin cross capillary walls and how these are affected by agents which alter permeability, we measured flow rate, protein and dextran concentrations relative to plasma of lymph from the dog's hindpaw. Endogenous plasma proteins were separated by disc electrophoresis or gel chromatography, dextrans by gel chromatography. Permeability surface area products (PS) were calculated from lymph flow (L) and lymph-plasma concentration ratio (R). $PS = LR \div (1-R)$. Under control conditions or after s.c. injection of saline, PS for plasma proteins decreased with increasing MW. PS for dextrans were much smaller than for proteins of comparable MW. A closer but still not perfect agreement was obtained on the basis of effective molecular size. Vasodilators (acetylcholine, methacholine) injected s.c. increased L but produced little change in R for proteins or dextrans. PS was increased proportionately for all components, indicating an increase in effective capillary surface rather than a change in permeability. Histamine (1 to 5.5 ug into each toe pad) greatly increased L and R for all substances. PS for both proteins and dextrans increased but the change was greater for the larger molecules. This indicates that the increase in PS is due not only to an increase in S, but to a change in permeability. We are presently trying to establish whether there is an increase in pore size or an acceleration of vesicular transport. (Supported by USPHS Grant HE-10936.)

TEMPORAL CHARACTERISTICS OF NERVE IMPULSE TRAINS EVOKED BY TASTE STIMULI. K.Y. Chan* and M.A. Biedenbach, Department of Physiology and Biophysics, University of Washington, Seattle, Washington 98105.

In anesthetized cats, potentials of single axons in the chorda tympani were recorded to establish whether temporal patterns of spike trains play a role in taste sensation. The tongue was perfused with solutions of the four basic taste stimuli (NaCl, acetic acid, quinine sulfate, sucrose) and one food substance (raw liver extract). Spike trains of 18 axons were recorded and later plotted as post-stimulus time histograms with 2 sec time bins. The envelopes of the resulting graphs divided into three main types: (1) Spike trains evoked by NaCl and liver extract displayed a high initial firing level (30-70 spikes/2 sec) which declined gradually (within 40 sec) to a low level (10-20 spikes/2 sec). (2) Spike trains evoked by acetic acid and quinine sulfate showed a high initial firing level which declined rapidly (within 2-5 sec) to a lower, tonic level. (3) Spike trains evoked by sucrose and more dilute acetic acid and quinine solutions than in (2) produced a rather flat envelope and a lower firing level (approximately 10 spikes/2 sec). Only a few axons, sensitive to several taste substances, generated spike trains with all three patterns. The majority generated two and a few only one of the described patterns. Thus, a given pattern is not unique to one taste substance. Nevertheless, temporal characteristics of spike trains appear to contribute information on taste quality in the sense that a given pattern was associated with the response to some taste solutions, but could not be elicited by other solutions. Supported by U.S.P.H.S. grant DE 02152.

OXYGEN AND ARTERIAL HELICAL STRIPS FROM SKELETAL MUSCLE VASCULATURE. Alfred Chang* and Reed Detar. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Contractile responses were produced in helical vascular strips taken from femoral and deep femoral arteries of the rabbit thigh with several agonists (e.g., epinephrine, norepinephrine, histamine, serotonin and KCl) at P_{O_2} levels between zero and 100 mm Hg. Strips from the larger extra- and intramuscular (adductor) vessel segments usually demonstrated a smooth curvilinear relationship between P_{O_2} and contractile tension (convex to the positive tension axis) with maximal contraction at 100 and almost no contraction at zero mm Hg P_{O_2}. Strips from the smallest intramuscular vessel segments demonstrated contractile responses which were only slightly diminished as P_{O_2} was reduced to as low as 10 mm Hg. At lower P_{O_2} levels, contractile responses in these strips were markedly diminished. Since contractile responses were greatly diminished in all of the strips when tested at the lowest P_{O_2} levels, it is suggested that ATP production in the smooth muscle cells of these arteries is primarily dependent upon oxidative energy pathways. The difference in the P_{O_2}-contractile tension relationship obtained in strips from the smallest intramuscular vessel segments as compared to that in strips from the larger vessel segments may possibly be related to reduced wall thickness and shorter distances for diffusion of oxygen into the vessel wall. (Supported by NIH grant # HE-12846 and NHHA grant #70.)

THE EFFECT OF pH ON THE MECHANICAL PROPERTIES OF TRACHEAL SMOOTH MUSCLE (TSM). Kilian W-K Cheung* and N.L. Stephens. Dept. of Physiology, Univ. of Manitoba, Winnipeg, Man., Canada.

We have previously reported that acidosis (pH 6.95, Po_2 600 mm Hg) was without any effect on isometric tetanic tension (Po) in TSM. Since muscle function should be described in terms of both Po and Vmax, the latter being the maximum rate of shortening, the effect of acidosis on force velocity (F-V) relationships were studied in this muscle. Eight experiments performed under conditions of respiratory acidosis (pH 7.075, pCO_2 108.0 mm Hg) and a metabolic acidosis (pH 7.068, pCO_2 41.2 mm Hg) revealed no significant changes in Po, Vmax and the a and b constants of Hill's equation $(P + a)(V + b) = (Po + a)b$, and no significant shift of the test F-V curve when compared to the control curve. This suggests that the effect acidosis exerts on TSM in vivo is not due to a local effect on the muscle. Whether the lack of effect is due to the buffering capacity of the TSM cell is to be studied in the future. Finally since we have also shown in the past that this degree of acidosis does impair contractile function in canine bronchial smooth, it appears that airway smooth muscle displays a heterogeneity in its response to acidosis.

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Skin Blood Flow Measured by ^{133}Xe Disappearance Compared to Venous Occlusion Plethysmography. J.E. Chimoskey and G. Rosenberg.* Stanford. Normal human digital skin blood flow was estimated by analysis of ^{133}Xe disappearance from intracutaneous injection sites measured by external scintillation detection. The two compartment, in-series exponential model of Sejrsen (Circulation Res 25:215, 1969) was employed, and the blood-tissue partition coefficient was taken as 0.7. The ^{133}Xe was administered in 0.02-0.04 ml sterile pyrogen-free physiological saline by a 27 gauge needle injection into the skin. Plethysmography was performed with an air-filled digital plethysmograph with the venous occlusion cuff on the digit. Four plethysmographic measurements spanning the interval of the Xe-disappearance were averaged and corrected for cuff artifact. The subjects were studied in a constant temperature room, supine, with the digit at heart level. Ambiant environmental temperature was manipulated over the range 15-30°C. Equilibration with each temperature produced skin temperatures over the range 21-36°C. Blood flow ranged from 0 to 31 ml/min/100 gm of tissue by plethysmography and from 1.0 to 35 ml/min/100 gm of tissue by ^{133}Xe disappearance. Thirteen observations in seven subjects gave a positive correlation coefficient of 0.914. The line of regression of ^{133}Xe (y) on plethysmography (x) is: $y=1.6+.915x$. It is concluded that the ^{133}Xe disappearance technique provides an acceptable measure of skin blood flow in man.

INFLUENCE OF THERMAL STRESS ON THE FEEDING BIORHYTHM OF RATS
B. J. Chou* and E. L. Besch. Dept. Physiol. Sci., Col. Vet. Med., Kansas State Univ., Manhattan, Ks. 66502

Relative food intake was measured, in series, in 24 adult, male, Sprague-Dawley rats housed in a controlled environment room. These animals were exposed to one photoperiod (12L:12D) but to two thermal conditions--a control (21.5°C) followed by an experimental (36.5°C) period. Food and water were available ad libitum. The heat stress resulted in 100% mortality between the 4th and 20th day of exposure. Relative food consumption of about 21% and 25% (N.S.) were observed during the light period under control and heat stress temperatures, respectively. However, in the three day period immediately preceding death, compared to control values there was a significant (<0.001) increase in relative food intake to 41% during the 12 hours of light. Moreover, by analyzing these data with appropriate mathematical transformation techniques (Fourier), changes in both the amplitude and shape of the feeding rhythm were observed. The amplitude of the rhythm for heat stressed rats decreased 11.9% from controls for the 3-day period immediately preceding death. During this same period, the shape of the feeding rhythm curve deviated 42% from the control curve. Thus, it appears that the physiological deterioration of rats exposed to heat stress may be detected from analyses of the food intake rhythms.

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MECHANISMS OF LOCAL VASODILATION CAUSED BY HYPERTONIC GLUCOSE IN THE CANINE JEJUNAL LUMEN.
C.C. Chou, T.D. Burns*, C.P. Hsieh*, and J.M. Dabney. Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

Hypertonic glucose solutions in the jejunal lumen raises local blood flow (Fed. Proc. 26:715, 1967). This present study inquired into the mechanisms involved. Using the double segment preparation (J. Lab. Clin. Med. 75:729, 1970), comparisons were made of the effect on venous outflow, plasma osmolarity ([O]), glucose concentration ([G]) and lumen pressure of 1) luminal placement of glucose (G) (2.5, 5.4, 20 and 50%) and non-absorbable polyethylene glycol (PEG)(8.5, 34, and 85%), 2) i.a. infusion of 2.5, 5.4 and 16.4% G, and 3) luminal placement of 50% G before and after exposing the mucosa to 0.4% dibucaine. Luminal placement of any G raised flow and venous [G]. Venous [O] and lumen volume were increased to the same extent by hypertonic G and PEG of the same [O] (20% G = 34% PEG, 50% G = 85% PEG) but 34% PEG did not change and 85% PEG raised flow less than did 50% G. This indicates that in addition to a direct vascular effect of hypertonicity, increased [G] either in the lumen or in blood contribute to increased flow. I.a. infusion of 2.5 or 5.4% G increased venous [G] in the range or higher than that caused by luminal placement of any G but did not alter flow indicating that hyperglycemia is not the factor increasing flow. The 16.4% G increased flow and venous [O]. The increased flow caused by luminal placement of 50% G was abolished or attenuated after exposing the mucosa to dibucaine. Hypertonic solutions increased motility and the factors involved were similar to those which increased flow. It is concluded that increased blood flow with hypertonic glucose in the jejunum is a local phenomenum and may in part be mediated by local vascular hypertonicity. The increased flow may also be mediated by the mechanisms that can be blocked by exposing the mucosa to a local anesthetic. (Supported by Michigan Heart Association.)

TOLERANCE OF NORMAL MAN TO THE INTERACTING STRESSES OF SEVERE EXERCISE AND ACUTE HYPERCAPNIA. J. M. Clark, R. D. Sinclair and J. B. Lenox. (intr. by S. M. Cain), USAF School of Aerospace Medicine, Brooks AFB, Texas.

During exposure to inspired P_{CO_2} ($P_{I_{CO_2}}$) levels of 0, 10, 20, 30 and 40 mm Hg, 9 volunteers in excellent physical condition ran at 4 different speeds on a treadmill at a 10% grac or a total time of 24 minutes. Treadmill speed was increased every 6 minutes and measurements were made during the last 2 minutes of each period. Average values of oxygen consumption ($\dot{V}_{O_2}$), which were not altered by changes in $P_{I_{CO_2}}$, were 1.08, 1.78, 3.00 and 3.57 L/min at the 4 speeds. Maximum $\dot{V}_{O_2}$ measured during air breathing in the same group of subjects was 4.43 L/min or 63 ml/kg min. Ventilation, arterial P_{CO_2} and arterial pH were altered smoothly and progressively in response to increasing severity of the interacting stresses of exercise and hypercarbia. Average values of these parameters for the highest $\dot{V}_{O_2}$-$P_{I_{CO_2}}$ combination were 169 L/min, 64 mm Hg and 7.12, respectively. Severe symptoms and ventilatory measurements indicated that physiological limits were approached during exercise at a $P_{I_{CO_2}}$ of 40 mm Hg. Two of the subjects collapsed while running at the highest speed in this atmosphere, but both were able to complete the entire run on subsequent attempts. Cardiac arrhythmias were not observed during exercise except for the random occurrence of occasional premature ventricular contractions. The data obtained from these experiments permit the derivation of predictive curves which describe physiological responses to any combination of exercise and $P_{I_{CO_2}}$ over the ranges that were studied.

URINARY GONADOTROPIN LEVELS DURING PREGNANCY IN THE CHIMPANZEE. M.T.Clegg Delta Regional Primate Research Center, Tulane University, Covington,La.

Urinary gonadotropin levels were studied throughout pregnancy in two chimpanzees. Weekly urine samples were collected following mating and gonadotropic activity determined by the following bioassay procedure: Immature female rats (21-23 days old) were injected twice daily for four days with either a urinary alcohol extract or unextracted material. Necropsy was performed on the fifth day and ovarian and uterine weight recorded. All assays were standardized against human chorionic gonadotropin and results expressed as HCG i.u. equivalents. Gonadotropic activity could be detected as early as the second week post-mating (chimpanzee#1, 10 iu/100 ml; chimpanzee#2, 150 iu/100 ml). Levels rose rapidly to reach a peak value by the fourth week (100 iu/100 ml,chimpanzee #1; 800 iu/100 ml chimpanzee #2). These elevated titres remained high and fairly constant through the eighth week after which they dropped precipitously. Some activity continued to persist up to the time of parturition (less than 10 iu in both chimpanzees). The discrepancy of almost a ten fold difference between the two subjects is the result of recovery loss in the urine from chimpanzee #1 following alcohol extration. Pregnant chimpanzee urinary gonadotropin appears similar to human chorionic gonadotropin based on biological and immunological tests. (Supported by USPHS Grant FR 00164)

BLOOD PRESSURE/FLOW RESPONSES TO LOW-PRESSURE EXPOSURE AT DIFFERENT DECOMPRESSION RATES. Julian P. Cooke*, Richard W. Bancroft, and Ronald Holden*. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

Femoral arterial blood flow and pressure measurements were made during and after rapid (1 sec) and slow (10 sec) decompressions of anesthetized dogs from a barometric pressure of 258 torr (27,000 ft) to 2 torr (130,000 ft) while breathing oxygen. The total exposure from the start of decompression lasted 2 min, followed by recompression to ground level within 1 min. During the 1-sec decompression, with almost immediate apnea, blood flow essentially ceased (<5 cc/min) within 20 sec and the A-V pressure gradient was essentially zero. Ten-second decompression resulted in a reduction to 50 cc/min in 20 sec or about one-half the pre-decompression flow while a favorable A-V differential was maintained and apnea was delayed. In both cases, flow generally ceased within less than 60 sec. During exposures after the 1-sec decompression the blood sequestered in the femoral blood-flow cannula appeared to be still oxygenated. In contrast, during the 10-sec decompression, blood that continued to flow through the cannula became essentially deoxygenated, as judged by its black color. This suggests that, during slower decompression, the body tissues were perfused and degassed with deoxygenated blood while flow continued. One-second decompressed animals may have had blood sequestered in the circulatory system that was still somewhat oxygenated. Recovery was much more delayed in animals that were decompressed slowly, further indicating a more profound degree of anoxia than when rapidly decompressed.

Length-dependent changes in the organization of contractile elements in smooth muscle fibers. P.H. Cooke and Fredric S. Fay (intr. by Fredrick E. Samson, Jr.). Dept. Physiol. & Cell Biol., Univ. Kansas, Lawrence, Kansas, and Dept. Physiol., Univ. Mass. Med. School, Worcester, Mass.

In order to investigate the structural basis for the length-tension (L-T) relationship of smooth muscle, changes in length and tension of muscle strips (taenia coli) were correlated with the length of the component fibers and the ultrastructural organization of their contractile elements. The L-T relationship consists of two phases as length is increased. In phase 1 (unstretched) active tension increases rapidly with only slight increases in passive tension, and in phase 2 (stretched) active tension decreases as passive tension rises rapidly. The mean length of fibers in stretched strips is 30% greater than in the unstretched strips. In unstretched fibers the 100 A dia. filaments, thick and thin myofilaments, and fusiform dense bodies are uniformly distributed throughout the cross-sectional profiles. In stretched fibers the 100 A filaments and dense bodies are consolidated into an amorphous mass near the center of the fiber profile, and the thick myofilaments are segregated into a surrounding ring. The particular pattern of distribution of 100 A filaments and dense bodies in the fibers shows a dependence on the length and tension of the muscle strip. The 100 A filaments and dense bodies form a network. A model describing the effect of stretch on the distribution of the network is proposed. Consolidation of the networks could occur upon stretching the fibers through a reorientation of the 100 A filaments that interconnect the dense bodies.

DETERMINATION OF PULMONARY EXTRAVASCULAR WATER (PEVW) USING OXYGEN-15 LABELLED WATER. J. D. Cooper, N. J. McCullough, R. Greene, E. Lowenstein, (intr. by M. B. Laver) Massachusetts General Hospital, Boston 02114.

The method of Chinard for measurement of in vivo lung water has been modified to avoid analysis of blood samples and enable rapid serial measurements without blood loss. Water tagged with $^{15}O_2$ is used as the diffusible indicator and indocyanine green as the vascular indicator. Since $^{15}O_2$ is an energetic gamma emitter with a two minute half life, sufficient quantity of isotope may be given for continuous counting without exceeding safe radiation limits or build up of background activity. The indicators are simultaneously injected into the right atrium. Arterial blood flows sequentially through a well counter, cuvette densitometer, constant infusion pump, and continuously back into the venous circulation. Electrical signals from the counter and densitometer are recorded directly on an ink recorder and stored on magnetic tape. PEVW is calculated from the indicated flow for the vascular indicator and the difference of the corrected transit times calculated for both indicators. The method has the potential for on-line measurement with a PDP9 computer. The standard deviation of triplicate determinations in 14 dogs was 3.5 ml. (4.6% of measured water).

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ABRUPT INFERIOR VENA CAVA OCCLUSION: A TECHNIQUE FOR THE EVALUATION OF CARDIAC PERFORMANCE IN THE CONSCIOUS ANIMAL. J.W. Covell, D.M. Davidson*, C.I. Malloch*, and J. Ross, Jr., UCSD, Dept. of Med., La Jolla, Calif. 92037.

The independent effects of preload and afterload on left ventricular (LV) performance have made the evaluation of myocardial contractile state in conscious animals and man difficult. A technique was developed for the study of left ventricular performance over a wide range of filling pressures in 7 trained conscious dogs in which left ventricular pressure (LVP), ascending aortic flow and intrapleural pressure were measured. A balloon cuff was implanted about the inferior vena cava for abrupt partial inferior vena caval occlusion (IVCO). During the initial 10 beats following IVCO, both LV end-diastolic transmural pressure (TMEDP) and stroke volume (SV) progressively decreased. When TMEDP was varied over a range of 25 to 4 mmHg there was no significant change in the ratio of dp/dt to active LVP determined at 40 mmHg (DPAP40) which averaged 87 $\pm$ 8 sec-1 at TMEDP's of 4-18 mmHg. However DPAP40 was significantly decreased to 80 $\pm$ 8 sec-1 at TMEDP below 3 mmHg ($p<.02$). DPAP40 was increased by isoproterenol and digitalis and was decreased from 66 $\pm$ 6 to 58 $\pm$ 7 following propranolol ($p<.02$). During IVCO, the relationship between TMEDP and SV over a range of TMEDP (25-4 mmHg) also was examined. However, the VF curve following the administration of propranolol was not significantly changed. It is concluded that DPAP40 is a more sensitive index of myocardial contractile state than the VF curve and that it is insensitive to alterations in LV end-diastolic transmural pressure above

SHORT TERM INTERRELATIONSHIPS BETWEEN THE RENIN-ANGIOTENSIN SYSTEM AND ARTERIAL BLOOD PRESSURE. A.W. Cowley, Jr.,* and A.C. Guyton. (Int. by B. Douglas). Dept. Physiol. & Biophys., Univ. Miss. School of Med., Jackson, Miss.

The changes in arterial blood pressure that occur during short-term graded constrictions of a single renal artery were related to the renal secretion rates of renin and the arterial renin activity. Quantitation of the various parameters was carried out in dogs in which the central nervous system components were eliminated by destruction of the spinal cord with ethanol followed by decapitation. The renal artery perfusion pressure of a single kidney with contralateral nephrectomy was altered by introducing 15 mm. Hg step decreases which were held constant while the rise in peripheral arterial pressure reached a maximum plateau value. Arterial and renal venous blood samples were then drawn for analysis of renin activity by radioimmunoassay of Angiotensin I (units expressed as nanograms Angiotensin I/hour incubation/ml plasma). Each 15 mm. Hg decrease in renal perfusion pressure between the range 100-50 mm. Hg elevated the net secretion of renin approximately 20 ng/min/g kidney, and the arterial renin activity approximately 8.0 ng/ml. Furthermore, each 15 mm. Hg decrease in renal perfusion pressure elevated peripheral pressure 15 mm. Hg resulting in an open-loop gain of -1.0. Below renal perfusion pressures of 50 mm. Hg, the renin secretion rates, renal blood flows and arterial renin activities declined. Corresponding decreases in the systemic arterial pressures were observed. There was a significant correlation ($P < 0.001$) between the arterial renin activity and the arterial blood pressure, as well as between the change in net secretion of renin and the change in arterial renin activity ($P < 0.001$). In summary, some of the major components of the renin-angiotensin system involved in short-term regulation of blood pressure have been quantitated. (Supported by Am. Heart Grant and NIH Grant HE 11678)

THE EFFECT OF HIGH PRESSURE HELIUM-OXYGEN ON THE CENTRAL NERVOUS SYSTEM AND BEHAVIOR IN THE RAT. J.A. Cromer*, S.J. Brumleve, J. Carman*, and E.S. Halas. Depts. of Physiology and Psychology, University of North Dakota, Grand Forks, North Dakota, 58201.

Electroencephalograms (EEG) were recorded from chronically implanted electrodes in rats before, during, and after compression and decompression, in order to determine the effect of high pressure (13 ATA) helium-oxygen or nitrogen-oxygen mixtures on the central nervous system. A comparison of EEG recordings suggest a state of light anesthesia in $He-O_2$ at 13 atmospheres. To determine the possible effects of $He-O_2$ on the behavior of rats, the conditioned anxiety paradigm of Estes and Skinner (1941) was used. The conditioned anxiety was obtained by repeated presentation of a warning stimulus (a light) upon a stable ongoing operant performance (lever pressing) maintained by food reinforcement. Termination of the warning stimulus was coincidental with the delivery of a brief, unavoidable foot shock. The behavioral consequence of this paradigm is one of reduced lever pressing during the warning stimulus, but these experiments indicate that $He-O_2$ at 13 ATA retards the speed of acquisition and reduces the absolute level of conditioned anxiety relative to that of rats under normal air, $He-O_2$ at ambient pressure, or N_2-O_2 at 13 ATA. However, the rate of lever pressing in the $He-O_2$ at 13 ATA is markedly increased and is an unexpected finding. The delayed conditioned anxiety acquisition supports the hypothesis that hyperbaric $He-O_2$ induces a slight anesthetic state. Supported by ONR Contract No. N00014-68-A-0499, and PHS 1-SO1FR-5407-04.

PLASMA CALCITONIN LEVELS IN FISH. Christopher G. Dacke°, Warren R. Fleming and Alexander D. Kenny°. Space Sciences Research Center, Division of Biological Sciences, and Department of Pharmacology, University of Missouri, Columbia, Missouri 65201.

Copp and others have demonstrated that calcitonin (CT) is present in the ultimobranchial tissues removed from fish and other lower vertebrates. No hypocalcaemic action of the hormone has been consistently demonstrated in these species however, and its role in lower vertebrates remains unexplained.

We are studying the plasma CT levels in fish using the techniques developed by Kenny (Endocrinology, in press) for other vertebrate species. Normal plasma CT levels have been surveyed in 3 species of fish, including Amia (bow-fin), Ictalurus (catfish) and Carassius (goldfish). The levels are generally higher than those previously reported in birds by Boelkins and Kenny (Fed. Proc. 29:253, 1970). In addition, 6 Amia have been challenged with iv calcium gluconate. In 4 fish a rise of up to 10-fold in plasma CT was noted 30 minutes following the injection. In the 2 remaining fish, CT levels remained undetectable throughout the experiment. Experiments are now under way to assess the influences of age, sex, and aquatic environment on plasma CT levels in goldfish.

Species	Age	No. Fish	Plasma CT levels μU/ml	
			Normal	Ca challenged
Bow-fin	-	6	<500-1500	<500-15000
Catfish	-	3	200-300	-
Goldfish	7 yr	14	<1000-5880	-

(Supported by NIH Grant AM12184, NSF Grant GB23798, and Space Sciences Research Center, University of Missouri).

HYPERBARIC MEDICINE IN THE TREATMENT OF THORACIC TRAUMA. Edward G. Damon and Robert K. Jones (intr. by Frederic G. Hirsch). Lovelace Foundation for Med. Educ. and Res., Albuquerque, New Mexico.

Exposure to air blast results in reproducible intrapulmonary damage that is indistinguishable from that occurring as a result of non-penetrating impact trauma to the thorax. Guinea pigs, rabbits, and Beagles were exposed to lethal reflected pressures in an air-driven shock tube and were subsequently treated in a hyperbaric chamber in which the oxygen tension (P_{O_2}) and chamber pressure were independently varied. Treatment involving increase in P_{O_2} resulted in increased survival times of guinea pigs whereas pressurization for 30 minutes at 72 psig with the P_{O_2} retained at the normal ambient level by use of an N_2-air mixture had no detectable effect on survival times of the animals. The effects of prolonged hyperbaric oxygenation was investigated in animals held at the initial pressure treatment level for 3 hours followed by a 26 hour decompression schedule. In rabbits, an initial P_{O_2} of 17.5 psia achieved either by air pressure at 72 psig or by pressurization to 15 psig with 65 percent O_2 - 35 percent N_2 resulted in full survival and recovery of all treated animals. In guinea pigs, treatment with 100 percent O_2 at 5.5 psig (P_{O_2} = 17.5 psia) or at 12 psig (P_{O_2} = 24 psia) resulted in increased survival times with no increase in overall survival and recovery in the first case and significantly increased survival and recovery in the second case. In Beagles, treatment with air at 72 psig (P_{O_2} = 17.5 psia) or with 100% O_2 at 12 psig (P_{O_2} = 24 psia) resulted in only an increase in survival time with the greatest effect seen in the latter experiment. (Supported by Contract DA-49-146-XZ-372, Defense Atomic Support Agency of the Department of Defense.

RELATIONSHIP OF INSPIRATORY MUSCLE ELECTROMYOGRAMS TO PRESSURE AND VOLUME DURING STATIC INSPIRATORY EFFORT. J. Danon*, W.S. Druz*, W. Machnach* and J.T. Sharp U. of Illinois Coll. Med. & VAH Hines, Ill.

Normal subjects generated varying degrees of inspiratory (negative) airway pressure against infinite resistance at volumes varying from residual volume to total lung capacity. Electromyograms (EMG) of intercostal, sternocleidomastoid and scaleni muscles were recorded from surface electrodes and that of the diaphragm was recorded from esophageal electrodes. All EMG's were rectified and integrated. Varying lung volumes were achieved and maintained passively by applying constant negative pressures to the body surface. The relationships of the integrated EMG to lung volume at constant inspiratory airway pressure and to inspiratory pressure at constant lung volume were evaluated for the different respiratory muscles. Striking differences were found when the diaphragm was compared to the other muscles studied. The integrated diaphragmatic EMG was approximately linearly related to lung volume when inspiratory airway pressure was kept constant. It was also linearly related to airway pressure when volume was kept constant. Integrated EMG's from the other muscles, however, bore quite non linear relationships to volume at constant airway pressure and to airway pressure at constant volume, with low levels of activity at small lung volumes and airway pressures and disproportionately great increases in activity at higher lung volumes and airway pressures. The latter relationships were approximately hyperbolic. An analysis of these data was attempted taking into account thoracic geometry and the length tension behavior of skeletal muscles. Summarizing, these data indicate that at a given airway pressure the state of activity of all inspiratory muscles is greater at large than at small lung volumes reflecting principally the length tension relationship of inspiratory muscles. Supported by N.I.H. Grant HE08789.

URATE AND PAH TRANSPORT BY ISOLATED, PERFUSED SNAKE RENAL TUBULES. William H. Dantzler. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724.

Urate and PAH are secreted by snake renal tubules, but previous work indicated that sites and mechanisms for transport might differ. In present studies, urate and PAH transport were examined in isolated, perfused snake (Thamnophis sp.) proximal and distal renal tubules. These can be teased apart without the use of enzymatic agents, held between glass micropipets in a bath of bicarbonate buffered snake Ringer and perfused with Ringer through a glass micropipet. Transport of ^{14}C-labeled urate and ^{3}H-labeled PAH from bath to perfusion fluid was studied at perfusion rates varying from about 0.08 to 8 nl/min. Active secretion of urate and PAH was observed with proximal tubules. With 2×10^{-5} M urate in bathing medium, urate perfusion fluid/outside bathing medium ratio (TF/B ratio) was as high as 10 at low perfusion rates. With 2×10^{-5} M PAH in bathing medium, PAH TF/B ratio was as high as 5 at low perfusion rates. Net transport of both urate and PAH from bath to tubular lumen increased significantly with increasing perfusion rates. The increase for both organic acids averaged about 40×10^{-15} M/mm/min for each 1 nl/min increase in perfusion rate. Net urate transport appeared to be slightly greater than net PAH transport at all perfusion rates. Net proximal tubular fluid reabsorption averaged about 2 nl/mm/min, and, although there was much variation, tended to be slightly greater at high than at low perfusion rates. Preliminary data suggest that urate secretion also occurs in distal tubules and that net secretion increases significantly with perfusion rates. Thus, in both proximal and distal tubules organic acid transport appears to be related to perfusion rate. (Supported by NSF GB-11788).

ADENYL CYCLASE ACTIVATION AND BINDING OF HUMAN CHORIONIC GONADOTROPIN TO COMPONENTS OF LUTEINIZED RAT OVARIES. Benjamin J. Donzo*, K. M. J. Menon*, Anil R. Sheth* and A. Rees Midgley. The University of Michigan, Ann Arbor, Michigan.

A highly specific binding protein for human chorionic gonadotropin (HCG) has been demonstrated in sedimentable fractions from luteinized rat ovaries. Incubation of 800xg pellets from ovarian homogenates with 10^{-12}-10^{-9} M 131-I-HCG at 4° and 37°C indicated the binding site to have an association constant of 2-3 x 10^{-8} M. The binding of 1/2 ng of labeled HCG can be inhibited 85-90% by 10 ng of unlabeled HCG, whereas, 100 ng of luteinizing hormone (LH), or HCG from which the sialic acid has been removed by treatment with neuraminidase (asialo-HCG) are required to produce the same degree of inhibition. One hundred ng of human growth hormone, 100 ng of ovine prolactin, 1000 ng of follicle stimulating hormone (FSH) or 1000 ng of thyroid stimulating hormone were not able to inhibit the binding of 131-I-HCG. On a weight for weight basis, radioiodinated HCG and asialo-HCG were bound to the same extent to the binding protein, but prolactin, FSH and LH were five times less active. Adenyl cyclase activity, present in the homogenates of luteinized rat ovaries, is stimulated 80% by 2 x 10^{-9} M HCG, but only 16% by the same concentration of asialo-HCG. Adenyl cyclase activity is also present in operationally defined nuclear, mitochondrial and microsomal fractions, but it has not yet been possible to demonstrate hormonal stimulation of the enzyme in these fractions. The highest degree of binding per mg of protein is obtained in those components that exhibit the highest endogenous adenyl cyclase activity, namely: the mitochondrial and microsomal fractions. It appears that a primary event in the mechanism of action of HCG is binding to sedimentable components present on or in the cells of luteinized tissue; a subsequent event seems to be stimulation of adenyl cyclase activity. (Supported by NIH HD-05318.)

THE DEPENDENCE OF THE DIFFERENCE IN P_{CO_2} BETWEEN CSF AND BLOOD ON THE RAPID HYDRATION OF CO_2. D.G. Davies*, G.H. Gurtner and B. Bromberger-Barnea. Department of Environ. Med., The Johns Hopkins University, Baltimore, Md. 21205 and Department of Physiology, The Albany Medical College, Albany, New York 12208.

We have previously shown that steady-state differences in P_{CO_2} can exist between CSF and blood (Davies, D.G., G.H. Gurtner and R.L. Riley, Fed. Proc. 30:1668, 1971) and that the magnitude of these differences is related to the arterial hydrogen ion concentration. We explained these differences in P_{CO_2} by the mechanism proposed by Gurtner, Song and Farhi (Resp. Physiol. 6:173-187, 1969). It has been calculated that for differences of this magnitude to be produced in a capillary with a transit time of 0.8 seconds, the hydration of CO_2 must proceed at a rate that is at least 100 times the uncatalyzed rate. If the hypothesis is correct there must be a source of carbonic anhydrase present in the system. One possible site is the CSF. In order to test the hypothesis we injected Diamox into the CSF of 2 mongrel dogs and followed the changes in P_{CO_2} in CSF and cerebral venous blood with a mass spectrometer. Preliminary evidence indicates that the magnitude of the difference in P_{CO_2} between CSF and blood is decreased when the carbonic anhydrase is inhibited. (Supported in part by HE 13721 and HE 10342.)

ABSENCE OF RESPONSE OF CAROTID BODY CHEMORECEPTORS TO PASSIVE AND STIMULATED HIND LIMB EXERCISE DURING HYPOXIA IN ANESTHETIZED CAT. Richard O. Davies* and Sukhamay Lahiri. School of Vet. Med. and Med., Univ. of Pa., Phila., Pa.

The effect of hypoxia on ventilation ($\dot{V}E$) in man is enhanced by muscular exercise. Since the stimulating effect of hypoxia is mediated through the peripheral chemoreflex mechanism, enhancement during exercise must involve a component of the reflex arc, such as (1) the chemoreceptor site, (2) and/or the central nervous system. To study this problem, we measured ventilation and carotid chemoreceptor activity (a few-fibre preparation) and oxygen uptake ($\dot{V}O2$) in anesthetized cats during rest, passive hind limb movement and during spinal cord stimulated hind limb exercise (increasing $\dot{V}O2$ by 2 to 3 times the resting value) at three levels of inspired P_{O2}: 710, 150 and 85 torr. The ventilation, carotid body chemoreceptor activity and femoral arterial blood pressure were recorded continuously on a Grass polygraph. During each steady state, timed expired air was collected for $\dot{V}E$ and $\dot{V}O2$, and arterial blood was sampled for P_{O2}, P_{CO2} and pH. $\dot{V}E/\dot{V}O2$ at rest and during active exercise was ca. 52 at P_aO_2 = 450 whereas during hypoxia (P_aO_2 = 38 torr) the corresponding values were 66 and 72 respectively. Muscular exercise, therefore, enhanced hypoxic ventilation. On the other hand, as P_aO_2 decreased, chemoreceptor activity changed to the same extent at rest (e.g., from 5.8 to 23.9 impulse/sec) and during exercise (from 5.7 to 25.1). Active exercise, therefore, did not enhance chemoreceptor activity either in hyperoxia or in hypoxia even after 5 min of duration of the stimuli. Also, passive exercise did not increase chemoreceptor activity, although $\dot{V}E$ did increase appreciably. We were thus unable to demonstrate any increase of chemoreceptor activity by exercise. We conclude that reflex enhancement of ventilation seen during hypoxic exercise occurs central to the peripheral chemoreceptors. (Supported in part by Grants NS-08383 and HE-08805.)

INPUT-OUTPUT CHARACTERISTICS OF PERIPHERAL NERVE-ANTERIOR TIBIAL ARTERY PREPARATION. D. L. Davis and Philip Dow. University of South Florida, Tampa, Florida, and Medical College of Georgia, Augusta, Georgia.

Vasoconstrictor responses of hemodynamically isolated but normally innervated in situ segments of dog anterior tibial arteries were recorded during electrical stimulation of the distal stump of the ipsilateral sciatic nerve. Isolated segments were perfused at constant inflow with autologous blood from the femoral artery of the opposite leg. Stimulations were made at 70 v, 3 msec pulse duration, 1-100 Hz, and continued for 3-60 sec. Vasoconstrictor responses were evaluated from segmental resistance changes calculated from differential pressures (Δp) across isolated segments and from inflow data. Frequency-response curves increased throughout the range of stimulation rates. When compared on the basis of response versus total number of stimuli in a given train, the largest resistance changes occurred at stimulation rates of approximately 15 Hz. When resistance changes were plotted against starting mean segmental pressures at various stimulation rates, similar shaped curves, which increase with stimulation frequency, were obtained until rates of 50 Hz were reached. Maximum $d\Delta p/dt$, employed to assess the rate of development of constrictor responses, varied inversely and linearly with mean resting pressure, and increased in a curvilinear relationship with stimulation frequency. The time required to reach maximum $d\Delta p/dt$ values showed a variable relationship to stimulation frequencies less than 15 Hz, and was relatively uneffected by stimulation rates above 15 Hz. (Supported by grants from Georgia Heart Association and USPHS, Grant HE-00240).

INDUCTION OF ICSH RELEASE AND TESTOSTERONE SECRETION FOLLOWING EJACULATION IN RABBITS. Claude Desjardins and Larry L. Ewing. Dept. of Physiological Sciences, Oklahoma State Univ., Stillwater, Okla. 74074.

Circulating levels of testosterone increase following ejaculation in rabbits (Haltmeyer, G. C., and K. B. Eik-Nes, J. Reprod. Fert., 19:273, 1969) but it is not known whether this is due to alterations in testicular blood flow or to the release of pituitary gonadotrophin or both. Hence, the present experiments were designed to measure ICSH release, circulating levels of testosterone, testicular blood flow and testosterone secretion in mature rabbits at specific intervals (10 replicates per interval) after ejaculation. Pituitary ICSH content averaged 3.0 µg/mg immediately after ejaculation (0 hr), dropped ($P<0.01$) to 1.0 µg/mg within 0.5 hr and increased ($P<0.01$) to 2.7 µg/mg after 3 hr. In comparison to pituitary ICSH, plasma ICSH levels averaged 0.45 µg/100 ml immediately after ejaculation (0 hr) increased ($P<0.01$) to 0.88 µg/100 ml within 0.5 hr and dropped ($P<0.01$) to 0.50 µg/100 ml after 3 hr. The temporal changes in pituitary and plasma ICSH levels following ejaculation coincided with a 55% increase in plasma testosterone (2.1 vs 5.9 mg/ml) between 0 and 0.5 hr after ejaculation. Testosterone secretion increased ($P<0.01$) from an average of 0.87 to 1.4 µg/hr/testis when testes were perfused (in vitro) with whole blood obtained from control and ejaculated (0.5 hr after) rabbits, respectively. Moreover, testes perfused with blood from control and ejaculated rabbits had similar ($P>0.50$) flow rates (5.8 vs 6.2 ml/hr) suggesting that changes in testosterone secretion were independent of blood flow. These results indicate that ejaculation causes a transitory increase in testosterone secretion that may be primarily attributed to increased ICSH release.
(Supported by USPHS Grants HD-04578 and HD-00636)

SITE OF AIRWAY OBSTRUCTION IN ASTHMA AND CHRONIC BRONCHITIS. P. Despas* and P.T. Macklem. Respiratory Division, Royal Victoria Hospital, Montreal, Canada.

Because maximum expiratory flow volume (MEFV) curves in normal subjects are dependent on gas density (Wood & Bryan JAP 27: 4, 1969) the resistance upstream (Rus) from equal pressure points (EPP) is mostly due to convective acceleration and turbulence. We measured MEFV curves breathing air and He - O_2 in asthmatics and chronic bronchitics. In the latter, MEFV curves did not change indicating that Rus is mostly due to laminar flow. Therefore, EPP must be further upstream than in normal subjects and the site of obstruction must be in small airways. MEFV curves in some asthmatics did not change, similarly indicating obstruction in small airways. In others, flow increased normally indicating obstruction in larger airways. The response to He - O_2 did not correlate with initial values for pulmonary resistance, the initial MEFV curves or the response to bronchodilators. We conclude that the site of airway obstruction is different among asthmatics but that this difference is not detectable by measuring the usual parameters of lung mechanics.
(Supported by a Grant from the Medical Research Council of Canada).

OXYGEN, ADENOSINE AND ISOLATED CORONARY ARTERIAL VASCULAR SMOOTH MUSCLE. Reed Detar and Miklos Gellai*. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Contractile responses of isolated helical strips of free-wall left ventricular coronary arteries produced by 0.2 to 0.5 μM acetylcholine were usually similar in magnitude at all P_{O_2} levels between approximately 5 and 100 mm Hg. At high P_{O_2} levels (> 40 mm Hg), adenosine produced dose-dependent relaxation of contractile tension in a range between 0.1 and 10 μM. When P_{O_2} was reduced to hypoxic levels (5 to 40 mm Hg), adenosine-induced relaxation was potentiated. With a constant concentration of adenosine present in the tissue bath, contractile tension of the isolated strips was directly dependent upon P_{O_2}. It is proposed that even under conditions in which the rate of release of adenosine from the myocardial cells may not change, variations in local oxygen pressure could act directly on the vascular smooth muscle of intact coronary arteries to regulate local vascular tone. (Supported by NIH grant #HE-12846 and NHHA grant #70.)

RESPIRATORY FUNCTIONS OF BLOOD OF RING-TAILED AND BLACK LEMURS. D. S. Dhindsa, J. Metcalfe and A. S. Hoversland*. Heart Research Lab., Dept. of Med., Univ. of Oregon Medical School, Portland, Oregon 97201.

The respiratory characteristics of whole blood from 12 ring-tailed lemurs (Lemur catta) and 10 black lemurs (Lemur macaco) were studied and compared. Adult animals of both sexes were used. Oxygen dissociation curves of whole blood were constructed at 38° C and corrected to a plasma pH of 7.40 by using specific Bohr factors determined in this study for each species. The mean blood oxygen capacities for ring-tailed and black lemurs were 21.5 ± 1.5 and 21.9 ± 2.3 vols%, respectively. The Bohr factor ($\Delta \log P_{O_2}/\Delta$ pH) for ring-tailed lemurs (-0.487 ± 0.051) was significantly higher ($P < .01$) than the Bohr factor for black lemurs (-0.446 ± 0.050). The mean partial pressures of oxygen required to half-saturate the hemoglobin (Hb) in the whole blood (P_{50}) were 37.0 ± 1.1 mm Hg and 32.9 ± 1.0 mm Hg for ring-tailed and black lemurs, respectively. These results indicate that blood from ring-tailed lemurs has a significantly lower ($P < .01$) affinity for oxygen than blood from black lemurs. Completely deoxygenated blood combines with more carbon dioxide than oxygenated blood at the same P_{CO_2}: this is called the Haldane effect and its values at a P_{CO_2} of 40 mm Hg were 4.7 and 4.4 vols% for ring-tailed and black lemurs, respectively. The concentration of 2,3-DPG in red cells was significantly lower ($P < .01$) in ring-tailed lemurs (4.45 ± 0.47 μM/gm Hb) than in black lemurs (5.75 ± 0.58 μM/gm Hb). Starch gel electrophoresis showed that hemoglobin from ring-tailed lemurs has two major components while hemoglobin from black lemurs has a single major component. (Supported in part by USPHS, NIH Grants HE-05499 and HE-06042; and the Oregon Heart Association.)

BILIRUBIN DEGRADATION AS AN INDIRECT MEASURE OF BACTERIAL ACTIVITY IN THE CAECUM OF THE RAT. John F. Dimmick (intr. by H. D. Green) Dept. of Biol., Wake Forest Univ., Winston-Salem, N. C. 27109.

Studies have shown that ingestion of certain foods result in the production of flatulence. Intestinal gas production is dependent upon changes in number, metabolism and type of microflora of the gut in rats, dogs and man. The conversion of bilirubin to urobilin-stercobilin is the result of reduction processes with a final oxidation. Measurements were made of pigment levels in the contents of the distal small intestine and the caecum of albino rats (RFS-Sherman-Wistar-three weeks of age at the beginning of a diet period) after the ingestion of either a casein or a soybean diet. A spectrophotometer and TLC were used to measure the relative amounts of pigment in the chyme of 20 cm of terminal small intestine, and the contents of the caecum, 12 hours after the ingestion of food. Diet periods were two weeks duration with 5.5 gms of diet fed daily. Extractions were made with petroleum ether and chloroform followed by methanol in Soxhlet extractors. Results: the bilirubin-mesobilirubin and stercobilin-urobilin in the caecal contents of rats fed soybean flour were of the same levels as that found in the intestinal contents of rats fed either diet; only the caecal contents of rats fed casein diet showed a shift in the absorption range (400 and 450-500 nM w/ methanol extraction) indicating an increase in bilirubin degradation for only the casein diet; chloroform followed by methanol extraction shows that bile pigments in the gut of the rat are in the conjugated form and are insoluble in chloroform. (Supported by the Wake Forest University Research and Publication Fund and the North Carolina Board of Science and Technology.)

PULMONARY EMBOLIZATION WITH SEPHADEX: EFFECTS ON HEART RATE, RESPIRATION FREQUENCY AND PERIPHERAL BLOOD FLOW. **J. DiSalvo and C. B. Montefusco (intr. by A. Corbin). Squibb Inst. Med. Res., New Brunswick, N.J. 08903**

Slow injection (1 min) of Sephadex G-25 (20 mg/kg, 50-150 μ) into the right ventricle of closed-chest dogs anesthetized with pentobarbital produced pulmonary embolization. Changes in systemic arterial blood pressure (SAP), central venous pressure (CVP), carotid (CBF), renal (RBF), and femoral (FBF) blood flows, heart rate (HR), and respiratory frequency (RF) were studied for 30 min after embolization. Sephadex embolization was repeated in 9 animals and changes in measured parameters were recorded for as long as 30 min. After initial embolization SAP, CBF, RBF, and FBF decreased transiently (10-60 sec), whereas HR, and RF increased. During 30 min after embolization, SAP was essentially equal to control, but CVP, HR, RF, CBF and RBF were above control; FBF and depth of respiration decreased. Calculated resistance to blood flow in the kidney and in the vasculature supplied by the carotid arteries decreased whereas femoral resistance increased. Immediately after the second injection of Sephadex into the right ventricle, SAP, CBF, RBF, FBF, and depth of respiration decreased; CVP and RF increased. All animals experienced intermittent periods of cardiac arrhythmia; of 9 animals, 8 expired in 3-30 min. At necropsy each dog showed multiple hemorrhagic foci in the lungs, particularly in the diaphragmatic lobes. The results, during the period of observation, show that nonlethal pulmonary embolization is accompanied by increases in HR, RF, and CVP, and differential changes in peripheral blood flow. In contrast, lethal embolization is accompanied by marked decreases in blood flow through the carotid, renal, and femoral vessels.

Effects of hemorrhage, endotoxin, and norepinephrine shock on the vasculature of collateral-free, innervated, naturally perfused canine gracilis muscles. David E. Dobbins*, Paul E. Parker*, W. Jeffrey Weidner*, Francis J. Haddy, and George J. Grega*. Department of Physiology, Michigan State University, East Lansing, Michigan 48823.

The response of skeletal muscle vasculature in circulatory shock appears to be variable. This variability may be related to the type and severity of shock, and to the particular skeletal muscle bed under study. To investigate the former two possibilities, the effects of different circulatory shocks on pressure, blood flow, and vascular resistance were investigated in the same skeletal muscle bed, the gracilis. Hemorrhage [60% blood volume depletion, rapid (n=6) and slow (n=6) bleeding] and endotoxin [5 mg/kg, I.V. (n=6)] reduced pressure and flow throughout the 4 hour period. Norepinephrine [3 mcg base/kg/min infused for 4 hours, I.V. (n=6)] transiently increased pressure and flow but both parameters rapidly waned gradually falling below control. Endotoxin transiently increased resistance but after 10 minutes resistance waned toward control. Norepinephrine transiently decreased resistance; resistance subsequently increased relative to control and was well maintained throughout the remainder of the infusion period. Slow hemorrhage was associated with marked increases in resistance which were maintained throughout the 4 hour period. Resistance transiently increased with rapid hemorrhage but soon waned to control levels. Many animals subjected to rapid hemorrhage died shortly after resistance waned despite partial transfusion of the shed blood. Pressure, flow and resistance were altered only slightly in saline control animals (n=6). These data show that the response of a particular skeletal muscle bed can be differentially affected depending on the type of circulatory shock and also on the severity of a given circulatory shock.

Isometric and isobaric stress developed by carotid vascular smooth muscle. P.B. Dobrin. Loyola University, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Segments of dog carotid artery were excised, cannulated and restored to in situ length. They were immersed in a Krebs-Ringer bath and inflated with 100% O_2 under non-oscillating pressures. Diameter was continuously monitored with a linear displacement transducer. The vessel segments were relaxed, then treated with norepinephrine to excite the muscle, but constriction was prevented by elevation of the pressure just enough to maintain a constant radius; this was termed an isometric contraction. Then the pressure was returned to the pretreatment level to permit the vessel to constrict; this was termed an isobaric contraction. Finally the vessels were x-rayed to obtain wall volumes. Maximum constriction occurred between 50 and 175 mm Hg. Isometric muscle stress (σ-ismet) was computed as the product of pressure *increase* and the ratio of internal radius to wall thickness. Isobaric muscle stress (σ-isbar) was computed as the product of pressure and the *change* in the ratio of internal radius to wall thickness. Circumferential length-active stress curves showed that σ-ismet and σ-isbar were equal for the rising limb of the curve, but σ-isbar was less than σ-ismet when the vessels were excited at large circumferences. These data were explained by a redistribution of lengths of contractile units at large muscle lengths, as A.V.Hill (Proc. Roy. Soc. 141:104, 1953) had proposed for skeletal muscle. Evidence to evaluate this interpretation was obtained by 1) treating vessels at large circumferences and observing their behavior during stepwise pressure decrements, and 2) by observing isobaric contractions with and without a preceding isometric contraction.
(Supported by NIH Grant HE 08682)

RELATIONSHIP OF SEX HORMONES AND CYCLIC 3', 5' AMP TO GINGIVAL FUNCTION. Homer L. Dorman, Fred Williams*, Albert Staples* and Jack G. Bishop
Baylor University College of Dentistry Dallas, Texas.

The function of the gingiva receives almost no attention until the pain of certain diseased states (periodontitis, periodontosis and desquamative gingivitis) brings its role in body function to the consciousness of the patient. A very painful and uncomfortable gingival dysfunction, desquamative gingivitis, is characterized by absence of sufficient cornified gingiva to resist the trauma of mastication. The result is reddened, swollen, hemorrhagic and painful gums. This disease is associated with or at least aggravated by dysfunction of certain sex steroid hormone relationships, e.g., the ovarian cycle. Restoration of a normal ovarian sex hormone cyclic pattern by therapy, parturition, or stopping contraceptive pills often allows the gingiva to resume normal cornification which cures the gingivitis. Cyclic 3'5' adenosine monophosphate is generally conceded to be the intracellular hormone or second messenger with the ability to cause allosteric changes and to effect activation of specific cellular processes. Ovariectomy resulted in a decline of cyclic 3'5' AMP content of the gingiva. Beta estradiol increased the cyclic 3'5' AMP content of gingiva in ovariectomized dogs but hydroxyprogesterone did not elicit the effect. Nor-epinephrine was also effective in increasing the C-AMP content of gingival slices when the incubation media contained the catecholamine to a concentration of at least 1.3×10^{-4}M.

^{85}KRYPTON WASHOUT CURVES IN ISOLATED PERFUSED KIDNEYS. Joseph C. Dougherty* and Frank J. Veith, Montefiore Hosp. & Albert Einstein College of Medicine, N. Y., N. Y. 10467

There is much evidence that renal function is dependent upon the intrarenal distribution of blood flow. This may be measured using an inert gas washout technic which we applied in a study of perfusion media for isolated kidneys. The perfusion circuit consisted of a pulsatile pump, membrane oxygenator and isolation chamber. Temperature was maintained in the 25-27°C range by means of a heat exchanger. The perfusate was either 1)crystalloid, 2)plasma or 3)dilute whole blood. The initial flow rate of 40 to 120 cc/min was the maximum that could be obtained without exceeding a pressure of 100 mm Hg. Disappearance curves were recorded with an external scintillation counter after the injection of 200 to 400 μc of ^{85}Kr dissolved in 0.5 ml of saline. The disappearance curve was resolved into components and flow calculated from the formula $F = (k \times \lambda \times 100)/e$. After each study the vasculature was injected with silicone rubber. No kidney could be perfused at normal flow rates. The initial washout curve had 3 rather than 4 components. The fastest component accounted for 60-80% of flow at a rate of 150-300ml/100 gm/min. The second component was between 20-50ml/100 gm/min. and the third 1-2ml/100 gm/min. With time as vascular resistance increased in kidneys perfused with blood or crystalloid and in 6/8 of plasma perfused kidneys the curves became uniexponential. After reimplantation plasma perfused kidneys with unchanged washout curves failed to function. In perfused kidneys, in contrast to the normal, both cortex and medulla were well filled with silicone rubber confirming the ^{85}Kr washout curve which indicated all areas to be equally perfused. Thus, ^{85}Kr washout curves were not helpful in assessing the adequacy of hypothermic perfusion technics.

PROTEIN, NUCLEIC ACID, AND HYDROXYPROLINE LEVELS IN ENLARGED HEARTS PRODUCED BY EXERCISE TRAINING, DOCA INJECTION, AND AORTIC CONSTRICTION. R. Thomas Dowell*, Charles M. Tipton, and Robert J. Tomanek*, Exercise Physiology Laboratory, University of Iowa, Iowa City, Iowa. 52240

The protein synthetic responses in various regions of rat hearts were measured from exercised trained (EX), DOCA injection (DOCA), aortic constriction (AC) and control (CON) groups (each group N=10). The experimental period was 21 days. In addition there were 80 day (EX) and (CON) groups. Determinations of protein, nucleic acid, and hydroxyproline levels were made. Significant increases in total heart weight were produced by 80 days of EX, DOCA, and AC. Atrial (A) and left ventricular (LV) regions were significantly heavier. Although no increased total heart weight was found after 21 days of EX, atrial weights were significantly elevated. Net protein synthesis was shown by increases of approximately 20%, 17%, and 44% in total protein content for 80 day EX, DOCA, and AC animals respectively when compared to (CON). No differences were found in hydroxyproline values that indicated augmented synthesis of connective tissue. Significantly increased total DNA content in AC animals (A, $\bar{X}$ = 61.8 ± 5.5 µg; LV, $\bar{X}$ = 560.4 ± 37.8 µg) compared to controls (A, $\bar{X}$ = 30.3 ± 3.5 µg; LV, $\bar{X}$ = 298.2 ± 27.6 µg) and reduced RNA/DNA (29%) and protein/DNA (32%) ratios suggested that hyperplasia had occurred. Normal total DNA content, RNA/DNA and protein/DNA ratios in 80 day EX and DOCA animals were interpreted as evidence for cardiac enlargement via hypertrophy. Since the 80 day EX animals had significantly lower systolic blood pressure ($\bar{X}$ = 113.7 ± 6.1 mmHg) than (CON) ($\bar{X}$ = 131.2 ± 3.5 mmHg), and had protein synthetic responses similar to DOCA animals, it was suggested that volume overload, rather than pressure overload, provides the major stimulus for cardiac enlargement with exercise training.

A MATHEMATICAL MODEL OF INTESTINAL VOLUME MOVEMENT. P.A. Duffy,* A.E. Taylor, and M.D. Turner. Dept. of Physiol. and Biophysics, Univ. of Miss. Med. Ctr., Jackson, Miss. 39216.

A mathematical model is developed for the volume movement into or out of the intestinal lumen. The model incorporates both mucosal volume flow and capillary filtration with the following assumptions: (1) The intestinal capillary bed is considered homogeneous. (2) The intestinal capillary and mucosal membranes are assumed to be homogeneous and in series. (3) Lymph flow is a function of interstitial fluid pressure. (4) Increases in interstitial fluid volume effect interstitial fluid pressure similar to that of subcutaneous tissue. The model also incorporates several important experimental findings: (1) an increase in the conductance of the mucosal membrane with increasing serosal pressures above mucosal pressure, (2) the effect of changing capillary pressure on the measured filtration coefficient, (3) decreases in the lymphatic protein concentration as lymph flow increases. Using the above assumptions and experimental findings, the model predicts that: (a) Mucosal volume flow is more sensitive to changes in blood colloid osmotic pressure than to changes in capillary pressure. (b) Volume movement will not occur into the intestine until the interstitial fluid pressure rises to a value high enough to increase the conductance of the mucosa and to overcome the effective colloid osmotic pressure of the interstitium. (c) The intestinal capillary normally filters but changes to an absorptive one when interstitial fluid protein concentration decreases and interstitial fluid pressure increases. (d) Any factors causing the capillary to filter into the interstitium will limit the volume flow across the mucosa unless the lymphatics can carry away both the transported and filtered volumes. (Supported by NIH Grant Nos. HE 11477 and HE 11678)

ACTION OF EPINEPHRINE ON Na^+ EFFLUX IN FROG STRIATED MUSCLE. T. M. Dwyer*, E. A. Hays* and P. Horowicz. University of Rochester; Rochester, N. Y.

Na^+ efflux from frog striated muscle can be fractionated into several components on the basis of its response to the addition of drugs such as strophanthidin and to the removal of external Na^+. In freshly isolated sartorius muscles about 45% of the resting Na^+ efflux is inhibited by maximally effective doses of strophanthidin. The strophanthidin insensitive Na^+ efflux can be largely inhibited by removing external Na^+; only 12% of the original Na^+ efflux remains after both addition of strophanthidin and removal of external Na^+. Removal of external Na^+ alone produces complex effects since both the strophanthidin sensitive and strophanthidin insensitive Na^+ efflux are altered in different ways. It was of interest to us, therefore, to determine the effect of epinephrine on the various fractions of Na^+ efflux. For concentrations in the range of 15 to 30 μg/ml, epinephrine produces, on the average, a 30% increase in the Na^+ efflux when muscles are in the normal Na^+-containing Ringer's fluid. In Li^+ containing, Na^+-free solutions these concentrations of epinephrine stimulate the Na^+ efflux by about 70%. When muscles are treated with strophanthidin, epinephrine reduces the remaining strophanthidin-insensitive Na^+ efflux by 20% on the average. Epinephrine has no effect on the residual Na^+ efflux in Na^+-free, strophanthidin containing solutions. These results suggest that epinephrine stimulates the active Na^+ transport system while inhibiting the Na^+ exchange diffusion system in frog muscle. (Supported by NSF Grant No.GB15662).

EFFECT OF LEVODOPA (L-DOPA) ON HUMAN HYPOPHYSEAL TROPHIC HORMONE RELEASE. R. L. Eddy, A. L. Jones*, Z. H. Chakmakjian*, and M. C. Silverthorne*, Clinical and Research Endocrinology, Scott and White Clinic and Mem. Hospital, Temple, Texas.

Studies in experimental animals have suggested a regulatory role for dopamine in the release of LH, FSH, and to a lesser extent for ACTH and GH. L-dopa, unlike exogenous dopamine, crosses the blood-brain barrier where it is believed to be converted to dopamine. This study was designed to investigate the effect of oral L-dopa upon human hypophyseal trophic hormone release. Seven healthy adult males were studied at bedrest in a fasting state. Single doses of 250 mg., 500 mg. and 1000 mg. of L-dopa were given on 3 successive days. Serial blood specimens, obtained through an indwelling venous catheter, were assayed for serum glucose, serum cortisol, and serum immunoreactive (IR-) LH, FSH, HGH, TSH and insulin (I). Significant ($P<0.001$) IR-HGH elevations consistently occurred between 60 and 180 minutes following L-dopa administration. IR-HGH returned to baseline levels within 180 minutes after the peak increment. All three L-dopa test doses induced an IR-HGH response. The magnitude of IR-HGH response was dose-related. No significant ($P>0.1$) changes in serum glucose, cortisol, IR-LH, IR-FSH, IR-TSH, or IR-I were found, however, a different L-dopa dosage schedule may be required for IR-TSH, IR-LH and/or IR-FSH responses to occur. These preliminary data show that levodopa has potential usefulness as a hypothalamic-hypophyseal axis function test, and suggest that an adrenergic mechanism may be involved in the regulation of human anterior pituitary secretion.

THE EFFECT OF HYPERTONIC INJECTIONS UPON RED CELL AND PLASMA TRANSIT THROUGH THE LUNGS. R.M. Effros. College of Medicine & Dentistry of New Jersey at Newark, Newark, New Jersey

Rapid injections of 4 to 6 ml of hypertonic saline (2 molal), sucrose (4.4 molal) or urea (4-17 molal) through a catheter in the superior vena cava of dogs were followed by falls in both hemoglobin and T-1824 labeled plasma protein concentrations in carotid artery blood (29 studies). The decline in concentration of these blood constituents was attributed to osmotic extraction of fluid from the pulmonary tissue. However, the fall in hemoglobin concentration produced by hypertonic saline and sucrose was invariably greater and earlier than the fall in T-1824 concentration. Thus, the early pulmonary venous outflow contained disproportionately less hemoglobin than T-1824 whereas later samples of blood contained disproportionately more hemoglobin than T-1824. In 16 studies 1.75 ml of a suspension of ^{51}Cr-labeled red cells and ^{125}I-labeled human serum albumin were simultaneously injected through a small catheter threaded through the superior vena cava catheter. In contrast to control studies in which water or saline were injected, hypertonic saline and to a lesser degree sucrose reversed the normal precession of labeled red cells over labeled albumin. Hypertonic urea at equivalent and greater concentrations failed to alter the ratio of hemoglobin to T-1824 concentrations in the pulmonary outflow and did not reverse the positions of the ^{51}Cr and ^{125}I indicator dilution curves. The effect of hypertonic saline and sucrose to slow the movement of red cells relative to plasma protein through the pulmonary capillaries is attributed to the loss of red cell deformability produced by their osmotic dehydration. The failure of urea to diminish the outflow of hemoglobin relative to T-1824 or slow red cell transit through the lungs is assumed due to rapid entry of urea into red cells with restoration of normal red cell deformability. (Supported by LIMRF and NIH HE 12879 Grants)

MULTIPLE ENDOCRINE RESPONSES TO COLD EXPOSURE IN THE MONKEY. A. L. Ehle, E. H. Mougey, F. E. Wherry and J. W. Mason (intr. by D. McK. Rioch). Walter Reed Army Inst. of Research, Washington, D. C.

Male Macaca mulatta monkeys, maintained under a basal temperature of 25°C, were subjected to a period of 5°C cold exposure for 4 to 6 weeks. Continuous urine collections were made and analysed for 17-OH steroids, epinephrine, norepinephrine, testosterone and epitestosterone. Weekly blood samples were obtained and plasma levels for TSH, thyroxine, free thyroxine, growth hormone and insulin determined. During the period of cold exposure, no physical effects were observed in the animals' conditions. Following the onset of cold exposure, urinary 17-OH steroids were observed to increase 1- to 3-fold over 3 weeks and then maintain an elevated value until the end of the cold period. The urinary catecholamines were found to behave in a parallel manner to the 17-OH steroids but had a relatively greater increase, especially norepinephrine, which was noted to increase up to 8-fold during the cold. In contrast to the adrenal hormones, the urinary excretion of testosterone and epitestosterone was found to decrease 50 to 80%. Plasma thyroxine and free thyroxine showed small but consistent increases to cold that reached a maximum 3 to 4 weeks after the onset of cold. The changes in TSH levels appeared to be more phasic with a peak occurring in conjunction with the peak free thyroxine values followed by a decline toward basal levels. In one animal subjected to 3 periods of cold, the TSH response was observed to increase on successive exposures. No significant change was noted in either fasting growth hormone or insulin levels during cold exposure. These experiments demonstrate that the endocrine response to cold exposure is a complex one and that marked changes from baseline values will persist for up to 6 weeks of cold exposure.

NON-OSMORECEPTIVE "THIRST NEURONS" IN THE CAT HYPOTHALAMUS. R. Emmers. Dept.of Physiol. Col.of Physicians and Surgeons, Col.U., New York, N.Y.

Historically, two observations have suggested that hypothalamic neurons involved in the regulation of body water are osmoreceptors, and that taste plays no significant role in water intake: 1)these neurons respond to intracarotid (IC) infusions of hypertonic NaCl, and 2) adequate water intake can be maintained when water is experimentally prevented from coming in contact with the oropharynx. - The present study indicates that hypothalamic "thirst neurons" are not osmoreceptors; their firing is modulated via the thalamic taste nucleus, semilunaris accessorius (nSA). Neurons of nSA respond not only to the application of a 3% NaCl to the tongue but also to an IC infusion of this solution. Furthermore, electrolytic destruction of the nSA leads to a decrease in the firing frequency of "thirst neurons" (unit recordings) and a reversal in the expected firing changes with IC infusions of a 1 ml 3% NaCl or a 1 ml distilled water (DW) as revealed by spike discharges of single neurons per 1000 sec intervals with counts repeated for the same neuron after the following: (average of 11 neurons) control, 5,308; after NaCl infusion, an increase by 3,762; after destruction of the nSA, a decrease by 3,062; after a repeat of NaCl infusion (nSA destroyed), a decrease by 1,568; after a DW infusion (nSA destroyed), an increase by 1,139. Single electronic pulses, when applied to the nSA produced an inhibitory-excitatory oscillation of the "thirst neuron" firing as seen on computer records obtained by a method described previously (Fed.Proc.28:396). This oscillation together with the reversal effect suggest that a negative feedback circuit operates between the supraoptic nucleus and the "thirst neurons". Histological analysis revealed that the "thirst neurons" were located in a bandlike area dorsal to the optic tract beginning approximately 1 mm posteriorly to the optic chiasm and extending into the entopeduncular nucleus (Aided by grant NS-03266 from NINDS)

POSSIBLE PHASIC MEMBRANE CHANGES ASSOCIATED WITH CALCIUM BINDING AND RELEASE IN CARDIAC RELAXING SYSTEM (SARCOPLASMIC RETICULUM). Mark L. Entman* and Arnold Schwartz. Div. of Myocardial Biol. and Dept. of Med., Baylor Col. of Med. and Methodist Hosp., Houston, Tex.

ATP-dependent calcium binding(B) by cardiac relaxing system (CRS)(sarcoplasmic reticulum), as measured by dual-beam spectrophotometry, shows a rapid initial binding rate (R_B) and a slower rate of release (R_R). Release is independent of method, since, under the same conditions, Millipore filtration reveals the same pattern; the nature of the release process is unknown. The following features are of interest: R_B is the major determinant of B and time to peak B (T_B); R_B is influenced by temperature (Q_{10} = 1.5), K_m (Mg^{++}) = 3 mM, K_m (ATP) = 5 μM and pH optimum is 6.8. Time to onset of release (T_R) is independent of [ATP] as long as ATP is present until peak binding occurs; in the presence of an ATP regenerating system, [ATP] from 5 μM to 2 mM did not alter T_R. T_R is markedly shortened by temperature (Q_{10} = 2.67), and prolonged by increased pH and aging of the CRS. R_R is a function of B. Ratio of R_R/B is influenced in the same manner as T_R; Q_{10} = 2.67, pH change and aging (increases). [Mg^{++}] exerts minor effect on T_R and R_R/B at 1-10 mM. After release of Ca^{++} is complete and, when all ATP is utilized, the CRS can be restimulated by ATP; in the presence of an ATP regenerating system, CRS is refractory to ATP. Data suggest that ATP induces cyclic changes in CRS leading to calcium binding and release that have different mechanisms of control. (Supported by USPHS grants HE-13870, HE-05435, HE-07906, HE-05925, HE-13837 and K3 HE-11,875).

ABNORMAL TESTOSTERONE EXCRETION IN MALE ALCOHOLICS
L. F. FABRE, JR.*, E. D. PELLIZZARI*, P. J. PASCO*, R. W. FARMER,
Texas Research Institute of Mental Sciences, Houston, Texas

Alcoholic male subjects exhibit several abnormal endocrine parameters (e.g. aldosterone, cortisol, ADH and insulin). Alcoholic subjects also frequently exhibit testicular atrophy and gynecomastia. This study was conducted to determine whether abnormal testosterone metabolism might also occur in alcoholic subjects. Male volunteers 24-45 years of age, with a documented history of alcoholism and no physical signs of gynecomastia or testicular atrophy and normal liver function tests, were studied on a Metabolic Ward. Consecutive 24-hr urine samples were obtained. Testosterone glucuronide was measured by the radioimmunoassay of Rosenfield. Mean testosterone excretion in abstaining alcoholic male, normal male and female populations were 153.1, 36.7 and 6.4 μg/24-hr, respectively. The data are significantly different among groups at the $p<.001$ level. In acute experiments with alcoholic males, testosterone glucuronide excretion showed no consistent changes related to ad lib alcohol consumption over a 6-day period. The mechanism of the persistent increase may reflect an increase in testosterone secretion or a change in its metabolism. Further experiments are in progress to elucidate the mechanism. (Supported by NIMH Grant MH 14434-03-S1).

ACIDIFICATION OF URINE BY THE TOAD' S BLADDER. Darrell D. Fanestil and James H. Ludens.* Dept. Med., Univ. Calif., San Diego, La Jolla, Calif.

Elimination of Na^+ transport in isolated urinary bladders of Bufo marinus of Colombian origin either by removal of mucosal Na^+ or by addition of 10^{-4} M amiloride to the mucosal solution results in reversal of the potential difference (RPD) such that the serosal surface becomes negative by 10 to 60 mV. We previously reported that RPD: (1) is dependent on the presence of CO_2 in the gas phase; (2) is abolished by the metabolic inhibitor, 10^{-5} M antimycin A; (3) is not inhibited by 10^{-4} M ouabain; (4) does not require mucosal Cl^-; and (5) does not require serosal K^+. However, 10^{-3} M acetazolamide in the serosal solution eliminated RPD. We have now monitored the reversed short-circuit current (RSCC) required to null the RPD when hemibladders are incubated as separate bags in Ringer's solution containing 4.8 mM HCO_3^-. The volume of the mucosal solution was 2 ml and the serosal solution was gassed with 1% CO_2 - 99% O_2. Na^+ transport was eliminated by placing 10^{-4} amiloride in the mucosal solution. After 3 hr. the mucosal solution was removed and equilibrated with the 1% CO_2 before measurement of pH and calculation of $[HCO_3^-]$ in the fluid. The net decrease in mucosal HCO_3^- ($\triangle HCO_3^-$) correlated with the RSCC ($n=8$, $r=0.95$, $p=.001$) and $\triangle HCO_3^-$ was not different from RSCC ($p > 0.2$). In the 8 paired hemibladders 10^{-3} M acetazolamide eliminated both the RSCC and $\triangle HCO_3^-$. These findings established that the toad's urinary bladder has a capacity for acidification of urine which (1) is acetazolamide sensitive and (2) can be rapidly quantitated by RSCC.
(Supported by AM-14915 and AHA 66-128)

ABOLITION OF GROWTH HORMONE LIPOLYSIS BY HEXAMETHONIUM GANGLIONIC BLOCKADE. R.W.FARMER, E.D.PELLIZZARI* and L.F.FABRE,JR.*. Texas Research Institute of Mental Sciences, Houston, Texas.

Growth hormone (GH) causes lipolysis at low doses in vivo but is inactive in vitro except in the presence of glucocorticoid. Adrenergic blockade with dihydroergotamine has been reported to accelerate rather than block GH lipolysis in vivo and in vitro. In these experiments ganglionic blockade with hexamethonium chloride (C_6) was tested for its effect upon GH lipolysis. C_6 was injected intravenously and 15 minutes prior to GH at an initial dose of 15 mg/kg and supplemented hourly with 2 mg/kg. GH (1 mg/kg) was singly injected intravenously. The drugs were tested singly and in combination in each of five dogs. FFA (percent of Time=0) for the three treatments were:

	HOURS						
	-0.5	0	0.5	1	2	4	6
GH	123	100	76	121±20.0	160±21.4	236±55.7	251±39.3
C_6	122	100	90	92±38.4	82±28.6	108±38.9	119±40.1
GH and C_6	124	100	92	93±26.8	65± 7.3	91± 8.5	107± 9.6

Blood glucose was not altered by any of the three treatments. In vitro hexamethonium (0.1 mg/ml) had no effect upon FFA release from rat epididymal fat pad due to GH in the presence of glucocorticoid. Therefore blockade did not occur at the level of adipose tissue. It was concluded that elements of the sympathetic nervous system participate in growth hormone induced lipolysis.

Supported by NIH Grant AM-14222

ENZYME STUDY OF THE PINEAL GLAND OF THE ALBINO RAT DURING THE ESTROUS CYCLE. A. V. Fasano*, Barbara A. Kasprow*, Frances A. Kovarik* and Joseph T. Velardo (intr. by Joseph R. Davis). Loyola University of Chicago, Stritch School of Medicine.

In an effort to establish cyto-, histo-, and biochemical assessments of the pineal gland in non-manipulated, Sprague-Dawley derived adult albino rats, it appeared of paramount interest to first determine the relationship between certain enzyme activities within this gland and the stages of the estrous cycle. Rats were obtained at 50 days of age, housed in groups of six in suspended stainless steel cages and fed Purina Rat Chow and water ad libitum. A light-dark cycle of 12:12 was maintained. Estrous cycles were followed by vaginal smears for a minimum of three cycles, then the animals were necropsied at precise times after both the onset of estrus and the onset of subsequent stages as determined by vaginal smears. Four enzymes were studied during seven distinctive stages of the cycle: Early Estrus (A_1), Late Estrus (A_2), Metestrus (B), Early Diestrus (C), Late Diestrus (D), Early Proestrus (E), and Proestrus (F). Comparative histochemical analysis revealed the following for succinic dehydrogenase: A_2 (maximal)>A_1>D>C>E>F>B (minimal); lactic dehydrogenase: F (maximal)>A_2>B>C>E>A_1>D (minimal); alkaline phosphatase: A_1 (maximal)>E>C>D>F>B>A_2 (minimal); and acid phosphatase: A_1 (maximal)>D>C>E>F>A_2 and B (similarly minimal). These data form a workable standard reference base-line for several of the important metabolic reactions associated with the pineal gland which can be effectively utilized in subsequent photoperiod and hormonal studies.

Ca^{++} EFFECTS ON RESPIRATION OF MITOCHONDRIA FROM LUNG HOMOGENATES. A.B. Fisher, A. Scarpa*, K. LaNoue* and J.R. Williamson. Depts. of Biophysics Physiology and Medicine, Univ. of Penna and Vet.Admin.Hosp., Phila.,Pa.

The addition of Ca^{++} in micromolar amounts to mitochondrial preparations from most mammalian tissues stimulates oxidation of added substrates. By contrast, we have found that the rate of oxidation of NADH-linked substrates by rat lung mitochondria (LM) is depressed by Ca^{++}. LM with a respiratory control ratio of 2-3 were isolated in 0.225 M mannitol, 0.075 M sucrose, 0.002 M EDTA. The rate of substrate oxidation was measured polarographically in 0.14 M KCl-0.005 M K_2HPO_4 medium after utilization of added ADP or in the presence of uncoupler of oxidative phosphorylation. With incremental addition of $CaCl_2$, oxidative rates with pyruvate, malate, α-ketoglutarate, glutamate, isocitrate and octanoate as substrates decreased progressively to 50% inhibition at 40-300 μM [Ca^{++}] and to 90% inhibition at 100-600 μM[Ca^{++}]. NAD added to the reaction chamber did not prevent Ca^{++} inhibition. In contrast to the NADH-linked substrates, Ca^{++} in small amounts stimulated oxidation of α-glycerophosphate (αGP), and up to 1 mM had no effect on the rate of oxidation of N,N,N',N'-tetramethyl-p-phenylendiamine plus ascorbate. Succinate oxidation was only partially inhibited by high[Ca^{++}]. To investigate the site of Ca^{++} inhibition, NADH oxidation measured fluorometrically, malate dehydrogenase activity followed spectrophotometrically and substate oxidation were studied after disruption of LM by sonic oscillation. Because no effect was observed in fragmented LM by [Ca^{++}] up to 5 mM, we conclude that neither electron transport nor inhibition of specific dehydrogenase activity was the mechanism of Ca^{++} effect and we suggest that Ca^{++} might alter permeability characteristics of inner membrane of LM. The effect of Ca^{++} utilization by LM to stimulate αGP and depress NADH-linked substrate oxidation may have physiological significance for the regulation of surfactant production by the lung.

The Active Transport of Methionine by Immature Rat Small Intestine. J.D. Fondacaro* and P. Nathan. Depts. of Physiology and Surgery and Shriners Burns Unit, Univ. of Cincinnati Coll. of Med., Cincinnati, Ohio

At the time of natural weaning in rats (18 to 21 days), important physiological changes occur in absorption of nutrients by the small intestine. Absorption of whole proteins ceases at about 18 days. Glucose transport by everted sacs of small intestine decreases sharply between 18 and 21 days. In this study, absorption of methionine was examined in vitro using small intestine from rats 15,18,21,24,27 and 30 days old. Everted sacs filled with 1.0cc of 2.0 mM methionine in Krebs-Bicarbonate Ringer were incubated in 5.0cc of the same solution (including l-methionine-^{14}C tracer) for 30 minutes at 37°C with constant shaking in an atmosphere of 95% O_2;5% CO_2. In jejunum, methionine transport to the serosal solution was 6.69 μmoles/gm/30 min at 15 days. At 18 days this rate dropped to 2.27 and at 21 days it was 1.21. Transport to the serosal solution was maintained in the 24-30 day old rats at about the rate observed in the 21 day old animals. The rate of methionine disappearance from the mucosal solution was 9.22 μmoles/gm/30 min at 15 days and 5.85 μmoles/gm/30 min at 18 days. This rate dropped to 3.37 at 21 days and was maintained near this level in the older animals. In ileum, methionine transport into the serosal solution at 15 days was 6.34 μmoles/gm/30 min and 5.02 at 18 days. At 21 days the rate dropped to 3.14 and was maintained near this level in the older animals. The mucosal disappearance rate of methionine in the ileum was 11.07 and 9.63 μmoles/gm/30 min in the 15 and 18 day group respectively. At 21 days the rate dropped to 7.37 and was maintained near this level in the older animals. The jejunal and ileal tissue uptake remained unchanged over the ages tested. Sacs of rat intestine from 15 to 21 day old animals show a rapid decline in transport of methionine to a stable level at about the time of natural weaning, 21 days of age.

LOCALIZATION OF DESCENDING SYMPATHETIC SPINAL PATHWAYS. Robert D. Foreman* and Robert D. Wurster. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Fibers mediating sympathetic activity from supraspinal regions to the peripheral sympathetic system have not been described in any detail. The purpose of this study was to localize a sympathetic fiber tract in the spinal cord responsible for relaying sympathetic activity. The pathway was localized by applying 0.1 ma of current through a small stainless steel stimulating electrode (15-20μ) at different regions of the spinal cord in anesthetized cats and dogs. The criterion for sympathetic activity was an increase of systemic arterial pressure. The region of maximal cardiovascular response was obtained on the surface of the lateral funiculus approximately 1 millimeter dorsal to the dentate ligament. The tract was 1 to 1 1/2 millimeters in width and extended into the white matter about 1 millimeter. Bilateral carotid occlusions were obtained before and after bilateral lesions of this fiber tract. A significant decrease in sympathetic cardiovascular responses was observed suggesting that these fibers may transmit sympathetic activity from baroreceptors. Conduction velocity experiments were also utilized in determining the location and fiber size of this tract. *(Supported by NIH HE 08682 and GM 999)*

IDENTIFICATION OF FUNCTIONAL BIOELECTRIC CONFIGURATIONS IN SPONTANEOUS ACTIVITY OF THE BRAIN. Stephen S. Fox and Hansook Ahn*. Department of Psychology, University of Iowa, Iowa City, Iowa 52240.

Prior studies from this laboratory with Rudell and Rosenfeld have indicated the feasibility of directly validating functional representation or coding in components and combinations of components of the sensory evoked potential. In those studies under direct control of reinforcement evoked potential components were demonstrated to be functionally independent and state dependent as were transforms between closely related sensory structures. The operant method of analysis has been extended in the present study to spontaneous activity of brain. Spontaneous activity from the brains of chronically implanted cats was recorded with computer aid. Individual 20-millisecond long units of spontaneous activity were identified, which occurred on the average of one/minute. Activity preceeding and following these brief bioelectric events was also recorded. For four animals large sequential potentials similar to evoked potentials followed these selected events but no regular potentials preceeded them. Averaging revealed dramatic similarity of this spontaneous event from day to day within each animal. Functional relevance of these events was demonstrated by increasing their probability independent of changes in frequency of EEG under reinforcement control. The significance of such repeatable functional units of bioelectricity for a theory of spontaneous bioelectric coding will be discussed.

CHARACTERISTICS OF H^+ AND NH_4^+ EXCRETION IN THE TOAD URINARY BLADDER. L. W. Frazier* and J. C. Vanatta. Univ. of Texas (Southwestern) Med. Sch., Dallas, Texas 75235.

The bladder of Bufo marinus excretes H^+ and NH_4^+ during NH_4Cl induced acidosis (Frazier and Vanatta, Fed. Proc. 30:365, 1971). In vitro studies were performed with bladders mounted between 2 ml chambers. Net H^+ flux into the mucosal medium in (nmoles)(100 mg bladder)$^{-1}$(min)$^{-1}$(I) and NH_4^+ flux in the same direction and units (II) were measured. Paired hemibladders were used for each experimental and control condition. CN^- (1 mM) inhibited both I ($P<0.005$) and II ($P<0.01$). Diamox inhibited I ($P<0.01$) but had no effect on II ($P>0.20$). Likewise anaerobiosis inhibited I ($P<0.01$) without effect on II ($P>0.20$). In the absence of exogenous CO_2 and a serosal medium of PO_4 buffered Ringer solution, pH 7.2, I averaged 15.0 $\pm$ 2.8 and II averaged 1.1 $\pm$ 0.3. In the presence of 5% CO_2 with the serosal medium a bicarbonate buffered Ringer solution, pH 7.2, I averaged 42.0 $\pm$ 5.5 and II averaged 1.1 $\pm$ 0.1. I was abolished by replacing the mucosal Na^+ with choline ($P<0.01$). II was also reduced by this procedure ($P<0.05$). K^+ was substituted for mucosal Na^+ and this reduced I significantly ($P<0.02$) but II was not affected ($P>0.50$). Substitution of mucosal Na^+ with Mg^{++} resulted in a significant increase in I ($P<0.02$) but caused an inhibition of II ($P<0.05$). In the choline substitution experiments there was a relation between mucosal Na^+ concentration and I but the importance of this finding is not clear since this relation did not hold in the K^+ and Mg^{++} sodium free medium. (Supported by NSF grant GB-17610).

THE EFFECTS OF NEPHRECTOMY ON THE IN VITRO BIOSYNTHESIS OF RENIN SUBSTRATE. R. H. FREEMAN* AND H. H. ROSTORFER. INDIANA UNIVERSITY, BLOOMINGTON, INDIANA 47401.

It is well known that, following bilateral nephrectomy, plasma renin substrate concentration increases 4 to 5-fold. The substrate levels begin to rise a few hours after nephrectomy and appear to reach maximum values within 24 hours. The mechanism for this rise in plasma substrate concentration is unknown, but could be either increased synthesis or decreased degradation of substrate, or, more likely, to a combination of these two processes. Since the half-life of renin is relatively short, 30-90 minutes, there can be no doubt that a decrease in substrate degradation plays some role in the augmentation of plasma substrate levels after bilateral nephrectomy. However, our results show that, following bilateral nephrectomy, there is also an increase in the biosynthesis of renin substrate by surviving rat liver slices. Moreover, the augmentation in synthesis is a function of time after nephrectomy, reaching its maximum value 5-6 hours after nephrectomy. This increase in the rate of substrate synthesis by surviving rat liver slices obtained from nephrectomized rats can be prevented by giving the antibiotic Actinomycin D 45 minutes before nephrectomy. We conclude that the rise in plasma renin substrate levels following bilateral nephrectomy is due to both a decrease in the rate of substrate degradation and an increase in the rate of substrate biosynthesis which, apparently, is subsequent to an increase in synthesis of hepatic RNA. (Supported by PHS HE 05625 and PHS 1 F01 GM 50057).

TRANSIENTS IN VENTILATION AND HEART RATE DURING EXERCISE. Y. Fujihara*, J.R. Hildebrandt, R. Winn*, M. Eisman* and J. Hildebrandt.
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Impulses in load, 2200 kgm/min in magnitude and 10 sec. in duration, were applied 4 minutes apart, while subjects pedalled a bicycle ergometer at 70 rpm and 200 kgm/min. Impulse responses (including $\dot{V}_E$, heart rate, respiratory rate, tidal volume and expired P_{CO_2}) were monitored continuously and averaged over at least 10 impulses for each subject. Heart rate rose rapidly within 2 seconds of the onset of exercise to reach a peak (mean increase 35 beats/min) about 5 sec after the end of the impulse; thereafter, it declined in an exponential manner. In most subjects there appeared an initial fast rise in $\dot{V}_E$ which was reversed by the off-transient of the impulse. During the following 5-15 seconds $\dot{V}_E$ fell, then rose to a second maximum about 30 sec after the end of the impulse, and finally returned slowly to baseline 2 min later. End-tidal P_{CO_2} began to rise about 6 seconds after the end of the impulse and reached a peak shortly before the peak in the slow $\dot{V}_E$ response. Graphical integration of the ventilatory impulse response yielded a predicted step response resembling those observed experimentally. The integrated response usually has an initial component which accounts for roughly 1/8 (up to 18%) of the total $\dot{V}_E$. Impulses of different height were compared with appropriate step and ramp responses. It appears that the major ventilatory response to "bolus" metabolic changes in muscle occurs only after a substantial time delay (about 25 sec) then is filtered by a time constant of about 50 sec. Changes in heart rate occur almost immediately with a time constant of 15-25 sec. Therefore, the ventilatory response could be principally humorally mediated, but cardioacceleration only neurally. Supported by NIH Grant HE 13233-01, CDA 1K04 HE 50169-01, and Cardiovascular Training Grant 1 T01 HE 05889-01.

CONTRACTILE MECHANICS OF PAPILLARY MUSCLES FROM RATS WITH EXPERIMENTALLY INDUCED CARDIAC NECROSES. H.H. Gale (intr. by D.F. Magee). Dept. of Physiology-Pharmacology, Creighton Univ. Medical School, Omaha, Nebr.

In animals a wide variety of chemical agents or a combination of chemical agents and stress will produce cardiac necroses grossly and functionally resembling myocardial infarction and resulting in death. The contractile mechanics of such hearts have not been studied. In this study 9-alpha-fluoro-cortisol and Na_2HPO_4 were administered during the course of 10 days to produce cardiac necroses in rats. Length-tension, force-velocity, and frequency-force relations were determined in isolated papillary muscles at 26 and 37°C. At low frequencies of stimulation, 1.5 or 6 beats per minute, length-tension and afterloaded force-velocity relations were the same for the hearts of treated animals and untreated controls. At high frequencies of stimulation, 480 beats per minute; isometric tension, velocity of shortening, total shortening, work output, and power output were all decreased in treated animals as compared to untreated controls. A simple index reflecting the general trend of the results is the amount of reduction in isometric tension between low and high frequencies of stimulation. Expressed as % P_o, 22 control animals show 30.8 percent force at high frequencies compared to low; whereas 22 treated animals show 16.8 percent. Animals were sacrificed after 2, 4, 6, 8, and 10 days of treatment. Statistically significant differences in mechanical properties were observed only after 6, 8, and 10 days of treatment. There was no correlation between gross signs of cardiac necroses and mechanical performance. Temperature had no influence on the differences between treated and untreated animals. The results suggest that a resting animal with cardiac necroses may have comparatively normal cardiac function while the same animal might show marked functional deficit during exercise.

EFFECTS OF ETHANOL INTAKE ON FLUID INGESTION AND DIURESIS IN RATS. Adriana Gallardo-Carpentier* and Kiyomi Koizumi. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

The diuretic effect of alcohol, at least in pharmacological doses, is very well known, even though the mechanism is still under discussion. However, during free choice ingestion of alcohol and tap water the effects of the former on fluid intake and diuresis are far from clear. We have studied the fluid intake and urine output in rats (Sprague Dawley) under conditions of both forced ethanol ingestion and free choice. When rats were forced to drink a 10% ethanol solution, total fluid intake (TFI) and urine volume were below those observed under normal condition (water only). When the same group of rats was changed to a free choice solution TFI increased reaching a value above that observed in rats drinking only water. The urine output also increased, but it did not exceed the value found in control conditions. The results seem to show that the effect of ingested ethanol on diuresis depended on its influence upon TFI and was not due to its diuretic effect. The analysis of the intake of alcohol in rats under free choice conditions showed two different populations: about 50% of the animals had an intake above 0.5 ml/100 g of body weight per day (criterion for "drinkers", Mardones J., Int. Rev. Neurobiol. 1960,2:41). Even though water intake was the same in both populations, TFI was significantly higher (approximately 25%) in rats with the high intake of ethanol solution. It is postulated that the increase in total fluid intake is due to a higher appetency for alcohol. The results indicate that an increase in TFI is responsible for diuresis.

(Supported by USPHS grant NS-6537).

PHARMACOLOGICAL INDUCTION OF SA BLOCK, AV BLOCK, AND WENKEBACH-LUCIANI PERIODICITY IN THE STANDING PONY. Harold E. Garner, James F. Amend, John P. Rosborough and Max E. Valentinuzzi (intr. by R.L.Vick) Baylor College of Medicine, Houston, Texas.

Intravenous administration of Bay Va 1470, a new sedative-analgesic chemical 2(2,6-Dimethylphenylamine)-4H-5,6-dihydro-1,2-thiazine hydrochloride to standing previously unmedicated ponies, consistently caused dose related responses of increased arterial blood pressure, bradycardia, SA block and AV block. Lower dosage (0.66 mg/kg) caused transient SA block while high dosage (1.1 mg/kg) resulted in AV block. Maximum blood pressure (systolic and diastolic) increases occurred at a mean time of 38.6 seconds and were significant ($p<0.01$) after rapid intravenous injection of the compound. Maximum bradycardia (longest single cardiac cycle) occurred at a mean time of 40.9 seconds following drug injection. Because of the virtually simultaneous occurrence of maximum bradycardia and peak blood pressure response, a baroreceptor reflex mechanism was assumed. When Bay Va 1470 was injected following alpha adrenergic blockade with phenoxybenzamine, a decrease in heart rate occurred in the absence of a rise in blood pressure. It is concluded that Bay Va 1470 acts to increase blood pressure by alpha adrenergic stimulation, and that the compound may decrease heart rate by direct cholinergic stimulation, as well as indirectly by baroreceptor reflex.

Wenkebach-Luciani periodicity was evident at the SA and AV levels of cardiac conduction depending solely upon dosage of Bay Va 1470. Wenkebach-Luciani periodicity was not observed following phenoxybenzamine. Ratios of block ranged from 3:2 to 12:11 at the SA level, and 2:1 to 9:8 at the AV level. It is concluded that pharmacologically induced SA and AV block in the laboratory pony could serve as a useful model for the study of cardiac conduction disturbances.

Venous Angiotensin I Levels During Lower Body Negative Pressure (LBNP) Experiments. W. R. Garner, R. A. Wolthuis, G. W. Hoffler, and C. S. Leach (intr. by W. Hull). NASA-Manned Spacecraft Center, Houston, Texas.

Five normal male subjects each participated in four paired incremental LBNP and sham LBNP experiments. An experiment consisted of a five minute resting control period, a 15-minute period of incrementally applied reduced pressure (actual or sham) and an extended 25-minute recovery period. Peripheral venous blood was sampled serially (total of nine samples) during the 45-minute experiment via an indwelling antecubital needle. Other measurements included the Frank lead vectorcardiogram, apex vibrocardiogram as an index of stroke volume, peripheral venous pressure as an index of CVP, calf volume and indirect blood pressure. Venous blood samples were analyzed for angiotensin I by the radioimmunoassay technique of Haber. Urine specimens were obtained before and following each experiment and were analyzed for electrolyte and catecholamine content. In a preliminary analysis, averages for each measurement were obtained for each subject, at each sampling period during both actual and sham LBNP experiments. Data from sham LBNP experiments showed no change or trend. With the actual LBNP experiments, however, individual mean heart rate, stroke volume, calf volume and blood pressure changes during reduced pressure were similar to those reported previously by this Laboratory. Each subject experienced a presyncopal episode during one of his actual LBNP tests. Individual mean angiotensin I levels during LBNP increased more than two fold in three of the five subjects, with peak levels occurring from 2 to 10 minutes into the recovery phase of the experiment. Angiotensin I changes during experiments in which presyncopal symptoms occurred did not appear to differ from changes seen in experiments without the appearance of these symptoms.

The Role of Microfilaments in Phagocytosis by Alveolar Macrophages: Reversible Effects of Cytochalasin B. J. Bernard L. Gee and Stephen E. Malawista*, Dept. Int. Med., Yale Univ. Sch. Med., New Haven, Conn.

The role of microfilaments in phagocytosis by alveolar macrophages (AM) was studied employing cytochalasin B, which reversibly disrupts contractile microfilaments in many biological systems (Wessels, Science, 171:135, 1971). Rabbit AM, obtained by pulmonary lavage, were studied in vitro in KRP-serum-glucose in the presence or absence of cytochalasin B (2-5 µgm/ml). Results: 1) uptake of live S. aureus by AM from shaking bacterial suspensions was inhibited at 20 and 40 min. of incubation. 2) $^{14}CO_2$ production from ^{14}C-labeled glucose (cpm/hr/10^6 AM/ 200,000 initial count) was also inhibited in both resting cells and cells stimulated by heat-killed S. albus (Table)

	No Bacteria		Bacteria	
Cytochalasin B	0	+	0	+
C-1-glucose	25	12	164	40
C-6-glucose	6	5	34	26

3) Effects both on phagocytosis and on ^{14}C-1-glucose oxidation were reversible by dilution and washing. (These same reversible effects are seen in human blood leukocytes. Malawista, S.E., Progress in Immunology 1st Internal. Cong. Immunol., D.B. Amos, ed., Acad. Press, N.Y., in press). 4) The ^{14}C-1-glucose effects did not occur in homogenized AM. 5) Cytochalasin did not affect $^{14}CO_2$ production from labelled pyruvate, acetate or succinate. These data provide indirect evidence for the presence in the AM of microfilaments which are involved in the phagocytic process. The reversibility and the lack of effects both on glucose in homogenized cells and on mitochondrial substrates in intact AM, support the specificity of action of cytochalasin B and its lack of general toxicity.

HEART RATE FOLLOWING CHRONIC CARDIAC DENERVATION. W. P. Geis, C.J. Tatooles*, and H.A. Spurgeon. Loyola University, Stritch School of Medicine, Dept. of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Following cardiac denervation, circulating catecholamines influence heart rate (HR). Whether alterations in cardiac chamber pressures or aortic pressure (AP) also influence chronotropic activity in the denervated heart is not known. Accordingly, seven non-denervated and eight denervated dogs were anesthetized, chests opened, and HR along with cardiac output (CO), AP, and left ventricular and atrial pressures monitored continuously. All animals received a constant infusion of hydrocortisone and acute bilateral adrenalectomy was performed to minimize effects of circulating catecholamines on HR. Right heart by-pass was instituted and AP was controlled using a variable resistor. A variety of CO were imposed at a fixed AP. Studies were repeated at each CO while AP was abruptly augmented in 25mm Hg increments from 75 to 200 mm Hg. During constant infusions of epinephrine, the interventions were repeated. Increments in CO at constant AP had little effect on HR. In contrast, stepwise augmentation in AP in the denervated group resulted in stepwise increment in HR. HR increment was approximately 10 beats/min. per each 25 mm Hg increment in AP. The response was not observed in the non-denervated group. During epinephrine infusion, initial HR (AP=75 mm Hg) was augmented accompanied by profound blunting in the HR response to AP augmentation, suggesting that the initial HR was above the level at which this response was operative. These data demonstrate that following cardiac denervation AP influences HR independent of CO - the mechanism of which may be intra-cardiac reflex or altered pulse pressure to the sinus node artery.

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OXYGEN AND ISOLATED PULMONARY ARTERIAL VASCULAR SMOOTH MUSCLE. Miklos Gellai* and Reed Detar. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Isolated pulmonary arterial strips equilibrated in a physiological salt solution at hypoxic P_{O_2} levels (zero to 40 mm Hg) for 2 to 6 hr, demonstrate paradoxical responses to changes in P_{O_2} only in a range between zero and 20 mm Hg. These responses consist of an abrupt increase in drug-induced contractile tension when P_{O_2} is diminished to zero mm Hg (hypoxic-induced contraction) and an abrupt relaxation of tension when P_{O_2} is subsequently raised to 20 mm Hg (oxygen-induced relaxation). Similar responses are observed in isolated strips exposed to higher P_{O_2} levels (100 mm Hg or above) for longer periods (e.g., 20 hr). However, the paradoxical responses observed in this latter group of strips can be produced by changes in P_{O_2} in a range above 20 mm Hg. These observations demonstrate a direct paradoxical effect of oxygen on contractility of isolated pulmonary arterial vascular smooth muscle. It appears that the intrinsic cellular processes responsible for paradoxical responsiveness of these vessel strips are regulated to operate within a particular P_{O_2} range according to the oxygen level of the environment in which the strips are equilibrated. (Supported by NIH grant #HE-12846 and NHHA grant #70.)

THE ESTIMATION OF STROKE VOLUME FROM VENTRICULAR DIAMETER IN DOGS, M. G. Gerin*, M. N. Boone* and D. A. McDonald, Dept. of Physiology, University of Alabama in Birmingham, Alabama 35233.

In an investigation of cardiac function we have been following left intraventricular diameter (V.D.) continuously with a mechanical gauge (Pieper, H., J. Appl. Physiol., 21, 1412, 1966). Ascending aortic flow was recorded with an electromagnetic flowmeter. Intraventricular and aortic pressures and the EKG were also recorded continuously and stored on magnetic tape and analyzed on a PDP-7 computer. The diameter gauge was inserted at the origin of the right subclavian artery and was positioned where the maximum ventricular excursion was observed. Various interventions used in anesthetized open-chest preparations resulted in stroke volumes (S.V.) ranging from 4.7-35 ml in dogs weighing 24-34 Kg. The V.D. measurements were converted to volumes by assuming that the ventricle was a sphere and the comparison was made of derived S.V. with flow S.V. in order to assess the accuracy of the gauge. Estimated values were found to be too large when the full excursion of V.D. was used, apparently due to a reduction in V.D. during isovolumic contraction. Calculations from the diameters measured at the opening and closing of the aortic valves gave considerably better values of S.V. Statistical analysis showed r=0.91, Y=0.17 + 0.87X ±2.1 ml S.E.E. (N=83 where each point was a mean of 4-8 successive beats). For the extrema of diameter change the corresponding values were r=0.62, Y=14.38 + 0.73X ±5.8 ml S.E.E. (N=83). The shortening of the recorded diameter in isovolumic contraction appears to be related to a real change in ventricular shape but may be exaggerated by instrument artifact and this will be discussed. (Supported by NIH Grant HE-11310-03-04, and International Fellowship to M. G. Gerin 5-F05-TW-1506.)

EFFECTS OF ADRENERGIC AGENTS ON PORTAL VEIN. A.M.Geumei, F.A.Bashour, S.J.Kechejian. Cardiopulmonary Institute, Methodist Hospital, University of Texas. Dallas.

Direct effects of adrenergic stimulants on portal vein were investigated in intact anesthetized dogs. Portal venous flow (PVF) was measured using electromagnetic flowmeter. Mean systemic arterial ($\overline{FA}$), portal venous ($\overline{PV}$), hepatic wedge ($\overline{HW}$) and vein pressures were measured simultaneously. Portal vein resistance (PVR) was calculated before and for 5 min. after intraportal administration of Norepinephrine (NE, 10 µg) epinephrine (EPI, 10 µg), Isoproternol (ISP, 10 µg) in normal (n=31) and after pretreatment with phenoxybenzamine (PNB, 1 mg/kg.IV) (n=18) and propranolal (PRP, 1 mg/kg.IV) (n=15). Immediate effects within 15 sec.) of adrenergic agents on PVR are summarized in table and reported as percent of control (%). FA remained unchanged.

	Normal	PNB	PRP	
NE	161 (16)	150 (12)	157 (11)	
EPI	169 (22)	146 (15)	185 (16)	
ISP	101 (0.7)	102 (1.1)	114 (5)	SEM = ( )

In conclusion, endogenous catecholamines (NE, EPI) constrict the portal vein directly while isoproterenol has an insignificant effect.

HEMISPHERE DIFFERENCES IN EATING BEHAVIOR IN SPLIT-BRAIN MONKEYS. A. R. Gibson* and M. S. Gazzaniga, Department of Psychology, N.Y.U., N.Y., N.Y.

Split-brain monkeys maintained on an ad-lib feeding schedule of monkey chow vary substantially in the amount of raisins they will eat depending upon which hemisphere receives visual input. This difference in eating cannot easily be explained by asymmetries in the primary perceptual or motor abilities of each half brain. Whether the difference reflects a natural asymmetry in hemispheric response hierarchies or an asymmetry caused by hypothalamic damage occasioned during the split-brain operation is not yet known. The fact that split-brain monkeys often show other abnormalities indicating hypothalamic damage, along with experimental evidence from unilaterally lesioned monkeys, favors an explanation based on a cortical-hypothalamic interaction. If true, this would imply lateral specificity in cortical-hypothalamic interactions underlying motivated behaviors.

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EDEMA "SAFETY FACTOR." H. Gibson*, A.E. Taylor, and A.C. Guyton. Dept. of Physiol. and Biophysics, Univ. Miss. Med. Ctr., Jackson, Miss. 39216

Edema fluid does not collect in the interstitial fluid spaces until the hydrostatic pressure or the effective osmotic pressure across the capillary wall is changed by 15-17 mm Hg. This filtration pressure, necessary to cause excessive interstitial edema, has been termed edema "safety factor." There are several factors that contribute to the total "safety factor." (1) As the interstitial fluid volume increases, the normally negative interstitial fluid pressure must be increased to a positive value. (2) The tissue proteins are washed out due to increased lymph flow, which increases the effective osmotic pressure across the capillary wall opposing filtration. (3) The increase in lymph flow associated with interstitial fluid expansion increases the pressure drop across the capillary wall. Previously, it has been shown that the interstitial fluid pressure must rise from -6.7 mm Hg to 0 mm Hg before edema would occur following massive intravenous infusion of fluid. Following such infusion we find the protein concentration in the lymph to be reduced from 2.0 gm % to .4 gm %, which increases the effective osmotic pressure across the capillary wall by 3.5 mm Hg. Our measurements show normal lymph flow from the paw lymphatic above the ankle to be .00006 ml/min/gm. Using Pappenheimer's filtration coefficient (K_f) of .00016 ml/min/mm Hg/gm, dividing the normal lymph flow by this K_f yields a normal pressure drop of .37 mm Hg across the capillary wall. We showed lymph flow to increase 20 times normal during edema formation which means that the pressure drop across the capillary wall increased to 7.4 mm Hg. Adding the above factors yield a calculated total "safety factor" against edema formation of 17.6 mm Hg. (Supported by NIH Grant Nos. HE 11477 and HE 11678)

THE EFFECT OF LEFT ATRIAL DISTENSION ON THE EXCRETION OF Na AND WATER IN THE DOG. D. J. Gillespie*, R. L. Sandberg*, and T. I. Koike. Dept. of Physiology, Univ. of Ark. Med. Ctr., Little Rock, Ark. 72201

Experiments were performed on 17 chloralose-anesthetized dogs to study the nature of the diuresis evoked by inflation of a small balloon placed in the left atrial appendage. All animals received DOCA and one series was given exogenous vasopressin (ADH). Mean left atrial pressure (LAP) during atrial distension increased by approximately 10 cm water. In animals not receiving ADH, atrial distension was associated with an increase in solute excretion, urine flow, and C_{H_2O}. In ADH-infused dogs solute excretion, $T^c_{H_2O}$, and urine flow increased during distension although the diuretic response was reduced. The increase in solute excretion was largely the result of increases in Na and K excretion and was independent of changes in renal hemodynamics. Enhancement of Na and K excretion and $T^c_{H_2O}$ suggests that delivery of Na to the distal nephron is increased during distension. A significant linear correlation was found between the increase in "distal Na load" and the increase in LAP, indicating that left atrial receptors play a role in Na homeostasis. The results indicate that the mechanisms underlying the diuretic response to an increase in left atrial pressure are dual in nature: 1) increase in urine flow due to reduction in endogenous ADH and 2) increases in excretion of water secondary to an increase in sodium excretion. (Supported in part by Public Health Service Grant AM-10393.)

RESPIRATORY RESPONSES TO LESIONS OF THE CEREBELLAR SUBCORTICAL NUCLEI. Richard L. Glasser, Walter M. St. John* and Richard A. King*. Department of Physiology and Neurobiology Program, University of North Carolina at Chapel Hill, North Carolina, 27514.

The respiratory effects of lesions of the cerebellar subcortical nuclei, midpontile decerebration and vagotomy, in various combinations and sequences, were studied in the anesthetized cat. Stereotaxic placement of lesions in the dentate, interpositus and fastigial nuclei produced moderate and inconsistent respiratory responses, when the pontile pneumotaxic areas and the vagal reflex systems were intact. Destruction of the cerebellar nuclei coupled with bilateral vagotomy typically produced augmentation of inspiratory amplitude and duration. However, the marked prolongation of inspiration characteristic of apneustic breathing was not observed in these animals. Destruction of the cerebellar nuclei in midpontile decerebrate cats resulted in marked prolongation of inspiratory duration usually accompanied by enhancement of inspiratory amplitude. Apneustic breathing patterns were exhibited. Vagotomy in midpontile decerebrate animals also produced apneustic breathing, as many investigators have reported. Combined elimination of the pontile pneumotaxic, vagal and cerebellar influences, regardless of sequence, produced greater exaggeration of inspiratory duration than was produced by destruction of any two influences. These data indicate that the cerebellum, in concert with the inspiration-inhibiting activity of the pontile pneumotaxic and vagal reflex systems, exerts an inhibitory influence on the inspiratory mechanisms of the lower brain stem. Among these three inspiration-inhibiting mechanisms, the data support the conclusion that the pontile pneumotaxic activity is preeminent.

EVIDENCE FOR A HUMORAL LINK BETWEEN ATRIAL RECEPTORS AND RENAL FUNCTION. Kenneth L. Goetz, and Gary C. Bond.* St. Luke's Hosp. and St. Luke's Fndn. for Med. Educ. and Res., Kansas City, Mo. 64111.

We have demonstrated that a reduction in atrial transmural pressure by "atrial tamponade" (AT) produces decreases in renal sodium excretion ($U_{Na}V$) and urine flow (V) (Am. J. Physiol. 219: 1417-28, 1970). The current studies were designed to identify the efferent pathway by which AT alters renal function. Results: 1) AT produced decreases in $U_{Na}V$ and V in the innervated kidney and in the contralateral denervated kidney of anesthetized dogs. There was no difference between the response of the innervated kidney as compared to that of the denervated kidney. Mean arterial pressure (MAP) was not changed significantly during AT in this series, but central venous pressure (CVP) increased approximately 2 mm Hg. 2) AT produced decreases in $U_{Na}V$ and V in conscious dogs with bilateral renal denervation, chronic DOCA administration, acute ADH loading, and alpha and beta adrenergic blockade. Glomerular filtration rate (GFR) decreased, and MAP decreased (8 mm Hg) during AT in this series. CVP increased approximately 2 mm Hg during AT. 3) AT also produced decreases in $U_{Na}V$ and V in anesthetized animals, blocked as above, during periods when MAP was held constant. GFR decreased and CVP increased during AT in these experiments. 4) Increases in renal venous pressure of about 2.5 mm Hg by balloon inflation in the inferior vena cava produced no decreases in $U_{Na}V$ and V. MAP was unchanged. The combined results of these studies provide evidence that AT in some way alters the concentration of a vasoactive, blood-borne agent which acts on the kidney to alter GFR, $U_{Na}V$ and V. (Supported by USPHS grant HE 13623).

PYRIDINE NUCLEOTIDES (PN) IN RESPONSE TO MODIFICATION OF PHOSPHOGLUCONATE (PG) SHUNT ACTIVITY IN HUMAN ERYTHROCYTES. J. M. Goldinger, P. L. Hawley,* and A. Omachi. University of Illinois at the Medical Center, Chicago, Illinois, 60612

Erythrocytes stored in ACD were washed and incubated in glucose-containing, Tris-Ringer's medium at 37° for 2.5 hours. The reduced (NADPH) and oxidized ($NADP^+$) forms of nicotinamide-adenine dinucleotide phosphate were measured after incubation of human erythrocytes under conditions that were expected to affect the PG pathway. It was shown previously (Biochim. Biophys. Acta, 184:139, 1969) that incubation without substrate results in a decline in NADPH and a rise in $NADP^+$. In the present study, oxythiamine (10 mM), which is known to depress transketolase activity, caused little change in PN although lactate production was increased by 30%. In a N_2 atmosphere, which might also be expected to depress PG activity, the sum of NADPH and $NADP^+$ declined although the decrease in each nucleotide was not significantly different. Methylene blue (0.1 mM), which is known to increase the activity of the PG pathway, caused a decrease in NADPH with an associated increase in $NADP^+$. When erythrocytes were incubated with 1 mM adenosine, NADPH was low and $NADP^+$ was high compared to cells incubated with 10 mM glucose. Addition of 0.1 mM iodoacetate to cells incubated with adenosine caused NADPH to rise and $NADP^+$ to decline in conjunction with a decrease in lactate production. These results indicate that PN changes can be produced experimentally in human erythrocytes by methods which modify PG activity and that these changes are generally consistent with conventional biochemical knowledge.

(Supported by PHS grants GM 738-09 and GRSG-333).

MYOCARDIAL AND SKELETAL MUSCLE SUBSTRATE UTILIZATION DURING HYPO- AND NORMOVOLEMIC HYPOTENSION. Nickole U. Gonzalez*, Robert F. Bond and Veryl B. Becker.* Bowman Gray Sch. Med. and Wake Forest University, Winston-Salem, N. C. 27103.

Our previous investigations have suggested that vasodilation of the skeletal muscle of a hypovolemic animal is the initiating factor of decompensatory shock. Other laboratories have presented data indicating a myocardial decompensation rather than a peripheral vascular collapse. Yet another team of investigators suggests that myocardial infarction (cardiogenic shock) initiates a reflex skeletal muscle vasodilation. The present study compares the myocardium and skeletal muscle utilization of glucose, lactate, pyruvate, β-hydroxybutyrate and inorganic phosphate, during the following stages: 1) control period; 2) hypovolemic hypotension (compensatory phase); 3) hypovolemic hypotension (decompensatory phase); 4) normovolemic normotension (immediately following the reinfusion of remaining shed blood), and 5) normovolemic hypotension (final decompensatory phase). Blood samples were taken from the coronary sinus, isolated thigh muscles and brachial artery of closed-chested innovar/pentobarbitalized dogs. Our preliminary data indicate that skeletal muscle used glucose through all five stages while myocardium did not. One animal which was able to maintain high arterial glucose, failed to enter decompensatory shock. Myocardium used lactate in stages 1, 3, and 5; skeletal muscle used none at any time. Pyruvate was released by skeletal muscle in stage 2 and by myocardium in stages 3 and 5. Skeletal muscle used β-hydroxybutyrate in all stages while myocardium used it only in stages 1 and 2, and possibly in 3. Large changes in phosphate were not observed. (Supported by NIH grants 344, 487, 5392; North Carolina Heart Association and Smithson Fund.)

ANTI-GONADOTROPIN TREATMENT AND SEXUAL DIFFERENTIATION OF THE BRAIN IN THE MALE RAT. R.A. Gorski, and B.D. Goldman*. Dept. of Anatomy, and Brain Res. Inst., UCLA Sch. of Medicine, Los Angeles, California.

Goldman and Mahesh (Biol. Reprod. 2: 444, 1970) found that neonatal injection of antiserum to GTH (anti-GTH) reduced fertility in the male rat. To study behavioral correlates of this infertility, anti-GTH or normal rabbit serum was injected on days 1,3,5 of life. When adult, the anti-GTH treated males did not impregnate cohabiting females, and in behavioral tests they exhibited fewer intromissions and ejaculations than the control males ($p<0.001$). Moreover, controls obtained intromission 56% of the times they mounted compared to 7% for the anti-GTH males ($p<0.001$). All rats were then castrated; the testes were equal in weight and structure in both groups. These males were next primed with ovarian hormones and tested for lordosis with stud males. The lordosis quotient (LQ = # lordoses x 100/# mounts) of controls was low (6.9) typical of the genetic male. However, anti-GTH males displayed an LQ of 72.3 ($p < 0.001$). Several weeks later all rats were given an sc graft of immature ovarian tissue. After one month all grafts were devoid of corpora lutea; anti-GTH had not prevented masculinization of pituitary control. These males were then primed with androgen for two weeks, tested with receptive females, and autopsied. Even under exogenous androgen, the anti-GTH rats had fewer intromissions and ejaculations ($p<0.001$), and a low % intromission (16.3 vs. 46.9, $p<0.001$). Prostate and vesicle weights were not different; however, the penis of the anti-GTH males was shorter and lighter than that of control males, and had fewer spines. We conclude: that infertility may be due to poor penile development and incomplete sexual behavior; that anti-GTH did have a central effect since these males displayed female levels of lordosis behavior; and that the lordosis regulating system in the male, as in the female, is less sensitive to androgen than the GTH controlling system. (NIH Grant HD-01182.)

REGULATION OF INTERSTITIAL FLUID VOLUME: A SYSTEMS ANALYSIS. H.J. Granger* and A.C. Guyton (intr. by C.E. Jones). Dept. of Physiol. and Biophysics, Univ. of Miss. Sch. of Med., Jackson, Miss. 39216

A mathematical model of interstitial volume regulation was developed. The model includes the following concepts: interstitium composed of gel and free fluid phases; negative interstitial fluid pressure; nonlinear interstitial pressure-volume relationship; lymphatic removal of fluid and proteins from interstitium; division of microcirculation into resistance, exchange, and capacitance compartments; and transcapillary protein and fluid fluxes. The forces which govern fluid movement across the gel-free fluid interface include free fluid pressure, Donnon osmotic pressure of the gel, and gel fluid pressure. Because the gel is permeable to proteins, only transient oncotic imbalances occur at the gel-free fluid interface. The analysis also considers partial exclusion of proteins from the gel phase. Transient and steady-state responses of the model to changes in venous pressure, arterial pressure, plasma oncotic pressure, and lymphatic activity were studied. The results demonstrate that fluid entering the interstitium is imbibed into the gel phase until the gel is saturated; further elevation of interstitial fluid pressure required to counteract filtration can only be produced by the large increases in free fluid volume characteristic of edema. Because of the rapid increase in imbibition forces as gel volume decreases the analysis also predicts that only 15 per cent of the interstitial fluid volume can be transferred to the circulation at the lowest capillary pressure occurring in hemorrhagic shock. Incorporation of this model into a computer analysis of overall cardiovascular regulation yields insights into the fluid shifts which occur in congestive heart failure, hypertension and nephrosis. (Supported by NIH Grant No. HE 11678)

COMPARATIVE STUDIES ON BLOOD VESSELS PERMEABILITY IN CEPHALOPOD MOLLUSCS. P. P. C. Graziadei and R. W. Beuerman*. Dept. Biological Science, Fla. State University, Tallahassee, Florida 32306.

In previous studies we have shown that cephalopods posses a highly vascularized nervous system with capillaries structure similar, however not identical, to that found in vertebrates. In the present studies we have examined the permeability of the brain vessels of cephalopods to intravascularly administered trypan blue, sodium fluorescein and fluorescein labelled globulin. These substances were injected into the dorsal aorta while an equal amount of blood was withdrawn. At controlled times after injection tissues were excised, frozen and cut at 30-60μ sections on a cryostat. Comparable experiments were performed with mice. Light microscope observations show that all of the dyes injected diffuse extravascularly in cephalopods but not in mice. The cortical zone of the cerebral ganglia of cephalopods, where the vascular supply is more dense than in the central neuropile or nerve bundles, is the zone where massive diffusion of the dye occurs. However, diffusion of the dye is observed all through the different zones of the CNS. The permeability of the dyes was in decreasing order from sodium fluorescein to trypan blue to fluoresein labelled globulin the last showing the least amount of extravascular staining for a 5 minute infusion period. EM observations have shown that cephalopod blood vessels have a discontinuous endothelial layer, a continuous basal lamina and a continuous pericyte layer. However, tight junctional complexes are not present between the cells lining the blood vessel walls. These differences are at present investigated at EM level and with the use of tracer substance to further clarify the anatomical differences between cephalopod and mammal blood vessels responsible for the different permeability of the dyes when intravascularly injected.

Research supported in part by grant NSF, GU-2612.

EFFECT OF CHANGES IN THE MAGNITUDE AND DIRECTION OF THE FORCE ENVIRONMENT ON REGIONAL DISTORTION OF LUNG PARENCHYMA IN DOGS. J. F. Greenleaf*, H. C. Smith*, A. A. Bove, D. J. Sass*, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

Regional displacements of lung parenchyma were studied in anesthetized dogs using 20-30 1-mm metallic markers 1-3 weeks after their percutaneous implantation in a spatial grid pattern (see Smith, H.C. et al, this Proc). Changes in the positions of the radiopaque tags were measured from biplane roentgenograms taken at end-inspiration and expiration at 1G and at the end of 1-minute exposures to 3 and 7G_y acceleration in the left decubitus position on a 15-foot radius centrifuge. Several animals were studied in a fluid-filled body plethysmograph allowing accurate measurement and control of lung volumes and pressures. Pulmonary arterial, aortic and esophageal pressures were measured with fluid-filled catheters. Relatively large degrees of compression and concomitant expansion of the dependent left and superior right lungs, respectively, occurred during the change from the supine to left decubitus position at 1G. Similar relatively smaller changes occurred during exposures to 3-7G_y acceleration in this position. Caudad and cephalad displacements of the superior right and dependent left domes of the diaphragm, respectively, cause relatively great distortions of the juxtaposed lung parenchyma due to the changes in weight of the relatively high specific gravity abdominal contents during acceleration. In addition, the distortion of the lung decreases with increases in alveolar volume. (Supported in part by grants USAF F41609-69-C-0058, AHA CI 10, NIH FR-7 and HE3532, and U.S. Navy.)

POSSIBLE FACILITATED TRANSFER OF O_2 AND CO_2 ACROSS THE SHEEP PLACENTA. G.H. Gurtner and B. Burns*. Department of Environmental Medicine, The Johns Hopkins University, Baltimore, Maryland 21205.

Measurements of the transfer of O_2, CO_2, Argon and Nitrogen were made in 3 term ewes using a mass spectrometer. The cord was severed and the fetal side of the placenta was flushed and perfused with an artificial solution of dextran in saline equilibrated with 100% Argon. Partial pressures of the gases were measured in umbilical artery (Pua), umbilical vein (Puv), maternal artery (Pma), and uterine vein (Pmv). We found that Puv/Pmv was close to unity for both oxygen and CO_2. Puv/Pmv for nitrogen, and Pmv/Puv for argon were both 0.3 approximately, indicating that O_2 and CO_2 come close to equilibrium in a single transit through the placenta whereas the inert gases do not. The effective permeability of the fetal-maternal exchange capillaries is greater to O_2 and CO_2 than to the inert gases. It is difficult to explain this large permeability to O_2 on a physical basis, since its physical properties are fairly similar to those of the inert gases. A possible explanation for the large apparent permeability to O_2 and CO_2 may involve facilitated (carrier-mediated) diffusion. Longmuir (Fed.Proc., 30:433,1971) has implicated a microsomal cytochrome (P-450) as a possible oxygen carrier. This cytochrome is present in the placenta and is important in drug metabolism in the liver. Infusion of a compound (SKF-525A), which binds to this cytochrome and inhibits hepatic drug metabolism, into the umbilical artery decreased O_2 transfer threefold and made O_2 transfer similar to that of the inert gases. CO_2 transfer was decreased similarly by infusion of acetazolamide into the umbilical artery, and unaffected by SKF-525A. In all instances, permeability to the inert gases remained unchanged and perfusion pressure in the umbilical artery did not vary. Supported in part by Public Health Service Grants #HE13721-01 and 5T01-MH-11110-02.

STRIATAL INHIBITION OF VESTIBULAR PROJECTIONS TO THE VISUAL CORTEX. G.R. Haase*, G.R. Narayanaswamy*, S. Morano* and E.G. Szekely. Dept.of Neurology, Temple Univ. School of Medicine, Philadelphia, Pa. 19140.

Electrographical studies (Spiegel et al.) indicated that labyrinthine impulses reach the second sensory area and also posterior cortical areas including part of the visual (vi) area II. Vestibular (ve) excitation activated the vi cortex (co) and neurons of the latter reacted often after long latency (Grüsser & Cornehls). Neurons of the vi co showed convergence of labyrinthine and retinal projections (Murato et al.). Ve and acoustic stimuli altered the discharge pattern of vi neurons (Jung et al.). Sequential to the findings mentioned we applied single electrical shocks to the ve nuclei that elicited responses in the electrogram recorded from the vi co (rat) or vi area II (cat) mostly contralateral to the stimulation. Additional neostriatal excitation (usually 40/sec) homolateral to the cortical responses diminished or abolished the ve responses during the paired excitation and for a few (5-20) seconds thereafter. The electrocorticogram during and after the coupled stimuli was only slightly altered. Ve stimulation with higher intensity needed a corresponding higher intensity for the neostriatal stimulation to subdue the evoked ve response from the co. Stronger ve stimuli activate larger number of neurons in the reticular formation. Immediately after 10-15 sec continuous stimulation of the neostriatum the summed and average ve responses from the vi co were diminished. The vestibulofugal cortical responses were abolished, the corticogram diminished one minute after insertion of 3-5 µg carbachol into the ipsilateral neostriatum.

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EFFECTS OF HYPOKALEMIA, HYPOMAGNESEMIA AND HYPOOSMOLALITY ON BLOOD PRESSURE IN THE ANESTHETIZED DOG. F.J. Haddy and J.B. Scott. Dept. of Physiol., Michigan State University, East Lansing, Mich. 48823

We have previously shown that perfusion of certain canine vascular beds with blood low in $[Na^+]$ (and therefore osmolality) or $[K^+]$ increases resistance (Am. J. Cardiol. 8:533, 1961; Am. J. Physiol. 204:202, 1963, 217:1216, 1969; Physiologist 12:343, 1969) and that rapid I.V. infusion of Ringer's solution low in $[K^+]$, $[Mg^{++}]$, or $[Na^+]$ raises blood pressure (P_S) relative to a control infusion (Am. J. Physiol. 218:234, 1970). We now report effects on P_S of steady state changes in cation concentration produced isovolemically. Plasma $[K^+]$, $[Mg^{++}]$, and $[Na^+]$ were lowered 1.0, 0.3 and 9 mEq/l (16 mOsm/kg), singly and in combination, within 83 min by injecting a duiretic (furosemide) I.V. and then replacing the lost urine with modified Ringer's solutions as previously described (J. Appl. Physiol. 29:523, 1970). In the case of lowered $[Na^+]$ (and hence osmolality) low molecular weight dextran was added to the replacement solution to maintain Hct and RISA plasma volume. Control animals received a replacement solution which maintained plasma cation concentrations normal. Relative to control animals, $\downarrow[K^+]$, $\downarrow[Mg^{++}]$, or $\downarrow[Na^+]$ was without effect on P_S but the combinations 1) $\downarrow[K^+]$ and $\downarrow[Mg^{++}]$, 2) $\downarrow[K^+]$ and $\downarrow[Na^+]$, and 3) $\downarrow[K^+]$, $\downarrow[Mg^{++}]$, and $\downarrow[Na^+]$ raised P_S. In the latter case, cardiac output (thermal dilution) increased; total peripheral resistance did not change. Administration of strophanthidin (50 ug/kg) at this time raised P_S further without measurably affecting cardiac output. The effects of $\downarrow[K^+]$, $\downarrow[Na^+]$ and strophanthidin on blood pressure may in part be related to $\downarrow[K^+]_i$, $\downarrow$membrane potential, $\uparrow$free $[Ca^{++}]_i$, and hence enhanced contraction of cardiovascular muscle. $\downarrow[K^+]$ and strophanthidin would $\downarrow[K^+]_i$ by depressing Na^+,K^+-ATPase and $\downarrow[Na^+]$ may further $\downarrow[K^+]_i$ by osmotic cellular dilution. $\downarrow[Na^+]$ may also produce mechanical effects subsequent to red cell, endothelial cell and vessel wall swelling.

STRETCH-INDUCED CONTRACTION OF BRONCHIAL MUSCLE - EFFECTS OF BLOCK OR DEPLETION OF NERVES. F. C. Hale* and C. R. Olsen. VA Hosp. (Wadsworth) and UCLA School of Med., Los Angeles, Calif. 90073.

To study mechanisms of stretch-induced contraction (SIC) of bronchial muscle (Fed. Proc. 29:662, 1970) we depleted or blocked sympathetic nerves and blocked parasympathetic nerves of dog airways in an in-vitro preparation. The airways ranged in size from tracheae to bronchi of less than 1 mm. i.d., and were equilibrated in oxygenated bicarbonate Krebs solution at 37° C for 2 hours prior to study. Changes in bronchial muscle tension were observed as changes in resting volume and compliance of the airway. The incidence of SIC in non-drugged airways (146) from untreated dogs was 33%. Viability of parasympathetic and sympathetic nerves was suggested by contraction of bronchial muscle in response to neostigmine methylsulphate alone in 85 of 114 airways and relaxation of neostigmine and acetylcholine chloride (or pilocarpine hydrochloride) treated airways after nicotine hydrogen D-tartrate (100 to 500 μg/ml [as base]) in 25 of 29 airways. Hexamethonium chloride blocked the relaxation with nicotine; after washing out the hexamethonium the response to nicotine returned. Following the depletion of catecholamines with reserpine (2 mgm/kg over 2 days), as indicated by lack of relaxation with nicotine, 30 of 79 airways (38%) showed SIC. All relaxed with isoproterenol hydrochloride. In-vitro block of β-adrenergic receptors with propanolol hydrochloride and of cholinergic receptor sites with atropine sulphate did not alter the incidence of SIC. In this in-vitro preparation the block or depletion of autonomic nerves did not appear to elicit or abolish the contraction of the bronchial muscle as a response to stretch.

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EXERCISE IN HIGH PRESSURES OF NEON, HELIUM AND NITROGEN. R. W. Hamilton, Jr. and T. D. Langley*. Ocean Systems, Inc., Tarrytown, N. Y. 10591

Deep sea diving at pressures beyond about 7 atm. is usually done using helium as the inert gas. We are investigating the use of crude neon (c. 75% Ne, 25% He) to avoid the excessive heat loss and speech distortion of He. We exposed subjects to pressures of 7, 10 and 13 atm in a dry pressure chamber using either He, N_2 or crude Ne and 10% O_2, and to 16 and 19 atm with Ne and He and 7% O_2. Following 15 minutes of performance testing, divers rode a bicycle ergometer for 10 min. at 140 watts. Breath-by-breath end-expiratory CO_2 was drawn by a nasal catheter into an infrared detector modified for pressure; there were no other restrictions to breathing. Heart rate showed slight increases over control in the pressure experiments, increasing somewhat more at the higher pressures. Respiration rate tended to be less at pressure than control, and was relatively higher in He than the other gases. CO_2 rose at first with exercise while at depth in all cases, returning toward normal with He but leveling off at 8-12 mm Hg above normal with Ne and N_2. No evidence of neon narcosis was seen, but narcosis was quite severe with nitrogen forcing the diver to stop work after 3 min. in the 400' dive. We see no reason why crude neon should not be safe and effective for diving to depths up to 500'.

AUTONOMIC CONTROL OF HEART RATE IN THE HORSE. Robert L. Hamlin, Charles R. Smith, Kay W. Gilpin*, and Wayne L. Klepinger*. Ohio State University, Columbus, Ohio 43210.

In the horse, heart rate (HR) varies between 20 (at rest) and over 250 (during exertion). Purposes of this study were to evaluate the roles of parasympathetic (P) and sympathetic (S) efferent activity and alterations in systemic arterial blood pressure (SAP) on HR. P or S blockade was produced with atropine (AT) or propranolol (PR). Reduction or increase in SAP was produced with nitroglycerine (NG) or phenylephrine (PE). Mean HR's, as studied in 12 healthy, 350 kg. horses by electrocardiography, were as follows:

control (C) = 34±4, after PE = 19±3, after NG = 75±10, after AT = 85±15, after PR = 34±4, after AT+PR = 90±15, after NG+PR = 75±10, after exertion (E) with no drugs = 220±40.

HR slows below C, because P increases (but not by decrease in S). HR increases from C to approximately 100 by either P decrease or S increase, but decrease in P, alone, can produce HR up to 100. HR above 100 is produced, only, by increase in S. That NG produced an increase in HR to, but not above, that produced by AT, indicates that a decrease in SAP causes reflex tachycardia by decrease P.

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AUTOREGULATORY ESCAPE IN THE CANINE LIVER. K. M. Hanson. The Ohio State University College of Medicine, Columbus, Ohio.

The phenomenon of autoregulatory escape has been studied in autoperfused in situ isolated canine liver preparations. Response of hepatic arterial (HA) and portal venous (PV) vasculature to prolonged periods (6 min or longer) of faradic stimulation (20 v, 10 cps) of the peripheral end of the hepatic nerve trunk was observed in 33 experiments. This produced increased pressure and resistance and decreased flow in both liver vascular beds. Maximum HA response was seen after 60-90 sec and showed some degree of escape from the vasoconstriction (mean 40% recovery) after 5 min stimulation in about 85% of the cases. Maximum PV response was seen after 90-120 sec of stimulation and also showed some tendency to escape from vasoconstriction (mean 30% recovery after 5 min stimulation). The constrictor responses were abolished or, in some cases, reversed by dibenamine. The HA constrictor response was decreased by DCI and that of the PV was decreased by propranolol; while the latter drug appeared to increase the HA constrictor response. When a 4 min stimulus was followed after 2 min by a repeat, response to the second stimulus was significantly less. Finally, in the experiments done thus far, we have seen little or no clear evidence of escape from the vasoconstrictor effects of HA infusion of norepinephrine at any dose given (1.5-28.6 μ gm/min) over a 10-20 min period.

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PHYSIOLOGICAL RESPONSES FOLLOWING HIGH VOLUME INTERVAL TRAINING. B. S. Harger,* R. L. Bartels,* E. L. Fox,* and D. K. Mathews. The Ohio State University Exercise Physiology Lab., Columbus, Ohio.

The purpose of this study was to determine differences in the effect of two frequencies of high volume interval training on the metabolic and cardiorespiratory responses of untrained college men. Specifically, the following variables were compared: max $\dot{V}O_2$, PWC, blood L.A. concentration, max anaerobic power, max $\dot{V}_E$, performance times, max and rec. HR, plus resting values for blood volume, heart volume, systolic intervals, and hemoglobin concentration. The subjects were divided into two groups; Group 2X (N=8) trained two times per week while Group 4X (N=5) trained four times weekly. The conditioning program was based on seven weeks of high volume interval training and was designed to have the groups attain peak mileages at the end of the sixth week. Group 2X progressed from 7.5 miles weekly to 18 and Group 4X increased its weekly totals from 15 to 35 miles per week. The results indicated that Group 4X improved more than 2X on the increase of $\dot{V}O_2$ max (ml/kg-min); however, a close scrutiny of the problems introduced by the small sample and 3 subjects who began the study surprisingly well trained casts doubt as to the validity of the statistical differences obtained. The groups were similar on improvements in max $\dot{V}_E$, max and rec. H.R., PWC, and performance times. There were no significant improvements for either group on any of the cardiac or hematological variables tested. High volume training produced an excessive amount of physical trauma in Group 4X.

THE EFFECT OF Ca-K INTERACTION ON THE PLATEAU OF THE CARDIAC ACTION POTENTIAL. J.E. Harris* and M. Morad. Dept. of Physiol., School of Med., Univ. of Pennsylvania, Phila., Pa. 19104.

The effects of variation in external potassium and calcium concentrations were studied with microelectrodes in frog ventricular strips, equilibrated in Ringer solution (temp 23°C). The duration of action potential (AP) and the repolarization waveform were found to be dependent on $(K^+)_o$ and $(Ca^{++})_o$. Lowering $(Ca^{++})_o$ from 1.0-0.01 mM, at constant extracellular potassium concentration (3 mM), produced an increase in AP duration up to 3.5 sec. Lowering $(K^+)_o$ from 3.0-0.6 mM at 1 mM$(Ca^{++})_o$ produced an increase in AP duration. At $(K^+)_o$ less than 0.6 mM the AP shortened to approximately 50 msec with a "spike"-type waveform and disappearance of the characteristic myocardial plateau. The extracellular potassium concentration at which the AP shortened to a "spike" form was directly correlated with the calcium concentration of the bathing medium; e.g., at 0.2 mM $(Ca^{++})_o$, the critical $(K^+)_o$ was 0.1 mM. This "spike" effect of low $(K^+)_o$ was not observed at very low $(Ca^{++})_o$, where the membrane potential depolarizes to a second "stable state" at about -40 mV for duration of exposure to low $(K^+)_o$ and low $(Ca^{++})_o$. In the presence of atropine and propanolol, the above results were reproduced. These experimental observations suggest a direct interaction between calcium and potassium in the determination of the duration of plateau and the rate of repolarization. A carrier-mediated transport system is compatible with these observations, in which the efflux of $(K^+)_o$ is coupled in a rate-limiting manner to the influx of calcium. Supported by AHA Grant #71-1026 and #GM-02046.

IMMUNOFLUORESCENCE OBSERVATIONS OF CROSS REACTIONS BETWEEN HAMSTER, BOVINE, AND HUMAN FETAL CELLS AND SERUM FROM HUMAN LYMPHOMAS. Warren W. Harris and B. W. Harrell (intr. by N. G. Anderson). Molecular Anatomy (MAN) Program, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830.

These studies concern the question of whether convalescent antibodies to an autochthonous human tumor thought to be of viral origin would react with embryonic or early fetal cells. Two convalescent sera from heterophile antibody negative infectious mononucleosis and from eight Uganda Burkitt lymphoma patients were used in tests against hamster 10-day fetal cells, nuclei from three-month-old bovine embryos, cultured human embryonic kidney cells, and SV40 transformed hamster cells. Positive tests for antibody attachment of both sera to each cell type were obtained with (a) direct FITC labeled sera, (b) blocking, and (c) indirect tests using goat anti-anti human serum. Thirteen out of fourteen normal human sera were not absorbed by HR_1K Burkitt cells. Absorption tests with 10-day hamster fetal cells dropped the mononucleosis titer from more than 1:200 to less than 1:10 and the Uganda titer from more than 1:500 to less than 1:50. These results demonstrate the presence of a cross-reacting antigen or antigens in infectious mononucleosis, certain leukemias, the Burkitt lymphoma, and fetal cells from two sources. Three possible explanations will be considered, one of which leads to the likelihood that many tumors express the embryonic features of changing associations and rapid cell division and exhibit the embryonic antigen associated with these properties. (Supported by NCI, NIAID, NIGMS, and AEC.)

COMPUTED MAXIMUM EXPIRATORY FLOW OF GAS AND LIQUID, J.H. Haynes*, W.H. Schoenfisch* and J.A. Kylstra. F.G. Hall Laboratory for Environmental Research, Duke University Medical Center, Durham, North Carolina

Mead et al. (J.A.P., 22, 95, 1967) have postulated that maximum expiratory flow ($\dot{V}_{max}$) is limited by the static recoil pressure of the lung (P_{stat}) and R_{us}, i.e. the resistance to flow through the airways upstream of equal pressure points (E.P.P.). We have computed the pressure drop (ΔP) in each generation of airways in the human lung, using dimensions given by Weibel (Hdbk. Physiol., Respiration, Vol. I, p. 303) and standard fluid flow equations. We assumed that $\dot{V}=\dot{V}_{max}$ when $\Sigma\Delta P=P_{stat}$. Our calculations clearly reveal that $\Sigma\Delta P$ upstream of generation 9 is very small for gases as well as for liquids and that ΔP is greatest at generation 3. Assuming P_{stat} = 15 cm. H_2O, computed $\dot{V}_{max}$ for air at 75% T.L.C. and 1, 2, 4, 6, 8 and 10 Ata, were 7.7, 5.4, 3.9, 3.2, 2.7 and 2.4 l/sec, respectively. These values agree closely with experimental findings in normal men (Wood & Bryan, 4th Symposium of Underwater Physiol., Philadelphia, 1969). $\dot{V}_{max}$ of air, Ne, SF_6, saline and FC-80 fluorocarbon in excised dogs' lungs also agreed closely with computed maximum flows in Weibel's lung model. For He at less than 5 Ata computed $\dot{V}_{max}$ is consistently greater than measured $\dot{V}_{max}$. In excised dogs' lungs at a given volume, $\dot{V}_{max}$ of air increased, but $\dot{V}_{max}$ of He at the same volume did not increase at progressively greater simulated altitudes up to 5500 m. We conclude: 1) That $\dot{V}_{max}$ in healthy lungs of men and dogs is a predictable function of P_{stat} and the dimensions of larger airways, for fluids with a density greater than 1.1 gm/l and a viscosity less than 1.4 cp., 2) That E.P.P. normally are fixed at the segmental bronchi by the geometry of the system and the characteristics of flow, 3) That $\dot{V}_{max}$ of He normally is limited by tissue resistance rather than by resistance to gas flow.

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UNIT ACTIVITY IN THE OCULOMOTOR NUCLEUS ASSOCIATED WITH EYE MOVEMENTS. Volker Henn* and Bernard Cohen. Department of Neurology, Mount Sinai School of Medicine, New York, N.Y. 10029.

Unit activity associated with vertical and horizontal eye movements was recorded in the brainstem of alert monkeys using tungsten microelectrodes. Several types of neurons were found in the region of the oculomotor nucleus. In one group discharge rates reflected eye position in a particular plane of movement and there was a dramatic increase or decrease in activity during saccades or quick phases of nystagmus in this plane. These cells have previously been described by several authors. Other cells were found which had tonic activity related to eye positions in particular spatial planes with little or no phasic activity during rapid eye movement. Still others had little or no steady activity but fired during rapid eye movement in specific directions of gaze. Some of these units also had steady discharges when the eyes were in extreme deviation in that direction. It is not known whether these neurons were oculomotor motoneurons but their cell bodies lay within the oculomotor nucleus. The data raise the possibility that, contrary to previous reports, there are motoneurons with different patterns of activity in the oculomotor nucleus.

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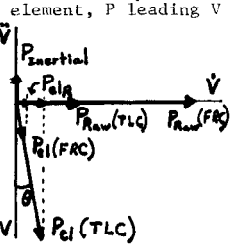
MEMBRANE ELECTRICAL PROPERTIES OF VASCULARIZED HAMSTER ATRIAL HOMOGRAFTS. Kent Hermsmeyer and Melvin Greenblatt.* Dept. of Physiology and Biophysics and Eppley Institute for Cancer Research, Univ. of Nebraska Col. of Med., Omaha, Neb. 68105.

Neonatal atria were implanted in cheek pouches of inbred, Syrian golden hamsters in optical chambers previously described (Microvasc. Res., 1:420, 1969, and Transplant., 11:50, 1971). The fragmented tissue vascularized in 3-4 days at which time spontaneous, rhythmic contractions were observed. Although an implant could be microscopically observed to be a continuous group of cells, there were usually several foci. Impalement of the cells showed resting E_m and action potentials (APs) generally similar to those of nodal (N), atrial (A), and conductile (C) cells. Impalements were made during pentobarbital anesthesia at an intrapouch temperature of 28-33°C. For the N type, firing at 140/min, average resting E_m was 63 mV, amplitude of the APs was 85 mV, and duration was 140 msec. In the A type, firing at 80/min, resting E_m averaged 74 mV, AP ampl. was 95 mV, and dur. was 120 msec. In the C type, firing at 100/min, resting E_m averaged 83 mV, AP ampl. was 112 mV, and dur. was 200 msec. In addition, some APs occurred at rates greater than 2/sec; these were similar to those seen in atrial tissue in fibrillation, and were accompanied by continuous, desynchronized contractions. These fibrillatory APs, at the rate of 3-6/sec, were very brief (<50 msec), and rose from a resting E_m of 72 mV, with an overshoot from 12 to 20 mV. At times there were cycles of activity and rest, in which the APs would begin at a slow rate, accelerate, decelerate, and cease; cycle durations were from 30 sec to 4 min. Thus, vascularized homografts in the hamster cheek pouch exhibit cellular characteristics similar to those in the in situ heart and may be useful in the study of cell membrane phenomena during cardiac transplantation.

LUNG HYSTERESIS COMPONENT OF TOTAL PULMONARY RESISTANCE IN OSCILLATORY METHODS. J. Hildebrandt. VMRC, 1000 Seneca, Seattle, Wash 98101

Resistance from oscillatory methods comprises an airway resistive component together with (surface + tissue) hysteresis. At lower lung volumes the latter is relatively small, but near TLC its energy dissipation could become comparable to that in the lower airways. The effect might be an apparent increase in resistance at high lung volumes (JAP 29:236, 1970). Two methods of dealing with the hysteresis component are suggested. (a) Instead of representing lung recoil by a perfect spring (P and V in phase) it can be approximated by a lossy elastic element, P leading V by roughly 7-8° (JAP 28:365, 1970). This angle seems not to vary greatly with either oscillating frequency or lung volume. Thus, as volume increases toward TLC, P_{Raw} diminishes while the tissue resistive component increases sharply along with P_{el}, resulting in a rise in total R_L. If compliance near TLC were 0.050, the resistive part of P_{el} would be $P_{elR} \simeq V_T \sin\theta/0.05$, while $P_{Raw} = R_{aw}\dot{V} = R_{aw}V_T\pi f$. For $R_{aw} = 0.2$, f = 4 and $\theta = 7°$, $P_{Raw} \simeq 2P_{elR}$. (b) Since hysteresis area A_H can be roughly described by $A_H \simeq kV_T^3/C$, where $k \simeq 0.1$ (JAP 30:493, 1971) one finds that near TLC, $A_H \simeq 0.1V_T^3/0.05 = 2V_T^3$. On the other hand, the energy loss/cycle in airways is $A_R = 2\int_0^{V_T} p\,dV$, where $p = R_{aw}\dot{V}$. Thus $A_R = \frac{4}{3}\pi R_{aw}V_T^3$. When $R_{aw} = 0.2$ and f = 4, $A_R \simeq 4V_T^3$, so that $A_R \simeq 2A_H$, in agreement with (a) above. By these methods any value of R_L could be corrected to yield R_{aw}, provided C at all points were known or estimable. It appears that almost no real increase in R_{aw} need occur near TLC.



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EFFECTS OF ENDOTOXIN ON MYOCARDIAL HEMODYNAMICS, PERFORMANCE AND METABOLISM DURING BETA ADRENERGIC BLOCKADE. L. B. Hinshaw, L. J. Greenfield, L. T. Archer*, and C. A. Guenter*. V.A. Hosp. and Univ. of Okla. Med. Ctr., Okla. City, Okla.

The question of the precise role of the heart in shock has been largely unresolved. Previous reports have shown that both excitatory and depressant actions on the myocardium after endotoxin are observed. The purpose of the present study was to assay the possibility of a direct myocardial toxic action of endotoxin or a circulating myocardial depressant factor released in the blood of endotoxin shocked animals. This was accomplished by utilization of beta adrenergic blockade (propranolol) under the experimental conditions of constant cardiac output and aortic pressure in an isolated canine heart preparation exchanging blood with an intact support animal. Results from the study fail to reveal a myocardial depressant effect following lethal injections of endotoxin administered to both isolated heart and intact dog. Marked systemic hypotension and acidosis in the support dog were observed. Cardiac performance is relatively unimpaired after endotoxin in the presence of beta adrenergic blockade as evidenced by normal cardiac work and power, dP/dT, left ventricular end diastolic pressure and oxygen uptake. Myocardial performance is postulated to be maintained in the presence of endotoxin and shocked blood by increased coronary blood flow under conditions of maintained cardiac output and coronary perfusion pressure. Findings from the present study do not preclude the possibility of adverse effects of prolonged systemic hypotension and hypoperfusion on myocardial performance.

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THE INFLUENCE OF HEMODYNAMICS ON THE DEVELOPMENT OF ATHEROSCLEROSIS
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The purpose of this study was to demonstrate that viscous shear stress on the endothelial surface of an artery could be causal in initiating lipid deposition and incipient atherosclerosis. Twenty-one male New Zealand white rabbits were fed a 1% cholesterol regimen for periods ranging from 45 to 60 days. The rabbits were sacrificed and the aortas excised, fixed, and stained with Sudan IV. Sudanophilic plaque deposition generally appeared as a crescent shaped pattern, concave on the proximal side, on the downstream surfaces of aortic branch ostia and on the apex of the aortic arch. The specific foci of incipient plaque deposition have been shown to be coincident with locally elevated values of viscous shear stress at the wall caused, in the case of ostia, by boundary layer development following flow division and, in the case of the aortic arch, by an asymmetrical velocity profile resulting from secondary flow phenomena. It was shown that these effects in addition to instantaneously high values of viscous shear associated with the pulsatile flow of blood, could result in critically large magnitudes of viscous shear stress at the arterial wall during part of the cardiac cycle. Under the conditions of abnormally high blood concentrations of lipoprotein, one concludes that arterial wall sites chronically exposed to high viscous shear experience endothelial deformation leading to increased permeability toward blood bourne lipoprotein. The accumulation of lipoprotein in the intima results in atherosclerotic pathogenesis.

OCCURENCE OF A HORMONE ANTAGONIST IN RAT EPIDIDYMAL FAT CELLS. R. J. Ho and E. W. Sutherland, Dept. of Physiology, Vanderbilt Univ., Nashville, Tenn. 37203

An antihormone factor that inhibits the ability of lipolytic hormones to increase cyclic AMP (CA) levels has been found in isolated fat cells from epididymal adipose tissue of rats. Epinephrine (6×10^{-7} M), ACTH (2 mU/ml) or glucagon (2.0×10^{-7} M) promoted the formation of this antagonist. It was formed in fat cells and released into the incubation medium during hormone stimulation. The activity appearing in the medium was dependent on both the concentration of hormone and the time of incubation. An increase in CA level in response to the hormones preceded the formation of the hormone antagonist, and the antagonist accumulated during a period when CA was decreasing toward the basal level. Antagonist formed by fat cells during the first stimulation by lipolytic hormone prevented the action of a second addition of that hormone, but the sensitivity to hormones could be restored by washing with new medium. The material that accumulated following epinephrine stimulation prevented the action not only of epinephrine but also of ACTH or glucagon. The antihormone substance was partially purified. Its activity was not mimicked by palmitate (1.5 mM) or oleate (1.5 mM). The inhibitory activity in the incubation medium was equivalent to nM prostaglandin E_1 (PGE_1). However, unlike PGE_1, it did not elevate CA in human platelets and rat spleen slices. The antagonist may be involved in a negative feed back loop moderating hormone response.
(Supported by USPHS HE08332, GM-16811 and American Heart Association).

SMALL VEIN CONSTRICTION DURING CAROTID ARTERY OCCLUSION AFTER URETHANE ANESTHESIA. L.F. Hodoval*, P.D. Harris, and D.E. Longnecker*. Microcirculatory Systems Research Group, Dept. of Vet. Physiol. and Pharmacol., Sch. of Vet. Med. and Depts. of Physiol. and Anesthesia, Sch. of Med., Univ. of Missouri, Columbia, Mo. 65201.

The effects of urethane anesthesia (800 mg/Kg) and bilateral carotid artery occlusion upon arterial pressure, heart rate, small artery diameter (34-45 μ) and small vein diameter (70 to 100 μ) were studied in bats (Myotis sodalis). The wings of a restrained unanesthetized bat were extended over a glass plate for observation with a trinocular microscope. Closed-circuit television was utilized to display the microscopic image at a total magnification of 1000X. One radial artery was cannulated for recording blood pressure and heart rate was monitored with subcutaneous needle electrodes. Five minutes after urethane administration (N=6), mean arterial pressure decreased to 68±6.5% of the pre-anesthetic value, heart rate decreased to 80±8.3%, artery diameter increased to 115±2.6%, and vein diameter was unchanged (103±6.9%). Data after bilateral carotid artery occlusion in the anesthetized animal appear in the following table.

	Time (min) after carotid artery occlusion			
% of Pre-occlusion	1	5	10	15
Arterial Pressure	119±3.4*	125±4.3*	120±4.1*	122±4.0*
Heart Rate	109±2.9*	111±3.5*	114±4.1*	113±4.6*
Artery Diameter	95±1.3*	92±2.2*	92±1.8*	91±2.0*
Vein Diameter	100±2.0	98±1.8	96±1.9*	95±2.0*

(Mean ± Standard Error: *P<.05 for N=20)

(Supported by HE 12614 from NHLI, GM 33611 from NIGMS and FR 5387-08 from Univ. of Mo.)

RATE DEPENDENT EFFECTS OF CALCIUM ON AUTOMATICITY IN CANINE PURKINJE FIBERS. P. M. Hogan and S. L. Sinclair*. Dept. of Physiology, State University of New York at Buffalo, Buffalo, New York 14214 USA.

Increases in extracellular calcium concentration are known to increase the spontaneous rate of isolated hearts, suggesting a direct membrane effect of calcium on cardiac pacemaker cells. To test this possibility transmembrane potentials of isolated, perfused canine Purkinje fibers were continuously monitored for changes in the electrophysiological parameters of automaticity as a function of extracellular calcium concentration. Preparations were driven electrically at a rate of 90/min as the extracellular Ca^{++} concentration was raised from 2.7 mM to 16.2 mM in Tyrode solution. Increased Ca^{++} caused a decrease in maximum diastolic potential (shift toward zero potential) and a simultaneous increase in the rate of slow diastolic depolarization. These changes favor an increased rate in spontaneously firing fibers. Furthermore, threshold potential decreased with increased extracellular Ca^{++}, thereby limiting the increase in automaticity of the fiber. Such calcium induced changes in automaticity were drive rate dependent. During periods of rapid drive Ca^{++} induced changes were increased, but reverted quickly upon return to the basic drive rate. The degree of such transient enhancement was directly proportional to the rate of rapid drive. The changes in maximum diastolic potential and slow diastolic depolarization were opposite to those observed during rapid drive in control Tyrode solution. It appears that increases in extracellular Ca^{++} may cause rate-dependent enhancement of automaticity in the canine Purkinje fiber.

METABOLIC ENERGY SOURCES AS AFFECTED BY A SEVEN-WEEK PROGRAM OF INTERVAL TRAINING. B. L. Hollering,* E. L. Fox,* R. L. Bartels,* and D. K. Mathews. The Ohio State University Exercise Physiology Laboratory, Columbus, Ohio.

Metabolic energy sources of four healthy men (23-34 years) were investigated before and after seven weeks of interval training. The 3-day/week workouts consisted of a series of 30-second high-intensity treadmill runs alternated with 45-second rest intervals. The subjects performed a short exhaustive treadmill run (before and after training) averaging 96 seconds in duration at workloads ranging from 12.9 to 16.1 km./hr. on 7 to 10 per cent grades. In addition, a duplicate run was performed after training at an identical workload and duration as the pretraining short exhaustive run. Measurements of oxygen consumption and blood lactate were used to determine the energy (kcal.) and power (kcal./kg.-hr) delivered via the aerobic, lactacid and alactacid energy sources. Comparison of the mean data between the pre-training short exhaustive run and the post-training duplicate run showed the following metabolic alterations: (1) total energy production decreased 7.2%, (2) the aerobic energy contribution was reduced 3.4%, (3) the lactacid energy delivery decreased by 20.5%, and (4) the alactacid energy contribution remained stable (0.8% increase). Analysis of the pre and post-training short exhaustive run data revealed the following mean changes as a result of training: (1) total energy production increased 12.8%, (2) aerobic energy delivery was 10.9% greater, (3) the lactacid energy contribution was improved 15.1%, and (4) a 14.5% alactacid energy increment was noted. When the same comparisons were made on the basis of power, similar metabolic trends were evident. (Supported in part by ONR contract N00014-67-A-0232-0008).

EFFECT OF VOLUME HISTORY ON TIME-DEPENDENT P-V CHARACTERISTICS OF EXCISED CAT LUNG. T. Horie* and J. Hildebrandt. Virginia Mason Research Center, 1000 Seneca, Seattle, Washington 98101.

Stress adaptation and dynamic compliance (Cdyn) were measured on excised cat lung for 20 min periods at 3 selected volume levels, 25%, 55% and 70% TLC. These were also the end-expiratory volumes (Ve) in dynamic experiments. Two volume histories were compared: (a) inflation to TLC, then deflation to Ve, and (b) deflation to zero Ptp, inflation to Ve + 15% TLC, then deflation to Ve. With air, history did affect Ptp at a given volume level, but almost no difference in Ptp was seen with saline. In static experiments, increases of Ptp by adaptation were about 0.5 cm H_2O with air and 0.1 cm H_2O with saline. After 20 min equilibration (air), static pressure differences at each volume level were: 1.5 cm H_2O (25% TLC), 2.1 cm H_2O (55% TLC) and 1.1 cm H_2O (70% TLC), and these differences were statistically significant ($p < 0.001$). Estimated surface tension (γ) (Physiologist 12: 162, 1969) revealed nonconvergence, ie, multiple equilibrium γ at the same surface area. In dynamic experiments with air and with a tidal volume of 15% TLC, initial Cdyn at a given Ve was higher following history (a) than following history (b). During 20 min ventilation, differences in Cdyn and in Ptp gradually diminished. Saline-filled lung showed small changes in Cdyn (1/10 that of air), however, the directions of change were the same as in the air-filled lung. Changes apparently continue beyond 20 min. Convergence of loops could be estimated (by extrapolation) to require 100-1000 hours. These times indicate that, effectively, a static hysteresis occurs in dynamic situations as in the static ones, and that a single equilibrium value cannot be attained in the times available for physiological experiments.

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THE INTERACTION OF SKIN AND HYPOTHALAMIC TEMPERATURE IN THERMOREGULATION OF THE UNANESTHETIZED CAT. W.S. Hunter* and T. Adams. Department of Physiology, Michigan State University, East Lansing, Michigan 48823.

Although average skin ($\bar{T}_s$) and preoptic hypothalamic (T_{hy}) temperatures have been identified as separate thermoregulatory inputs in warm-blooded animals, their possible interaction in a homeothermic control system has not been examined. $\bar{T}_s$ and T_{hy} were independently varied in 116 experiments on 6 lightly restrained, unanesthetized, adult cats (2 to 5 kg body wgt.), while measurements of metabolic heat production (M), respiratory evaporative water loss (E), respiratory frequency (f) and internal abdominal temperature (T_{re}) defined resultant thermal balance. $\bar{T}_s$ was adjusted between 33.9°C and 38.3°C by allowing each animal to reach a thermal steady state at a mild cold (23°C), thermoneutral (29°C) or mild heat-stressing (35°C) ambient temperature (T_a); T_{hy} (monitored by an implanted thermistor) was adjusted in increments as much as 2.3°C above or below a resting level at each T_a using a water-perfused heat exchanger chronically implanted in the presphenoid sinus. Vasodilation of the ear, forefoot, lower hind leg and tail in response to hypothalamic heating was partially or totally inhibited by a low $\bar{T}_s$. Vasoconstriction in the same areas induced by hypothalamic cooling was inhibited by a high $\bar{T}_s$. An increase in M with hypothalamic cooling was greater the lower $\bar{T}_s$. The augmentation of the heat dissipating responses of elevated E and f by T_{hy} increases was facilitated by a high and diminished by a low $\bar{T}_s$. These data are interpreted as indicating that although both $\bar{T}_s$ and T_{hy} function as thermoregulatory control inputs, their respective influence is mutually modulated.

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EXPIRATORY FLOW LIMITATION, THE CAUSE OF SO-CALLED "AIRWAY CLOSURE" OR "CLOSING VOLUME". R.E. Hyatt and G.C. Okeson*, Mayo Fdn., Rochester, MN.

When O_2 is inhaled from residual volume (RV) to total capacity and a slow expiration to RV performed, there occurs in normals a characteristic rise in N_2 concentration as RV is approached. Dollfuss and associates (Resp. Physiol. 2:234, 1967) demonstrated a similar phenomenon by introducing a bolus of ^{133}Xe at the onset of inspiration and termed the concentration change phase IV and suggested its cause was "progressively rising closure of airways from base towards apex as RV is approached". Phase IV has been taken by some as evidence of "trapping" and possibly of early small airway disease but Jones and Clarke (Clin. Sci. 37:343, 1969) have recently shown that the volume at which Phase IV occurs varies with expiratory flow rate ($\dot{V}exp$). We noted the same. We have studied nine normal seated males. Control FV curves were obtained in a body box. Single-breath O_2 tests were initiated from RV. $\dot{V}exp$ was held relatively constant either voluntarily or by an orifice. $\dot{V}exp$ was varied between 0.3 - 5.0 l/sec. With $\dot{V}exp$ relatively steady, a volume was reached, defined by the FV curve, where flow-limitation and dynamic compression (sharp rise in transpulmonary pressure) began. At this volume N_2 concentration rose consistent with Phase IV. By changing $\dot{V}exp$ this volume could be varied from 15-50% VC above RV. Dynamic compression of airways beginning in dependent regions appears to be the explanation of Phase IV. Dependent regions do not close but continue to empty at slower rates. Phase IV does not represent a unique volume. We suggest that reported changes in closing volume with age, etc. may basically reflect changes in slope of the FV curve. Correlations between "closing volume" (Phase IV) and altered gas exchange may not be simply explained by airway closure and trapping. (Supported by PHS Grant HE 12229).

CLINICAL MEASUREMENT OF PLASMA COLLOID OSMOTIC PRESSURE. Edwin J. Jacobson,* Max H. Weil, Rudolf Ritz,* and Sybil Michaels.* USC School of Medicine, Los Angeles, California.

Measurements of plasma colloid osmotic (oncotic) pressure are made using a modification of techniques of Prather, et al[1]. A pool of preserved human plasma or dextran (M. W. 70,000) were used as standards together with bovine albumin in increments from 1 to 7%. The maximum differences between all of these standards over 33 days was 1.7 (torr). The fit of curves obtained with albumin increments were within 95 percent confidence range of those reported by Prather, et al[1] and Hansen[2]. In three critically ill patients, two of whom had clinical signs of circulatory shock, oncotic pressures were reduced to 11.9, 13.5 and 15.2 (torr); serum albumin was 1.6, 1.7 and 2.5 gm% determined by separation with 2,4 hydroxyazobenzine benzoic acid. Total protein was 4.2, 4.8 and 5.5 gm% by Biuret method. In each case, there was unequivocal x-ray evidence of pulmonary edema. However, right atrial (3), pulmonary artery (3), pulmonary artery wedge (3), and left ventricular end diastolic pressure (1) were all within normal ranges. We therefore recognize a clinical syndrome of pulmonary edema associated with oncotic hypotension, in the absence of pulmonary venous hypertension. Since these were selected from only 14 cases which were comprehensively studied over a period of 2 months, changes in oncotic pressure, not fully reflected in measurements of plasma proteins, are likely to be an important cause of pulmonary failure in critically ill patients. (Supported by United States Public Health Services grant HS 00238.)

[1] Prather, J. W., et al. J. Appl. Physiol. 24(4): 602-605, 1968.

[2] Hansen, A. T. Acta Physiol. Scand. 53: 197-213, 1961.

EFFECTS OF PROSTAGLANDIN $F_{2\alpha}$($PGF_{2\alpha}$) ON MECHANICAL AND ELECTRICAL PARAMETERS OF RAT PAPILLARY MUSCLE. C. T. January* and B. A. Schottelius. Dept. of Physiology & Biophysics, Univ. of Iowa, Iowa City, Ia. 52240.

Prostaglandins have been reported to have positive inotropic and chronotropic effects on cardiac tissue *in vivo* and *in vitro* in some species. Rat left ventricle posterior papillary muscles were driven electrically (12 beats/min) for simultaneous mechanical and intracellular microelectrode study. The muscles were bathed with a modified Krebs-Ringer solution containing $PGF_{2\alpha}$ when indicated. All experiments were conducted at 37±1 C with each muscle serving as its own control. The parameters measured included: isometric twitch tension, maximum rate of tension development (dP/dt), time to peak tension (TPT), resting potential (RP), action potential amplitude (AP), maximum rates of depolarization (dV/dt) and repolarization (-dV/dt), and action potential duration. With $PGF_{2\alpha}$ (100 ng/ml), augmentation of twitch tension (1.01 g/mm^2 for control-1.31 g/mm^2 with $PGF_{2\alpha}$) and dP/dt (19.77 to 27.15 g/sec) was found. TPT was not significantly altered. The RP (69.6 mV for control) and AP (85.5 mV) were unchanged while dV/dt was reduced from 93 to 74 V/sec. $PGF_{2\alpha}$ increased the duration of the action potential. The potential was prolonged 62.7% at the 0 mV level, 51.0% at 50% repolarization and 35.4% at the -60 mV level. Correspondingly, -dV/dt was reduced from 5.3 to 3.7 V/sec. Following double washout, rechallenging the muscle with the same concentration of $PGF_{2\alpha}$ produced essentially similar results, but of reduced magnitude. The results indicate a distinct positive inotropic effect with $PGF_{2\alpha}$ which appears tachyphylaxic on second perfusion. In addition, the results suggest that the inotropism may, in part, be mediated through an increase in the action potential duration.
(Supported in part by USPHS, NIH Grant 08550.)

EFFECT OF PROSTAGLANDIN (PGE_1) ON RENAL FUNCTION AND THE DISTRIBUTION OF RENAL BLOOD FLOW.[1] Dusit Jirakulsomchok* and W.W. Moore. Dept. of Physiology, Mahidol Univ., Bangkok, Thailand.

Nine anesthetized male mongrel dogs were used in a study where PGE_1 was infused either in the right or left renal artery and the contralateral kidney was used as the control or sham side. An estimation of the intrarenal distribution of blood flow was made using Reubie's hypothesis, e.g. extraction of para-amino-hippuric acid (PAH). No changes in heart rate, mean arterial blood pressure or glomerular filtration rate followed PGE_1 infusion. However, PGE_1 did induce significant increases in total renal blood flow, total renal plasma flow, cortical plasma flow, medullary plasma flow, urine flow, osmolar clearance, and urinary sodium, potassium and chloride excretion, but induced a decrease in free water reabsorption. The cortical plasma flow increased 110% and 108%, whereas medullary plasma flow increased 172% and 190% following the infusion of PGE_1 at rates of 0.01 and 0.1 ugm/Kg min., respectively. It was clearly shown that PGE_1 had a direct effect upon the kidney, because the changes occured only in the kidney infused with PGE_1. The primary effect appears to be a vasodilator effect and this seems to be most prominent in the medullary circulation, and therefore medullary flow increases more than does cortical flow, or it must be assumed that cortical plasma flow is much better regulated than the medullary flow. The increases in electrolyte (Na^+, K^+, and Cl^-) loss and the increase in renal loss of water are assumed to be a result of the increased medullary flow. It can be concluded that PGE_1 has a direct effect on renal hemodynamics, and these changes alter electrolyte and water excretion.
(Supported by The Rockefeller Foundation).

CONTROL OF RENIN SECRETION BY THE RENAL SYMPATHETIC NERVES.
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The present studies were designed to investigate the role of the renal nerves in promoting renin secretion in the absence of a functional macula densa or renal baroreceptor mechanism. In the first experiment, 7 female dogs were prepared with a non-filtering kidney by the method of Blaine, et al. (Circulation Res. 27:1081, 1970); the renal nerves were left intact. During the acute experiment, papaverine was infused into the renal artery (5 mg/min) to block the renal baroreceptor mechanism. After two control determinations of renin secretion, the animals were hemorrhaged 20 ml/Kg of body weight and measurements made at 15, 30, 45, and 60 min. after hemorrhage. Renin secretion increased from a mean control value of 161 ng angiotensin/min. to an average value of 1068 following hemorrhage ($P<.05$). In the second study, a series of 7 dogs similarly treated, but with denervated kidneys, failed to show an increase in renin secretion in response to hemorrhage. In a third experiment, in 7 dogs with non-filtering kidneys, the renal nerves were stimulated electrically to study the effect on renin secretion. Renal nerve stimulation was continued for 25 min. and renin secretion was measured at 5, 15, and 22 min. A papaverine solution was then infused into the renal artery and the renal nerves stimulated again; renin secretion was determined at 5 and 22 min. Prior to papaverine, renin secretion averaged 132 ng angiotensin/min., and during renal nerve stimulation increased to an average of 405. During papaverine infusion, renal nerve stimulation increased renin secretion from 142 to 386 ng angiotensin/min. Both increases were statistically significant ($P<.05$). These studies suggest that the renal nerves are capable of increasing renin secretion independent of macula densa or renal baroreceptor mechanisms. Supported by NHLI grants HE 10612, HE 05810, and HE 29993.

EFFECT OF ISOTONIC SALINE LOADING ON RENAL NERVE ACTIVITY AND RENAL FUNCTION. W. V. Judy*, J. R. Thompson* and M. F. Wilson. Dept. of Physiology & Biophysics, W. Va. Univ., Med. Ctr., Morgantown, WV. 26506

Six unconditioned dogs (10-14 kg) were anesthetized with 30 mg/kg sodium pentobarbital. They were infused intravenously with an acute isotonic saline load (1/2 estimated blood volume in 30 min.) followed by a sustaining load (0.5 ml/kg/min. for 60 min.) and then allowed to recover from the saline infusion. Mean arterial pressure (MAP), mean pulse pressure (MPP) and mean renal nerve activity (MRNA) were recorded continuously. Urine volume (U_V) was collected in 5 min. aliquots for determination of sodium (U_{Na}) and potassium (U_K) excretion. During acute loading MAP, MPP, U_V, U_{Na} and U_K increased to peak values of 10, 50, 287, 206 and 129% above control respectively. MRNA was inhibited to 23% of control. During the sustaining phase MAP and MPP leveled off to 4 and 35% above control respectively. MRNA remained inhibited whereas U_V and U_{Na} continued to increase and peaked at 450 and 290%. U_K decreased abruptly during the latter part of the acute infusion to control levels and remained there during the sustained period. During recovery all parameters returned to or near control levels. The overshoot and plateau of MAP and MPP show the reflex control of blood pressure during saline loading. Evidence of reflex inhibition is supported by the reduced MRNA. The rapid increase and then decrease in U_K during loading resembles washout. The reduction of MRNA and the increase in U_V and U_{Na} during loading shows that such a hydration method effectively denervates the kidneys. Under such conditions renal function resembles that of the isolated or denervated kidney and the diuresis and natriuresis responses are inversely related to the neural inputs to the kidneys. (Supported in part by NASA Grant No. NGL 49-001-001.)

EQUALITY OF URINE/BLOOD pCO_2 AND OSMOLALITY RATIOS AT HIGH URINE pH AND BUFFER CAPACITY. J.T. Kaim (intr. by F.P. Chinard) New Jersey Coll. of Med. Dent. at Newark, Newark, New Jersey.

The ratio, urine/blood pCO_2, comes within 5% of the ratio of urine to blood osmolality in alkalotic, concentrated urine. Urine flow 0.1cc/min/40gm kidney; urine pCO_2 50-120mmHg; and mOsm 600-1200. pCO_2 ratios exceed mOsm ratios at higher flows in urine with little non-HCO_3 buffer; but urine buffered with phosphate at pH 7.8-8.0 maintains this near equality pCO_2 and osmolality ratios up to flows of 0.5cc/min/kidney. In addition to low flows and phosphate loading maneuvers to lessen the delivery of carbonic acid to the collecting duct such as Diamox administration and production of urine against increased pelvic pressure gave similiar results. Under these conditions it would appear that urine-blood "gradients" of CO_2 gas are more closely related to mechanisms of urine concentration in a region of apparent CO_2 impermeability than to delayed dehydration of carbonic acid. Carbonic Anhydrase reduces the size of the pCO_2 gradient. It is possible that the enzyme may facilitate the diffusion of CO_2 gas from the collecting duct since the diminished CO_2 gradients obtained during Carbonic Anhydrase infusion generally resemble those CO_2 gradients obtained during brief periods of urine stop-flow.

THE EFFECTS OF DIMINISHED CAROTID SINUS PRESSORFLEX ON THE PULMONARY CIRCULATION IN RESPONSE TO INCREASED VENOUS RETURN. John E. Kallal* and Bernell Coleman. The Chicago Medical School, Chicago, Illinois.

Thoracic surgery was performed on a group of dogs anesthetized with chloralose (125-150 mg/kg) in order to obtain recordings of aortic flow and/or pulmonary arterial flow with the use of an electromagnetic flowmeter. The dogs were heparinized (10 mg/kg) and catheterized to obtain aortic pressure, pulmonary arterial pressure, and either right or left ventricular pressure. A pressure reservoir was attached to both common carotid arteries so that flow through these arteries was not abolished. With the pressure reservoir closed to the arterial system, venous infusions of 12-17 ml/kg of blood in one minute resulted in marked increases in aortic and pulmonary flows and pressures on the order of one hundred percent increase. After hemorrhaging an amount of blood equal to that infused and obtaining a steady state control level, the carotid pressure reservoir was opened so as not to alter the carotid pressure. Repeating the venous infusion resulted in an increased pulmonary flow to double its control value but little change in pulmonary arterial pressure or aortic flow. The tendency for carotid pressure to rise was buffered by permitting blood to enter the pressure reservoir which was maintained at the control pressure level. The results reflect the pulmonary system's capacity as a reservoir and the influence of pressoreceptor activity on such a capacitance system. (Supported by grant HE 12285 from the National Heart and Lung Institute, U.S.P.H.S.)

PHYSIOLOGICAL EFFECTS OF THE ARTIFICIAL HEART IN CALVES SURVIVING UP TO TEN DAYS. J. Kawai*, F. Donovan*, J. Peters*, H. Zwart*, T. Kessler*, N. Eastwood*, and W. Kolff, Division of Artificial Organs, University of Utah College of Medicine, Salt Lake City, Utah.

A total artificial heart was implanted in 14 calves surviving up to 260 hours. Three calves, surviving over 100 hours (mean time 7½ days), showed a consistent pattern of hemodynamic and pulmonary changes. The mean arterial pressure remained at or above 90 mm Hg. Central venous pressure increased to an average of 10 mm Hg. Blood volume gradually increased with the time of pumping to over 140% of the control value. Pulmonary function studies showed a decreased functional residual capacity and tidal volume with time of pumping. Oxygen consumption remained normal. Terminally, arterial PO_2 and O_2 saturation decreased. Respiratory support by a Bird respirator or nasal O_2 was supplied intermittently. One calf required no respiratory support for 167 hours. Arterial PCO_2 during spontaneous respiration remained normal. The calves appeared to be normal neurologically, as indicated by the eating, drinking, spontaneous breathing, defecation, micturition, self-support and interest in surroundings. Terminally, two of the long-surviving calves showed signs of cerebral damage. In all experiments there was evidence of degrees of disseminated intravascular coagulation at autopsy. These experiments demonstrate the capability of longer term support by a total artificial heart.

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ULTRASTRUCTURAL MANIFESTATIONS OF HEPATIC MICROSOMAL INSUFFICIENCY IN WALKER TUMOR-BEARING RATS AND THEIR REVERSAL BY PREGNENOLONE-16α-CARBONITRILE (PCN). J. D. Khandekar*, J. Werringloer*, D. Dardachti*, B. D. Garg*, B. Tuchweber and K. Kovacs*. Institut de médecine et de chirurgie expérimentales, Université de Montréal, Montreal, Quebec, Canada.

Rats bearing intramuscular Walker tumor transplants but exhibiting no evidence of circulatory insufficiency were studied at weekly intervals, for 28 days. Hexobarbital anesthesia and zoxazolamine paralysis were prolonged in these animals, which also showed an increase of hepatic microsomal proteins and a decrease of cytochrome P-450 content and aniline p-hydroxylation. These changes were associated with progressive rough-surfaced endoplasmic reticulum (RER) dilatation, disruption and degranulation as well as smooth-surfaced endoplasmic reticulum (SER) proliferation. Hutterer et al. (Lab. Invest., 20: 455, 1969), using dieldrin and methyl butter yellow, noted similar hypertrophic, hypoactive SER. It remains to be established whether the livers of cancer patients also display similar abnormalities, yet such hepatic alterations might be responsible for aberrations in hormone and drug metabolism. PCN, which protects against many chemical toxicants mainly through hepatic microsomal enzyme induction (Selye, H. J. Pharm. Sci., 60: 1, 1971), reverses the RER changes that are known to occur in Walker tumor-bearing rats. This conditioner also alters in vivo drug metabolism and increases cytochrome P-450 content, ethylmorphine demethylation and aniline p-hydroxylation. These PCN-induced changes could be beneficial to cancer patients. (Supported in part by the Medical Research Council of Canada and The Cancer Research Society Inc.)

EFFECTS OF STEROID PRECURSORS IN HYPOPHYSECTOMIZED RATS. K. S. Kim and J. A. Straw, Dept. Pharmacology, The George Washington Univ. School of Medicine, Washington, D.C. 20005.

Tropic hormones for the adrenals and gonads regulate the synthesis of steroid hormones by controlling the rate of conversion of cholesterol to pregnenolone. Maintenance of glandular size and of the enzymatic pathways for conversion of pregnenolone to end products of secretion possibly involves other actions of the tropic hormones. However, the glandular levels of the rate-limiting intermediate, pregnenolone, may in part regulate the levels of enzymes essential for its conversion to end products and thus regulate glandular size. This hypothesis was tested by studying the effects of large doses of pregnenolone and its derivatives in hypophysectomized rats. When treatment was initiated 3 days after hypophysectomy in adult males, pregnenolone 17OH-pregnenolone, progesterone and 17OH-progesterone (20 mg/rat in two equally divided doses daily for 14 days) maintained testicular weight and to a lesser extent the weights of seminal vesicles. Pregnenolone was without effect on seminal vesicle weight in castrated hypophysectomized rats. Loss of adrenal weight was less in rats treated with pregnenolone and 17OH-pregnenolone than in control hypophysectomized rats (sesame oil treated) or in rats treated with progesterone or 17OH-progesterone. When treatment was initiated 17 days after hypophysectomy, pregnenolone (20 mg/rat for 14 days) partially restored the weights of the testis, thus demonstrating the gonadotropic action of pregnenolone. It is likely that testosterone produced from pregnenolone in the testis is responsible for this gonadotropic action. When treatment with pregnenolone was started 17 days after hypophysectomy no effect on maintenance of adrenal weight could be demonstrated. (Aided by USPHS Grant GM13749.)

PREPARATION AND PROPERTIES OF CYCLIC 3',5'-AMP-DEPENDENT PROTEIN KINASE ACTIVITY IN TOAD BLADDER EPITHELIUM. M. Kirchberger,* I.L. Schwartz and R. Walter,* Department of Physiology, Mount Sinai Medical and Graduate Schools of the City University of New York, New York, N.Y. 10029

Toad urinary bladder epithelium has been found to contain high cyclic 3',5'-AMP-dependent protein kinase activity. Partially purified protein kinase was stimulated over a wide range of cyclic 3',5'-AMP concentrations; kinase activity was enhanced at cyclic 3',5'-AMP concentrations less than 5×10^{-9} M and showed a maximal 3.5-fold stimulation at 5×10^{-7} M. Protein kinase activities, stimulatable and non-stimulatable by cyclic 3',5'-AMP, were found to be linear with time up to at least 10 minutes and at amounts of protein ranging from 2 γ to at least 20 γ per sample. The enzyme activity was found to be pH-dependent (with an optimum at approximately pH 6.5 when tested from pH 5.5 to 7.5) and Mg^{++}-dependent (optimal Mg^{++} concentration 10 mM when tested from 0 to 100 mM). Histone (mixture) was found to be an effective substrate. Preliminary results indicate that epithelial cell membranes may serve as a substrate for toad bladder epithelial protein kinase. These findings are an encouraging point of departure for an identification and characterization of the specific protein(s) phosphorylated in response to neurohypophyseal hormone-stimulated adenylate cyclase activity. These proteins may be implicated in epithelial membrane permeability changes.

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UTEROTROPIC ACTIVITY OF SEVERAL PROSTAGLANDINS IN RHESUS MONKEYS. K. T. Kirton and A. D. Forbes (intr. by G. W. Duncan). The Upjohn Company, Kalamazoo, Michigan.

Prostaglandins, 20 carbon unsaturated fatty acids, include some of the most potent known stimulants of myometrial contractility. The present study was conducted to determine the uterotropic activity of several of the prostaglandins in an *in vivo* test system. Changes in intrauterine pressure were monitored through a fluid-filled open-ended catheter introduced transabdominally into the amniotic sac. Activity was quantitated by comparing the initial change in resting tone of the uterus, following acute intravenous (saphenous) injections. Two naturally occurring prostaglandins, PGE_2 and PGA_2, were compared to $PGF_{2\alpha}$. Prostaglandin E_2 (differing from $F_{2\alpha}$ by replacement of the 9α-OH with a keto group) was more potent (≅10X), and PGA_2 (dehydrated PGE_2) was slightly less potent than $F_{2\alpha}$. Replacement of the 15α-OH by a 15-keto group greatly reduced potency of $PGF_{2\alpha}$. These results indicate that alteration of molecular structure of the prostaglandin molecule as noted above affected uterotropic activity *in vivo* in this species of primate.

DISSOCIATION OF PERITUBULE ONCOTIC FORCES AND PROXIMAL REABSORPTION IN THE DOG. Franklyn G. Knox, L. R. Willis*, Jon Bates*, R. E. Lynch* and E. G. Schneider. Mayo Clinic, Rochester, Minnesota 55901.

Experiments in rats indicate a direct causal relationship between uptake of reabsorbate by the peritubule vasculature and active sodium reabsorption by the proximal tubule. To test this hypothesis, the effect of infusion of 25% albumin solution, and subsequent equilibration, on peritubule protein concentration and proximal reabsorption was simultaneously determined with micropuncture methods in 11 dogs. Protein concentrations in efferent arteriolar plasma were determined with an ultramicrocolorimeter. Following protein infusion, systemic protein concentration increased .52 $\pm$ SE .06 gm% ($P < .001$). Protein concentration in efferent arterioles was unchanged (from 8.06 $\pm$ .48 to 7.84 $\pm$ .48 gm%) due to a decrease in filtration fraction (-.10 $\pm$ .02, $P < .001$). Renal plasma flow increased significantly (56.3 $\pm$ 8.3 ml/min, $P < .001$). The post-glomerular oncotic load calculated from efferent arteriolar plasma flow and protein concentration increased from 5.47 $\pm$ .58 to 9.48 $\pm$ .73 gm/min, $P < .001$). GFR, single nephron GFR, and blood pressure were not significantly altered. Proximal fractional reabsorption was significantly decreased from 38.5 $\pm$ 2.3% to 26.7 $\pm$ 4.0% ($P < .005$). Since the increase in post-glomerular oncotic load was not accompanied by an increase in either fractional or absolute sodium reabsorption, it is concluded that colloid oncotic forces in the peritubule microcirculation are not the sole regulators of active sodium reabsorption by the proximal tubule of the dog. (Supported in part by NIH HE-14133, HE-18518 and Mayo Foundation).

ACTIVITY OF SINGLE SYMPATHETIC POSTGANGLIONIC NERVE INNERVATING MUSCLE. K.Koizumi & A.Sato. II Physiol.Inst.,Univ.of Heidelberg and Dept. of Physiol.,State Univ. of New York, Downstate Med. Ctr., Brooklyn, N.Y.

Patterns of resting and reflex discharges of single postganglionic sympathetic fibers have been studied in rats anesthetized with chloralose. Fibers in nerves innervating gastrocnemius-soleus (GS) and posterior biceps-semitendinosus (PBST) were prepared by microdissection and identified by direct electrical stimulation of lumbar sympathetic trunk. Average conduction velocities were 0.73 ± 0.13 m/sec for postganglionic fibers contained in GS muscle nerve (53 fibers) and 0.74 ± 0.09 m/sec for PBST (13 fibers). Activities of these GS and PBST muscle nerves were similar. Of 66 dissected, 59 units showed resting discharges at rates of 1.8 ± 1.2 impulses/sec, while 7 were silent. Single pulse stimulation of group II and III somatic hind-limb afferents produced reflex excitation in sympathetic fibers (40%) with latencies of 250-400 msec for GS nerves and 190-300 msec for PBST. Duration of the excitatory response was 50-300 msec and this was followed by clear depression of resting activities lasting for 200-400 msec. Depression was observed in 86% of fibers; in many without preceding excitatory response. Stimulation of group II afferents alone produced only depression without excitatory response in 30% of fibers tested. Activation of group IV afferents along with group II and III, by stimulating with 3-5 pulses at 200/sec, evoked an additional late excitatory response with latency of 550-700 msec in majority (83%) of fibers. Repetitive stimulation of afferents or asphyxia produced remarkable augmentation of discharges in sympathetic fibers, reaching a maximum frequency of 15-25 impulses/sec. Resting discharges of all sympathetic fibers in muscle were inhibited by central stimulation of depressor nerve or vagus nerve. The inhibitory effect was greater when group IV afferents in the depressor nerve were also excited (supported in part by USPHS grant NS 847).

EFFECT OF SELECTIVE PHARMACOLOGICAL DESTRUCTION OF CENTRAL CATECHOLAMINERGIC (CA) NEURONS AND OF L-DOPA ADMINISTRATION ON OVULATION IN THE RAT. C. Kordon*and M. Héry*(introduced by C. H. Sawyer). Lab. d'Histophysiologie du Collège de France, Paris, France.

We tested the effects of 6-hydroxy-dopamine (6-OH-DA), a drug known to induce pharmacological destruction of central CA neurons, on cyclic and provoked ovulation and on dopamine (DA) stores in the hypothalamus. In PMS-treated immature rats, intrahypothalamic (iht) infusion (5 to 100 μg)of the drug is more effective in inhibiting ovulation than the standard intraventricular (ivc) (twice 200 μg) route of administration (14 and 51% of ovulating animals respectively, vs. 75% in corresponding controls). In adult cyclic rats, ivc administration results in 10 to 13 days of vaginal diestrus in 70% of the subjects (but not in pseudopregnancy); ovulation and irregular cycles resume after this interval. The time of treatment in the cycle does not seem relevant, provided the drug is given prior to the "critical period". Treatment with increasing doses of L-dopa (0, 50 or 100 mg/kg ip) increases the number of eggs released per ovulating animal, in normal animals (10.9 ± 4.6; 18.1 ± 5.5 and 28.3 ± 3.1 respectively), as well as in subjects given iht 6-OH-DA (1.2 ± 1.8; 9.6 ± 3.0 and 19.8 ± 2.5 respectively). It is concluded that: 1) Standard ivc administration of the drug does not result in complete destruction of hypothalamic CA neurons, since ovulation resumes after a transient interruption and hypothalamic DA stores are less affected than those of the brain stem. 2) Intrahypothalamic infusion of the drug has a very rapid effect upon LH release regulation in contrast to a much slower action on central endogenous CA stores. 3) Even after extensive damage to hypothalamic CA neurons caused by iht infusion of 6-OH-DA, DA formed by non-specific decarboxylation of its direct precursor in neurons other than CA ones may still stimulate LH release.

CELLULAR HYPERPLASIA AND HYPERTROPHY IN EXPERIMENTAL CARDIOMEGALY OF RATS. B.Korecky, J.Neffgen*, Department of Physiology, University of Ottawa.

In our previous studies a twofold cardiomegaly (+100%) was found in rats subjected to low iron diet after weaning (21st day);stimulated growth of the heart was accompanied by a proportional synthesis of cardiac DNA (Korecky,French,1967). In order to localize the newly synthesized DNA,groups of control and anemic rats between the ages of 24-34 days were given three intraperitoneal injections of H_3-thymidine (1μc/g of body weight 22c/mM) in four hour intervals. Autoradiographs were prepared from PASH-stained sections of the left ventricle and the percentage of labelled cardiac muscle and non-muscle nuclei were determined microscopically. A significantly higher number of labelled nuclei was found in both cardiac muscle (80-160 per 1000) and non-muscle cells (81-149 per 1000) in faster growing hearts of anemic rats as compared to controls(35-61 per 1000 and 31-59 per 1000). These results provide further evidence for cellular hyperplasia in cardiomegaly induced during early post-natal period. If adult rats (80 days old) were subjected to low iron diet, a cardiomegaly (+50%) was produced but it was not accompanied by new synthesis of myocardial DNA. After intraperitoneal injection of H_3-thymidine a small but significantly higher number of labelled nuclei (10-26 per 1000) was observed in the anemic groups but this labelling was almost entirely confined to non-muscle cell nuclei. It is concluded that during the stimulated growth of the heart hyperplasia of cardiac muscle cells and connective tissue cells develops in young rats, while in adult rats only hyperplasia of connective tissue cells was observed.

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QUANTITATIVE ENHANCEMENT OF MYOCARDIAL REACTIVE HYPEREMIA FOLLOWING BETA ADRENERGIC STIMULATION.
E. J. Kosinski* and G. S. Malindzak, Jr. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

It is generally accepted that vasoactive metabolites and adrenergic receptors play a role in the regulation of coronary blood flow. Recent experiments have shown that the coronary dilator response following a period of maximum myocardial ischemia (MMI) can be enhanced or diminished by β-adrenergic stimulation (Isoproterenol (ISO); Epinephrine (EPI); Norepinephrine (NE)) or β-blockade (propranolol (PRO)), respectively. Mean arterial pressure from the arch of the aorta (effective coronary perfusion pressure) and coronary blood flow (anterior descending branch) were measured in open-chest anesthetized mongrel dogs, before and after MMI (via a ligature placed distal to the flow probe). Adrenergic stimulation was produced by maximum intravenous injections of ISO, EPI, NE, while PRO diminished the adrenergic contribution. Results showed that ISO caused a 12% reduction in the MMI response, while EPI and NE produced an 80% and 40% enhancement, respectively. PRO alone produced a 46% reduction in the MMI response. ISO, EPI and NE all showed a decreased MMI response following β-blockade.

It is concluded that β-adrenergic stimulation can significantly enhance the reactive hyperemic response, while β-blockade diminishes the response by either (a) unmasking α-receptors or (b) decreasing myocardial oxygen utilization. (Supported by NIH grants H-487, HE-344 and HE-5392.)

"Pacing" Left Ventricular Function Curves in Conscious Dogs.
Frances Kraft-Hunter and Edward Wm Hawthorne. Department of Physiology, Howard University, Washington, D.C.

The left atrium was paced for short periods at 2, 2.5, 3 and 3.5 Hz using bipolar electrodes, in a series of conscious instrumented dogs. The animals were instrumented so as to permit simultaneous recordings of d lnP/dt, dP/dt, aortic, left ventricular and atrial pressures, left ventricular internal diameter, and the left ventricular electrocardiogram. The recording of these primary variables permitted the calculation for each of a series of cardiac cycles, derived variables such as left ventricular volumes, stroke work, total peripheral resistance, stroke power, cycle lengths and a variety of other variables. A small digital computer and A to D converter was used for the on-line data acquisition and reduction. End-diastolic volume/stroke work function curves were constructed using the data derived from the stepwise atrial pacing. It was observed that V_{ce} (muscle lengths/sec) increased systematically with each increase in heart rate. The function curves were straight as opposed to the usual curvilinear character shown by Samoff et. al. These "pacing" ventricular function curves were shifted to the left during periods of norepinephrine infusion and to the right after beta blockade using propanolol. Atrial pacing appears to provide usable left ventricular function curves in conscious instrumented dogs.

FACILITATION OF SOMATOSENSORY RESPONSES FOLLOWING LESIONS OF THE VENTROMEDIAL MESENCEPHALON. G. Krauthamer and M. Dalsass*. Department of Anatomy, Rutgers Medical School, New Brunswick, N. J. 08903.

Field potential were recorded on primary somatosensory and association cortex of cats anesthetized with chloralose (80 mg/kg) and immobilized with Flaxedil. The responses were evoked by electric shocks to the contralateral and ipsilateral forepaws or by free field clicks. The polysensory responses recorded from association cortex displayed the typical sensory convergence properties, including their selective inhibition by caudate stimulation. Lesions restricted to the ventral tegmental area of Tsai resulted in a marked facilitation of the primary S I response to contralateral forepaw stimulation. The amplitude of the positive and negative deflections increased up to 40% above control values; there was no change in response latency. The effect on polysensory responses was either minimal and variable or absent. The inhibition of polysensory cortical responses by caudate stimulation remained unaltered for all parameters studied (stimulus intensity, onset, duration and effectiveness of inhibition). A specific functional linkage between this area and the lemniscal projection system is indicated. Lesions placed more laterally and dorsally in the region of the medial lemniscus, abolished not only the primary somatosensory response (S I) but also the polysensory responses to contralateral forepaw stimulation. These preliminary observations suggest that in the caudal mesencephalon the polysensory responses tend to be lateralized and travel in or near the medial lemniscus rather than in the mesencephalic reticular formation. (Supported in part by NIH grant no. FR-05576.)

MEMBRANE CURRENT ASSOCIATED WITH THE FAST EPSP OF SYMPATHETIC NEURONS. K. Kuba* and S. Nishi. Loyola University Stritch School of Medicine, Maywood, Illinois 60153.

The fast EPSP of bullfrog sympathetic ganglion cells, which are devoid of dendrites and have synapses mainly on the lower hemisphere of soma, was investigated with the voltage-clamp technique. The B type neurons having a relatively large diameter (40 to 60 microns) were subjected to the analysis. The relationship between the amplitude of excitatory postsynaptic current (EPSC) and the membrane potential was almost linear in the range of membrane potential between -100 mV and +20 mV. The reversal of EPSC was found to occur at the membrane potential between -10 mV and +5 mV. When the membrane potential was clamped at a depolarized level beyond +20 mV, the increase in amplitude of the reversed EPSC became much smaller than that which one would expect from linearity. The rise time of EPSC varied from 1.0 msec to 2.5 msec, and the half decay time ranged between 2.5 msec and 6 msec, in different cells. The half decay time was dependent upon the membrane potential; it was shortened by depolarization and lengthened by hyperpolarization. The results suggest that the receptor activation may be affected by the membrane potential. (Supported by NIH Grant NB06672-06).

GAS SECRETION INTO THE FISH SWIMBLADDER BY COUNTERCURRENT MULTIPLICATION
Howard Kutchai. Dept. of Biol., The Johns Hopkins Univ., Baltimore, Md.

Kuhn et al. first quantitatively formulated the idea that countercurrent multiplication in the rete mirable is responsible for high gas tensions that exist in the fish swimbladder. In this paper the model of Kuhn et al. is modified to include the permeability of the retial capillaries to lactic acid (a substance presumed to be involved in the countercurrent multiplication) and the possible kinetics of the change in gas partial pressure when lactate is added to or removed from the blood. It is shown that the permeability of the capillaries has no effect on the steady-state gas tensions generated by the system, but that the reaction kinetics may have the effect of markedly increasing the theoretical maximum gas pressure generated by the system.

PENIN-ANGIOTENSIN SYSTEM IN RATS WITH HEREDITARY HYPOTHALAMIC DIABETES INSIPIDUS. J. Kyncl, L. Miksche, M. Khayyal, J. Möhring, F. Gross, (intr. by P. A. Khairallah) Pharmacol. Inst. Univ. Heidelberg, Germany

In rats with hypothalamic diabetes insipidus (D.I.), two stimuli are present which may influence plasma renin activity (PRA): fluid loss, a primary stimulus for volume or osmoreceptors, should increase PRA, while a high Na level in extra-and intracellular space is supposed to have an opposite effect via hypothetical chemoreception. In spite of known higher Na levels the PRA in the compensated stage in D.I. rats is higher than in their non D.I. strain mates: ♂, 282.8 vs 146: ♀, 339 vs 162 ng AII/ml. Also the plasma angiotensinogen level is significantly higher in D.I. rats: ♂, 586 vs 488: ♀, 333 vs. 300 ng AII/ml. The D.I. rats have a significantly greater renal mass as per cent of body weight, but heart weights are the same. After 24 hours of water deprivation, PRA markedly increases in D.I. rats: ♂♀, control, 315: after dehydration, 2225.7 , and after rehydration, 325 ng AII/ml. The hematocrit is pronouncedly higher only after severe dehydration. The changes in body fluid volume plays, thus, a major role in control of PRA in this model. Four weeks after unilateral clamping of a renal artery, the D.I. rats reduced their already slow body growth, markedly increased water intake, built up their right-left kidney coefficient and increased the hematocrit and markedly already high PRA, but did not develop hypertension or heart hypertrophy. The non D.I. litter mates developed all signs of renal hypertension. They increased their water intake and PRA only moderately.

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Effect of Imipramine & Related Drugs on the Urinary Bladder - Peregrina Labay, M.D.* and Saul Boyarsky, M.D.; Washington University Medical School & Allied Hospitals; Saint Louis, Missouri 63110

The mechanism of action of Imipramine on detrusor muscle strips was studied by the isometric, in vitro method. One end was fixed in a 50 ml bath containing oxygenated Locke's solution at 37°, and the opposite end attached to a force displacement transducer, loaded with one gram of tension. Changes in the muscle tension were recorded on a Grass Polygraph. The bladder strips responded uniformly to Acetylcholine, 0.1-5.0 ug/ml with an elevated tension and more frequent activity. Imipramine, 0.1 to 3.0 ug/ml produced depression of the baseline tension, decrease in the force, and a slowing of contraction. With doses of 5.0-100 ug/ml, spontaneous activity ceased within 1 to 15 minutes, until the drug was washed out from the bath. Imipramine effects were compared to Atropine, 0,1-1 ug/ml, Norepinephrine, 1.0-10 ug/ml, Isoproterenol, 10-20 ug/ml, and Phenoxybenzamine, 10-40 ug/ml. Atropine blocked the spasmogenic action of ACh. Both NE and Isoproterenol dropped the baseline tension and amplitude of contraction. Phenoxybenzamine completely blocked the response to ACh. Imipramine might be said to act as an anti-cholinergic, like Atropine, by blocking the spasmogenic effect of ACh, but subtle differences in their actions existed. By preventing the uptake of released NE, Imipramine could be stimulating the beta-receptors of the detrusor muscle as NE can, and Isoproterenol does. Also, the parasympathetic pathway may discharge over sympathetic pathways in the bladder as suggested by the altered response to ACh after alpha-blockade by Phenoxybenzamine.

IN VIVO CO_2 "BUFFERING" OF SKELETAL AND CARDIAC MUSCLE AS A FUNCTION OF TIME. Lai, Yih Loong*, B. Attebery* and E. B. Brown, Jr., University of Kansas Medical Center, Kansas City, Kansas.

Previous work in dogs (Clancy, R. L. and E. B. Brown, Jr., Am. J. Physiol. 211:1309, 1966) established that cardiac muscle had a much larger CO_2 buffer value (defined as $-\Delta HCO_3^-/\Delta pH$) than skeletal muscle when values were determined after 2 hours of breathing increased concentrations of CO_2. It was the purpose of this investigation to determine the change in these buffer values with time. Rats were kept in an environmental chamber in which 10% CO_2, 22% O_2, 26°C, and 40% relative humidity were maintained constant. After 1, 2, 4, 6, 10, 16 and 24 hours the animals were lightly anesthetized and without removing them from the chamber blood was drawn from the inferior vena cava. Skeletal muscle samples were taken from the thigh and the entire ventricle was taken for cardiac tissue. P_{CO_2}, pH, and P_{O_2} were measured on whole blood and intracellular pH was determined by distribution of DMO-^{14}C. Skeletal muscle pH was lowest at 1 hour and increased gradually over the next several hours. Conversely, cardiac muscle pH decreased over the first 6 hours. These changes are reflected in increasing CO_2 "Buffer Values" in skeletal muscle and decreasing "Buffer Values" in cardiac muscle during the initial 6 hours of hypercapnia. (Supported by USPHS grant HE 12231)

DETERMINATION OF AMINOCHROMES PRODUCED IN THE RAT DURING O_2 AT HIGH PRESSURE (OHP) BY GAS-LIQUID-CHROMATOGRAPHY (GLC). Brian LaLone* and Rodney T. Houlihan. Michigan State University, Pontiac, Michigan.

There is good supportive evidence that adrenolectomy protects animals from oxygen toxicity. It has been proposed that the cyclic oxidation products of epinephrine, namely adrenochrome and adrenolutine, can account for the mechanism of adrenal involvement in the manifestations of oxygen poisoning. Our earlier work utilizing a combination of paper chromatographic and fluorescent spectral techniques supported this hypothesis. Although highly sensitive, these techniques afforded little knowledge as to the nature of the particular aminochrome metabolites involved. In an effort to obtain a higher degree of specificity a GLC method was adapted for our use. This GLC method utilizes the formation of trimethylsilyl derivatives from purified extracts of plasma. The silylated derivatives are then gas chromatographed on a 6 ft. glass 3% SE-30 column in a Varian 1200. Individual aminochromes can be determined via chemically stable derivatives that possess good resolution and specificity. A series of experiments were designed to determine the effects of OHP (60 psig) on the production of aminochromes in the intact verses the adrenalectomized rat. The relative amounts of adrenochrome and adrenolutine were higher in the intact than in the adrenalectomized animals exposed to OHP. Data taken from rat plasma assayed for epinephrine oxidase activity would suggest that the plasma from the intact animal subjected to OHP has a greater ability to cyclically oxidize epinephrine. Corticosterone injected one hour prior to OHP in the adrenalectomized animal indicates that the steriod removes the animal from his protected state by increasing the amount and ability to form aminochromes from epinephrine.

EFFECTS OF ANTRAL CLAMPING AND/OR ANTRECTOMY ON THE ENDOGENOUS RELEASE OF GASTRIN BY VAGAL STIMULATION IN THE DOG. George Lanciault*, Carol Bonoma* and Frank P. Brooks. School of Med., Univ. of Penna., Philadelphia, Penna. 19104.

Continuous electrical stimulation of the cervical vagi in anesthetized dogs increases the level of serum gastrin and the output of HCl from the stomach (Lanciault et al., Fed. Proc. 30:748, 1971). Similar stimulations in 4 dogs for 2 hr produced an elevation of gastrin in portal blood of 204±30 (SEM) pg/ml. The pylorus was then isolated from the circulation by applying clamps to the vessels and wall of the stomach and vagal stimulation continued. Serum gastrin levels fell 104±26 pg/ml shortly after clamping. Acid output fell 4.4±0.2 mEq/30 min. Similar results occurred when the antrum was removed (verified by histology) in 4 other dogs. The presence of continuing fasting levels of gastrin after antral exclusion and removal is consistent with Trudeau and McGuigan's results after vagotomy and antrectomy in humans (24±5.1 pg/ml) 6 months after surgery (Gastroenterology, in press). The results suggest that the principal source of gastrin released by vagal stimulation is the pyloric antrum and that most of the excitatory effect of vagal stimulation on acid secretion is mediated via gastrin releases. (Supported by USPHS NB-IR01-AM 14563-01)

ACETYLCHOLINE AND PHYSOSTIGMINE EFFECTS ON ISOLATED NERVE FIBERS. Timothy G. Lane* and Edward M. Lieberman. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

Ach and physostigmine were externally applied to crayfish medial giant axons to test the functional significance of the Ach-Achesterase system to permeability characteristics of the axon membrane. Internal stimulating and recording electrodes were used to monitor excitability properties of the membrane. Ach ($\geq 10^{-3}$M) and physostigmine ($\geq 10^{-5}$M) consistently and reversibly depolarized the membrane by 7 and 10 mV respectively. These responses occurred in the absence of venom, enzyme or detergent pretreatment. Ach (10^{-6}-10^{-4}M) and physostigmine (10^{-8} - 10^{-6}M) caused 2 - 4 mV hyperpolarizations. Lowering the temperature of the bath from 27 - 28°C to 20 - 22°C caused a reversal of low [Ach] response. Low [physostigmine] mimicked this effect. During the rapid Ach-induced depolarization phase (15 - 45 sec) excitability increased significantly followed by inactivation during the steady depolarization (3- 5 min). Physostigmine (10^{-5}M) decreased action potential amplitude 15 - 20% and increased AP duration by 50%. A significant increase in the positive after potential was seen. Within 2 - 3 min 10^{-5}M physostigmine enhanced the excitability of the preparation to induce repetitive spiking on application of a long duration stimulus. Instantaneous rates of spiking were 250 - 300 spikes/sec. It is tentatively proposed that low [Ach] and [physostigmine] externally applied to this axon causes an increase in steady-state K^+ permeability and conductance (hyperpolarization). Higher [Ach] or [physostigmine] increases both Na^+ and K^+ permeability and conductance favoring Na^+ conductance (depolarization). (Supported in part by NIH grant NSO 8773).

THE EFFECT OF INCREASED NITROGEN PRESSURE ON THE ENDOCRINE MAINTENANCE OF HOMEOSTASIS. C. S. Leach*, W. C. Alexander, C. L. Fischer*, and P. C Johnson*, Clinical Laboratories, Preventive Medicine Division, NASA-MSC, and Baylor College of Medicine, Houston, Texas.

The endocrine response of six normal subjects was studied during a 14 day exposure to four atmospheres absolute pressure containing 5.2% O_2 and 94.8% N_2. Urine and blood samples were taken sequentially before, during, and after the exposure. During the exposure, we found a significant reduction in urinary antidiuretic hormone (ADH) (-50%) accompanied by a volume diuresis (+70%). The blood results demonstrate a hemoconcentration with a significant increase in venous hematocrit, a decrease in plasma volume (-16%), an increase in total proteins and albumin concentration and an increase in plasma electrolytes (Na and K). These reflect the vascular water deficit resulting from an initial diuresis which occurred with no significant change in aldosterone excretion. These changes show the subjects' adaptation to the chamber environment, with a new homeostatic balance established as compensatory mechanisms are activated in response to the stress of the hyperbaric atmosphere and the narcotic effect of increased nitrogen pressures. The endocrine changes are believed to reflect the central nervous system (CNS) effect of chronic exposure to hyperbaric nitrogen. The observed changes are consistent with CNS depression of ADH production. The increased mechanical work required to breathe in a hyperbaric environment cannot be ruled out as a contributing factor; however, the observed findings are less compatible with this explanation.

EFFECTS OF OUABAIN ON SPONTANEOUS PENICILLIN SEIZURE DISCHARGE IN THE CAT HIPPOCAMPUS. R.M. Lebovitz and F.E. Lybrand*. University of Texas Southwestern Medical School, Dallas, Texas.

Penicillin induced spontaneous spike discharge seen in the surface electrical activity of archicortex (hippocampus) corresponds to synchronous,self-limited discharge of a large fraction of the pyramidal cells at the site of penicillin application. This preparation provides a means for examining metabolic mechanisms that may underly the genesis and control of epileptiform activity. Cats were prepared under ether and maintained on the paralytic gallamine to avoid the corticodepressive action of barbiturates. Na-penicillin was applied to localized sites on the surface of the exposed hippocampus. After the surface record showed regular and stable spiking, ouabain was applied to the same sites either directly or via 0.5 mm^2 bits of filter paper saturated with 10^{-7} to 10^{-4} M ouabain solution.Under these conditions the latency of action of the Na-K ATP-ase inhibitor varied from one to thirty minutes, depending on concentration and method of application. The initial effect was a marked increase in the rate of penicillin spiking; this was followed by a gradual alteration in the spike form and amplitude that terminated in full seizure. Bursts of spontaneous seizure-like activity tended to occur for a considerable period following the ouabain placement. During the ictal seizure and persisting for several hours thereafter, there developed a marked reduction in the field potential evoked by brief fornix stimulation that was more profound than that to be expected from the seizure itself. It was also common for the hippocampal excitability to remain depressed for several hours as judged by the ineffectiveness of trains of stimuli that had been seizure producing prior to ouabain application.

EFFECT OF ESTRADIOL AND PROGESTERONE ON PITUITARY SENSITIVITY TO HYPOTHALAMIC EXTRACT. Sandra J. Legan and Vernon L. Gay (intr. by H. W. Davenport). The Univ. of Michigan, Ann Arbor, Mich.

In a series of experiments designed to investigate the increased pituitary sensitivity to hypothalamic extract following administration of estradiol benzoate and progesterone to ovariectomized rats, we attempted to determine: (1) the time after steroid injection at which maximal increase in pituitary sensitivity occurs; (2) the optimal length of time between castration and administration of steroids; and (3) the specific steroid requirement for increased pituitary sensitivity. To characterize the time course of increased pituitary sensitivity Holtzman rats ovariectomized 4 weeks earlier were treated with a combination of estradiol benzoate (50 ug/rat) and progesterone (25 mg/rat). One, three and five days later they were injected via a carotid cannula with 150 or 250 ul of crude hypothalamic extract (5 hypothalami/ml in 0.1N HCl). Pituitary responsiveness, as measured by increased plasma LH in response to hypothalamic extract injection, was greatest 3 days after steroid treatment. To determine the effect of length of time of castration on increased pituitary responsiveness, hypothalamic extract was injected on the third day after steroid administration into rats ovariectomized 5 wks, 3 wks, 1 wk or 2 days earlier. The sensitivity to exogenous "LRF" increased with the duration of castration. To ascertain the specific steroid requirement for increased pituitary sensitivity, partially purified hypothalamic extract was injected into ovariectomized rats 3 days after administration of estradiol benzoate (50 ug), or progesterone (25 mg), or both. Estradiol benzoate, whether injected alone or in combination with progesterone, caused the same increase in pituitary sensitivity, and following an initial depression of plasma LH which occurred within 24 hrs, a spontaneous and rapid 15-fold increase in plasma LH was seen approximately 48 hrs after injection. (Supp. by NIH HD-05318.)

ISOLATION OF IMMUNOGENIC RNA FROM RAT MACROPHAGES.
P.E. Lentz and N.R. Di Luzio. Tulane Univ. School of Medicine, New Orleans, La. 70112.

Previous studies have demonstrated that immunogenic RNA can be isolated from peritoneal macrophages after in vivo or in vitro phagocytosis of particulate antigens. The recently developed technique to isolate Kupffer cells and splenic macrophages prompted an evaluation of the comparative ability of macrophage RNA to initiate an immune response to sheep red cells (SRBC). Significant and comparable titers of hemagglutinating antibody were found in the sera of rats seven days after injection of 300 ug of RNA prepared from either peritoneal macrophages, Kupffer cells or spleen macrophages which had phagocytized SRBC. in vivo and in vitro. The amount of antibody was related to the time of phagocytosis as the highest titers were found when RNA was prepared from macrophages which had phagocytized SRBC for 45, 90, or 120 minutes in vivo and in vitro; RNA prepared from macrophages exposed to antigen for 4 or 24 hours in vivo was associated with reduced antibody titers. In significant amounts of hemagglutinating antibody were observed when RNA was prepared to non-antigen exposed macrophages. Treatment of rats with Actinomycin D (18 ug/100 g) inhibited the formation of macrophage immunogenic RNA. These results indicated that an immunogenic RNA can be isolated from three different populations of rat macrophages after in vivo and in vitro phagocytosis of SRBC. However, the contribution of each macrophage population to an immune response in vivo under physiological and pathological conditions requires further investigation. Supported by the Atomic Energy Commission, an Institutional Research Grant and American Cancer Society.

INTRACELLULAR RESPONSES OF PALLIDAL AND ENTOPEDUNCULAR NEURONS.
M. Levine*, C. D. Hull and N. A. Buchwald, Univerisity of California, Los Angeles.

Intracellular responses were recorded from cells in the entopeduncular nucleus, globus pallidus and caudate nucleus in cats. Cells in the area of the entopeduncular nucleus responded both to sensory and to electrical stimulation of the caudate nucleus. Auditory stimulation and somatosensory stimulation of forepaws and tail elicited responses. Visual stimulation appeared to be ineffective. Responses in pallidum and entopeduncularis to these sensory stimuli were characterized by EPSP-IPSP sequences. These cells also responded to single pulse stimulation of the caudate nucleus with similar postsynaptic sequences. They did not respond, however, to single pulse stimulation of the precruciate cortex of sufficient intensity to induce postsynaptic sequences in caudate nucleus neurons. Cells in the caudate nucleus also responded to auditory and somatosensory stimuli of the forepaws and tail. Their responses were characterized by small EPSPs followed by longer IPSPs and terminated by rebound depolarization. These results demonstrate that the basal ganglia receive and integrate sensory information and underscore the role of these structures in integrative brain mechanisms.

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INCREASED ADRENAL AND HYPOTHALAMIC NORADRENALINE WITH PERIPHERAL DEPLETION IN ADULT RATS FOLLOWING POSTNATAL INJECTION OF 6-HYDROXYDOPAMINE. Gloria M. Lew* and W. B. Quay. Department of Zoology, University of California, Berkeley, California.

It is known that 6-hydroxydopamine (= 6-OHDA) produces in adults persistent depletion of noradrenaline (= NA) in sympathetically innervated peripheral organs and does not impair nerve cell bodies, although in newborn rats and mice repeated injections of 6-OHDA cause irreversible lesions of neuroblasts in all sympathetic ganglia, with a complete sympathectomy persisting for at least 6 months. We have measured tissue and brain region NA contents in 23-weeks-old female rats which had been injected subcutaneously daily for 7 days with 6-OHDA (50 μg/g) starting within 12-24 hours of birth. Fourteen treated animals and thirteen untreated, matched sibling controls (= C) were weaned and set up in adjacent individual activity recording cages when 25-26 days old. A 24-hour rhythmicity in running activity and normal activity levels were observed in all animals. At autopsy they were decapitated, quickly dissected, and the tissues frozen in vials on dry ice (CO^2). Fluorimetry of NA (μg/g tissue) showed expected depletion in heart (6-OHDA - 0.145±0.013; C - 0.324±0.021) and spleen (6-OHDA - 0.049±0.006; C - 0.709±0.068), but increase in hypothalamus (6-OHDA - 0.875±0.032; C - 0.663±0.040) and adrenal gland (6-OHDA - 56.38±3.96; C - 43.84±3.27). Studies of tissue and brain region NA contents in other experiments with 6-OHDA and in animals of other ages allow some tentative conclusions. In general, it is suggested that the response to 6-OHDA by the sympathetic system is complex and is regionally differentiated, with the possibility of compensatory mechanisms occurring in adrenal medulla and hypothalamus. (Supported by USPHS-NIH research grants NS-06296 and HD-04103.)

EFFECT OF THE PROTEIN INTAKE ON THE NUTRITIONAL STATUS OF RHESUS MONKEY. S. C. Li*, Y-T Li* and A. J. Riopelle. Tulane University Delta Regional Primate Research Center, Covington, La.

Although rhesus monkeys have been widely used in various biomedical investigations for a number of years, our knowledge about the minimum daily protein requirement for this animal is still inadequate. We have studied the effect of the protein level in the diet on plasma-protein concentration and on the ratio of nonessential (NE) to essential (E) amino acid in rhesus monkeys. Female adult rhesus monkeys weighing 4-9 kg were divided into 3 groups of 5 animals each. Each group was fed with a semisynthetic diet supplying 1, 2 or 4 g protein kg body weight/day respectively for a period of 4 months. Protein was supplied in the form of casein. It was found that in the adult rhesus monkeys, the NE:E ratio is more sensitive to the protein deficiency than the plasma protein concentration. Those animals fed with 4 g protein/kg body weight/day maintain a fairly constant NE:E ratio, while elevated values of NE:E ratio were found in those animals fed with 1 or 2 g protein/kg body weight/day. No significant changes in the total plasma protein concentration were found in all three groups, however, the albumin to globulin ratio became lower in the animals fed with 1 g and 2 g protein kg body weight/day. It appears that daily intake of high-quality protein much below 4 g/kg/day will produce adverse changes which are detectable by appropriate biochemical means before the appearance of frank illness. (Supported by USPHS NIH Grant HD 05340 and RR-00164.)

THALAMIC GROSS POTENTIAL WAVES PRODUCED BY HIGH FREQUENCY STIMULATION OF THE CAUDATE NUCLEUS IN UNANESTHETIZED CATS. Samuel L. Liles. Louisiana State University Medical School, New Orleans, La, 70112.

A previous study in unanesthetized cats with permanently-implanted electrodes showed that high frequency electrical stimulation (20-100 Hz) of the anteroventral part of the caudate nucleus induced rhythmic slow waves in gross electrical recordings from the motor cortex (submitted to J. Neurophysiol.). These rhythmically-recurring (about 1/sec) potentials were usually diphasic positive-negative waves of long duration (positive, 150 msec; negative, 200 msec). At appropriate stimulus frequencies it was evident that the individual slow waves were triggered by selected pulses in the stimulus train, with the onset of the positive part of each slow wave occurring about 20 msec after a triggering pulse. In the present study, recordings from the thalamus have revealed that the cortical slow waves are accompanied by gross potential changes in specific parts of the thalamus. The thalamic responses appear to be localized in the ventroanterior-ventrolateral (VA-VL) complex, and consist primarily of a large negative wave occurring more or less simultaneously with each cortical diphasic wave. Recordings from the more rostral part of the VA-VL area show an additional smaller negative wave which precedes by a variable time (about 50 msec) the larger thalamic wave. This initial thalamic wave rises in about 10 msec to a slowly-declining plateau. The first caudate stimulus pulse occurring during this negative plateau appears to be the pulse which triggers the large thalamic and cortical slow waves. These data suggest that the VA-VL area of the thalamus plays a fundamental role in generation of the cortical slow waves produced by high frequency stimulation of the anteroventral caudate area. (Supported by USPHS, NIH Grant NS98907)

OXYGEN SUPPLY-DEMAND AND BREATH-HOLD BREAKING POINTS. Y.C. Lin, D.A. Lally*, T.O. Moore*, and S.K. Hong. Univ. of Hawaii, Honolulu, Hawaii.

The effect of oxygen supply on the breath hold (BH) breaking points (b.pt.), physiological (onset of involuntary respiratory effort) and conventional, were studied in 5 male volunteers at rest ($\dot{V}o_2$=305 ml/min) and during steady state exercise ($\dot{V}o_2$=712 ml/min). Exercise was employed to obtain a spectrum of $\dot{V}o_2$. At the onset of BH two levels of alveolar oxygen were provided for the resting and exercising conditions: 1)BH with air, and 2) normal breathing with O_2 for 10 min. and then BH. TLC was employed in all cases. The relationship between $\dot{V}o_2$ (X,ml/sec) and BH time (Y,sec.) can be expressed as Y=a(1/X) + b, where the intercept, b, is small and statistically insignificant from zero (Table 1). The slope, a, represents the amount of O_2 supplied by the lung and the blood during the period of BH. The above equation predicts that the O_2 supply, a, dictates the conventional but not the physiological b.pt. Our results indicate that at the physiological b.pt. the blood oxygen store was not altered ($a<600$) since the lung can provide enough oxygen for the first 2 min. during BH with air (Hong et al., JAP 30:540, 1971). Hence the diaphragmatic contraction is initiated by the level of P_{Aco2}. Our results confirmed those of Agostoni (JAP 18:30,1963) in that P_{Aco2} at the physiological b.pt. is independent of P_{Ao2} (P_{Aco2}=0.00903P_{AO2} + 43.8 mm Hg over a wide range of P_{Ao2}). In contrast, at the conventional b.pt. the P_{Aco2} increases as a function of BH time and P_{Ao2}.

Table 1. Oxygen supply, BH time, and Vo2.

BH with	Physiological b. pt.	t_1*	t_2*	Conventional b. pt.	t_1	t_2
air	Y=388(1/X) + 0.1	90	32	Y=747(1/X) + 7.4	162	66
O_2	Y=491(1/X) + 2.7	104	40	Y=1190(1/X) + 19	275	102

*t_1 and t_2 are the BH time (sec) for rest and exercise, respectively.

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DIFFERENTIAL EFFECT OF THYROID HORMONES ON RIGHT AND LEFT VENTRICLE. H.A. Lindsay and M.B. Mowery*. Dept. Physiol. & Biophys., W.V.U. Med. Ctr., Morgantown, W. Va. 26506.

Exogenous thyroid hormone in excess causes cardiac hypertrophy. This study was undertaken to determine whether the hypertrophy is equal, relative to control weight, in the right and left ventricle (RV and LV). Male, Sprague-Dawley rats were used. Change in body weight was limited as much as possible by control of food intake. Triiodothyronine (T3) was given at 1.2 (group I), 6 (II), 30 (III), or 150 γ/kg/day (IV) for 14 days. Heart rate and the ratio of heart weight to body weight were decreased in I, unchanged in II and increased in III and IV. The atrophy in I was statistically equal in RV and LV but the hypertrophy in III and IV was relatively greater in RV. We have verified then that RV hypertrophies relatively more than does LV in response to T3. A similar study was performed with T4 in doses ranging from 15 to 405 γ/kg/day for 14 days. At the highest dose hypertrophy occurred and was relatively greater in LV than in RV. The relative contribution of LV and RV to cardiac hypertrophy in response to thyroid hormones depended on the identity of the hormone. Supported by W. Va. Heart Association.

OLFACTION AND PUBERTY IN THE LABORATORY RAT. Robert F. Locke Jr.* Barbara A. Kasprow,* and Joseph Thomas Velardo. Department of Anatomy, Loyola University, Stritch School of Medicine, Maywood, Illinois.

A series of experiments was undertaken to determine whether or not young, female, albino rats could be stimulated to undergo early puberty by exposure to mature, male rats or their odors. It is known (Vandenbergh, 1967, 1969) that female, albino mice undergo both canalization and first estrus earlier than normal when exposed directly to mature, male mice or the soiled bedding material from the cages containing mature, male mice. Five groups of 24 young (21 day old) female rats were housed in plastic cages (three animals per cage) on san-i-cel bedding and fed Purina Rat Chow and water ad libitum. The five experimental groups were exposed to one of the following stimuli: (1) one mature, male rat; (2) the urine of one mature, male rat: (3) one mature, orchidectomized rat; (4) one mature, orchidectomized rat given 1.5 mg. testosterone propionate (T.P.) daily or (5) two mature, male mice. Control female rats were isolated from birth. In every group exposed to intact male rats or their urine, the time of canalization was not accelerated, but first estrus was advanced significantly ($P = 0.05$ and 0.02 respectively). In groups exposed to orchidectomized rats and orchidectomized rats + T.P., canalization was delayed significantly ($P = 0.02$ and 0.001 respectively), and first estrus was not advanced. Male mice failed to elicit either early canalization or first estrus in the females.

HISTOGENESIS OF NORMAL AND MUTANT RETINAE OF MICE. Richard N. Lolley (intr. by W. G. Clark). VA Hospital, Sepulveda, and Dept. of Anatomy, University of California School of Medicine, Los Angeles, California.

Histological, physical and biochemical changes in mouse retinae with inherited blindness (C3H/HeJ) were compared to normal retinae (DBA/1J) during postnatal development. Dry weight and protein content of DBA retinae increased rapidly to near adult levels during the first 10 postnatal days. Comparable measurements of C3H retinae were similar initially but both parameters decreased sharply after 5 days, the decrease in protein content preceding that of dry weight. The DNA content of DBA retinae increased sharply from birth to 5 days, then decreased slightly to adult levels while that of C3H retinae increased normally from birth to 5 days, then decreased abruptly to adult levels. The cellular population of the retina was estimated from DNA measurements by assuming the average cell of the retina was diploid. After birth, cellular division and differentiation proceeded sequentially in both DBA and C3H retinae. Thereafter in DBA retinae, the majority of photoreceptor cells grew and matured but a minority died and were autolyzed. After achieving partial differentiation, the complete photoreceptor population of C3H retinae died and were autolyzed. A decrease in protein content of C3H retinae preceded by 2 days the first changes in ultrastructure of the C3H photoreceptor cells. This observation suggests that some aspect of protein metabolism is disrupted by the mutant gene of C3H mice. (Supported by USPHS Grant EY0395.)

ENDOTOXIN SENSITIVITY IN MALARIA INFECTED MICE. L.D. Loose*, R. Trejo* and N. R. Di Luzio. Tulane Univ. School of Medicine, New Orleans, La. 70112.

The influence of P. berghei infection on endotoxin susceptibility and detoxification in white mice was studied. Malaria infected mice showed a 41 fold increase in endotoxin susceptibility. To elucidate the mechanism of endotoxin enhancement, studies were conducted of endotoxin detoxification by liver and spleen of control and malarial infected mice by our recently developed bioassay procedure. Liver and spleen homogenates from normal control animals possessed a significant endotoxin detoxification ability. In contrast, liver homogenates prepared from malaria infected mice possessed no significant endotoxin detoxifying ability. The endotoxin detoxifying ability of splenic homogenates prepared from malaria infected donors was, however, normal. These findings indicated that endotoxin hypersensitivity in malaria infected mice may be due to an impairment in hepatic endotoxin detoxification. The loss of endotoxin detoxification ability by liver adds another dimension to hepatic functional alterations induced by malaria.

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EVIDENCE OF A STATIC FLOW ZONE IN THE INTERNAL CAROTID BULBUS OF THE ANESTHETIZED DOG. P. R. Lynch, A. Bonakdarpour*, H. M. Stauffer**, J. Heckman*, and M. S. Lapayowker*. Departments of Physiology and Radiology, Temple University Med. Sch., Philadelphia, Pa. 19140.

Flow separation is associated with changes in vessel geometry. Evidence that quiescent or static zones exist in vivo has been demonstrated in the internal carotid bulbus of the dog. A red Odman catheter was introduced into the common carotid artery using the Seldinger techniques via the femoral artery. A dose of 5.0 ml of Methylglucamine diatrizoate (Renografin 76) was injected into the common carotid artery, while cross-table lateral or AP X-ray films are made of the carotid bifurcation. An Elema-Schonander serial filmchanger takes an exposure every second for ten seconds and then a 12- and 15-second film after the injection of the contrast medium. The X-ray factors were 75 kvp, 100 ma, 1/20 of a second at forty inches T.F.D. Junta mural stasis of the radionaque media in the carotid bulbus was observed in all of the six animals examined. This is considered to be a normal finding in the anesthetized dog. (Supported by NIH, NHLI Grant HE 08886)

** Deceased

DEPRESSION OF THE ISOLATED HEART MUSCLE BY BACTERIAL ENDOTOXIN. Malcolm F. Macnicol, Alan H. Goldberg and George H. A. Clowes Jr. Departments of Surgery and Anesthesiology, Harvard Medical School and the Sears Surgical Laboratory, Boston City Hospital, Boston, Massachusetts, 02118.

The effect of endotoxin (Rudbach) on an isolated heart muscle preparation was assessed using the toxin in a concentration similar to that found in the septic state by Limulus assay. Left ventricular trabeculae carneae muscles were obtained from 250 G male Sprague Dawley rats and induced to contract isometrically once every 4 seconds in a 10 ML bath containing Krebs solution. Endotoxin in a bath concentration of 0.1 ug/ML caused a depression in peak developed tension (Tpd) observable only after 15 minutes, but becoming significant (70% of initial value) by 60 minutes. Control preparations showed no significant change over the same period. Maximum rates of tension development (+dp/dt) and relaxation (-dp/dt) were reduced to a lesser extent while time to peak tension (Tpt) and resting tension (Tr) were not consistently affected. The observed myocardial depression could be reversed by increasing the bath concentration of Calcium from 4.5 to 6.75 Meq/L. Cortisone, only if given prior to the endotoxin, had a protective effect. It is stressed that the direct depressant effect of endotoxin on the heart muscle occurs only if the toxin bathes the tissue for an appreciable time, 30 minutes or more, and that its rapid washout may mask this effect. This may explain the discrepancies seen in the literature concerning the effect of endotoxin on the isolated heart.

EFFECTS OF CYANIDE ON RENAL TUBULAR SODIUM ABSORPTION IN THE RAT. David A. Maddox (intr. by Marshall A. Cortney). Dept. of Physiology and Biophysics, Univ. of Iowa, Iowa City, Iowa 52240.

To study the inhibitory effect of cyanide on proximal tubular sodium absorption microinjections were made of small isosmotic samples of NaCl and solutions of other Na salts containing tracer amounts of ^{22}Na. ^{22}Na recovery in ureteral urine was measured after injections into proximal tubules of female rats undergoing diuresis produced by i.v. infusion of 10% mannitol in saline at 0.2 ml/min. Other salts substituted for NaCl were NaCN (70 and 140 mM) to determine if an inhibitor of aerobic metabolism would affect ^{22}Na efflux from microinjections, $NaHCO_3$ (35 mM) and NaSCN (140 mM) to determine whether the cyanide effect was specific for that anion, and $Na_4Fe(CN)_6$ (28 mM) to test the effect of an impermeant anion on ^{22}Na efflux. Also, the ureteral recovery of tracer ^{14}CN in 140 mM NaCN solution was measured to see if cyanide could act as an impermeant anion. Recovery of ^{22}Na from injections of NaCl solutions was low when injections were into early segments of the proximal tubule, 11-40% of the proximal tubular length, and averaged 4%. It was higher from late injections, 40-67% proximal tubular length, and averaged 16%. Addition of NaCN to the injectate increased ^{22}Na recovery. With 70 mM NaCN, ^{22}Na recovery averaged 13% from early and 26% from late injections. With 140 mM NaCN, recovery averaged 20% from early and 30% from late injections. With either $NaHCO_3$ or NaSCN in the injectate recovery was similar to that obtained with NaCl injections. Recovery averaged 18% from early and 40% from late injections with $Na_4Fe(CN)_6$ in the injectate, indicating that the presence of an impermeable anion affects ^{22}Na recovery. Cyanide was readily absorbed since recovery of ^{14}CN averaged 6% from early and 11% from late injections. It is concluded that the tubule is readily permeable to cyanide, and cyanide affects sodium absorption rapidly, presumably due to its metabolic effects as suggested by other investigators.

CARDIOREGULATORY ROLE OF THE ABDOMINAL GANGLION OF Aplysia. George Maeda* and Bernell E. Baldwin. Loma Linda Univ. School of Med., Loma Linda, Calif. 92354

An isolated heart-abdominal ganglion preparation was developed and used to study the cardioregulatory function of the ganglion and nerves. The heart was perfused with artificial sea water through an atrial cannula and blood pressure monitored at the gastro-esophageal artery. The presence and cardioregulatory effects of axons in the nerves was investigated by electrical stimulation. Microelectrodes were used to determine relationships between ganglionic neuronal activity and cardiac rhythm. The principal results are listed below.

1. The siphon nerve exerts a strong inhibitory influence on the heart, probably acting as part of a feedback pathway.
2. Primarily inhibitory responses are obtained from both right and left connective stimulation, with some evidence for excitatory axons.
3. Predominantly acceleratory responses are elicited from pericardial nerve stimulation (confirming work of Wright, 1960, and Carlson, 1905).
4. A high frequency spike burst in L7 precedes bradycardia, a coincidental but not deterministic relationship observed in one subject.

This investigation was supported in part by Public Health Service Training Grant No. HE05171 from the Department of Health, Education, and Welfare.

MYOCARDIAL FUNCTION AND ULTRASTRUCTURE IN CHRONICALLY HYPOXIC RATS. J. T. Maher*, A. L. Goodman*, W. D. Bowers*, L. H. Hartley, and E. T. Angelakos. US Army Res. Inst. of Env. Med., Natick, Mass. 01760 and Hahnemann Med. Col., Philadelphia, Pa. 19102.

Cardiac output and stroke volume decrease in man consequent to prolonged exposure to high altitude. Previous studies have suggested that an alteration of myocardial function may be the immediate cause of the decrement. In order to pursue the mechanism(s) involved, myocardial function was studied in isolated cardiac muscle from 10 rats exposed to a simulated altitude of 5800 meters for 24 days (Hy) and compared with those of 9 weight-matched (WM) and 7 age-matched (AM) controls. Left ventricular columnae carneae were suspended in a chamber containing oxygenated Krebs solution at 30°C and were stimulated at a frequency of 30/min. The velocity of shortening at the lightest load (0.5 g/mm^2) did not differ significantly among groups (Hy = 2.09 ± .12, WM = 2.07 ± .10, AM = 2.02 ± .23 muscle lengths/sec). Peak isometric tension was likewise similar in muscles from the 3 groups (Hy = 2.64 ± .25, WM = 2.54 ± .23, AM = 2.58 ± .32 g/mm^2), as was passive compliance. However, both time from onset to peak tension development and latency were significantly ($p < .05$) prolonged in Hy rats. Neither ventricular norepinephrine (NE) content nor inotropic responsiveness to exogenous NE showed significant group differences. Electron microscopic examination of the myocardium from Hy animals revealed structural alterations in the capillaries with marked swelling of the endothelial cells. Thus, it is concluded that although evidence of ultrastructural changes was present, no depression of myocardial contractile function could be demonstrated in the rat as a result of chronic exposure to hypobaric hypoxia.

URINARY KALLIKREIN EXCRETION IN RATS UNDER LOW AND HIGH SODIUM INTAKE. M. Marin-Grez* and O.A. Carretero. Department of Medicine, Henry Ford Hospital, Detroit, Michigan 48202.

Although urinary kallikrein (UK) was first discovered in 1926 by Frey, its physiological role is still unknown. This enzyme is probably produced by the kidney. To see if the UK has any relation to water and Na metabolism, 8 rats were fed a low Na diet. The drinking fluid had .1% NaCl for 3 days and 1% NaCl for another 3 days. Water intake and urinary Na, K, volume, and UK were measured daily. UK activity was measured by incubating 1 µl of urine with .5 ml of plasma. The peptidases and the kallikrein inhibitor were inactivated by treating the plasma 3 hours at 57°C and by the addition of phenanthroline to the incubation mixture. The kinins released, were bioassayed in the perfused hind leg of the dog, the daily excretion was expressed as µg of bradykinin. During the 1st day of high Na intake the urinary volume and UK increased. The UK on the last day of the low Na period was 34 ± 13.2 µg (± S.D.) and on the 1st day of the high Na period it was 49.5 ± 14.8 µg ($p < 0.05$). The r between UK excretion and the following parameters was calculated:

	Low Sodium Period		High Sodium Period	
Parameter	Urine Vol.	Na Excret.	Urine Vol.	Na Excret.
r	.59	.56	.72	.74
p	<.003	<.004	<.001	<.001

These results showed a high correlation between the UK and Na excretion and between the UK and urine volume. The correlation was stronger during the high Na period. It is postulated that the kallikrein-kinin system may play a role in the water and/or Na excretion, acting as a natriuretic hormone. (Supported in part by KFM)

BLOOD AND BILIARY LIPID FLUCTUATIONS DURING PREGNANCY IN THE RHESUS MONKEY. D. E. Martin*, R. C. Wolf, and R. K. Meyer. Wisconsin Regional Primate Research Center, Madison, Wisconsin 53706.

Weekly blood samples were obtained from eight cycling Macaca mulatta, beginning five weeks prior to mating and ending three weeks after parturition. From five of the animals, a blood sample was obtained within 12 hours following delivery. Analyses were made for total cholesterol, phospholipids, nonesterified fatty acids, triglycerides, and total lipids. Plasma phospholipids, total cholesterol, and total lipids significantly decreased during pregnancy. These alterations were initially observed after the fifth week of gestation, reached a maximum by the 11th week, and were maintained at this level essentially throughout pregnancy, with a small upward trend noted during the terminal few weeks. Nonesterified fatty acid and triglyceride levels fluctuated randomly during most of pregnancy, but were elevated during the last month of gestation and at parturition. All measured lipid moieties returned to non-pregnant levels by the second postpartum week. In an attempt to assess whether alterations in biliary excretion of lipids could aid in explaining this marked hypolipemia, the concentrations of cholesterol, phospholipids, and total lipids in gallbladder bile were measured in four Macaca mulatta, two of which were mated shortly following delivery in the preceding experiment. Samples were obtained prior to mating, at four week intervals during gestation, and one month postpartum. No significant changes in biliary lipid levels were detected, suggesting that an elevated biliary concentration of lipids probably does not account for the depressed plasma levels observed during pregnancy.

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ALTERATION IN PLASMA ALDOSTERONE LEVELS IN ANEPHRIC MAN IN RESPONSE TO HEMODIALYSIS. R. E.McCaa*, V. H. Read*, J. D.Bower *, C. S. McCaa*, and A. C. Guyton. Dept. Physiology and Biophysics, Univ. of Miss. Medical Center, Jackson, Miss.

Of the four known humoral factors([Na^+], [K^+], angiotensin II, ACTH) which affect aldosterone secretion when they are varied within physiological limits, the renin-angiotensin mechanism is generally considered to be the major physiological controlling factor in regulating aldosterone secretion. Therefore, the anephric patient provides an excellent model to study the influence of humoral factors other than the renal renin-angiotensin system in controlling aldosterone secretion. Peripheral plasma levels were determined using a sensitive radioimmunoassay method in nine anephric patients before and after hemodialysis. Average patient weight fell 2.0 kg (56.0 $\pm$ 3.84 to 54.0 $\pm$ 3.92) following 12 hours dialysis on the Kiil dialyzer. Plasma Na^+ decreased from 139 $\pm$ 1.06 to 132 $\pm$ 0.81 mEq/l($p < 0.05$), plasma K^+ from 4.8 $\pm$ 0.29 to 3.2 $\pm$ 0.06 mEq/l ($p < 0.0001$), while Na/K ratio increased from 32.0 $\pm$ 2.0 to 42.0 $\pm$ 0.91($p < 0.0001$). Plasma aldosterone levels increased in each individual patient (12.0 $\pm$ 1.57 to 20.0 $\pm$ 2.13 ng/100 ml plasma) $p < 0.02$, while plasma cortisol levels did not change significantly (17.5 $\pm$ 2.0 to 14.8 $\pm$ 1.89 µg/100 ml plasma). These results show that aldosterone secretion increases in the anephric patient in response to hemodialysis. This increase occurs without an increase in cortisol secretion and is independent of the renal renin-angiotensin system. (Supported by USPHS Grant 2 R01 HE 09921-06).

IN VITRO ADRENAL MITOCHONDRIAL 11β-HYDROXYLATION FOLLOWING HYPOPHYSECTOMY OR EXPOSURE TO A STRESSOR. John L. McCarthy, R. S. Sohal* and Wanda L. Green*. Dept. Biol., Southern Methodist Univ., Dallas, Tx.

Adrenal mitochondria were prepared from rats subjected to hypophysectomy or to crowded housing conditions and incubated in vitro to determine 11β-hydroxylation capacity. Previous studies indicated that after exposure of rats to ACTH in vivo it was possible to demonstrate an increased conversion of deoxycorticosterone (DOC) into corticosterone (B) in vitro in the presence of oxidizable substrate (Laury and McCarthy, Endocrinol. 87, 1380, 1971). On the first day following hypophysectomy B production by mitochondria incubated with isocitrate, or succinate were 2 to 3 times the control values. The data suggest the effects result from high levels of ACTH induced by anesthesia and surgery. Malate supported 11β-hydroxylation was consistently below control values from day 1 to day 10 following hypophysectomy. When rats were housed up to 10 animals/1000 cm^2 (control 1 rat/200 cm^2) for 1 to 4 weeks the rate of substrate supported B production in experimental groups was virtually unchanged from control. Increased conversion of DOC into B was found in adrenal mitochondria from rats housed 1 animal/78 cm^2 for 3 weeks. In experimental preparation B production supported by α-ketoglutarate, succinate or malate was 2 to 3 fold above control values. It is suggested that the increase in mitochondrial substrate supported B production reflects the onset of enhanced capacity to carry out 11β-hydroxylation following elevated levels of ACTH.
(Supported by USPHS Grant AM-05744 and NASA Grant NGL 44-007-006)

SIMULATION OF MUSCLE MODELS ON A SMALL COMPUTER. Thomas W. McIntyre (Intr. by J. Clifford Stickney) Dept. of Physiology & Biophysics, W. Va. University Medical Center, Morgantown, W. Va. 26506

The sliding filament model of muscle contraction has been simulated on a digital computer by J. Julian (1969) from the framework developed by A. F. Huxley (1957). I have converted Julian's simulation to run on a PDP-12 computer. The simulation is programmed in BASIC and allows simple modification of some of the basic parameters of the model such as the activation function, rate constants and external compliance. The behavior of the model can be compared to the behavior of muscle preparations having the same external compliance.

1) Huxley, A. F. 1957. Prog. Biophys. Biophys. Chem 7: 255.
2) Julian, F. J. 1969. Biophys. J. 9: 547. (Supported in part from P.H.S. General Research Support W.V.U. School of Medicine Grant No. 5 S01 05433.)

COUPLING BETWEEN Na^+, Cl^- AND WATER DIFFUSION IN RAT INTESTINE. J. R. McKenney and T. R. Morgan*, Dept. Physiol., Med. Col. Ga., Augusta, Ga. 30904.

The effects of 1200R X-irradiation on interaction between Na^+, Cl^- and water diffusion across isolated rat jejunum and ileum were examined. Everted segments were used in apparatus for ^{22}Na, ^{36}Cl and ^{3}HOH flux measurements. It was previously observed that with $[K^+]$ = 50 mM in the incubation medium, to depress net transport, permeabilities to ^{22}Na, ^{36}Cl and ^{3}HOH were closely related over a wide range of Na^+ and Cl^- concentrations. The same relationships were observed following depression of net transport at three days post X-irradiation for the condition $[K^+]$ = 5 mM. One of the relationships is that the unidirectional fluxes for monovalent anions and cations appear to be about equal. A possible interpretation for this relationship is that passive diffusion of ions in some barrier in the tissue occurs predominantly by co-diffusion steps for anion, cation pairs. Since a constraint of co-diffusion steps should reduce the average velocity for ions by one-half, it may be significant that the relationship observed between the permeabilities for ^{22}Na, ^{36}Cl and ^{3}HOH can be derived on the basis that the average velocity for ions in the tissue is about one-half that for water. These observations indicate that there is marked interaction between anion, cation and water diffusion within a barrier in rat small intestine. Work supported by U.S.A.E.C. Contract No. AT-(40-1)-3882.

BETA-ADRENERGIC BLOCKADE IN CARDIAC DENERVATED DOGS UNDER FIXED CARDIAC PRE-LOAD. John C. McMahon* and Arthur W. Merrick. Department of Biological Sciences, Illinois State University, Normal, Ill.

The influence of a beta-adrenergic blocking agent (Propranolol) on cardiac function was evaluated in extrinsically denervated, stressed dogs. A fixed pre-load stress was imposed on 12 cardiac-denervated animals by means of an abdominal arterio-venous fistula. Measurements obtained before and after each surgical procedure included arterial blood pressure, cardiac output, right atrial pressure, heart rate, and the electrocardiogram. Norepinephrine and isoproterenol were infused intravenously before and after the intravenous injection of Propranolol in order to determine the effectiveness of the blocking agent. The data was evaluated by analysis of covariance. Results indicated that the denervated dogs respond to a fixed pre-load with significant positive chronotropism which could be only partially reduced by treatment with Propranolol. A positive inotropic response accompanied the rate increase. It was concluded that increased conduction velocity in the atrium, due to atrial distention, and the heterometric response, initiated by the elevated right atrial pressure, were, in part, responsible for the rise in heart rate and the increase in cardiac output. The suggestion also is offered that one or more intrinsic beta-adrenergic agents may contribute to the positive responses. Beta-adrenergic blockade, in this particular experimental design, appeared to increase cardiac performance and efficiency. (Supported by NHLI Grant HE-12452.)

CARDIOVASCULAR LITERATURE--CITATION PRACTICES. Frances McMurtray* and John M. Ginski. Univ. of Tenn. College of Basic Medical Sciences, Memphis, Tennessee.

In an attempt to further amplify the characteristics of the cardiovascular serial literature, citation patterns were studied. As previously shown, 1/3 of the 5,860 papers from the National Heart Institute grantees for 1967 appeared within 13 journals (JASIS 21, 338, 1970). After the exclusion of the abstract journals, the remaining journals were used to obtain a basic pool of 300 cardiovascular related articles. To determine the citation patterns emanating from these original articles, SCIENCE CITATION INDEX was used. Statistics were gathered relative to citing author, journal and year. The 300 articles in the basic pool were cited a total of 2,545 times; therefore, on the average, an article was cited 8 times during this 4 year period (1967-1971). The figures concerning citation rate by year serve to uphold the idea that journal citation reaches a peak during the third year after publication and falls off at a regular rate thereafter. Also, some definite patterns of self-citation were noted. It was found that, when analyzed solely on the basis of the first author, 15% of the 2,545 citations were self-citations. Statistics show that the 10 basic pool journals tend to be cited mostly within themselves; 1/3 of the citations were found in these journals. Although the citations were found throughout 349 various journals which indicates an extensive scatter, a relatively high percentage of the papers were found in relatively few journals.

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GASTRIC ACID AND PEPSIN SECRETION IN CONSCIOUS MINIATURE SWINE AFTER INTRAVENOUS 2-DEOXYGLUCOSE. A.M. Merritt (intr. by F. P. Brooks). School of Veterinary Med., Univ. of Pennsylvania, Philadelphia, Pa.19104

This study was designed to begin defining the role of the vagi in the control of porcine gastric secretion. Pitman-Moore miniature swine of both sexes were prepared with a gastric fistula and a chronic jugular catheter. Animals between 2 and 6 months of age were given 50, 100, or 200 mgm/kg of 2-DG by rapid iv infusion; only 1 dose was used per experiment. A gastric secretory effect was evident within 15-20 minutes, with a peak response occurring in 45-60 minutes, following 2-DG administration. The exception was no increase in pepsin output following 50 mgm/kg of 2-DG. Both acid and pepsin were stimulated in greatest amounts by 200 mgm/kg, the output's being 1.287 ± 0.218 (SEM) mEq/kgBW/hr and 2.21 ± 0.46 P.U. x 10^{-1}/kg/hr respectively which were not significantly different from maximal histamine responses (Merritt & Brooks; Gastroenterology, 58: 801, 1971). The results suggest that the acid component of gastric secretion in the miniature pig responds to 2-DG infusion in a manner similar to the dog (Hirschowitz & Sachs, Am. J. Physiol., 209: 452, 1965) with regard to the dose-response curve and peak acid output in the range of a maximal histamine response. In contrast to the dog, pepsin response following 2-DG in the pig is roughly equivalent to that following histamine.

PULMONARY INTERSTITIAL VOLUME ESTIMATION IN DOGS BY KINETIC ANALYSIS OF PLASMA TO LYMPH ALBUMIN TRANSPORT IN THE RIGHT DUCT. E. C. Meyer*, R. Ottaviano* (SPON: M.H.F. Friedman), Mercy Catholic Medical Center, Darby, Pa. 19023.

As baseline data for pulmonary edema studies we measured interstitial fluid volume relative to lymph (V_I) in the thoracic (TD) and right ducts (RD) in dogs. V_I was calculated from plasma-lymph appearance of I^{131} RISA assuming bulk transport and first order kinetics. Asymptotic, steady-state lymph I^{131} RISA concentration at time $\rightarrow \infty$ was estimated from lymph concentration of equilibrated I^{125} RISA injected 3-5 days previously. In 8 dogs with TD and RD, V_{IRD} = 0.9 ± .47 ml/Kgm; V_{ITD} = 3.1 ± 0.8 ml/Kgm. In 12 additional dogs with no RD found, V_{ITD} = 3.3 ± 1.5 ml/Kgm. Mean TD flow was 10 times mean RD flow. We analyzed the lungs from dogs with TD and RD for lung tissue water (Q_{LW}), lung blood water, and I^{125} activity by homogenization. Mean Q_{LW} = 4.7 ± 0.8 ml/Kgm corresponding to a mean lung/body weight of 0.98 ± 0.08%. We assumed lung interstitial water (Q_{IW}) was 0.36 Q_{LW}. (Vaughan: Fed. Proc. 30:1041). Subtracting homogenate plasma activity from total homogenate activity we calculated that lung interstitial fluid/plasma albumin concentration = 0.72 ± 0.3. Corresponding right duct lymph/plasma albumin concentration was 0.73 ± 0.1. These data suggest that V_I in pulmonary lymph estimates Q_{IW} but that only V_{IRD}/Q_{IW} = .52 measures Q_{IW} passing in the right duct in dogs. (Supported by N.I.H. Grant No. 08601).

EFFECTS OF THERMAL ACCLIMATION ON MUSCLE LYSOSOMES OF RAINBOW TROUT. Albert A. Milanesi* and John W.C. Bird. Dept. of Physiology, Rutgers University, New Brunswick, N.J.

The distribution and particle properties of striated muscle lysosomes of the rainbow trout, Salmo gairdneri, were studied at acclimation temperatures of 5°, 12° and 18°C to gain an understanding of the organism's ability to modify and regulate its internal environment. Tissue homogenates of dorsal muscle in 0.25 M sucrose were tested for optimum enzyme assay conditions by exploring such variables as pH, incubation temperature, protein concentration, and incubation time. The subcellular distribution of enzyme activity was determined by differential centrifugation of the homogenate into five fractions. Particulate enzymes have their greatest concentration in the light mitochondrial fraction. Sedimentation and equilibrium characteristics of lysosomal particles were studied by rate and isopycnic zonal centrifugation in linear sucrose gradients (10-30% and 30-50%, respectively). These experiments illustrated the heterogenic nature of muscle tissue lysosomes by demonstrating the existence of at least two distinct populations. In rate zonal fractionation a slow sedimenting population peak of acid hydrolases was found around fraction four while a fast sedimenting population was found with the mitochondria against the gradient cushion. Cold and warm acclimated lysosomes had an increase in activity at the cushion. Isopycnic zonal centrifugation demonstrated the following modal equilibrium densities for the different temperature acclimations: 5°C, 1.17; 12°C, 1.18; and 18°C, 1.19. (Supported in part by N.I.H. grants NS-07180 and NS-12524).

ACTIVE NEUROGENIC VASODILATION IN SKIN. Ronald W. Millard* and Kjell Johansen, Center for Bioengineering and Dept. of Zoology, Univ. of Washington, Seattle, Wash.

Regulation of skin blood flow (SBF) is poorly understood since most preparations studied have included substantial amounts of muscle and other vascular tissues. We have found birds with large webbed feet offer superior preparations for direct study of SBF and its regulation. In the giant petrel (Macronectus giganticus) skin makes up 35% of foot weight while 65% is bone and tendon. SBF with changes in ambient temp. was studied by electromagnetic flow meter, intracutaneous and intravascular temps. and local a-v O_2 differences in the foot. Foot immersion in iced brine greatly steepened intravenous temp. gradients in the foot central to peripheral from 35 to 30 to 30 to 4°C. Immersion promptly elevated SBF 2-1/2 times to 50 ml/min. This cold flush response was associated with increased web venous pressure, web arterial and venous temps. and heart rate, while systemic pressure decreased. Stimulation of cut peripheral nerve ends to the foot caused vasodilation or constriction depending on selection. Responses were mimicked by autonomic agents injected intraarterially in the foot. Atropine blocked vasodilation from nerve stimulation and Ach injection. A-v O_2 differences revealed that Q/VO_2 for the foot increased more than fivefold from 70 to 150 ml/mlO_2 when compared at thermoneutrality and heat stress or the initial phase of a cold flush. The conspicuous blood flow variations are largely effected by changes in a-v shunt flow and controlled by a synergistic neurogenic mechanism.

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THE EFFECT OF EDGE DAMAGE ON THE MEASUREMENT OF ELECTRICAL RESISTANCE OF FROG SKIN. David A. Miller and Sandy I. Helman (intro. by D.F. Sears). Tulane Univ. Medical School, New Orleans, La. 70112

The steady state current-voltage relationship of frog skin was studied in Cl Ringer using techniques that avoid edge damage (Science, in press). In 141 skins, the I-V relationship (Between 0 and +200 mV, inside positive) characteristically showed 3 distinct regions of resistance. Resistance R_1, 4858 ± 278, R_2, 3418 ± 196, R_3, 2312 ± 142 (mean ± SE ohm cm^2) fell into regions above open circuit voltage, around open circuit voltage, and around short circuit current conditions, respectively. Edge damage produced by compression in 6.4 cm^2 chambers caused R_1, R_2, and R_3 to fall 39%, 36%, and 33% and in 0.64 cm^2 chambers they fell 75%, 69%, and 58%, respectively. From these results the resistance of the damaged edge was estimated to be 5432 ohm per cm edge. Solving for the parallel combination of R_{edge} and R_{skin} for all areas (circular chambers), a curve relating measured resistance to chamber area was generated. This curve gave values that correspond well to the results of others using chambers in the range of 8.3 to 0.38 cm^2.

INTRACELLULAR POTENTIALS FROM MEDULLARY RESPIRATORY NEURONS IN THE CAT. Robert A. Mitchell and Dorothy A. Herbert* Dept. of Anesthesia and Cardiovascular Res. Inst., Univ. of Calif., San Francisco, Calif. 94122

Two unresolved questions concerning the role of medullary respiratory neurons are (1) does CO_2 have a direct effect on them and (2) are they primarily involved in rhythm generation. We recorded intracellular potentials from 57 inspiratory and 11 expiratory neurons in the caudal medulla of anesthetized cats. Inspiratory neurons (ave. resting membrane potential (RMP) - 62 mv.) had rhythmic depolarizations and firing synchronous with inspiration as indicated by phrenic nerve activity. On termination of inspiration, the firing ceased and the membrane potential rapidly returned to the RMP. Hypercapnia caused either no change in RMP or slight hyperpolarization. However during inspiration the magnitude of the rhythmic depolarizations and frequency of firing were increased. Carotid chemoreceptor stimulation by NaCN increased the magnitude of rhythmic depolarization and firing frequency without significantly altering the RMP during expiration. Expiratory neurons (ave. RMP - 52 mv.) showed rhythmic depolarization and firing during expiration with a return to RMP at the termination of firing. However, during inspiration these cells were hyperpolarized. The magnitude of the hyperpolarization fluctuated within one inspiratory cycle and the fluctuations were closely related to variations in phrenic discharge during that cycle. Our results indicate that tonic chemoreceptor stimulation and presumably a non cyclic input into the "respiratory centers" produced an increase in cyclic input to medullary respiratory neurons. We therefore suggest that medullary inspiratory cells (1) are neither themselves chemoreceptors nor directly influenced by chemoreceptors and (2) are not primarily involved in the generation of normal respiratory rhythm, since the input into inspiratory neurons resulting from hypercapnia, as well as from other respiratory stimuli, appears to be synaptic and is already gated to a respiratory rhythm. (Supported in part by USPHS, NIH Grants GM15571 and 5-K3-HE-19411.)

ROENTGEN VIDEODENSITOMETRIC DETERMINATION OF LEFT-TO-RIGHT SHUNTS IN EXPERIMENTAL VENTRICULAR SEPTAL DEFECT (VSD). K. Miyazawa*, H. C. Smith*, A. A. Bove, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

Dilution curves of 69% renovist were used for the detection and quantitation of intracardiac left-to-right shunts in 6 anesthetized dogs 21-45 days after creation of a defect through the mid portion of the ventricular septum. Spontaneous closure of the defect occurred in 2 dogs. Following injections of an indocyanine green-renovist solution into a peripheral pulmonary artery or vein, left atrium, or left ventricle, left-to-right shunts, as % of pulmonary flow, were determined from the ratios of areas of dilution curves of indocyanine green and renovist recorded from the pulmonary and systemic circulations using densitometer-catheter sampling from pulmonary artery and aorta and roentgen videodensitometry sampling windows at the same sites on simultaneously recorded videotape angiograms. In all dogs, a small increase in roentgen opacity was observed over the right heart and lungs immediately following renovist injection into the ascending aorta due chiefly to renovist traversing the coronary and bronchial circulations. In the 4 VSD dogs, correlation between the two methods was good but videodensitometric shunt flow values were generally higher. This difference was eliminated when the coronary-bronchial/systemic circulation renovist area ratios following aortic injections of renovist were subtracted from the ratios following injections into a distal pulmonary artery. The phasic rate of opacification of videodensograms recorded from the right ventricle near the VSD, i.e., phasic shunt flow, was greater during diastole than systole in all dogs at low heart rates (<110) despite greatly reduced interventricular pressure gradients. Increased heart rates by atrial pacing did not alter the amount of shunt but appeared to increase systolic and decrease diastolic components. (NIH 3532, 4664, FR-7, AHA CI 10.)

FREQUENCY RESPONSE OF EXERCISE HYPEREMIA. D.E. Mohrman*, J.R. Cant*, and H.V. Sparks, Univ. of Michigan, Ann Arbor, Michigan.

The flow response following brief tetanic exercise is too rapid to be controlled by mechanisms related to oxidative metabolism (Mohrman, D.E. and P.H. Abbrecht, Fed. Proc. 30:211, 1971). To determine whether the same is true during continuous non-tetanic work we have studied the dynamic response of resistance and O_2 consumption ($\dot{V}O_2$) to sinusoidal variations in exercise rate of dog calf muscle. If the resistance changes associated with this type of work are to be explained by a mechanism related to oxidative metabolism, changes in $\dot{V}O_2$ must occur at least as fast as changes in resistance. The blood supply of the calf of 7 dogs was isolated and pump perfused at constant flow. Perfusion pressure and venous O_2 (% hemoglobin saturation) were continuously monitored. O_2 measurements were corrected for vascular transit using the distribution of transit times of arterially injected dye. The stimulation rate of the sectioned sciatic nerve was modulated sinusoidally between 0.5 and 1.0 twitches/sec. The modulation frequency ranged from 0.003 to 0.05 Hz. Both resistance and $\dot{V}O_2$ varied sinusoidally in response to this stimulus. The amplitude of the oscillations were constant at modulation frequencies below 0.01 Hz and diminished in an identical fashion (12 db/octave) at higher frequencies. This similarity of resistance and $\dot{V}O_2$ changes exists because the resistance changes during continuous exercise are slower than those after brief tetanus. This indicates that during continuous exercise the resistance response could be controlled by a mechanism directly related to oxidative metabolism. Thus, exercise hyperemia may be controlled by at least two mechanisms, one dominant after brief tetanus and another during continuous exercise. Supported by USPHS Grant GM01289 and Mich. Heart Assoc.

EFFECT OF DIFFERENT ALCOHOLS ON MYOCARDIAL CONTRACTILITY. S. E. Moore* and J. Nakano. Dept. of Pharmacol. and of Medicine, Univ. of Oklahoma Sch. of Med., Oklahoma City, Oklahoma 73104

Ethanol (ETOH) depresses directly myocardial contractile force (MCF) in vivo and in vitro. Regan et al. (J.C.I. 43: 1289, 1964) postulated that the myocardial depressant effect is caused by hyperosmolarity of the plasma induced by administration of ETOH. The present study was conducted to examine the effect of different alcohols, i.e. methanol (MEOH) ETOH, n-propanol, i-propanol, n-butanol, i-butanol, n-pentanol and i-pentanol, on the MCF in the isolated guinea-pig ventricular strip. The strips were bathed in Chenoweth-Koelle solution (pH 7.4, 30°C, 300 milliosmol/liter) gassed with 95% O_2 and 5% CO_2. The rate of contraction (120/min) was kept constant with a Grass stimulator. ETOH in concentrations from 1 x 10^{-2}M to 3 x 10^{-1}M reduced MCF by 11 to 65%. Similarly, geometrically increasing concentrations of the 7 other alcohols (1 x 10^{-3} to 1 M) decreased MCF essentially in proportion to the concentration. The magnitude of MCF depression by the 8 alcohols is proportional to the length of their carbon chains and their dielectric constants. When the pD_2 value of each alcohol studied was related to its structure, among the 8 alcohols, MEOH and n-pentanol caused, respectively, the least and the greatest depression of MCF. Sucrose (1 x 10^{-2} to 3 x 10^{-1} M) when added to the media to produce hyperosmolarity equivalent to the same molar concentrations of ethanol (415 milliosmol/liter) did not alter MCF significantly. The present study suggests that the MCF depressant effect of ethanol and other alcohols is not caused by hyperosmolarity but by their affinity to the myocardial cell structures. (Supported in part by research grants from the Licensed Beverage Ind., Inc. and from U.S.P.H.S., HE-11848).

Effect of insulin-induced hypoglycemia on pancreatic amylase secretion and enzyme synthesis. J. MORISSET, Y. COUTURE and J. DUNNIGAN (intr. by P.D. Webster). Unité de Recherche Gastro-intestinale. Fac. Sci., Sherbrooke Univ. Sherbrooke, Canada.

It is known that insulin-induced hypoglycemia increases pancreatic volume flow and protein output. It is also known that this secretory effect is abolished by vagotomy. These experiments were designed to determine mechanisms whereby insulin hypoglycemia increases pancreatic enzyme secretion and synthesis. Male albino rats were used. Insulin 6 Units/100 gr. B.W. was administered SC. Pancreata were incubated in tissue culture media with ^{14}C-labeled amino acids and protein synthesis was studied. Amylase secretion following insulin was determined directly by cannulation of the pancreatic duct as well as indirectly by determining residual amylase content. Results show that insulin is associated with a significant decrease in pancreatic amylase content as well as an increase in amylase output. Increased protein synthesis occurs only one hour after hypoglycemia has been established. These effects were abolished by vagotomy and by acid into the stomach with a duodenal ligature. These results suggest that the stimulus involved is under vagal control and confined to the stomach; this stimulus is believed to be gastrin. (Supported by grants A-6369 and A-1963 from Nat. Res. Council of Canada).

VASCULAR RESPONSE OF THE CAT INTESTINE TO NOREPINEPHRINE FOLLOWING INFUSION OF TETRODOTOXIN (TTX). Nicholas A. Mortillaro* and Leif Horn. College of Medicine and Dentistry of New Jersey at Newark, Newark, N.J.

In cats, eviscerated and adrenalectomized, autoperfused isolated loops of small intestine (ileum) were intra-arterially infused with norepinephrine (1.0-2.5 ug/min) before and following infusion of TTX (10 ug/min). The former taken as the control. In each case the concentration of norepinephrine before and following the infusion of TTX was the same. Total blood flow (ml/min x 100 g) through the intestinal segment was measured utilizing a flowmeter activated by a photoelectric cell in a drop chamber. During infusion of TTX, the TTX containing efflux from the segment was discarded and blood was cross perfused from a donor cat. Both splanchnic nerves were cut and the peripheral ends were mounted on double ring electrodes. Marked inhibition of sympathetic outflow to the TTX perfused segment was indicated by the absence of vascular response during splanchnic nerve stimulation (5-8 imp/sec), i.e., blood flow remained relatively constant during the stimulation period. Intestinal vascular constrictor response to norepinephrine, as indicated by a decrease in blood flow, ranged from 41 to 48% (control) of resting blood flow, whereas following TTX infusion the range was only 13 to 28% of resting blood flow. The results suggest that a condition similar to denervation hypersensitivity results from TTX's inhibition of sympathetic activity, and this condition is seen to develop minutes after the infusion of TTX. The results will be discussed in relation to the "autoregulatory escape". (This research was supported by Contract DADA-17-68-C8058 with the U.S. Army Medical Research and Development Command and National Science Foundation Grant #FJ5024.)

SINGLE UNIT ACTIVITY IN SOMATOSENSORY CORTEX OF WAKING MONKEYS. D.G. Mountjoy* and M.A. Baker. Department of Physiology, University of Southern California, School of Medicine, Los Angeles, California.

We studied the activity of single neurons in the postcentral gyrus of conscious pigtail macaques (M. nemestrina) which had been prepared for chronic extracellular microelectrode recording. Both spontaneous activity and response to peripheral stimulation were observed for each unit isolated. "Natural" stimuli, delivered by brush, blunt probe or needle, or by movement of joints, were used to drive the cells. One hundred and fifty single neurons were studied. In the waking animal, 50% of the cells showed no spontaneous activity, but could be driven to fire if appropriate stimuli were delivered to the receptive field. The remaining cells showed varying levels of spontaneous activity, most firing at rates below 5 spikes/second. Eighty per cent of the units could be driven by light touch on the skin or by hair movement, and the remaining 20% responded to firm touch or joint movement. Nearly all units responded to both punctate and moving stimuli, but some cells responded only to moving stimuli. Several of the cells were direction-sensitive. Of the neurons showing a high spontaneous activity, a small proportion could be inhibited by natural stimulation outside of the excitatory receptive field. None of the units showed attenuation of evoked responses with repeated peripheral stimulation. The high proportion of somatosensory cortical cells showing no spontaneous activity in the waking monkey is consistent with findings in the waking cat (Baker, Fetz & Towe, Physiologist, v.12, 1969) and contrasts with the activity of neurons in the ventrobasal thalamus, where most somatosensory neurons show high levels of spontaneous activity in the awake animal (Baker, J. Physiol. Lond., in press 1971).
(Supported in part by NIH Grant NS 09599-01)

THE EFFECT OF PULMONARY EDEMA ON THE REDISTRIBUTION OF BLOOD FLOW IN DOGS. Muir, A.L., Hall, D., Despas, P., J.C. Hogg, (intr. by P.T. Macklem). Respiratory Division, Royal Victoria Hospital, Montreal, Canada.

We measured the effect of pulmonary edema on regional pulmonary blood flow in intact, vertically upright, anesthetized dogs. Edema was produced by raising left atrial pressure and by hemodilution with intravenous saline. Regional pulmonary perfusion was determined before and after edema in multiple lung samples using two radioactive macroaggregates with different emission characteristics. Regional gas volume per gram of lung tissue (Vg/gm) was determined from lung density (1) and lung edema was determined from wet to dry weight ratio (W/D) and histological examination. Nine dogs were studied; in 3 dogs no edema was produced ($W/D < 5.5$); in 2 dogs histological interstitial edema was produced ($5.5 < W/D < 7.0$); in 4 dogs alveolar edema was identified histologically ($W/D > 7.0$). In the 4 dogs with alveolar edema there was a redistribution of pulmonary blood flow with proportionately less flow at the base of the lung. Similar changes were not observed in the dogs with interstitial edema. The reduction in blood flow in individual lung samples correlated more closely to Vg/gm than to W/D. These results suggest that the reduction in Vg/Gm. associated with alveolar edema has a greater effect on pulmonary vascular resistance than interstitial fluid collection.

(1) Hogg, J.C. & Nepszy, S., J. Appl. Physiol. 27; 198, 1969
(Supported by a grant from the M.R.C. of Canada).

A METHOD OF COMPARTMENTAL ANALYSIS OF THE INSECT NERVE CORD. G.G. Myers*, D.J. Weidler*, A.L. Bennett and P.J. Gardner*, Dept. of Physiology and Biophysics and Dept. of Anatomy, University of Nebraska College of Medicine, Omaha, Nebraska.

At the previous Autumn Meeting, efflux studies on nerve cords of Periplaneta were reported, in which six components were described. Insect nerve cords generally deteriorate after about 40 hr in vitro; as a result, it is impossible to completely saturate all compartments (i.e., to achieve the same specific activity in all compartments). The purpose of the present study was to develop a computer method of estimating saturated levels in all compartments of the insect nerve cord. Nerve cords of the grasshopper Melanoplus differentialis were removed and incubated 14 hr in solution containing ^{22}Na; then they were desaturated 22 hr in solution not containing ^{22}Na and the radioactivity in the nerve cord was monitored as a function of time. Using a digital computer method, the desaturation curve was integrated and converted into an uptake curve. The latter curve was fitted into raw uptake data by means of a scale factor which was computed by a least squares method. The asymptote of the curve represents the saturation value approached by the experimental data if it were possible for the experiment to continue indefinitely. Beginning with this computed saturation value, a desaturation curve was simulated on the digital computer, using the original desaturation dynamics. Graphical analysis of the latter curve yielded estimated apparent saturated component sizes. The latter values may be used to calculate concentrations only after corrections are made for interactions between components.

THE EFFECT OF TEMPERATURE ON PLATELET MIGRATION IN VITRO. P. Nathan and Rosalin W. Lowenhaupt. Shriners Burns Unit and the Depts. of Physiology and Surgery, Univ. of Cincinnati Coll. of Medicine, Cincinnati, Ohio.

Previous work from our laboratory has shown that platelets rapidly accumulate in dog kidneys transplanted to specifically sensitized recipients. The need to study platelet migration under controlled conditions led to the development of an in vitro system for migration of platelets. The procedure was modeled on the macrophage migration test of David et al. J. Immunol. 93, 264, 1964. Dog blood was collected in tubes containing EDTA. The platelets were isolated from the blood by differential centrifugation. Platelets were packed at the bottom of flame sealed hematocrit tubes. The tubes are cut off about 1 mm above the platelet button and mounted in sealed MacKaness chambers. The platelets were incubated at 10,22,30 and 37°C for 24 hrs. in Eagles solution with added antibiotics and EDTA. An image of the migrating platelet pattern was magnified with an overhead projector and the area of migration measured with a planimeter. No migration was observed at 10°C. The migration area for 16 tubes was averaged for each temperature. At 22°C the average migration measured in the projection was 35cm^2, at 30°C 55 cm^2 and at 37C the area projection was 32 cm^2. Optimum temperature for migration in vitro was at approximately 30°C. This observation is consistent with the report of another platelet activity, namely that platelet adhesiveness is greater at 20°C than at 37°C. The structure of the platelets was observed by electron-microscopy and many were found to be greatly extended and to possess bizarre shapes. The technique described permits a direct approach to platelet migration in vitro.

EFFECT OF HYPERONCOTIC DEXTRAN INFUSIONS ON SEGMENTAL RENAL VASCULAR RESISTANCES AND GLOMERULAR PRESSURE. L.G. Navar, P.G. Baer,* and S.L. Wallace.* Dept. Physiol. & Biophys., Univ. Med. Ctr., Jackson, Miss.

To determine effects of increased plasma colloid osmotic pressure (PCOP) on renal hemodynamics and segmental vascular resistances, 12% dextran (MW 100,000) solutions were infused into anesthetized dogs both systemically (n = 11) and directly into the renal artery (n = 5). Systemic infusion of 300-500 ml of solution increased PCOP by 60%. Renal blood flow and intrarenal venous pressure increased by 110% and 137%, and arterial pressure increased slightly from 128 mm Hg to 134 mm Hg. Glomerular filtration rate was not significantly altered. Arterial pressure-renal blood flow curves revealed that the vasodilatory effect was restricted to the autoregulatory portion of the curve. Renal blood flow recovery patterns after one-minute renal arterial occlusion demonstrated that renal vascular contractility was maintained. Direct infusion revealed a 40-60 second lag-time for measurable blood flow response; and no blood flow increase was recorded when renal arterial pressure was held at 55-60 mm Hg during infusion. On the basis of these data it is suggested that elevation of PCOP causes decreased intrarenal resistance at the pre-glomerular autoregulating segments by interfering with the intrarenal mechanism normally responsible for renal blood flow autoregulation. Resistance at this segment is apparently reduced to a minimal level while post-glomerular resistance and venous resistance are not altered. Calculated glomerular pressure increased from 52 mm Hg to 106 mm Hg following systemic infusion, and the calculated filtration coefficient was decreased. It would appear that in addition to its colloid osmotic pressure effects, dextran directly interferes with filtration by decreasing the permeability of the glomerular membrane. (Supported by Grants HE 11428 and HE 11678)

UREA AND URINE VOLUME IN BEARS. R. A. Nelson, H. W. Wahner,* J. D. Jones* and P. E. Zollman.* Mayo Clinic and Mayo Foundation, Rochester, Minn.

Blood urea does not increase in bears after 100 days of winter sleep despite no intake of food or water or output of urine. An intravenous injection of 10 gm of urea was given to two black bears during winter sleep to determine their ability to handle urea. The bears were studied for 24 hours, before, during, and at the end of winter sleep while immobilized with phencyclidine and promazine HCl. Before winter sleep, the 24-hour volume of urine was 1,872 and 970 ml and total urea was 31 and 22 gm, respectively. After 84 days without food or water, 24-hour volume of urine was 104 and 78 ml and total urine urea was 4 gm in each collection. The values for blood urea and water content of plasma (0.90/ml) and of red blood cells (RBC) (0.69/ml) were unchanged from control values. Three weeks later, 10 gm urea/50 ml saline was injected. Blood urea increased from 9 to 42 mg/100 ml and returned to levels considered normal for winter sleep (<33 mg/100 ml) in 1 hour. Urine output doubled and 58 and 90% of the injected load was excreted. Water excreted came from intracellular sources because in 24 hours the RBC water content decreased from 0.69 to 0.63 ml/ml RBC and that of plasma was unchanged. Urine volume was an exponential function of urea excretion, $V = 66\ e^{0.12\ U}$, the equation derived from data collected before, during, and at the end of winter sleep. It was concluded that during the bear's winter sleep the decrease in urea produced from dietary and endogenous sources of protein removed a potent stimulus for urine formation. When the bear was conserving water and when urine volume was at its lowest level, a net increase in blood urea promptly stimulated increased formation of urine and with its excretion most of the injected bolus of urea also was excreted.

CEREBRAL LACTATE (LA) METABOLISM IN INSULIN-INDUCED HYPOGLYCEMIC DOGS. E.M. Nemoto☆ J.T. Hoff☆ and J.W. Severinghaus. Cardiovascular Research Inst., U.C. Med. Ctr., San Francisco, Calif.

During sustained (6 hr.) elevation of arterial LA to 6-8 mM at normal pH and Pco_2, a mean (A-V) LA of .55±.14 (se) mM and gradual rise of CSF LA, suggested cerebral metabolism of LA (Fed. Proc. 30:970, '71). We have tested whether LA uptake spares glucose (G) consumption and might be increased during hypoglycemia. In 8 hyperoxic, isocapneic dogs we measured, at 30 min. intervals, CBF (^{133}Xe clearance), arterial and sagittal sinus LA, G and O_2 content, CSF G, LA and pH, and $Paco_2$, Pao_2 and pHa. After 3 control samples, hypoglycemia was induced with 800-1600 U regular insulin i.v. and 3 samples were drawn. 1M NaLA and 0.6M HLA were infused at programmed rates inducing a step rise of LA (to 10.5± .77 se mM) at constant pH and Pco_2, and 5 more samples were drawn. During control and hypoglycemic periods, before raising LA, CMR_{LA} (cerebral metabolic rate) was zero. CMR_G, CMR_{O_2} and CBF were reduced 38%, 22% and 23% resp. by hypoglycemia. CSF G fell progressively from 4.3 mM control to 0.68 mM at the end. At 30 min intervals after LA loading, CMR_{LA} accounted for the following fractions of CMR_{O_2}: .58, .34, .12, .24 and .24. CBF and CMR_{O_2} rose to 94% and 90% of control, resp, while CMR_G remained 42% below control. Over the entire 2 hr lactate infusion, lactate and glucose accounted for 28% and 78% of O_2 uptake resp, the sum (106%) suggesting that 6% of the lactate uptake was stored in brain and CSF or otherwise metabolized. CSF LA rose faster (half time < 1 hr), to 0.63 and 0.60 of arterial LA at 1.5 and 2.0 hr, while in our previous study with normoglycemia at similar lactate levels half time = 2 hr, with a similar final CSF/arterial ratio. We conclude that, under these conditions, LA can replace about 0.3 of glucose needed by brain. Rising CSF LA suggests that the limitation is unlikely to be blood brain barrier permeability to LA. Supported by HE06285, GM00063 and 5-K6-HE 19,412 grants of the NIH.

EFFECTS OF CHANGES IN EXTERNAL SALINITY ON RENIN ACTIVITY IN PLASMA AND KIDNEYS OF TWO EURYHALINE TELEOST FISHES, ANGUILLA ROSTRATA AND OPSANUS TAU. H. Nishimura*, W.H. Sawyer and R.F. Nigrelli*. Dept. of Pharmacology, College of Physicians & Surgeons of Columbia Univ., New York, and the Osborn Lab. of Marine Science, New York.

Renin activity has been found in the kidneys and plasma of a variety of bony fishes from both sea water (SW) and fresh water (FW). It has been suggested that the renin-angiotensin system (RAS) may respond to changes in external salinity and may serve some osmoregulatory function. In an attempt to determine whether activity of the RAS is related to sodium balance we have studied plasma renin activity (PRA), kidney renin activity (KRA), and renin substrate levels in two euryhaline fishes transferred from SW to hypoosmotic environments. American eels (Anguilla rostrata) show decreased PRA 3 days after transfer from SW to FW but this may return toward the original SW levels after 3 weeks in FW. KRA also decreases but at a slower rate than does PRA. Aglomerular toadfish (Opsanus tau) in SW have lower PRA and higher KRA and substrate levels than do glomerular SW fishes. After transfer of toadfish to dilute SW (5%) PRA levels show inconsistent changes but may be slightly depressed. Thus renin activity in these euryhaline fishes either remains unchanged or decreases with adaptation to a hypoosmotic medium. In adapting to FW euryhaline fishes excrete excess water by increasing urine flow while actively absorbing sodium through their gills. From the above results we cannot conclude that the RAS in these fishes works in the direction of sodium retention, as has been observed in some mammals. It may serve different functions in euryhaline fishes. (Supported by NIH Grants AM 01940 and HE 12738 and NSF Grant GB 4932).

RESPONSES OF THE RIGHT VENTRICLE DURING STIMULATION OF VENTRAL ROOTS. Jeanne Norris*, Robert D. Wurster, and Robert Foreman*. Loyola Univ., Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Force of contraction of four areas of the right ventricle were monitored with strain gauges during stimulation of thoracic ventral roots in eleven anesthetized dogs. Systemic pressure and right ventricular pressure were also monitored. Significant increases in systemic pressure were noted during stimulation of the first right thoracic root and the first three left thoracic roots. Significant heart rate increases accompanied stimulation of the first three right thoracic roots. Force of contraction increased with stimulation of the first five thoracic roots of both sides. The magnitude of this increase varied with the root stimulated, with second thoracic root of both sides giving the greatest response. In general, the left roots gave a greater increase in force of contraction than did the right. Stimulation of the fourth and fifth thoracic roots caused an increase in force of contraction in some animals but the magnitude of the increase was significantly less than that noted with stimulation of the upper roots. Stimulation below the fifth thoracic level gave no response in ten of the eleven dogs studied. These findings indicate that the first three roots of both sides participate in both rate and force responses. It is also suggested that the rate response is controlled by the right side of the cord while both sides of the cord participate in increasing force of contraction. *(Supported by NIH HE 08682 and GM 999)*

EFFECT OF ACUTE HYPOXIA ON THE HEART BEAT OF THE CONSCIOUS DOG. David W. Northup, Michael Soulsby* and Michael F. Wilson. Dept. Physiology and Biophysics, W.Va. University Medical Center, Morgantown, WV.26506

Pairs of miniature coils chronically attached to the left ventricle of dogs were so arranged that signals varying with the width and length of the left ventricle were generated. These signals after appropriate processing were fed through an analog computer giving a continuous record of left ventricular volume. The EKG was also recorded. The dogs were subjected to acute hypoxia in a low pressure chamber at a simulated altitude of 10 km with a rate of ascent of 914 meters/min, remaining at 10 km for 30 minutes. During ascent the diastolic volume of the left ventricle decreased and continued to decrease during the stay at 10 km. The stroke volume increased during the ascent to a maximum as 10 km was reached. During the stay at 10 km the stroke volume decreased, arriving at about the control value at the end of 30 min. Heart rate increased during the ascent to an altitude of 6 km and then fell off, reaching a minimum of 10% below control at 10 km. During the stay at 10 km it again rose. As a result of these changes the cardiac output rose during ascent and for the first 10 min of the stay at 10 km, then fell off. After 10 min at 10 km it was only 8% above control value. During descent to ambient pressure the cardiac output continued to fall to 13% below control at 2 km. After 10 min at ambient the output was 6% below control. The diastolic volume failed to recover during descent and after 10 min at ambient pressure was 24% below the control value. The ejection fraction increased during ascent from an altitude of 6 to 10 km, then declined toward control values. The decrease in cardiac output while at 10 km indicates inability of the cardiac regulatory mechanisms to compensate fully for the stress imposed on it. Supported in part by W.Va. Heart Grant No. 70-AG-12C.

THE EFFECT OF CEREBRAL ISCHEMIA ON CAROTID VASCULAR HEMODYNAMICS AND CORTICAL ELECTRICAL ACTIVITY IN GOATS. Richard K. O'Hern* and Guido Ascanio. Dept. of Physiol., Temple Univ. Med. Sch., Phila., Pa. 19140.

The anatomy of the goat cephalic arterial vasculature permits measurement of cerebral blood flow with minimal admixture of blood from extracerebral sources. Since analysis of corrosion casts and angiograms has demonstrated that the entire cerebral blood supply in goats is derived from the external carotid arteries, they serve as convenient vessels for producing total cerebral ischemia through bilateral vascular occlusion. In addition, their accessibility permits the application of electromagnetic cuff flow probes without significant surgical trauma. The plotting of systemic blood pressure-carotid blood flow relationships before and after bilateral external carotid arterial occlusion revealed a loss of cephalic vascular autoregulation following cerebral ischemia of 20 minutes duration. External carotid blood flow ranged from 200 to 300% of control following the release of carotid occlusion. At the same time, cerebral venous oxygen tension (PVO_2) was elevated to 55.1 ± 4.2 ($M \pm SE$) from a control of 41.8 ± 3.7 mm Hg ($P < 0.05$). Furthermore, cerebral venous blood pH decreased to 7.286 ± 0.055 from a control of 7.343 ± 0.027. CO_2 cephalic vascular reactivity was also diminished following carotid occlusion. Under normal ventilation conditions, before induction of cerebral ischemia, EEG frequency increased linearly with elevations of external carotid blood flow. The coupling of flow and electrical activity was lost following the cerebral ischemia episode. This spectrum of hemodynamic and metabolic alterations associated with cerebral ischemia indicates a profound disturbance of cerebrovascular function, which renders the normal relationship between brain blood flow, metabolism and electrical activity inoperative. (Supported by USPHS Grant 5 T01 HE05362.)

A NONDESTRUCTIVE TECHNIQUE TO MEASURE WALL DISPLACEMENT IN THE THORACIC AORTA. R. M. Olson*, D. K. Shelton, Jr.*, and H. L. Stone. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas, 78235.

This paper presents a simple, microscopically precise, nonsurgical technique to continuously monitor pulsatile changes in thoracic aortic radius. The radius contours which result can be used in much the same way as pressure contours, because both contours are practically congruent. Pressure contours have been used to estimate cardiac output, to detect some valvular heart diseases, and to detect such abnormalities of the aortic arch as coarctation. The technique utilizes an ultrasonic crystal mounted on an esophageal probe by means of a platform which can be tilted. Ultrasound is passed across the esophageal wall and reflects from the walls of the aortic arch. The reflected signals are processed, like radar, to track the position of the reflecting surface—i.e., the aortic walls. The results of using this technique show that the intact aorta expands 8-11% of its diastolic diameter with each beat. This is considerably bigger than the 2-4% expansion reported by many other investigators using invasive techniques. Group propagation velocities calculated using the Moens-Korteweg equation and the measured data agree well with the expected value of about 4-5 meters/sec.

STATIC AND DYNAMIC RESPONSE CHARACTERISTICS OF CO_2-SENSITIVE CHEMORECEPTORS IN THE AVIAN LUNG. J. L. Osborne and R. E. Burger (intr. by R. S. Fitzgerald). Dept. Environ. Med., The Johns Hopkins Univ. and Dept. Avian Sci., Univ. of Calif., Davis.

Single unit activity was recorded extracellularly with tungsten microelectrodes from the nodose ganglion. Ventilation was regulated artifically by passing gas mixtures unidirectionally through the respiratory system. Results indicate an inverse relation between F_{ICO_2} and discharge frequency. Individual units showed a diversity in their sensitivity to static levels of ventilatory CO_2. However, the stimulus-response curve for a population of 35 units was linear between 0.01 and 0.04 F_{ICO_2}. Based on their static discharge patterns, pulmonary chemoreceptors were divided into two types. Type I pulmonary chemoreceptors were characterized by a regular discharge pattern and Type II pulmonary chemoreceptors were characterized by an irregular discharge pattern. Step and sinusoidal forcing functions were utilized to characterize the dynamic response of pulmonary chemoreceptors to CO_2. The results indicate that these receptors were both proportional and bidirectionally rate sensitive, and characterized by a faster response time to a step decrease in F_{ICO_2} than to a step increase in F_{ICO_2}. The mean response time for a step decrease and for a step increase in F_{ICO_2} were 0.4 and 2.1 sec respectively. Some units were capable of responding rhythmically to sinusoidal variation in F_{ICO_2} at 188 cpm. We conclude that chemoreceptors are in close association with the intrapulmonary bronchi of the avian lung and transmit information to the CNS concerning the mean level, the rate of change and the direction of change in F_{CO_2} during eupneic breathing; that an inverse linear relationship exists between pulmonary chemoreceptor activity and vertical sternal deflection (an index of ventilation). Supported in part by USPHS Grant ND 05125.

INCREASED SENSITIVITY OF CNS CYCLIC AMP TO NOREPINEPHRINE (NE) in vitro FOLLOWING 6-HYDROXYDOPAMINE DEPLETION OF NE STORES in vivo. Gene C. Palmer* (intr. by Helmuth Vorherr) Univ. New Mexico, School of Med., Albuquerque, N.M.

Depletion of CNS NE stores with reserpine and ablation of the superior cervical ganglion in rats followed by a subsequent in vitro incubation of respective brain tissue with NE may result in enhanced activity of adenyl cyclase - cyclic AMP. The increased adenyl cyclase activity ("supersensitivity") to NE seems to be an integral component of the effects of previous adrenergic depletion. Because 6-hydroxydopamine (6-HDA) can also cause depletion of NE stores in rat brain as well as degeneration of adrenergic nerve endings, it was of interest to determine whether this compound also can produce an enhanced cyclic AMP response to NE in vitro. For that purpose, adult male rats were injected intraventricularily with 6-HDA (250 µg/day for 2 days). Before, during and after the 6-HDA treatment urinary levels of cyclic AMP were estimated. Seven days later, the animals were sacrificed and 0.75 mm thick tissue slices from the hypothalamus, brain stem, cortex and cerebellum were incubated with NE (10^{-5}M). No daily changes in urinary cyclic AMP were noted during intracisternal 6-HDA treatment. After 6 minutes incubation with NE the cyclic AMP content in tissue slices of brain cortex, hypothalamus and brain stem from 6-HDA treated rats was significantly increased when compared to respective controls. These studies with 6-HDA in addition to other investigations utilizing different means of CNS-NE depletion support the hypothesis that adenyl cyclase is an integral component of the molecular mechanisms responsible for adrenergic denervation supersensitivity to catecholamines. (Supported by USPHS Grant No. MH 19893 and New Mex. GRS Fund 5-S01-RR05583.)

MYOCARDIAL FREE ENERGY PURINES DURING CARDIAC ARREST AND RECOVERY. J.C. Parker* and E.E. Smith. Dept. of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, Mississippi 39216

Adenine nucleotides involved in free energy metabolism (ATP, ADP, AMP) and their metabolic degradation products (IMP, adenosine, inosine, hypoxanthine) were determined in myocardial tissue samples from mongrel dogs under different conditions of cardiac arrest and recovery. Compounds were separated and quantitated by thin layer chromatography. Ventricular fibrillation by electric shock produced a decline in myocardial ATP from 4.35 ± .14 (S.E.M.) μM/gm to .85 ± .3 μM/gm in 25 minutes while anoxic beating hearts had a decline to 1.34 ± .24 μM/gm in 30 minutes. Total adenine nucleotides fell from 5.98 ± .44 μM/gm to 2.24 ± .36 μM/gm in 35 minutes while the total of other compounds rose from 0 to 2.37 ± .27 μM/gm. The total of all compounds during unperfused arrest did not change significantly. The effect of the resumption of coronary perfusion after arrest was evident in the recovery groups. The group receiving a statistically non-lethal period of cardiac arrest (4 min) had average values over a 40 minute period of recovery, of 6.02 μM/gm for all compounds, 5.16 μM/gm total adenine nucleotides, and .86 M/gm total other compounds. A statistically lethal arrest period (15 min) had average values during recovery of 1.25 μM/gm ATP, 2.26 μM/gm adenine nucleotides, .57 μM/gm total other compounds, and 2.81 μM/gm total all compounds. The build up of inosine and other diffusible intermediates in arrest, with their subsequent wash-out during re-perfusion, caused a decline in total purine substrate and was an important factor in the difficulty of reestablishing the myocardial high energy compounds necessary for survival of the heart after anoxic injury. Supported by NIH Grant No. HE 11780.

VASCULAR RESPONSES IN THE CANINE FORELIMB DURING INTRAARTERIAL INFUSION OF PROSTAGLANDIN A_1. J.L. Parker*, T.E. Emerson, Jr., and R.M. Daugherty, Jr., Departments of Physiology and Medicine, Michigan State University, East Lansing, Michigan 48823.

Steady-state muscle (brachial) and skin (cephalic) venous outflows were measured in the naturally perfused, isolated, innervated dog forelimb during intrabrachial artery infusion (N=16) of Prostaglandin A_1 (PGA_1; 0.2-10.0 ug/min). Large and small artery and vein pressures were measured and total and segmental vascular resistances calculated in both skin and muscle. Limb weight was monitored continually. PGA_1 decreased skin and muscle small artery pressures, small vessel resistances (arteriolar) and total limb resistance (R_T) at each level of infusion. There was a progressive fall in all R_T until blood pressure fell (1 ug/min) at which point R_T increased but still remained below control. The major fall in R_T occurred in the small vessel segments. Blood outflow and limb weight increased at all infusion rates. In another group of animals, forelimb blood flow was held constant and PGA_1 infused proximal to the blood pump (N=9; 0.2-10 ug/min). Brachial (perfusion) and small artery pressures and R_T decreased due to active vasodilation in small vessel segments of both skin and muscle. No redistribution of blood flow between skin and muscle beds occurred. Weight changes in all preparations suggest little change in transcapillary fluid movement. Low dose infusion of PGA_1 (0.02-0.2 ug/min) in 5 additional constant flow limbs produced changes qualitatively similar to those seen in the previous constant flow group over the lower infusion rates. In addition, PGA_1 did not produce changes in responses to norepinephrine or histamine different from those observed during infusion of acetylcholine. These data demonstrate that PGA_1 causes active vasodilation in the skin and muscle beds of the dog forelimb and that the major site of action is in the small vessel segment. (Supported by NIH Grant HE 10899.)

CARDIOVASCULAR EFFECTS EVOKED BY SELECTIVE STIMULATION OF THE CAROTID BODIES WITH O_2 AND CO_2. P. Parker*, J. Dabney, J. Scott, and F. Haddy. Dept. of Physiol., Mich. State Univ., East Lansing, Mich. 48823.

We studied in anesthetized dogs the effects of changes in O_2 and/or CO_2 in blood perfusing bilaterally isolated carotid sinuses on heart rate (HR) and systemic arterial pressure (P_S). We also measured brachial perfusion pressure at constant flow (P_{BA}), and outflows from cephalic (F_{CV}) and brachial (F_{BV}) veins of collateral-free innervated forelimbs. Arterial blood was pumped through an isolated lung ventilated with various gases and then pumped at constant flow through the sinuses at pressure (P_{CS}) set nearly equal to P_S by varying outflow resistance. Sinus outflow was returned to the jugular vein. PO_2 and PCO_2 of systemic blood were held normal by positive pressure ventilation. Carotid body stimulation was verified by monitoring the animal's respiratory pattern. All gas changes were made before and after vagotomy and the table shows post-vagotomy data.

Ventilatory Mixture (Isolated Lung)	PCS	PS	PBA	FBV	FCV	HR	PO2	pH
5% CO_2-20% O_2(Control)	118	119	119	45.8	55.8	156	115	7.28
20% CO_2-0% O_2	117	156*	140*	46.1	58.6	156	19	6.92
5% CO_2-20% O_2(Control)	115	111	124	43.5	57.1	159	110	7.25
5% CO_2-0% O_2	114	127*	135*	44.0	57.8	157	14	7.27
5% CO_2-20% O_2(Control)	114	100	127	42.6	57.9	157	110	7.27
20% CO_2-20% O_2	112	115*	141*	43.3	57.4	164*	129	6.91

*$P<0.05$ when compared to preceding control; n=13

Before vagotomy the only change seen was a rise in systemic pressure and only when the carotid bodies were exposed to both low O_2 and high CO_2. These studies suggest that low O_2 and high CO_2 act on carotid chemoreceptors to elicit changes in autonomic outflow to heart and blood vessels similar to those induced by lowering pressure in the carotid sinus.

THE EFFECT OF ACUTE COLD EXPOSURE ON GLUCOSE METABOLISM IN NORMAL AND THYROIDECTOMIZED DOGS. P. Paul, W. L. Holmes,* and G. A. Reichard,* Division of Research, Lankenau Hospital, Philadelphia, Pa.

Glucose-^{14}C(UL) was infused i.v. at a constant rate into unanesthetized normal and surgically thyroidectomised (THY) dogs in the basal state at 22°C and during acute cold exposure at 4-5°C. O_2 uptake, CO_2 output, and specific activities of CO_2 and plasma glucose were determined, from which the rates of glucose turnover and glucose oxidation were calculated. Normal dogs in the basal state had an average glucose level of 109 mg% and a turnover rate of 17 μmole/mg min, of which 33% was immediately oxidized accounting for 12.5% of the caloric expenditure of 0.74 kcal/m^2 min. When subjected to acute cold exposure glucose level and turnover rate of normal dogs remained the same, but the percent of glucose turnover oxidized was increased to 46.9%, accounting for 12.9% of the increased caloric expenditure of 1.0 kcal/m^2 min.

THY dogs had a significantly lower caloric expenditure, 0.50 kcal/m^2 min, but a similar glucose level of 107 mg% and a turnover rate of 15.6 μmole/kg min, of which 28.3% was oxidized accounting for 14.7% of the total caloric requirement. A significantly higher glucose turnover was found in THY dogs when it was expressed as mmole/cal BMR. No differences were observed during acute cold exposure between normal and THY dogs with respect to their caloric expenditure, the amount of glucose oxidized, or the percent of calories derived from plasma glucose oxidation. (Supported by NIH grants HE-07687&FR-5585).

RESPONSES OF RESISTANCE AND CAPACITANCE VESSELS TO CAROTID CHEMORECEPTOR STIMULATION BY HYPOXIA AND HYPERCAPNIA. L. C. Pelletier* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The effect of stimulation of carotid chemoreceptors by hypoxic or hypercapnic blood on systemic resistance and capacitance vessels was examined in 12 dogs anesthetized with chloralose and artificially ventilated. Bilateral cervical vagotomy was performed. Both carotid bifurcations were isolated from the systemic circulation and perfused at constant pressure with blood from a donor dog. The P_{O_2} and P_{CO_2} of the perfusing blood were altered by ventilating the donor dog with different gas mixtures; the systemic arterial blood gases of the experimental dog were kept normal. The hind limb and saphenous vein (perfused at constant flow) and the isovolumetric spleen were studied. Hypoxia of the carotid chemoreceptors resulted in increases in aortic blood pressure, perfusion pressure of the hind limb, and venous pressure of the isolated spleen (mean increases [$\pm$ SE]: 56.6 $\pm$ 10.8, 57.7 $\pm$ 5.7, and 13.1 $\pm$ 4.0 mm Hg, respectively) and in a decrease in perfusion pressure in the saphenous vein (30.9 $\pm$ 6.3 mm Hg). Combined hypoxia and hypercapnia caused similar changes, whereas with hypercapnia alone the changes were about 50% of those seen with hypoxia. These responses were abolished by sinus nerve anesthesia. The dilatation of the saphenous vein could not be blocked by atropine, antihistamine, or propranolol but was prevented by phenoxybenzamine; the latter also decreased the responses in the other beds. Thus, the effect of carotid chemoreceptor stimulation is an increase in sympathetic activity to the resistance vessels of the hind limb and to the splanchnic venous bed and a decrease in sympathetic activity to the cutaneous veins. (Supported in part by NIH Grant HE-5883 and the Medical Research Council of Canada).

DECREASED GLUCOSE TOLERANCE IN THE RAT PRODUCED BY AMINOPHYLLINE. J.C. Penhos, N. Yamaguchi*, R. De Santis* and L. Recant* VA Hosp., Endoc. Res. Unit; Dept. Physiol, Geotwn. Univ.; Dept. Med., Geo. Wash. Univ., Washington, D.C.

Recent evidence indicates that prediabetes is characterized by a lag in insulin response to glucose which can be "normalized" by aminophylline. A similar lag in insulin response was also observed in hypophysectomized rats (with intact pancreas). It seemed of interest to examine the effects of aminophylline in this experimental animal model (studied 3 weeks post-operatively). In hpx rats we demonstrated that a "diabetic" state exists characterized by the following: (1) Markedly impaired oral and i.v. glucose tolerance test, (2) Diminished insulin response to glucose and (3) A significant lag in the insulin response to glucose. Treatment of these animals with a single dose of aminophylline (I.P., 5 mg/100 g b.w.) prior to glucose load resulted in (1) Intensification of the glucose intolerance, (2) Striking elevation of the plasma insulin levels, (3) No shortening or alteration in the lag in insulin release and (4) No increase in FFA. Control rats treated with aminophylline showed significant hyperglycemia and hyperinsulinemia though less marked than the hypophysectomized rats and an elevation of the FFA levels. Thus, aminophylline administration produced a syndrome of insulin resistance in both groups of rats. Furthermore, aminophylline was not able to correct in hpx rats the lag in insulin response to glucose administration.

BRAINSTEM MODULATION OF THE CARDIOVASCULAR SYSTEM. J.L. Peters, Dept. of Surgery, Univ. of Utah, Salt Lake City, Ut., J.A. Posey+, C.S. Leach, Endocrine Laboratory, NASA, Houston, Texas, H.E. Hoff*+, J. Smith+ and L.A. Geddes*+ (intr. by H.E. Hoff).

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Cardiovascular function was studied in midcollicular decerebrate dogs with intact vagus nerves and patent carotid arteries for up to 15 hours. Parasympathetic, sympathetic and somatic neural facilitation were demonstrated. Heart rate decreased on the average 43%, 39%, 37% and 35% at ½, 1, 2 and 3 hours, respectively, after decerebration. Heart rate was further decreased by blood pressure, respiration (Biot's breathing and apnea) and periods of extreme extensor rigidity. Systolic blood pressure was increased an average 39%, 42%, 48% and 47% at ½, 1, 2 and 3 hours, respectively, after decerebration. Average arterial pulse pressure was 2.8 times the control value at 1-3 hours post decerebration. Stroke volume and cardiac index varied only slightly from control values. Plasma catecholamines, epinephrine and norepinephrine were measurable after decerebration and at times were 2-3 times greater than control values. These data suggest that the main role of the brainstem is to modulate cardiovascular function by decreasing the heart rate, increasing systolic blood pressure and pulse pressure and increasing the concentration of plasma catecholamines. These cardiovascular parameters are further modified by the spontaneous respiration and extreme muscular activity of the decerebrate preparation.

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CARDIAC OUTPUT (ELECTROMAGNETIC FLOWMETER) IN RATS: COMPARISON OF URETHANE, PENTOBARBITAL, AND ETHER ANESTHESIA. Marc A. Pfeffer,* Janice M. Pfeffer,* and Edward D. Frohlich. University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

Although the rat is being used with greater frequency in cardiovascular studies continuous measurement of quantitative blood flow has not been reported. Heart rate and arterial pressure are recorded often but flow changes are not examined. In this study, either a 1.5 or 2.0 mm electromagnetic flow probe was placed around the ascending aorta of 18 male Wistar rats (age: 16-20 wks; weight: 282-500 Gm) under either urethane (U) (1.4 Gm/Kg, s.c.), pentobarbital (P) (40 Mg/Kg, i.p.), or ether (E) anesthesia. Carotid arterial pressure and aortic flow were measured continuously for one hour. Control values for pressure (mm Hg), heart rate (beats/min), cardiac index (ml/min/Kg), and peak flow velocity (ml/sec) were: U - 104/44, 306, 139, and 39; P - 108/63, 366, 144, and 40; and E - 125/65, 356, 231 and 51, respectively. These values remained constant with U so that at the end of one hour they were 109/46, 326, 127, and 40, respectively. Under P, the preparation gradually deteriorated; by one hour pressure, cardiac index and peak flow velocity fell to 102/55 mm Hg, 120 ml/min/Kg and 35 ml/sec, respectively. Although the E anesthetized rats also showed a gradual decline in pressure and flow, the indices of cardiac function were always higher than either U or P. After a one hour period under E, the values were: pressure 110/48 mm Hg; heart rate 351 beats/min; cardiac index 186 ml/min/Kg; and peak flow velocity of 47 ml/sec. Thus, these data demonstrate that, in the doses used, U provides the best cardiovascular stability (although lowest arterial pressure), and E provides the most optimal cardiac function.

CENTRAL VENOUS PRESSURE CHANGES DURING APNEA AND APNEIC WATER IMMERSION. Andrew A. Pilmanis* and John P. Meehan, University of Southern Calif. Department of Physiology, School of Medicine, Los Angeles, California

Central Venous Pressure was used to study dynamic changes in thoracic blood volume resulting from breath-holding in air and during whole body water immersion. Seven young, healthy male subjects had EKG electrodes attached and a venous catheter was advanced to approximately the right atrium. For control apnea data in air, the supine position was used to approximate the cardiovascular state of weightlessness during immersion. Lung volumes were controlled by a spirometer and several levels of water temperatures were used. A total of 246 breath-holds were performed. Control apnea in air showed only slight changes in both heart rate and CVP. With total body immersion apnea, as well as neck deep immersion apnea, there was a relatively large and steady rise in CVP. Simultaneously, a pronounced bradycardia developed. Both parameters reached maximum levels at the end of apnea. Composite data showed a rise in CVP to 60% over control levels by the end of apnea, and concurrently a 25% reduction in heart rate. Apnea with face immersion and with arm immersion only, showed similar bradycardias which were greater than that in air and less than that with total body immersion. The steady rise in CVP during underwater breath-holding is a measure of increasing intra-thoracic engorgement, which is due to (1) a gradual decrease in cardiac output and (2) active redistribution of peripheral venous blood centrally. Both parameters recovered only gradually after termination of breath-holding, reflecting a gradual redistribution of the enlarged central blood volume back to the peripheral reservoir.

RADIO-PROTECTION OF AROUSING GROUND SQUIRRELS. Russell Prewitt* and X.J. Musacchia. Dept. of Physiology and Space Sciences Research Center, Univ. of Mo., Columbia, Mo.

Radio-protection by catecholamines has been reported. The protection is thought to be due to a local tissue hypoxia in the bone marrow as a result of vasoconstriction and/or decreased blood pressure(i.e. after isoproterenol). Radio-protection has been previously demonstrated only after administration of extremely high doses of catecholamines and the possibility that this occurs naturally from endogenous catecholamines has never been reported. It was thought that protection of ground squirrels(Citellus tridecemlineatus) arousing from hibernation could be due to the release of catecholamines that occurs at this time. To test this hypothesis a group of animals hibernating at 6 C, rectal temperature, was given 10 mg/kg of phentolamine mesylate i.p., a second group was given equivalent amounts of physiological saline. Both groups were allowed to arouse at room temperature to 12 C and were then exposed to 1450 rads (^{60}Co). A control group was given phentolamine but not exposed to irradiation. The three groups were allowed to complete arousal in a normal manner, individually caged, and given food and water ad libitum. They were observed daily for 90 days. Survival was 80% for controls, 60% for the irradiated-saline group, and 20% for the phentolamine-irradiated group. Thus, the radio-protection of arousing ground squirrels can be blocked with an alpha blocker and appears to be due to the release of endogenous norepinephrine. (Supported by Grants USPH, 5-F01-GM-41418-03 and NASA NGR 26-004-021S5)

FSH PATTERNS IN NORMAL ADULT MALE RATS. C.M.Proudfit*, D.C.Johnson, Dept. of Physiology, U.Kansas Med. Center, Kansas City, Kansas.

Male rats (60-65 days old; lights on 6AM-8PM) were used in these studies. Animals in the first series (3 per group) were sacrificed on the even-numbered hours over a 26 hour period from 10AM on D1 through noon on D2. Serum was pooled within groups and assayed for FSH (NIAMD RIA used to assay all serum samples). Serum FSH concentrations rose at 2AM and remained above the 24 hour mean at 10AM on D2. In a second series of animals (4-5 per group) killed hourly on another day from 7PM through 2AM, serum samples from each rat were collected and assayed separately. Serum FSH in these animals rose at 9PM and remained high throughout the duration of the experiment. A third series of animals was sacrificed (4 per group) on the odd-numbered hours over a 26 hour period from 9AM on D1 through 11AM on D2. Serum samples were again collected and assayed separately for each animal. Serum FSH concentration rose at 5PM and remained high through the 11PM sampling. In contrast to the findings of Yamamoto et al. (Endocrinology 87: 798,1970), these data show that our normal adult male rats do experience significant changes in serum FSH levels throughout the day. Results from the assay of serum of individual rats in the second and third series show that these levels are synchronized among animals in a given group. The fact that periods of elevated serum concentration did not occur at the same time of day in the 3 series tested (each series done on different days) suggests that the Zeitgeber effecting these changes is other than (or in addition to?) a signal related to the daily light-dark-activity regimen. Supported by NIH grant #HD03097.

A PERIPHERAL REFLEX ARC AND AFFERENT PERIKARYA IN AN AUTONOMIC GANGLION. P. T. Purinton, T. F. Fletcher, and W. E. Bradley (intro. by G. F. Ayala). Departments of Veterinary Anatomy, Neurology and Neurosurgery, University of Minnesota, Minneapolis, Minnesota.

The presence of reflex activity mediated through autonomic ganglia has long been debated. We investigated the pelvic ganglion of the rat for electrophysiologic evidence of peripheral reflex activity and the location of afferent perikarya of the reflex. Electrical stimulation of a postganglionic branch from the pelvic ganglion produced a synaptically transmitted response in a second postganglionic branch. The response persisted following chronic isolation of the pelvic ganglion from the spinal cord as well as chronic transection of the stimulated postganglionic branch. The response could not be influenced by preganglionic conditioning except that intense preganglionic stimulation produced some depression of the response. The results of this investigation indicate that a postganglionic to postganglionic response was mediated through a peripheral reflex arc having afferent perikarya in the pelvic ganglion.

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INFLUENCE OF GONADAL HORMONES ON SOCIAL, SEXUAL, MATERNAL, EMERGENCE AND OPEN FIELD BEHAVIOUR IN THE RAT. [1]D. M. Quadagno*, [2]C. Anderson*, J. Shryne* and R. A. Gorski. BRI and Dept. of Anatomy, UCLA Med. School, Los Angeles, Calif.

The influence of the postnatal and adult hormonal environment on lordosis, open field, emergence and maternal behaviour and on social behaviour as measured by analysis of the response of a test rat when exposed to a control male or female in a test arena was measured. Oil-injected and androgenized females, neonatally castrated males, males castrated on day 20, and sham castrates were studied as young adults, and again after gonadectomy of all groups. Neonatal androgen treatment "masculinizes" sexual, maternal and non-sexual behaviour of the female rat. Although only neonatal castration of the male results in the retention of the capacity to show normal female levels of lordosis behaviour, non-sexual behaviour with the exception of maternal behaviour of the male for the most part is not altered specifically by neonatal castration.

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RADIO TELEMETERED RENAL RESPONSE TO EXERCISE IN THE DOG. R. Rader*, R. Krutz*, J. P. Meehan and J. P. Henry. Univ. of So. Calif., Dept. Physiol., School of Med., Los Angeles, California

Application of implant telemetry creates the capability of investigating renal hemodynamics under broad environmental conditions (Rader, R., Nat.Tel.J.,V6,#3, Apr.May'71). Data analysis develops directly from consideration of blood pressure, blood flow and the hydraulic impedance relating the two. An exercise episode illustrates the utility of the device. An instrumented dog was exercised on a treadmill inclined at 15 degrees sequentially at speeds of 2, 3, 4.5 and 2 mph for respective periods of 3, 3, 5 and 3 min. Three min. control periods preceded and followed exercise. From taped dynamic pressure and flow, mean pressure and flow were electronically calculated and the absolute resistance to flow determined by electronically dividing mean pressure by mean flow. Salient renal pressure and flow data follow:

	Precontrol	2 MPH	4.5 MPH	Postcontrol
Renal Pressure S/D-M(mm Hg)	145/85-110	90/65-85	115/85-110	120/80-100
Renal Flow S/D-M(ml/sec)	7.5/5-6	9/4-6	7/1-4.4	5.5/4-4.4
Renal Flow Resistance(PRU)	18	14	25	23

One apparent conclusion is that at the start of exercise mean renal flow remained constant as a consequence of vasodilatation, but throughout exercise decreased because of vasoconstriction. As exercise commenced, diastolic flow decreased in direct proportion to pressure, but paradoxically systolic flow increased as systolic pressure decreased. This intriguing finding might be explained on the basis of a proportionate flow increase through relatively larger and more compliant renal vessels. This concept is supported by experiments suggesting that cholinergic vasodilatation follows reduced renal pressure. (Stinson, J.M. et al., Am.J.Physiol. 217, p. 239, 1969).

THE EFFECT OF WHOLE BILE ON INTESTINAL MICELLAR LIPID TRANSPORT IN VITRO. Alfred J. Rampone and Lawrence R. Long*. Dept. of Physiology, University of Oregon Medical School, Portland, Oregon.

This study examines natural bile as a possible source of components complementary to bile salts in the intestinal transport of micellar lipid. Everted sacs of rat intestine containing 2 ml of phosphate-buffered saline were incubated 1 hour at 37°C in 25 ml of the same buffer containing glucose plus bile salt (2.4 mM), glyceryl monoleate (0.3 mM) and C^{14}-labelled oleic acid (0.6 mM) in micellar form. C^{14} incorporation into the lipid fractions isolated by thin layer chromotography was measured in mucosal tissue and serosal fluid. Control rats were compared with bile fistula rats (external bile drainage for 48 hours). The effects of adding fresh rat bile to the incubation fluid in addition to the other components was also studied. In the absence of fresh bile the bile fistula group showed a significantly increased C^{14} uptake in the tissue as free fatty acid compared to controls (481 n moles per g. vs. 255 n moles per g.). Adding 1-3 ml of fresh bile to the incubation fluid significantly decreased this value in both groups and increased the incorporation of C^{14} into the triglyceride fraction recovered from the tissue and the serosal fluid. Results suggest that fresh bile may facilitate intestinal triglyceride synthesis from fatty acid or triglyceride transport through the wall by mechanisms other than bile salt-induced micelle formation.

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HEART RATE, PRESSURE, AND MYOCARDIAL CONTRACTILITY RESPONSES TO EXERCISE AND EMOTIONAL CONDITIONING IN THE NONHUMAN PRIMATE. David C. Randall* and Orville A. Smith. Dept. of Physiology and Biophysics and Regional Primate Research Center, Univ. of Washington, Seattle.

Rhesus monkeys, seated in primate restraining chairs, were habituated to a darkened, sound shielded chamber until they sat quietly; they were then trained to exercise on signal by turning a wheel, and later, to lever press for food reward. They were also conditioned to a one-minute tone followed immediately by a two-second shock. Following training, cannulae were surgically implanted in the left and right ventricles, as well as in the axillary artery. The ventricular cannulae were shown to yield tracings of reasonably high fidelity, thus warranting measurement of end diastolic pressure relative to thoracic pressure (EDP), time rate of change of pressure (dp/dt), and an index of myocardial contractility based on an adjusted ratio of dp/dt and the corresponding isovolumic pressure. In addition, isometric strain gauge arches were sutured onto both the right and left ventricular myocardium to assess localized changes in myocardial contractility. Heart rate (HR) was continuously measured. After the animal had recovered from surgery, marked changes (generally increases) in HR, ventricular pressures, and dp/dt occurred in response to exercise and in anticipation of shock. Significant increases in contractility occurred, as shown by both the index and the isometric arches, which,since they could not be attributed primarily to changes in HR, afterload, or preload, were probably produced by activation of cardiac sympathetic nervous pathways. These responses are thought to reflect ventricular innervation patterns which had previously been described for the primate. (supported by NIH Grants HE04741, PR00166 and HE05889-01.)

Effects of Acute Renal Ischemia on the Metabolism and Function of Cortical Slices. Howard M. Randall, Jr. Department of Physiology, Louisiana State University Medical Center, New Orleans, Louisiana, 70112.

It has been shown that the rate of aerobic metabolism of cortical homogenates of dog kidney is not reduced by 1 hr of ischemia induced by total occlusion of either the renal artery (RA) or renal vein (RV). The present experiments of a similar nature done on slices of cortex were designed to determine: (1) whether the rate of aerobic metabolism of slices is as resistant to ischemia as mitochondria and (2) whether the rates of several specific energy-dependent renal functions are altered to the same degree by the stress. Ischemia was induced in the left kidney by occluding either the RA, RV or renal pedicle (RP). The right kidney served as a paired control. The parameters of aerobic metabolism studied were the rates of O_2 consumption (Q_{O_2}) and α-KG utilization. Energy-dependent functions studied were rates of PAH and K^+ uptake and gluconeogenesis. All experiments were done in Warburg flasks incubated at 30° in O_2. Occlusion of the RA was without effect except for a decrease in K^+ uptake. In contrast, occlusion of the RV resulted in a significant decrease in Q_{O_2}, and in the rates of K^+ and PAH uptake; the rates of gluconeogenesis and α-KG utilization were unchanged. Occlusion of the entire pedicle resulted in a significant decrease in all parameters studied. The rates of each specific function appeared to be changed by approximately the same degree. These data indicate that metabolic changes occur in slices before they occur in homogenates and suggest that the cell membrane may be one of the first structures to be altered by RV or RP occlusion. The reduction in each function appears to be related to the reduction in metabolism. (Supported in part by the Louisiana Heart Association and USPHS National Institutes of Health Grant 11987-02).

REGENERATION OF MOTOR FIBERS INTO SENSORY PATHWAYS SHOWN BY ACETYLCHOLINESTERASE. N. Ranish,* S. Ochs and C. Barnes, Dept. of Physiology, Indiana Univ. Med. Cent., Indianapolis, Indiana, 46202.

The regeneration of ventral root fibers into the dorsal roots of the opposite side was previously shown by axoplasmic flow (Ochs and Barnes, Brain Res. 15: 600, 1969) where fibers were found to regenerate successfully across a graft within two to three weeks. Functional innervation occurred within 8 weeks (Barnes and Worrall, J. Neurophysiol. 31; 689, 1968). Another method of showing regeneration was to determine acetylcholinesterase (AChE) and pseudocholinesterase (PsChE) in axons growing into the dorsal roots of the opposite side. A modification of the Ellman method was used for enzyme determination. The changes in enzyme activities were calculated in terms of root weight, length and protein in the sample homogenates. The expected low levels of AChE and PsChE were found in control dorsal roots. When regenerating ventral root fibers entered the dorsal roots a significant increase of AChE activity of about 2x control level was seen in 2 weeks. The AChE activity increased continually thereafter for about 100 days before reaching a plateau of approximately 20x control levels. The increase of AChE showed regeneration of ventral root fibers across the graft. The gradual increase and plateau of enzyme activity is in accord with a maturation of the fibers which had regenerated into the grafted dorsal roots. PsChE in the dorsal roots changed in parallel with the changes in AChE, in a ratio of 1:10. This suggests that PsChE may in part be localized in the regenerating axons.

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EFFECT OF SYMPATHETIC NERVE STIMULATION ON CEREBRAL AND CEPHALIC FLOW. C. E. Rapela. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

Previous work (Rapela et al., Circ. Res. 21: 559, 1967) indicated that the carotid sinus reflex has no influence on the cerebral vascular tone and on the autoregulatory responses of cerebral blood flow to changes in perfusion pressure. Also, most workers have observed that the cervical sympathetic has no or slight effect on the cerebral vasculature. Recently D'Alecy and Feigl (Fed. Proc. 29: 520, 1970) have postulated that stimulation of the stellate ganglion, or nerves arising from it to the superior cervical sympathetic ganglion of the dog, produces marked constriction of the cerebral vasculature. We have studied the effect of stimulating the stellate ganglion and its nerve branches on the canine cerebral and cephalic blood flow. The cerebral venous blood flow was measured at the confluence of sagittal, straight and lateral sinuses with the lateral sinuses occluded (Rapela et al., Fed. Proc 20: 100, 1961). The blood flow in the common carotid ipsilateral to the nerve stimulated was measured with a non-cannulating electromagnetic flowmeter. All branches from the stellate ganglia were isolated via a cervical approach and prepared for stimulation with a bipolar electrode. Monophasic pulses of 10 msec duration and 3 volts were applied at a frequency of 14/sec during 1 min. Stimulation of the nerve branches of the stellate ganglion to the superior cervical sympathetic ganglion induced a marked decrease of common carotid blood flow and dilation of the ipsilateral pupil but no change in the cerebral vascular conductance.

Conclusion: Electrical stimulation of the stellate ganglia or its nerve branches via a cervical approach, has no effect on the cerebral vasculature. Effects of sympathetic stimulation on measured cerebral blood flow were observed only if significant communications between intra- and extracranial venous vasculature were present. Supported by NIH grants HE 487, HT 344, HT 5392 and North Carolina Heart Association.

RESPONSES OF PIAL VESSELS TO CHANGES IN CSF pH AND PCO_2. A.J. Raper*, H.A. Kontos, and J.L. Patterson, Jr. Dept. of Medicine, Medical Col. of Virginia, Virginia Commonwealth University, Richmond.

The action of CO_2 on pial arterioles could operate via changes in carbon dioxide tension or via induced pH changes, or via both mechanisms. Paralyzed anesthetized cats (18) were fitted with a modified Forbes window. Pial arterioles (16-77 μ) were visualized by a compound reflected light microscope (138 X), and diameter was measured by the image-splitting television system described by Baez. Ventilation was controlled, and arterial blood PCO_2 and PO_2 were maintained constant. Arterial blood pressure was also monitored. Artificial CSF was prepared to allow independent variation of pH (6.8-8.1) and PCO_2 (13-150 mm Hg) in both directions by altering bicarbonate content appropriately and by equilibrating with different CO_2 concentrations. Fluid was flowed at a constant rate and low (< 2 mm Hg) pressure beneath the window. It was found that the arterioles reacted to changes in pH, but not to independent changes in PCO_2. These results show that CO_2 acts on pial arterioles via pH changes induced in interstitial or cerebrospinal fluid.

CAPACITY OF THE CORONARY COLLATERAL CIRCULATION. W. R. Rassman and C. W. Lillehei (Intr. by K. G. Swan). New York Hospital, New York.

Coronary collateral circulation was measured in anesthetized dogs. Following a left thoracotomy the left circumflex (LC), left anterior descending (LAD), and right (R) coronary arteries were cannulated at their origins. The coronary sinus (CS) was also cannulated. The septal branch of the left coronary artery was left intact. During the control period CS flow measured 49 $\pm$ 8 (S.E.) ml/min and this rate did not differ significantly ($p > .10$) from the rate of coronary inflow which was controlled with a perfusion pump. Increasing myocardial work, either mechanically (aorta cross clamped) or pharmacologically (norepinephrine or phenylephrine), resulted in a CS flow value which exceeded the value for coronary inflow. Stimulation with norepinephrine (1.0 µg/kg, I.V.) permitted a reduction in coronary inflow to near zero while CS flow increased to 196 $\pm$ 15 ml/min. Oxygen saturation of the CS blood under these circumstances was 20%. When the aorta was clamped or phenylephrine injected the flow differentials were smaller. Alpha adrenergic receptor blockade (phenoxybenzamine, 1.5 mg/kg, I.V.) did not alter these responses in coronary collateral circulation. The results indicate that there exists a significant cavitary - coronary communication in the canine heart. These findings have been corroborated with silicone rubber injection techniques and found to be independent of the septal coronary circulation.

BLOCKADE OF AMNIOTIC FLUID INDUCED PULMONARY HYPERTENSION BY ASPIRIN AND OXYGEN. John T. Reeves, Fuheid S. Daoud* and Tracy Wilkins*. Dept. of Medicine, University of Kentucky Medical Center, Lexington, Kentucky, 40506.

Fourteen Bovine amniotic fluids were collected from fetuses 70 to 90% of term. The fluids in doses of 7 to 40 µL/Kg were given intravenously to calves 2 to 11 weeks old. Five fluids caused an early monophasic rise in pulmonary arterial pressure with a peak in 2 minutes. Nine fluids caused biphasic pulmonary hypertension with an early peak in 2 minutes and a delayed peak in 10 to 30 minutes. Pulmonary vascular resistances increased up to 6 fold and pulmonary hypertension lasted from 1 to more than 4 hours. Pretreatment of recipient calves with diphenhydramine, dibenzyline, or methysergide did not alter either the early or delayed pulmonary hypertension caused by amniotic fluid. The effects of amniotic fluid were largely prevented when the calves breathed oxygen and were completely prevented by pretreatment with I.V. aspirin (.5 mg/Kg). The anti-inflammatory properties of aspirin (Piper and Vane, Nature, 1969) may account for the blockade of the amniotic fluid effects. The active substance in amniotic fluid appears to be a glycoprotein and may play a role in maintaining high pulmonary vascular resistance in the fetus. (Supported by N.I.H. Grants HE 06780 and HE 08932).

POIKILOTHERM ACID-BASE BALANCE: ARE CARBON DIOXIDE STORES INDEPENDENT OF BODY TEMPERATURE? Robert Blake Reeves. State University of New York at Buffalo, Buffalo, New York 14214.

The effect of temperature on blood pH and carbon dioxide tension were compared in vivo and for blood of constant carbon dioxide content in vitro. Animals used were large 300 g bullfrogs (Rana catesbiana) which had been at the experimental temperature for at least a week before measurements or samples were taken. A glass electrode at each individual animal's body temperature was used for pH measurements; carbon dioxide tensions were measured using the Astrup technique. As previously described (Howell et al., AJP 218: 600-606, 1970) blood pH in vivo decreases with increasing body temperature, -0.016 units/°C. Carbon dioxide tension increases with body temperature from near 5 torr at 5°C to about 20 torr at 30°C. Considerable interest attaches to the fact that blood obtained anaerobically and cooled or heated in a closed volume at constant carbon dioxide content, closely parallels these values, both in pH values and carbon dioxide tensions. For example, blood from eight frogs at 12°C with a total blood carbon dioxide content of 24.2 ± 2.5 (s.d.) mmoles/liter showed a decrease in blood pH in vitro of 0.0145 - 0.0155 degrees/°C and an increase in carbon dioxide tension from 0.58 - 0.71 torr/°C (temperature ranged from 5 - 38°C). In neither parameter is the behavior in vitro significantly different from in vivo. These results suggest that ventilation at each body temperature is adjusted to maintain in the steady state a constant blood carbon dioxide content.

MELATONIN INHIBITION OF LUTEINIZING HORMONE RELEASE AND OVULATION IN IMMATURE RATS INDUCED TO OVULATE WITH PREGNANT MARE'S SERUM (PMS) GONADOTROPIN. R.J. Reiter and S. Sorrentino, Jr.*, Univ. Rochester, Rochester, New York 14620.

Initially, 5 I.U. of PMS were injected at 8:00 A.M. into 27-day-old female Sprague Dawley rats. One and one-half mg of melatonin (0.5 mg each at 1:30, 2:30 and 3:30 P.M.) given on the second day after PMS administration inhibited ovulation in 27 of 31 animals. The mean number of ova recovered from the Fallopian tubes of those animals that did ovulate was 6.3. Eleven of 14 rats that received diluent only at the critical time of LH release shed an average of 6.5 ova. When blood samples were collected at 4:30-5:30 P.M. on the second day after PMS injection, no rise in plasma LH (radioimmunoassay) could be detected regardless of whether the rats had received melatonin or ovulated. In the second study the quantity of PMS was increased to 20 I.U. Twelve of 13 diluent-treated rats ovulated and they shed an average of 35 ova. After the injection of melatonin (0.5 mg each at 1:30, 2:30 and 3:30 P.M. on second day after PMS) only 8 of 18 rats ovulated. The number of ova per ovulating rat was 32. Diluent-injected rats had a 6-12 fold rise in plasma LH (blood collected between 4:30 and 5:30 P.M. on second day), thus correlating well with the incidence of ovulation. Conversely, only two melatonin treated rats exhibited a detectable rise in plasma LH at the critical time. The results indicate that melatonin, injected about the time of LH release, either inhibits or delays the release of this hormone from the anterior pituitary and thus ovulation does not occur. (Supported by grant HD-02937. R.J. Reiter is an NIH Career Development Awardee; S. Sorrentino, Jr. is an NIH postdoctoral fellow).

IN VIVO COMPARISON OF ELECTROMAGNETIC (EMF) AND DOPPLER FLOWMETERS (DF). R. S. Reneman*, H. Clarke*, N. Simmons* and M. P. Spencer. Virginia Mason Research Center, Seattle, Washington.

In open chest dogs, instantaneous tracings of the ascending aorta (AA), descending thoracic aorta (DA) and femoral artery (FA) obtained with an EMF and a 10 mHz DF were compared at rest and during i.v. infusion of Isoprenaline (I). The tracings of the AA were also compared during cardiac pacing up to 186 beats/min, and those of the FA during reactive hyperemia (RH). The electromagnetic probes on the AA and DA were alternately proximal and distal to the Doppler probes. A probe was built for simultaneous measurements on the AA. ECG and aortic pressure were also recorded. The instantaneous tracings were compared on the recorder and in x-y plots.

To process an adequate Doppler flow signal at rest, the peak-to-peak voltage had to be adjusted properly before the signal was fed into the zerocrossing meter (Hewlett-Packard 500B). High pass filters were necessary, especially on the AA, where heart and vessel wall motion, as well as turbulences were more pronounced. During acceleration, induced by cardiac pacing, the DF followed the EMF. On the AA and DA, the DF could not follow the EMF during the increase in peak velocity due to I; on the FA, the DF followed only partially. On the FA, the DF followed the changes in peak velocity after occlusions of 3 sec. After occlusions of 15 sec, however, the DF did not reflect the highest velocity components at peak RH, which were reflected by the EMF. Maximal peak velocity in the FA during I and RH was 102 cm/sec. This will produce a Doppler shift of ± 14.5 kHz, which should have been reflected by our Doppler system with a frequency response of at least 17 kHz-3db. The zerocrossing meter probably limits the DF in completely following increases in peak velocity. (Supported by the Dutch Organization ZWO and NIH Grant HE-10258.)

RADIOISOTOPE CLEARANCE BY THE CAT MESENTERY by J.E. Rikel* and W.G. Frasher. Univ. of So. Calif. School of Med., Dept. of Physiol., Los Angeles, Calif. 90033.

Kety's method for clearance of radioisotope from tissue was used to determine the ability of the cat mesenteric microcirculation to remove freely diffusible substances. The procedure sequestrates an identical area of both surfaces of the mesenteric membrane with control of the tissue's extracellular environment and without alteration of circulation. By placing $Na^{131}I$ on the upper surface of the tissue the disappearance of isotope from the upper surface and the flux across the membrane to the lower surface was monitored by scintillation. From the difference of these two curves a circulation uptake curve was drawn. The results demonstrate that the mesenteric microcirculation is an extremely active exchange bed. By comparison an average clearance constant of .05 has been reported for the resting human gastrocnemius muscle, while the present study found an average of 0.122 for the mesentery. It is of specific interest that the results for the isotope crossing a layer of epithelium and then entering the circulation from mesenteric interstitium are compatible with results obtained by injecting directly into the interstitial space. With these transport results and available quantitative dimensions a structural-functional correlation can be made. Supported by N.I.H. Grant #HE-11153 and L.A. County Heart Assoc. Grant #218.

PROTEIN LEVELS AND FOOD PREFERENCES OF RHESUS MONKEYS. Arthur J. Riopelle and Charles W. Hill*. Tulane University Delta Regional Primate Research Center, Covington, La.

Ten female monkeys were started on a semisynthetic diet providing 4 grams of protein (casein) and 120 calories per kilogram of body weight daily. Five others received 2 gms per day and five others only 1 gram per day. One month later they were offered three samples of each of seven food types: vegetable, nut, meat, fruit, cereal, milk, candy. The three samples differed in protein concentration. We recorded the time required to pick up seven pieces of food, limiting each version to three minutes if the animals failed to eat. The 3-minute limit was exceeded in 67% of the tests in the 4 gm group, 87% of the tests in the 2 gm group, and only 5% of the tests in the 1-gm group. Median elapsed times followed the same pattern. The data suggest diets that are adequate or slightly deficient in protein produce finicky eaters, however markedly deficient diets produce eaters with catholic interests. Indeed, 4 of 5 animals in the 1-gm group ate bits of raw beef and pork. A nonlinear relationship exists between dietary levels of protein and food acceptability in rhesus monkeys. Supported by grants RR-00164 and HD-05341 from the National Institutes of Health.

REGULATION OF VASCULAR FLOW BY CAPSULAR PERMEABILITY. Simon Rodbard. City of Hope Med. Center, Dept. of Cardiology, Duarte, Calif.

Mechanical properties of the capillaron (one or more permeable collapsible capillaries enclosed with extracapillary fluid and parenchymal cells in a relatively impermeable capsule) exhibit many of the physiological reactions (hyperemias, autoregulations, basal flow, etc.) observed in vascular beds (Circ. Res. Supp. #1, 28, Jan. 1971). The present study examines the effects of capsular permeability in a capillaron model. As capsular permeability is increased, some of the intracapsular fluid drains away [as "lymph" (Curr. mod. Biol. 3:27, 1969)]. This lowers local tissue pressure and increases capillary flow and capillary transmural bulk fluid flow. In a parallel system of several capillarons, increased capsular permeability of one capillaron results in a striking increase in flow through it while the parallel capillarons receive a reduced flow. Capsular permeability increases the duration of hyperemia, prolonging the time constant of the system. The results show that factors that increase capsular permeability will increase local flow, prolong post-occlusion and post exercise hyperemias and the time required for autoregulation; it also delivers more fluid to the extracapsular space from whence it enters the lymphatic system. Capsular permeability has a multiplier effect on flow; a transcapsular flow of 1 ml min^{-1} increases vascular flow by about 100 ml min^{-1}, while also increasing transcapillary bulk flow. The possibility that parenchymal catabolites can increase capillary flow and fluid exchange, and thereby increase vascular conductance and lower arterial pressure is suggested.

THE EFFECTS OF COLCHICINE ON CELLULAR AND INTRACELLULAR MOVEMENT. Fred J. Roisen and Lionel I. Rebhun (intr. by S. Malamed). Rutgers Medical School, New Brunswick, N. J., and University of Virginia, Department of Biology, Va.

In vitro embryonic chick cardiac fibroblasts, L-929 fibroblasts and chick dorsal root ganglia treated with colchicine have been studied by timelapse and high speed cinematography employing differential interference microscopy. The locomotory cells of the leading edge of explant outgrowth display a high degree of axial orientation. Colchicine reversibly destroys this orientation, stops whole cell locomotions, and increases the number of random surface movements. Colchicine also reversibly affects intracellular movement. The velocities, orientations, displacements and durations of saltations (non-random particle movements) are reduced; in contrast, the number of particles undergoing saltatory events is increased. Neurites of embryonic dorsal root ganglial cultures treated with colchicine undergo similar changes, i.e., elongation ceases, the displacement of intra-axonal particles decreases, but the number of saltations increases. High levels of colchicine initiate neurite retraction. Since colchicine specifically disrupts microtubules, (Borisy and Taylor, J. Cell Biol., 1967) our findings indicate that the orientation of moving cells and the orientation of intracellular particle movements depend upon intact microtubules, but that microtubules are not essential for the movements themselves.

PHYSIOLOGICAL ASSESSMENT OF HYPERTENSIVE AND NORMOTENSIVE PONIES. John Rosborough, Harold E. Garner and James F. Amend (intr. by W. J. Schindler.) Baylor College of Medicine, Houston, Texas.

Studies in the laboratory pony indicate that some animals within this species grouping (small, domestic ponies) revealed remarkable physiological similarities to hypertensive human patients. Eleven young (1-4 years) ponies were subjected to electrocardiographic, phonocardiographic, aortic manometric and cardiac output measurements in the standing, unmedicated state. Of these eleven, four exhibited hypertension based upon the criteria advanced by Frohlich, et. al. (Circ. Res. 27: Suppl. I, 55-63, 1970).

These hypertensive ponies exhibited significant ($p<0.05$) increases in arterial systolic, diastolic and mean pressures, cardiac indices, and left ventricular ejection rates when compared to normotensive ponies. Additionally, left ventricular work and power, right ventricular work and power, and total work and power were all significantly ($p<0.05$) increased. These findings suggest that these hypertensive ponies possessed hyperkinetic circulatory systems in the absence of retinopathy, cardiac enlargement, and gross kidney dysfunction, and were classified as labile hypertensives.

It is concluded, on the basis of the physiological and pathological evidence, that the pony represents a useful model for the longitudinal study of progressive essential hypertension. The value of such studies would be that etiological mechanisms and treatment regimes could be critically and experimentally controlled and the results evaluated at necropsy at a time designated by the investigator.

POLYAMINE BIOGENESIS IN THE RAT MAMMARY GLAND. Diane H. Russell and Thomas A. McVicker. (Intr. by E. D. Hendley) Laboratory of Pharmacology, Baltimore Cancer Research Center, C, NCI, National Institutes of Health, Baltimore, Maryland 21211.

Polyamine synthesis and accumulation is an early event in rapid growth systems. Although the precise role or roles of putrescine and the polyamines, spermidine and spermine, are not completely understood, there is increasing evidence that they affect primarily RNA metabolism. The relationships between polyamines and RNA can be studied in rat mammary gland since it is easily cycled through growth and regression; i.e., pregnancy, lactation, and involution. The enzymatic activities of both ornithine decarboxylase (the enzyme that synthesizes putrescine) and S-adenosyl-methionine decarboxylase (the enzyme that synthesizes spermidine from putrescine and S-adenosyl-methionine) are greatly elevated in the mammary gland both during late pregnancy and during the first weeks of lactation. The spermidine pool is also greatly increased. Indeed, the spermidine concentration is higher than 5 mM in the 13-day lactating mammary gland. This is 40-fold greater than the amount of spermidine found in the mammary gland of normals or of rats six days after pregnancy. Maximal RNA content (16-fold greater than the control level) coincides with the high spermidine concentration occurring during lactation. Further, during pregnancy and early lactation there are gradual and parallel increases in both spermidine concentration and in RNA content. Studies are in progress to determine the species of RNA that are being synthesized and to determine whether polyamines affect either the amount or the rate of synthesis of a particular species of RNA.

STUDIES ON Z-DISCS ISOLATED FROM HONEYBEE FLIGHT MUSCLE. Judith D. Saide* and William C. Ullrick. Boston Univ. School of Med., Boston, Mass.

Treatment of preparations of honeybee myofibrils with 0.4% lactic acid solution solubilizes myofilaments but leaves the resistant Z-disc "backbones" intact. These structures have been purified with a series of differential and sucrose density gradient centrifugations. Electron micrograph studies have shown that although the isolated Z-discs as viewed "face on" have an open hexagonal lattice, they lack the appearance of an hexagonal array of triangular tubes with dense rims characteristic of the "in situ" honeybee Z-discs. When viewed on edge the isolated Z-discs show numerous thin projections extending about 1,300 Å from both surfaces. These projections may represent attachment points for thick or thin filaments. In further studies preparations of isolated Z-discs separated from all cellular debris and washed free of proteins soluble in 0.4% lactic acid (pH 2.6) and in distilled water were analyzed for amino acid composition and lipid content. Total lipid, extracted with chloroform-methanol, was found to comprise less than 1% of the isolated Z material. The amino acid composition of the Z-disc backbones (which may of course be comprised of more than one protein) showed no similarity to that of tropomyosin. (Supported by a grant from the Muscular Dystrophy Associations of America, and USPHS grants T1 HE 5680 and 4-FO1-GM-35, 131.)

EFFECT OF ADENINE COMPOUNDS ON H^+ SECRETION OF HISTAMINE-STIMULATED IN VITRO GASTRIC MUCOSA OF RANA PIPIENS. S. S. Sanders,* J. O'Callaghan,* C. F. Butler* and W. S. Rehm, Dept. of Physiol. and Biophys., Univ. of Alabama in Birmingham, Ala.

Addition of ATP (10 mM) to nutrient bathing medium decreases H^+ rate by an average of 80% (range 40-100%) and increases PD and resistance; the effect is reversible. We have previously shown that H^+ inhibition is not due to chelating action on ambient Ca^{++} and/or Mg^{++}. In present study we found that ADP (10 mM) had essentially the same inhibitory effect as ATP while adenosine (10 and 20 mM) did not inhibit. Sometimes adenosine increased H^+ rate slightly. 5'-AMP (10 mM) caused a small decrease in H^+ rate while cyclic-AMP (10 mM) was virtually without effect. When secretion was inhibited by ATP and ADP there was an increase in PD and resistance while the other tested compounds had very little effect on these parameters. It is unlikely that inhibition is due to entrance of ATP and ADP into cells since inhibition starts usually within 6 min. and sometimes is evident within 2 min. In previous work we found that motility of muscularis mucosa was inhibited by all of above compounds (threshold conc. much less than for effect on secretion). Inhibition of H^+ secretion is not due to effect on motility since adenosine (10 mM) abolishes motility but has no effect on H^+ rate. It appears that we must look for a mechanism of H^+ inhibition that involves an action on the limiting membrane on the nutrient side. Tentative working hypothesis: H^+ inhibition by ATP and ADP is due to an inhibition of the postulated neutral carrier exchange mechanism for Cl^- and HCO_3^- in the nutrient membrane. Effect could be due to net charge and conformational characteristics of ATP and ADP. (NIH and NSF support.)

COMPARISON OF TWO CHOLINESTERASE INHIBITORS ON EEG OF SQUIRREL MONKEYS. John A. Santolucito, EPA, Perrine Primate Laboratory, Box 490, Perrine, Florida 33157.

Squirrel monkeys have been fed a carbamate (carbaryl) and an organophosphate (parathion) at the rate of 0.007 and 0.03 mg/kg body weight/day respectively for 33 months. Anesthetized-sleep EEG records (stable for 15 min.) were analyzed visually and with computer assistance. The mean zero-potential crossover (ZPC) rate per 5 sec epoch for carbaryl-treated and control monkeys was 33.4 and 19.7 ($p<0.01$) respectively. The coefficient of variation for ZPC rate during 30, 5-sec epochs was also higher ($p<0.05$) in carbaryl-treated than in control monkeys. Parathion treatment did not affect these characteristics. Interval histograms revealed an increased number of waveform intervals in the 10-90 msec (11-50 Hz) class for carbaryl ($p<0.05$) but not parathion-treated monkeys compared to controls. Both carbaryl and parathion treatment resulted in an increase of intervals less than 10 msec. (>100 Hz) while carbaryl but not parathion showed a decrease in 0.9-2 Hz class. Carbaryl treatment resulted in decreased amplitude of slow-wave (0.5-2 Hz) and both parathion and carbaryl reduced amplitude of 10-15 Hz waveforms. The ratio of mean amplitude of ROxMF/ROxLO activity was used as an index of right-left hemisphere correspondence. Carbaryl-treatment reduced this ratio ($0.05<p<0.1$), i.e., increased bilateral correspondence over controls while parathion did not.

EFFECTS OF ACCELERATION ON PULMONARY BLOOD FLOW IN DOGS BREATHING ORGANIC LIQUIDS. D. J. Sass*, J. F. Greenleaf*, H. C. Smith*, A. A. Bove, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

Dogs were supported in the left decubitus position in a whole-body water-immersion respirator which provided control of rate, tidal and residual volumes of ventilation. Successive injections of differentially tagged microspheres (15±5μ) were made into the right ventricle at $1G_y$ and during exposures to $7G_y$ when being ventilated with room air and then an organic liquid (3M fluorocarbon FC80 or Dow Corning silicone oil DC 200, 1.0cs). The lungs were excised, inflated, dried, embedded en bloc in styrofoam then cut into 1-cm thick sections and blood flow per ml of lung tissue determined for each condition by computer controlled high resolution scintiscanning of each section. Pressures in the aorta, pulmonary artery, right and left atria, left pulmonary vein, upper airway and lower trachea, and right and left pleural spaces were recorded. Oxygen saturation of aortic, pulmonary arterial, and left pulmonary venous blood were recorded continuously by cuvette oximetry. When at $1G_y$, the fraction of cardiac output traversing the left (dependent) lung was frequently less than for the right. However, fractional flow to the left lung was increased during exposures to $7G_y$ when breathing air and silicone oil (sp gr 0.8) but was shifted to the right (superior) lung when breathing FC80 (sp gr 1.76), as would be expected. (Supported in part by grants USAF F41609-69-C-0058, AHA CI 10, and U.S. Navy.)

SUGAR TRANSPORT IN ISOLATED INTESTINAL EPITHELIAL CELLS. M. M. Sayeed, A. Mitchell* and A. E. Baue. Washington University School of Medicine and the Jewish Hospital of St. Louis, Missouri 63110.

There have been few studies of intestinal transport functions by the use of isolated epithelial cells. The purity and possible alterations in the functional capability of these cells during isolation are critical factors. We have determined the capability of isolated epithelial cells to transport 3-methyl glucose (3MG). Isolated cells were prepared by incubating segments of everted rat small intestine in a Ca and Mg free medium containing Na^+, K^+, Cl^-, HCO_3^-, glucose, phosphate buffer (pH 7.3), enzyme hyaluronidase and EDTA. The cells were washed, suspended in Krebs-Ringer-bicarbonate solution and incubated (37C) with 3MG and/or radioactive mannitol in an oxygen environment (95% O_2 + 5% CO_2). At the end of incubation 3MG and mannitol space were analyzed in the final incubation medium and packed cells. The effects of replacement of sodium ion in the incubation mixture by potassium or choline and the addition of metabolic inhibitors (0.1 mM dinitrophenol and iodoacetamide) and anaerobiosis were also determined. An accumulation of 3MG in the isolated cells to approximately 4 times its concentration in the medium was observed only in the control. The mean 3MG uptake (±SE) by cells under various conditions in umoles/ml intracell water was: 65.62 ± 5.59 in control, 24.75 ± 2.49 with potassium, 28.46 ± 4.27 with choline, 35.22 ± 3.17 in anaerobic medium, 35.25 ± 2.34 with iodoacetamide, and 42.87 ± 5.05 with dinitrophenol. These results indicate that isolated cells were capable of accumulating 3MG against a concentration difference only in the presence of a sodium gradient. The active uptake was inhibited in the absence of oxygen and in the presence of metabolic inhibitors. (Supported by National Institute of Health Grant HE-12278).

A QUANTITATIVE STUDY OF THE RELATIONSHIP BETWEEN CORONARY COLLATERAL RESISTANCE AND PERIPHERAL CORONARY RESISTANCE DURING CHRONIC CORONARY OCCLUSIONS. K. W. Scheel, C.E. Ott, M. Banet, and P.H. Lehan (Intr. by H.K. Hellems). Depts. of Physiol. and Med., Univ. Miss. School of Med., Jackson, Miss.

In an isolated dog heart preparation the circumflex, anterior descending and right coronary arteries were simultaneously perfused and blood flow was monitored by electromagnetic flow probes. The retrograde flow method was used to determine the potential collateral flow. In a group of 9 (control) animals the collateral flows as well as the antegrade flows were measured during an acute occlusion of one of the coronary arteries. In a second group of 12 animals (experimental) the collateral as well as the antegrade flows were determined after an ameroid occluder had been placed on one of the left coronary arteries for several months. The antegrade flow of the occluded vessel was measured by cannulating the vessel just distal to the occluder. The collateral conductance in the experimental group increased up to 100 fold in comparison to the control group. The lowest collateral resistance was observed between the circumflex and anterior descending coronary arteries; while the right coronary artery favored collateral development to the circumflex rather than the anterior descending coronary artery. Antegrade flows distal to the occlusion decreased relative to control flows, and further decreased with the length of time the artery had been occluded. Concomitantly, the flow in the other coronary arteries increased. After a 4 month occlusion of the circumflex artery the collateral resistance was almost 3 times smaller than the peripheral resistance of the artery supplied by the collaterals. After several months of coronary occlusion the naturally developing collaterals seem to be able to supply a more than basal need to the occluded vessel.

RECOVERY CYCLES OF SINGLE NEURONS IN THE LATERAL LEMNISCUS AND INFERIOR COLLICULUS OF ECHOLOCATING BATS. P. A. Schlegel* and N. Suga, Dept. of Biol., Washington Univ., St. Louis, Mo.

In order to study the specialization of single neurons for echo-detection and -ranging, recovery cycles of single neurons in anesthetized bats, Myotis lucifugus and Pipistrellus subflavus were measured with a pair of tone pulses set at the best frequency of each neuron, with a 0.5 msec duration and 0.2 msec rise-decay time. Amplitude for the first and second tone pulse was 80 dB SPL or, sometimes, was independently varied. The delay of the second pulse was varied systematically, and the responses of single neurons to it were quantitatively processed with a computer. Almost all neurons in the lateral lemniscus (L.L.) showed very short recovery (50% at 0.5-2 msec), while neurons in the inferior colliculus (I.C.) showed a wide spectrum of recoveries, from short (50% at 1 msec) to long (50% at over 20 msec). The L.L. neurons often discharged only one impulse with a short latency of 3-5 msec. For long tone bursts, however, they showed multiple discharges. On the contrary, many I.C. neurons showed very phasic on-responses with long latencies ranging between 5-15 msec, regardless of stimulus duration. The probability of responses was rather low, 20-50%, unlike that of the L.L. neurons. The recovery cycle was characterized by either short, long or delayed inhibition, undelayed or delayed facilitation or temporary recovery. 22% of the L.L. and 12% of the I.C. neurons showed undelayed, or more often delayed facilitation. Delayed inhibition was frequent in I.C. neurons (42%) and rare among L.L. neurons (7%). Temporary recovery was rarely found in either nucleus. Since these neurons show temporary recovery and/or facilitation after distinct time lags or show inhibition for a certain time gap, they may be considered to be specialized for the reception of echoes from specific distances. (Supported by NSF, GB-13904 & NIH, FR-504, FR-07054 & NS-07498).

POSSIBLE EXISTENCE OF PORTAL RECEPTORS AFFECTING HYPOTHALAMIC NEURON ACTIVITY. M. Schmitt* and K. Koizumi. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, N.Y.

Several authors have proposed the existence of glucoreceptors (Nature, 197:79), osmoreceptors (Pflüg. Arch. 281:39) and proteoreceptors (Fed. Proc. 29:658) in the portal vein-hepatic area and that this is a logical site for signaling higher centers involved in control of food intake and water balance. In order to investigate neural connections between portal vein-hepatic area and hypothalamic neurons known to be involved in such controls microelectrode recordings of hypothalamic cell activity were made in rats anesthetized with urethane. Portal vein injections of 0.25 ml. of NaCl (0.85M) and glucose (1.7M) produced an increase or a decrease in rate of discharge of neurons located in lateral hypothalamus (LH); no cells responsive to NaCl and/or glucose were found in ventromedial nuclei nor in supraoptic and paraventricular nucei. In LH area 18% of cells responded only to glucose, 22% to NaCl and 31% to both injections, while 29% were non-responsive. Cells in the cortex and thalamus were nonresponsive, except for certain cells located in ventral thalamus. Fiber connection between LH and this area have been reported. Section of bilateral splanchnic nerves or of spinal cord at T5 eliminated effects produced in LH neurons by portal vein injection, while vagal section accentuated the responses. Repetitive stimulation of splanchnic afferents increased rate of firing of LH cells. Injection of the same amount of NaCl and glucose into tail vein had no effect on hypothalamic neurons. Small dose of ammonium chloride given by portal vein had no effect but larger dose (0.25 ml of 0.85M) had central effects which were not abolished by severance of afferent nerves. Diurnal rhythmic variations of "spontaneous" discharges in LH neurons were found to play a prominent part in the type of response elicited from portal injections. (Supported by USPHS Grants NS-6537 & -847).

MAXIMUM EXPIRATORY FLOW FROM SALINE AND FLUOROCARBON FILLED LUNGS. W.H. Schoenfisch* and J.A. Kylstra. F.G. Hall Laboratory for Environmental Research, Duke University Medical Center, Durham, North Carolina

Pseudo-static pressure-volume and expiratory pressure-volume-flow characteristics of air, saline and fluorocarbon (FC-80) filled excised lungs of 11.8 to 16.8 kg mongrel dogs were determined by volume displacement plethysmography. Deflation isovolume static recoil pressure (P_{stat}) of air filled lungs > FC-80 filled lungs > saline filled lungs. In each experiment, flow started at a volume at which P_{stat} of the air filled lung was 20 cm H_2O. Maximum expiratory flow ($\dot{V}_{max}$) of air was reached at a pleural pressure (P_{pl}) of approximately 40 cm H_2O; $\dot{V}_{max}$ of saline and FC-80 at P_{pl} of approximately 10 cm H_2O. Peak flow and cessation of flow occurred at a lung volume which was much greater when the lung was filled with liquid than when the lung was filled with air, precluding meaningful isovolume pressure-flow comparisons. At P_{pl} = 50 cm H_2O, the mean $\dot{V}_E$ of the first 500 ml of air exhaled was 4.35 $\pm$ 0.26 l/sec (n=5); of the first 500 ml of saline exhaled 0.112 $\pm$ 0.025 l/sec (n=3); and of the first 500 ml of FC-80 exhaled 0.081 $\pm$ 0.034 l/sec (n=3). In the left lung of a healthy 40 year old man, the maximum mean $\dot{V}_E$ of saline from FRC + 830 ml to FRC + 330 ml was 53 ml/sec, i.e. 38 times slower than the maximum mean flow of air over the same range of lung volumes. It is concluded: 1) That FC-80 does not abolish surface tension at the alveolar interface, suggesting the presence of polar groups facing the alveolar lumen, 2) That the minimum P_{pl} required to reach $\dot{V}_{max}$ reflects the pressure needed to overcome tissue resistance, 3) That the MVV of a mechanically assisted liquid breathing human diver could be considerably greater than the previously estimated 3.5 l/min (Leith and Mead, Fed. Proc. 25,506, 1966), in particular, if time alotted for inspiration and expiration were proportioned optimally.
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FINE STRUCTURE OF GOLGI TENDON ORGANS IN THE CAT. T. W. Schoultz* and J. E. Swett. Univ. Colo. Med. Center, Denver.

Increased interest in the functional role of the Golgi Tendon Organ (GTO) requires more precise morphological data. GTOs were found in samples of E. Carpi Ulnaris. An example shows a GTO receiving collagen bundles from 22 muscle fibers. An abrupt constriction occurs at the musculo-tendinous junction where collagen bundles become tightly compartmentalized by heavy inward extensions of the external capsule and by septa originating from fibroblasts. Capsular cells of the GTO are continuous with perineural epithelium surrounding the afferent nerve. Collagen, occasional fibroblast nuclei, and capillary plexes are present in intralamellar spaces of the capsule. Progressing distally the compact collagen bundles begin to disperse within thin-walled compartments. It is in these loosely packed compartments that axon profiles make their first appearance. The longitudinal compartments formed by thin septa do not retain a consistent relationship to the original muscle fiber groupings. Preterminal axonal branches originate from the large axons of a central compartment and distribute themselves to outlying compartments where they form clasp-like structures around small longitudinally oriented bundles of collagen. Collagen bundles often come into close relationship with axonal membranes in places where Schwann cell sheaths disappear leaving an intervening basal lamina. Less frequently the basal lamina may be absent in patches allowing a more intimate association between collagen and the axonal membrane.

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EFFECTS OF HYPOOSMOLARITY AND HYPONATREMIA ON RESISTANCE TO FLOW THROUGH SKELETAL MUSCLE. J. Scott, B. Brace*, D. Anderson*, and F.J. Haddy. Depts. of Physiol. & Chem. Eng., Mich. State Univ., E. Lansing, Mich.

We have previously shown with a dilutional technique that perfusion of the renal or forelimb vascular beds with hypoosmolar blood increases the resistance to flow. These studies also suggested that the Na^+ per se was not vasoactive. Since the dilutional method alters the concentration of all the blood components (cells, protein, Ca^{++}, Mg^{++}, K^+, etc.) as well as of water, the responses must be interpreted in the light of a isoosmolar control infusion. This objection has been partially obviated in the present study. The in situ canine gracilis muscle was alternately perfused at constant flow with normal and hypoosmolar blood or with normal and hyponatremic blood (isoosmolar) while measuring perfusion pressure (Pp). Osmolarity was lowered by interposing a minature hemodialyzer in the muscle's arterial supply and dialyzing the perfusing blood against a modified Ringer's solution low in NaCl. To create isoosmolar hyponatremic blood, mannitol was used to replace NaCl in the Ringer's dializate. Blood [Ca^{++}], [Mg^{++}], [K^+] and pH were not affected by the dialyzer, hematocrit varied slightly and inversely with osmolarity. Hypoosmolar blood quickly produced a rise in Pp which promptly disappeared on returning osmolarity to normal. In animals where control Pp was $\cong$ to systemic pressure the response was linear, a 10% decrease in osmolarity producing a 22% increase in Pp. Isoosmolar hyponatremic blood produced a slight increase in Pp (11% decrease in [Na^+] causing a 10% increase in Pp) but the response more often than not failed to disappear on returning [Na^+] to normal. These studies add support to the concept that simple changes in plasma [H_2O] can cause striking alterations in the resistance to blood flow through a vascular bed. The ambiguous response to hyponatremia affords little definitive data on the vasoactivity of the Na ion.

TEMPORAL AND DIFFERENTIAL REGENERATION OF CANINE VAGAL MOTOR AND SENSORY FIBERS FOLLOWING CRUSH. W. J. Sears*, S. E. Poppell*, and H. L. Stone. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

Following crush injury, the afferent and efferent fibers in the vagus may follow a different time course during regeneration. If this occurs, techniques may be established to allow investigation of a conscious, chronic, sensory or motor animal, uncomplicated by normal cardiovascular reflexogenic compensatory mechanisms. To examine this possibility, an insulated cooling coil was surgically implanted around the right cervical vagosympathetic nerve in ten animals. Following recovery, control heart rates were recorded in response to right vagus cold block, infusion of aramine, and aramine in conjunction with cold block. The left vagus was then crushed and the animals' responses were studied at weekly intervals to establish the return of motor function. Return of sensory function was confirmed by electrically recording from single left vagal afferent fibers at varying intervals over a 28-week period. Afferent input from respiratory receptors was recorded at 20 weeks, while aortic and atrial cardiac receptor firing was demonstrated in the animals only at or after the 23rd week post crush. The number of afferent spikes per burst increased to normal levels by the 28th week. Little or no change was noted in the motor response with time, to cold block, infusion of aramine, or even to electrical stimulation of the distal end of the severed left vagus through the 27th week. These data suggest that, following crush injury to the vagus nerve, the afferent fibers follow an earlier time course for regeneration than the efferent fibers.

EFFECT OF NEONATAL SPLIT-BRAIN SURGERY ON SHOCK THRESHOLDS AND AVOIDANCE LEARNING IN RATS. Jeri A. Sechzer. Dept. of Psychiatry, Cornell Med. Coll., White Plains, NY 10605

Split-brain surgery was performed on 22 Sprague Dawley and 6 Long-Evans rats within 8 hours of birth. They were raised in the laboratory and weaned under the same conditions as untreated control rats. At 120 days all animals were housed individually. Shock threshold levels were determined in milliamperes (ma.) in ascending, descending and random order. Shock threshold levels were found to be significantly lower in the neonatal split-brain group. "Y" maze learning, on the other hand, was significantly prolonged. Many neonatal split-brain rats never reached an 8 out of 10 criterion. Comparison with shock threshold levels and subsequent avoidance learning in adult commissurotomized rats emphasizes the importance of age of separation of the hemispheres in evaluating the development of interhemispheric interrelations.

PULMONARY CAPILLARY BLOOD FLOW AND PULSATILITY OF YOUNG NORMAL SUBJECTS: EFFECTS OF TILTING, ANTI-G SUIT INFLATION AND EXERCISE. N. SEGEL*, R. DOUGHERTY* AND M.A. SACKNER. Divisions of Cardiology and Pulmonary Diseases of Dept. of Medicine, Mount Sinai Hospital, Miami Beach, Fla.

Pulmonary capillary blood flow ($\dot{Q}c$) and capillary pulse amplitude(CPA) of 10 resting subjects in the postabsorptive state were measured in the supine and 90° vertical positions before, during and after anti-G suit inflation and immediately after isometric exercise in a tiltable body plethysmograph (Lee,Dubois:JCI 34:1380, 1955; Sackner, Culver: Physiol. 12: 345,1969).Passive tilting from the supine to 90° position caused a striking fall in $\dot{Q}c$ in every subject,mean from 3.8L/min/M^2 to 1.5L/min/M^2,and a significant decrease in stroke volume (SV) and CPA. Normal pulsatility was no longer evident. Neither fainting nor bradycardia occurred. These circulatory changes were greatly reduced if the anti-G suit was inflated before passive tilting to 90°. Inflation of the anti-G suit in the vertical position restored $\dot{Q}c$, SV and heart rate(HR)towards the supine control values and pulsatility returned. Similarly, isometric exercise performed for 30 sec in the upright position caused an even greater reversal of the changes induced by passive tilting. In the supine position, isometric exercise for 30 sec produced a mean increase in HR of 32/min,$\dot{Q}c$ of 2.0L/min/M^2 and CPA of 9.1 L/min while SV remained unchanged. Hence,passive tilting to 90° caused a profound fall in cardiac output, SV and CPA probably due to a large shift of intrathoracic blood volume to the splanchnic bed and limbs. The disappearance of normal capillary pulsatility in this position is related to the very low SV and its reappearance after anti-G suit inflation or exercise to the substantial rise in SV. In contrast, we believe that the marked pulsatility induced by supine isometric exercise in the face of unchanged SV is probably a result of the accompanying increase in $\dot{Q}c$ and a decrease in pulmonary vasomotor tone.

MECHANISMS REGULATING RENIN RELEASE IN DOGS WITH THORACIC CAVAL CONSTRICTION. R.E. Shade*, J.O. Davis, R.T. Witty*, J.A. Johnson* and B. Braverman*. Dept. of Physiol., Univ. of Mo. Sch. Med., Columbia, Mo.

In 6 dogs with chronic caval constriction, renal denervation was followed by a fall in plasma renin activity (PRA) from an average of 82.1 ± 1.5 ng angiotensin per ml of plasma over a 9 day control period to 40.8 ± 2.3 ng/ml for a 13 day period after denervation ($P<.001$); normal PRA was 4.7 ± 0.7 ng/ml ($P<.001$). There was no effect of denervation on the marked Na retention. It is concluded that the renal nerves contributed to the high PRA but were not essential for increased activity of the renin-angiotensin system. In a second group of 6 caval dogs, the non-filtering kidney model was produced and renin secretion was measured before and after papaverine infusion into the left renal artery. Papaverine decreased renin secretion from 1156 ± 188 ng angiotensin/min to 497 ± 140 ng/min ($P<.005$). This initial rate of renin secretion of 1156 ng/min was higher than that from a non-filtering left kidney of 190 ± 50 ng/min in otherwise normal dogs ($P<.001$). Therefore, the initial high renin secretion in dogs with caval constriction and the decrease in renin secretion with papaverine occurred in the absence of a functional macula densa; the data suggest that a baroreceptor mechanism was partly responsible for increased renin secretion. In a third series of 6 dogs with caval constriction but with filtering kidneys, papaverine produced a similar decrease in renin secretion and an associated increase in Na excretion. This decrease in renin secretion could conceivably have resulted from inhibition of the baroreceptor mechanism alone or a combination of this effect with a change in Na load at the macula densa. Collectively, the data support a role for the baroreceptor mechanism and the renal nerves in control of renin secretion in this model but observations are needed to define the role of the macula densa.

Primacy of the (Mg + Na + K)-E-ATP complex in the (Na + K)-ATPase sequence. Adil E. Shamoo and William A. Brodsky, Div. Biophys. Chem. and Dept. Physiol., Mt. Sinai Sch. Med., CUNY., New York.

Microsomes obtained from the epithelial cells of turtle bladder were incubated with ATP, 0.01mM. The mean level of Ca-dependent ATPase, 141 nmoles/mg prot./hr., was one third that of the Mg-dependent ATPase. Addition of Na and K together increased the hydrolysis by 20% in the presence of Mg, but had no effect in the presence of Ca. The addition of Ca to the (Mg + Na + K)-system eliminated the (Na + K)-increment of hydrolysis. The amount of E-ATP formed in 50 sec. at $0^{o}C$ was 13 pmoles/mgm in the presence of Ca alone or Mg alone. The addition of Na and K together resulted in a 32% increase in the Ca-dependent but not in the Mg-dependent binding of ATP. The amount of phosphoprotein formed after 50 seconds was 19.2 pmoles/mgm protein with Ca alone and 76 with Mg-alone. Addition of Na caused a three-fold increase in the amount of Ca-dependent phosphoprotein formation. The addition of K reduced the level of (Ca + Na)-dependent E-P to the underlying Ca-dependent level; while the same addition of K reduced the level of (Mg + Na)-dependent E-P to less than half (31 pmoles) that of the underlying Mg-dependent level. It is inferred that the simultaneous presence of Mg, Na and K is required in the very first intermediary reaction step of the (Na + K)-ATPase sequence. Calcium substitutes for Mg in this first step, but forms an irreversible complex. The sodium-induced increment of phosphoenzyme is not one of the sequential steps in the (Na + K)-ATPase. (Supported by NIH grant AM 13037 and NSF grant GB 7764).

LOCAL CONTROL OF TISSUE OXYGEN DELIVERY: A THEORETICAL ANALYSIS. A. P. Shepherd, Jr. and H. J. Granger (Intr. by W. L. Williams). Dept. of Physiol. & Biophysics, Univ. of Miss. School of Med., Jackson, Miss.

A mathematical model of metabolic regulation of oxygen delivery in the microvasculature has been developed. It includes the following: nonlinear hemoglobin dissociation curve; nonlinear tissue oxygen utilization-intracellular pO_2 relationship; transcapillary diffusive flow of oxygen as a function of capillary density, capillary pO_2 and intracellular pO_2; and metabolic control of arteriolar and precapillary sphincter tone. Basically, flow regulation by the arterioles serves to minimize changes in capillary pO_2, whereas the precapillary sphincters regulate capillary density and thereby determine diffusion parameters (diffusion distance and surface area). The transient and steady-state responses of the model to changes in arterial pressure, venous pressure, arterial oxygen content, and metabolic rate were studied. Following slight to moderate reductions of the oxygen availability-to-demand ratio, oxygen delivery is maintained primarily by precapillary sphincter adjustments of diffusion parameters. With more severe reduction of this ratio, arteriolar flow control becomes more important in maintaining adequate tissue oxygenation; this result could account for the greater degree of blood flow autoregulation under conditions of low venous pO_2. If one assumes intracellular pO_2 is 5 mm Hg and that capillary density may increase 3-4 times control, the maximum oxygen delivery is 4-5 times control, a value much lower than the 10-15 fold increase observed in exercise. However, the model agrees with the experimental data if an intracellular pO_2 of 15-20 mm Hg is used. In addition, the simulation of reactive hyperemia offers a possible explanation for the difference in flow patterns observed after arterial vs. venous occlusion.(Supported by NIH Grant HE 11678 and a grant from the Miss. Heart Association.)

PROSTAGLANDIN E_2 STIMULATION OF HUMAN PLATELET AGGREGATION
Hideo Shio* and P.W. Ramwell. Alza Corp., Palo Alto, Calif.

The potent inhibitory action of prostaglandin E_1 on platelet aggregation has been established in various experimental systems and is generally believed to be mediated via cyclic AMP. However, PGE_2 also stimulates rat platelet aggregation as well as adenyl cyclase activity. This anomaly has been examined in human citrated platelet-rich plasma (c-PRP) using the turbidometry method.

The effect of PGE_2 (10^{-7}-10^{-6}M) on the two phases of aggregation induced by ADP is (i) slight inhibition of the first aggregation phase when added before ADP, (ii) significant enhancement of the second phase, especially when PGE_2 was added during the first aggregation phase. Collagen-induced platelet aggregation, which is believed to be similar to the second phase of ADP-induced platelet aggregation, was (iii) enhanced by PGE_2. On the other hand, the (ii) and (iii) effects of PGE_2 were minimal or absent on samples of human c-PRP which do not exhibit the second phase. The (i) effect seems to be closely related to adenyl cyclase stimulation. However, the enhancing effect of PGE_2 on platelet aggregation in the rat and the second aggregation phase in human platelets is independent of cyclic AMP.

These results indicate that intravenous PGE_2 may have a thrombogenic effect when infused into those human subjects who possess a secondary phase of aggregation.

CIRCADIAN VARIATION OF NOREPINEPHRINE RATIO (NER) IN HEALTH, SLEEP DEPRIVATION AND SCHIZOPHRENIA.
R.N. Shiotsuka*, A. Reinberg*, F. Ungar*, R. Sonstroem*, R.B. Sothern*, W. Nelson*, Z. Kahane*, P.B. Vesteraaard*, A.H. Esser*, J. Fröberg*, L. Levi*, N.S. Kline* and F. Halberg. Chronobiology Laboratories, Univ. of Minnesota, Minneapolis, Rockland State Hospital, Orangeburg, N.Y. and Karolinska Sjukhuset, Stockholm, Sweden.

Circadian variation characterizes urinary corticoids, norepinephrine (NE), epinephrine (E) & also NER=NE/(NE+E) -- for groups of healthy subjects either deprived of sleep or not (including individuals sampled for weeks or months) and for (8 institutionalized) patients with schizophrenia. The mean NER (& SE) are comparable in healthy subjects (0.80 $\pm$ .02) and patients with schizophrenia (0.81 $\pm$ .01) (t=.12). Rhythmometry reveals statistically significant changes in NER approximated by least squares fits of 24-hour cosine curves, perhaps reflecting, inter alia, changes in relative NE conversion to E. Whether subjects sleep or not for a day or two and whether or not they are institutionalized, a high NER [acrophase, ϕ (Annual Rev. of Physiol.31: 675,1969)] usually occurs during the habitual sleep span (95% confidence arc of ϕ covers 4 hours for patients with schizophrenia -- span between 00^{00} and 04^{00}). The mean circadian amplitude, C+SE, of NER for institutionalized patients with schizophrenia was .09 $\pm$ .01; it was .082 + .01 for sleep-deprived healthy subjects whereas C was much lower ($P<.05$) or barely demonstrable as statistically significantly different from zero in other presumably healthy individuals. NER decreases as blood corticoid levels spontaneously increase during the habitual sleep span, in the absence of known exogenous stimulation and of sleep. Rhythmometry thus scrutinizes possible adrenal cortical and medullary interaction when classical rhythm-unqualified approaches fail to reveal differences.

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MECHANISM OF COLLAGEN DEGRADATION BY SNAKE VENOM. John W. Simpson. Univ. of Texas Dental Science Institute, Houston, Texas.

Venoms from Crotalus atrox, Agkistrodon contortrix contortrix, Agkistrodon piscivorus leukostoma and Bitis nasicornis contained an enzyme which was capable of reducing the specific viscosity of collagen solutions. Venom from Vipera russelli, Ophiophagus hannah and Naja naja did not degrade collagen. The collagenolytic activity from C. atrox venom was studied in detail. Reaction mixtures containing collagen and C. atrox venom were examined by acrylamide gel electrophoresis. Venom activity converted collagen β chains into α chains. In addition, a collagen fragment was formed which traveled in front of the α chains on the acrylamide gels. A portion of the collagenolytic activity from C. atrox venom was stable after exposing crude venom to pH 2.5. Electrophoretic patterns obtained from reaction mixtures containing venom exposed to low pH showed a reduction of both α and β collagen components coincident with the formation of collagen fragments. Samples of a partially purified trypsin-like protease from the venom did not contain collagenolytic activity. Crude venom and venom exposed to pH 2.5 were capable of degrading native collagen fibers of rat mesentery in tissue cultures. The results of this study show that C. atrox venom contains enzymes specific for collagen degradation. The presence of collagenolytic enzymes in snake venoms may provide a mechanism for penetration of toxins through connective tissues. (Supported in part by a grant from the Robert A. Welch Foundation, Houston, Texas and USPHS Grant No. DE 02743-03.)

METABOLIC RESPONSES TO THE INTERACTING STRESSES OF SEVERE EXERCISE AND ACUTE HYPERCAPNIA. R. D. Sinclair, J. M. Clark, and J. B. Lenox (intr. by R. W. Bancroft). USAF School of Aerospace Medicine, Brooks AFB, Texas.

The effect of respiratory acidosis on the metabolism of heavy exercise was studied in 9 subjects who were exposed to inspired P_{CO_2} ($P_{I_{CO_2}}$) levels of 0, 10, 20, 30 and 40 mm Hg while running on a treadmill at a 10% grade. Average oxygen uptakes ($\dot{V}_{O_2}$) at 4 different speeds were not altered by changes in $P_{I_{CO_2}}$ and approximated 25, 40, 68 and 81% of the maximum $\dot{V}_{O_2}$ which was 63 ml/kg min. In contrast, CO_2 elimination ($\dot{V}_{CO_2}$) for a given workload was enhanced by increasing concentrations of $P_{I_{CO_2}}$. Calculation of the metabolic component of the total change in arterial hydrogen ion concentration $[H^+]$ showed that, for 68 and 81% maximum $\dot{V}_{O_2}$ runs, it increased in a progressive manner with elevations in $P_{I_{CO_2}}$ and reached a value at the heaviest workload in 40 mm Hg which was approximately 40% greater than that in air. The observed increases in $\dot{V}_{CO_2}$ paralleled closely the calculated changes in metabolic acidosis for the two highest workloads. Arterial lactate and pyruvate concentrations were also measured and excess lactate was calculated for each experimental condition. Changes in arterial lactate and excess lactate were not consistently different at the same workload in the five CO_2 environments. The average lactate values were 0.91, 1.65, 4.89 and 9.29 mM/L for the stepwise increments in treadmill speed. A progressive decrease in arterial pyruvate was found with rising $P_{I_{CO_2}}$ for the two highest workloads and the same trend persisted at the end of a 5-minute recovery period. The failure of measured changes in lactate and pyruvate to explain the concurrent changes in arterial $[H^+]$ suggests that severe respiratory acidosis may have altered the metabolism of free fatty acids normally associated with exercise in air.

A PROGRAMMED TEACHING LABORATORY IN MEDICAL INSTRUMENT RECORDING. J. E. Sipe* and G. S. Malindzak, Jr. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

Because electronic instrumentation is a vital tool in investigative physiology and medical diagnosis, first year medical students and graduate students were introduced to the use and operation of a typical laboratory recording instrument through a program consisting of prerecorded instructions and physiological data. The program was introduced in a scheduled laboratory rotation in the beginning of the medical physiology segment of the curriculum. The objectives of the exercise were (a) to enable the students to understand the basic components of the polygraph to the extent that they could execute a standard calibration procedure for the polygraph amplifiers and (b) to enable the students to derive quantitative data from the strip chart recordings and arrive at a reasonable interpretation of the results. Direct evaluation of the program by written examination demonstrated that these objectives were achieved. Subjectively, participating faculty observed increased student participation and interest in other laboratories utilizing similar instrumentation, and the Teaching Laboratories experienced some reduction in time for and cost of maintenance of these instruments. Additional programs utilizing prerecorded instructions and data are being planned in connection with a variety of physiological and pharmacological experiments. (Supported by USPHS grants ME-1085 and HT-344.)

EFFECT OF INFLATION LEVELS AND BODY POSITION CHANGES UPON REGIONAL PULMONARY PARENCHYMAL MOVEMENT IN DOGS AT 1G. H. C. Smith*, J. F. Greenleaf*, D. J. Sass*, A. A. Bove, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

The spatial distribution of inspired air and pulmonary blood flow during respiratory maneuvers of man and dog in various body positions and force environments have been reported but data regarding regional shifts in the pulmonary parenchyma under these conditions is not available. In this study, 25-50, 1-2 mm radiopaque stainless steel tags were implanted percutaneously in the pulmonary parenchyma of anesthetized dogs in a grid pattern without significant hemorrhage or pneumothorax. The dogs were examined in the prone, supine, left decubitus, head-up and head-down positions at various levels of lung inflation 1-2 weeks after implantation. Pleural pressures were recorded simultaneously from fluid filled catheters positioned in the superior and dependent pleural spaces. The position of the pulmonary parenchymal tags was determined from biplane orthogonal roentgenograms with correction for magnification in the two planes. Upon completion of the study, the lungs were removed and air dried while inflated to 30 cm H_2O transpulmonary pressure to achieve uniform alveolar size, and the parenchymal tag positions determined as above. No pleural adhesions were noted, and minimal ($<100\mu$) fibrosis was found surrounding the parenchymal tags. The effects of the magnitude of the resultant vector of the force environment on the weights of mediastinal structures and abdominal contents, the direction of this vector in relation to the body, plus the level of lung inflation all interact to influence the observed non-uniform regional displacements of the pulmonary parenchyma. (Supported in part by grants NIH FR-7, HE3532, HE4664, AHA CI 10, and MRC 100-2S-122.)

GLUTATHIONE SYNTHESIS IN SHEEP ERYTHROCYTES. Joseph E. Smith and Margaret Lee (intr. by Ronald Gronwall). Department of Pathology, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas.

Two enzymes are necessary for the de novo synthesis of reduced glutathione in the erythrocyte. The first enzyme, glutamylcysteine synthetase, forms γ-glutamylcysteine from glutamic acid, cysteine, adenosine-5'-triphosphate and magnesium. The activity of this enzyme in six normal sheep hemolysates was 0.537 ± 0.0699 μmoles/minute/Gm hemoglobin. The second enzyme, glutathione synthetase, requires GC, glycine, adenosine-5'-triphosphate and magnesium to form reduced glutathione. The activity of glutathione synthetase in six normal sheep hemolysates was 0.104 ± 0.0232 μmoles/minute/Gm hemoglobin. Six additional sheep had reduced glutathione concentrations which were 25% of that found in normal sheep. Erythrocyte glutamylcysteine synthetase activity in these animals was 0.285 ± .0487 μmoles/minute/Gm hemoglobin and glutathione synthetase was 0.0849 ± 0.0065 μmoles/minute/Gm hemoglobin. The GSH levels of the combined groups were significantly ($P < 0.001$) correlated with the glutamylcysteine synthetase activity. The activity of glutamylcysteine synthetase was inhibited by adenosine-5'-diphosphate, reduced glutathione, oxidized glutathione, reduced nicotinamide adenine dinucleotide phosphate and reduced nicotinamide adenine dinucleotide.

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EFFECT OF FOOD AVAILABILITY ON RENAL DEVELOPMENT OF NEONATAL RATS. Sidney Solomon, Univ. of New Mex. Sch. of Med., Albuquerque, N.M.

Litters of rats were reduced to a total of 4 or 5 within five days post-natally. When compared to controls, such animals grow faster than animals from intact litters. It has previously been shown that under such conditions, renal functional development and morphological development also increases with the increase in body weight (Capek and Solomon, Fed. Proc. 1971). Differences are, however, found between animals from reduced and intact litters. The ratio of kidney weight to body weight is less in the animals from reduced litters. For comparable total kidney GFR, superficial nephron GFR (SNGFR) is less in the animals from reduced litters. Dividing GFR by SNGFR gives an apparent nephron number. In animals from reduced litters, the number is higher than in animals from intact litters until both groups are over thirty days old. These observations suggest that in animals from reduced litters, there is either underperfusion of superficial nephrons or enhanced development of functional nephrons, perhaps including nephrogenesis. (Supported by NSF Grant GB 25112.)

PROGESTIN AND LUTEINIZING HORMONE LEVELS IN PLASMA OF FEMALE DOGS. J. Spano*, W. J. Tietz, J. F. Masken and M. L. Hopwood, Dept. of Physiology and Biophysics, Colorado State Univ., Fort Collins, Colo.

Luteinizing hormone (LH) and progestins were determined in plasma of purebred beagles. LH was measured by radioimmunoassay using a rabbit anti-bovine LH (Niswender et al., Endocrinology 84:1166, 1969) in 24 cycling bitches sampled daily during proestrus and estrus (means of 6.6 and 9.1 days, resp.). Progestins were assayed by radioligand binding in all the dogs bled daily during the estrous cycle and through pregnancy. The dogs were divided into 3 groups of 8 dogs each. One group was bred at estrus to fertile sires, one to vasectomized males and the third was not bred. LH values peaked to a mean of 24.6 ng/ml (NIH-LH-B5) at 12 hours after the onset of estrus. Through proestrus and the remainder of estrus LH values did not exceed the peak. Progestins were low at 2 to 5 days before the onset of estrus, rose gradually to peak at 25-30 days, then declined gradually to a low at 63-67 days in all groups of dogs. No significant differences in progestin levels were found between groups. It appears that pregnancy and pseudopregnancy are the two conditions that follow estrus in the bitch and that pseudopregnancy terminates at the expected time of parturition. The canine placenta does not appear to contribute progestins to maternal plasma. (Supported by a grant from the Morris Animal Foundation.)

METABOLIC CHANGES IN MALE PATIENTS WITH OSTEOPOROSIS. Herta Spencer, Clemontain Norris*, Lois Kramer*, and Joseph Samachson*. Metabolic Section, Veterans Administration Hospital, Hines, Illinois.

Previous studies carried out in this Research Unit have shown that female patients with osteoporosis absorb less calcium from a high calcium intake than patients without osteoporosis. Very few data are available on the intestinal function of male patients with osteoporosis in regard to the intestinal absorption of calcium from different intake levels of calcium. Studies were performed in male patients with osteoporosis under strictly controlled dietary conditions. Calcium balances and ^{47}Ca absorption studies were determined during both a low calcium intake of about 200 mg and during a high calcium intake of approximately 2000 mg per day. A tracer dose of ^{47}Ca was given orally in both study phases. During low calcium intake, the slightly negative calcium balances and the ^{47}Ca absorption values of these patients were similar to those observed in patients without osteoporosis. However, on a high calcium intake the calcium balances became only slightly positive or remained negative despite the marked increase in calcium intake. In agreement with these findings were the lower than normally observed absorption values for ^{47}Ca during high calcium intake. Also, on performing the calcium tolerance test, the retention of intravenously infused calcium was lower than normal in two of these 3 patients similar to the retention of calcium observed in female patients with osteoporosis. The studies have shown that the low absorption of calcium during high calcium intake is not characteristic of female patients with osteoporosis but is also found in male patients with osteoporosis. (Supported in part by U.S. Atomic Energy Commission and in part by National Dairy Council.)

RESPIRATORY METABOLISM OF THE KILLER WHALE (ORCINUS ORCA) M.P. Spencer, A.C. Van GOETHEM*, D.W. Kenny*, K. Burgess*, D. White*. Virg. Mason Res. cntr., Seattle, Wash; Sea World, San Diego, Calif. and Vancouver Acquarium Vanc. B.C.

Four orca were trained to breath through a special low-resistance, twin-valve device placed over their blowholes at pool-side. Quantitative collections of expired air in large polyethelene tubes extended to 10 min. End alveolar (ea) & bag air were analysed for Po_2 & Pco_2. From the volumes, collection times and number of breaths, tidal volume (TV) l/breath, minute volume (MV) l/min., respiratory interval (RI) seconds and O_2 uptake (U) were calculated. Measurements of body weight (BW) Kgms, overall body length (L) meters, heart wt. (HW) Kgms & lung weight (LW) Kgms were made on additional orca. # of data points are given in (). (20)$BW=13.5L^{3}$; (6)$HW=.034BW^{.77}$, (6)$HW=.28L^{2.28}$ (6)$LW=.07BW^{.81}$; (6)$LW=.54L^{2.48}$; (3)$RI=3.2BW^{.36}$ (8)$RI=8.3L^{1.15}$; (3)$TV=1.4BW^{.55}$; (3)$TV=11L^{1.30}$ (6)$MV=4.6BW^{.52}$; (29)$MV=2,350\ RI^{-.84}$ (6)$U=.056BW^{.66}$ averaging both resting (r) & post-excercise (pe)data. $MV=.76\ U^{1.70}$RI median of 3 orca decreased from 27/sec. immediately pe. Resting ea P_{O_2} for 27 sec. RI averaged 98 mmHg and decreased to 65mm in 60 sec. and 32mm during a 240 sec. breath-hold submergence. pe Po_2 decreased to 75mm for a 20 sec. RI & 50mm in 60 sec. Maximal breath hold r/metabolic rate/Kgm decreases with increasing BW suggesting O_2 conservation advantage for larger whales. Long volunteer breath-hold dives may be prolonged by bringing into play special O_2 conservation mechanisms not used during normal RI. (NIH grant HE-10258)

A STUDY OF THE MATERNAL-FETAL WEIGHT RELATIONSHIP IN SEVERAL MAMMALIAN SPECIES. Richard P. Spencer. Section of Nuclear Medicine, Yale Univ. School of Medicine, New Haven, Conn. 06510.

Efforts to obtain a general statement, descriptive of the maternal-fetal (birth) weight relationship in mammalian species, have not been reported. As a preliminary attempt, we can note that the weight of an organ can often be expressed as a power function of the body weight (allometric relationship: Huxley, 1932; Stahl, 1965). Fetal weight was given in terms of a constant (q) and the maternal weight (M) raised to an exponent x. Thus $F = q.M^{x}$, or $\log F = \log q + x.\log M$. This was tested by plotting log F against log M for 36 mammalian species (data principally from Spector (1956), Heinroth (1930) and the Interzoo Yearbook). Fetal weight was considered to be the weight of the entire litter if there was more than 1 offspring. The least squares equation was $\log F = -0.47 + 0.83 \log M$, or $F = 0.34\ M^{0.83}$. The correlation coefficient was 0.92. This was true even though the maternal weights varied by over 5 orders of magnitude (mouse to elephant). Using gram weights for calculations, the equation was precise for man (60,000 gm maternal, 3,300 gm fetal), but tended to overestimate fetal weight in the bears and in the "large cats". That is, in these species the newborn are smaller than expected on the basis of generalization from other mammals. The description, while good for man and the Rhesus monkey, also overestimates the weight of the newborn gorilla. It is likely that many sub-rules are operating, which result in an overall close approximation to the allometric equation. It will be of value to recalculate data for various families of mammals, as well as on the basis of placental type and other physical parameters.
(Supported by USPHS CA 06519 and by T-492 A from Am. Cancer Soc.).

CEREBRAL REMOVAL OF KETONE BODIES IN NEWBORN PUPPIES. J.J. Spitzer & J.T. Weng* Hahnemann Med. Coll., Philadelphia, Pa.

Thirty-one puppies (1-8 days old) from 5 litters, were anesthetized with Nembutal and given a constant intravenous infusion of Na-DL-3-hydroxybutyrate-^{14}C at the rate of 92,000 dpm (in 0.02 ml) per min. Following more than 120 min of infusion simultaneous arterial and cerebral venous (from confluens sinuum) blood samples were taken for analysis of acetoacetate (AcAc), D-β-hydroxybutyrate (βOHB), O_2, CO_2, $^{14}CO_2$ and glucose. Not all determinations were performed on all animals. The following table summarizes the main findings (mean ± SEM):

	Arterial Conc.	A-V Diff.	# of animals
AcAc (μmole/ml)	0.140±0.018	0.034±0.008	31
βOHB (μmole/ml)	0.077±0.018	0.023±0.008	29
Glucose (μmole/ml)	7.76±0.72	1.17±0.29	23
O_2 (μmole/ml)	5.17±0.43	2.27±0.27	21
CO_2 (μmole/ml)	23.17±1.06	-2.60±0.41	21

While the cerebral removal of ketones was a consistent finding, there was no significant production of $^{14}CO_2$ across the brain. There was a positive correlation between the arterial concentration of AcAc or βOHB, and the A-V difference of AcAc or βOHB across the brain. If all the removed ketones had been oxidized, ketones would have accounted for 16% of the cerebral O_2 consumption. Lipid classes in 6 different areas of the brain have also been separated in 7 animals. Significant ^{14}C radioactivity was consistently found in the phospholipid and free cholesterol fractions of all 6 brain areas studied. (Supported by NIH Grant HE 03130.)

EFFECTS OF GASTRIN AND SECRETIN ON ACID OUTPUT AND PARIETAL CELL COUNT. Michael D. Stanley*, Robert E. Coalson* and Leonard R. Johnson. University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

Rats were surgically prepared with gastric cannulas and divided into four groups of five animals each. Basal and maximal acid outputs in response to 250 μg/kg pentagastrin were determined three times prior to the start of chronic injections. The animals were injected three times per day for fourteen days with either 250 μg/kg pentagastrin, 250 μg/kg pentagastrin and 100 unit/kg secretin, 100 unit/kg secretin, or saline. Basal and maximal acid output were collected on the 7th and 14th day of chronic injection. The rats were sacrificed and the stomachs removed for histological studies. At fourteen days the gastrin group showed a 78% increase in basal and 82% increase in maximal acid output. Secretin decreased basal output 7% and decreased maximal output 3%. The pentagastrin-secretin group increased basal output 13% and decreased maximal output 27%. In the saline control basal output decreased 6% and maximal output increased 42%. The average parietal cell count for the gastrin group was $(56.5 \pm 1.5)10^6$, for the secretin group $(28.6 \pm 1.2)10^6$, $(38.6 \pm 10)10^6$ for the pentagastrin-secretin group, and $(37.7 \pm 4.8)10^6$ for saline controls. We conclude that gastrin acts as a trophic hormone on parietal cells causing an increase in the number of parietal cells. Secretin blocks the trophic effect of gastrin and thus retards both the stimulated and normal growth of parietal cells. Supported by NIH Grant AM 14392.

PLASMA LUTEINIZING HORMONE (LH) IN OVARIECTOMIZED (OVX) PRE AND POST-PUBERAL RATS DURING CONTINUOUS INFUSION OF ESTRADIOL (E_2). Ronald E. Steele and Judith Weisz (intr. by C. W. Lloyd). Worcester Fndn. for Exptl. Biol., Shrewsbury, Mass.

This study was conducted to determine whether continuous intravenous infusion of E_2 into the conscious, semi-restrained animal over a long period of time produced a difference in the level of plasma LH in the ovx prepuberal rat as compared to the ovx postpuberal rat. Rats were ovx at 19 or 45-55 days of age. Vaginal opening occurs in the intact rat between 32-37 days of age. One week after ovariectomy, a polyethylene catheter was inserted into the vena cava via the right external jugular vein and fastened. The rats were then semi-restrained according to a modification of the technique of Dalton et al (J Lab Clin Med 74:813-815, 1969). The catheter was utilized for collection of blood and infusion of E_2. Between 1500-1700 hrs EST on the day of catheterization, a blood sample was obtained and infusion of E_2 (1.14 cc/day) initiated. The E_2 vehicle consisted of .7% ethanol/100 g body weight (bwt) in saline. At 24 hr intervals the infusion was interrupted for about 10 min. for blood collection. Plasma LH was measured by radioimmunoassay. One week after ovariectomy plasma LH levels exceeded 250 ng/ml (LER 1213 A) in both pre and postpuberal rats. Continuous infusion of .08μg of E_2/100 g bwt/day into ovx prepuberal rats lowered plasma LH levels to less than 30 ng/ml within 72 hrs of infusion. In ovx postpuberal rats no effect was seen after 72 or 120 hrs of administration of the same dose. These findings are consistent with the hypothesis that a change in the negative feedback effects of E_2 on LH release and/or synthesis occurs at the time of sexual maturation.

VISUAL AND POLYSENSORY NEURONS OF CAT SUPERIOR COLLICULUS. Barry E. Stein and Makanjuola O. Arigbede (intr. by L. Kruger). Dept. Anat., UCLA Ctr. Hlth. Sci., L.A. 90024.

Neurons in the upper layers of the superior colliculus were selectively excited by visual stimuli and were usually best activated by moving visual stimuli. These neurons were not, however, affected by those nonvisual stimuli which were found capable of influencing deeper collicular neurons. A number of deeper collicular neurons driven by moving visual stimuli or stationary luminous stimuli were also excited by tactile (predominantly hair receptors) and/or low intensity acoustic stimuli. Tactile receptive fields of polysensory neurons were usually widespread and bilateral with zones of maximal sensitivity. Repeated presentations of tactile stimuli resulted in periods of diminished responsiveness, however, the distinction between response fluctuation and what has sometimes been interpreted as habituation could not be secured. Cortical inactivation by local cooling of visual and suprasylvian cortex selectively inhibited visual activation while responsiveness to tactile and acoustic stimuli were unaltered.

THE CARDIOVASCULAR RESPONSES TO BREATH-HOLD DIVING IN THE FREE-SWIMMING CALIFORNIA SEA LION ZALOPHUS CALIFORNIANUS. Christopher M. Stevens* and John P. Meehan. Univ. of So. Calif., Dept. Physiology, School of Med., Los Angeles, California

Central venous pressure and the electrocardiogram (EKG) were recorded from a trained sea lion diving 'on command' in the ocean. The EKG was obtained from skin-mounted electrodes and the intravascular pressure transducer was implanted in the thoracic inferior cava. Data were recorded directly on magnetic tape by the use of a small underwater recorder attached to a harness. The well-known diving or apneic immersion bradycardia (Elsner, Hvalrad. Skr. 48:24, 1965) occurred with an average decrease of 59%. After 80% of the dive the rate increased, following a time course similar to the initial gradual decrease. The central venous pressure increased sharply by 4.8 mm Hg at the onset of the dive and returned after 10% of the dive time, to a steady value of 1.5 to 2.0 mm Hg above the predive level. When the animal surfaced, the central venous pressure returned to control. Conclusions: The bradycardia response was under higher center control as evidenced by the adjustment of the magnitude of the decrease to the subjective assessment of the metabolic demands of the dive and its reversal with anticipation of surfacing. The low central venous pressure, i.e. the absence of thoracic vascular engorgement during swimming and diving, suggests the operation of a regulatory mechanism to meter blood flow into the thoracic circulation. The inferior vena caval sphincter (Harrison and Tomlinson, Symp. Zool. Soc. 13:59, 1964) is an anatomical entity capable of exercising this regulatory function.

TESTOSTERONE (T) DIMETHYLPOLYSILOXANE (DPS) IMPLANTS:DAILY SPERM PRODUCTION (DSP), LIBIDO AND ACCESSORY SEX ORGAN (ASO) FUNCTION IN MALE RABBITS. L. Stratton*, L. Ewing and C. Desjardins, Dept. Physiological Sci., Okla. State Univ., Stillwater, Okla. 74074

Administration of testosterone propionate to men results in azoospermia that is reversible upon withdrawal (Heller et al., Fertil. Steril. 1:415,1950). We hypothesized that subcutaneous (SQ) T filled DPS implants would maintain peripheral levels of T at concentrations sufficient to inhibit spermatogenesis without inducing ASO hypertrophy. Results show that T-^{3}H passes through DPS capsules suspended in water at constant rates, that release (µg/24 hrs) into water is dependent upon capsule surface area (SA), that release from SQ implants depends upon SA and that release in vivo is constant over 3 mos. As expected castration (7 rabbits) abolished libido, caused ASO atrophy and resulted in non-detectable plasma T levels. In contrast peripheral T levels, libido and ASO function in 7 castrate rabbits receiving SQ T filled implants (300 mm^{2}) were identical to 7 intact rabbits receiving cholesterol (C) SQ implants for 3 mos. Intact rabbits with C filled implants had: 2.1 ngT/ml plasma; sex behavior score of 8.6; 7.1 g paired testes weight; DSP of 210 X 10^{6} sperm/day and seminal vesicle, vesicular, prostate and bulbourethral gland wts. of 0.5, 0.9, 0.7 and 0.6 g respectively. Seven intact rabbits containing SQ T filled implants (300 mm^{2}) for 3 mos. were similar to control rabbits in all respects except for a significant ($P<0.01$) reduction in testes wt. (1.6 g) and the absence of testicular sperm. These data demonstrate conclusively that T filled DPS implants may be used to inhibit spermatogenesis and maintain libido in rabbits without causing accessory sex organ hypertrophy.
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THE PRODUCTION OF INTESTINAL FLUID BY CHOLERA TOXIN IN THE RAT. Donald R. Strombeck, (intr. by R.C. Ingraham) University of Illinois, School of Basic Medical Sciences, Chicago, Illinois 60680

In vitro methods, used to study the effect of cholera toxin in the rat small intestine, have failed to support the hypersecretion hypothesis. In vivo methods have verified that the rat can be used as a cholera model but differs from others in the effects of acetazolamide and cycloheximide on toxin induced fluid production. Fluid production in 40 cm loops of small intestine (distal half) increased 50% in rats given 6 mg/kg isoproterenol and decreased 26% in rats given 2 mg/kg propanolol with 20 mg/kg diphenhydramine. These three drugs did not inhibit the complete absorption of a bactopeptone solution. The composition of intestinal fluid induced by cholera toxin (3ml 20mg cholera toxin/ml, Wyeth,NIH lot 001 in each loop) was in mEq/l: Na^+,144.1; K^+,5.9; Cl^-, 72.4; HCO_3^-,37.9 and osmolality was 288.7 mosm. Plasma composition was: Na^+,142.3; K^+,4.4; Cl^-,102.0; HCO_3^-,20.1 and osmolality was 304.1 mosm. HCO_3^- content increased to 43.9 with 10mg/ml cholera toxin and decreased to 34.1 when 30mg/ml was used. Fluid production was also dose dependent over the range of toxin tested (10-30mg/ml). Another group of rats were used to prepare 40cm loops of the proximal half of the small intestine. Fluid production was twice as great as that in the distal loops when 30mg/ml toxin was present. HCO_3^- content of this fluid was 15.0 mEq/l. The altered fluid production by agents which affect microcirculation suggests that changes in circulatory parameters and/or permeability may occur with cholera toxin. The inverse relationship between fluid production and HCO_3^- content does not support the hypothesis that cholera toxin induces a HCO_3^- rich secretion as a means of the fluid production. The greater fluid production in the proximal loop is consistent with the fact that fluxes of H_2O and ions are greater at this site.

MATHEMATICAL CORRELATION BETWEEN VENTRICULAR PRESSURE-VOLUME RELATIONSHIP AND MYOCARDIAL FORCE-VELOCITY CURVE: A NEW INDEX OF CARDIAC CONTRACTILITY. Hiroyuki Suga* and Kiichi Sagawa. Dept. of Biomed. Eng., Johns Hopkins Univ., Baltimore, Md.

Instantaneous left ventricular volume was measured by a cardiometer in open-chest dogs whose right heart was completely bypassed. A multitude of pressure-volume relationships under various preload, afterload, inotropism and heart rate were generally formulated by $p(t)=e(t)\{v(t)-v_d\}$. $e(t)$ is instantaneous ventricular pressure/volume ratio, $p(t)$ and $v(t)$ left ventricular pressure and volume, and v_d a constant volume below which the ventricle can not develop any systolic pressure. It was empirically found that the $e(t)$ in any ventricular contraction could be normalized with respect to a control $e_o(t)$, which was determined under a control inotropism and heart rate, by a general form: $e(t)=ae_o(bt)$. Both a and b increased or decreased as the inotropic state was enhanced or depressed. Only b increased with heart rate. This pressure/volume ratio was then mathematically correlated with myocardial force (F)-velocity (V_{ce}) relationship by the use of a myocardial two-element model and geometrical models of the ventricle. It was shown that $F(t)=aHe_o(bt)$ and $V_{ce}=bK\{de_o(x)/dx\}e_o(bt)$ with $x=bt$. Both H and K are functions of $v(t)$, specific to a type of the geometric model used and a mode of afterload. The F-V curves mathematically derived from $e(t)$ were similar in shape to the experimentally established F-V curves. The characteristic shifts of the F-V curve by changes in inotropism, heart rate and preload reported in literatures were reproduced in the above formula by the experimentally observed range of variations in a, b, H and K. On these bases, $e(t)$ is concluded to express explicitly the dynamic characteristics of myocardial contraction as well as the contractile state of the ventricular chamber.

EFFECT OF ANGIOTENSIN II ON ACTIVITY OF THE SYMPATHETIC NERVOUS SYSTEM.
T. Suga*, W.M. Manger and T. Reich*, Institute of Rehabilitation Medicine and Departments of Medicine and Surgery, N.Y.U. Medical Center, New York, N.Y.

It has been suggested that some type of interaction may exist between angiotensin II (A) and the sympathetic nervous system. To evaluate such an interaction, A was injected (25-300 ng/Kg) and infused (5-500 ng/Kg/min) into the vertebral artery and femoral vein of chloralose anesthetized cats and unanesthetized cats immobilized with Flaxedil. No increase in spontaneous discharge occurred in the splanchnic nerve following administration of A. Elevation of blood pressure (BP) induced by A caused a decrease in splanchnic nerve discharge and an increase in spontaneous discharge in the vagus nerve, similar to that induced by equipressor doses of norepinephrine. Furthermore, no remarkable or consistent changes occured in the electroencephalograms recorded from bipolar depth electrodes in the pressor and depressor areas respectively in the hypothalamus and medulla oblongata. No remarkable potentiation of the BP response to stimulation (3-10 volts for 10-20 seconds) of these pressor areas was observed during A infusion. The results do not support the concept that the vasopressor action of A is due to activation or potentiation of the central sympathetic nervous system in the cat.

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SIMULATION IN NORMAL TISSUE OF THE PROPERTIES FOUND IN IRREVERSIBLE DIFFUSE OBSTRUCTIVE PULMONARY SYNDROMES ($DOPS_I$).
T. Sugihara* and C. J. Martin. Inst. Resp. Physiol., Virginia Mason Res. Ctr. and Firland Hospital, Seattle, Wash.

We have shown that lung tissue from the aged and patients with $DOPS_I$ (clinical emphysema) have a decreased maximum extensibility ($\lambda_{max} = L_{max}/L_o$) and discussed the evidence for believing this to be due to an increase in the resting length of the tissue (J. Appl. Physiol. In press). The changes in $DOPS_I$ are significantly greater than in those without DOPS of the same age. Means of simulating this permanent deformation are under investigation. The length-tension (L-T) relationships of cat lung tissue (ca 30 x 30 x 200 μ) were measured in a 100 cc bath filled with a buffer solution controlled as to pH and temperature. Control tracings were obtained following which selected enzymes (elastase, trypsin, collagenase, hyaluronidase) were added. L-T curves were repeated at 15 to 30 min. intervals. A decrease in the breaking force of this tissue was particularly marked in tissues exposed to colleganase. An increase in the resting or unstressed length was demonstrated by elastase. All these enzymes except hyaluronidase increased the compliance of alveolar wall, or reduced the force necessary to reach a given extension. Such a change in tissue properties would reduce the elastic recoil of intact lung. Elastase more closely simulated the effects of aging and $DOPS_I$ through its effect upon tissue compliance and altered resting length.

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SUPPRESSION OF CELL FIRING IN THE SUBSTANTIA NIGRA BY CAUDATE STIMULATION. Jerome Sutin and John McNair*. Dept. of Anatomy, Emory Univ. School of Medicine, Atlanta, Ga.

Cats anesthetized with barbiturates show a unique 8-12/sec continuous rhythmic activity in the subthalamic nucleus and ventral tegmental area which is correlated with the "barbiturate tremor". Pallidal stimulation inhibits subthalamic nucleus slow wave and single unit activity, while nigral stimulation produces a phasic discharge in subthalamic neurons. In contrast to pallidal stimulation, caudate stimulation does not inhibit the firing of subthalamic nucleus cells. In view of this and the action of the substantia nigra upon the subthalamic nucleus, we studied the effects of caudate activation upon extracellularly recorded single unit responses in the nigra of barbiturate anesthetized cats. A total of 51 units were analyzed. Of these, 24 were localized to the tegmentum just above the substantia nigra, 25 in the nigra, and 2 in the cerebral peduncle. The predominant effect of single caudate stimuli was suppression of firing of nigral (95%) or tegmental (58%) cells for either 70 or 150 msec, or more. These effects were seen in both medial and lateral portions of the nigra, and at rostral and caudal levels of the nucleus. No short latency spikes were seen in nigral cells following caudate stimulation, and only a few in units localized to the tegmentum. In the barbiturate anesthetized cat, caudate stimulation leads to a suppression of firing of cells throughout the substantia nigra. Aided by NINDS Grant NS06948.

EFFECTS OF CATECHOLAMINES ON THE MESENTERIC CIRCULATIONS OF DOG AND MONKEY. K.G.Swan, R.W.Barton* and D.G.Reynolds*. WRAIR, Washington, D.C.

Recent studies of the mesenteric circulatory responses to endotoxemia indicate that a species difference exists between dog and subhuman primate (Brobmann, Am.J.Physiol., 1970 and Swan, Gastroenterology, 1971). The present study was designed to compare the effects of norepinephrine (NE) and epinephrine (E) upon mesenteric arterial blood flow (MBF) in anesthetized dogs and baboons. MBF was measured with an electromagnetic flowmeter. Arterial and portal venous pressures were monitored. NE and E were administered through a catheter placed in the first branch of the superior mesenteric artery. Under these circumstances injections of either NE or E, in doses ranging logarithmically from 10^{-3} to 10^{0} $\mu g\ kg^{-1}$ (base), caused a progressively increasing vasoconstrictor response in the dog. At 10^{-2} $\mu g\ kg^{-1}$ NE decreased MBF 140 $\pm$ 10 (S.E.) ml min^{-1} below control (310 $\pm$ 25 ml min^{-1}). At the same dose E caused significantly less ($p<.01$) vasoconstriction (100 $\pm$ 10 ml min^{-1} below control). Infusions of NE and E (0.5 $\mu g\ kg^{-1} min^{-1}$) caused a vasoconstrictor response characterized by autoregulatory escape within minutes. Escape occurred more rapidly with E. In the baboon NE was a vasoconstrictor at all doses of injections. At 10^{-2} $\mu g\ kg^{-1}$ E caused an increase in MBF (20 $\pm$ 25 ml min^{-1} above control). At higher doses E was a vasoconstrictor. Infusions of both drugs caused vasoconstriction in the primate gut. Autoregulatory escape occurred near the end of the infusions. Although the endogenous catecholamines are vasoconstrictors in the gut of dog and baboon the responses are sufficiently different to support the theory that a species difference does exist which may account for some of the observed differences in the mesenteric circulations of the dog and monkey during experimental shock.

PREMATURE DELIVERY WITHOUT ACCELERATED LUNG MATURATION IN FETAL LAMBS TREATED WITH LONG ACTING CORTICOSTEROID. H. William Taeusch, Jr.*, Joseph Sugg*, Richard Catchlove* and Mary E. Avery. Department of Pediatrics, Anesthesia, and Physiology, McGill University, Montreal.

In 1968, Liggins demonstrated that ACTH, hydrocortisone, and dexamethasone induced premature delivery when administered to fetal lambs (J. Endocr. 42:323, 1968, and 45:515, 1969). DeLemos et al., showed that hydrocortisone infusions could also accelerate lung maturation in fetal lambs. (Am. Rev. Resp. Dis. 102:459, 1970). To study these effects, six lamb fetuses of approximately 125 days gestation were injected while in utero with a single intramuscular dose of 80 mg of methylprednisolone acetate in a glycol base. Five control fetuses were similarly injected with saline. All of the steroid injected fetuses were delivered spontaneously within 85 hours of injection. None of the controls were delivered within 10 days of injection. When compared to a group of non-injected fetuses of similar gestational age, the steroid injected fetuses had no acceleration of lung maturity as measured by lung weight, pressure volume deflation curves, minimum surface tension, wet weight/dry weight ratios, and distensibility. These findings indicate an ability to separate two previously described effects of fetal corticosteroid administration by the use of methylprednisolone.

DECREASED FOOD INTAKE AS MAIN CAUSE OF GROWTH RETARDATION (GR) IN EXPERIMENTAL PULMONARY STENOSIS (EPS) IN RATS. Yet-Sim Tan* and Hugh A. Lindsay. Dept. Physiology & Biophysics, W. Va. University Medical Center, Morgantown, W. Va. 26506

Wet and dry body weight, body and femur length, food intake, food consumption (food intake-fecal output), nitrogen consumption, presence of congestive heart failure, activity index, and hematocrit were determined in 38 albino rats with EPS. The main pulmonary artery was banded at 21 days with tantalum rings 0.75 (T), 0.85 (M) and 0.95 (L) I.D. There were 19 unoperated controls and 17 rats pairfed (PF) with the M group. GR manifested in all EPS rats as decreased wet and dry body weight, body and femur length ($P < .001$). The severity of GR increased with decreased band size. GR was present in every EPS rat although 40% of them showed no signs of congestive heart failure at autopsy. The decreased body weight in the EPS rats was significant by the third week when decreased food intake became significant. Decreased food consumption became significant one week later, suggesting compensatory improved absorption during this period. Nitrogen consumption was the same in the M and PF groups, tending to negate deficient absorption as cause of GR in EPS. Activity was greater in group PF than in M, and thus could not account for GR in the EPS rats. Increased hematocrit, reflecting hypoxia, was seen only in the T group ($P < .001$). Mean body weight was arithmetically less in group PF than in M; this trend was probably real but too small to show statistically and was probably accounted for by increased activity in the pairfed rats. Thus, GR in EPS is due to decreased food intake mainly, worsened by heart failure and hypoxia. (Supported in part by NIH Grant HD02919)

DYNAMIC STIFFNESS OF PAPILLARY MUSCLE DURING CONTRACTION AND RELAXATION. G.H. Templeton*, T.C. Donald, III*, J.H. Mitchell, and L.L. Hefner. Depts. of Physiol. & Med., U. Tex. Southwestern Med. Sch. at Dallas, Dallas, Texas; and Dept. of Med., U. Alabama Med. Sch., Birmingham, Alabama.

Use has been made of a sinusoidal forcing function to investigate the dynamic mechanical properties of a feline papillary muscle preparation. Sinusoidal length changes (ΔL) of less than 0.6% Lmax in amplitude, at frequencies of 10 and 30 Hertz (Hz), were induced in 5 papillary muscles contracting isometrically. The resulting sinusoidal tension changes (ΔT) were measured during contraction and relaxation. A linear relation between stiffness ($\Delta T/\Delta L$) and tension (T) was present throughout the contraction-relaxation cycle in the control state. That relation was unaltered by changes in preload, rate of contraction, or Ca^{++} level while the perturbation frequency was held constant. When the perturbation frequency was increased from 10 to 30 Hz a significant increase in stiffness for any given tension occurred, with the increase being greater during contraction. Thus, measured stiffness at any given tension is independent of the inotropic state or length of the muscle; it is dependent, however, on the rate of change of L and T, suggesting that a sinusoidal forcing function will be useful in characterizing the dynamic mechanical properties of cardiac muscle. The results of this *in vitro* study are comparable to our previously reported results obtained with intact hearts *in vivo* subjected to sinusoidally-induced changes in volume.

EFFECT OF ADRENALECTOMY ON A CIRCADIAN RHYTHM IN THE MULTIPLE-UNIT ACTIVITY (MUA) OF HYPOTHALAMIC AND PREOPTIC NEURONS IN THE FEMALE RAT. J. Terkel*, J. H. Johnson*, D. I. Whitmoyer* and C. H. Sawyer. Department of Anatomy and Brain Research Institute, UCLA, Los Angeles 90024.

A method of recording MUA in the freely moving rat has recently been developed in our laboratory. With chronically implanted bipolar (70 μ) stainless steel electrodes we have recorded integrated MUA simultaneously from the hypothalamus and preoptic area (POA) for several consecutive days. MUA varied with the sleep-wakefulness cycle and was highest during paradoxical sleep. A circadian rhythm, independent of sleep-wakefulness changes, was observed in most animals with electrodes in the basal hypothalamus and POA. This diurnal rhythm consisted of two stable levels of MUA, the higher of which was maintained during the dark period (1900-0500). The shift from one level to the other developed over a period of about 2 hr in close relationship with light changes (14L:10D) but not triggered directly by light or darkness. The diurnal rhythm was observed consistently in the preoptic area (10 cases), the basal hypothalamus (VMH - 5 cases), the anterior hypothalamus (AHA - 4 cases) and the septum-diagonal band of Broca (3 cases). It was not affected by estrous cycles, ovariectomy or treatment with exogenous estrogen. Neither prolactin nor LH affected it. However, following adrenalectomy the circadian rhythm disappeared from POA (4 cases), AHA and VMH in the 5 animals treated to date. Attempts are now being made to restore the circadian rhythm in adrenalectomized animals by continuous infusion of corticosterone, mimicking the normal diurnal variations of this steroid in the blood. (Supported by grants from the Ford Foundation, NIH NB 01162 and the American Medical Association Education and Research Foundation.)

EFFECTS OF MERCURY COMPOUNDS ON THE GENERATION TIME OF TETRAHYMENA PYRIFORMIS. J. D. Thrasher, J. Adams (intr. by R. S. Pogrund). UCLA School of Public Health, Los Angeles, California.

The effects of four mercury compounds [methyl HgCl (MMC), Phenyl Hg Ac (PMA), Ethyl HgCl (EMC) and $HgCl_2$(HC)] on the generation time (G.T.) of T. pyriformis WH14 were studied. T. pyriformis were cultured in 1% proteose peptone, acetate-phosphate buffer (pH 7.2) at 34°C in 250 ml flasks. The mercury compounds were tested in the following concentrations by addition to the growth medium: MMC (0 to 0.30 mg/l), PMA (0 to 0.54 mg/l), EMC (0 to 0.36 mg/l) and HC (0 to 5.3 mg/l). MMC was the most toxic of the four compounds tested. The G.T. increased by 36% at .042 mg/l, 50% at 0.074 mg/l, 100% at 0.14 mg/l and 100% death at 0.30 mg/l. Similar effects of PMC occurred at 0.108, 0.215, 0.430 and > 0.54 mg/l; of EMC at 0.06, 0.08, 0.20 and > 0.36 mg/l; and HC at 2.3, 3.0, 4.5 and > 5.3 mg/l. The order of toxicity on a Molar basis was MMC, PMC, EMC and HC. MMC and EMC form mercaptides, and, therefore, their primary action probably inhibits S-S bonds in microtubular proteins of cilia and the mitotic apparatus. PMC may interfere with the formation of secondary bonds of these proteins.

IONS RESPONSIBLE FOR NET FLUID SECRETION AT TWO DIFFERENT LEVELS OF CANINE SMALL INTESTINE. C.S. Tidball, B.B. Bon* and R.W. Barton*. Dept. of Physiology, George Washington Univ. Med. Ctr. and Dept. of Gastroenterology, Div. of Medicine, Walter Reed Army Inst. Res., Washington, DC.

Reproducible net fluid accumulation (secretion) into the lumen of the small intestine was brought about by experimental obstruction (Shields, Brit. J. Surg. 52:774-779, 1965). Surgically, the jejunum or the ileum was transected; the cut ends were closed with hemostatic and inverting sutures. After 48-120 hours of recovery, the abdomen was reopened under pentobarbital anesthesia. The bowel above the obstruction was distended but appeared otherwise normal. 25 cm segments above and below the obstruction were isolated, flushed with saline, and filled with isotonic glucose-saline-bicarbonate. Whereas loops below the obstruction always had net fluid losses, loops above the obstruction invariably exhibited secretion. By modification of chemical gradients and measurement of electrical potential differences between mucosal and serosal surfaces it was possible to identify the mechanism of transport for the principle ions involved. In jejunum only Cl^- entered the loop by active transport during secretion. In ileum only HCO_3^- entered the loop by active transport during secretion. The results suggest that the dog responds to the same stimulus (intestinal obstruction) by invoking active transport of two different ions at higher and lower levels in the small intestine.

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CELLULAR CALCIUM AND MAGNESIUM ALTERATIONS ASSOCIATED WITH HISTAMINE RELEASE FROM RABBIT PLATELETS. M.E. Tidball and R.W. Scherer*. Dept. Physiol., The George Washington Univ. Med. Ctr., Washington, DC.

Rabbit platelet histamine, Ca^{++} and Mg^{++} were measured at regular time intervals during histamine release and under conditions previously reported to be inhibitory to histamine release. In controls, histamine was completely released by 45 min; platelets first gained and then lost Ca^{++}; and platelet Mg^{++} efflux closely paralleled histamine release. When buffered EDTA was added to the control medium after 30 min of incubation it did not alter these findings. Incubation in a Ca^{++}-free medium resulted in a markedly delayed onset of histamine release; however, once release began it continued to completion and was accompanied by Mg^{++} efflux but no net movement of Ca^{++}. If acetazolamide was added to the Ca^{++}-free medium before the delayed onset of release, no histamine or Mg^{++} left the platelet and platelet Ca^{++} remained at a low level. The results indicate that Ca^{++} uptake enhances histamine release but is not obligatory; that platelet Mg^{++} and histamine translocations are interdependent under both release and non-release conditions; and that carbonic anhydrase inhibition occurs by a means unrelated either to Ca^{++} uptake or to the relationship between histamine and Mg^{++}. The mechanism for histamine release in the rabbit platelet thus appears to be Ca^{++}-sensitive, Mg^{++}-dependent, and contingent upon intact intracellular pH regulation.

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EVALUATION OF TRAINING AND DETRAINING EFFECTS IN DOGS. Charles M. Tipton, William C. Eastin* and Rita A. Carey*, Exercise Physiology Laboratory, University of Iowa, Iowa City, Iowa 52240

Selected changes associated with training and detraining were evaluated using a 7-stage (21 minute) sub-maximal treadmill (TM) exercise test. Venous blood measurements for free fatty acids (FFA), glucose (G), lactate (L), pyruvate (P), hemoglobin (Hb), and hematocrit (Hct) levels were obtained before and after the exercise bout. The speed remained constant at 6.4 km/hr. while the grade was progressively elevated until a maximum of 20% was achieved. Heart rates (HR) were obtained before, during and after the test. In addition, training effects were evaluated by a resting HR response to an injection (IV) of atropine sulfate (200 µg/Kg.). Pre and post exercise results ($\bar{X}$ and SEM) from 23 "normal" male dogs were; HR: 73 $\pm$ 3 - 233 $\pm$ 5, L: 1.73 $\pm$ .13 - 2.40 $\pm$ .28 mM/L, P: 0.11 $\pm$ .01 - 0.18 $\pm$ .02 mM/L, G: 83 $\pm$ 4 - 79 $\pm$ 5 mg/100 ml, FFA: 402 $\pm$ 40 - 652 $\pm$ 74 µeq/L, Hct: 40 $\pm$ 1 - 43 $\pm$ 1%, Hb: 13 $\pm$ .3 - 15 $\pm$ .4 gm/100 ml. Eleven non-trained dogs repeated the exercise HR test 4 weeks later and correlation coefficients ranged from .41 to .86 for stages 3 to 7. The peak HR response to atropine was 234 $\pm$ 5. Dogs were trained (T, N=8) for 8-10 weeks by running on a TM for 1-1.5 hrs/day and then detrained for 4-6 weeks. When compared to the nontrained controls, T animals had consistently lower resting HR, significantly lower exercise HR, lower post-exercise L values, and less cardiac acceleration after atropine. The other measures did not effectively differentiate the two groups. Since these differences were absent after detraining, it was concluded that the exercise HR and atropine test procedures were suitable for identifying group changes associated with training. (Supported by funds from USAF School of Aerospace Medicine.)

REFLEX INHIBITION OF ABDOMINAL MUSCLES DURING GASTRIC DISTENTION.
Edmund Y. Tong and D. T. Tjioe (intr. by - W. B. Youmans), Department of Physiology, University of Wisconsin, Madison, Wisconsin.

We have demonstrated decreased electromyographic activity in the external oblique abdominal muscles during distention of the stomach by inflation of a balloon with a pressure of 18-40 mm Hg in twenty dogs anesthetized with sodium pentobarbital. The same or greater inhibition occurred during gastric distention in each of six of these animals which was tested after laparotomy in which case there was little or no concomitant rise in the intraabdominal pressure. In acute experiments on animals with abdomen opened and having the greater and lesser splanchnic nerves sectioned and the abdominal sympathetic chains removed bilaterally there was an increase in activity of the abdominal muscles during gastric distention. This may have been a manifestation of the muscle stretch reflex. After vagotomy only at the mid-cervical level in animals with abdomen intact or after laparotomy the reflex inhibition was still present. On the other hand, in two chronically abdominally sympathectomized dogs the augmentation of tonus of the abdominal muscles in response to gastric distention did not appear until both vagi had been sectioned. It is concluded that a gastroabdominal inhibitory reflex is elicited by gastric distention and afferent impulses are carried mainly through the thoracic system, but a less important vagal afferent pathway also appears to be involved.

THE ROLE OF MACROPHAGES IN IRON TRANSPORT TO PREIMPLANTED BLASTOCYSTS IN THE BITCH.
C. A. TORBIT*, J. H. ABEL*, and W. J. TIETZ.
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A positive reaction for ferric iron has been obtained in macrophage cells within the myometrial and endometrial connective tissues of pregnant dogs. During early metestrus iron bearing macrophages gradually accumulate in the regions of future trophoblastic invasion. These cells occur in their greatest concentration just prior to implantation. As invasion begins a large number of the macrophages are found closely associated with the basement membrane of uterine glands. At the same time a positive iron reaction is observed in intercellular channels, in the apices of glandular epithelial cells and in their secretions. After implantation very few iron bearing cells are evident. Autoradiographic time course studies using intravenous injections of radioactive ^{55}Fe indicate: (1) macrophages facilitate the transport of iron to the uterine glands prior to invasion; (2) during the early stages of invasion iron is transferred directly from newly developed capillaries to and through uterine glands; and (3) after invasion is complete iron is transferred directly from the maternal blood to embryonic membranes at the polar hematomas. (This investigation was supported in part by a National Institutes of Health Fellowship (5 F01 GM 35121-04) from the General Medical Sciences Division.)

EFFECT OF DIETHYLSTILBESTROL (DES) ON THE INTRAVASCULAR CLEARANCE, TISSUE DISTRIBUTION AND DETOXIFICATION OF S. ENTERITIDIS ENDOTOXIN. Rafael A. Trejo*, Leland D. Loose*, and N. R. Di Luzio. Dept. Physiol. Tulane Univ. School of Med., New Orleans, La.

Previous studies indicate that resistance to endotoxins is largely dependent upon the population and functional status of reticuloendothelial (RE) cells. The present study was undertaken to evaluate the influence of DES, an agent which profoundly enhances phagocytic activity, on the intravascular removal rate of ^{51}Cr-labeled S. enteritidis endotoxin and on endotoxin detoxification by liver and spleen. The phagocytic activity in DES-treated mice was increased approximately 8 fold due to an enhancement of hepatic uptake of the "RE test lipid" emulsion. DES treatment also significantly enhanced the removal rate of S. enteritidis endotoxin as indicated by a t/2 of 51.0 min. vs 96.0 min. in the controls. The enhanced removal rate was attributed to an increased uptake by liver and spleen. Liver and spleen homogenates prepared from normal mice possessed significant endotoxin detoxifying activity as bioassayed in Actinomycin D-treated mice. Endotoxin detoxification was not altered by DES treatment. Susceptibility of DES-treated mice to the lethal effect of endotoxin was similar to the control group. These results indicate that while DES significantly enhances the phagocytic activity of the RES, it does not modify inactivation of endotoxin by liver and spleen. The normal susceptibility of DES-treated animals to endotoxin is in marked contrast to the enhanced susceptibility noted with other RES stimulants. These studies indicate that host defense against bacterial endotoxins is mainly concerned with a macrophage intracellular event, such as endotoxin detoxification, rather than phagocytosis per se. (Supported in part by the American Heart Association).

EVIDENCE OF THE AUTOMATICITY OF THE CANINE A-V NODE. W. W. F. Tse (intr. by - L. D. Davis), Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Spontaneously discharging canine A-V nodal preparations in which the A-V node was exposed were immersed in Tyrode's solution. Action potentials of single fibers of the A-V node and adjacent tissues were registered by conventional microelectrode techniques. Action potentials from fibers in the middle and lower node were identical and characterized by an amplitude ranging from 55 to 90 mv (mean 72 ± 12 S.E.M./min) and a duration of about 300 ms. These fibers also had inherent steep diastolic depolarization. Many fibers had a smooth gradual transition from phase 4 to phase 0 which is a characteristic of true pacemaker fibers. Artificial stimulation faster than the intrinsic rate caused an abrupt onset of phase 0. Cessation of artificial stimulation again resulted in spontaneous discharge of the fibers. Simultaneous recordings from the A-V node and His bundle showed that discharge of the A-V node preceded that of the His bundle in each of 7 experiments. After transection of the tissue between the A-V node and His bundle each area discharged independently. In 5 of 7 hearts the A-V nodal rate of discharge was higher than the His bundle. In one instance no difference in rate was noted, while in one instance the His bundle discharged faster. In conclusion, automaticity probably is a property of the canine A-V node.

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THE DISTRIBUTION OF VENTILATION IN CLINICAL EMPHYSEMA. S. Tsunoda* and A. C. Young. Inst. Resp. Physiol. Firland Hosp. and Virginia Mason Res. Ctr., Univ. of Wash., Seattle, Wash.

Uneven ventilation ($\Delta V/Vo$) of the human lung is often assessed from a nitrogen washout. Such analyses usually group units having similar alveolar dilution ratios ($ADR = FN_{2_{i+1}}/FN_{2_i}$) into compartments and determine their volumes. We have previously described an analog which determines such compartmental ADR's and the contribution of each to the expired gas concentration.* By selecting nitrogen concentrations at specific expired volumes, the changing contributions of the compartments to the expirate can be assessed. Dead space is treated as one compartment in this model ($ADR = 0$) accepting that all the nitrogen is swept from this compartment in inspiration. We can then describe the pattern of emptying of the dead space and the various lung compartments as well as the compartmental expired volumes and their initial volumes (FRC). Patients with clinical emphysema have uneven ventilation and measures of dead space volume (V_D) are uncertain using single breath techniques. We have used the sequential analog to study 20 patients with clinical emphysema and found the dispersion of $\Delta V/Vo$ was increased over that found in normal subjects of the same age. In all, the dead space delivery was prolonged and in none did it empty completely before end-expiration. V_D was significantly increased in these patients as was FRC. There was, however, no significant difference in the V_D/FRC ratio between normals and those with clinical emphysema.

*Ref. Physiologist, Vol. 13, No. 3, August 1970.

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CONTRIBUTION OF TACHYCARDIA TO THE CORONARY DYNAMIC RESPONSE TO SEVERE EXERCISE IN UNTETHERED DOGS. Stephen F. Vatner*, Charles B. Higgins*, Dean Franklin and Eugene Braunwald. U. of Calif., San Diego and Scripps Clinic and Research Foundation, La Jolla, California.

In order to define the contribution of tachycardia to the response of the coronary circulation in severe exercise, measurements of coronary flow (CF) and arterial pressure (AP) were telemetered from normal, healthy dogs as they ran 15-25 mph behind a mobile recording unit in the field for distances averaging 1.5 miles. The dogs had recovered from implantation of Doppler ultrasonic flow probes on the left circumflex coronary artery, miniature pressure gauges in the aorta and stimulating electrodes on the left atrium. In 11 normal dogs severe exercise increased HR from 77 to 244/min, AP from 91 to 135 mm Hg, CF from 38 to 124 ml/min and decreased coronary resistance (CR) from 2.34 to 1.10 mm Hg/ml/min. The role of tachycardia in the coronary hemodynamic response was elucidated by restudying the response to exercise after raising heart rate (HR) at rest with atrial pacing to exercise levels and in other dogs by preventing exercise tachycardia with surgically induced A-V block. Atrial pacing to exercise levels in 6 dogs increased CF from 40 to 69 ml/min, and decreased CR from 2.34 to 1.37 mm Hg/ml/min, while AP remained constant. With heart rate constant exercise further increased CF to 121 ml/min and decreased CR to 1.03 mm Hg/ml/min. In 3 heart block dogs exercise increased HR from 42 to 76/min, CF from 29 to 60 ml/min and decreased CR from 2.78 to 1.38 mm Hg/ml/min while AP remained constant. Thus, tachycardia accounts for approximately one-third of the increment in CF and three-fourths of the reduction in CR during severe exercise. The additional changes in CF and CR are presumably related to alterations in inotropic state and arterial pressure that also occur during exercise.

EFFECT OF MSH ON THE SOMATIC EVOKED RESPONSES. Marcos Velasco and Abba J. Kastin. Research Department, National Medical Center, IMSS. México, D. F. and Department of Medicine, Tulane University Med. School, New Orleans, La.

The present investigation is concerned with the effect of melanocyte-stimulating hormone (MSH) on the processes of general alertness and selective attention in man by means of the analysis of the somatic evoked response (SER) and other related electrophysiological parameters. In 7 hypophysectomized and 2 normal patients SER was produced by electrical stimulation of the median nerve and recorded at the somato sensory projection and vertex skull regions. Changes in amplitude of the various SER components were studied before and after I.V. injection of synthetic MSH to patients in 3 different conditions: 1) awake and relaxed, 2) general alertness, 3) specific attention. Prior to MSH injection, the late components of SER of the relaxed patient (peaking 90 and 230 msec.) increase amplitude with specific attention and decrease during general alertness. After MSH injection these components were larger during relaxation and specific attention and smaller during general alertness than the previous controls. Concomitantly, the spontaneous EEG activity was synchronized and the reaction time faster, while the afferent nerve potential and the SER's earlier components were unchanged. Since injection of equivalent amounts of other hormones did not produce any significant change, it was assumed that MSH may have a specific role in the process of human selective attention.

EFFECT OF HYPOXIA, HYPERCAPNIA, AND ISCHEMIA ON BLOOD-BRAIN BARRIER PERMEABILITY. Lester A. Wade* and Alan M. Thompson. Kansas Univ. Med. Ctr., Kansas City, Kansas.

A rat head-perfusion technique (J. Appl. Physiol. 24:407,1968) was used to investigate the effect of several metabolically important perfusate conditions on rate of uptake of materials across the blood-brain barrier (BBB). Terminal tissue and venous plasma isotope concentrations were determined after perfusions for 5,10,20,30, and 45 minutes. Most results were expressed as the rate of increase of tissue/plasma concentrations (T/P ratio) after the first five minutes (ml H_2O/g tissue/min). This was assumed to be a measure of BBB permeability. Under control perfusion conditions, each of four regions of the brain took up urea-^{14}C at the same rate after five minutes, although there were differences of 0.01 to 0.04 ml/g in absolute T/P ratios due to more rapid initial uptake in cerebellum and brain stem than in cerebral hemispheres and diencephalon. These differences appear to be partly, but not entirely, due to differences in vascular volume, as indicated by RIHSA and inulin-^{3}H. Hypercapnia (mean Pa_{CO_2}=120 mm Hg) significantly increased the rate of urea uptake of whole brain from 0.0054±0.0003 to 0.0080± 0.0008 ml/g/min. Essentially the same increase occurred in all four regions of the brain and the same regional differences in T/P ratio occurred as in controls. Hypoxia alone (mean Pa_{O_2}=15 mm Hg) had no effect on urea uptake (0.0060 ± 0.0005 ml/g/min). Perfusion for ten minutes under normal conditions, but after two or more hours of ischemia, increased the urea T/P ratio from 0.094± 0.004 to 0.148± 0.016, while the RIHSA T/P ratio increased from 0.018 ± 0.001 to only 0.028 ± 0.002 ml/g. Maintenance of the blood-brain barrier does not appear to depend directly upon an energy source, but is affected by metabolic parameters. (Supported in part by USPHS, NIH grant NS-07059).

Acclimatization of Pre- and Postpubertal Boys to Work in the Heat. J. Wagner*, S. Robinson and S. Tzankoff*. Indiana Univ., Bloomington, Ind. 47401

Three groups of male subjects (ages 11-14, 15-16 and 25-30) were exposed to 45 to 90-minute treadmill walks at 5.6 km/hr on the level in dry heat for 8 consecutive days. The experiments were terminated after 90 minutes or when the rectal temperature (T_{re}) reached approximately 39.0°C in the boys or 39.5°C in the young men. The results of the first and eighth walks (49°C db, 26.6°C wb) can be summarized as follows:

	Unacclimatized			Acclimatized		
Age (yrs)	11-14	15-16	25-30	11-14	15-16	25-30
Duration (min)	50	67	79	90	90	90
T_{re}, initial (°C)	37.8	37.9	37.4	37.6	37.5	37.3
T_{re}, final (°C)	39.1	39.1	39.2	38.7	38.4	38.4
T_s, final (°C)	38.1	37.9	37.8	37.1	36.8	36.5
Heart rate	160	160	160	146	131	129
Evap. (kcal/m^2·hr)	265	318	321	323	346	350
MR (kcal/m^2·hr)	167	200	188	168	186	178

During the first walk the slope of the rise in mean T_{re} was similar for all of the groups and the higher initial T_{re} of the boys may partially explain the shorter mean duration of their first walks. After acclimatization the mean T_{re} for all groups approached a steady state during the final 30 minutes of the walk; consequently, the initial T_{re} had no effect on the duration of the eighth walk. Prepubertal boys substantially improved in their ability to regulate body temperature; however, they were handicapped both before and after acclimatization to work in the heat due to a limitation in the ability to sweat. (Supported by PHS Grant RO1 HD-4056-03.)

EFFECTS OF DIFFUSION IMPAIRMENT ON THE O_2 and CO_2 TIME COURSE ALONG PULMONARY CAPILLARIES. Peter D. Wagner* and John B. West. Dept. of Medicine, University of California, San Diego, La Jolla, California.

A modified Bohr integration procedure has been simultaneously applied to O_2 and CO_2 exchange along pulmonary capillaries allowing for chemical reaction rates, dissolved oxygen and interaction between the O_2 and CO_2 dissociation curves. Calculations were made over a large range of ventilation-perfusion ratios ($\dot{V}A/\dot{Q}$). The reaction of CO_2 with blood was taken to be exponential with a half time of 0.15 sec. When oxygen diffusing capacity (D_{LO_2}) fell below 15 ml/min/mm Hg, alveolar-endcapillary differences exceeded 1 mm Hg for both gases, with $\dot{V}CO_2$ being relatively more depressed than $\dot{V}O_2$ at $\dot{V}A/\dot{Q}$ values above 1.5. For example, at a $\dot{V}A/\dot{Q}$ of 10 and D_{LO_2} of 3 ml/min/mm Hg, the alveolar-endcapillary P_{O_2} difference was 79.7 mm Hg and that for CO_2 8.6 mm Hg, causing reductions of gas transfer of 18 and 22% respectively. For both gases diffusion impairment generally had relatively greater effects at higher $\dot{V}A/\dot{Q}$ values, the exception being a reduction in alveolar-endcapillary P_{O_2} difference at medium values of D_{LO_2}, which was ascribed to the shape of the O_2 dissociation curve. No such recovery occurred for CO_2. When the $\dot{V}A/\dot{Q}$ was less than 0.4 and F_{IO_2} greater than 0.6, endcapillary P_{CO_2} exceeded mixed venous P_{CO_2} by up to 5 mm Hg, while when $\dot{V}A/\dot{Q}$ was above 3 and F_{IO_2} normal or reduced, endcapillary P_{O_2} fell below mixed venous P_{O_2} by up to 3 mm Hg. Effects of pulsatile blood flow and a distribution of transit times were examined; the resulting impairment of $\dot{V}O_2$ and $\dot{V}CO_2$ compared with steady flow conditions was never more than 15% at any combination of D_{LO_2} and $\dot{V}A/\dot{Q}$.

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FEEDBACK CONTROL OF ALVEOLAR CO_2 VIA RESPIRATORY FREQUENCY. R.M. Weissberg*, A.L. Kunz, and M.S. Peery*. Department of Physiology, The Ohio State University College of Medicine, Columbus, Ohio 43214.

This laboratory reported at last year's A.P.S. Meetings about a preparation using a computer in the feedback loop of alveolar CO_2 control. It used an awake, unidirectionally-ventilated chicken preparation in which input gas flow was kept constant at 5 L/min (9x normal). Inspiratory % CO_2 was modulated as a function of frequency and depth of respiratory movements as monitored by a whole-body plethysmograph. The algorithm used for feedback was:

$$\% CO_2 \propto \int (\dot{Q} - k\bar{V}_T f)\, dt$$

where $\dot{Q}$ is the electronic analog of CO_2 production, k is a constant of proportionality, $\bar{V}_T$ is mean tidal volume and f is frequency. With this system the % CO_2 drifts up between breaths at the rate $\dot{Q}$ and is brought down with each breath proportionally to the tidal volume. This system seeks a stable equilibrium alveolar CO_2 level. When arbitrarily displaced from this equilibrium level appropriate changes occurred in respiratory movements to return alveolar CO_2 to this equilibrium level.

The experiments to be reported used basically the same preparation except a different algorithm was used to close the feedback loop:

$$\% CO_2 \propto \int (\dot{Q} - cf_e)\, dt$$

where $\dot{Q}$ is again the analog of CO_2 production, c the amount alveolar CO_2 is lowered with each breath that is greater than a set threshold, and f_e is the effective frequency, or number of breaths per min which trigger CO_2 lowering. This system was found to regulate alveolar CO_2 at a physiological level (3 to 5 %). The effects of different values for $\dot{Q}$, c and trigger level were examined. At higher values of $\dot{Q}$ regulation of alv. CO_2 was by frequency modulation; at lower values of $\dot{Q}$ regulation was accomplished by interspersing ineffective breaths (below threshold). (Supported in part by Office of Naval Research Grant N.R. 101-733.)

Myocardial metabolism during endotoxic shock. J.T. Weng,* A.A. Bechtel, J.J. Spitzer, and J.C. Scott. Hahnemann Medical College, Philadelphia, Pennsylvania.

The effects of endotoxin (E. coli) administration were studied in 8 closed-chest dogs under Nembutal anesthesia. Simultaneous arterial and coronary sinus blood samples (through catheter) were removed before, and 60 & 120 minutes after the injection of endotoxin (~LD 90). Mean arterial blood pressure and total body O_2 consumption (TBO_2) decreased markedly in 3 minutes following the injection, then gradually rose and leveled off at 50% and about 85% respectively. At both blood sampling periods cardiac output and coronary sinus blood flow were decreased (by 33 & 45% and 32 & 29% respectively). Heart rate remained unchanged. Arterial free fatty acid (FFA) concentration did not change significantly. Myocardial FFA uptake decreased by 35 & 22%, FFA oxidation by 53 & 51%, O_2 consumption by 41 & 45% at 60 & 120 minutes following endotoxin. Before endotoxin administration, 90% of the removed FFA was oxidized by the myocardium, following the toxin this figure dropped to 65 & 56%. Left ventricular O_2 consumption accounted for 10% of TBO_2 during the control period, and for 7 & 7% during shock. Arterial lactate increased, pH dropped. Myocardial lactate uptake remained high during both sampling periods. During endotoxic shock a shift was observed in myocardial metabolite utilization characterized by a more extensive reliance on blood lactate and a greatly diminished FFA oxidation. (Supported by Project Themis of the U.S. Navy and by NIH grants HE 04619 and HE 03130.)

EFFECT OF PHENOBARBITAL AND CATATOXIC STEROIDS ON HEPATIC MICROSOMAL MIXED FUNCTION OXIDATION REACTIONS AND CYTOCHROME P-450. J. Werringloer (intr. by H. Selye). Institut de médecine et de chirurgie expérimentales Université de Montréal, Montreal, Quebec, Canada.

In female rats, phenobarbital (PhB) and certain catatoxic steroids, such as spironolactone (SNL), SC-11927 (SC) and ethylestrenol (EE) (Selye, H.: J. Pharm. Sci. 60: 1, 1971) -- at the dose of 0.2 mM/kg p.o. twice daily for four days -- enhanced sex-dependent microsomal hexobarbital (HB) oxidation and ethylmorphine (EtM) N-demethylation. In male rats, SNL decreased the rate of HB metabolism, but stimulated EtM demethylation. Under the same conditions, PhB elicited a parallel increase of both these enzyme activities. SNL, unlike SC, EE and PhB, failed to stimulate sex-independent aniline (AN) p-hydroxylation or to increase cyt. P-450 content. Yet, like SC, it elicited a slight shift of the 450 mμ peak in the CO difference spectrum of this cytochrome to a lower wave length. In the ethyl isocyanide difference spectrum, a decrease of the ratio of the 455/430 mμ peak heights -- similar to that which occurs in male rats during maturation -- was observed in females in response to SNL, SC and even more to EE and PhB treatment. In male rats, SNL elicited an increase of this ratio, whereas PhB was ineffective. Changes in cyt. P-450 concentration and AN p-hydroxylation activity were closely related. HB oxidation was markedly affected by both cyt. P-450 concentration and qualitative changes as reflected by the ratios of the 455/430 mμ peak heights. No such relationships were observed for EtM demethylation. Thus, in rats, the variety of changes in drug metabolism induced by catatoxic steroids and PhB is not only influenced by quantitative but also by qualitative changes of cyt. P-450 which are in part related to the endogenous factors controlling the sex differences in microsomal mixed function oxidase activity. (Supported by the Ministère de la Santé, Québec.)

DISSIPATION OF BODY HEAT IN DOGS IN A CONTROLLED ENVIRONMENT. J. E. Woods* and E. L. Besch. Institute for Environ. Res., Col. Engg. and Dept. Physiol. Sci., Col. Vet Med., Kansas State University, Manhattan, Ks 66502

Four mature greyhound dogs, two male and two female, each with an average body weight of 22.7 kg. were confined, individually, in standard dog cages. These cages and dogs were placed in a controlled environment room and maintained under ambient conditions of 24°C, 50% relative humidity and 12 air changes per hour. Heat dissipation rates were determined for the group and calculated on an individual dog basis. Food and water were available ad libitum. The photoperiod was held constant at 24L:0D or at 0L:24D for a period of 24 hours prior to the collection of data. There were no significant differences in heat dissipation rates irrespective of photoperiod employed. Heat dissipation was found to be 11.15 Kcal/hour/sq. meter body surface area which is approximately three times the previously published standard metabolic rate. However, the ratios of actual heat dissipation to standard metabolic rate were found to be similar to previously reported data for other animals on ad lib feed and water. The sensible to total heat dissipation ratio of 0.52 in these dogs indicates similar latent and sensible heat dissipation rates as man at a medium level of activity. Further, these data suggest that heat dissipation rates in dogs or other animals will allow for the characterization of animal heat equivalents.

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SERUM ENZYME CHANGES IN CARDIAC DENERVATED DOGS AFTER STRESS. Kenneth E. Wozniak* and Arthur W. Merrick. Department of Biological Sciences, Illinois State University, Normal, Ill.

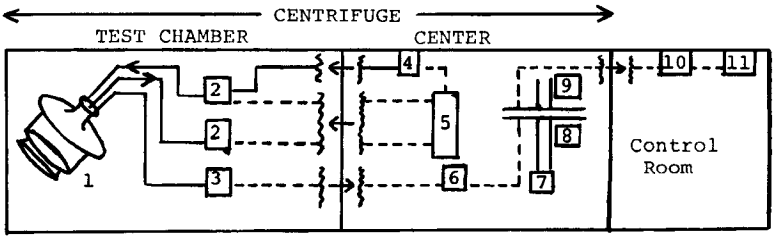
The effects of stress on several serum enzymes were investigated in dogs that had undergone extrinsic cardiac denervation. The stress was effected through an arteriovenous (A-V) shunt of the inferior vena cava and abdominal aorta just below the kidneys. Enzymes investigated were glutamic oxalacetic transaminase (SGOT), glutamic pyruvic transaminase (SGPT), alkaline phosphatase (AP), creatine phosphokinase (CPK), aldolase (A), malate dehydrogenase (MDH), alpha-hydroxybutyric dehydrogenase (α-HBD), and lactic dehydrogenase (LDH) and its isoenzymes. No attempt was made to place the A-V shunt until the effects of surgery on the serum enzymes was evaluated. The serum was analyzed 1, 3, 5, 7, 9, and 20 days following placement of the A-V shunt. SGOT, SGPT, AP, CPK, A, MDH, and total LDH were significantly elevated; α-HBD and the heart-type LDH remained within normal limits. We conclude from these results that although the shunt may place considerable stress on the right side of the heart, depending upon shunt size, the serum enzyme assay indicates there is no cardiac damage or necrosis. However, the serum enzyme changes do indicate liver involvement. (Supported by NHLI Grant HE-12452.)

ACCELERATED MATURATION OF FETAL RABBIT LUNGS BY THYROXINE. B.Wu*, Y.Kikkawa*, M.M.Orzalesi*, E.K.Motoyama, M.Kaibara*, C.J.Zigas* and C.D.Cook, Depts. of Ped. and Anesth., Yale Sch. of Med., New Haven and Dept. of Pathol., Albert Einstein Col. of Med., New York.

The maturation of the lung can be accelerated by administration of cortisol directly to the fetus (Kotas & Avery, 1970; Motoyama et al., 1970). Since thyroxine is known to stimulate growth, its effect on the development of fetal rabbit lung was evaluated. In a first series of experiments involving 26 pregnant does with known gestational days, 11 were given thyroxine intramuscularly (20-40 μg/day) and 15 were given saline for 2 days prior to premature delivery of fetuses by cesarean section at 26 to 28 days gestation (full term: 30 days). There was no significant difference in body weight, crown-rump (C-R) length, and in bubble stability ratio (BSR) of the lung wash in the fetuses from treated and control animals. In a second series of experiments of 20 pregnant does, thyroxine (1-2 μg/fetus) was injected directly into the fetuses and amniotic sacs in one uterine horn at 24 to 25 day gestation; saline was given to the fetuses in the other horn which served as controls. When delivered 2 days later, thyroxine treated fetuses in comparison to the controls showed a significantly ($P<.001$) higher BSR (mean difference in BSR = $0.271 \pm .06$ (SEM)), indicating increased surface activity although there was no appreciable difference in body weight, C-R length and lung weight. Electronmicroscopy revealed an increase in number of inclusion bodies and early disappearance of glycogen in the type II alveolar cells in the treated fetuses. Thus direct injection of thyroxine into fetal rabbits accelerates lung maturation. (Supported by: USPHS HD-03119, FR-05358, HD-02459; Grant-in-aid, N.Y. Heart Assoc. and Winchester Fund.)

MEASUREMENTS OF INCREASED O_2 INTAKE BY WHITE MICE CONTINUOUSLY CENTRIFUGED AT 7 G'S. C.C. Wunder, W.G. Fethke*, K.M. Cook* and S.M. Porter*, University of Iowa, Iowa City, and Coe College, Cedar Rapids, Iowa.

A 70% increase was noted for 4 mice centrifuged in a desiccator (1) isolated by solenoid valves (2), activated 6 times/day by a timer switch (5) which also inactivated an air pump (4) during 30 minute measurements of pressure drop with a transducer (3). Signal was frequency modulated at (6, Ia. Bioeng. Resource, Facility #252C) for telemetry at the centrifuge shaft (7) from a rotating condensor plate (8) to a stationary plate (9) and then electrically transmitted to a demodulator (10), and then to a recorder (11). After 3 days, O_2 volumes dropped toward control ones with subbaseline values on return to 1G after a week's exposure. Effects were less drastic at 2 and 4 G's with a consistent depression of day-night rhythm and decreased food intake.



INFLUENCE OF HEAD SKIN TEMPERATURES UPON TYMPANIC AND ORAL TEMPERATURES. Robert D. Wurster, Melburn W. Stocks* and Robert D. McCook. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Tympanic membrane and oral temperatures have been often used as correlates of both brain temperature and "core" temperature. In previous experiments heating the whole body, but not the head, of human subjects suggested that cutaneous head temperatures alter these central temperatures. In the present studies various regions of the head were unilaterally heated or cooled while bilateral tympanic membrane and deep sublingual temperatures were measured. Results suggest that a significant counter-current exchange occurs between descending cutaneous venous blood from the head skin and ascending arterial blood to the tympanic membrane and oral cavity. This exchange could affect the brain temperature significantly in cases where the face is exposed to extreme ambient temperatures. Such alterations in brain temperature could cause thermoregulatory responses. (Supported by NIH HE 08682 and GM 999)

MAZE LEARNING IN SPLIT-BRAIN MACAQUES. Kenichi Yamaga* and Robert W. Doty. Center for Brain Research, University of Rochester, Rochester, New York 14620.

In man the right hemisphere is dominant for analysis of spatial relations. The present experiments suggest that macaques are more variable in this regard. Four monkeys were trained in a 1.8 x 3.0 m maze with a transparent cover and 5 choice points. A criterion of 10 errorless consecutive passages required 30 - 200 trials. An opaque contact lens on one eye did not disturb performance, but covering both eyes produced severe confusion. After cutting optic chiasm, corpus callosum, psalterium and anterior commissure, performance was comparable with either eye open in two animals, best for right eye and brain in one, and for left eye and brain in the other. General visual behavior seemed equivalent for either eye in the latter two animals. One of these always used the left hand to take food; yet maze behavior was best with the left eye and became slow and confused when the right eye only or both eyes were open. This suggests that the less skillful, right hemisphere assumed dominance when both eyes were open. (Supported by NSF Grant GB-7522X1 and NIH Grant NS-03606)

EFFECT OF SIMULATED METABOLIC LOADING ON RESPIRATION. S.M. Yamashiro*, F.S. Grodins, and M. Gordon*. Biomed. Engr. Univ. of S. California, Los Angeles, California.

Controversy persists over the relative roles of neural and humoral factors which mediate the hyperpnea of exercise. Supporters of a primarily humoral theory feel that although there is no measureable change in steady-state chemical concentrations of respiratory stimulants during exercise, the dynamic pattern of these concentrations still remains as a possible explanation of this hyperpnea. We tested this hypothesis experimentally on nembutal anesthetized dogs by manipulating inspired gas mixture in such a way as to simulate metabolic loading. An oxygen and carbon dioxide load is used which is equivalent to that of exercise but introduced at a different point in the system. Respiratory responses were compared to that obtained by conventional inspired CO_2. Preliminary results suggest that fluctuations in blood gas concentrations provide independent respiratory stimuli since mean blood concentrations cannot completely explain responses to simulated metabolic loading.

Development of a Special Restraint to Enable Chronic Measurement of Cerebral Blood Flow in the Macaque Monkey. H.M. Yanof and J.G. Albernaz*, Medical College of Ohio at Toledo, Toledo, Ohio.

A surgical procedure was developed to measure blood flow through both vertebral and internal carotid arteries using the electromagnetic flowmeter. The authors have found that available methods for restraining the monkey, following implantation of the transducers, often failed. The restraint allows the monkey to move with relative freedom inside his cage while his cerebral blood flow is being measured. The restraint consists of a hard plastic jacket into which a Fafnir misallignment coupler has been fit. The coupler acts as a universal ball joint. A similar coupler is attached to the back of the cage and a length of 3/4" electrical conduit is welded to the coupler fittings. The jacket is fabricated using standard techniques as used by a prosthetist to make an artificial leg. The animal is first given a tranquilizer (Sernylan, Parke-Davis Co.) and then fitted with a body stocking. An orthopedic plaster cast is made of the monkey's thorax, being careful to hold him in the correct position. The cast is then removed from the monkey and put back together, using plaster gauze. The head and arm holes are closed. The cast, used as a mold, is filled with plaster. When hard, the original plaster mold is removed and finished. The back of the cast is built into the shape of a box and the flange of the coupler is attached. A Hosmer laminating jig and vacuum pump are then used to make a polystyrene impregnated dacron felt jacket. The jacket is adjusted to avoid bony highpoints and lined with foamed silastic rubber. When complete, cables and catheters may be inserted from the inside of the jacket to the outside of the cage through the electrical conduit. This technique can be used to form an extremely durable container of almost any shape. This jacket is but one example.
(Supported, in part, by Northwestern Ohio Chapter of the A.H.A.)

THE ROLE OF DEOXYCORTICOSTERONE ACETATE (DOCA) ON IMPLANTATION AND MAINTENANCE OF PREGNANCY IN OVARIECTOMIZED PREGNANT RATS. Shao-Yao Ying* and Roy O. Greep. Harvard Medical School, Boston, Mass.

Ovarian steroids in proper ratio and/or adequate amounts are necessary for the implantation of blastocysts and the maintenance of pregnancy in ovariectomized pregnant rats. However, the role of corticoids has not been studied. Thus adult female rats ovariectomized on day 3 of pregnancy and treated with a daily dose of 4 mg DOCA and a single injection of 0.25 μg estradiol-17β given two days after ovariectomy produced implantation. The induction of implantation and maintenance of early pregnancy were obtained with daily administration of 4 mg DOCA when the rats were ovariectomized on day 5 or day 6. In all cases, the size and number of implantation sites were normal in DOCA-treated rats. Higher doses of DOCA were needed to maintain mid- or late pregnancy. Animals ovariectomized on day 8 of pregnancy following daily injection of 10 mg DOCA produced a 60% or 45% maintenance of pregnancy when examined on day 12 or day 15, respectively. Maintenance of embryos in ovariectomized rats from days 15 to 20 was also obtained with daily dose of 10-20 mg DOCA. However, fetal and uterine weights were subnormal and fetal numbers were less in DOCA-treated rats. These results indicate that other than progesterone and estrogen, DOCA also plays a significant role in the regulation and maintenance of pregnancy. (Supported by NIH Grant HD 03736, The Ford Foundation, The Bing Fund, and The Population Council.)

THE ROLE OF FETUS IN THE ONSET OF PARTURITION IN THE RAT. Koji Yoshinaga. Laboratory of Human Reproduction and Reproductive Biology and Department of Anatomy, Harvard Medical School, Boston, Mass.

The role of fetus in the onset of parturition was studied in super-implantation rats which carry two sets of fetuses at two different developmental stages in the uterus. The super-implantation rats were produced as previously reported (Yoshinaga, J. Reprod. Fert. 2, 35, 1961). Parturition took place at one time, term being dependent on the ratio of old/young fetuses (5 days difference in age). When the ratio was less than 0.3, parturition usually took place when young fetuses became mature and old fetuses died *in utero*. When the old/young ratio was more than 0.3, parturition usually took place when old fetuses became mature and the young ones were aborted. In the rats where the old/young ratio was more than 0.3 and the old fetuses were removed or decapitated on day 19, pregnancy was maintained until the young fetuses became mature. Thus, it has been shown that (1) some positive factor(s) for the initiation of parturition are produced by fetuses when they become mature. (2) The factor exerts its action by antagonizing the young placenta-corpus luteum system. (3) The source of the factor(s) is located in the head of mature fetuses. (Supported by NIH Contract 69-2203 and a grant from the Population Council, N.Y.)

ELEVATION OF SERUM LACTATE DEHYDROGENASE IN RATS SUBJECTED TO CHRONIC CENTRIFUGATION. H. L. Young and H. Lee*. NASA-Ames Research Center, Moffett Field, Calif. and Pacific Medical Center, San Francisco, Calif.

Alteration of body temperature, heart rate, carbohydrate and lipid metabolisms has been reported by different investigators in rats during acute centrifugation. These changes imply tissue hypoxia which has been confirmed by measurements of arterial blood oxygenation in animals and man. The purpose of this study was to determine if serum lactic dehydrogenase(S-LDH), the terminal enzyme of anaerobic glycolysis, was affected by centrifugation. Isoenzymes were also determined to predict which tissues might be preferentially affected. 170 rats were divided into two groups; a tested group and a paired-control group. Tested rats were divided into 8 groups and centrifuged at either 2.3 G or 4.2 G for 1, 2, 4.5 or 7 days. Following each experimental period the rats were etherized and blood samples were collected by cardiac puncture, allowed to clot in an ice bath, then centrifuged. S-LDH activity was assayed within 24 hours by following the formation of reduced nicotinamide adenine dinucleotide at 340 mμ. In the 8 control groups the mean S-LDH ranged from 0.68 ± 0.07 to 0.94 ± 0.08 μm/min/ml serum. S-LDH was significantly elevated in all centrifuged rats. Mean values at 2.3 G were 1.92 ± 0.12, 1.61 ± 0.13, 1.34 ± 0.18 and 2.04 ± 0.12 for 1, 2, 4.5 and 7 days of centrifugation respectively; and corresponding values at 4.2 G were 1.85 ± 0.28, 1.40 ± 0.27, 1.63 ± 0.29 and 1.55 ± 0.38. Serum isoenzyme pattern of centrifuged rats showed that all 5 isoenzymes increased proportionally and indicated that elevated S-LDH was due to a generalized change in cellular permeability rather than an effect on a specific tissue. The increased S-LDH is thought to result from generalized hypoxia associated with centrifugation.

THE ROLE OF CALCIUM IN THE VAGAL INHIBITORY EFFECT

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The vagal inhibitory effect in the isolated vagal heart preparation of Rana pipiens was used as quantitative assay of acetylcholinesterase (AChE) activity in situ to study the role of calcium in humoral transmission. The AChE activity is inversely proportional to calcium concentration in the perfusing medium within a narrow range of 0.5-3.5mM. There is a linear relationship between the degree of inhibition and the limited range of calcium concentration, beyond which the relationship is nonlinear. EDTA reduces the vagal inhibition by partially removing the calcium from Ringer's solution and by chelating the calcium bound to the anionic site of AChE. Magnesium inhibits the in situ AChE of the vagal heart system. Cardiolipin reduces the vagal inhibition by chelating the calcium from the membrane. All these effects reported here are reversible when normal Ringer is used. The inhibitory effect of acetylcholine injected into the cardiac sinus is also conditioned by the concentration of calcium in the perfused fluid. This casts some doubt on the role of calcium on the release of acetylcholine from the nerve endings. It appears more likely that calcium blocks the anionic site of AChE in the postsynaptic membrane as well as in the neuromuscular junction.

Mesenteric Blood Flow and Small Intestinal Motility in the Dog.

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The relationship between intestinal motility and mesenteric blood flow was studied in anesthetized dogs comparing responses to intra-arterial infusions of saline, acetylcholine (ACh, 1.5μg/kg-min), and methacholine (MCh) at a low dose (0.3μg/kg-min), an intermediate dose (0.5μg/kg-min), and a high dose (0.7μg/kg-min). Mesenteric arterial blood flow (MBF) was measured electromagnetically. Motility was recorded from a four ml saline filled balloon in the proximal jejunum. Motility index in units was calculated from amplitude times frequency of contractions divided by time interval in seconds. ACh increased MBF from 343 ± 39 ml/min to 534 ± 31 ml/min ($p<.001$) in the first minute of infusion. Motility increased to a maximum of 5.7 ± 1.5 units in the second minute and diminished gradually. This response was not significantly different ($p>.10$) from spontaneous motility during saline infusion. MBF did not increase ($p>.25$) during low dose MCh infusion. Motility increased to 6.8 ± 2.0 units in the fourth minute and diminished gradually. This response was not significantly different ($p>.10$) from motility stimulated with ACh. The intermediate dose of MCh did not alter blood flow ($p>.25$) or motility ($p>.10$) when compared to the low dose. High dose MCh caused no significant increase ($p>.25$) in MBF. Motility increased to 14.7 ± 4.9 units in the fourth minute. This response was greater than that with ACh and low dose MCh ($p<.001$). These findings indicate that intestinal smooth muscle contraction can be stimulated over a wide range of values without altering mesenteric blood flow.

MECHANISMS OF PHOTORECEPTOR CURRENT GENERATION IN LIGHT AND DARKNESS. Ralph Zuckerman (intr. by K.T. Brown). Department of Physiology, University of California, San Francisco, California.

Measurements of the retinal "dark" voltage and light-evoked receptor potential were made in isolated frog retina preparations in which responses were limited to the receptor layer by sodium aspartate Ringer's. Two components of the net retinal "dark" current were revealed. A "dark" current flowing in the proximal-to-distal direction results from a passive transport mechanism whereby Na^+ influx is greater at a distal site, such as the outer segment, than at a proximal site, such as the inner segment. This component is immediately dependent upon $[Na^+]_o$, is abolished by ouabain (10^{-4}M) in 25 minutes, and may be re-established in the absence of Na^+ pumping by developing an artificial Na^+ gradient across the membrane. In addition, there is a second type of "dark" current which flows mainly in a distal-to-proximal direction, and which appears to be generated by an electrogenic Na^+ pump. Increasing $[K^+]_o$ by as little as 4mM can increase this current by 100%. It is not immediately affected by changing $[Na^+]_o$, and is abolished by 10^{-4}M ouabain in 60 seconds. The rod-dominant receptor potential of aspartate-treated retina appears to result mainly from a light-induced change in membrane Na^+ conductance. The electrogenic Na^+ pump is hypothesized to be located in the receptor inner segment and to serve as a source of constant current over short periods of time. It is proposed that light makes the outer segment less of a current sink, causing a transient decrease in the amount of pump current flowing into the outer segment and a concomitant increase in the amount of pump current flowing proximally into the synaptic terminal. (Supported by NIH grants EY00187 and EY00468.)

EFFECTS OF PARTIAL AND COMPLETE TRANSARTERIAL LEFT VENTRICULAR BYPASS ON HEMODYNAMICS OF THE FAILING LEFT VENTRICLE. Hans H.J. Zwart*, Alexander C. Kralios* and Willem J. Kolff. Division of Artificial Organs, Department of Surgery, University of Utah, Salt Lake City, Utah.

For transarterial bypass, blood is removed from the left ventricle with a wide bore, flexible cannula, inserted via the right axillary or carotid artery past the aortic valve. The blood is returned via a femoral artery with a roller pump. Left ventricular failure was produced in ten sheep by ligation of coronary arteries. The effects of maximum bypass were studied in 100 failure periods. Mean left atrial, systolic left ventricular and arterial pressure (mmHg) changed from 15.3 70.8 and 47.5 during failure to 3.6, 36.3 and 68.4 during bypass. Mean systemic flow (flow pulmonary artery or aortic flow + bypass flow) increased from 1.5 to 2.7 L/min. Bypass flow was increased with steps of 1 L/min in thirty failures. At 1 L/min, mean aortic flow increased from 2.0 to 2.1 L/min but circulation was maintained better and the left ventricle was unloaded more at higher flows when aortic flow decreased to zero. The optimal condition was reached at 3 L/min bypass unless decompression of the left ventricle to atmospheric pressure would be of benefit. The latter could be effected only at maximum bypass. Right atrial pressure remained normal in all failures and during and after bypass. Ventricular fibrillation occurred seven times, bypass maintained mean arterial pressure at 53.6 mmHg and kept left atrial and ventricular pressure at atmospheric pressure. Defibrillation was accomplished without difficulties. Left ventricular bypass is unique for its capability to unload the ventricle to this extent.

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