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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.

CORONARY HEMODYNAMICS AND LEFT VENTRICULAR FUNCTION DURING ELEVATED CARBON MONOXIDE IN THE CONSCIOUS DOG. J. D. Adams,* H. H. Erickson, and H. L. Stone, Sealed Environment Branch and Biodynamics Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

Exposure to elevated levels of carbon monoxide (CO) results in hypoxemia, since CO replaces oxygen in hemoglobin. The myocardium is flow dependent for its oxygen requirements; thus, any change in oxygen demand by the myocardium is met primarily by a change in coronary flow. In this study, the effects of elevated CO on coronary hemodynamics and left ventricular function have been determined in the conscious dog. A tracheostomy was performed on each of 4 dogs to permit rapid introduction of CO (1500 or 3000 ppm) in room air through an endotracheal tube. Each dog was instrumented with a Doppler ultrasonic cuff transducer to measure the velocity of blood flow in the left circumflex coronary artery. A solid-state pressure transducer was implanted within the left ventricle to determine left ventricular pressure and dP/dt. A catheter was placed in the left atrium in order to determine left atrial pressure, blood gases, pH, and the carboxyhemoglobin saturation (COHb) of arterial blood. COHb was determined by a chemical extraction and spectrophotometric method. Each dog was exposed to CO for approximately 30 minutes, a total of 8 exposures for 4 dogs. Five per cent COHb caused a 14% increase in coronary blood flow ($p < .025$), 8% increase in coronary stroke volume ($p < .01$) and 4% increase in heart rate ($p < .005$). Twenty per cent COHb caused a 57% increase in coronary flow ($p < .001$), 37% increase in coronary stroke volume ($p < .01$), and 20% increase in heart rate ($p < .005$). At 5% and 20% COHb there was no significant change in dP/dt. These results indicate that low levels of COHb can cause significant changes in coronary blood flow and heart rate.

CHARACTERISTICS OF THERMOREGULATION IN THE UNANESTHETIZED CAT. T. Adams, M.L. Morgan*, W.S. Hunter* and K.R. Holmes*. Dept. of Physiol., Mich. State Univ., East Lansing, Mich. 48823.

The establishment of acclimatization indices for body temperature regulation first requires the identification and evaluation of an animal's physiological responses uninfluenced by its thermal exposure history. Oxygen consumption ($\dot{V}_{O_2}$), internal (T_{re}) and skin surface temperatures (T_s), respiratory frequency (f), and evaporative heat loss (E) were measured on 5, female, short-haired, adult, non-acclimatized, unanesthetized, domestic cats (2.0 - 3.3 kg.) in separate tests as animals rested in steady state adjustments to ambient temperatures (T_a) of 20, 23, 26, 29, 32, 35, 38, and 41°C. Animals regulated at statistically higher internal body temperatures during mild cold (at T_a 20°C, T_{re} = 39.0°C) and heat stresses (at T_a 41°C, T_{re} = 40.5°C) than during thermoneutral exposures (at T_a 29°C, T_{re} = 38.5°C); T_{re}'s during exposure to T_a's both lower and higher than 29°C showed a progressive elevation. E, f and M were better predicted by average skin temperature ($\bar{T}_s$) than by T_{re}; with the animal in a steady state, $\bar{T}_s$ was a linear function (r = 0.99) of T_a over the entire exposure range. Progressive increases in M during exposures below T_a 35°C were paralleled by increases in the thermal insulation of the distal but not proximal extremity or central body skin regions. A "fine control" function in whole body thermal balance appeared as variable skin blood flow in one or more of the distal extremities during exposure to T_a less than 38°C, and as a cyclic (freq. of 1.5 per min.) variations in E during heat stress. The domestic cat appears to confront both acute cold and heat stresses by thermoregulating at higher internal thermal loads compared to normothermic exposures, and by rapid, controlled, brief shifts in thermal exchange superimposed on stable T_{re} and $\bar{T}_s$ adjustments. (Supported under NSF Grant No. B8-2130R.)

ELECTRON MICROSCOPY OF WIDENED AND MULTIPLE INTERCALATED DISCS OF PULMONARY ARTERIAL BANDED CANINE HEARTS. G.E. Adomian*, M. Laks,* F. Morady*, H.J.C. Swan. Department of Cardiology, Cedars-Sinai Medical Center, Los Angeles, California 90029.

The purpose of this study was to investigate the ultrastructure of widened and multiple intercalated discs (MID) observed in the pulmonary arterial banded (PAB) heart. Tissue samples were taken from the trabeculae carneae of the right ventricular base from normal and PAB hearts. The width of the intercalated disc transverse segment (IDTS) was measured at the maximum fold of its membranes; the IDTS widths ranged from 0.6 to 3.0μ in the PAB heart and from 0.6 to 1.0μ in the normal. The width of the dense filamentous mat, 0.02 - 0.14μ, was the same in the normal and PAB hearts. The widths of the fascia occludens, macula adherens, and fasciae adherentes in widened IDTS's were unchanged from normals. We have defined MID as two, three, or four intercalated disc transverse segments lying along the same myofibrils, each two of which are separated by one to ten sarcomeres. The sarcomeres within the MID's were either bounded on two sides by membranes connecting the IDTS's to each other, or lacked a membrane on one side. Some of the A-band borders were irregular in sarcomeres adjacent to the transverse segments of MID's compared to sarcomeres more distant.

In summary, the following changes were observed after banding the pulmonary artery: (1) broadening of the membrane folds of the IDTS's, without broadening of the filamentous mat or membrane junctions. (2) arrangements of MID's which we postulate to be due to projections of the myocardial cell. (3) irregular A-band boundaries similiar to those in embryonic sarcomeres. We hypothesize that the observed structural alterations in the intercalated discs of PAB hearts are involved in myocardial cell growth. (Supported by NIH grant HE-10382 and RR05468).

APPLICABILITY OF CUSUM TECHNIQUES FOR MONITORING PULMONARY FUNCTION IN NORMAL AND ABNORMAL CONDITIONS. Y. Alarie (intr. by D. Minard), Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pa. 15213.

The CUSUM (Page, E. S. Technometrics, 3, 1-9, 1961) and regression analysis techniques were used to analyze data on distribution of ventilation (nitrogen washout), respiratory rate and tidal volume of groups of cynamolgus monkeys (M. irus) during a period of 86 weeks. It was found that the CUSUM technique was well suited to detect small deviations in group mean level following exposure of these animals to pulmonary irritants. The technique was also used in sequential sampling and was found to be very effective in detecting changes occurring within a short time period as exposure to pulmonary irritants progressed. Data from the literature on airway conductance (Graham, W. G. B. et al. Am. Rev. Resp. Disease, 96, 266-274, 1967) in normal and asthmatic patients were also analyzed and the CUSUM technique was found to give an excellent indication of pulmonary function changes.

We conclude that when the objective is to detect changes due to irritation of the pulmonary system or amelioration of asthmatic or emphysematous conditions by medication or exercise the CUSUM technique can be used to analyze the data obtained from pulmonary function tests after the experiment or to follow the progress during the experiment. The technique is simple but requires a minimum of 8 sequential data points and can be best applied in series exhibiting sudden changes.

HELIUM-COLD HYPOTHERMIA: ECG, MYOCARDIAL CONTRACTILITY AND RESISTANCE TO ANOXIA. G.L. Anderson* and X.J. Musacchia. Dept. Physiology and Space Sciences Research Center, University of Missouri, Columbia, Missouri 65201.

Exposure to $He:O_2$ (80:20) and low temperature induces hypothermia in hamsters. Survival in the hypothermic state ranges between 18-24 hrs. The factor(s) limiting survival of these preparations are unresolved. The aim of this study was to determine if there is an increase in the sensitivity of the myocardium to hypoxia following a hypothermic exposure. Electrocardiograms of hypothermic hamsters were taken intermittently throughout the hypothermic exposure (7°C ambient). Changes which appeared to be solely temperature dependent were: a reduction in rate to 15-18 beats/min, 2:1 and 3:1 A-V block and depression of the T wave. In those animals judged to be acutely failing, atrial fibrillation, erratic ventricular beats and depression of what appears to be the R' component of the QRS complex were frequently observed. The right ventricle was isolated from animals which were judged not to be acutely failing and resistance to experimental anoxia tested. The mean resistance time of these preparations was 12.5 min as compared to 16.8 min for ventricles isolated from normothermic controls. This difference may be attributable to a reduction in contractility of the myocardium of hypothermic hamsters rather than an increased sensitivity to anoxia. The mean generated tension for these preparations was 0.38 gms as compared to 0.76 gms for controls. (Supported by NASA Grant NGR 26-004-021 S 4 & 5 and SSRC funds).

OBSERVATION OF MAMMALIAN INTESTINAL VILLI WITH THE SCANNING ELECTRON MICROSCOPE. James H. Anderson* and A. B. Taylor, Department of Physiology and Biophysics, University of Illinois, Urbana, Ill.

The scanning electron microscope (SEM) has been used to obtain better three dimensional concepts of structures including intestinal villi. Segments of the jejunum or ileum were prepared for study using modifications of the techniques described by Boyde & Wood '69. Villi from each species studied present a characteristic pattern, shape, length and structural configuration. Those of the dog and hamster are cone shaped being somewhat longer and more pointed in the dog and shorter and blunter tipped in the hamster. In contrast the villi from the rat are leaf-shaped structures. Each villus surface is distinguished by relatively deep fissures which increase the total absorptive surface and permit greater flexibility of movement during digestion and absorption. Both the surface of the villi and the intervillus floor exhibit a number of clear, or mucous containing pores believed to be orfices of goblet cells. The area between villi in the hamster is characterized by a number of mound shaped structures perforated by pores, the openings of the crypts of Lieberkühn, through which the secretions of the intestinal glands reach the lumen of the intestine. These slightly elevated structures are frequently interconnected by ridges and may be continuous with the base of the villus. In the hamster the openings of the pores, the intervillus ridges, and the villi frequently exhibit a spiral configuration suggesting that cells may migrate from the crypts of Lieberkühn to the tips of the villi following such a spiral pathway. In conclusion we believe that the SEM provides a better three dimensional concept of the intestinal villi than other available instruments.
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Action of the Superior Colliculus on Neck Motoneurons in the Cat. M.E. Anderson*, M. Yoshida* and V.J. Wilson, The Rockefeller University, New York.

Activation of the superior colliculus (SC) results in contraction of contralateral neck muscles (Apter, 1946). Electrical stimulation, in chloralosed cats, of the contralateral SC evokes a predominant EPSP (contra EPSP) in all motoneurons studied that innervate the splenius or other dorsal neck extensor muscles. Stimulation of the ipsilateral SC tends to evoke an IPSP (ipsi IPSP), although stimulation of either side may elicit mixed responses. Contra EPSPs evoked by stimulation of the middle to deep SC layers have latencies of 1.6 to 3.2 msec., with a mode of 2.0 msec. They are seldom evoked by single shocks, show marked facilitation with repetitive stimuli, and are evoked polysynaptically, some being disynaptic. The amplitude of the contra EPSPs usually is not markedly diminished at stimulus frequencies up to 20-50/sec. Ipsi IPSPs have latencies of 2.0 to 4.3 msec. and are also evoked polysynaptically. Cuts in the ipsilateral lower medulla that should interrupt the crossed tectospinal fibers do not abolish contra EPSPs, although their amplitude is often reduced and latencies are more variable. The ipsi IPSPs are not abolished by cutting the tectospinal tract in the lower medulla on either side. Pathways other than the direct tectospinal tract play a dominant role in the production of tectal-evoked PSPs in neck motoneurons.
Supported by grants NS02619 and NS05463

CORRELATIVE CHANGES BETWEEN RETINAL SHIELDING PIGMENTS POSITION AND ELECTRORETINOGRAM IN CRAYFISH. H. Aréchiga and B. Fuentes. (intr. by J. J. Izquierdo). Universidad Nacional Autónoma de México, Facultad de Medicina.

The amplitude of the electroretinogram (ERG) in the crayfish Procambarus bouvieri, undergoes gradual enhancement under dark adaptation, at first (15 to 20 min) rapidly and then slowly proceeding for several hours. Measurements simultaneously made of ERG amplitude and of retinal shielding pigment position, the latter in terms of area of seudopupil, show that changes are parallel during the slow phase of ERG enhancement. In long term records, ERG amplitude and seudopupil area undergo, at dusk, further increase, remain at high values during night, and both decrease at dawn, attaining in 60 to 90 min, steady low values which persist until next dusk. In fully dark adapted animals, injections of sinus gland extracts, known to induce migration of retinal shielding pigments towards a light adapted position, reduce ERG amplitude. These results point to a close dependance of activity of retinal photoreceptors, from a modulatory mechanism for light admittance to the eye.

INTERVENTRICULAR SEPTAL FUNCTION IN THE CANINE HEART. J.A. Armour* and W.C. Randall, Department of Physiology, Loyola University, Maywood, Illinois.

To investigate interventricular septal function, strain gauge arches were sutured onto the right and/or left sides of the septum; two miniaturized pressure transducers (Scientific Advances model SA-SA-M-7BW) were also placed in the interventricular septum, one beneath and parallel to each of the endocardial surfaces. Patterns of contraction demonstrated that the left side of the septum contracted first followed by the right side; the apex contracted before the base. The septal portion of the left ventricular outflow tract contracted after the overlying anterior epicardium. Right septal intramyocardial pressures (33± mmHg) were above those recorded simultaneously in the right ventricular chamber (20±2 mmHg); the left septal control pressures (98±11 mmHg) were slightly less than those in the cavity (118±5 mmHg). Pressures of the right septal wall were considerably below those within the left ventricular free wall superficial musculature (93±7 mmHg) and are considered to reflect events in the right ventricular portion of the septum. Augmentation of contraction via stellate ganglion stimulation demonstrated a preponderance of excitation by the right nerves to the right septum and left nerves to the left septum. Inotropic agents administered intravenously augmented pressures and forces proportionately on both sides, the left side developing the greater pressures and showing onset of contraction well in advance of the right.

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EFFECT OF DNP AND ANOXIA ON TRANSMURAL P.D. AND SHORT CIRCUIT CURRENT OF ISOLATED BULLFROG SMALL INTESTINE IN SODIUM FREE MEDIA.
W. McD. Armstrong, T.K. Suh* and G.A. Gerencser*. Dept. Physiology, Indiana Univ. School of Med., Indianapolis, Ind.

When isolated segments of bullfrog small intestine are mounted between identical oxygenated Na free tris chloride Ringer's containing glucose, the serosal side of the tissue becomes negative with respect to the mucosal side and a short circuit current is observed which is consistent with a net mucosal to serosal flow of Cl ions. 1 mM DNP (2,4 dinitrophenol) added to either the mucosal or serosal medium greatly enhances both the serosal negative transmural p.d. and the short circuit current. These effects are reversible for moderately long exposure (up to 1 hour) to DNP. During exposure to DNP the mucosal to serosal flux of Cl (measured isotopically) is increased and the serosal to mucosal Cl flux is decreased compared to control values. Simultaneous anoxia (N_2) on both sides of the tissue produces a similar reversible increase in transmural p.d. and short circuit current. The effect of N_2 is dependent on an external supply of metabolizable substrate (e.g. glucose or fructose). It is not observed in substrate free media, or in Ringer's containing actively transported but non-metabolized sugars (e.g. 3-O-methyl glucose) or amino acids (e.g. L-valine) only. Similarly, it is not seen in the presence of sorbose which is neither transported nor metabolized. These results suggest the presence, in bullfrog small intestine, of an active mucosal to serosal Cl pump which is directly dependent on glycolysis as a major source of energy. (Supported by USPHS grants AM 12715 and HE 06308).

EFFECTS OF STAPHYLOCOCCAL ENTEROTOXIN B ON INTESTINAL TRANSPORT.
Tomoaki Asano and Sr. Rosemary Sullivan*. Dept. of Microbiol., U. of Notre Dame, Notre Dame, Ind.

Studies were made on the mechanism of staphylococcal enterotoxin B in inducing diarrhea in the small intestine of rats in vitro as well as in vivo. In in vitro experiments, under the influence of enterotoxin, a decrease in net absorption was shown for water, glucose, Na, K and lactic acid while Cl reversed direction to become net secretion. Metabolic indices of the intestinal wall, such as oxygen uptake and lactic acid production, did not change significantly. In in vivo experiments a portion of the small intestine was perfused with Ringer's fluid and serial samples were taken from the perfusate before and after addition of the toxin in order to determine the net transport of water and solutes. The action of enterotoxin was most salient in the middle segment where water, Na, K, Cl and bicarbonate ion were secreted into the lumen. Only glucose continued to be absorbed under the toxin action. The time course of the change was rapid in that 10 minutes after the addition of the toxin the net secretion was observed and 10 minutes later the net transport returned to the net absorption comparable to the control period. In the upper segment the change was similar but to a lesser degree, although 20 minutes after the toxin the net absorption became greater than the control period. In the lower segment the net absorption of water, Na and Cl decreased while the secretion of bicarbonate increased independently with respect to Cl absorption. The osmolarity of the perfusate remained nearly isoosmotic with the plasma before and after the toxin, indicating that the net absorption in the control period and the net secretion after toxin were carried out in isoosmotic fashion. The electric potential difference across the intestinal wall determined in vivo was 6.8 mv on the average, the serosal side being positive, in the control period and did not change during the toxin action.

IS THYROTROPIN RELEASING FACTOR (TRF) ALONE RESPONSIBLE FOR MAINTAINING THYROTROPIN (TSH) SYNTHESIS IN THE PITUITARY GLAND? R.L.W. Averill and J.S. Evans, University of Tennessee Medical Units, Memphis, Tennessee.

Continuous perfusion of rat pituitary autografts with extracts of porcine hypothalamus increased the rate of thyroidal release of 131I to 16-20% from 3-8%/day in rats with uninfused or saline infused autografts. When infusions changed from hypothalamic extract to saline the enhanced rates of release reverted to 4%/day. The high rate of release in rats with grafts infused with hypothalamic extract was maintained for more than 15 days. For this to have occurred TSH synthesis must have been reinitiated in the grafts. This study has been repeated using synthetic TRF (TRH Abbott-38579) to determine whether TRH could reinitiate synthesis in the absence of other components of crude extracts. Synthetic TRH at a concentration (4 ng./ml.) which would release TSH by intrapituitary infusion in phenobarbital treated rats at 34 C (49.0 $\pm$ 5.11% increase in blood 131I) to the same extent as the crude porcine extract (52.8 $\pm$ 4.45% increase) was unable to re-establish TSH synthesis in infused autografted pituitaries. Synthetic TRH at 1 µg/24 hr (4 µg/ml) was required to duplicate the effect of crude hypothalamic extract. TRH at 1 µg/ml was ineffective. As 1000 x the concentration able to release TSH from pituitaries of intact rats was needed to re-establish synthesis in grafted pituitaries, it is suggested that the maintenance of TSH synthesis by the TRF normally requires potentiation by some other humoral agent. (Supported by Grants AM-11379 and HD-02457)

MECHANISM OF INCREASED PLASMA CORTISOL LEVELS FOLLOWING INTRAVENOUS GLUCOSE INFUSION. **Habeeb Bacchus. Department of Medicine, Riverside General Hospital, Riverside, Calif. 92503 and Loma Linda University, California 92354.**

Marked increases of plasma cortisol levels were observed in normal human subjects within 5 minutes after intravenous infusion of 20-25 ml. of 50% glucose in water over the course of 1-2 min. There occurred a mean increase of 120% at 5 min., lasting until 60 min. post-infusion. The cortisol returned to baseline levels within 3 hrs. Similar infusions to patients who received single or multiple suppressive doses of dexamethasone resulted in significant elevations of cortisol, but with a more rapid return to baseline. In two patients with adrenocortical insufficiency who had only trace amounts of plasma cortisol the hypertonic glucose infusion failed to result in detectable rises in cortisol. One patient who underwent a hypophysectomy for craniopharyngioma 4 yr. previously, and one who was adrenalectomized for breast cancer were also studied. These patients were given single doses of 20 mgm. Hydrocortisone at 6:00 a.m. and the plasma levels were then measured for 3 hrs., at this time intravenous infusions of hypertonic glucose were given. Plasma cortisol levels increased significantly within 5 min. after the infusion, and returned to pre-infusion levels at 2 hrs. Normal saline, or hypertonic saline infusions failed to alter the plasma cortisol levels. During oral glucose tolerance tests (GTT) the plasma cortisol levels increased only in patients who exhibited diabetic type GTT curves, suggesting an hyperglycemic threshold for the cortisol increases. The data are consistent with an effect of glucose to decrease the degradation of cortisol; these data are consistent with our other findings of altered corticosteroid excretion following glucose infusion (Metabolism 18:277, 1969).

MEASUREMENT OF CARDIAC OUTPUT BY ETHYL-ETHER-DILUTION AND DIRECT FICK METHODS. Hans Bachofen*, David A. Bloom* and Leon E. Farhi. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N.Y. 14214.

In a previous report Chinet et al (Fed. Proc. 28:653, 1969) proposed a new "bloodless" method for measuring cardiac output. Ethyl-ether dissolved in saline is infused as tracer at a constant and known flow rate into the vena cava or the right atrium. The equilibrium pressure of ethyl-ether between alveolar air and mixed venous blood can be measured during a rebreathing maneuver performed simultaneously to the infusion. This value in turn allows one to calculate the ether concentration in the mixed venous blood, the dilution of the infused tracer, and hence the cardiac output, provided that the blood/gas partition coefficient of ethyl-ether at body temperature is known. In the present experiments the accuracy of the ether-dilution technique was tested in 9 dogs by comparison with the direct Fick method. The corresponding values obtained simultaneously by the two methods were in good agreement; on an average the differences did not exceed 6%. These results indicate the usefulness of the new technique which is repeatable within short time intervals and does not require blood analysis. (Supported by ONR Contract No. N00014-68-A-0216 (NR 102-722) and AF Contract No. #F-41609-70-C-0019).

INTERFERENCE BY HISTAMINE AND BETAHISTINE HCl WITH HYDROCORTISONE POTENTIATION OF RESPONSES TO EPINEPHRINE, NOREPINEPHRINE AND METHOXAMINE IN SINGLE SMOOTH MUSCLE CELL IN SITU. S. Baez, J. Lorenzo* and L.R. Orkin*, Departments of Anesthesiology and Physiology, Albert Einstein College of Medicine, Yeshiva University, Bronx, New York 10461

Histamine (H) and the synthetic analogue Betahistine HCl (Bh), even in non-relaxant amounts, interfered with the smooth muscle cell (smc.) shortening action of a number of agonists, including epinephrine and norepinephrine (The Physiologist 12:162, 1969, Fed. Proc. 29:388 Abs., 1970). To further explore whether such interference by the above depressant molecules with the catecholamines might be enzymatically mediated, experiments were designed in which the interaction of the opposing musculoactive molecules was evaluated before and following potentiation of responses to the stimulants by hydrocortisone. In 10 arterioles each in 22 rats, lightly anesthetized with pentobarbital sodium (25 mg/kg), changes in smc. thickness (th.) was monitored by the method of image-shearing. Before decadron, the gain in smc. th. produced by topical epinephrine and norepinephrine (aver. 39.0%), and vasoxyl (aver. 48.3%) were effectively suppressed by as little as 0.01 mg/ml of histamine and 0.05 mg/ml of betahistine HCl. After decadron (0.2 mg/ml), and potentiation of responses of the same target smc. to the standard doses of the catecholamines (aver. incr. +90%) and vasoxyl (aver. incr. +120%), suppression of the stimulants was still effective by such non-relaxant amounts of H and Bh. These results indicate that interference by H and Bh upon the agonist is not mediated through enzymatic pathways affected by hydrocortisone.

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SYMPATHETIC CONTROL FACTORS IN RENAL HAEMODYNAMICS. Roger J. Bagshaw*, Masahiko Iizuka*, and Lysle H. Peterson. Bockus Research Institute, University of Pennsylvania, Philadelphia, Pennsylvania, 19146

This study was designed to evaluate the effects on renal haemodynamics of stimulation of the hypothalamus and the carotid sinus; also, to study the modulation of the hypothalamus by the carotid sinus upon the renal bed. Renal pressure and flow was measured as a function of hypothalamic stimulation and pulsatile pressure changes in the isolated perfused carotid sinuses of nine vagotomized dogs anaesthetized with chloralose. The hypothalamus was stimulated with square waves at 100 hz, 1 msec duration, 1-6 volts at carotid sinus pressures (c.s.ps.) varied between zero and 275 mm Hg. Under these open loop conditions sufficiently raising the c.s.p. completely inhibited changes in renal resistance to hypothalamic stimulation at low intensities (1-2 v). The renal response to higher intensities of stimulation (5-6 v) was relatively unaffected by c.s.p. changes with proportionately variable inhibition of changes to stimulation of intermediate intensities. At all c.s.ps. the renal hydraulic input impedance represented a relatively high fraction of the D-C impedance and the corresponding phase angles were negative at all frequencies. A direct relationship between renal impedance and c.s.p. at all significant harmonics was observed. These results demonstrate that interaction between the carotid sinus and the hypothalamus, previously demonstrated on efferent neural outputs (Pitts, Larrabee and Bronk, Am. J. Physiol. 134:359, 1941) produces haemodynamic changes in the case of the kidney, and that these changes are reflected in pulsatile as well as non-pulsatile blood flow (Support by USPHS HE 07762 and ONR 551 (54).

EFFECT OF IMMOBILIZATION UPON BONE METABOLISM AND THE PARATHYROID GLANDS. P. K. Bajpai, C. E. Miller and M. A. Hayat. Department of Biology, University of Dayton, Dayton, Ohio 45409.

Experiments were conducted to observe the interrelationship between the parathyroid glands and disuse osteoporosis. Three trials were conducted. Sixteen rats (200 grams each) were used in each trial. Blood and urine were obtained from all the animals before performing the operative procedures. Serum was analyzed for calcium and inorganic phosphate. Urine was analyzed for calcium, inorganic phosphate, and hydroxyproline. The animals were divided into two groups of eight each. Eight animals in one group were immobilized by sectioning the sciatic nerve. The other eight animals were sham-operated. After thirty days, the animals were sacrificed and observed for the following: serum calcium and inorganic phosphate; urinary calcium, inorganic phosphate, and hydroxyproline; bone calcium, inorganic phosphate, dry weight and ash content; and ultrastructural changes in the parathyroid gland. No significant variation was observed in serum calcium, bone calcium, and bone phosphorus. Serum inorganic phosphate, urinary calcium, inorganic phosphate, and hydroxyproline increased significantly in the immobilized animals; dry weight and ash content of the bones in the immobilized animals were significantly lower than the sham-operated animals. Studies of ultrastructures revealed that the parathyroids of the immobilized animals are not as active as the parathyroids of sham-operated animals.

EFFECTS OF CHRONIC HYPERCAPNIA ON RED CELL, PLASMA VOLUME AND TOTAL BLOOD VOLUME OF GUINEA PIGS. George T. Baker III* and Karl E. Schaefer. University of Miami School of Medicine, Miami, Florida and Submarine Medical Research Laboratory, Groton, Connecticut.

Blood volume in guinea pigs, estimated on the basis of simultaneous measurement of red cell volume using chromium-51 tagged red cells and plasma volume with iodinated human albumin (I-125), was found to be more accurate than blood volume data calculated from separate determinations of red cell volume (chromium-51) and plasma volume (I-131). In chronic hypercapnia induced by prolonged exposure of guinea pigs to 15% CO_2 in 21% O_2 total blood and cell volume was found to rise during the uncompensated phase and increase to a greater extent during the compensated phase, while the plasma volume did not change significantly. The first rise was attributed to the release of blood stores from the spleen and liver while the later rise was attributed to an increased rate of erythropoiesis, as indicated in a significant elevation of reticulocytes. The fifty percent survival time of normal guinea pig erythrocytes was determined to be 11.6 days.

THE ACTION OF ANTIDROMIC IMPULSES ON TROCHLEAR AND ABDUCENS MOTONEURONS. R. Baker and W. Precht (intr. by R. Llinás). Dept. of Neurobiology, Institute for Biomedical Research, AMA/ERF, Chicago, Ill.

Following electrical stimulation of either the IVth or the VIth nerve in the orbit of the eye, a triphasic field potential (sharp positive-negative field succeeded by a slow positivity) was recorded close to the center of the trochlear (TRN) and abducens (ABN) nucleus with 10 MΩ micropipettes. The negative wavefront travelled dorsoventrally in the TRN and in the reverse direction in the ABN. The slow positivity, which had the same threshold as the preceding negativity, was very similar in both nuclei (0.5-1 mV in amplitude and 10-20 msec in duration). Double shock (condition-test sequences) demonstrated a reduction in the amplitude of the test antidromic field potential (negativity) for a duration of 20-30 msec in the TRN and 30-40 msec in the ABN. At short intervals (ca. 2.0 - 10.0 msec), however, the negative field showed a facilitation which had the same time course as the slow positivity. Intracellular recordings from the above ocular motoneurons demonstrated that direct or antidromic activation of the impaled neuron was followed by a depolarizing-hyperpolarizing after-potential sequence. The time course of these potential changes which are non-synaptic in nature is well correlated with the results of the interaction experiments at the field potential level. Their mechanism of origin may be related to electrotonic depolarization following somatofugal dendritic invasion and delayed rectification respectively.

Dissociation of Intestinal Transmural Sugar Transport from Transmural Na^+ Transport. R. David Baker, Malcolm J. Wall*, and Jo Ellu Long*. Univ. of Texas Medical Branch, Galveston.

Transmural potential difference (PD) and short-circuit current (I_{sc}) were measured across flat sheets of rat and hamster jejunum in an Ussing chamber. PD and I_{sc} in oxygenated Krebs-Ringer-bicarbonate solution were about 4 mV and 40 $\mu a/cm^2$, respectively. Gassing the serosal solution with 95% N_2 instead of O_2 usually caused PD and I_{sc} to drop to about zero within 5 min even when mucosal oxygenation continued. Gassing the mucosal solution with 95% N_2 usually had no effect on PD and I_{sc} if serosal oxygenation was maintained. Thus, in keeping with current concepts, we should conclude that Na^+ pumping by basal-lateral membranes of epithelial cells requires O_2 from the serosal side but cannot be maintained by O_2 from the mucosal side. When basal-lateral Na^+ pumping is abolished by serosal anaerobiosis, intracellular Na^+ concentration ought to increase, and, according to the Na^+-gradient hypothesis, uphill transport of sugars should consequently be depressed. However, everted segments of hamster jejunum (which showed the same PD responses as the flat sheets) transported galactose uphill just as well with serosal N_2 as with serosal O_2. Galactose transport was totally dependent upon mucosal O_2. It seems that Na^+ pumping by basal-lateral membranes is not important for sugar transport. This result is incompatible with the Na^+-gradient hypothesis for uphill sugar transport as currently formulated. (Supported by USPHS Grant No. AM-05778.)

OXYGEN UPTAKE BY A PARALLEL FIBERED MAMMALIAN SKELETAL MUSCLE DURING TWITCH CONTRACTIONS. J. K. Barclay* and W. N. Stainsby. Dept. of Physiology University of Florida College of Medicine, Gainesville, Florida.

Steady state oxygen uptake by the in situ dog semitendinosus muscle, a parallel fibered muscle, was determined for twitch contractions at a frequency of 1 per second. The contractions were isometric, isotonic afterloaded, isotonic freeloaded or isotonic constant load-variable rest length. Oxygen uptake was calculated from measurements of blood flow and arterio-venous oxygen differences. In the experiments, there appeared to be no consistent relationship between oxygen uptake and load, tension, external work or muscle length; oxygen uptake appeared unrelated to any mechanical variable measured. Even though the internal work should be much less in semitendinosus, these findings agree with previously reported work on gastrocnemius.

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EFFECT OF PORTAL HYPERTENSION ON HEPATIC ARTERIAL INFLOW
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Effect of extrahepatic portal hypertension was investigated in 2 groups of mongrel dogs. Group I included 21 normal dogs, and II 8 dogs with porta-caval (PC) shunt. Hepatic arterial inflow (HAI) was measured directly using an electro magnetic flowmeter in Group I, and indirectly using the extraction-clearance technique of Bradley in II. Mean portal venous ($\overline{PV}$) systemic arterial, hepatic wedge pressures and cardiac output (CO) were measured simultaneously before (control) and following partial obstruction of portal vein. During control, ratio of HAI to CO averaged 8.2% (SEM=1.0). In moderate (1.5-2.0 x control $\overline{PV}$) to marked (greater than 2x) portal hypertension, this ratio rose to 123% and 151% (control=100%). HA resistance rose to 120 and 129%, whereas systemic resistance to 137% and 180% respectively. Phenoxybenzamine-pretreatment and bilateral vagectomy failed to block this effect. Obstruction of IVC proximal to site of PC shunt increased HAI/CO ratio from 8.1%(0.9) to 13.9%(1.6). In conclusion, extrahepatic portal hypertension increased the hepatic arterial inflow. Mechanism of action is probably reflex.

Supported by NIH Grant (HE-07739)

EFFECTS OF JUVENILE HORMONE ON PROTEIN SYNTHESIS IN THE TISSUES AND HEMOLYMPH OF THE FIFTH INSTAR MILKWEED BUG.
Sukh Dev Bassi* and Dorothy Feir. St. Louis University, St. Louis, Mo.

Since juvenile hormone (J.H.) inhibits adult differentiation, we attempted to find a protein associated with differentiation in the milkweed bug. Fifth instar bugs were injected with J.H. and ^{3}H-leucine at different times during the stadium. Proteins were separated by electrophoresis on disc gels, the gels were scanned on a densitometer, sliced into small equal fractions, and used for liquid scintillation counting. The results show that J.H. increases the rate of synthesis in one band and inhibits the synthesis of proteins in another band. The effect of J.H. in altering the rate of synthesis is possibly caused by the activation and inactivation of specific chromosomal loci. Since presumably little or no endogenous J.H. is present in the fifth instar but it is present in the fourth instar, we compared the protein bands from the J.H. treated fifth instar and the normal fourth instar bugs. The results show that one of the bands altered by J.H. treatment in the fifth instar appears the same in the normal fourth instar as in the J.H. treated fifth instar bug. Histochemical studies on the gels showed that one of the bands altered by J.H. treatment is positive for acid phosphatase. There is less acid phosphatase activity in the J.H. treated fifth instar and the fourth instar than in the untreated fifth instar bug. Supported in part by NSF grant GB16688 to D.F.

EFFECTS OF ANGIOTENSIN II, HYPERKALEMIA, SODIUM DEPLETION, AND ACTH ON ADRENAL CORTICAL ELECTROLYTES IN DOGS. J.S. Baumber*, J.O. Davis, J.A. Johnson*, and R.T. Witty*, Univ. of Mo. Sch. of Med., Columbia, Mo.

Adrenocortical Na and K content was studied during use of 4 potent stimuli to increase aldosterone secretion in an attempt to define a relationship of Na or K to the synthesis of aldosterone. Thirty five dogs were maintained on a constant daily diet containing 70 mEq Na and 55 mEq K for 4 days. During acute experiments the animals received 1) a 4 hour infusion of normal saline at 0.5 ml/min (n=6), 2) a pressor dose of angiotensin II for 4 hrs. at 1.5 ug/min (n=6), 3) a non-pressor dose of angiotensin II at 0.29-0.39 µg/min (n=7), and 4) a 4 hour infusion of 1 mEq/min KCl in normal saline (n=5). Five animals were given an infusion of saline alone at exactly the same rate as the KCl infusion; the rate of the KCl infusion was adjusted to avoid fatal arrythmias from the high plasma K. Six dogs were Na depleted for 2 days with 2 ml mercuhydrin per day and with a daily diet containing 5 mEq Na and 55 mEq K. Six animals were given a series of 5 injections of ACTH at 12 hr. intervals. At the conclusion of the infusion periods or after Na depletion or ACTH administration, the dogs were killed and the adrenal cortex and psoas muscle analyzed for Na and K content; this was expressed in mEq/100 gm fat free tissue solids. The K content of the adrenal cortex was increased with all stimuli. This was associated with a decreased Na content in the sodium depletion and KCl infusion series. There were no changes in psoas muscle K. The only change in plasma electrolytes was an increase in plasma K from 4.1 to 7.6 mEq/L with the KCl infusion. The increased K content of the adrenal cortex with 4 stimuli known to stimulate steroidogenesis suggests that a change in the ionic environment of the zona glomerulosa cells influenced aldosterone synthesis.

NEUROENDOCRINE INFLUENCE ON LUNG COMPLIANCE IN HEAD INJURY. David L. Beckman, John W. Bean and Donald R. Baslock*, Univ. of Mich., Highway Safety Research Institute and Dept. of Physiology, Ann Arbor, 48105.

It has been shown (Proc Soc Exp Biol Med 130:5, 1969)that lethal mechanical head injury in rats results in pulmonary pathology which can be prevented or ameliorated by pretreatment with sympatholytic, antiepinephrine or general anesthetic agents(J Appl Physiol 27:807, 1969); that this head injury decreases pulmonary compliance in rats with this lung pathology by 30%, (Physiologist 12:172,1969)and in squirrel monkeys (Fed Proc 29:594,1970)in the absence of any attendant gross lung pathology by 50%.The present experiments were carried out in a further evaluation of the changes in alveolar surface tension forces in the causation of the decreased compliance(P-V curves)of excised lungs of monkeys following lethal head injury.Preliminary fillings to vols. of control lungs were carried out to counteract airway blockage or pulmonary collapse. Head injury did not alter lung wt/body wt ratios, but initial minimal air vol. (trapped air) was increased by 90%. However, after preliminary fillings to equal lung volumes, it was found that control lungs contained more minimal air than lungs from traumatized monkeys. Such evidence of absence of consistent pneumoconstriction or air trapping minimizes the possibility of smooth muscle involvement. Sympathetic blocking by Dibenzyline pretreatment prevented this "traumatic" compliance decrease; however, isoproterenol or atropine pretreatment had no effect, further ruling out any smooth muscle involvement. The compliance decrease was not evident in saline curves. The data support the earlier conclusion (Physiologist 12:172,1969) that the decrease in pulmonary compliance in head injury is due in large part to a change in surface tension forces through involvement of the sympathetics. Supported by USPHS RG-GM-16912 and HE-01646.

DISSOCIATION OF PROXIMAL TUBULE AND EFFERENT PERITUBULAR CAPILLARIES OF THE SAME GLOMERULUS. Reinier Beeuwkes III (intr. by A. C. Barger). Harvard Medical School, Boston, Mass.

Some theories of "glomerulo-tubular balance" assume close association between the peritubular capillaries and proximal tubule of the same glomerulus. Little evidence for or against such association is available. Dog kidneys were perfused in vivo by perfusion with glutaraldehyde in Tyrode's solution, thus preserving the tubules in an open state. The vasculature was then filled with "Microfil" silicone rubber and the organs were dehydrated, cleared and sliced. A micropipet filled with silicone was inserted into Bowman's space, and rubber of contrasting color injected into the corresponding proximal tubules. Thus both efferent vascular and tubular structures of the same glomerulus were made visible. Close association was found only in the subcapsular zone. In the bulk of the cortex proximal tubules were generally associated with efferent vessels from different glomeruli. Accordingly, close association should not be invoked to explain glomerulo-tubular balance in the whole kidney. In addition, those nephrons most studied by micropuncture appeared to be different in tubular perfusion from those in the bulk of the kidney. A short film showing the injection of representative tubules in different zones of the cortex will be shown.

PLASMA GLUCOSE CAN SUPPORT LONG-TERM ANAEROBIC BRAIN FUNCTION IN TURTLES. Daniel A. Belkin. Dept. Physiol., Univ. of Fla., Gainesville.

In the absence of O_2, the central nervous systems of most non-marine chelonians can function more or less normally for about ten times as long as can those of other reptiles. Since this tolerance of anoxia is lost if perfusion of the brain is stopped, or if the turtle is given an aerobically sublethal dose of iodoacetate (which is thought to depress anaerobic glycolysis), it appeared likely that metabolism of plasma glucose provides the energy needed for CNS function in O_2-free turtles. A system was devised whereby the brains of unanesthetised, cardiectomized turtles (Chrysemys picta) were perfused at constant pressure with a completely inorganic artificial plasma to which known concentrations of D-glucose were added. The perfusion fluid was equilibrated with either O_2 or N_2. Its pH was maintained at about 7.6 by a CO_2-bicarbonate buffer system. Brain function was monitored by observing breathing movements and by periodically measuring cortical evoked potentials elicited by visual stimuli. Since the perfusion fluid contained no large molecules to maintain osmotic balance, the turtles' heads became progressively edematous during the perfusion. After 30 to 48 hours this edema usually blocked the flow of perfusion fluid into the brain; therefore experiments were arbitrarily terminated at 24 hours. Without O_2, 22 mM glucose was sufficient to maintain brain function for 24 hours at 22°-25°C (In two cases in which flow was maintained, brain function continued for about 72 hr.); with O_2, 6 mM glucose was needed. (Plasma glucose concentration usually exceeds 40 mM in intact anoxic C. picta). In the absence of glucose, brain function persisted for about 1.6 hr. without O_2 and for about 6 hr. with it. It is concluded that plasma glucose is a sufficient fuel for anaerobic brain function in turtles. (Supported by NSF G 6014 and NIH Research Career Development Award K3-GM-31, 779).

CHANGES IN CANINE RENAL FLUID DYNAMICS EFFECTED BY ACETYLCHOLINE. R. D. Bell* and M. J. Keyl. University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

Previous experiments have suggested that elevated intrarenal venous pressure is the immediate determinant of the increased renal lymph pressures which follow increases in renal pelvis pressure and external renal venous pressure. The present experiments were designed to examine these relationships during alterations in renal hemodynamics produced by acetylcholine. Close arterial infusion of acetylcholine was shown to be accompanied by a significant increase in intrarenal venous pressure (IRVP). The increase in IRVP appeared to result from an increase in renal blood flow with only slight changes in venous outflow resistance. Capsular renal lymph pressure was found to follow a course similar to that of IRVP. These experiments thus support the hypothesis that IRVP is the major variable responsible for renal lymph formation in the dog. (Supported in part by NIH Grant #HE 12832 and the V.A. Hospital, Oklahoma City, Oklahoma)

THE EFFECT OF HEMATOCRIT ALTERATION ALONE ON URINE VOLUME AND SODIUM EXCRETION. H.H. Bengele*, E. Houttuin* and J.W. Pearce. Department of Physiology, University of Toronto, Toronto, Ontario, Canada.

The blood of anesthetized male rats (Sprague Dawley) was equilibrated, via an arterial-venous (A-V) shunt, with a reservoir containing donor blood. After two hours, while the A-V shunt continued, the reservoir blood was centrifuged. In three separate series, the plasma, red cells, or whole blood was returned to the reservoir. Equilibration continued for an additional two hours in order to evaluate the effect of acute alterations in hematocrit, unaccompanied by other changes in blood composition or changes in vascular volume, on urine excretion. The results indicate that a decrease in hematocrit (40.3%→23.1%) is associated with an increase in urine volume and sodium excretion of 0.35 ± 0.62 µl/min.g and 282.5 ± 193.4 mµEq/min.g (mean ± S.E.) respectively. An increase in hematocrit (40.4%→50.0%) is associated with decreases of 2.81 ± 0.98 µl/min.g and 371.7 ± 176.9 mµEq/min.g for these variables. The changes are different from each other ($P<0.05$). Regression analyses yield negative correlations ($P<0.01$) between the alterations in hematocrit, and the changes in sodium excretion ($r=-0.66$) and urine volume ($r=-0.63$). These findings indicate an influence of hematocrit on both the urine volume and sodium excretion. (Supported by M.R.C., Canada)

EYE AND HEAD COORDINATION OF NORMAL SUBJECTS AND PATIENTS WITH DEFECTIVE OCULOMOTOR OUTPUT. Peter Herman Ben-Zur,* Martin Feldman,* Morris B. Bender. Departmentof Neurology, Mount Sinai School of Medicine, New York, New York.

Normal subjects and patients with defective eye movements as a result of lesions of the oculomotor system were given the command "look at the wall" (on the right). This induced eye and head movements from direct forward to lateral gaze. Eye and head movements were recorded by DC electrooculography on a polygraph.

In six normal subjects, the eyes began to move before or at the same time as head movement. The eyes moved with average velocity of 150°/sec. over an amplitude of 40°. The head moved with an average velocity of 40°/sec. over an amplitude of 25°. The head usually began to move 50-150 msec. after the initiation of eye movement.

In the patient group: (1) Head movement usually began before eye movement. (2) Average eye velocity was diminished. (3) Eye amplitude was diminished. (4) The eye movement was broken down into multiple steps. (5) Head movement tended to be of larger amplitude. In the presence of defective oculomotor output (slow and small amplitude eye movements) the head contributed a larger proportion to the total eye movement in space (gaze) by moving over larger amplitude.

Patients were selected with prominent defects in eye movement. However on testing, each such patient also had defects in head movement. The defects in head movement were less apparent and were of lesser severity than those of eye movement. The presence of head movement defects in patients with lesions of the oculomotor system suggests that the neural organization responsible for oculomotor output is also, in part, responsible for head movement (Supported by USPHS Grant NB 04576).

EFFECT OF SEROTONIN ON GASTRIC SECRETION IN THE PERFUSED RAT STOMACH USING A CONTINUOUS RECORDING OF pH AND H^+ SECRETION. Gerrit H. Besselaar, Ronald Geller, and Walter Lovenberg (intr. by K. S. Kim). Natl. Inst. of Health, Bethesda, Md. and George Washington Univ., Washington, D.C.

The model for continuous recording of pH in the perfused stomach of the rat as described by Gosh and Schild was adapted in the following way. The stomach of the anesthetized rat is perfused with .9% NaCl (pH 7, 30°C), delivered at a rate of 1 ml/min. The pH of the effluent is measured in a T-tube, and the effluent is collected in a 500 ml beaker, containing a combination pH electrode connected with an automatic titrating pH meter. The endpoint of the titration unit is set at pH 7, so that the amount of .004 N NaOH used by the titrator is a direct measure of the amount of H^+ ions secreted by the stomach. Blood pressure is continuously monitored. The experimental rates of secretion are consistently within 10% of those calculated from the recorded pH and the rate of perfusion. With this sensitive method we have studied the influence of serotonin on gastric acid secretion. Unlike the reported inhibitory effects of serotonin on histamine induced gastric secretion in the dog, we were unable to demonstrate any inhibitory effect of serotonin infusions or single injections on gastric secretion stimulated by histamine or carbamylcholine. Pretreatment with parachlorophenylalanine, a serotonin synthesis inhibitor, did not result in an augmented response to histamine. This is in contrast to the increase in gastric acid secretion after histamine stimulation we observed in parachlorophenylalanine pretreated Shay rats. The possible cause for the discrepancy in the results obtained in the two different preparations has not yet been determined.

THE EFFECT OF CORONARY VASODILATION ON HEMORRHAGIC SHOCK. H. L. Bethea*, J. W. Crowell, and C. E. Jones*. Univ. of Miss. School of Med., Jackson, Miss.

The effect of pharmacological coronary vasodilation on hemorrhagic shock was studied in two groups of dogs. All dogs were bled to an arterial pressure of 30 mm Hg. and maintained at this hypotensive state until irreversible shock was developed. In the first series, 20 closed chest dogs were used; 10 were treated with a pharmacological coronary vasodilator, Persantin, and 10 were used as controls. Bleeding rate and peak bled volume were not significantly different in the two groups ($p > 0.05$). The mean reversal time was 108 ($\pm$ 12 SEM) min. in the Persantin group and 64 ($\pm$ 7 SEM) min. in the control group. This difference is significant ($p < 0.05$). In the second group of 10 open chest dogs, the effect of Persantin on circumflex blood flow was studied. In 5 dogs treated with Persantin there was a significantly greater flow during the first 75 minutes of hypotension. These data indicate that reduced coronary flow during hemorrhagic hypotension may be a contributing factor to the development of irreversible shock since pharmacological vasodilation appeared to have a protective effect.
Supported by NIH Grant HE 02494.

FUNCTIONAL AND ANATOMIC CORRELATION OF PULMONARY ARTERY MEDIAL HYPERTROPHY IN THE CAT. Sanford P. Bishop and William Rogers (intr. by C.R. Smith) Dept. of Pathology, Ohio State University, Columbus, Ohio

Hypertrophy and hyperplasia of the medial smooth muscle of pulmonary arteries in the cat (MPH) was correlated with age, sex, breed, disease status, electrocardiographic and hemodynamic parameters, and heart weight to body weight ratios in conventional and specific-pathogen-free (SPF) cats. Histologic study was completed in 120 cats; in 35, hemodynamic and electrocardiographic studies were done under sodium pentobarbital anesthesia. Histologically lung sections were graded as no MPH present (I), mild MPH (II), moderate MPH (III), or severe MPH (IV). MPH was found in 39% of 120 cats and there was no correlation of MPH with age, sex, breed, method of euthanasia or presence of disease. MPH was observed with the same frequency in both SPF and conventional cats, indicating that the cat lungworm, Aelurostrongylus abstrusus, is not a priori necessary for the condition to be present as others have suggested. Although no difference was found in right ventricular or aortic peak systolic pressure, calculated pulmonary vascular resistance ($N = 7$ in each group) was higher in cats with MPH (0.180 $\pm$ 0.08 S.D. mm Hg/ml/min/kg) than in cats without MPH (0.086 $\pm$ 0.057) and cardiac output was lower in cats with MPH (98.8 $\pm$ 47.1 ml/kg/min) than in cats without MPH (183.8 $\pm$ 73.1). No differences were found in the electrocardiograms or heart and ventricular weight to body weight ratios in cats with and without MPH. It was concluded that MPH is a lesion of unknown cause in the cat which, at least in the anesthetized state, produces increased pulmonary vascular resistance which is compensated for by decreased cardiac output. Myocardial hypertrophy was not present. (Supported in part by USPHS Grant HE-09884.)

TRANSFER OF INERT GASES AND TRITIATED WATER ACROSS THE SHEEP PLACENTA. J. M. Bissonnette* and G. H. Gurtner. Dept. of Environmental Medicine, The Johns Hopkins University, Baltimore, Maryland 21205.

Measurement of the transfer of inert gases across the placenta was made in 9 term ewes using a mass spectrometer. The fetal side of the placenta was perfused with a saline-dextran solution at various flow rates after removal of the fetus. Partial pressures of the test gases were measured in umbilical artery (Pua) umbilical vein (Puv) and maternal artery (Pma). The results showed that when the test gases were presented via the umbilical artery that Puv/Pua was almost independent of fetal perfusion rate for the gases Argon and Ether but different for each gas (Ether > Argon), Puv/Pua was less for N_2O than for any of the other gases at low flow rate but increased with increased fetal perfusion rate. When the ewe was respired with the test gases Puv/Pma was greater for N_2O than for Argon or Ether. The transfer of tritiated water under the same conditions was greater than with the gases. It is difficult to explain these results on the basis of diffusion across a single membrane between maternal and fetal capillaries since such a membrane would be required to have a higher permeability to water than to gases. We have postulated a three-compartment unit on the fetal side of the placenta which allows exchange between inflow and outflow compartments as well as exchange between maternal and fetal capillaries. The results could be due to different permeabilities of the barriers between inflow and outflow compartments (K_1) and the fetal maternal capillaries (K_2). According to this model $K_1 > K_2$ for Ether and Ar, $K_1 < = K_2$ for N_2O and $K_1 < K_2$ for water. It seems possible that K_1 characterize a predominantly lipid membrane and K_2 may be due t predominantly aqueous membrane. Supported in part by USPHS Gran 10342.

URINARY CORTICOSTERONE EXCRETION IN LABORATORY RATS EXPOSED TO PRESSURES OF 10, 20, AND 30 ATA. (He-O_2). R.A. Bitter and T.W. Nielsen (intr. by T.K. Akers). Dept. of Physiology and Pharmacology, School of Medicine, Univ. N. Dak., Grand Forks, North Dakota, 58201.

It is generally accepted that corticosterone is the major adrenal corticosteroid excreted in response to stress in the laboratory rat. The purpose of this study was to investigate some of the possible relationships between high pressure and adrenal cortical activity. Adult male Sprague-Dawley rats (250-350 gm) were exposed in a high pressure chamber to He-O_2 (80-20% at 1 atm) while control urine samples were collected. Animals were then exposed to He-O_2 mixtures at 10, 20, and 30 Ata. The partial pressure of O_2 was kept between 150 and 250 mm Hg during experimental periods. Animals were exposed to the high pressure He-O_2 mixture for 24 hours and then stage decompressed in 8 to 12 hours. Excreted corticosterone levels were measured along with appropriate standards according to the method of Mattingly (1964). Urinary corticosterone, expressed as ug/24 hour sample, was found to be 0.95 ± 0.27(S.D.) for room air (N_2-O_2), and 1.83 ± 0.29 (S.D.) for He-O_2 at normal pressure. At 10, 20, and 30 Ata, the urinary steroid levels were 3.04 ± 0.87; 3.95 ± 0.75; and 2.79 ± 0.39; respectively. Urinary corticosterone excretion returned to normal levels during the 24 hour period following exposure. Unexplained but statistically significant differences were found between the N_2-O_2 and He-O_2 control samples. Significant increases over control values were noted in the groups of animals treated at 10, 20, and 30 Ata. This study was supported in part by ONR N0001468A0499.

CIRCULATORY RESPONSE TO HEMORRHAGE DURING HYPOXIC HYPOXIA. Clark M. Blatteis. Department of Physiology & Biophysics, University of Tennessee Medical Units, Memphis, Tennessee 38103.

Hemorrhage was produced by the method of Walcott (Am. J. Physiol. 143:254, 1945) in 18 pentobarbitalized, heparinized dogs; 25% of the shed blood volume was returned immediately. Throughout the experiments 9 dogs breathed air, i.e., normoxic (N) group ($P_{a_{O_2}}$ = 86.5 ± 6.7 mmHg, $S_{a_{O_2}}$ = 96.9 ± 0.5%), and 9 other dogs inspired 10% O_2 in N_2, i.e., hypoxic (H) group ($P_{a_{O_2}}$ = 38.6 ± 2.9 mmHg, $S_{a_{O_2}}$ = 73.7 ± 5.3%). The volume (N = 31.3 ± 2.0, H = 31.2 ± 1.9% of the control total blood volume) and duration (N = 6.6 ± 0.7, H = 7.9 ± 0.9 min) of bleed-out were equal in the two groups. Twenty-two % of the normoxic and 77% of the hypoxic animals (P = .05) died within 2 hr after bleeding. One hour after hemorrhage, the following results were obtained:

	N	H
Plasma volume, ml/kg	40.1 ± 2.1	30.9 ± 3.1*
Cardiac index, ml/kg^{-1}min	70.9 ± 5.7	43.4 ± 7.6*
Mean arterial press, mmHg	80 ± 6	46 ± 5*
TPR, dynes·sec/cm^5	5534 ± 532	4448 ± 700
Central venous press, mmHg	-2.3 ± 1.4	3.6 ± 3.8
Lactate/pyruvate, ratios	33.6 ± 5.9	105.5 ± 34.7*

(The values are means ± S.E.; * indicates significant differences.)

These findings suggest that hypoxic inhalation may sensitize anesthetized dogs to acute blood loss by provoking failure of the precapillary sphincters. (Supported in part by Tennessee Heart Association Grant No. 243030 4609R.)

IDENTIFICATION AND ELECTRICAL POTENTIAL OF ISOLATED OXYNTIC CELLS. A. L. Blum*, C. P. Sung*, G. Shah*, V. D. Wiebelhaus* and G. Sachs. University of Alabama Medical Center, Birmingham, Ala. and Smith, Kline and French Laboratories, Philadelphia, Pennsylvania.

In viable preparations of isolated cells from amphibian gastric mucosa (Necturus and Rana catesbeiana, Physiologist 12:179, 1969), oxyntic cells could be identified biochemically (ATPase activity proportional to concentration of oxyntic cells), histochemically (positive succinic dehydrogenase and ATPase stain) and morphologically (electron and light microscopy). Identification was also possible in a system which allowed cell punctures with KCl filled glass microelectrodes. The mean oxyntic cell potential was 44 ± 3 mv (S.E.M.) and was sensitive to changes of K^+ and Cl^- concentrations in the nutrient solution. With this technique electrical responses of oxyntic cells alone can be directly determined. (NSF).

EFFECT OF BILATERAL AORTIC NERVE SECTION ON PLASMA ADH TITER. G. C. Bond* and J. W. Trank. Univ. of Kan. Med. Ctr., Kansas City, Kan.

The hypothesis that aortic arch and right subclavian baroreceptors influence plasma antidiuretic hormone ([ADH]p) concentration was tested by determining the effect of bilateral aortic nerve section (BANS) on [ADH]p. BANS was performed in: a) intact rabbits; b) vagotomized rabbits; and c) vagotomized rabbits in which arterial pressure was controlled. For each experiment, two 20 ml arterial blood samples were drawn for determining [ADH]p: one prior to BANS; and one three minutes after BANS. Control experiments indicated that sample withdrawal had no effect on [ADH]p. Subsequent to BANS in intact rabbits [ADH]p went from 2.9 ± 0.2 μUnits/ml (mean ± SE) to 5.0 ± 1.3 μUnits/ml. The plasma ADH concentrations are not significantly different ($p > .10$). Significant differences were obtained in pulse pressure ($p < .005$) and mean arterial pressure ($p < .001$). Subsequent to BANS in vagotomized rabbits [ADH]p increased from 2.9 ± 0.1 μUnits/ml to 5.8 ± 1.2 μUnits/ml. The plasma ADH concentrations are significantly different ($p < .05$). A statistically significant change also occurred in mean arterial pressure ($p < .005$). Finally, subsequent to BANS in vagotomized rabbits in which arterial pressure was controlled, [ADH]p rose from 3.0 ± 0.8 μUnits/ml to 10.5 ± 2.9 μUnits/ml. The plasma ADH concentrations are significantly different ($p < .025$). For any experiment no statistically significant changes occurred in heart rate or central venous pressure after BANS. Based on the results, it is suggested that aortic arch and right subclavian baroreceptors influence [ADH]p and therefore may play a role in the regulation of blood volume. (Supported in part by a grant from the Kansas Heart Association.)

EFFECTS OF NOREPINEPHRINE ON ACTIVE TRANSPORT AND AUTOMATICITY OF CARDIAC PURKINJE FIBERS. Pier Giorgio Borasio* and Mario Vassalle. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

The aim of the present project was to investigate whether norepinephrine increases K-uptake directly or indirectly and can independently affect pacemaker activity and active ionic transport. Purkinje fibers from canine ventricles were perfused in a tissue bath in close proximity to a beta probe. Tissue radioactivity and transmembrane potentials were measured at the same time. In fibers driven at constant rate, norepinephrine (0.1 μg/cc) increased both potassium uptake and the spontaneous rate of discharge (which was measured during brief interruptions of the stimulation). In the same preparations, tetrodotoxin (10 μg/cc) inhibited the stimulation of automaticity and of K-uptake induced by norepinephrine. Either the substitution of glucose with 2-deoxy-D-glucose or omission of Mg^{++} from the Tyrode solution markedly reduced the norepinephrine-induced K-uptake, but not the increase in automaticity. Substitution of Na^{+} with choline inhibited both increase in K-uptake and in automaticity induced by norepinephrine. Dibutyryl 3',5'- AMP (0.5 mg/cc) increased K-uptake (as norepinephrine did) but increased automaticity only very slightly. It is concluded that the sodium-potassium pump is stimulated by norepinephrine but indirectly (possibly through an enhanced Na^{+} influx). No K-uptake is induced by norepinephrine when active transport is blocked either by absence of Mg^{++} or the presence of 2-deoxy-D-glucose. The action of norepinephrine on K-uptake, but not on pacemaker activity, can be mimicked by dibutyryl 3',5'- AMP. Several of these results suggest that the action of norepinephrine on active transport can be dissociated from that on automaticity. (Supported by a grant from New York Heart Association)

OPTIMUM FRAME RATE FOR QUANTITATIVE CARDIAC CINERADIOGRAPHY. A.A. Bove*, P.R. Lynch, and M.C. Ziskin* (intr. by M.P. Wiedeman) Temple University School of Medicine, Philadelphia, Pa.

Left ventricular pressure (LVP), volume (LVV) and length (LVL) were calculated from biplane cineradiographs taken at 270 frames/second (fps) during intraventricular contrast injection. A computer data reduction system provided rapid calculation of LVV using numerical integration applied to ventricular dimensions obtained from the films. X-ray magnification and image intensifier face distortion were corrected automatically with the computer program. LVP was recorded directly on the cine film for precise timing. Discrete samples at 270 fps were used to construct continuous curves for each parameter throughout the cardiac cycle. Fourier analysis of the LVV, LVP and LVL curves gave frequency and signal energy spectra for each curve. One complete heart cycle was analyzed with a premature beat included. From 75 to 85% of the signal was found between 0 and 15 Hz for pressure, 0 and 5 Hz for volume and length, 99% of signal energy is contained in the same frequency bands. The low frequency characteristics of these signals indicate that film speeds of 60 fps are more than adequate for reconstruction of continuous curves of cardiac parameters for discrete samples calculated from cine frames.

Supported by USPHS, NIH, NHI Grant HE 08886 and Grant GM 14548. A.A. Bove: Postdoctoral Fellow in Physiology, USPHS Fellowship 1-F2-GM-37,295-01.

CALORIGENIC EFFECTS OF ISOPROTERENOL DURING PRODUCTION OF CARDIAC NECROSIS. P.O.Bramante and E.L.Nirdlinger*, Dept. of Physiology, University of Illinois College of Medicine, Chicago, Illinois.

Little is known about the calorigenic effects of isoproterenol, a potent β-stimulator capable of eliciting myocardial necrosis. Changes of O_2 consumption in rats treated with a single dose of this drug were measured utilizing an automatic apparatus (J.A.P.14:1063,1959) and technique of quantitation (J.A.P.16:982,1961 & 24:11,1968) which permit partitioning of the continously registered total $\dot{V}_{O_2}$ of the animal into several components (The Physiologist,12:182,1969). Values of Minimal Calculated Metabolic Rate (MCMR) can thus be obtained representing the metabolic effects of experimental procedures as a function of time, unbiased by the influence of spontaneous muscular activity (SMA). Isoproterenol administration (40 mg/Kg,s.c.) resulted in a rapid increase of the animal's "net" $\dot{V}_{O_2}$ (MCMR). Results of individual determinations in 2 series of rats of different strain,age and weight were highly reproducible and yielded smooth curves of the average $\dot{V}_{O_2}$ changes. Peaks of +150 and +110% respectively were observed within one hour,followed by return to normal values over a period of several hours. Determinations performed after 24 & 48 hrs revealed normal resting metabolic rates. However, episodes of SMA of animals with severe cardiac lesions, confirmed at autopsy,elicited disproportionate increases of $\dot{V}_{O_2}$. It is noteworthy that a rapid increase of $\dot{V}_{O_2}$ after isoproterenol injection is immediately followed by an increase of Ca concentration in cardiac mitochondria (Nirdlinger and Bramante,this issue). The decreased caloric efficiency of animals with severe cardiac lesions,as shown by these experiments,may provide a simple diagnostic tool for the evaluation of experimentally produced myocardial damage. (Supported by USPHS grants HE 10373 & GM 738 and the University of Illinois Graduate College)

Potassium-induced inhibition of proximal tubular fluid reabsorption. M.Brandis*, J.Keyes*, and E.E. Windhager. Cornell Univ. Med. College, N.Y. 10021.

Using micropuncture techniques, the effect of elevation of peritubular capillary K conc. on proximal tubular fluid reabsorption was studied in rat kidneys. In one series, free-flow collections were done at the same site prior to and during i.v. infusion (0.05ml/min) of 140 mM/l KCl. Arterial plasma K ranged from 4.0 to 4.7 mM/l in controls and from 5.7 to 8.0 under exper. conditions. The average (exper./contr.) rate of fluid reabsorption was 0.65 ± 0.09 (SEM,14obs.), significantly different from 1.0 ($p<0.01$). In a second series, peritubular capillaries were perfused with isosmotic Ringer's containing 10 mM/l K. Reabsorptive rates, measured in split drop experiments averaged 3.64×10^{-4} $mm^3/mm^2.sec$ ±0.31(SEM,19obs.). During capillary perfusion with Ringer's containing 5 mM/l KCl the mean split drop reabsorptive rate was $5.36\times10^{-4}mm^3/mm^2.sec$ ±0.48(SEM,9obs.), and during normal blood perfusion of capillaries 5.60×10^{-4} $mm^3/mm^2.sec$ ±0.44(SEM,14obs.). Reabsorption was significantly decreased during high K perfusion of capillaries ($p<0.05$ for high K-low K; $p<0.01$ for high K-norm.blood). In separate free-flow recollections during 10 mM K-Ringer perfusion of capillaries the mean (exper./contr.) rate of fluid reabsorption was 0.71 ± 0.06(SEM,12obs.), a value significantly different from 1.0($p<0.01$). The results demonstrate that elevation of K-concentration in peritubular fluid depresses proximal sodium and water reabsorption.

THE EFFECTS OF CHANGES IN SODIUM CONCENTRATION ON RENIN RELEASE IN VITRO FROM RAT KIDNEY SLICES OBTAINED FROM RATS ON NORMAL AND SODIUM DEFICIENT DIETS. Berton Braverman* and Howard H. Rostorfer. Anatomy and Physiology Dept., Indiana University, Bloomington, Indiana.

Kidney slices obtained from rats either on a normal diet or a sodium deficient diet (more than 14 days) incubated in Warburg flasks in Robinson's solution containing 160mEq Na and a 100% nitrogen atmosphere released significantly less renin than neighboring slices in the same solution but incubated in flasks that were sparged with oxygen. Release was negligible in the presence of nitrogen and 10^{-5}M arsenite-arsenate. Kidneys from rats on a sodium deficient diet contained 3-6 times more renin than those from rats on a normal diet, but slices from either group released the same percentage of their renin content into the surrounding solution on incubation in 100% oxygen at 37°C. Oxygen consumption and renin release were significantly greater in solutions containing either 100 or 160mEq Na than a solution with only 20mEq Na (300 milliosmolar concentration maintained with mannitol). It appears that in vitro renin release is an active metabolic process which is a function of renin content, pre-existing in vivo parameters, and in vitro sodium concentration. It also appears that renin release in vitro proceeds at a maximally possible rate due to the lack of a physiological control. (Supported by USPHS Grant 2R01-HE05625-09)

ATRIAL RECEPTORS AND THEIR INFLUENCE ON PLASMA ADH AND RENIN LEVELS. Leonard A. Brennan, Jr.*, Richard L. Malvin, Kenneth E. Jochim, Donald E. Roberts*. University of Michigan, Ann Arbor.

The role of atrial receptors controlling secretion of renin and ADH was investigated in dogs anesthetized with either pentobarbital or morphine, urethane-chloralose mixture. Atrial pressures were increased by an inflatable balloon placed in the atrial appendages. Atrial pressures were recorded from cannulas inserted into the appendage. Cardiac output was recorded by means of a flow probe placed around the ascending aorta. Mean arterial pressure was recorded from a femoral arterial cannula. Plasma ADH and renin concentrations were determined by bioassay. Inflation of the left atrial balloon consistently reduced plasma levels of ADH but did not predictably alter plasma renin levels. Increases in left atrial pressure reliably produced cardio-acceleration in dogs anesthetized with morphine, urethane-chloralose but not in those with pentobarbital anesthesia. These effects occurred without consistent changes in either cardiac output or arterial pressure. Increases in right atrial pressure by as little as three cm. H_2O produced a decrease in plasma renin levels. Our investigations have confirmed that increases in left atrial pressure reduces plasma ADH levels in the anesthetized dog. Further evidence has been obtained which indicates that renin levels can be altered by stimulation of the right atrial but not the left atrial receptors.

OBSERVATIONS ON A PARADOXICAL HYPOSTHENURIA. E.H. Bresler, K. Nielsen*, and R. Odell*.

We have previously reported that dogs given 300 ml of 5% NaCl at 10 ml/min and then infused with n-saline at 10 ml/min over a period of hours frequently produce a urine during some portion of this period which is markedly hyposmolal to contemporary plasma. Slowing of urinary flow by partial ureteral obstruction, surprisingly, leads to a further reduction in urinary osmolality. Pitressin administration is without effect. In the present study observations on this phenomenon were extended. A procedure involving collection of serial samples following a 10 minute ureteral occlusion (similar to stop-flow procedure) was carried out. These were analyzed for Na, K, urea and creatinine and total osmolality computed. Comparison of the serial plots so obtained in the same animal during a period when urine hypertonic to plasma was being formed with those obtained during a period of hyposthenuria shows that at corresponding points on the plots the molar ratio of solutes remains unchanged. This signifies that the formation of dilute urine is not the result of preferential removal of a single solute such as NaCl but rather to a failure to abstract water. The plot of osmolalities for the serial samples shows a marked minimum which coincides with a sodium minimum during hyposthenuria. The osmolar minimum but not the sodium minimum, is either markedly blunted or not present during the formation of a urine more concentrated than plasma.

EFFECTS OF MASSIVE DOSES OF NEOMYCIN ON GUT MORPHOLOGY AND LIPID TRANSPORT IN THE RAT. Kenneth R. Brody*, Richard P. Spencer, Section of Nuclear Medicine, Yale Univ. School of Medicine, New Haven, Conn.

A readily produced animal model of the steatorrheic state would be of use in evaluating the intestinal absorption of lipid analogues (such as the ^{75}Se-selenofatty acids). Steatorrhea can be produced in man by the prolonged oral administration of neomycin B sulfate. At a dose of 0.06 gm/kg body weight for 19 days, human fecal fat is greatly elevated. In an effort to induce this state in rats, male Sprague-Dawley animals (150-200 gm) were given a diet of Lab Chow (13.95 gm), triolein (0.75 gm), and neomycin (0.3 gm, or 1.5 gm/kg body weight). Drinking water contained 0.5 gm of neomycin/15 ml. A macromethod was devised for lipid assay in the feces. This estimated all the free fats, as well as fatty acids and soaps (determined in the form of liberated free fatty acids, and calculated as glyceryl tristearate for reference purposes). The assay showed a daily excretion of about 0.14 gm/day in the control period before neomycin was added. In 4 rats, the fecal fat excretion did not increase significantly during a period of up to 18 days of neomycin addition to the diet. This was true despite signs of toxicity in the animals, and the presence of microscopic changes in the liver and intestine. Hence the rat is not a suitable species for producing steatorrhea due to neomycin. (Supported by USPHS CA 06519).

TEMPERATURE, SKELETAL MUSCLE MITOCHONDRIAL FUNCTIONS, AND OXYGEN DEBT. G. A. Brooks,* K. J. Hittelman,* J. A. Faulkner, and R. E. Beyer. The University of Michigan, Ann Arbor, Mich.

O_2 debts measured after exercise are invariably larger than theoretical O_2 debts. Compared to resting liver and skeletal muscle temperatures of 38.6°C and 37.7°C, respectively, post-exercise values were 43.4°C and 44.1°C *in vivo*. To determine the relationship between temperature and cell respiration, the O_2 consumption of isolated rat skeletal muscle mitochondria was measured at temperatures between 25° and 45°C *in vitro*. Increasing temperature had a striking effect on mitochondrial functions. Between 37° and 45°C, state 3 respiratory rate increased from 470 to 754 n atoms $O_2 \cdot mg^{-1} \cdot min^{-1}$, state 4 respiratory rate increased from 98 to 295 n atoms $O_2 \cdot mg^{-1} \cdot min^{-1}$, the ADP:O ratio decreased from 2.47 to 2.04, and mitochondrial oligomycin sensitive ATPase activity increased from 223 to 429 n moles $Pi \cdot mg^{-1} \cdot min^{-1}$. Due to the increase in non-conservative (state 4) respiration and decrease in phosphorylative efficiency (ADP:O ratio), a portion of the post-exercise O_2 consumption is not associated with recovery from anaerobic metabolism. The classical definition of O_2 debt, therefore, requires revision. Furthermore, observed decreases in energy-conserving efficiency at elevated temperatures suggest a molecular mechanism for muscle fatigue under conditions of exercise-induced hyperthermia. (Supported by grants from the National Institute of Arthritis and Metabolic Diseases [AM-10056-05], the National Science Foundation [GB-13496], the Western Electric Company, and PHS Training Grant No. 5 T01 GM 00989.)

MOTOR EFFECTS FROM INTERPOSED NUCLEI. V. B. Brooks, A. Atkin,* I. Kozlovskaya,* and M. Uno.* Dept. of Physiology, New York Medical College, New York, N.Y. 10029.

In a study of cerebellar control of voluntary movement, brief stimuli (20 msec trains of 0.1 - 0.2 msec pulses, 1000/sec, 0.2 - 0.5 mA) were administered through implanted electrodes to the interposed nuclei (IP) of a Cebus monkey while it moved a handle with the ipsilateral arm between two target zones along a horizontal arc centered at the elbow. Supra-threshold IP stimulation evoked a flexional acceleration (onset latency about 30 msec, duration 30-40 msec) that was immediately followed by an extensional acceleration of longer duration (70-90 msec) and then by 2 or 3 progressively smaller accelerations of the same or slightly greater duration. This IP-induced flexor jerk tended to lengthen voluntary flexions and to shorten extensions. Electromyographic surface recording revealed an increase of flexor (biceps) activity of about 100 msec duration and concomitant reduction of extensor (triceps) activity for about 200 msec immediately after each stimulation. When stimulation was applied during extension the initial flexor acceleration was smaller (sometimes nearly disappearing) than when equal stimulation was applied at rest or during flexion. Nevertheless the magnitude of the subsequent extensor acceleration generally remained large. Cooling of the ipsilateral dentate nucleus decreased the initial IP-induced acceleration and changed the differential actions of IP stimulation on flexions and extensions. These results reveal differences in motor reactivity during voluntary flexion and extension, which depend on dentate outflow. Effects from IP seem to be under functional control of other motor systems.
(Supported by USPHS Grants NB 05508 and NB 05544, and NSF Grant GB 8018)

AUTOREGULATION OF SPLANCHNIC BLOOD VOLUME. Gerald A. Brooksby* and David E. Donald. Mayo Foundation, Rochester, Minnesota.

Studies in anesthetized dogs showed that autoregulation of splanchnic blood volume and blood flow occurred concurrently. Moment to moment changes in splanchnic blood volume were calculated from continuous simultaneous measurements of blood flow (electromagnetic flow transducers) into and out of the vascularly isolated coeliac and superior mesenteric circulation in bilaterally splanchnicectomized dogs with intact abdomens. Aortic blood pressure was held constant at desired values with a 40 L windkessel. In some cases separate simultaneous measurements were made of blood flow in the coeliac and in the superior mesenteric artery. Perfusion pressure was varied between 80 and 200 mmHg, either in continuous steps of 20 mmHg, or in isolated varied increments. In those dogs in which only minor changes in splanchnic blood flow attended changes in perfusion pressure, splanchnic blood volume likewise remained relatively constant. Dogs with none or minimal autoregulation showed changes in blood flow and blood volume directionally similar to the change in perfusion pressure. Autoregulation of blood flow was more pronounced in the superior mesenteric than in the coeliac circulation. Separate increments in pressure and increase in pressure were more effective in eliciting autoregulation than were continuous change in pressure or a decrease in pressure. Autoregulation of splanchnic blood flow and blood volume was observed in about two-thirds of the dogs studied. (Supported in part by N.I.H. Grant HE-06143).

LEARNING OF LEG POSITION BY SPINAL RATS. A. A. Buerger and A. Fennessy.* Harvard University, Cambridge, Mass.

Experiments by Horridge (Proc. Roy. Soc. B., 1962, 157:33-52) and others indicate that all or part of the ventral nerve cord of insects are capable of learning leg position. Our experiments suggest that the lumbosacral cord of mammals is also able to learn leg position. All experiments were performed on young adult rats with thoracic or lumbar spinal cord transections. In a previous experiment (Nature, 1970, 225:751-752), experimental rats received shocks whenever they lowered an electrode attached to one hindfoot into an electrolyte bath; yoked-control rats received the shocks along with the experimental animals. Experimental animals consistently held the foot with the electrode above the electrolyte. During the early minutes of the second phase--a testing situation--in which the experimental and control animals were both shocked for leg lowering, the experimentals received fewer shocks than the controls; the controls eventually withheld the foot. In the present experiment, one-animal preparations were used; one hindleg was a yoked control for the other. The results of both experiments were analogous, although the differences between the experimental and control legs were less distinct in the one-animal experiment than in the two-animal experiment. These results suggest that the lumbosacral spinal cord of mammals relates shock to leg position, and directs the leg to avoid shock when leg position is contingent on shock. Hence, the spinal cord might be used as a simple system for the study of mammalian learning.

ELECTRICAL STIMULATION OF HUMAN SWEAT GLANDS AND LOCAL HEATING ENHANCEMENT. Robert W. Bullard, John B. Pierce Foundation Laboratory, New Haven, Conn. and Indiana University, Bloomington, Ind.

Using a specially designed clamp electrode mounted on the forearm skin surface, branchlets of either the medial or lateral antebrachial cutaneous nerves were stimulated to produce sweating which was continuously recorded from a nearby skin area using a ventilated capsule and a resistance hygrometry system. Square wave stimuli, with a duration of 2.5 m/sec, a frequency of either 5 or 10 H, and a strength of 20 to 30 volts were used throughout this series. By means of a water jacket, the temperature of the skin area under the capsule could be controlled in the range of 30°C to 40°C and recorded with a small thermocouple mounted on the skin area. Plots of the sweating rates obtained by constant electrical stimulation versus local skin temperature yielded Q_{10} values between 5 and 6. With higher frequencies (maximal stimulation) a lower Q_{10} was obtained. The experiments indirectly support a previously published hypothesis that local heating enhances sweat gland production by an action at the neuroglandular junction wherein the amount of transmitter released with each sudomotor neural impulse is increased with temperature. The maximum limit of sweating produced from electrical stimulation is presumably determined by the rate of resynthesis or handling of the transmitter substance at the neuroglandular junction, and thus a lower thermal increment would be expected.

THE EFFECT OF VASOPRESSIN ON SECRETIN-STIMULATED PANCREATIC SECRETION IN THE RABBIT, in vivo and in vitro. Paiboon Buranarugsa * and Ward W. Moore. Dept. of Physiology, Mahidol Univ., Bangkok, Thailand.

Recent reports have indicated that high doses of vasopressin (ADH) alter the response of the pancreas to secretin. The present study shows the effects of ADH administration on secretin-stimulated pancreatic juice flow and HCO^-_3 and Cl^- concentration in the rabbit, in vivo and in vitro. The intravenous administration of ADH (10 mU/kg/min) for 30 minutes significantly reduced the rate of secretin-stimulated (20 mU/kg/min) pancreatic juice flow and HCO^-_3 concentration and increases the Cl^- concentration in an in vivo preparation. ADH at this dose also significantly reduced the arterial blood pressure and produced evidence of cardiac ischemia. ADH (either 4 mU/min or 8 mU/min) infused intra-arterially for 30 minutes in an in vitro pancreas preparation (Rothman and Brooks. Amer. J. Physiol. 208: 1171, 1965) produced no significant effect upon secretin-stimulated (8 mU/min) pancreatic juice flow rate, HCO^-_3 or Cl^- concentration. These doses of ADH however, increase the perfusion pressure of the preparation. The perfusion rate (1 ml/min), and therefore, the delivery rate of secretin to the pancreas remained constant. The data suggest that ADH does not reduce pancreatic juice flow rate by enhancing the reabsorption of HCO^-_3 and H_2O from the ducts. The reduction in flow rate and HCO^-_3 concentration observed in vivo are probably the result of the effect of ADH on pancreatic blood flow and a resultant reduced rate of delivery of secretin to the pancreas. (Supported by The Rockefeller Foundation).

CHANGES IN REGIONAL CEREBRAL TISSUE pO_2 AND BLOOD FLOW IN ANIMALS BREATHING AIR AND O_2 AT ATMOSPHERIC (OAP) AND HIGH PRESSURE (OHP). D.W.Burgess* & J.W.Bean, Dept. of Physiol.,Bioeng. Prog.,Univ. of Mich.

Regional measurements of pO_2 and blood flow have been made by combining a 75 micron gold polarographic electrode and a thermal flow probe (J. Appl. Physiol. 23: 585, 1967) into one integral unit, which allows the two different measurements to be taken from the same site. Experimental results are taken from two chronic implantation sites (lateral geniculate and rostral thalamic regions) of rats in air, OAP, and OHP. Initial results show many areas of positive correlation between increase in pO_2 and increase in flow, the best and most striking correlation being obtained during periods of flow increases produced by the addition of CO_2 (4%) to the inspired gas. Studies on chronic awake rats show that in some areas of the brain, only a small but definite increase in tissue pO_2 is observed on changing from air to O_2, coupled with a negligible change in blood flow. Shifting to OHP (65 psig) results in a further small slow increase, followed after a delay of 5 to 10 min. by an abrupt and massive increase in pO_2 (as much as 500% of its OAP value) coupled with an equally abrupt large parallel blood flow increase in the two regions, associated with a massive convulsive EEG discharge. This increase in pO_2 usually precedes any visable overt epileptiform O_2 seizure episodes. Subsidence of the EEG and overt seizures are attended by a decrease in pO_2 and blood flow, this sequence of events is repeated in successive seizures. Data support the conclusions that one component of regional vascular control is neurogenic in nature, which under the stress of high pO_2 fails. The convulsive seizure is apparently causally related to the abrupt regional increase in pO_2 that takes place on breakdown of the control system.
Supported by NIH Fellowship No. 2F03GM39386-03 and NIH RG HE-01646.

A Na^+ REQUIREMENT FOR THE BINDING OF AN ACTIVELY TRANSPORTED AMINO ACID TO A FRACTION OF DISRUPTED INTESTINAL BRUSH BORDERS. Mary Jo Burns* and Robert G. Faust. Univ. of North Carolina, School of Med., Chapel Hill, N.C.

Isolated intact brush borders from hamster jejunum were disrupted by incubation in 10 ml of distilled water for 30 min at 37°C. Disrupted brush borders were separated into 5 fractions by density gradient centrifugation on 10,20,30,35 and 40% Ficoll. The top fraction I was employed for binding studies because previous experiments had indicated that it was the only fraction which had preferentially bound actively transported ^{14}C-labelled amino acids. The suspension of fraction I employed contained many filaments and had a Na^+ concentration of 10 μM. Preferential binding of actively transported ^{14}C-L-histidine to fraction I was completely inhibited when NH_4^+ and Li^+ were substituted for Na^+ in the buffers of the incubation medium. The replacement of Na^+ by K^+ produced an 81% inhibition of preferential binding. ^{14}C-L-histidine binding was dependent on the Na^+ concentration in the incubation medium. No binding occurred at a 1 mM concentration of Na^+. Maximum preferential ^{14}C-L-histidine binding was measured at 32.3 mM Na^+, and there was no increase in this binding even though the Na^+ concentration was elevated to 100 mM. These results support the hypothesis that preferential binding of actively transported amino acids to a component within the brush border membrane is related to the initial step in the mechanism of active amino acid transport by the small intestine. Supported by N.I.H. grant AM07998.

EFFECT OF ANOREXIGENS ON PULMONARY ARTERY PRESSURE IN THE CALF. Edward Byrne-Quinn* and Robert F. Grover. Department of Medicine, Univ. of Colorado Medical Center, Denver, Colorado 80220.

Primary pulmonary hypertension has been reported in obese patients treated with the anorexigen aminorex (2-amino-5-phenyl-oxazoline). Therefore, we attempted to induce pulmonary hypertension in the experimental animal with this drug, and also with amphetamine which has a similar sympathomimetic action. Young calves were selected because of their marked pulmonary vascular reactivity. Three groups of 4 calves were treated daily for 4 weeks as follows: 1) 6 ml N. saline I.V. (controls) 2) aminorex 0.25 mg/kg I.V. 3) amphetamine 0.25 mg/kg I.V. Serial mean PA pressures were (± SEM):

Week of Rx	0	1	2	3	4
controls	26.5±1.3	27.5±1.0	25.5±1.7	28.8±3.5	28.8±1.0
aminorex	26.3±1.0	31.0±3.0	30.8±2.3	32.8±2.9	31.7±1.9
amphetamine	32.0±4.1	33.5±1.9	32.8±2.3	36.3±3.3	38.3±0.9

Significant pulmonary hypertension did not develop in any group. In contrast acute hypoxia produced an average increase in PA pressure of 140% in all animals throughout the study. Systemic arterial pressure also remained constant. The acute haemodynamic effects of both drugs I.V. was similar in that PA pressure was unaffected but mean systemic arterial pressure rose significantly 30-50 mmHg. At the completion of the study each animal was challenged with 0.1 mg/kg tyramine I.V. The response was similar in all animals and consisted of no change in PAP but a significant rise in mean systemic arterial pressure, indicating no depletion of endogenous norepinephrine. Thus calves with a high degree of pulmonary vascular reactivity did not develop significant pulmonary hypertension during one months daily treatment with aminorex or amphetamine.

SYMPATHETIC NERVOUS CONTROL OF AIRWAYS IN DOGS. G.A. Cabezas*, P.D. Graf*, and J.A. Nadel. Cardiovascular Research Institute, University of California, San Francisco, San Francisco, California

We studied (1) the influence of sympathetic vs. cholinergic nervous effect on airway dimensions and (2) the possible role of alpha adrenergic pathways. We outlined airways roentgenographically in 31 dogs using insufflated powdered tantalum. After bilateral cervical vagotomy, electrical stimulation of a stellate ganglion had no effect on airway size. When moderate cholinergic tone was present (e.g., electrical stimulation of cervical vagi; intensity, 5 volts; frequency, 10 per sec; duration, 3 msec), supramaximal electrical stimulation of one stellate ganglion (intensity, 12 volts; frequency, 60 per sec; duration, 1 msec) increased airway size only on the homolateral side. Bilateral adrenalectomy or cutting the right splanchnic nerve did not modify the response. When the vagi were stimulated supramaximally, the dilation during stellate stimulation diminished. After vagotomy, propranolol (1-2 mg/kg, i.v.) or dichloroisoproterenol (10 mg/kg, i.v.) had no effect on airway dimensions; subsequent i.v. injection of methoxamine (0.5 mg/kg), norepinephrine (2-6 ug/kg), isoproterenol (2-6 ug/kg) also had no effect on airway size, nor did electrical stimulation of a stellate ganglion. We conclude that the dilator effect of sympathetic nervous stimulation depends on the presence of airway tone and is weak compared with the constrictor effect of the vagus nerves. We found no evidence of alpha adrenergic constrictor action on airways. (Supported in part by Program Project Grant HE-06285 from the National Heart and Lung Institute.)

PREPARATION OF A FIBRINOGEN ANTIBODY BY A NEW METHOD. William A. Cain*, Ira T. Priluck*, John A. Anderson* and James W. Hampton. Univ. of Oklahoma School of Medicine and Okla. Medical Research Found., Okla. City, Okla.

Previous attempts at the preparation of a specific antibody to Factor I (fibrinogen) have yielded antisera which were not highly specific because of the contaminants of the starting fibrinogen fraction. For starting material a commercial fibrinogen fraction (Cutter) was used which is free of profibrinolysin activity. The fibrinogen was dissolved and dialysed 72 hrs. against tris-phosphate buffer, pH 8.6, then applied to a 2.2 x 35 cm. DEAE cellulose (DE-23) column according to the varigrad procedures of Finlayson and Mosesson. The effluent was followed for protein concentration and clottability and the ascending limb of peak I was pooled, lyophilized and injected (25 mgm) into the flanks of two white New Zealand rabbits. Five weeks later the antisera was harvested and characterized by Ouchterlony gel diffusion, immunoelectrophoresis and hemagglutination assay. The antisera compared favorably in concentration to other antisera (1:32,000) by hemagglutination and demonstrated no cross-reaction with normal serum. No differences were noted on gel diffusion between peak I and peak II (fibrinogen plus Factor XIII). On immunoelectrophoresis a small band was noted migrating in advance of the fibrinogen which probably represents a contaminating plasmin-trypsin inhibitor. This method affords a more specific antisera preparation and should provide an improved technique for examining abnormal fibrinogens.

MEMBRANE POTENTIAL TRAJECTORIES IN MOTONEURON REPETITIVE FIRING. *William H. Calvin.* Departments of Neurological Surgery and of Physiology & Biophysics, University of Washington, Seattle, Washington

The form of the membrane potential between spikes (the *trajectory*) changes in two very different ways, suggesting that the firing rate is controlled by several different mechanisms. The firing rate of cat lumbosacral motoneurons was manipulated by steps of current injected through the recording microelectrode. The initial firing rate adapts to a lower steady-state rate; both rates are directly proportional to current strength. The membrane potential scoops downwards after a spike and then rises quite linearly towards the firing level for the next spike. The steepness of this linear rise (the *ramp*) may be directly proportional to current strength, allowing the firing rate *vs.* current curve to be predicted quite simply. The declines in firing rate during adaptation, however, are not typically effected by such changes in ramp steepness. The interspike interval is instead lengthened by a longer *scoop* early in the trajectory, as if the ramp were delayed by some other process. Thus, two types of trajectory change emerge: *Ramp delays* and *ramp steepness*. Although both trajectory change types may participate in one type of firing rate change in some cells, selected motoneurons show adaptation rate changes due only to ramp delays, and current-induced rate changes effected solely by ramp steepness. Other manipulations, such as interjecting extra spikes during rhythmic firing, lend support to the theory that the ramp itself is a process which may be delayed or entered at different points. Similarly, the early scoop seems to exhibit trans-spike summation, providing one mechanism for adaptation.

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DYNAMIC RESPIRATORY AND CIRCULATORY RESPONSES TO HYPOXIA IN THE ANESTHETIZED DOG. D. E. Carrell* and H. T. Milhorn, Jr. University of Mississippi Medical Center, Jackson, Mississippi.

To evaluate the dynamic response of the oxygen transport system to hypoxia, eighteen mongrel dogs weighing 12-17 kg (avg 13.9 kg) were anesthetized with chloralose (60 mg/kg) and urethane (600 mg/kg). They were then subjected to step changes to 10, 8, and 6 per cent oxygen for 10 minute periods alternating with 10 minute periods at room air control values. The following variables were recorded: Pao_2, mixed venous Po_2, external jugular Po_2, femoral vein Po_2, heart rate, blood pressure, aortic blood flow, carotid blood flow, femoral blood flow, respiratory rate, tidal volume, and minute ventilation. All variables, with the exceptions of blood gases, increased in response to hypoxia at all levels. The increase in heart rate was approximately 22 per cent and the increase in blood pressure was 8 per cent at each level. Ventilation and blood flow increased progressively for each level of hypoxia. The response time of ventilation was consistently fast at all levels, while circulatory responses occurred fastest at 8 per cent and slowest at 6 per cent oxygen. Arterial oxygen partial pressure responded to low oxygen with a time lag of about 8 seconds and a half time of 20 seconds while venous oxygen lag was around 20 seconds with a half time of 40 seconds. Smallest half times for blood flow occurred in the carotid artery while largest half times were seen in femoral flow. Return to room air showed larger half times for most variables.

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IDENTIFICATION OF THE PRESSOR SUBSTANCES GENERATED BY RENIN ISOZYMES
O.A. Carretero, B. Bujak*, J. Houle*; Department of Medicine, Henry Ford Hospital, Detroit, Michigan.

Renin-like enzymes (R.L.E.) with the capacity to release pressor substances (P.S.) have been extracted from various tissues. Some investigators have suggested that they play a role in the control of the blood pressure in normal and in some pathological states through the renin (R.)-angiotensin (ang.) system. However, it has been unclear whether the end product of the enzyme substrate reaction corresponds to ang. or other P.S. These P.S. were generated by R.L.E. extracted from kidney or uterus of the dog, human amniotic fluid, or mouse submaxillary gland (Na_2 EDTA present). Also, P.S. was produced when uterine R. was incubated with plasma from which renin substrate (R.S.) had been removed previously by digestion with kidney R. and subsequent dialysis. The P.S. released was 1/3 that formed when plasma with substrate was used. Submaxillary R. incubated with plasma without R.S. didn't release P.S. To identify the P.S. generated by these R.L.E. antibodies (A.B.) that specifically inhibit the pressor effect (P.E.) of ang. I and II were used. Zero to 30% and 70 to 100% of the P.E. was inhibited when each of the P.S. were incubated with A.B. against ang. II and I, respectively. Complete recovery of P.E. was observed following destruction of the A.B. by boiling. These results clearly show that ang. I is the product generated by these R.L.E. in the presence of EDTA. Since these R.L.E., with the possible exception of uterine R. (which was able to digest another substrate in addition to kidney R.S.), consume the same substrate to release the same product, they may be regarded as renin isozymes. The physiological significance of these renin isozymes remains to be explained.

STUDIES ON METABOLIC RATE OF COLD AND HEAT ACCLIMATED MACACA MULATTA.
R.R.J. Chaffee and J.R. Allen*. Dept. of Ergonomics, Univ. of Calif., Santa Barbara, Calif.

Young male Macaca mulatta (body weight 3.1-4.7 kg) were divided into three groups: cold acclimated at 6°C, controls at 23°C and heat acclimated at 35°C. Animals were acclimated for over 20 months. Cold acclimation inhibited growth; controls and heat acclimated animals gained weight at the same rate. Oxygen uptake (MR) was measured in a closed circuit system at a chamber temperature of 24 ± 1°C. The unanesthetized animals were held in restraining boxes to which they had been previously conditioned but in which activity was not completely eliminated. The degree of restlessness appeared to be comparable in all three groups during the period of MR measurements. MR results at 24°C, calculated over a period of 30 min or longer, are as follows: cold acclimated = 0.99 ml $O_2/cm^2/hr$, controls = 0.98 and heat acclimated = 0.80. Thus it appears that heat acclimated monkeys have a depressed MR at 24°C in spite of the fact that this temperature is cool for them. MR measurements at 10°C and 35°C are now in progress. In a series of monkeys fitted with indwelling stainless steel hypothalamic inserts, both hypothalamic temperature and MR are being monitored during progressive changes in ambient temperature between 10° and 35°C. Thus the stability of hypothalamic temperature in the face of ambient temperature transients can be assessed as a function of temperature acclimation. [Supported by Contract # DADA 17-68-C-8064, U. S. Army Medical Research and Development Command.]

BRAIN STEM RETICULAR FORMATION EFFECTS ON LUMBAR MONOSYNAPTIC REFLEXES. Samuel H.H. Chan* and Charles D. Barnes, Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

Experiments were performed on cats made decerebrate at the precollicular level. Stimulation of reticular formation (RF) sites was done with a 20 msec train of rectangular pulses at 500/sec using concentric bipolar electrodes 0.5 mm in diameter and with a tip separation of 0.5 mm placed stereotactically. The monosynaptic reflex elicited from stimulation of the left gastrocnemius-soleus or common peroneal was recorded from VRL7 and tested at various time intervals with relation to RF stimulation. Stimulation of the medullary or pontine RF causes a pattern of facilitation, followed by inhibition, of lumbar flexor and extensor monosynaptic reflexes. When the extensor monosynaptic reflex is under the influence of spino-bulbo-spinal reflex inhibition or facilitation, medullary RF stimulation causes the same temporal sequence, but is depressed by additional inhibition. When stimulation is at the anterior end of the pontine reticular formation, the pattern is usually tripnasic in extensor monosynaptic reflexes with an early inhibitory phase impinging on the start of the facilitation.
(Supported by USPHS Grants NB 07834 and NB 34986)

MICROPERFUSION AND MICROPUNCTURE STUDIES OF TRYPTOPHAN TRANSPORT IN RAT KIDNEY. Y.L. Chan*, C.G. Campbell* and K.C. Huang. Univ. of Louisville, School of Med., Louisville, Ky. 40202.

The renal tubules of rat and dog kidneys handle the excretion of D- and L-glucose differently (Am. J. Physiol. 214:342, '68 Pflugers Arch. 305:155 '69); D-glucose is reabsorbed while its L-isomer is secreted. Knowledge on how do the tubules handle the excretion of L- and D-amino acids is still lacking. In this investigation, the microperfusion technique of Sonnenberg et al. was used to study the tubular reabsorption of D- and L-tryptophan. Spraque-Dawley rats were anesthetized with "Inactin" 100 mg/Kg i.p. The test amino acid and inulin were dissolved in a steady state solution used to perfuse a surface loop of proximal tubule at a rate of 16 nl min^{-1}. It was found that L-tryptophan rapidly disappears from the perfused solution but D-isomer does not. This indicates that D-tryptophan is not actively reabsorbed and consequently the permeability coefficient calculated which was found to be 2.36×10^{-5} cm sec^{-1}. L-phenylalanine was found to inhibit the tubular reabsorption of L-tryptophan with the inhibition proportional to the concentration of L-phenylalanine in the perfused solution. 10^{-3} M sodium azide had no effect on L-tryptophan reabsorption. Free flow micropuncture study with D-tryptophan showed that the ratio of $TF/P_{D\text{-try.}}$ to TF/P_{inulin} in proximal tubular fluid was greater than one, suggesting tubular secretion; but in final urine samples this ratio was less than one, suggesting that D-tryptophan is reabsorbed somewhere beyond the proximal convoluted tubules. This finding confirms the data obtained from dog's experiment that L-tryptophan is reabsorbed and D-tryptophan is secreted by renal tubules.
(Supported by grants NIAMD AM2217-12 and NSF GB-8435).

UREA REMOVAL BY UREASE AND AMMONIA ABSORBENTS IN THE INTESTINE. T.M.S.Chang and S.K.Lo*. Dept.Physiol.,McGill Univ. Montreal.Canada.

Microencapsulated urease in an extracorporeal shunt system effectively lowered blood urea levels(Chang 1966 TASAIO). The ammonia so formed could be removed by ammonia absorbents. This combined use of urease and ammonia absorbents has since been investigated for the removal of urea in uremia. This paper reports the use of this combination in the intestinal tract. In the intestine,bacterial urease converts urea into ammonia which is reabsorbed. Therefore,there is little intestinal excretion of urea or ammonia. However, in the present experiments, 4 hours after the oral adminstration of Zirconium phosphate(ammonia absorbent),the systemic blood urea levels were 11.0 ± 1.1mgm % as compared to 14.5 ± 1.5mgm % in the control rats. The serum calcium levels were 10.22 ± 0.77 mgm% in the treated group and 10.65 ± 0.40mg% in the control group. Similar results were observed when another ammonia absorbent,Dowex 50W-X12 was administered orally into rats. Within 4 hours, the systemic blood urea levels had decreased to 65.0 ± 4.5 % of the control values. When animals were treated with an antibiotic mixture(sulfaguanidine,terramycin,penicillin and neomycin) to eliminate the urease producing bacteria,oral administration of ammonia absorbents had little effects on the systemic blood urea levels (89.1 ± 6.0 % of the control values). In these antibiotic treated rats, the oral administration of both microencapsulated urease and ammonia absorbents lowered the systemic blood urea levels to 60.6 ± 5.0 % of the control levels within 4 hours. Thus microencapsulated urease efficiently replaced the bacterial urease activity. In conclusion, a combination of exogenous ammonia absorbents and bacterial or microencapsulated urease in the intestine can efficiently remove systemic urea. (Supported by the Medical Research Council of Canada).

DISTRIBUTION OF GLYCOGEN IN DOG AND CAT SKELETAL MUSCLE. C. K. Chapler and W. M. Moore (Intr. by D. B. Jennings) Dept. of Physiology, Queen's University, Kingston, Ontario.

The small sample needle biopsy technique has been extensively used in exercising human subjects to investigate the quantitative contribution of glycogen in skeletal muscle metabolism. The technique offers the obvious advantage of allowing multiple samples to be obtained from a single muscle. A necessary prerequisite for interpretation of data from small samples requires that distribution of glycogen within the muscle be constant. The present study was undertaken to investigate glycogen distribution in the gastrocnemius-plantaris muscle group of dogs and the medial gastrocnemius of cats. All animals were anaesthetized with sodium pentobarbital. The muscle group in each leg was surgically exposed and multiple samples were obtained from both peripheral and central locations at about 1 cm intervals along the muscle. Visible connective tissue was removed and the samples rapidly frozen. Duplicate glycogen analyses were performed using anthrone reagent following digestion in KOH. In the dog, small samples ranging from .087-1.0 g had widely varying glycogen concentrations ranging from 1.64-7.53 mg/g in individual muscles while larger samples, 1.0-4.7 g, ranged from only 0.5-3.9 mg/g. Using 1-2 g samples from the medial gastrocnemius of the cat, variation within an individual muscle tended to be even less than that observed in large samples from the dog, ranging from 0.10-1.80 mg/g. Preliminary studies suggest that wide variations in glycogen concentrations also occur in the rectus femoris of the dog. The results of this study demonstrate the extreme variability of glycogen concentrations within individual muscles. Thus the needle biopsy technique appears unsuitable for evaluating changes in glycogen concentrations in the muscles investigated.
Supported by a grant from the Medical Research Council of Canada.

Variation of Retinal Structure in Diverse Species of Echolocating Bats. Julia Chase (intr. by Roderick A. Suthers). Indiana University, Bloomington, Indiana.

The great diversity of behavioral patterns among echolocating bats is reflected by differences in both echolocation and visual acuity. Previous anatomical studies of Microchiropteran eyes, however, have described uniformly small, but typical, nocturnal eyes with a dense all-rod receptor layer converging on less numberous bipolars and scanty ganglion cells. In this study, light microscopy on 27 species of echolocating bats and preliminary electron microscopy on 3 of these have revealed notable differences between species of different habits. The eyes of the nocturnal insectivorous bats may be as little as 1/10 to 1/40 the weight of those from nocturnal fruit-, blood, or nectar-feeding species of similar body size. The retinae of all the nocturnal species have a densely packed receptor layer and an approximate receptor to ganglion cell ratio of 100:1. In the three species of Emballonuridae, which roost in well lighted places and not infrequently fly in daylight, however, this ratio is approximately 10:1. This difference is accounted for by a receptor layer that is only about one-fifth as dense in the three partially diurnal species as in the nocturnal bats and an increase in the cells of the inner nuclear and ganglion cell layers. Contrary to earlier studies, such features as eye movement, a nictitating membrane, an ovoid lens and an apparent macular area were noted in various species. In addition, scattered cone-like receptors with large, triangular, multisynaptic pedicles, large tigroid nuclei, and short conical outer segments have been demonstrated in several species.

EFFECT OF LOCAL STIMULATION OF DOG JEJUNUM ON INTESTINAL MOTILITY AND AORTIC PRESSURE. W.T. Chen*, C.P. Hsieh*, C.C. Chou and J.M. Dabney. Dept. of Physiology, Mich. State Univ., East Lansing, Michigan 48823.

Utilizing in situ jejunal segments we studied the effect of local mechanical and chemical stimuli on systemic pressure (SP) and segment motility. While monitoring SP and lumen pressure (LP), the following stimuli were given: 1) acute distension of the segment (Avg. Δ LP, 30-90 mmHg), 2) clamping of the mesentery, 3) local i.a. infusion of KCl (0.5-2.0 ml/min, 300 mOsm/l) and 4) local i.a. infusion of hyperosmotic NaCl (H-NaCl) (0.5-2.0 ml/min, 1500 mOsm/l). All stimuli caused an immediate rise in SP. Acute distension caused a transient rise of about 10 mmHg in SP. Clamping caused a greater and more prolonged rise in SP and an increase in segment motility. I.A. infusion of KCl or H-NaCl caused the most prolonged increase in SP and a rise in LP with phasic contractions. These responses were not abolished by vagotomy. Since venous outflow was not returned to the animal during any stimulus, the rise in SP must be neurally mediated. This finding was studied by infusing KCl and H-NaCl before and after 10 min i.a. infusions into the segment of atropine (100 ug/min), dibucaine (2 mg/min) or tetrodotoxin (2.5 ug/min). The SP response was abolished by dibucaine, attenuated by tetrodotoxin but not affected by atropine. Atropine, dibucaine, or tetrodotoxin abolished the rise in LP and phasic motility induced by H-NaCl but only attenuated these responses to KCl. The results show that these local stimuli can induce a rise in SP and LP via a non-vagal pathway. The rise in SP during KCl or H-NaCl is not secondary to increases in LP or phasic motility. Increases in LP and phasic contractions by H-NaCl are mediated via nerves; increases by KCl are partly by nerves and partly by a direct action of K^+ on intestinal muscle.

EFFECTS OF MODERATE AND EXHAUSTIVE EXERCISE PROGRAMS ON PLASMA CATECHOLAMINE AND CORTICOSTERONE LEVELS. Alan K. Chin* and Eugene Evonuk. Ctr. of Res. for Human Performance. Univ. of Oregon, Eugene, Oregon 97403

Male adult rats were administered moderate and exhaustive exercise programs for six weeks. There were no significant differences (P .05) in the plasma norepinephrine, epinephrine, total catecholamine and corticosterone levels between the non-exercised control animals and the moderately exercised group. However, markedly significant differences (P .05) in the plasma norepinephrine, epinephrine, total catecholamine and corticosterone levels were found between the exhaustively exercised animals and the control and moderately exercised groups. The exhausted animals exhibited an increase in norepinephrine to levels 41.5% above control values and 48.1% above moderate exercise concentrations. The animals exercised to exhaustion demonstrated a decrease in epinephrine to concentrations 50.2% below control levels and 50.4% below moderate exercise values. The exhausted animals showed an increase in total catecholamines to levels 14.2% above control values and 19.2% above moderate exercise concentrations. The animals exercised to exhaustion exhibited a decrease in corticosterone to levels 31.5% below control concentrations and 23.9% below moderate exercise values. These results suggest that prolonged exhaustive exercise may cause physiological impairment to the adrenals resulting in below control levels of plasma corticosterone and epinephrine. In addition, chronic exhaustive exercise appears to elicite a compensatory increase in plasma norepinephrine and total catecholamines.

THE INFLUENCE OF ANIMAL HANDLING ON PLASMA GLUCOSE AND LIVER GLYCOGEN. B. J. Chou* and E. L. Besch. Department of Physiological Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas 66502.

In animal experimentation it is not uncommon to excite an animal during manipulative procedures even though some caution may be exercised to keep this at a minimum. Thus, the experimental variables may not represent true absolute or relative values of the physiological parameter being measured. Accordingly, plasma glucose and liver glycogen values were determined for several groups of male, Sprague-Dawley rats which had been exposed to varying amounts of animal handling. Prior to these determinations, all animals were exposed, for 3-4 weeks, in a controlled environment room, to 24-hour days in which 12 hours of light (27°C) were followed by 12 hours of dark (16°C). The ether anesthesia group displayed a hyperglycemia which was about 25% greater than the plasma glucose values of the decapitated group of rats and about 40% greater than the group receiving a sudden blow to the head. There were no significant differences in packed cell volume, plasma protein or per cent dry matter of the liver between treatment groups. The results indicate that the degree of animal handling was related to the plasma glucose and liver glycogen levels.

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CYCLIC VARIATION IN ESTROGEN RETENTION BY HAMSTER TISSUES DURING THE ESTROUS CYCLE. Leonard A. Ciaccio* and R. D. Lisk, Princeton University, Princeton, N. J.

Groups of female hamsters were injected (i.v.) with ^{3}H-E(2,4,6,7-^{3}H estradiol-1/β, 100 Ci/mM) at 12 hr intervals during the 4 day estrous cycle. Two hours after injection females were etherized and perfused with 0.9% saline. Tissues were collected, dried at 60°C, homogenized in tris EDTA, and extracted 2X with 5 ml of EtOAc. Activity was expressed as DPM/100mg tissue dry weight. Activity retained in pituitary, uterus and vagina was minimal on the evening of proestrus, increased significantly by the morning of estrus and remained high through the day of diestrus one. Through diestrus two and the morning of proestrus activity was slightly reduced but remained significantly higher than at the evening of proestrus. Within the C.N.S. the preoptic area, arcuate nucleus and amygdala displayed cyclic retention. However, these areas did not show a sharp drop in activity on the evening of proestrus. No cycle was observed for muscle, hippocampus or cerebellum. Competition studies were conducted on the morning of diestrus one and proestrus by injecting (i.p.) 15 μg of estradiol or 300 μg of progesterone 30 minutes before injection of ^{3}H-E. Estradiol pretreatment depressed activity in pituitary, uterus, vagina, preoptic areas, arcuate and amygdala but not that of blood, muscle, hippocampus or cerebellum. Progesterone did not compete with ^{3}H-E. This implies that retention is specific for estrogen and is of limited capacity. Cyclic fluctuations in the ability to retain ^{3}H-E displayed by the somatic tissues suggest changing endogenous estrogen levels; this implies highest estrogen levels occur on the evening of proestrus. Since somatic tissue and tissues of the C.N.S. display different cycles these tissues may have different mechanisms for retaining estrogen. (Supported by Grant HD-02615 U.S.P.H.S.)

EFFECT OF TRACHEALIS MUSCLE CONTRACTION ON THE TIME-DEPENDENT PRESSURE VOLUME RELATIONSHIPS OF THE IN VIVO DOG TRACHEA. R.F.Coburn and B. Palombini* Sch of Med., Univ. of Pennsylvania, Philad., Pa.

Eight to 12 cm segments of intrathoracic trachea of open-chest dogs were converted into closed chambers and held at constant length. The animals were respired with a cannula attached to the trachea just above the carina. These segments were then filled with saline. Tracheal volumes could be altered by adding or removing liquid and the resultant transmural pressures (TMP) determined. Starting at the tracheal volume where TMP=0 (resting volume) we added 2 ml of fluid over 0.2 to 0.3 sec period every 15 sec until TMP reached +50-70 cm H_2O. Measurements under collapsing TMP were made by stepwise removal of 2 ml of fluid starting at resting volume. Time-dependent changes in TMP at each volume were expressed as stress relaxation, in % of the peak pressure change resulting from volume change. We computed TMP changes during the first 4 sec after each volume change (SR_4) and during 5 to 15 sec (SR_{5-15}). The same measurements were made during constant electrical stimulation of the cervical vagosympathetic trunks. We estimated active muscle tension with measurements of intraluminal pressure. In 6 dogs SR_4 without electrical stimulation averaged 27.7±SE 2.1% (26 measurements) at 110 to 175 % of resting volume, and 46.9±SE 3.0% in 46 measurements performed during electrical stimulation. Trachealis Muscle contraction had no consistent effect on SR_{5-15}. With collapsing TMP equivalent increases in active muscle tensions were associated with much smaller increases in SR_4. These data show that when the trachea is exposed to distending pressures increases in Trachealis Muscle active tension are associated with marked increases in muscle viscosity although tissue extensibility measured under static conditions did not change. Thus Trachealis Muscle viscosity appears to be related to contractile elements. Time-dependent change occurring 5 to 15 sec after volume changes are apparently not related to the contractile element. The small effect on SR_4 with collapsing TMP suggests that under conditions where tracheal cartilages are articulating, time-dependent effects are related more to fibrocartilages than to smooth muscle.

N-METHYLHISTAMINE--A POTENT STIMULANT OF GASTRIC SECRETION. C. F. Code, S. M. Maslinski,* H. Navert* and F. Mossini.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Navert et al (Physiologist 12:313, 1969) have shown in dogs that N-methylhistamine (N-MH) and N-dimethylhistamine (N-DiMH), derived from injected histamine (H), occur in gastric mucosa and in the juice secreted. Lin et al (Ann NY Acad Sci 99:30-44, 1962) found N-MH and N-DiMH to be more potent gastric secretagogues in dogs than histamine. The prospect emerges that part, or all, of the secretory effects of histamine may be due to the production, in the gastric mucosa, of N-MH and N-DiMH. This study further tests this concept. First, the observation of Lin et al that N-MH in dogs with Heidenhain pouches is a more effective stimulant than H was confirmed (Table). We also found that in conscious healthy cats with gastric fistulas N-MH is a more potent gastric secretagogue than H (Table). To determine whether aminoguanidine (A) would block the oxidative degradation of N-MH as it does that of H, 0.625 gm/hr of A was given intravenously to dogs with Heidenhain pouches, alone and during continuous injections of H or N-MH. The secretory effects of H and N-MH were equally increased by simultaneous administration of A. It appears possible that N-MH and N-DiMH may have an influence in the gastric secretory effects of H.

	Tests	μM/hr	Output, mEq HCl/hr N-MH	H	Ratio output, N-MH/H
3 Dogs	3	1.0	2.416	1.765	1.37
	3	2.0	3.867	2.923	1.32
4 Cats	3	0.250	2.169	1.540	1.41
	1	0.500	2.900	2.076	1.40

CALCARINE POTENTIAL CHANGES ASSOCIATED WITH RAPID EYE MOVEMENT IN LIGHT IN THE RHESUS MONKEY. Bernard Cohen and Martin Feldman*. Department of Neurology, Mount Sinai School of Medicine, New York, New York 10029.

In light each saccade, quick phase of nystagmus, or blink is associated with a prominent potential change in the region of the calcarine cortex. This potential change is similar in waveform and anatomical distribution to potential changes evoked by light flash. Its waveform is independent of the direction of eye movement. It can be induced by passive movement of one or both eyes. It is not present during eye movement in darkness. Therefore, it is a light-evoked response to rapid eye movement which originates in the retina. Slow eye movements do not induce these potential changes.

The amplitude of the calcarine potential change is dependent upon the level of background illumination, the size of the pupil, and the size of the rapid eye movement which induced it. It is independent of the presence or absence of contrast in the external visual fields. Its latency is a function of the level of background illumination and the size of the pupil. These potential changes are present at light levels which are in the photopic or the scotopic range. When animals are put into dim illumination ($\sim 1 \times 10^{-3}$ ft. Lamberts) with the pupils fixed and constricted, the size of calcarine potentials associated with eye movement increases after 10-15 minutes of dark adaptation. Neither the amplitude nor waveform of these potential changes is affected by foveal destruction. This suggests that these calcarine 'eye movement' responses arise largely as a result of activity in rods in the periphery of the retina.

LGB and pontine potentials associated with rapid eye movement reflect efferent oculomotor output. In contrast, calcarine potential changes may be an afferent signal to the visual cortex which code the amount of light energy reaching the retina and the size of the rapid eye movement which induced them. Aided by NIH Grants NS-00294 and 1K3,34,987.

TEMPERATURE OPTIMA FOR AMINO ACID TRANSFER RIBONUCLEIC ACID LIGASES ISOLATED FROM THE POIKILOTHERM, ONCORHYNCHUS NERKA. F. P. Conte and V. Cvancara*. Dept. of Zoology, Oregon State Univ., Corvallis, Oregon 97331

Thermal lesions of protein synthetic apparatus have been reported for several obligatory low-temperature microorganisms. The most heat sensitive components appear to be aminoacyl-tRNA synthetases and ribosomes. Haschemeyer[1] investigating *in vivo* protein synthesis and its role in temperature adaptation of poikilothermic toadfish (*Opsanus tau*) reports that changes in net protein synthesis in cold acclimation are directly related to changes in levels of aminoacyl transferase and not aminoacyl-tRNA ligases. Present study investigated optimal temperature range for *in vitro* formation of aminoacyl-tRNA incubated at temperatures from 0° - 40°C utilizing tRNA and ligases isolated from the liver of sockeye salmon (*O. nerka*). Preparation and purification of activating enzymes and tRNA were identical to methods described by Yang and Novelli (Methods in Enzymology XII, pt. C, eds. Grossman and Moldave). Alanine, glycine, valine, phenylalanine and lysine exhibited a very restrictive temperature range in which maximum activity occurred between 5° - 15°C. Aspartic acid, proline, isoleucine and leucine had much broader ranges (0° - 25°C).

(Supported by AEC Contract AT(45-1)-2013).

[1]Haschemeyer, A. (1969). Proc. Natl. Acad. Sci. U.S. 62, pp. 128-135.

EFFECTS OF DILUENT HELIUM AND NITROGEN UPON INTRAOCULAR PRESSURE DURING DECOMPRESSIONS TO A NEAR-VACUUM. Julian P. Cooke (intr. by R.W. Bancroft) USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

To evaluate the effects of different breathing gases upon directly measured intraocular pressure (IOP) during and after a near-vacuum exposure, anesthetized and unanesthetized dogs were rapidly decompressed from 258 torr to 2 torr for a 2-min exposure while breathing either (1) 100% O_2, (2) 70% O_2:30% He, or (3) 70% O_2:30% N_2. Comparisons were also made with N_2 at ground level pressure. Other measurements included arterial (P_a) and venous (P_v) pressure.

With O_2 breathing, IOP increases 2X during the exposure, and it increased 3X or 4X when O_2:He or O_2:N_2, respectively, was breathed. Retinal vascular recovery was more rapid when O_2 was breathed, with O_2:He being more similar to O_2 than to O_2:N_2. Hypoxia produced by N_2 breathing caused a 0.5X IOP increase. The IOP increases during the low pressure exposure were associated with elevated P_v, venous congestion, and an ineffective blood flow. The IOP increases, along with a drop in temperature, effectively reduced the frequency of retinal hemorrhage. During recompression, IOP returned to control levels and then increased temporarily. This transient increase, along with retinal cupping, was associated with venous congestion in retinal vessels, concurrent with elevated P_a. At operational altitudes, should a decompression occur, O_2 is slightly favored for early visual recovery. If either gas mixture was breathed before the decompression and during recompression, then administration of pure O_2 immediately after the recompression should speed retinal recovery.

RESPONSES OF RAT ETHMOIDAL NERVE UNITS TO CUTANEOUS AND OLFACTORY STIMULI. G.P. Cooper. Univ. of Cincinnati College of Medicine, Cincinnati, Ohio

Anesthetized Wistar rats were used. One eye was removed and the ethmoidal nerve dissected free and cut posteriorly. With the head rotated to one side, the orbit served as a convenient recording chamber. Differential recordings were made under oil from fine strands of the ethmoidal nerve. Unit responses to mechanical stimulation of the skin showed that (a) no spontaneous firing occurred, (b) the only effective stimulus was a distinct depression of the skin; light touch or movements of the hair or vibrissae had no effect, (c) all responses were rapidly adapting, many units yielding only one spike at the beginning and end of stimulation, (d) receptive field size ranged from 2x2 mm near the nares to 5x15 mm overlying the nasal bone, (e) many units followed vibratory stimuli for variable periods of time in a one-for-one fashion at frequencies up to about 1000/sec. These data indicate that cutaneous fibers of the ethmoidal nerve distribute largely to encapsulated receptors. Units innervating the nasal mucosa (a) often fired spontaneously, usually at rates below 1/sec, (b) spike amplitude was always less and spike duration longer than those of cutaneous units recorded in the same nerve strand, (c) units which responded to cutaneous stimulation did not respond to odors and vice versa, (d) responses to different odors clearly depended on the type of odor and the concentration, with very little difference between units with respect to relative response to a particular odor. (Supported by USAEC contract AT(11-1)-1669 and USPHS grant P510-ES-00159-04.)

VESTIBULAR PROJECTIONS TO THE CAUDATE NUCLEUS. P. Copack*, M. Potegal*, G. Krauthamer, and S. Gilman. Columbia U. Coll. P&S, New York

Encephale isolé cats were used to determine whether projections from the vestibular system reach the caudate nuclei, as suggested by previous experiments. The peripheral branches of the vestibular and ipsilateral cochlear nerves were stimulated with separate bipolar electrodes. Responses were recorded with macroelectrodes from the vestibular and primary auditory projection areas of cortex and the heads of the caudate nuclei. To evaluate the degree of current spread between nerves, excitability cycle studies were performed using paired pulses to vestibular and to cochlear nerves. Different curves were found for each response, indicating that current spread was negligible. Vestibular-evoked responses in cortex had latencies of 3-7 msec and amplitudes of 20-100 μV. Vestibular-evoked responses in caudate had latencies of 5-15 msec, amplitudes of 5-30 μV , and were localized to the dorsomedial portion of the ipsilateral and dorsolateral portion of the contralateral nucleus. Vestibular responses were found usually in regions of the caudate responsive to cochlear nerve or click stimulation and interactions were found between these responses. In some cases, vestibular responses were found in regions unresponsive to cochlear stimuli. The vestibular responses remained intact following ablation of the vestibular projection area of cortex but were decreased in amplitude following coagulation of the medial geniculate nuclei bilaterally. We conclude that there is a projection from the vestibular system to the caudate nuclei bilaterally in a localized distribution which overlaps that from the auditory system.

REGIONAL BRAIN BLOOD FLOW AND EEG IN O_2 CONVULSIONS. J.D.Coulson*, J.W. Bean, & J.Lignell*. Dept. of Physiol., Univ. of Mich., Ann Arbor, Mich.

Earlier reports of blood flow changes recorded by thermo probes implanted in lateral geniculate and rostral thalamic regions of unanesthetized rats (Fed. Proc. 25: 700, 1966) indicated that such changes might be precipitating factors in O_2 convulsions (Arch. Neurol. 20: 396, 1969). Further studies of such changes and their relationship to EEG activity confirm earlier findings that in rats at rest in air or O_2 at atm.press. there are commonly reciprocal cyclic regional flow changes differing in time relationship and magnitude. These changes are enhanced in O_2 at high pressure (OHP) preceding onset of overt convulsions at which time the reciprocal pattern abruptly shifts to an in-phase relationship with rapid parallel flow increases in both regions. Similar increases recur in successive convulsions with reciprocal patterns reappearing in postictal periods and on return to atm. press. Spiking in the EEG precedes onset of overt convulsions with massive synchronization appearing immediately before convulsions and blood flow increases. Reciprocal flow changes are absent under anesthesia. The data support the conclusions that cyclic reciprocal changes in regional brain blood flow occur normally (Am. J. Physiol. 201: 1192, 1961) due to neurogenic vascular control mechanisms within the CNS; that in contrast to this the mechanisms responsible for flow changes induced by CO_2, possibly myogenic, control a wider area, probably the whole brain; that although the onset of overt O_2 convulsions is associated with an abrupt shift in regional flow pattern, the initiating factors in such convulsions are neurogenic rather than circulatory; that regional changes in brain pO_2 as previously determined by O_2 electrodes in rats exposed to OHP are due in large part to regional changes in blood flow which are masked in mixed venous brain blood (O_2 in the Animal Organism, Pergamon Press. p. 496, 1963).
Supported by NIH RG HE-01646

CORTISOL DISAPPEARANCE IN DOGS DURING ENVIRONMENTAL STRESSES. Gladys A. Courtney* and S.F. Marotta. University of Illinois at the Medical Center, Chicago, Illinois.

Although adrenocortical steroids are necessary for the maintenance of homeostasis and resistance of an organism to adverse conditions (stress) relatively little is known concerning the in vivo metabolism of these steroids during environmental stresses. The removal of injected cortisol (4-pregnen-11β, 17α, 21-triol-3,20-dione) from the plasma of dogs exposed to a wide variety of environmental stresses was investigated. Male mongrel dogs were divided into 6 groups: ground (control animals breathing ambient air at 23°C), 10% O_2 (hypoxia), 100% O_2 (hyperoxia), heat (41°C), cold (0.5°C), and positive pressure breathing (10-18mmHg). Blood samples were obtained before cortisol infusion and 2,15,30,60,90, and 120 minutes after infusion. Plasma samples were analyzed for Porter-Silber chromagens (17-OHCS). The disappearance of 17-OHCS in plasma was calculated according to the method of Matthews for an open two-compartment model with a fast and a slow component. Rate constants to and from compartments, half-lives and volumes of compartments were determined. No significant differences in any of the calculated values were observed between the stressed groups and the control group or between any of the experimental groups. These data suggest that the discrepancies reported in the literature relative to the elevation or depression of peripheral plasma 17-OHCS during stress are due to the differences in the response of the adrenocortical-hypothalamic-pituitary system and not necessarily the subsequent rate of 17-OHCS removal.
(Supported in part by the Office of Naval Research, NR101-580).

EXHAUSTING WORK LIMITED BY EXTERNAL RESISTANCE AND INHALATION OF CARBON DIOXIDE. F. N. Craig, W. V. Blevins* and E. G. Cummings. Medical Research Laboratory, Edgewood Arsenal, Maryland.

The purpose was to examine reasons suggested for the reduction in endurance imposed by an external respiratory resistance, such as oxygen debt, hypercapnia or peak pressure limits, in the hope of finding some objective feature that, consciously or not, might provide a basis for a subject's decision to halt.

In the absence of heat stress 13 men worked to exhaustion on a treadmill at grades up to 22 per cent at respiratory resistances from 2 (R1) to 15 (R4) cm H_2O/l/sec and expiratory resistance of 2 cm H_2O/l/sec. In 3 men oxygen debt was measured after exhaustion at R4 and after the same length of time at R1. In 5 men effects of inhalation of carbon dioxide mixtures up to 4 per cent were compared with those of resistance.

In six comparisons the average walking times were 11.3 min with R1 and air, 6.9 min with R1 and 3 per cent carbon dioxide, and 5.1 min with R4 and air. High resistance did not affect the oxygen debt in either exhausting or non-exhausting work. As work progressed the time devoted to expiration decreased. At exhaustion, in 38 of 48 comparisons of R1 with carbon dioxide and with R4, the duration of expiration was the same within $\pm$ 0.1 sec.

It was concluded that for some unexplained reason the sense of impending exhaustion was associated with an insufficiency of time for the expiratory phase of the respiratory cycle.

MEASUREMENT OF RAPID HYDROXYL ION MOVEMENTS ACROSS THE HUMAN ERYTHROCYTE MEMBRANE. E.D.Crandall*, R.A.Klocke* and R.E.Forster. University of Pennsylvania, Philadelphia, Pa.

We have developed a stopped-flow rapid-reaction apparatus which can follow changes of $\pm$0.02 pH units in 0.1 ml of solution in <0.005 sec, utilizing a commercially available pH-sensitive glass electrode. This instrument was used to measure extracellular pH at 37°C in mixtures of equal volumes of the following CO_2-free solutions, from <0.01 to 300 sec after mixing: (A) normal human red blood cells, washed 3 times and resuspended in 150 mM NaCl at pH 7.2 and 20% hematocrit; and, (B) 150 mM NaCl adjusted with HCl or NaOH to pH 3 to pH 10.4. A minimum of 2 ml of mixture had to flow through the electrode chamber to ensure complete washout. The mixing process produced a step change in the pH of the extracellular fluid, after which exchanges across the red cell membrane and buffering by intracellular hemoglobin caused it to return toward 7.2. When the pH of B was 3, the initial pH of the extracellular fluid of the mixture was 3.5, and the equilibrium pH was 7.1. The corresponding values when B was pH 10.4 were 9.7 and 7.3. The time course of extracellular pH was approximately exponential. Under the assumption that pH changes after mixing represent exchanges of OH^- for Cl^- across the cell membrane, OH^- permeabilities (P_{OH^-} in cm/sec) were calculated and found to vary from 2×10^{-4} at pH 9 to 2×10^{-1} at pH 3 according to the empirical relationship: $P_{OH^-} = 322 \exp(-1.54\ pH)$. The strong dependence of P_{OH^-} on external pH is compatible with the fixed charge theory of membrane permselectivity.

HEART RATE IN THE EXTRINSICALLY DENERVATED CANINE HEART WITH CHRONIC ARTERIOVENOUS FISTULA. N. D. Crisp,* D. W. Lucke,* D. K. Meyer, and M. L. Zatzman.* Univ. of Missouri School of Med., Columbia, Missouri.

Dogs with hearts surgically denervated by the technique of selective neural ablation were subjected to a chronic cardiac preload introduced by the surgical placement of an aortic-caval fistula. Heart rate was measured prior to thoracotomy, after thoracotomy (prior to shunt placement) and after aortic-caval shunt placement. This included data collection in awake and anesthetized dogs with and without beta adrenergic blockade. The beta adrenergic blocking agent propranolol was administered to dogs who had compensated for the increased cardiac preload with an increased heart rate. The denervated dogs observed in the awake unsedated state showed an increased heart rate of 32 beats per minute as a consequence of the aortic-caval shunt. The heart rate of sham denervated shunted dogs increased an average of 61 beats per minute. In the sedated anesthetized denervated shunted dogs, the heart rate increased an average of 49 beats per minute. Beta adrenergic blockade with propranolol in the awake and in the sedated anesthetized dogs did significantly reduce the stress induced heart rate, but did not decrease the heart rate to levels achieved as a consequence of propranolol administration prior to the shunt placement. Propranolol blockade revealed that 60% of the stress induced tachycardia in the denervated dog was due to beta adrenergic receptor mediated agents and that the remaining 40% of the stress induced tachycardia was mediated by an unknown mechanism.

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IN VITRO STIMULATION OF GLUCOSE UPTAKE AND UTILIZATION BY DIAPHRAGM OF RATS EXPOSED TO CHRONIC CENTRIFUGATION. B.C. Daligcon* and J. Oyama. Environmental Biology Division, Ames Research Center, NASA, Moffett Field, California 94035.

Differences in metabolic activity of liver and adipose tissue of centrifuged rats have been previously reported from our laboratory. The objective of the present study was to investigate the effects of chronic centrifugation on glucose metabolism of muscle tissue. Glucose uptake and uniformily labeled glucose-^{14}C incorporation into glycogen and $^{14}CO_2$ production by isolated diaphragm tissue of centrifuged and non-centrifuged rats were determined. Weanling female rats were centrifuged at 4.15 G or 2.76 G for periods of 1, 2, and 3 months. The hemidiaphragms obtained from rats immediately after sacrifice were incubated for 90 minutes at 37°C in 3.0 ml of Gey and Gey buffer medium containing 2 mg/ml glucose and 1.0 μC glucose-^{14}C. The diaphragms of centrifuged rats showed significant increases in glucose uptake (31%) and $^{14}CO_2$ production (101%); no increase in ^{14}C incorporation into glycogen was observed. Addition of insulin (0.1 mU/ml) stimulated glucose uptake and ^{14}C incorporation into glycogen more than two-fold in diaphragms of centrifuged rats as compared to controls. Insulin had no effect on $^{14}CO_2$ production. The results from these in vitro studies lend further support to the view that metabolic activity and insulin sensitivity of rats exposed to chronic centrifugation are significantly increased.

COMPARATIVE EFFECTS OF HYPEROXIA AND HYPERBARIC PRESSURE IN TREATMENT OF PRIMARY BLAST INJURY. Edward G. Damon and Robert K. Jones (intr. by Frederic G. Hirsch). Lovelace Foundation for Med. Educ. and Res., Albuquerque, New Mexico.

Guinea pigs and rabbits were exposed to lethal reflected pressures in an air-driven shock tube and were subsequently treated in hyperbaric chamber in which the oxygen tension (P_{O_2}) and chamber pressure were independently varied. Treatments involving increases in P_{O_2} resulted in increased survival times of guinea pigs whereas pressurization for 30 minutes at 36 or 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. To study the effects of prolonged hyperbaric oxygenation in treatment of blast injury, guinea pigs and rabbits were treated on a 29-hour schedule having an initial 3-hour hold at the pressure-treatment level followed by 26 hours for decompression. 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 compared to that of untreated controls in the second case. The pathophysiology of primary blast injury is discussed with special reference to the roles of air embolism and cardiopulmonary pathology in the etiology of death. (Supported by Contract DA-49-146-XZ-372, Defense Atomic Support Agency of the Department of Defense.)

THE ROLES OF AORTIC CHEMORECEPTORS, VAGAL TONE, AND ANESTHESIA IN REGULATION OF CIRCULATION IN THE FETAL CALF. Fuheid S. Daoud*, Charles Eastin* and John T. Reeves. University of Kentucky College of Medicine, Lexington, Kentucky.

In the anesthetized fetal lamb bilateral cervical vagotomy (denervation of aortic chemoreceptors) led to hypotension, acidemia, and hypoxemia. The effects of bilateral cervical vagotomy on blood pressure, heart rate and arterial blood gases were studied in 17 unanesthetized and 3 Chloralose anesthetized fetal calves age 187-259 days gestation. Vagotomy caused hypotension and rapid deterioration of blood gases in 2 unanesthetized and one anesthetized fetuses that had hypoxemia and acidosis with CO_2 retention. In the remaining 17 calves vagotomy caused tachycardia but no hypotension or change in blood gases. Within 5 seconds of a one minute cord occlusion in the intact unanesthetized fetal calves sinus bradycardia and 1° and 2° A-V block occurred. These effects were abolished by anesthesia and by vagotomy. Recovery within 6 minutes of arterial pressure, heart rate and blood gases following cord occlusion occurred only in the 17 fetuses in good condition.

It appears that unlike the fetal lamb, the fetal calf is less dependent on aortic chemoreceptor function for maintenance of blood pressure and blood gas values. Failure to observe A-V conduction disturbances due to increased vagal tone in previous studies in the fetus may have been due to anesthesia. (Supported by NIH grants HE 06780-09 and HE 08932-06).

ACID-BASE RELATIONSHIPS BETWEEN CSF AND BLOOD. D. G. Davies*, R. S. Fitzgerald* and G. H. Gurtner. Dept. of Environmental Medicine, The Johns Hopkins University, Baltimore, Maryland 21205.

Time course measurements of the changes in the acid-base composition of CSF were made following a step increase in the $[H^+]_a$ of 20 ± 5 nN, made by the intravenous infusion of HCl at constant arterial P_{CO_2} in 16 anesthetized dogs. Prior to the infusion of acid the $[H^+]_{csf}$ was significantly higher than the $[H^+]_a$. A significant increase in the $[H^+]$ of CSF was observed 20 minutes after the infusion of acid. After two hours no significant difference in the H ion concentration between CSF and blood existed. CSF P_{CO_2} increased in spite of constancy of arterial and jugular venous P_{CO_2}. This increase in CSF P_{CO_2}, as well as a slight fall in the CSF bicarbonate concentration, accounted for the increase in the H ion concentration of the CSF. The mechanism of the increase in the CSF-arterial P_{CO_2} difference could be the same as that proposed previously to explain the concentration of the weak acids, DMO and Barbital, in the CSF (Fed. Proc. 29:270, 1970). This mechanism was originally proposed by Gurtner, Song and Farhi (Resp. Physiol. (1969) 6:173-187) to explain CO_2 differences across the alveolar wall in a fluid-filled lung and involves rapid movement of H^+ from blood buffers toward the negatively charged capillary wall and a slower movement of HCO_3^- away from the wall resulting in a net increase in P_{CO_2} near the capillary wall and hence in the CSF. This study suggests that such a mechanism could be involved in the regulation of CSF and brain interstitial fluid pH. Supported by USPHS Grants # 5 TO1 HE 0553 and 5 PO1 HE 10342.

RIGOR IN VASCULAR SMOOTH MUSCLE. Thomas Davin* and Reed Detar, Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

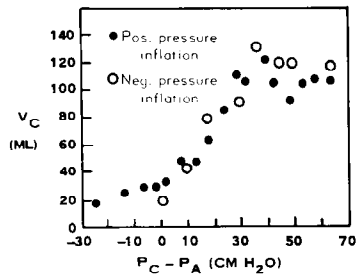
It has been questioned as to whether rigor occurs in vascular smooth muscle. Studies directed toward this problem were carried out using isolated helical strips of rabbit aorta and pulmonary artery suspended isometrically in a physiological salt solution (PSS) at 37°C and pH 7.4. After obtaining control responses to epinephrine, 1 μM, using normal PSS and 100 mm Hg P_{O_2}, strips were exposed to glucose-free PSS at P_{O_2} = < 1 mm Hg. Under these latter conditions the strips do not contract in response to epinephrine. After washing epinephrine out of the bath and allowing the strips to remain in the glucose-free PSS at P_{O_2} = < 1 mm Hg, contractile tension gradually increases to levels 500-1000 mg above resting values. This "contracture" is readily relaxed by the addition of oxygen or glucose to the bathing medium. Normal responses to epinephrine are obtained on returning to normal PSS at 100 mm Hg P_{O_2}. It is suggested that the contracture observed in the unstimulated strips exposed to substrate-free, oxygen-free conditions may represent rigor in vascular smooth muscle. (Supported by NIH grant #FR-05392.)

AMINO ACID ONTOGENESIS IN DISCRETE AREAS OF THE RABBIT BRAIN. J. M. Davis* and W. A. Himwich. Galesburg State Res. Hosp., Galesburg, Ill.

This study is a continuation of our efforts to elucidate the biochemical changes in the CNS of different mammalian species as the young achieve morphological and behavioral maturation. New Zealand white rabbits bred in our animal colony were studied at 0, 5, 10, 15, 20, 25 and 30 days of age as well as adult rabbits one year of age. Glutamic acid, glutamine, GABA, aspartic acid and alanine were determined by two-dimensional paper chromatography in the cortex, cerebellum, pons-medulla, hippocampus-amygdala and mesodiencephalon. Glutamic acid increased throughout development in all brain areas studied until 20-30 days of age. The largest increments were found in the cortex and mesodiencephalon by 20 days of age. Glutamine decreased in the cerebellum and pons-medulla from birth to 5 days. This decrease was followed by an increase to mature levels. Little change occurred in the glutamine level of the hippocampus-amygdala. GABA matured to adult levels in all brain areas by 20 days of age except in the pons-medulla where there was a significant rise from 30 days to adulthood. In general aspartic acid attained mature levels some 10 days earlier than the other constituents and alanine either did not change or decreased to 40 or 50% of its birth values as in the cortex and cerebellum. These data illustrate the caudad to rostral maturation of the parts of the CNS but raise a number of questions as to the functional relations of the amino acids in the various areas. The large relative proportion of GABA in the mesodiencephalon suggests either more GABA available for inhibition in these areas or a larger metabolic pool. The functional reason for either possibility cannot be given at this time.

PRESSURE-VOLUME CHARACTERISTICS OF THE PULMONARY CAPILLARY BED. J.A. Dean*, V.E. Doty* and R.L. Johnson, Jr. (intr. by J.H. Mitchell). U. Tex. (Southwestern) Med. Sch. at Dallas, Dallas, Texas.

The interrelationships among pulmonary capillary blood volume (V_C), capillary blood pressure (P_C), and alveolar pressure (P_A) were measured in isolated perfused dog lungs during intervals when blood flow was stopped. V_C was calculated from the capillary blood's capacity to absorb carbon monoxide after lung inflation with a gas mixture containing 5% carbon monoxide and 0.5% neon in room air. The neon served to indicate the initial dilution of the inspired mixture in the alveolar volume. Measurements were performed at different levels of P_C and P_A. Results are summarized in the figure. P_C had to be higher to achieve the same V_C at a high P_A than at a low P_A but relationships between V_C and (P_C-P_A) were the same during negative or positive pressure lung inflation and were unaffected by changes in lung volume or by norepinephrine.



EFFECT OF DRUGS ON CA EXCHANGE IN THE FROG HEART. J.F. Delahayes* and Emil Bozler. Dept. of Physiology, The Ohio State University, Columbus, Ohio.

Effect of drugs on Ca exchange in the frog heart. Uptake of Ca^{45} was determined continuously by circulating a small known volume of solution through the inside and outside of the ventricle by means of a pump and determining the changes in Ca^{45} at regular intervals with high accuracy. To ensure that diffusion within the muscle does not introduce a lag in the movement of Ca, the ventricle was rhythmically expanded by placing the ventricle inside a chamber to which suction was applied about once per second. The rate of uptake of Ca^{45} varied considerably in different muscles. In the quiescent muscle the addition of epinephrine (10^{-6}g/ml) had no effect. Confirming results of previous investigators electric stimulation increased uptake to a variable extent, while acetylcholine had no effect. In high Ca Ringer solution (25 mM Ca) epinephrine as well as acetylcholine caused an increased Ca influx. These effects as well as those obtained with normal Ringer solution, were most striking in muscles showing a slow Ca exchange. The effects of drugs on Ca influx paralleled the effects on contractures (Bozler and Baker) only partly.

CYCLICAL VARIATION OF RATE OF HEME DESTRUCTION AND CARBON MONOXIDE PRODUCTION ($\dot{V}_{CO}$) IN NORMAL WOMEN. Maria Delivoria-Papadopoulos*, Ronald F.Coburn, and Robert E. Forster (intro by Leonard D. Miller) School of Medicine, University of Pennsylvania, Philadelphia, Pa.

Normal $\dot{V}_{CO}$ values for women are not available. We measured $\dot{V}_{CO}$ (J.Clin.Invest. 42:1172,1963) in 9 young healthy women. All subjects were non-smokers who had a normal menstrual history and no hematological disease. They were studied during both phases of their menstrual cycles. Mean $\dot{V}_{CO}$ during the estrogen phase was 0.32±SE 0.04 ml per hour, and during the progesterone phase 0.62±(SE) 0.06 ml per hour ($p<0.001$). In addition $\dot{V}_{CO}$ was determined in 6 young healthy male volunteers before and after administration of oral progesterone, 0.014 to 0.025 mg per kg each day for 10 days. Baseline $\dot{V}_{CO}$ averaged 0.43±(SE) 0.05 ml per hour. After progesterone $\dot{V}_{CO}$ averaged 0.73±(se) 0.09 ml per hour ($p<0.01$). These data suggest that rates of body heme catabolism and resultant CO production vary with the menstrual cycle in the female and that cyclic variation in blood progesterone levels may be related. A possible mechanism is that progesterone induces liver heme which results in increases in rates of liver heme catabolism.

EFFECTS OF COMPRESSION UPON THE LUNGS OF SEA-LIONS AND DOGS. D.M.Denison and D.A.Warrell (intr. by J.B.West). Department of Medicine, University of California, San Diego, La Jolla, California.

Scholander has suggested that the rigid airways of marine mammal lungs allow the alveoli to collapse completely during a dive so limiting gas exchange, although in terrestial mammals collapse of small airways prevents this. Pressure volume characteristics and alveolar size have been determined on the isolated lungs of four California sea-lions (Zalophus californianus) and seven mongrel dogs during identical cycles of compression and decompression, and for a simulated breathhold dive to a depth of 230 feet. Histological sections were prepared after fixation by a rapid-freezing technique. The dog lungs ceased to empty at pleural pressures of 0 to +3 cm H_2O above airway pressure and the simulated dive at that time caused an eight fold reduction in apparent alveolar volume. The sea-lion lungs emptied much more fully on mild compression and the simulated dives caused almost complete atelectasis. The findings are consistent with the view that the site of airway closure in dog lungs is very close to the alveoli and with Scholander's suggestion that such closure is prevented in the cartilage-reinforced small airways of diving mammals.

POTASSIUM AND ISOLATED CORONARY VASCULAR SMOOTH MUSCLE. Reed Detar and James M. Norton*. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Helical strips cut from rabbit coronary arteries (280-800μ O.D.) were suspended isometrically in a physiological salt solution at 37°C, pH 7.4, and a P_{O_2} of 100 mm Hg. In strips equilibrated at $[K]_o$ between 4 and 10 mM, active tension produced by acetylcholine (1 μM) or histamine (1 μM) is not diminished when $[K]_o$ is increased 1-5 mM by injecting KCl into the bathing medium. Active tension of strips equilibrated at $[K]_o$ less than 4 mM is relaxed abruptly and usually completely by increasing $[K]_o$ 3-5 mM; increasing $[K]_o$ by only 1 mM produces variable degrees of relaxation in these strips. Occasionally spontaneous recovery of tension is observed within five minutes after the onset of the relaxation produced by the added potassium. The potassium-induced relaxation is not blocked by propranolol. These results show that variations in $[K]_o$ within the physiological range can produce changes in contractile tension of isolated coronary strips. It is suggested that potassium may be important in the local control of coronary vascular tone in situ. (Supported by NIH grant # HE 12846.)

EFFECT OF CAROTID SINUS PRESSURE ON CANINE CORONARY VASCULAR RESISTANCE, HEART RATE AND VENTRICULAR CONTRACTILE FORCE. J. DiSalvo*, P. Parker*, J. Scott and F. Haddy. Physiol. Dept., Mich. State U., E. Lansing, Mich.

Changes in systemic arterial pressure, coronary sinus blood flow, coronary sinus pressure, coronary vascular resistance, left ventricular contractile force, and heart rate were measured during pulsatile pressure changes in bilaterally isolated carotid sinuses in 11 open-chested dogs anesthetized with pentobarbital. Control steady-state values for all measured parameters were established by adjusting carotid sinus perfusion pressure to equal mean systemic arterial pressure (~90 mmHg). At low carotid sinus perfusion pressure (48 mmHg), systemic arterial pressure, coronary sinus blood flow, left ventricular contractile force, and heart rate increased, but coronary vascular resistance did not change. At high carotid sinus perfusion pressure (193 mmHg) systemic arterial pressure, coronary sinus blood flow, left ventricular contractile force, and heart rate decreased, while coronary vascular resistance increased. After administration of propranolol (0.5 mg/kg, i.v.) in 4 dogs, reduced carotid sinus perfusion pressure still produced a rise in systemic arterial pressure. Coronary sinus blood flow decreased slightly, coronary vascular resistance increased markedly and left ventricular contractile force was unaffected, contrasting with responses seen in the absence of propranolol. At high carotid sinus perfusion pressure, systemic arterial pressure, coronary sinus blood flow, and left ventricular contractile force still decreased and coronary vascular resistance still increased but the decrease in left ventricular contractile force was reduced. The study shows that the carotid sinus reflex influences coronary sinus blood flow, coronary vascular resistance, and left ventricular contractile force. In addition, it suggests that direct neural effects on the coronary vascular bed are antagonized by metabolic factors, at least at low carotid sinus perfusion pressure.

BEHAVIORAL DISCRIMINATIVE CAPACITY AND CORTICAL UNIT RESPONSES IN CATS WITH DORSAL COLUMN LESIONS. P. J. K. Dobry* and K. L. Casey. Dept. of Physiol., University of Michigan, Ann Arbor, Mich. 48104.

Recent physiological and behavioral studies have suggested that the somatic spatial discriminative capacity of cats might be maintained by a fraction of the fibers in the dorsal columns (DC), or by systems other than the DC-medial lemniscal pathway. This was tested by a roughness discrimination task, 7 cats with high cervical DC lesions being compared with 5 intact controls in tasks of 4 graded levels. Two cats with 97% and 100% destruction of their total DC cross-sectional area failed to reach criterion beyond the second and first discrimination grades; cats with up to 66% DC lesions learned the highest discrimination grade as quickly as intact controls. Extensive (67% to 100%) DC lesions in pretrained cats, however, failed to produce evidence of post-operative deficits when compared with pretrained, sham-operated controls. Cortical unit recording (546 units) from the coronal forepaw focus showed that, in the cats with over 95% DC destruction, 73% (76/104) of the units did not respond to natural or electrical stimulation, as compared to 31% (39/126) in intact controls; smaller acute or chronic DC lesions or total bilateral dorsolateral pathway lesions did not produce this effect. As compared to all other groups, units recorded from cats with over 95% DC destruction had larger receptive field sizes; and cats with chronic DC lesions (38% to 100%) had a higher proportion (9% vs. 0 to 1.6%) of units with prolonged depression of post-stimulus excitability. No significant differences were found with respect to latency to CFP stimulation or porportion of modalities encountered. These findings suggest that only extensive DC destruction detectably alters cortical sensory function and impairs behavioral discriminative capacity. (Supported in part by NIH Grant NS 06588)

ADENINE NUCLEOTIDE DEGRADATION IN HEART AND SKELETAL MUSCLE. James G. Dobson, Jr.*, Rafael Rubio and Robert M. Berne. Dept. of Physiology, University of Virginia School of Medicine, Charlottesville, Virginia.

Adenosine appears to be a mediator in the regulation of myocardial blood flow and has been suggested to play a similar role in the regulation of skeletal muscle blood flow. In the light of improved methodology it seemed appropriate to investigate the latter possibility. Adenine nucleotides (AN) compounds and their derivatives were determined in heart and contracting (5/sec) skeletal muscle of the rat after 20 minutes of ischemia. Histochemical localization of 5' nucleotidase, the enzyme responsible for adenosine formation, was done with the aid of electron microscopy in both cardiac and skeletal muscle. Cardiac and skeletal muscles were perfused with glutaraldehyde for fixation, sectioned (40-50μ) and incubated in a Wachstein-Meisel media containing 5'-AMP, 5'-IMP or 2,3'-AMP as substrate. Adenosine levels increased 20 fold and 2 fold above control levels in ischemic heart and skeletal muscle, respectively. The formation of nucleosides from nucleotides was 4.6 times greater in heart than in skeletal muscle. Myocardial 5'-nucleotidase activity was associated with endothelium, T-tubules, sarcolemma, intercalated discs and sarcoplasmic reticulium, i.e. mostly with membranes bordering compartments open to the extracellular space. In skeletal muscle, the nucleotidase activity was found in endothelium and in localized zones within muscles cells in close proximity to blood vessels. The higher adenosine concentration in ischemic heart as compared to ischemic skeletal muscle and the intracellular distribution of 5'nucleotidase in the two tissues are consonant with the ideas that AN degradation occurs primarily via adenosine in myocardium and via 5'-IMP in skeletal muscle and that adenosine is involved in control of vascular resistance in the heart but probably not in skeletal muscle.
Supported by USPHS Grant #HE 10384.

NATRIURESIS FOLLOWING INTRAVENOUS INFUSION OF CEREBROSPINAL FLUID. Janice Dorn*, Gary E. Kaufmann*, Gary S. Kahn*, Kemp Clark* and John C. Porter. Depts. of Physiology and Surgery, Univ. of Texas (Southwestern) Medical School at Dallas, Dallas, Texas.

Infusion of hypertonic saline (0.85M NaCl) into the third ventricle of anesthetized rats elicits large increases in sodium excretion (Dorn & Porter, Endocrinology 86: 1112-1117, 1970). In an attempt to ascertain whether changes in the electrolyte composition of cerebrospinal fluid (CSF) are responsible for this natriuretic response, CSF from 36 neurosurgical patients was infused into the jugular vein of rats. Thirty-three of these samples contained normal amounts of sodium and potassium and all had normal osmolalities. Intravenous infusion of these samples did not alter the urinary sodium levels of rats. Three of the samples, which possessed low sodium concentrations and low osmolalities, produced highly significant increases in urinary sodium levels when infused into rats at the rate of 0.15, 0.051, 0.025 or 0.013 ml/min. The extent of the observed natriuresis varied significantly with infusion rate ($P < 0.001$) and with time throughout each experiment ($P < 0.001$). The results suggest that the alterations in the composition of cerebrospinal fluid may be instrumental in eliciting increases in urinary sodium excretion. (Supported by NIH Grant AM01237, a grant from the Medical Research Foundation of Texas, and a grant from the American Heart Association, Texas Affiliate.)

EFFECTS OF NEUROHYPOPHYSEAL HORMONES (NHH) AND ANALOGS ON RENAL MEDULLARY ADENYL CYCLASE (RMAC). T.Dousa* and O.Hechter. Inst.Biomed.Res., American Med. Assn., Ed.Res.Fndn., Chicago, Ill., and R.Walter* and I. L. Schwartz. Dept. of Physiology, Mt. Sinai Med. & Grad. Schools, New York, N.Y.

In vitro effects of NHH on RMAC have been compared with their relative antidiuretic potencies. Arginine vasopressin (AVP), lysine vasopressin (LVP) and oxytocin (OXY) selectively stimulate RMAC preparations from rabbit, rat and mouse. In RMAC preparations from these three species, saturating concentrations of AVP and LVP evoke the same maximal response (a measure of intrinsic hormonal activity), while the maximal response to OXY was significantly lower. Studies of the full dose-response range indicated the following order for affinity: AVP> LVP>OXY (as evaluated by the concentration of hormone required to elicit an half-maximal response). This order corresponds to the known relative antidiuretic potencies of AVP, LVP and OXY in the rat. The molecular requirements for RMAC stimulation were studied in detail with the rabbit preparation utilizing a number of NHH analogs possessing structural changes in positions 1,2,3,4,5,8 and 9. The foregoing studies introduce the neurohypophyseal peptide-sensitive RMAC preparation as a tool for the analysis of NHH receptor interaction and suggests the possibility that these mammalian cyclase systems may provide an in vitro bioassay procedure for antidiuretic hormone activity.

INFLUENCE OF TRAINING ON THE HEART RATE RESPONSES OF RATS TO ISOPROTERENOL AND PROPRANOLOL. R.T. Dowell*, and C.M. Tipton. Exercise Physiology Laboratory, Univ. of Iowa, Iowa City, Iowa.

Changes in the resting heart rates (HR) of unanesthetized trained (T) and nontrained (NT) male rats after an IP injection of isoproterenol (ISOP) (50 μg/kg) were measured before and after an 80 day training program. Prior to training, ISOP caused changes of 211±4 and 203±4 beats/min. for the T and NT groups respectively. After training, injections of ISOP produced increases of 220±4 for the T animals and 196±4 for the NT animals. These findings were significant and were obtained from more than 100 rats. When the-beta receptor blocking agent propranolol (PROP) was injected (2 mg/kg, IP), NT rats had a greater decrease (15%) in HR than T rats (9%). Isolated hearts from T and NT animals were perfused with ISOP (.2 μg/ml) and PROP (3 μg/ml) using a modified Langendorff preparation. ISOP perfusion was associated with a greater increase in HR (31%) by the hearts from the T animals than with the hearts from the NT animals (19%) whereas PROP resulted in a greater decrease in HR by NT hearts (35%) than with the T hearts (28%). These findings suggested that hearts from T animals have an increased responsiveness to ISOP that could be associated with a decreased sympathetic tone in the resting state. (Supported by funds provided by Iowa Heart Association)

EFFECT OF MYOCARDIAL STRAINS ON DISTRIBUTION OF CORONARY BLOOD FLOW IN SYSTOLE. James M. Downey*, H. Fred Downey and Edward S. Kirk*. Dept. of Physiology & Biophysics and Dept. of Vet. Med. Physiology & Pharmacology, Univ. of Illinois, Urbana, Illinois.

Although a preferential distribution of coronary blood flow (CBF) to epicardial layers during systole has been ascribed to a gradient of intramyocardial pressure (IMP) (Kirk, E.S. The Physiologist 9:219,1966), deformation of coronary vessels caused by myocardial strains may also influence the transmural distribution of CBF. In this study effects of deformation were separated from effects of IMP by comparing measurements in hearts of anesthetized dogs that were either ejecting into a severed aorta (low afterload) or contracting against an isovolumic balloon. A quantitative index of local CBF during systole was provided by the myocardial uptake of a bolus of ^{42}K or ^{86}Rb injected when constant pressure perfusion of the cannulated left coronary artery was restricted to the period of systole with a solenoid-controlled diaphram pump. Use of both isotopes permitted control and experimental measurements in each heart. Phasic perfusion of the myocardium limited to systole in normally beating hearts, which could be obtained by perfusion with ventricular pressure as well as by the diaphram pump, resulted in twice the uptake of isotope in epicardial layers than in endocardial ones. Similar results were obtained in isovolumic hearts where cardiac strains are minimal. In contrast, maximizing cardiac strains while reducing cardiac pressures by suddenly decreasing afterload abolished the gradient of CBF during systole. We conclude that at least a 2-fold transmural gradient of tissue blood flow occurs during systole which is not caused by myocardial strains. It appears that IMP alone, and not shear or traction forces, acts on the coronary vessels to determine this gradient. (Supported by NIH grants HE-10788 and FR-5460.)

STUDY ON THE ELECTROCHEMICAL ACTIVITY OF BLOOD COAGULATION FACTORS (PROTHROMBIN AND THROMBIN) L. Duic*, S. Srinivasan*, and P.N. Sawyer Electrochem. and Biophys. Lab. of the Vasc. Surg. Serv., Dept. of Surg., SUNY, Downstate Med. Ctr., Brooklyn, N.Y.

On metallic surfaces, thrombosis is accelerated at potentials more positive then 0mv vs N.H.E. while it is inhibited at negative potentials. There are two types of electrochemical reactions, electrosorption (potential dependent adsorption) and charge transfer, which could take place in the overall thrombosis process. In the present study, potential sweep technique has been used to study the electrochemical and related biological activity of prothrombin and thrombin. In this technique, the electrode potential is increased at a constant rate from negative to positive values and then returned to the starting potential. The recorded current-potential (I-V) transient indicates adsorption of species investigated as well as any charge transfer process in which the species is involved. Studies on prothrombin show that electrosorption of prothrombin on the electrode occurs coincident with a charge transfer process. I-V transients, recorded at different sweep rates of potential, show that at least two electron transfer processes take place in the overall electrochemical reaction - one at positive and the other at negative potentials. Similar data have been obtained with thrombin. Electrosorption precedes charge transfer reactions. At physiological concentrations, thrombin shows much lower electrochemical activity than prothrombin. These studies support the evidence for electrochemical reactions taking place in the overall thrombosis process.

EFFECT OF DEHYDRATION ON TOLERANCE TO EXERCISE IN HEAT AS INFLUENCED BY ACCLIMATIZATION, OBESITY, AND SEX. F.N. Dukes-Dobos, E.R. Buskirk, O. Bar-Or* and A. Henschel. Laboratory of Physiology and Ergonomics, Bureau of Occupational Safety and Health, ECA, EHS, PHS, Cincinnati, Ohio and Laboratory for Human Performance Research, The Pennsylvania State University, University Park, Pennsylvania.

Subjects (Ss) were ten college students, 4 lean and 2 obese males and 2 lean and 2 obese females. Each subject (S) was exposed in a climatic chamber to successive 20 min. exercise and 20-40 min. rest periods in 6-7 hours until Ss reached a fluid loss of approximately 2.7 or 4.2% of body weight. Exercise consisted of treadmill walking at 3 mph at 0-5-10% grade, respectively, and of step tests corresponding in intensity to that of the treadmill walks. Each S was exposed twice to each of the two conditions. On one occasion the Ss received complete fluid replacement while on the other no fluid intake was permitted. The climatic conditions were kept in all sessions within the limits of $38.0\text{-}39.5T_a$ and $20.0\text{-}24.1T_{wb}$. All but 2 lean-male Ss were moderately acclimatized to the same test conditions by three previous exposures for about 4 hours each. All Ss had higher heart rates (HR) and rectal temperatures (T_{re}) when dehydrated. In the test series with 2.7% fluid loss there was no difference in HR and T_{re} elevation between male and female or lean and obese Ss. In the 4.2% fluid loss series the obese Ss had higher elevations in HR and T_{re} than the lean Ss. Unacclimatized lean male Ss' increments in HR were the highest. Although absolute values of HR and T_{re} were higher in the female Ss, elevation of these parameters due to dehydration was greater in the male Ss. (Partially supported by Office of Civil Defense Work Order OCS-PS-64-126).

EFFECT OF TEMPERATURE ON GROWTH AND ADRENAL FUNCTION. T.G. Dunn*, S.P. Wilson*, D.P. Doolittle* and P.V. Malven. Dept. Animal Sciences, Purdue University, Lafayette, Ind.

Male and female mice of breeding age were placed together in one of three environmental temperatures (55, 70, or 85 F). Litters from these parents were born and were reared to 43 days of age in their respective environments. Body weight, tail length, adrenal weight, and whole blood corticosteroid concentration were measured and correlated in 294 mice. Mice reared at 55 F had smaller body weights at 42 days than mice reared at 70 and 85 F (18.8 vs 22.1 and 21.6 g). Females, across environments, had larger adrenal glands than males (4.9 vs 3.4 mg) and greater corticosteroid concentrations (136 vs 103 ng/ml). Adrenal weights in both sexes tended to increase as temperature decreased. The 55 F environment elevated blood corticosteroids only in males and eliminated the sex difference which was observed in the other environments. Tail length was markedly reduced in animals reared in the 55 F environment. Correlation coefficients between adrenal weight and blood corticosteroid concentrations were generally small and nonsignificant. In males but not females, blood corticosteroids were negatively correlated with body weight at 42 days across all environments ($r=-0.45$, $P<0.01$) as well as within each environment. In females but not males, adrenal weight was positively correlated with body weight at 42 days across all environments ($r=0.25$, $P<0.01$) as well as within the 55 and 70 F environments. These data suggest that the effect of temperature on adrenal weight and blood corticosteroid concentrations varies between sexes.

THE EFFECTS OF SODIUM PENTOBARBITAL ANESTHESIA ON CANINE MYOCARDIAL FFA METABOLISM. B.C. Durham*, P.W. Prestileo*, A.M. Mulford* and H.I. Miller. Div. of Research, Lankenau Hospital, Philadelphia, Pa.

Many studies of myocardial metabolism have been undertaken on anesthetized experimental animals and the findings reported as indicating normal metabolic functioning of the heart. In order to determine if metabolic data collected from dogs under narcosis represented truly normal values, experiments were performed on unanesthetized mongrel dogs fitted with indwelling catheters in the coronary sinus, and pulmonary and carotid arteries who were later anesthetized with sodium pentobarbital (26 mg/kg, iv) and samples were drawn one and two hours later. Palmitic acid - 1 -^{14}C was infused throughout the duration of the experiment. Sodium pentobarbital markedly decreased plasma levels of FFA and glucose while the pyruvate, lactic acid or glycerol concentrations did not change. FFA turnover was greatly decreased by anesthesia as was the % CO_2 coming from plasma FFA. The total body O_2 consumption decreased significantly but no change was seen in the ventilatory RQ. Both myocardial removal and oxidation of FFA decreased after one hour. At two hours, the FFA removal rate continued to decrease while the oxidation rate returned to control value. Uptake of glucose, glycerol and lactic acid seemed unaffected by anesthesia. Interestingly, at one hour after anesthesia the uptake of pyruvate by the heart significantly increased and returned to the control value by two hours. Myocardial RQ, cardiac output and coronary blood flow did not seem to change significantly. Although the efficiency of the heart was unaffected at one hour, in two hours it decreased. It appears that sodium pentobarbital anesthesia markedly decreases free fatty acid metabolism not only in the entire animal but in the heart as well. (Supported in part by N.I.H. grant # HE 12636-01)

CONTROL OF THE CIRCULATION BY CARDIOPULMONARY RECEPTORS IN THE DOG. A. J. Edis* and J. T. Shepherd, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Experiments were carried out in dogs (thiopentone-chloralose anesthesia) to assess the role of cardiopulmonary (CP) afferents in control of the circulation. Eight dogs with aortic nerves cut were atropinized and subjected to a standard bleed (8% blood volume) and the ability of CP receptors to reflexly maintain aortic blood pressure and to accelerate the heart was compared with that of the carotid sinuses. Carotid sinus reflexes were eliminated by vascular isolation and CP reflexes by vagotomy. When the carotid sinuses were the sole controlling mechanism aortic blood pressure decreased 17% and heart rate increased 15 beats/min. With the CP receptors alone intact comparable values were 24% and 10 beats/min. respectively. With neither reflex intact blood pressure decreased 41% and there was no significant increase in heart rate. Since the control blood pressure before the bleeds was similar these results indicate that CP receptors, although less effective than carotid sinus receptors, can play an important role in maintaining blood pressure during hemorrhage. In nine dogs the aortic nerves were cut and the hindlimbs and left kidney perfused at constant flow. The reflex vascular responses in these beds to a standard decrease in carotid sinus pressure were compared before and after vagotomy. Before vagotomy the hindlimb and renal pressures increased 46 and 17 mmHg respectively; after vagotomy comparable increases were 56 and 76 mmHg. These results suggest that intrathoracic receptors subserved by vagal afferents have a more powerful action on the kidney than on muscle vessels in opposing the constriction caused by carotid sinus hypotension. Supported in part by NIH Grant HE-5883.

POTENTIATION BY HEXAMETHONIUM OF ADRENALINE ACTIONS ON SUDOMOTOR TRANSMISSION IN THE CAT. A.E.U. Edisen and D.P.C. Lloyd, The Rockefeller University, New York, N.Y. 10021.

Hexamethonium, an antinicotinic ganglionic blocking agent, allegedly pure in its action upon nicotinic cholinergic junctions, in dose range from 5 to 20 mg/kg, produced a slight transitory depression of action potentials of sweat glands without sign of depolarization at this classically muscarinic junction, as did in greater intensity phentolamine and tolazoline (Edisen and Lloyd, Fed. Proc. 29, 478, Abs.). Responses were induced by 4/min. stimulation of the distal plantar nerve of the cat's hindlimb; recorded by zinc-zinc-sulfate electrodes, one on the footpad and the indifferent lead beneath the skin. Adrenaline (0.3 to 100μg/kg) always produced an immediate depression of action potentials, usually accompanied by baseline negativity indicating depolarization of sweat gland cells, followed by positivity indicating sweat secretion. These effects varied with dose levels (Edisen and Lloyd, 1970). Therefore, adrenaline, by depolarizing sweat gland cells, leads to cathodal-type block of neuroglandular transmission (that can approach completeness) and to secretion of sweat. Responses to standard low doses, 5 to 10μg/kg, of adrenaline were greatly potentiated by prior dosage of hexamethonium. All actions of adrenaline were greatly enhanced, mimicking the effect of increased dosage of adrenaline. (Supported in part by U.S.P.H.S. grant No. 02816 from N.I.N.D.S., U.S.P.H.S.)

Interaction of Sinusoidal Vibration and Cardiovascular Function in Dogs. Richard G. Edwards, Ernest P. McCutcheon, Charles F. Knapp, and Robert Boone, (Intr. by Donald T. Frazier).

The problem of defining how the various composite systems in the human body respond to accelerations transmitted from vehicles and machinery has been the object of much research in recent years; however, few data exist from direct experimental measurements of pertinent parameters associated with critical cardiovascular system function in a dynamic environment. This investigation established magnitudes of effects and mechanisms by which sinusoidal vibration can alter blood flows and pressures in dogs. Electromagnetic flow transducers chronically implanted around the aorta and the pulmonary and carotid arteries enabled the recording of flow velocity during vibration. Catheter-tip pressure gauges were used to simultaneously monitor arterial blood pressure. The animals were restrained in a vertical attitude with respect to both gravity and vibration acceleration vectors (y-axis). They were placed on an electrohydraulic "shake table" vibration exciter and exposed to vibrations in the 2 to 12 HZ frequency range at acceleration amplitudes of from 1 to 3g, i.e. from 980 to 2940 cm/sec2. The results indicated that compared to flow rates in the resting dog, flows occuring during low frequency vibration (frequencies close to the heart rate) can be increased by more than 100% or decreased to approximately zero for a given flow cycle in a major artery. The changes in pressure corresponded to the changes in flow. These alterations were shown to be a function of (1) the phase relationship between the vibration motion and cardiac systole, (2) the vibration-induced movement of internal organ systems, and (3) the vibration frequency and acceleration intensity. (Supported in part by Air Force Office of Scientific Research Contract F4460-69-C-0127.)

THE EXTRACTION OF SOLUTE-FREE WATER FROM THE LUNG BY OSMOTIC TRANSIENTS. R.M. Effros* (intr. by F.P. Chinard). New Jersey College of Medicine, Newark, New Jersey

A new indicator dilution technique is used to quantitate and characterize the flux of fluid from pulmonary tissues induced by hypertonic solutions. Following rapid injection of hypertonic urea or NaCl into a jugular vein of an anesthetized, intact dog, blood is pumped from the carotid artery into serial sample tubes at 1/3 second intervals. Hemoglobin concentrations are measured in the collected blood. Hemoglobin dilution is assumed to reflect fluid flux from tissue to blood while hemoglobin concentration reflects the flux from blood to tissue. As much as 40% of the pulmonary space as measured with tritiated water and T-1824 is removed by the osmotic bolus within 10 seconds indicating that alterations in tissue concentration are rapid and local equilibration with the bolus may occur. The dilution of albumin and urea (labelled by prior administration of T-1824 and urea -^{14}C) and sodium and potassium by extraction of fluid from the lung is essentially equal to that of hemoglobin. The flux of water from the tissue is apparently not accompanied by the movement of these solutes which therefore must have reflection coefficients close to 1.0. Indeed no significant amounts of osmotically active materials appear to be carried by solvent drag into the pulmonary capillaries. In contrast, outflow tritiated water concentrations do not decline indicating a reflection coefficient close to zero. These studies demonstrate that rapid flows of solute-free water between pulmonary tissue and blood are elicited by osmotic gradients. This technique may provide the means of estimating the reflection coefficients of solutes in other capillary beds in vivo. (Supported by NIH Grant HE 12879)

NORMAL AND ABNORMAL CARDIAC DYNAMICS VISUALIZED BY ULTRASONIC VENTRICULAR CATHETER. Reginald C. Eggleton*, Julia Herrick, and Thomas Franklin*. Interscience Research Institute, Champaign, Ill. 61820.

A computer derived display of ultrasonic data shows detail of cardiac dynamics for normal and infarcted dog hearts. Four catheter-borne 10 MHz transducers spaced 90° apart in a plane normal to the axis of the catheter are pulsed sequentially at the rate of 1000/sec and the catheter is rotated slowly through 90°. The cardiac cycle is arbitrarily divided into 24 equal increments or frames. The data are ordered and stored in a computer and displayed on a cathode ray tube. The 24 ventricular contours are a composite of approximately 16 cardiac cycles. A motion picture showing the cardiac dynamics will be presented. A three-dimensional representation of ventricular shape and volume at various stages during the cardiac cycle may also be reconstructed by combining a series of ventricular contours. The results on the display indicate the function of trabeculae carneae and papillary muscles in the performance of the cardiac cycle. Infolding of the ventricular wall visualized by this technique is explained on the basis of cardiac morphology. Experimental myocardial infarcts are induced by ligation of the anterior interventricular branch of the left coronary artery. Changes in the contractility of the infarcted myocardium may be visualized. (Supported in part by NIH Grant HE 12144-02.)

PLASMA GROWTH HORMONE RESPONSES TO AMYGDALOID STIMULATION IN CONSCIOUS MONKEYS. A. L. Ehle, L. L. Pennington and J. W. Mason (intr. by D. McK. Rioch). Walter Reed Army Institute of Research, Washington, D. C.

Chair restrained rhesus monkeys with chronic implanted electrodes and venous catheters were used in this study. Plasma growth hormone levels were determined by radioimmunoassay. Following the onset of repetitive electrical amygdaloid stimulation, plasma growth hormone levels were found to increase significantly ($p < .005$) if the prestimulation base line had been stable and less than 13 mug/ml. Under these conditions increases in plasma growth hormone from 5 to greater than 20 mug/ml were observed. The latency of the response ranged from 10 to 20 minutes and reached its maximum value in 30 to 40 minutes. When base line levels were greater than 20 mug/ml there was no further increase seen during the stimulation period. In most experiments stimulus strengths were used that resulted in a short afterdischarge in the amygdala and large increases in growth hormone were seen. However, in one instance a small increase was observed without the occurrence of an afterdischarge. These experiments demonstrate the ability of amygdaloid stimulation to increase plasma growth hormone levels subject to the existence of a low, stable base line and suggest a possible mechanism for the mediation of known psychological influences on growth hormone levels. However, the validity of this suggestion and the possible role of amygdaloid influence on growth hormone secretion in other circumstances remains to be demonstrated.

THE RELATIVE CONTRIBUTION OF CENTRAL AND PERIPHERAL INPUTS TO UNIT ACTIVITY IN THE LUMBO-SACRAL SPINAL CORD OF DEVELOPING CHICK EMBRYOS. M. Eisenstadt and S. C. Sharma (Intr. by N. Suga). Biology and Psychology Departments, Washington University, St. Louis, Mo.

Firing patterns of single neurons at active loci in the lumbo-sacral spinal cord of developing chick embryos (15, 17 and 19 days of incubation) were recorded through micro-electrodes (KCl-agar glass pipettes 2-4μ in diameter). For each stage, the average number of units per probe was computed for a) normal embryos, b) embryos with the spinal cord transected between the 1st and 2nd vertebrae, c) embryos with the spinal cord transected at the 21st vertebra, and d) embryos with the dorsal roots (23-30) transected bilaterally. The unit activity of normal embryos increases between 15 and 17 days and remains approximately constant through 19 days. In preparations b, c and d there was a decrease in number of units per pass in all stages. More units were found, however, than in preparations of spinal cord both transectioned at the level of 21st root and bilaterally deafferented in the lumbo-sacral region at the same stages of development (Sharma et. al., 1970 P.N.A.S. 66, No. 1). The hypothesis that the influence of central and peripheral inputs into the lumbo-sacral spinal cord increases between 15 - 19 days is supported by the present study. (Supported by USPHS Grants NB-0571 to Dr. Hamburger and GM-01900 to Dr. Sandel.)

THE EFFECT OF SHORT TERM HEAT ACCLIMATION ON SWEAT GLAND FUNCTION. Reynaldo S. Elizondo*, Mukul R. Banerjee, Tokuo Ogawa* and Robert W. Bullard. Indiana University, Bloomington, Indiana. 47401.

The purpose of this investigation was to study by resistance hygrometry the changes in sweat gland function occurying in man following short term acclimation to heat. A battery of functional tests was performed on male subjects before and after short term acclimation produced by the procedure described by Lind and Bass (Fed. Proc. 22:704, 1963). The sweating activity over an 8 cm^2 area on the forearm was continuously recorded during each test which included local heating in a warm environment (34-or 38°C), 7% CO_2 inhalation, leg cooling, and local heating in a cold environment (18°C.) following the stimulation of the glands by an intradermal injection of acetylcholine (1:100,000). No significant change in the cyclic nature of the sweating pattern was observed following acclimation. The latent period for sweating was decreased and the rate of sweating on the forearm tended to decrease or remained unchanged. Short term acclimation to heat produced a significant decrease in the sensitivity of the sweat glands to local heating. This observation was true both in a warm environment where the sweat glands were being stimulated by the central nervous system and in a cold environment where the sweat glands were stimulated by the intradermal injection of acetylcholine. These observations suggest that after short term acclimation to heat the function of eccrine sweat glands is less dependent upon local skin temperature and may be more directly controlled by the central thermolregulatory processes. (Supported by U.S. Air Force C-0014 and Army MD 17-68-G-8066).

EFFECTS OF EXERCISE ON PULMONARY ARTERIAL IMPEDANCE AND HYDRAULIC ENERGY. Ronald C. Elkins* and William R. Milnor. Johns Hopkins Univ. School of Med., Baltimore, Maryland.

Exercise produces a much smaller increase in mean pulmonary arterial pressure than in pulmonary blood flow, suggesting some active or passive alteration in the properties of the pulmonary vessels. To investigate this response, and to examine the changes in pulsatile flow and pressures with exercise, we carried out experiments on 5 dogs after implanting transducers to measure pulmonary arterial pressure and flow, and left atrial pressure. Observations were made at rest (prone), standing, and running on a horizontal treadmill at about 10 km/hour. Effects of exercise on cardiac output and pulmonary vascular resistance (PVR) were similar to those reported by others: pulmonary blood flow doubled, approximately, (averages, 2.59 L/min at rest, 5.30 L/min with exercise), and PVR fell, though in only one instance was the fall greater than 10%. At rest, the spectrum of input impedance (which expresses pulsatile pressure/flow relationships) contained moduli that averaged 280 dyne sec/cm^5 in the range 1 to 12 Hz, with frequency-dependent oscillations of ±45 dyne sec/cm^5. Two kinds of change in impedance were noted with exercise: (1) a decrease in the oscillations (average change 46%); (2) an increase in average modulus (average change 55%). These modifications of the impedance spectrum do not resemble those produced by altering sympathetic stimuli to the pulmonary vessels, but they are compatible with the passive effects of vascular distention by increased transmural pressure. The levels of kinetic power reached during exercise (range 41 to 208 milliwatts) indicate that conversion between kinetic energy and pressure within the bed, which is negligible at rest, may become significant during exercise.

LEFT VENTRICULAR FUNCTION DURING ACUTE HYPERCAPNIA IN THE CONSCIOUS DOG. H. H. Erickson, E. L. Fitzpatrick,* and H. L. Stone, Biodynamics Branch and Data Processing Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

The impairment of cardiac performance during hypercapnia is a function of pH or P_{CO_2}, or of both parameters; however, the mechanisms responsible for the changes in cardiac function have not been completely defined. In this study a tracheostomy was performed on each of 12 dogs to permit rapid introduction of hypercapnia through an endotracheal tube. Each dog was instrumented with Doppler ultrasonic flow transducers to measure the velocity of blood flow in the left circumflex coronary artery and ascending aorta. A solid-state pressure transducer was implanted within the left ventricle to determine left ventricular pressure and dP/dt. A catheter was placed in the left atrium to measure left atrial pressure, blood gases and pH. After a recovery period of at least 10-14 days each dog was subjected to 6% CO_2. Approximately 3-4 minutes' exposure to 6% CO_2 in room air elevated the arterial P_{CO_2} from 27 to 40 mm Hg, the arterial P_{O_2} from 88 to 113 mm Hg and decreased the arterial pH from 7.40 to 7.36. At rest, the average values of: heart rate was 85 beats/min, cardiac output was 3.62 L/min, left atrial pressure was 2.6 mm Hg, and left ventricular systolic pressure was 142 mmHg. There was no significant change in these parameters during hypercapnia. Left ventricular dP/dt, however, decreased from 3086 to 2769 mm Hg/sec ($p < .001$) while there was essentially no change in coronary flow, 43 to 48 ml/min ($p < .10$). These results indicate that acute hypercapnia has a negative inotropic effect on the myocardium in the absence of a negative chronotropic effect, and at the same time causes a small increase in coronary blood flow. The negative inotropic effect of acute hypercapnia in the resting animal is likely the direct effect of P_{CO_2} since intracellular pH changes rather slowly.

EFFECT OF PROPRANOLOL (PPNL) ON STEADY STATE PENTAGASTRIN-INDUCED HCl SECRETION AND GASTRIC MUCOSAL BLOOD FLOW (MBF) IN DOG. D. C. Evans* and T. M. Lin. Lilly Research Laboratories, Indianapolis, Indiana

We found that the steady state "pentagastrin" (PG)-induced acid secretion in dogs was augmented by β-blocking adrenergic agents. The purpose of this study is to show the effect of PPNL on PG-induced acid secretion and the gastric MBF in dogs with vagally denervated pouch (HP) and innervated gastric fistula (GF). Seven dogs were infused with PG (1.2 μg/kg-hr) and aminopyrine (5 mg/kg-hr) at a rate of 60 ml/hr for a 6-hr period. PPNL 0.5 mg/kg was given in a single injection i.v. after steady states were established. Measurements were made for volume (V) $\{H^+\}$ conc., total H^+, aminopyrine clearance (C) and ratio (R) of aminopyrine in the gastric juice to that in the blood at 15 minute intervals. The net % changes of these parameters from their respective controls are as follows:

	V	H^+	Total H^+	C	R
HP	↑80-85	↑8-15	↑60-85	↑ 46*	↓ 34*
GF	↑40-45	↑ NS	↑35-50	↑P>.05	↓P>.05

↑increase, ↓decrease, *at 30-45'

Thus the steady state acid secretion and clearance of aminopyrine in both HP and GF were increased by PPNL. The results suggest that one of the mechanisms by which PPNL affects acid secretion is by increasing MBF. However, the decrease in R values suggests that PPNL may also have a direct effect on the acid secretory mechanism.

ACTIVITY OF VENTRALIS LATERALIS NEURONS PRIOR TO MOVEMENT IN THE MONKEY. E. V. Evarts. Natl. Insts. of Health, Bethesda, Md.

Studies of single unit activity in man by Jasper et al. have shown that neurons in nucleus ventralis lateralis (VL) become active prior to voluntary movement, and indicate that the thalamic projection to the motor cortex plays a role in initiating movement. The present study on VL neurons in relation to movement in the monkey was carried out to extend these observations, and to compare the onset times of VL and motor cortex discharges prior to movement. Monkeys were trained to maintain wrist flexion (or extension) until the onset of a light stimulus and to extend (or flex) the wrist following stimulus onset. Following training, a microelectrode was introduced vertically down into thalamus. The entrance of the microelectrode into the thalamus in the inactive, relaxed monkey was signalled by the appearance of rhythmic burst activity. It has been wondered whether such bursts by VL neurons are involved in control of movement. The results of the present experiment indicate that this is not the case. Of more than 30 neurons in VL which were involved in the wrist movement, none had the burst pattern during the movement, and yet all of these same neurons which were observed during drowsiness exhibited rhythmic bursts. During the steady state prior to movement, VL neurons were either silent or showed regular discharge; increases or decreases of activity in VL neurons were found to precede movement by as much as 100 msec, a lead time which is approximately the same as that of the earliest motor cortex neurons. This result points to a role of thalamic neurons in controlling motor cortex activity prior to movement. Such a role does not in any way militate against the undoubted function of VL in the relay of sensory feedback information following movement initiation, but indicates that VL (like cerebellar) neurons may have a dual function, coming into play before as well as after movement.

MESENTERIC VASOMOTOR RESPONSE TO REDUCED MESENTERIC BLOOD FLOW. M.E. Everhard,* J.A. Regan,* F.J. Veith, and S.J. Boley* Montefiore Hosp. and Med. Ctr. and the Albert Einstein Coll. of Med., New York, N.Y.

Both vasoconstriction and vasodilatation of the mesenteric vascular bed are described in response to diminished mesenteric blood flow. To study the importance of the duration of ischemia the effects of prolonged 50% diminution of superior mesenteric artery (SMA) flow were determined in 11 anesthetized dogs. SMA, celiac and ascending aortic or femoral arterial flows, and mesenteric and systemic arterial pressures were measured. After SMA flow was reduced 50% with an hydraulic occluder, mesenteric arterial pressure (MAP) fell 36-71% and celiac artery flow rose 18-250%. However, within 1-6 hours MAP returned to control levels while 50% SMA flow was maintained and celiac flow fell, indicating active vasoconstriction in the mesenteric bed. If the occluder was released when MAP first returned to control, the SMA flow immediately rose to control levels. However, if the SMA occlusion was continued ½-4hours after MAP had returned to control, SMA flows remained at 30-53% of control even after removal of the occluder. These low SMA flows persisted and were observed up to 5 hours, but in several animals papaverine injected into the SMA produced an immediate return to normal SMA flow. During all studies aortic and femoral blood flows and systemic arterial pressure were unchanged. While the initial response to 50% SMA flow is probably autoregulatory active vasodilatation, with prolonged ischemia this is replaced within hours by active vasoconstriction which persists as long as the SMA is partially occluded. If prolonged, vasoconstriction may persist even after release of the SMA occlusion causing continued diminished SMA flow. This may explain why low mesenteric flow of only a few hours duration can produce mesenteric ischemia persisting for many hours after the primary problem is corrected.

EFFECTS OF AN ADRENAL CORTEX INHIBITOR (AMINOGLUTETHIMIDE) ON WATER AND ELECTROLYTE BALANCE. W.J.Eversole, George P. Pollock* and R.E. Zimmerman,* Indiana State University, Terre Haute, Ind., 47809.

The purpose of this study was to determine whether aminoglutethimide (AG) induces changes in water and electrolyte metabolism similar to those known to occur in adrenal insufficiency. Aminoglutethimide was injected by various routes into animals in daily doses ranging from 25 to 100 mg/kg BW. Studies were made on water intake in normal, adrenalectomized and nephrectomized rats, and water duiresis tests were conducted in male and female rats after administration of AG by stomach tube or by subcutaneous injection. Effects of varying doses and the duration of effects of given doses on blood electrolytes were determined in rats, dogs, chickens, turtles, and frogs. The results show that AG induces a polydinsia in non-adrenalectomized rats and acute effects on water and electrolyte metabolism occur in a pattern characteristic of that known to occur in chronic adrenal insufficiency. Also, AG augments the adrenal-insufficiency-like syndrome in adrenalectomized rats. No changes in electrolyte balance were detected in poikilothermic vertebrates (turtle & frog). Symptoms of adrenal insufficiency were induced in homoiotherms (rat, dog, chicken) so rapidly after injection that it appears unlikely that such effects were caused by inhibition of adrenal cortical secretion.

THE EFFECT OF ETHANOL ON ALDOSTERONE SECRETION IN MAN. L.F.Fabre, Jr.*, R. W. Farmer*, E. D. Pellizzari*, G. Farrell, Texas Research Institute of Mental Sciences and J. H. Mendelson, NIMH, Chevy Chase, Maryland.

Ethanol has been shown to alter a variety of endocrinologic systems, e.g., vasopressin and cortisol metabolism. In earlier studies, we found as well, alterations in aldosterone secretion in anesthetized dogs, and aldosterone excretion in human subjects in response to ethanol. The present study is an investigation of the effect of ethanol on human aldosterone secretion. Alcoholic subjects were admitted to a Metabolic Ward and thoroughly screened and found free of hepatic, renal, endocrine or cardiovascular disease. Compartmental analysis estimates of aldosterone secretion were then performed during control and ethanol consumption periods. Serial blood ethanol levels performed during alcohol consumption indicated a range of 100 to 300 mg%. Aldosterone determinations were performed by a gas chromatographic method and by a new radioimmunoassay. Control aldosterone secretion averaged 6.42 µg/6 hr; ethanol-treated subject's aldosterone secretion averaged 11.30 µg/6 hr. The mean difference (4.88 µg/6 hr) analyzed by the paired t-test was significant; $n=21$, $t=3.03$, $p<.01$. Aldosterone excretion was also elevated in confirmation of earlier studies: $\bar{X}$ control 2.66 µg/6 hr, $\bar{X}$ alcohol 4.97 µg/6 hr, $\Delta\bar{X}$ 2.35 µg/6 hr, $n=26$, $t=2.58$, $p<.02$. These results demonstrate increased aldosterone secretion in human subjects receiving moderate ethanol intake, and suggest that ethanol-induced electrolyte abnormalities may be, in part, mediated by altered aldosterone metabolism.

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FURTHER ANALYSIS OF COLD ADAPTATION OF NA-K ATPASE OF HIBERNATING MAMMALS. Leslie S. T. Fang* and John S. Willis, Department of Physiology and Biophysics, University of Illinois, Urbana, Ill.

Like ion transport, Na-K ATPase from kidney of hibernating species has been shown to be less affected by decrease in temperature than that from non-hibernating species. Experiments were done to examine in greater detail two aspects of this adaptation. In earlier work on Na, K transport, kidney slices from hibernating hamsters were seen to have an initial rate of K uptake that was about twice that of slices from awake hamsters. Present studies indicate that, upon entry into hibernation, the specific activities of both Na-K ATPase and K-stimulated p-nitrophenol phosphatase (K-NPPase) were increased by about two fold at four different assay temperatures. It is probable that an increase in production of the enzyme takes place during the preparation for hibernation. A second line of investigation is designed to determine how low temperatures block the Na-K ATPase reaction in non-hibernating species. The Na-K ATPase reaction can be subdivided into several partial reactions, the last of which is a K-dependent phosphatase reaction involving the release of phosphate from a phosphorylated intermediate. K-stimulated NPPase activity is thought to be a reflection of this last reaction. In rat renal cortical preparations, K-NPPase activity is fairly similar to that of the hamster and is less inhibited by low temperature than the Na-K ATPase reaction. These results may suggest that the principal difference in the enzyme between these two species lies at an earlier step in the reaction. Further studies are being done to examine the rates of turnover of the phosphorylated intermediates.

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THE SPECIFICITY AND ROLE OF CHOLYCYSTOKININ IN THE MESENTERIC VASODILATATION INDUCED BY INTRADUODENAL FAT. J.W. Fara*, E.H. Rubinstein, and R.R. Sonnenschein. Dept. of Physiology, UCLA School of Medicine, Los Angeles, California 90024.

We have shown (Science 116: 110-111, 1969) that the instillation of 1.5 ml of fat directly into the duodenum of chloralose anesthetized cats produced a superior mesenteric vasodilatation (blocked by atropine) of characteristic latency, amplitude and duration, and that this vasodilatation could be mimicked by intravenous infusion of cholycystokinin (CCK). Present experiments on anesthetized cats demonstrate that the intraduodenal instillation of 1.5 ml fat (corn oil) or 127 M (0.1-0.2cc/min) l-phenylalanine produces an increase in superior mesenteric blood flow, gall bladder pressure, duodenal motility and pancreatic enzyme output, which can be closely mimicked by the intravenous infusion of CCK (0.6-3.5 units/kg/hr.); while intraduodenal saline, 5% lactose or 5% dextrose fail to produce comparable responses. The intravenous infusion of CCK failed to elicit blood flow changes in the renal, femoral, gastric or large intestinal vascular beds, but did produce a comparable vasodilatation in the pancreas and small intestine. The vasodilatation in the small intestine and pancreas following intraduodenal fat or l-phenylalanine and intravenous CCK is accompanied by increased oxygen consumption of these tissues. (Supported by USPHS grants HE-05157 and HE-5696, AMA-ERF, and AHA 69880 and 69127)

DEVELOPMENT OF VENTILATORY CONTROL MECHANISMS IN THE VIRGINIA OPOSSUM. J. P. Farber* and S. M. Tenney, Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

The opossum must undergo much of its fetal development in the mother's pouch without benefit of a placental connection to provide for its gas exchange. Early use of pulmonary respiration is required in a pouch environment containing less O_2 and more CO_2 than room air. In this investigation, the development of chemical control of breathing (high CO_2; low O_2; asphyxia) and the ventilatory effects of pulmonary inflation and deflation were studied by plethysmography in unanesthetized pouch young, aged from 4-6 days to weaning at about 95 days. A sustained increase in ventilation was evoked with high CO_2 or low O_2 breathing in the youngest animals. Hypoxic-hypercapnic interaction was observed by the 15-20th day but the effect was much decreased by weaning time along with the hypoxic response. Ventilation on room air was characterized in the youngest animals by inspiratory pauses and usually by an irregular rhythm. On the 15-20th day a regular breathing pattern without inspiratory pauses could be seen. Carbon dioxide or asphyxia provoked a more regular ventilatory pattern, while low O_2 caused an irregular ventilation, which only gradually became smoother with increasing age. Breathing with positive pressure immediately decreased tidal volume and frequency of ventilation at all ages; while negative pressure caused deep breaths with inspiratory pauses in young animals, but produced an increase in respiratory frequency by the 40-50th day. These results indicate that specific receptor and effector mechanisms are present early in pouch life which respond to low O_2, high CO_2, asphyxia, and lung volume changes. Modification of the asphyxia, hypoxia, and negative pressure responses with age may result from development of higher central nervous influences upon primitive ventilatory control mechanisms. (Supported by NIH grant # HE 02888-14.)

GROWTH HORMONE DOES NOT CAUSE GLUCAGON SECRETION. R. W. Farmer*, L. F. Fabre, Jr.*, Texas Research Institute of Mental Sciences, Houston, Texas and T. Sugase*, K. Nonaka*, and P. P. Foa, Sinai Hospital of Detroit, Detroit, Michigan, (intr. by R. A. Huggins, Baylor College of Medicine, Houston, Texas.)

Previous work in the Houston laboratory showed that pancreatectomy abolished the lipolytic response to growth hormone (GH). This finding revitalized the theory that GH causes glucagon secretion. Dogs were anesthetized with pentobarbital and the GI tract removed, leaving the pancreas intact. Pancreatic venous glucagon was measured by the radioimmunoassay of Nonaka and Foa. Porcine GH or buffered saline was injected intrajugularly (1 mg GH/kg) or infused intrapancreatically. Pancreatic venous glucagon increased variably after both GH and saline. When eviscerated dogs were infused intrapancreatically with GH, glucagon concentration was increased 90-120 minutes after termination of surgery. Varying the time of initiation of GH infusion from 0 to 60 minutes post-surgery did not modify the time of the glucagon response. Glucagon secretion is independent of plasma GH concentration. The increased glucagon secretion observed herein appears to be the result of surgical trauma.

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MAXIMUM CARDIOVASCULAR RESPONSES TO BICYCLING AND RUNNING. J. A. Faulkner, D. E. Roberts,* R. L. Elk,* and J. F. Conway. The University of Michigan Medical School, Ann Arbor, Michigan 48104.

The CO_2 rebreathing method was used to estimate the cardiac outputs of 8 men during selected work loads on a bicycle ergometer and on a motor-driven treadmill. Oxygen uptake was measured and heart rate was calculated from the ECG. Our purpose was to investigate the interrelationships between stroke volume and heart rate at maximum cardiac output and between cardiac output and $(a\text{-}v)O_2$ difference at Max VO_2. In both cycling and running cardiac output was linearly related to submaximum work but as maximum work was approached cardiac output declined. The decline in cardiac output was due to a marked decrease in stroke volume from 164 to 137 ml as heart rate increased from 168 to 180 beats/min. Max VO_2 was reached at a higher work load or later in time than maximum cardiac output. Max VO_2 was attained through an increase in $(a\text{-}v)O_2$ difference from 144 ml/liter to 162 ml/liter at a time when cardiac output was declining. Since $(a\text{-}v)O_2$ differences were maximum (160 $\pm$ 10 ml/liter) in both activities, we conclude that Max VO_2 cycling and running were limited by the inability of the heart to maintain stroke volume as heart rate increased. The 11% decrease in Max VO_2 cycling (3.56 $\pm$ .65 L/min) compared to the Max VO_2 running (3.96 $\pm$ .66 L/min) was in good agreement with published data. The heart rate at Max VO_2 was 177 beats/min at Max VO_2 both cycling and running and the difference in cardiac output was completely due to a lesser stroke volume cycling (128 ml) than running (141 ml). (Supported by a grant from the Michigan Heart Association.)

HEPATIC LYSOSOMAL HYDROLASE ALTERATIONS DURING STARVATION
James P. Filkins, Dept. of Physiology & Biophysics, Univ. of Tennessee Medical Units, Memphis, Tennessee.

Based primarily on morphological data, lysosomes and their constituitive acid hydrolases have been implicated as mediators of various physiological tissue regressions - including the mobilization of hepatic cytoplasm during starvation. The present study focused on alterations in four representative hepatic lysosomal hydrolases accompanying fasting of male rats for 24 to 168 hours; both "free" and "total" hydrolase activities were measured by the Triton X100 labilization method. Liver regression within 24 hours of fasting was manifest in a 33% decrease in wet liver weights, and a 50% increase in cellularity expressed as nuclei per gram of wet liver. During continued starvation, liver weights and protein content decreased while cellularity increased. Within 24 hours and through 96 hours of fasting, total activities of acid phosphatase, beta-glucuronidase, acid ribonuclease, and cathepsin D were increased when expressed either per gram of liver wet weight, or per gram of protein; however, hydrolase activities were decreased when expressed either per total wet weight of liver or per cell nuclei. By 168 hours of fasting the free activities of acid phosphatase and acid ribonuclease were enhanced 75-100%. Both the persistence and increase in free acid hydrolase activities during prolonged starvation are consonant with a role for the lysosomal apparatus in hepatic cell regression during starvation. (Supported by USPHS Grant HE 11499.)

RESISTANCE OF ALVEOLI TO SEVERE HYPOXIA. A.B.Fisher*, R.W. Hyde, J.Reif*, and J. Sonnemann*. Depts. of Graduate Physiology and Medicine, School of Medicine and School of Veterinary Medicine, Philadelphia, Pa.

Seven anesthetized dogs were studied to determine the resistance of alveoli to local hypoxia in the presence of normal systemic oxygenation. After insertion of a tracheal divider and occlusion of the left pulmonary artery with a balloon catheter,the left lung was ventilated for 3-7 hours with a gas containing 95% N_2 and 5% CO_2. Left lung-end tidal P_{O_2} during the experiments ranged from 1 to 6 mmHg. At the end of the exposure period, the pulmonary artery balloon was deflated, differential single breath diffusing capacity ($D_{L_{CO}}$) and pressure-volume (P-V) curves were measured and the dogs were sacrificed. Subsequently, large lung sections were examined by light microscopy. Surface active properties of lung washings from 2 dogs were evaluated with a modified Wilhelmy balance. One dog was allowed to recover and was restudied 3 days later. Compared to pre-exposure values, mean D_L decreased 16% in the control right lungs and 2% in the experimental left lungs, while the P-V slope decreased 18% on the right and increased 5% on the left. No differences of minimal surface tension were noted among the lung washings and there were no histologic differences between right and left lungs. These studies suggest that alveolar cells of the dog lung are relatively resistant to lack of oxygen and that lung edema associated with acute hypoxia is probably not due to a direct effect on alveolar permeability.

FROG RETINAL RESPONSES: RELATIONSHIPS BETWEEN ADAPTATION LEVEL AND BRIEF INTERMITTENT STIMULATION. D. E. Fleming and H. K. Merrill*. Veterans Administration Hospital, Phoenix, Arizona.

Electroretinographic (ERG) responses elicited by short-duration two-pulse trains are characterized by variable amplitude b waves, the first being larger than the second. Presumably a light adaptive process is involved, as the amplitude of the second b wave increases with an increase of inter-pulse interval. Arden, Garnit and Ponte (1969) demonstrated that the amplitude of the second b wave is proportional to the exponential decay of a suppressive process following the first b wave. In the present study, it was questioned whether similar b wave amplitude interrelationships could be demonstrated with longer pulse trains and under different levels of retinal adaptation. Five-pulse trains were used with frog eyecup preparations. Four levels of adaptation were used. It was found that with the dark-adapted retina the first b wave was the largest, the second markedly smaller than the first, and the successive b waves were intermediate in amplitude to the first and second. By increasing the level of light adaptation, the amplitude of the first b wave was correspondingly reduced, with the remaining b waves correspondingly increased in amplitude. The greatest increase in amplitude was observed with the b wave elicited by the second pulse in the train. These results suggest that the decay rate of retinal suppressive processes can be modified by adaptation from surround illumination and by the successive presentation of light pulses.

GLOMERULAR FILTRATION AND RENAL PLASMA FLOW IN URANIUM POISONED RABBITS. E. C. Foulkes, Depts. of Env. Health & Physiol., Univ. of Cinti., Col. of Med., Cincinnati, Ohio.

We have previously reported (Toxicol. Appl. Pharmacol. 13:89, 1968) a decreased ratio of creatinine or mannitol to inulin clearances in U poisoned rabbits (0.2 mg/kg IV) and have attributed this to backdiffusion of smaller molecules from tubular fluid. To determine whether absorption of filtered inulin also occurs, intrarenal distribution volumes of inulin and Na were determined. These volumes, calculated in ml/100 gm from mean A-V transit times, remained unchanged (control V_{In} 21 ± 5, S.D., V_{Na} 27 ± 3; poisoned V_{In} 20 ± 7, V_{Na} 26 ± 6). In further experiments, excretion of dextran (Mol. wgt. 70-90000) was determined: C_{Dex}/C_{In} controls $0.24\pm.06$ (n=8), poisoned $0.22\pm.09$ (n=14). Extraction of PAH fell from 87 to 31%. Directly measured RPF remained constant at 8 ml/min/kidney. To test whether redistribution of blood flow could explain low PAH extraction, tubular saturation was determined as function of plasma PAH levels. Maximal secretion was approached in controls only at 1.5-2 mM PAH, compared to approx. 0.5 mM in poisoned animals. We conclude that in rabbits exposed to low doses of U, 1) C_{In} can serve as measure of GFR in patent tubules; on that basis, 2) no gross alteration in glomerular permeability could be demonstrated; and 3) reduced ERPF reflects inhibition of PAH transport as previously shown in vitro, and not blood flow redistribution. (Supported by AEC contract AT(11-1)1691, NIH grant 5P10 ES00159).

DYNAMIC RESPONSE OF HYPOTHALAMIC TEMPERATURE TO LOCALIZED HEATING. J.R. Fox and K. G. Kastella (intr. by A. C. Brown). Dept. of Physiology and Biophysics, University of Washington, Seattle, Washington 98105.

The object of these experiments was to determine the thermal properties of brain tissue in intact, conscious animals (baboons). Thermal transients were introduced by a cylindrical thermode (1.07 mm.O.D.) chronically implanted in brain tissue; thermode temperature was controlled by a servosystem, and could be made to duplicate various functions. Temperature was measured at the thermode and also some distance from the thermode in brain tissue. The data so obtained were compared to numerical solutions of the heat equation, in cylindrical coordinates with appropriate boundary conditions, expressing heat transport in terms of conduction in the tissue and convection due to capillary blood flow. Good agreement between experimental and theoretical curves was obtained for values of k (thermal diffusivity) of 0.0017 - 0.0019 cm^2 - sec and $\emptyset$ (blood flow per unit volume of tissue) of 0.3 - 0.7 cm^3/cm^3 - sec. The predicted temperature response at a given tissue location was not greatly affected by either changes in k and $\emptyset$ over the physiological range or by small errors in describing experimental geometry. However, inaccuracies in describing boundary locations or failing to account for the relatively avascular scar tissue around the thermode changed the value of $\emptyset$ needed to fit the data by as much as 50%. Thus, we conclude that the model presented in this paper can be used for a description of thermal gradients surrounding a thermode but extreme caution should be exercised if such a model is used to quantitatively evaluate blood flow.

THE RESPONSE OF THE RETINAL CIRCULATION TO EXPOSURE TO ALTITUDE. Regina Frayser, Gary Gray*, A. C. Bryan, C. S. Houston*, and Drummond Rennie*. Indiana U. School Medicine, Indianapolis, Ind., Defense Research Establishment, Toronto, Canada, U. Toronto, Toronto, Canada, and Presbyterian-St. Luke's Hospital, Chicago, Ill.

The retinal circulation affords the opportunity to study an intact microvascular system under a variety of circumstances. Individuals were studied at ground level, immediately after arrival at 17500 ft., after 4 days and after 7 weeks at this altitude. Measurements were made of retinal arterial and venous diameter, blood oxygen saturation by a photographic technique, and retinal mean circulation time following the IV injection of fluorescein. Retinal arterial blood oxygen saturation at ground level is 98%, venous saturation is 59%. Retinal arterial oxygen saturation was 70% and venous saturation 44% after 4 days at altitude. Arterial saturation was 75% with venous saturation 47% after 7 weeks at altitude. Arterial and venous diameter increased 20% over control within 2 hours of arrival at altitude with a maximal increase in arterial size (27%) and venous size (33%) occurring after 4 days. Retinal mean circulation time was 5.0 sec. at ground level, 3.4 sec. after 4 days, and 2.8 sec. after 7 weeks at altitude. These data indicate a marked reduction in retinal vascular resistance. Calculations of retinal flow indicate that there is a 2.5 times increase in flow following acute exposure to altitude and that flow tends to decrease with longer exposure to altitude. These changes in retinal flow occur despite an average systemic arterial carbon dioxide tension of approximately 27 mmHg. Acute exposure to such carbon dioxide tensions has been shown previously to markedly reduce retinal flow. The volume of blood contained within the retinal vasculature at altitude is more than double the ground level volume.

DEPRESSION OF GASTRIC SECRETION BY ELECTROANESTHESIA. M.H.F. Friedman and Allen R. Gordon*. Department of Physiology, Thomas Jefferson University, Phila., Pa.

Insulated 18 gauge stainless steel hypodermic needle electrodes were applied directly to the skull of 9 cats in an extracranial bitemporal arrangement. The uninsulated needle tips were located opposite the foramina in the base of the sphenoids. Current from a Hewlett-Packard constant current generator (Model 3380A) was supplied to the skull electrodes by Cinch-Jones connectors. All 9 cats were provided with cannulated fistulas of the whole stomach. With a current rising to 50 ma. and 6000 Hz. during a ten-minute induction period there was superimposed a current of 100 Hz. at 27 percent of read-out amperage levels. Complete immobolization of the animal and abolition of most reflexes occurred. Basal gastric secretion, as well as gastric secretion induced by histamine and other secretogagues, was arrested during the whole time of current application. Within 15 minutes after termination of the electroanesthesia gastric secretory rates returned to control levels. Salivary secretion however was very profuse during the time of current application.

CONTROL OF BLOOD FLOW IN THE HAMSTER CHEEK POUCH: ROLE OF ARTERIAL PO_2.
R. Fuhro* and H. Berman, Dept. of Biology, Boston U., Boston, Mass.

Gas mixtures with various PO_2's were delivered intratracheally at 52cc/min. Flow velocity in individual vessels was measured with a particle velocity meter. Blood gas tensions and pH were determined on blood taken from the femoral artery. In animals breathing air, flow velocities in first order arcuate arterioles (A_4;~70μ), second order arcuate arterioles (~40μ); preterminal arterioles (~15μ), and in venules~40μ and ~60μ in diameter averaged 6.4, 5.1, 3.9, 0.9, and 1.7 mm/sec, respectively. Arterial PO_2's (mmHg), ratios of mean velocities to those of air-breathing animals, and total blood volumes and oxygen volumes (Q, QO_2: $\mu L \times 10^{-2}$/sec) entering the cheek pouch were:

Inspired Gas	P_AO_2	V/V control	Q	QO_2
Air	70	1.00	10.0	1.97
98% O_2, 2% CO_2	437	0.76	5.6	1.16
10% O_2, 90% N_2	33	0.67	4.8	0.54
30% O_2, 70% N_2	120	0.83	8.9	1.83

Arteriolar vasoconstriction was evident in hyperoxic and hypoxic groups. It was established that a significant amount of O_2 leaves the arterial blood before the capillary bed is reached. Blood from A_4's had lower PO_2 than did blood from the femoral artery. For control, hyperoxic and hypoxic groups, the femoral and A_4 PO_2's were: 69, 61; 475, 254; and 39, 35mmHg, respectively. Further evidence supporting the hypothesis of diffusion of O_2 from arterioles was a rapid 40mmHg rise in PO_2 at the wall of A_4's when the inspired gas was changed from air to 98%O_2. The study indicates that blood flow in the hamster cheek pouch is probably under central sympathetic control, but that the pouch may also maintain some control over its own blood flow. Arterial PO_2 is one parameter that strongly affects these controls. (Supported by NIH grant HE-00902 and Contract DA-49-193-MD-2696.)

DETERMINATION OF YOUNG'S MODULUS OF ELASTICITY AND THE DAMPING COEFFICIENT FOR CAT PAPILLARY MUSCLE BY A DYNAMIC METHOD.
H. Fung and L. E. Bailey (intr. by I. R. Innes). Univ. of Manitoba, Winnipeg, Canada.

The activity of the contractile element in cardiac muscle is modified by the elastic and viscoelastic properties to produce the observed mechanical events. These physical properties can be estimated by Young's modulus of elasticity and the damping coefficient of the muscle. The passive displacement of the papillary muscle after each contraction was characteristic of an underdamped oscillation when an appropriate moment of inertia was selected for the mechanical system. Solution of the second order differential equation which describes this passive motion yields Young's modulus and the damping coefficient for each contraction of the papillary muscle. Young's modulus determined in these experiments ranged between 5 and 6 x 10^6 dynes/cm^2 at low resting tensions. These values were constant for all papillary muscles and were independent of resting tensions. When the critical resting tension was exceeded, Young's modulus increased by two- to threefold to between 11 and 16 x 10^6 dynes/cm^2. Such quantitative determinations of Young's modulus and the damping coefficient may allow estimation of the activity of the contractile element for single contractions of the papillary muscle.

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THE HYPERCHOLESTEROLEMIA OF STREPTOZOTOCIN-INDUCED DIABETES MELLITUS IN DOGS. Joseph H. Gans. Univ. of Vermont Col. of Med. Burlington, Vt.

Hypercholesterolemia is a common hematologic abnormality of diabetes mellitus in man suggesting a regulatory role for insulin in cholesterol or lipoprotein metabolism. To study the relationship of insulin to lipoprotein metabolism streptozotocin was dissolved in citrate buffer 0.1 M, pH 4.5, and administered intravenously in a dose of 50-55 mg/kg to adult dogs of both sexes. Hyperglycemia and glucosuria were evident 48 hours after the antibiotic had been given. Dogs were maintained on a high fat diet and diabetic dogs were given isophane insulin 0.4 U/kg/day. Plasma cholesterol concentrations 4 weeks after streptozotocin increased from 161 mg/100 ml to 268 mg/100 ml, a significant change from control dogs. High plasma cholesterol concentrations were maintained in diabetic dogs for more than 2 months despite insulin maintenance therapy. Paper electrophoresis and separation of low density lipoproteins by $MnCl_2$-Na Heparin precipitation indicated that the hypercholesterolemia in diabetic dogs resulted from an increase in both the low density and high density lipoproteins. High insulin doses, 0.8 U/kg/day, and strict attention to diet reduced plasma cholesterol concentrations in diabetic dogs. Insulin withdrawal for 3 to 5 days results in a restoration of high plasma cholesterol concentrations. These results indicate that insulin deficiency may either 1) permit an increase in the production of plasma lipoproteins or 2) decrease lipoprotein catabolism. Dogs made diabetic with streptozotocin may be effectively utilized as models for analyses of hormonal regulation of cholesterol and lipoprotein metabolism. This experimental hypercholesterolemia may be analogous to both diabetic hypercholesterolemia and the more elusive problem of "essential" hypercholesterolemia. (Supported by PHS Grant HE 11681.)

THE SINGLE BREATH O_2 DIFFUSING CAPACITY (D_{LO_2}) AT REST AND EXERCISE; ITS USE IN DETERMINING PULMONARY DIFFUSION/PERFUSION RELATIONSHIPS. R.F.Garman*, R.W.Hyde, A.B.Fisher*, R.E.Forster (intr. by S.Y.Botelho), University of Pennsylvania, School of Medicine, Philadelphia, Pa.

In order to evaluate the effect of exercise on the relationship between O_2 and CO diffusing capacity, we studied five normal subjects in the supine position at rest and at a work load of 90 watts (O_2 consumption approximately 1200 ml/min). After rebreathing to mixed venous levels, the simultaneous uptake of $^{34}O_2$, CO, and C_2H_2 from the lung during a single breath was measured, and pulmonary diffusing capacity for O_2 (D_{LO_2}) and CO (D_{LCO}) and capillary blood flow ($\dot{Q}c$) calculated. With exercise D_{LO_2} increased from 28 $\pm$ 10 (mean $\pm$ SD) to 40 $\pm$ 4 ml/min x mm Hg (+43%), D_{LCO} increased from 36 $\pm$ 10 to 45 $\pm$ 6 ml/min x mmHg (+25%), $\dot{Q}c$ increased from 8 $\pm$ 2 to 13 $\pm$ 2 L/min (+63%). Using separate measurements of D_{LCO} at varying alveolar O_2 partial pressure, pulmonary capillary blood volume (Vc) and membrane diffusing capacity (D_{MCO}) were determined. These data were used to calculate a theoretical D_{LO_2} ("True" D_{LO_2}) as follows: $1/\text{"True"}\ D_{LO_2} = 1/(D_{MCO})(1.19) + 1/(Vc)(\Theta_{O_2})$. The experimental values of D_{LO_2} ("Obs" D_{LO_2}) were always lower than the "True" D_{LO_2}, which is interpreted as evidence of uneven $D_L/\dot{Q}c$ in the lung. The ratio "Obs" D_{LO_2}/"True" D_{LO_2} increased from 51 $\pm$ 20% during rest to 72 $\pm$ 8% during exercise, indicating improvement in $D_L/\dot{Q}c$ matching.

RIGHT VENTRICULAR HEMODYNAMICS AND COMPLIANCE IN THE CONSCIOUS DOG STUDIED BY THERMODILUTION TECHNIQUES. D. Garner*, M. Laks*, W. Ganz*, E. Rice*, A. McCullen* and H.J.C. Swan. Department of Cardiology Cedars-Sinai Medical Center, Los Angeles, California 90029 & UCLA, Los Angeles, California 90024.

The purpose of this experiment was to study in the conscious dog the right ventricular hemodynamics with emphasis on 1) its compliance and 2) the relation of stroke volume to right ventricular end-diastolic volume, right ventricular systolic pressure, right ventricular end-diastolic pressure, aortic pressure, and heart rate. The thermodilution technique for the determination of right ventricular end-diastolic volume and stroke volume in the conscious dog has been reported (Fed. Proc. 29:2, 525).

In the conscious dog, the right ventricular end-diastolic volume of 30 to 76 ml/m^2 produced an end-diastolic pressure of only 0 to 4 mm Hg. In contrast in the fresh post mortem canine heart, the same ranges of right ventricular volumes produced pressures from 0 to greater than 40 mm Hg. The end-systolic volumes were small, varying from 6 to 24 ml/m^2. The stroke volume, 18 to 54 ml/m^2, correlated positively with the end-diastolic volume. ($r = 0.83$, $p < 0.001$). In contrast, the stroke volume did not correlate with the ranges of heart rates, 65 to 95; right ventricular pressures, 27/9 to 35/4 mm Hg; and aortic pressures, 100/70 to 150/90 mm Hg ($p > 0.05$).

In summary, in the conscious dog the right ventricle 1) was more compliant than the fresh post mortem heart, and 2) can almost completely empty. We postulate that the major determinant of stroke volume is end-diastolic volume. (Supported in parts by USPHS, NIH Grant HE-10382).

REGULATION OF PHOSPHOENOLPYRUVATE SYNTHESIS IN LIVER MITOCHONDRIA. L. Garthoff*, R.B. Tobin, M.A. Mehlman*, and V. DeVore*. (Intr. by D.P.J. Goldsmith). University of Nebraska College of Medicine and V.A. Hospital, Omaha, Nebraska 68105.

The formation of phosphoenolpyruvate (PEP) from oxalacetate (OAA) by guinea-pig liver mitochondria is catalyzed by phosphoenolpyruvate carboxykinase (PEPcK). The mitochondrial OAA concentration is an important regulator of PEP synthesis. In the present study we have examined the synthesis of PEP from succinate-^{14}C, ATP, Pi, $MgSO_4$ and HCO_3 under conditions that lead to alterations in levels of mitochondrial OAA and PEP. The oxidation of succinate-^{14}C to $^{14}CO_2$ was greatly increased by ATP or ADP in liver mitochondria from rabbit, rat and guinea-pig. Oligomycin decreased succinate-^{14}C oxidation in the presence of ADP or ATP. Increases in the redox state of NADH/NAD^+ from oxidation of fatty acids as indicated by the B-hydroxybutyrate/acetoacetate ratios, or in the presence of rotenone inhibited PEP synthesis. A decrease in the redox state caused by DNP or malonate stimulated succinate metabolism and PEP synthesis. The synthesis of PEP from succinate is highly sensitive to the concentration ratios of pyridine and adenine nucleotides. Mitochondrial PEP may play an important role in providing phosphorylated intermediates to the cytosol for gluconeogenesis. (Supported by NIH Grant AM 13-782-02 and Veterans Administration).

COMPARISON OF INCORPORATION USING LABELED GLYCEROL AND PALMITATE INTO LUNG LECITHIN. L.N. GASSENHEIMER AND R.A. RHOADES (Intro.by J.Kollias). The Pennsylvania State University, University Park, Penna., 16802

Saturated lecithin is considered to be an essential component of the pulmonary surfactant system. Different biological half-life (t1/2) values have been reported for lung lecithin. Part of the discrepancy in reported half-life could stem from the fact that the fatty acids are exchanged more freely than the glycerol moiety of the lecithin molecule. In an attempt to see if the glyceride-glycerol portion of the lecithin molecule is exchanged at a different rate than the fatty acid portion, incorporation of ^{14}C-(U)-glycerol into lecithin from lung washings (alveolar lecithin, AL) and lung homogenates (lung tissue lecithin, LTL) was studied and compared to that of ^{14}C-1-palmitate. Specific activity (dpm/μgP) for both labeled precursors was obtained at 5 time intervals ranging from 1-24 hours after I.V. injection into rats. Specific activity for lecithin labeled by palmitate and glycerol revealed that AL and LTL decayed exponentially with respect to time and were parallel. Hydrolysis of LTL following glycerol incorporation showed that 86% of the radioactivity was in the glyceride-glycerol fraction and this moiety yielded a t1/2 of 11 hours. A t1/2 of 12 hours was obtained following palmitate incorporation and did not differ significantly from the glyceride-glycerol t1/2 ($P>.05$). Hydrolysis of the LTL at maximum incorporation of labeled palmitate (1 hr.) revealed that 94% of the radioactivity was in the fatty acid portion. The results show: 1) that palmitate and glycerol more or less exclusively label specific moieties of the lecithin molecule; and 2) the glyceride-glycerol portion is being exchanged at approximately the same rate as the fatty acid portion, and suggests that the lecithin molecule is degraded as an entity. (Supported by USPHS Grant ES 00335).

AREA LOCALIZATION OF SUPRAVENTRICULAR PACEMAKER ACTIVITY BEFORE AND AFTER SA NODE EXCISION. J.M.Geesbreght* W.C. Randall,and G.Brynjolfsson Dept. of Physiology and Pathology, Loyola, Maywood, Illinois.

Acute open-chest experiments were performed on decentralized canine hearts to study supraventricular pacemaker activity and atrial activation. Data from multiple electrodes and a lead II ECG were recorded on an FM electromagnetic tape at 3.75 ips while playback was effected at 0.375 ips resulting in an expanded time-scale of 1 msec/mm as a direct ink read-out on a Grass model 7 polygraph. Unipolar electrodes were positioned endocardially during inflow occlusion onto the middle and posterior internodal conduction pathways and at the region of the bundle of HIS. By an epicardial approach, leads were placed in the SA node, anterior internodal pathway, left atrium and right ventricular sinus. Spontaneous pacemaker activity was identified with the SA node in only 69% of control observations, with localization in the internodal pathways in the remaining 31%. Right stellate stimulation (RSS) was characterized by an SA nodal pacemaker in 93% of the stimulations while left stellate stimulation (LSS) resulted in only 31% incidence of SA nodal precedence. During LSS, pacemaker activity was located in the posterior internodal pathway at the coronary sinus in 50% of the stimulations. Excision of the entire SA node resulted in pacemaker activity at the middle (72%) and posterior (28%) internodal pathways. Histologic confirmation by serial section of the excised tissue was performed. RSS then elicited initial depolarization in the middle (64%) anterior (27%) and posterior (9%) internodal pathways. Except for the absence of SA nodal precedence, LSS induced pacemaker function and depolarization patterns similar to those observed prior to SA nodal excision. These experiments suggest a mobile nature in pacemaker function and give information as to the functional distribution of sympathetic nerve terminations of the atria. (Supported by NIH Grant HE08682)

Cyclic Variations in Carotid Body Chemoreceptor Activity.
J. L. Gehrich* and G. P. Moore. Biomedical Engineering, University of Southern California, Los Angeles, California.

Previous investigators (1, 2), using averaging and counting techniques, have detected the presence of rhythmic variations in the activity of carotid body chemoreceptors which have the same period as respiration. Their recordings, with few exceptions (2), have been of chemoreceptor activity in whole sinus nerve or for few fiber preparations. Investigations were undertaken in our laboratory to confirm and extend these results. Activity on single carotid body chemoreceptor afferent fibers in the cat was recorded in conjunction with heartbeat and respiration. These data were analyzed using a number of statistical methods such as histograms, autocorrelograms, and crosscorrelograms to detect the presence of periodic variations in single chemoreceptor firing patterns. It was determined that every carotid body chemoreceptor tested exhibited, to some degree, a time varying firing pattern in phase with respiration. Moreover, it was established that there also exists a cyclic change in the activity of single chemoreceptors which has the same period as heartbeat. It is further proposed that these patterns, and the statistical methods employed to detect them, can be utilized to provide a dynamic model of the response of carotid body chemoreceptors to changes in the pH, P_{CO_2}, P_{O_2}, pressure, and flow of arterial blood.

(1) Hornbein, T. F., et al. (1961). J. Neurophysiol. 24, 561-568.
(2) Biscoe, T. J., and M. J. Purves.(1967). J. Physiol. 190: 389-412.

REFLEX CARDIOVASCULAR RESPONSES FOLLOWING ISOLATED CARDIAC DENERVATION.
W.P.Geis†, C.J.Tatooles† and M.P.Kaye, Depts. of Physiology and Surgery, Loyola University, Maywood, Illinois.

Isolated cardiac denervation was carried out in twenty-four mongrel dogs by: (1) circumferential stripping of the adventitia from the root of the pulmonary artery and aorta, (2) transection and re-anastomosis of the atria at its pericardial reflection, (3) transection and re-anastomosis of inter-atrial septum. Two to four weeks later functional denervation was demonstrated by lack of heart rate, myocardial contractile force, and ventricular pressure responses to infusions of tyramine and to electrical stimulation of the stellate ganglia and vagal trunks. In selected animals with no pharmacological intervention, cardiac catecholamine content was significantly depressed: LV-0.030 mgm/gm, RV-0.037 mgm/gm. Baroreceptor reflexes elicited a moderate blood pressure response of slow onset reflecting changes in peripheral resistance. Electrical stimulation of somatic afferent nerves, the central vagus and hypothalamic stimulation resulted in an abrupt rise in systemic pressure and end-diastolic chamber pressure similar to the response to cross-clamping of the aorta. Heart rate increased 12-to 18 seconds following the onset of each intervention along with increase in inotropic activity indicating the role of the adrenal medulla in these cardiovascular responses. These findings elucidate the role of neural control of preload, afterload, and circulating catecholamines in modulating cardiovascular dynamics in the presence of the denervated heart. Acute adrenal vascular ligation resulted in depression of heart rate along with a decrease in systemic pressure to less than 25% of control values. Infusion of epinephrine 1.0 ugm/kg/min. prevented cardiovascular deterioration reflecting the dependence of the denervated heart on circulating catecholamines for adequate cardiovascular function.
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A HIGH ALTITUDE SYNDROME IN THE SQUIRREL MONKEY. M. J. Gerben, L. G. Jones, and J. A. Smoake (intr. by R. J. T. Joy). U. S. Army Research Institute of Environmental Medicine, Natick, Mass. 01760

Behavioral and physiological responses of ten unanesthetized squirrel monkeys (S. Saimiri) were measured at simulated high altitude in hypobaric (HB) and/or N_2 + O_2 gas mixture (GM) atmospheres. Results indicated: 1) Unacclimatized, unrestrained monkeys exposed to both HB, from 10,000 to 15,000 ft., and GM, rapidly decreased core temperature, became lethargic and anorexic and assumed head-down postures. 2) Chronically catheterized chair-restrained monkeys acutely exposed to graded GM (13 to 7% O_2) evidenced marked falls in mean systemic arterial blood pressure, heart rate and rectal temperature, as direct functions of the degree of hypoxia. 3) When exposed to GM, the frequency of respiration decreased in those animals with high respiratory rates in ambient atmospheres (AO) and increased in those with low respiratory rates in AO. 4) GM hypoxia produced performance decrements under a variety of operant behavioral schedules. 5) In GM the administration of carbonic anhydrase inhibitors and carbon dioxide improved operant shock-avoidance performance, increased respiratory rates, and attenuated the hypoxia-induced fall in mean arterial blood pressure. 6) Chronic exposure to 15,000 ft. HB for up to seven weeks produced partial to complete "acclimatization" as measured by behavioral and physiological indices. The greatest improvement accrued during the first week of exposure. These observations in the squirrel monkey suggest a similarity to the signs of acute mountain sickness in humans. The squirrel monkey may provide a useful model for the study and treatment of acute mountain sickness.

METABOLISM OF THE HUMAN FOREARM MUSCLES AT REST. M. G. Gerin, N. Gerin-Portier, J. M. Detry and A. A. Charlier (intr. by D. A. McDonald). Cardiopulmonary Lab. Univ. of Louvain Med. School. Belgium and Dept. of Physiol. and Biophys. Univ. of Ala. in Birmingham, Ala.

In order to explore the metabolic functions of the forearm resting muscles during leg exercise, the metabolic exchanges of forearm muscles were first measured at rest in 7 medical students. An arterial catheter-needle was inserted into the humeral artery and a catheter was positioned under fluoroscopic control into one of the deep forearm veins. The following determinations were made on the blood samples from 27 arterio-venous measurements: oxygen capacity and saturation, lactic acid (LA) content and glucose (GLU) content, pO_2, pCO_2, pH. The deep venous blood had a pO_2 of 22.7±4.8 (S.D.) mmHg; the oxygen arterio-venous difference was 12.7±2.6ml O_2 per 100 ml blood. Simultaneously, the veno-arterial difference of CO_2 was 8.40±2.58ml CO_2 per 100 ml blood In all cases but 3 a net uptake of LA was found, as estimated from the arterio-venous differences measured: 0.205±0.181 mMole per liter blood; this arterio-venous difference is dependent on the AL arterial level (Y=0.477X-0.457;r=0.87). There was also an uptake of GLU, with an arterio-venous difference of 0.986±0.438 mMole GLU per liter blood; this difference is not dependent on the GLU arterial level (r=0.36). The AL uptake is not dependent on the venous blood pO_2 within the range of pO_2 observed (34.0-16.6mmHg). The ratio of AL arterio-venous differences to oxygen arterio-venous differences is also not dependent on the venous blood pO_2. These results suggest that the muscles at rest are able to metabolize LA, even at low pO_2, in direct proportion to its arterial level. LA is probably not oxidized but transformed into glucose and glycogen, as suggested from the low values of the local respiratory quotients.

NON-CYCLE LENGTH DEPENDENT ACTION POTENTIAL SHORTENING IN PURKINJE FIBERS. Leonard S. Gettes, Nancy W. Morehouse* and Borys Surawicz. University of Kentucky College of Medicine, Lexington, Kentucky.

Cycle length (CL) is a known determinant of action potential duration (APD). However, in purkinje fibers, the APD shortening of premature responses (PR's) originating from incompletely repolarized fibers may be greater than accounted for by the preceding CL, i.e., non CL dependent (NCLD). We compared in the pig moderator band, the APD of purkinje fibers PR's originating during phase 3 of the AP preceding the PR, to the APD of non PR's having the same CL and found that both the duration of the AP preceding the PR and the level of phase 3 from which the PR arises contribute to NCLD shortening. When PR's followed AP's of similar duration, NCLD shortening increased as the PR arose progressively earlier during phase 3 of the preceding AP, i.e., as the difference between the resting potential and the membrane potential at the onset of depolarization (TOP) increased. At each level of decreased TOP, NCLD increased as the duration of the AP preceding the PR increased. These findings suggest that the APD of PR's arising from incompletely repolarized fibers are influenced by repolarizing currents generated during phases 2 and 3 of the preceding AP and that the earlier the onset of the PR during phase 3, and the longer the duration of phase 2 in the preceding AP, the greater the influence of these currents.

ADRENERGIC RECEPTOR MECHANISM IN THE HEPATIC CIRCULATION A. M. Geumei, M.D.,* F. A. Bashour, M.D. Cardiopulmonary Institute, Methodist Hospital and University of Texas at Dallas, Texas.

Using the isolated liver preparation technique, the actions of adrenergic stimulators (l-Norepinephrine, NE3γ, Nylidrin, NY2γ) and blockers (Phenoxybenzamine, PEN5γ, Propranolol, PRP3γ) on the intrahepatic segments of the hepatic artery (HA) and portal vein (PV) were studied in dogs. The isolated liver was perfused under constant pressure (hepatic arterial at 120 mm Hg and portal venous at 10 mm Hg respectively) with "physiological" Tyrode's solution (5% CO_2 and 95% O_2 were bubbled for 30 min.). Both temperature and pH of the solution were maintained constant. Each adrenergic agent was tested in 10 dogs. Both NE and PRP reduced HA inflow, -64% and -18% respectively; whereas NY, PEN increased HA inflow by +57% and +20% respectively. All agents decreased PV inflow (-84% NE, -88% NY, -42% PEN and -54% PRP). Pretreatment with PRP abolished the effects of NY and PEN on HA inflow. In conclusion, stimulation of α-receptors caused constriction of both HA and PV intrahepatic segments, whereas activation of β-receptors resulted in dilation of HA and constriction of PV segments.

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HORMONE INFLUENCE ON OSMOREGULATION IN THE NEWT. Thomas Gieske* and Wm. L. Frantz. Dept. of Physiol., Mich. State, E. Lansing, Mich. 48823

The hypophysectomized aquatic form of the adult spotted newt survives in fresh water only after a combined injection of ovine LTH and thyroxin. To determine whether their impaired osmotic regulation is corrected by LTH and thyroxin, 5 groups of hypophysectomized newts were treated with either: 125 μM arginine vasotocin; 25 μg aldosterone; 25 μg thyroxin; 25 μg LTH; or 25 μg thyroxin with 25 μg LTH, dissolved in aqueous solutions at concentrations such that 0.05 ml of solution injected intraperitoneally each day delivered the desired quantity of hormone. Sham groups were given 0.05 ml of isotonic amphibian Ringer solution. On the 7th day a cannula collected ureteral urine, then the newt was decapitated, a cardiac blood sample was taken and the abdominal skin was removed for permeability studies. The short-circuiting method of Ussing and spectrometric methods were used to measure the fluxes of $^{22}Na^+$, $^{36}Cl^-$ and ^3HOH across the isolated skins. Hypophysectomy increased Na^+ efflux, water permeability and the passive chloride flux. Since Na^+ influx was unaltered, the net uptake of Na^+ decreased. Also after hypophysectomy plasma osmolality fell, osmolar clearance increased but free water clearance (C_{H_2O}), ureteral urine osmolality and volume were unchanged. Only the combined LTH-thyroxin treatment effectively prevented the changes indicated; LTH alone was less effective, thyroxin alone, aldosterone, arginine vasotocin or isotonic Ringer solution were completely ineffective. Since the LTH-thyroxin treatment also elevated C_{H_2O}, it has a diuretic as well as a skin permeability effect in this salamander.

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Closed Loop Optimization of Atrial-Ventricular Stimulus Interval. B.K. Gilbert*, M.Bourgeois*, D.Mair*, and E.H.Wood. Mayo Clin., Rochester, Minn.

Electromagnetic flowmeters were implanted around the aortic roots in five mongrel dogs. Following implantation, complete atrial-ventricular block was induced by a closed-chest technique. After recovery, the relationships between cardiac function and varied atrial-ventricular stimulus interval (A-V delay) at different heart rates were studied in the anesthetized dogs with a monitoring and controlling real-time computer program. A-V delay and heart rate were controlled with computer-actuated coupled atrial and ventricular pacemakers. Respiration with room air was maintained by a computer-driven intermittent positive pressure device. Pressure and flowmeter calibrations and operating parameters were transferred to the computer. Control data was then recorded at a specified heart rate and A-V delay of 100 msec. The A-V delay was then switched automatically to a preset minimum value, and the pressure and flowmeter data were analyzed on a beat by beat basis in real time. The computer repeatedly incremented the A-V delay up to a preset maximum, after a given number of pulses from the end-expiratory periods at each A-V delay were sensed (constant heart rate). The complete procedure was then repeated in a decremental mode. The optimum A-V delay, defined as maximum stroke volume and maximum ventricular end-diastolic pressure at minimum mean atrial pressure, was searched for during the incremental and decremental passes. At the end of each double determination, made within 2-8 minutes, the summarized results were graphed on a Calcomp plotter. Later detailed analysis of the data confirmed the immediate results, which indicated an optimum A-V delay in the 100 to 150 msec range. The optimum range was not influenced systematically by change of heart or by infusion of propranalol or atropine. (Supported in part by research grants NIH H-3532, FR-00007, and 1 FO1 GM43045-01, and AHA GI 10)

RESPIRATORY ACTIVITY IN AWAKE CATS WITH CHRONIC PONTILE PNEUMOTAXIC LESIONS AND SECTIONED VAGI. Richard L. Glasser, Walter M. St. John* and Richard A. King*. Department of Physiology and Neurobiology Program, University of North Carolina at Chapel Hill, N. C. 27514.

This investigation explored the phenomenon of apneustic breathing under awake and anesthetized conditions. Fifteen male cats under Nembutal anesthesia were subjected to bilateral lesions in the pontile pneumotaxic areas. These P-Lesion animals were maintained for 1 or 3 months. They were then subjected to bilateral vagotomy under Brevital anesthesia. Vagotomy produced the marked prolongation of inspiration typical of apneustic breathing in all 15 P-Lesion animals. Control animals failed to exhibit apneustic breathing. Two P-Lesion animals died in deep apneusis without recovering from the anesthetic state. The remaining P-Lesion animals exhibited diminishing inspiration-holding times with recovery of the awake state. Four hours after vagotomy, the respiratory rates and inspiratory durations of the P-Lesion animals were not significantly different from those of the Control animals. Twenty-four hours after vagotomy, the animals were anesthetized with alpha-chloralose. The P-Lesion animals again exhibited apneustic breathing without exception. These data indicate that awake cats with chronic lesions in the pontile pneumotaxic areas and with sectioned vagi are able to maintain a normal pattern of respiration. General anesthesia permits the dominance of the pontile apneustic mechanism and the resultant manifestation of apneustic respiration. It is concluded that respiratory influences from higher levels of the brain compensate for the loss of the pontile pneumotaxic and vagal Hering-Breuer mechanisms and assist in the support of a normal respiratory pattern in the awake condition. (Supported by NIH Grant NS-06795.)

Inorganic and Organic Anions Inhibit Folate Influx in Ehrlich Ascites and L1210 Tumor Cells:A Possible Mechanism for Uphill Transport. **I. D. Goldman (Intr. by R.G.Faust) Univ. of No. Carolina, Chapel Hill, N.C.**

Folate transport was studied using the analog, methotrexate, (MTX) which shares the same carrier mechanism as the naturally occurring folates. MTX transport is uphill but,paradoxically,metabolic poisons further increase the electrochemical-potential (EP) for intracellular (IC) MTX. The unidirectional influx of MTX (MTX_{in}) is unchanged when extracellular (EC) Na^+ is completely replaced by K^+ or Li^+. Substitution of sucrose,mannitol,or urea for NaCl stimulates MTX_{in} suggesting inhibition by Cl^-. When Cl^- is replaced with the Na^+ salts of other anions the sequence of inhibition is $(HPO_4^= / H_2PO_4^-) > SO_4^= > NO_3^- > Cl^-$. Organic anions including the phosphates also inhibit MTX_{in}. This is not related to the energy-potential of these compounds since 5mM AMP and ADP are at least as inhibitory as equimolar ATP. The kinetics of riboflavin-PO_4 inhibition is competitive. MTX-anion interactions could lead to a countertransport of MTX into the cell if (1)the anion inhibitory effects also occur within the cell to reduce the unidirectional efflux of MTX,(2)a transmembrane EP difference (IC>EC)exists for the anion, (3)the anion can pass through the membrane as it interacts with the MTX carrier. Organic phosphates,synthesized in the cell to mM levels are asymmetrically distributed across the cell membrane which is impermeable to them; however, a small leak via the MTX carrier which has a V_{max} of 1-5 μMoles/l cell water/min,while negligibly affecting the cell organic phosphates, might markedly affect the MTX carrier. This possible countertransport could account for uphill transport of MTX in the presence of metabolic poisons since hydrolysis of ATP ($\rightarrow AMP + 2P_i$)would not immediately diminish the anion gradient. The augmented MTX-EP under these conditions might be due to a transient increase in the anion gradient or to inhibition of an energy-dependent mechanism which pumps MTX out of the cell.

THE PASSIVE VOLUME-PRESSURE CHARACTERISTICS OF THE RIB CAGE. Michael D. Goldman* and Jere Mead. Harvard School of Public Health, Boston, Mass.

We obtained passive volume-pressure characteristics of the rib cage in 4 standing subjects who relaxed against an occluded airway at different lung volumes, and represented them graphically in two ways: (1) by relating estimates of rib cage volume (Vrc) based on changes in its anteroposterior and transverse diameters, to trans rib cage pressure (Prc); and (2) by relating Vrc to trans abdominal pressure. In the former, abdominal compression produced by a pneumatic cuff displaced the characteristic in the inspiratory direction (i.e., greater Vrc at a given Prc) progressively at volumes below FRC. In the latter representation, abdominal compression shifted Vrc and abdominal pressure nearly along the same relaxation characteristic (i.e., same Vrc for a given Pab). In explanation we suggest that the two major influences on volume of the relaxed rib cage, namely, trans rib cage pressure and diaphragmatic tension, are simply additive when the latter is expressed as the transdiaphragmatic pressure (Pdi) it generates. That is,

$$Prc + Pdi = (Ppl - P_B) + (Pab - Ppl) = Pab - P_B ,$$

where pl = pleural, B = atmospheric, and ab = abdominal. We conclude that the effective driving pressure distending the passive rib cage in the standing posture is abdominal pressure relative to atmospheric; and that the diaphragm increases rib cage volume only to the extent that it changes abdominal pressure. A corollary of this conclusion is that contraction of the diaphragm alone will move the chest wall along its relaxation characteristic. Supported in part by USPHS Grants ES 00044 and GM 12564.

TRANSPORT AND EXTRACTION OF OXYGEN IN SKELETAL MUSCLE. J. M. Gonzalez-Fernandez and S. E. Atta. Mathematical Research Branch, NIAMD, National Institutes of Health, Bethesda, Maryland. (Intr. by W. Rall).

A mathematical analysis for the extraction of oxygen in skeletal muscles is developed. The formulation considers: inside the capillary, the flow transport and the oxyhemoglobin-hemoglobin chemical kinetics; in the tissues, the non-equal longitudinal and radial diffusion coefficients, and the oxygen consumption dependence on the oxygen pressure through a Michaelis-Menten relationship. Steady state conditions are assumed. A first model considers a finite cylinder with a central capillary. The experimental results of Stainsby (W. N. Stainsby, Proc. int. Symp. cardiovasc. resp. Effects Hypoxia, Kingston, Ontario, 1965, pp 29-40) of high oxygen extraction in exercising gastrocnemius were examined. The model required a capillary density of 1370 capillaries/mm^2, substantially higher than the figure of 750 obtained by histological measurements. A second model incorporates the following geometrical inhomogeneities. 1) Every capillary is assumed to branch so that the number of terminating capillaries is three times the number of beginning ones (M. Wiedeman, Circulation Res. 12: 375, 1963). 2) The fibers with low consumption are accompanied by fewer capillaries than the ones with high consumption (F. C. Romanul, Arch. Neurol. 12: 497, 1965). 3) The consumption is higher near the capillaries (F. C. Romanul loc. cit.). By incorporating 1) and 2) in the calculations a capillary density of 818 was inferred. By further incorporating 3) a further reduction in the inferred capillary density was obtained. It is concluded that the geometrical inhomogeneities are necessary and perhaps sufficient to explain the high oxygen extractions found experimentally.

LENGTH-TENSION, FORCE-VELOCITY AND ACTIVE-STATE CHARACTERISTICS OF SMOOTH MUSCLE. A.R. Gordon* and M.J. Siegman. T. Jefferson University, Phila., Pa.

The mechanical properties of rabbit taenia coli were studied at 22°C; the absence of tone was confirmed by test applications of epinephrine. The muscles were tetanically stimulated by means of a maximal 60 Hz AC transverse field. The tissues exhibited an optimum length for tension development at which the passive tension was 30% of the total tension. P_o was 0.89 ± 0.11 Kg/cm^2. The force-velocity relationship of the tetanized muscles was hyperbolic. The dynamic constants from the Hill equation were independent of the initial muscle length (a/P_o = 0.331 ± 0.051; b = 0.010 ± 0.001 lengths/sec; and V_{max} = 0.031 ± 0.003 lengths/sec.). The active-state characteristics were obtained by the quick-stretch method of Hill following single DC shocks (6-9 volts, 5 msec duration). The maximum intensity of the active-state occurred 0.5 second after the shock and was maintained for 0.5 second. The active-state decayed exponentially through the peak of the twitch. The relative magnitude of the twitch was 35% of the maximum active-state intensity and the time to the peak of the twitch was 7 seconds. The maximum intensity of the active-state was less than P_o. The intensity of the active-state and twitch varied with $[Ca^{++}]_o$ in the range 1.0-2.5 mM. Caffeine (1 mM) potentiated the twitch by increasing the intensity and decreasing the rate of decay of the active-state when $[Ca^{++}]_o$ was 1.0-2.5 mM. No twitch response could be elicited with 0.5 mM $[Ca^{++}]_o$, with or without caffeine. P_o was independent of $[Ca^{++}]_o$ (0.5-2.5 mM) and was unaffected by caffeine. (Supported in part by USPHS, NIH Grant HD03622, and an RCA Fellowship in Physiology).

A NON-ULTRAFILTERABLE PRESSOR SUBSTANCE FORMED BY THE ACTION OF RENIN ON PLASMA. David B. Gordon and Carrie E. Lee*, Veterans Administration Hospital, San Francisco, California 94121

Grollman (Clin. Pharmacol. & Therap. 10:755, 1969) and others (Helmer and Judson, Hypertension A.H.A. Publ. 8:38, 1960) have reported the presence of a non-dialyzable pressor or vasoconstrictor substance in renal vein blood plasma from ischemic human kidneys. We have looked for a similar substance in rat plasma incubated with rat renin. Rat renin was added to rat plasma in such small quantity (about 0.02 G.U. per ml) that 0.1 ml of the cold mixture gave only a modest pressor effect in a sensitive bioassay rat (15-25 mm Hg). After incubation for 30 min. at 38°C, 0.1 ml of the mixture was injected and gave a larger pressor response (40-55 mm Hg) which was not distinguishable from that due to angiotensin. No reagents for protection against angiotensinase activity were used. Pressor activity was measured in the ganglion-blocked, saline loaded rat and matched against known quantities of angiotensin I. After development of pressor activity the mixture was ultrafiltered by centrifugation for 30 min. at 4°C through an "Amicon" centricone ultrafilter (which retains molecules 50,000 M.W. and larger). The results of 8 experiments were: after incubation and prior to ultracentrifugation, mean 75.0 ng angiotensin/ml ±12.6 S.D., ultrafiltrate, mean 30.0 ng angiotensin/ml ±9.5 S.D. This indicates 60% of the pressor product did not pass through the ultrafilter. It can be distinguished from renin by the shape of its pressor curve and from angiotensin by its non-filterability and greater resistance to angiotensinase. The pressor material which does go through the ultrafilter is presumably angiotensin and that which does not (other than the renin added) is a larger molecular species, either different from angiotensin or consisting of angiotensin bound to some plasma protein.

IN VITRO UPTAKE OF AMINO ACIDS BY ERYTHROCYTES OF THE HAGFISH EPTATRETUS STOUTI. Robert A. Gorkin* (intr. by Grover C. Stephens) University of California, Irvine.

Eptatretus erythrocytes have a free amino acid pool of approximately 200 mmols/liter of cell water; the serum amino acid concentration averages 1.8 mmols/liter. Column chromatography of cell extracts and of serum indicates standing ratios of 3:1 (cells:serum) to more than 300:1 for the major amino acids. Erythrocytes were suspended in filtered artificial sea water and supplied with C^{14}-labelled amino acids. Six amino acids were supplied in separate experiments at medium concentrations of 10^{-5}- 10^{-7}mols/liter. Amino acids are rapidly accumulated under these conditions. Entry rates are not modified when choline is substituted for external sodium. The non-metabolizable amino acid analogue, cycloleucine (1-aminocyclopentane-1-carboxylic acid), was used to establish the following points: The steady state is achieved with a half-time of approximately 5 to 50 minutes depending on the external concentration. Leakage from cells into artificial sea water is slow even at high internal cycloleucine concentrations but rapid exchange occurs if sufficient cycloleucine is present in the medium. The steady state concentration ratio between cells and suspending medium depends upon the external concentration. Steady state concentration ratios range from approximately 22:1 (cells:medium) at an external concentration of 8×10^{-3} M to 2200:1 at 2×10^{-8} M. The system parameters allow only a ten-fold change in the internal concentration over the external concentration range of 10^{-2} M to 10^{-4} M. Below 10^{-5} M the steady state concentration ratios are constant at approximately 2200:1. (supported by USPHS Grant GM-12889)

EXCURSIONS OF CAT HIND LIMB MUSCLES DURING UNRESTRAINED LOCOMOTION. George E. Goslow, Jr.* and Douglas G. Stuart. Department of Biological Sciences, Northern Arizona University, Flagstaff and Department of Physiology, University of Arizona, Tucson, Arizona.

While the relation between spinal reflex activity and locomotion was discussed thoroughly in the earlier literature (cf Philippson 1905, Sherrington 1910) it remained for Engberg and Lundberg (1969) to report on the temporal sequence of muscle participation in the natural locomotion of the cat and to relate this sequence to current knowledge of the properties and connections of spinal neurons and muscle receptors. It was not implied that within the confines of laboratory experimentation, their data are intended to reflect the peak rate and extent of angular movement possible in the cat hind limb. Such information would be of particular use in assessing the relative Ia, Ib and group II input to the spinal cord during locomotion. To this end we have made: 1) a cinematographic analysis of the cat hind limb (N-11) during various patterns of locomotion; and, 2) measurements relating cat size (N-55) to joint angle and muscle length. From these data it is possible to simulate normal muscle stretches during acute experiments. For our purposes it is of particular interest that the peak rate and extent of muscle stretch are over double those generally employed in studying the properties of muscle spindles and Golgi tendon organs. Furthermore it has been possible to extend the range of Engberg and Lundberg's (1969) observations on the eccentric (lengthening) contractions that occur during locomotion. These contractions elicit peak Ib discharge (Stuart et al 1970) and are particularly pronounced during jumping as well as galloping. (Supported in part by USPHS Grant NB 07888).

AUTOREGULATION OF FLOW IN THE EXCISED PERFUSED ABDOMINAL AORTA. Jerry Franklin Green* and Solbert Permutt. The Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Maryland 21205.

We observed autoregulation of flow in the excised perfused canine abdominal aorta, treated with epinephrine, under the condition where the outflow pressure (P_O) was low enough to collapse the vessel partially at its outflow end. After soaking in a concentrated epinephrine solution (1.36×10^{-3} M), excised canine aortas were cannulated and perfused with an oxygenated Krebs-Ringer bicarbonate solution from a tubing arrangement which allowed us to vary independently the inflow pressure (P_I) and P_O. At low levels of P_O, an elevation of P_O caused no change in flow ($\dot{Q}$) or P_I until P_O was raised above a critical level (P_O'). When $P_O > P_O'$ increasing P_O caused a decrease in $\dot{Q}$ at constant P_I. Under the condition where $P_O' > P_O$, $\dot{Q} = (P_I - P_O') / R$, where R is the resistance to flow. P_O' and $\dot{Q}$ were determined simultaneously at varied levels of P_I, and R was calculated from the above relation. Our data showed that in general both P_O' and R increased as P_I was raised. In a typical experiment at a P_I of 20 mm Hg, P_O' = 7 mm Hg, R = 0.0326 mm Hg/ml/min, and $\dot{Q}$ = 400 ml/min. In the same aorta at a P_I of 100 mm Hg, P_O' = 43 mm Hg, R = 0.0507 mm Hg/ml/min, and $\dot{Q}$ = 1300 ml/min. If there had been no increase in P_O' and R with an increase in P_I from 20 to 100 mmHg $\dot{Q}$ would have been 2800 ml/min rather than 1300 ml/min. This difference of 1500 ml/min we take as evidence for autoregulation of flow. After 24 hours, P_O' was close to zero and an increase in P_I caused no change in P_O' and a small decrease in R.

EXERCISE TEMPERATURE REGULATION IN MAN DURING HYPOHYDRATION AND HYPERHYDRATION. J. E. Greenleaf and B. L. Castle*. Biotechnology Division, NASA-Ames Research Center, Moffett Field, Ca. 94035.

To investigate the mechanism of the excessive rise in exercise core temperature with water depletion, rectal (T_{re}) and mean skin ($\overline{T}_s$) temperature were measured in 8 healthy male subjects who exercise for 70 min on a cycle ergometer at 49% of their maximal O_2 uptake (4.55 l/min) in an ambient temperature of 23.6 C and relative humidity 50% at 3 hydration levels performed in random order on non-consecutive days: hyperhydration (Δ body wt = +1.2%), normohydration (Δ body wt = -1.6%) and hypohydration (Δ body wt = -5.2%). Equilibrium levels of T_{re} were: hyperhydration = 37.64 C, normohydration = 37.89 C and hyperhydration = 38.51 C ($P<.001$). Compared with hyperhydration values (a) average V_{O_2} and heart rates were increased; (b) equilibrium levels of $\overline{T}_s$, and average $V_{E_{BTPS}}$ and respiratory water loss were unchanged; and (c) sweating and evaporative heat loss were reduced with hypohydration. There is a linear relationship between percent body wt change and equilibrium level of T_{re}; i.e., T_{re} is elevated 0.1 C for each 1% of body wt loss. Equilibrium levels of $\overline{T}_s$ and $\Delta\overline{T}_s$ are constant and independent of hydration levels between +1% and -5%. Eighty percent of the difference in equilibrium T_{re} between hyper- and hypohydration was accounted for by reduced sweating. It is concluded that the major mechanism for the excessive rise in exercise core temperature with hypohydration is due to reduced evaporative heat loss.

CHANGES IN DISTRIBUTION OF PULMONARY BLOOD FLOW DURING ACCELERATION
J. F. Greenleaf*, E. L. Ritman*, D. J. Sass*, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

The effect of duration and magnitude of the gravitational-inertial force environment on regional distribution of pulmonary blood flow (RDPBF) was measured using radioactive microspheres in 6 dogs and 4 chimpanzees in the left lateral decubitus position. RDPBF was determined from the regional concentration of 15 or 35 μ diameter radioactive microspheres resulting from their injection into the right ventricle. Microspheres tagged with different isotopes were injected during 1G control, and at two (dogs) or three (chimpanzees) successive points in time during 2-3 minute exposures to centripetal acceleration of 5.6-8G. High resolution measurements of the RDPBF in the dogs were obtained by scanning individual 1 cm thick cross-sections of the excised fixed lungs. Pressures in the thoracic aorta, pulmonary artery, right ventricle, left atrium and left pulmonary vein were recorded. Three cuvette oximeters measured oxygen saturation of blood continuously withdrawn from the thoracic aorta, pulmonary artery and left pulmonary vein. Results indicate 1) the fraction of blood flow (BF) traversing the left and right lungs is independent of duration and magnitude of acceleration, but 2) is strongly affected by the occurrence or absence of fast deep breaths which cause an increase or decrease, respectively, in ventilation and concurrently in BF through the dependent lung, 3) $+G_y$ acceleration resulted in a RDPBF with greatest perfusion at the midthoracic region of both lungs and least perfusion at the most superior and most dependent regions of the lungs. Result 2) may be mediated primarily by the hypercapnic pressor response and is superimposed on and may override the hydrostatic effects of acceleration. (Supported in part by NASA grant NGR 24-003-001, USAF F41609-69-C-0058, NIH HE3532, FR-00007, and AHA CI 10.)

EFFECTS OF ETHANOL ON GASTRIC SECRETION IN CATS.
N. Grego*, M.H.F. Friedman and A. Janson*. Department of Physiology, Thomas Jefferson University, Phila., Pa.

Experiments were performed on 7 unanesthetized cats provided with cannulated fistulas of the whole stomach. In addition, 3 other cats were equipped with isolated pouches of the antrum and fistulas of the corpus. The stomach of each animal was perfused several times with ethanol solutions of different concentrations. Following an initial prompt increase in output of acid, neutral chloride and acid chloride, there occurred a secretory depression of relatively long duration. A dose-response curve of the biphasic acid secretion was obtained with ethanol concentrations between 2.5 and 10.0 percent. Both gastric juice sodium and potassium levels were also depressed. The depression of secretion was not correlated with mucus secretion and no inflammatory effects of alcohol on the mucosa were noted. Pepsin output was increased throughout the observation period. Similar perfusion of the stomach with saline had no effect.

ASCENDING AND DESCENDING MLF ACTIVITY FROM VIIIth NERVE STIMULATION. Eunice J. Grey*and Charles D. Barnes, Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

Studies were done on cats decerebrated at the precollicular level and fixed in a Horsley-Clarke head holder. Coaxial bipolar electrodes were placed bilaterally on the VIIIth nerves. Pairs of recording electrodes were placed in the ascending and descending MLF. Responses were averaged in groups of 80 by a Northern Scientific digital memory oscilloscope. Threshold determinations were made for the mono- and polysynaptic responses. With increasing VIIIth nerve stimulus intensities, in the ascending MLF both mono- and polysynaptic amplitude increased smoothly to a maximum at 5 x Threshold (5T), whereas in the descending MLF, a maximum was reached at 2T then reduced at 3T to 70% for the monosynaptic response and to 60% for the polysynaptic response. Conditioning with one VIIIth nerve and testing with the contralateral at 4-6 msec produced no change in the ascending MLF response. In the descending MLF, the monosynaptic was decreased to<50% of the unconditioned response when the conditioning stimulus was at 3T and the test at 2T. Facilitation occurred when the test was at 3T. When the conditioning stimulus was at 2T, this pattern was reversed. Similar changes were noted in the polysynaptic responses. With increasing time intervals there was still no change in the ascending responses, but in the descending responses, inhibition decreased or gave way to facilitation. When 2 stimuli were delivered to the same VIIIth nerve at various time intervals, the ascending mono- and polysynaptic responses were inhibited longer than 500 msec. The descending responses, however, showed considerable facilitation. It is concluded that different populations of neurons are involved in the ascending and descending vestibular projections to these levels. (Supported by USPHS Grants NB 07834, NB34986 and GM 41650.

STUDIES ON THE SITE AND MECHANISM OF ACTION OF GROWTH HORMONE (GH) William E. Groves and Claude F. Baxter (intr. by C. E. Grosvenor) St. Jude Children's Research Hospital, Memphis, Tennessee 38101, and V.A. Hospital, Sepulveda, California 91343.

Since GH previously has been shown to stimulate rat liver RNA polymerase, studies were designed to learn more about the mechanism of this activation. To see if the hormone acts directly on liver, GH was enzymatically iodinated and injected intravenously into young mice, which subsequently were frozen and sectioned. Autoradiography of resulting whole-body sections showed I^{125}-GH localized predominantly in liver and in kidney cortex. To learn more about the subcellular site of action of the hormone in liver, mice again were injected with I^{125}-GH and subcellular organelles then separated using sucrose density-gradient centrifugation. Data on isolated fractions showed I^{125}-GH was bound mainly to plasma membranes and nuclei; no free I^{125}-GH was observed. These results suggest GH may activate RNA polymerase by altering a plasma or nuclear membrane function, such as metal ion transport. Since rat liver RNA polymerase activity is altered by metal ions, the concentration of Ca++, Mg++, Na+, and K+ was determined in nuclei, as well as whole cells and blood serum, during the first few hours after GH injection. To prevent unwanted translocation of metal ions, livers were frozen in situ and nuclei isolated using a non-aqueous procedure. In nuclei the concentration of Ca++ and Na+, but not Mg++ and K+, decreased significantly over a 4.5 hour period, whereas in whole cells Ca++ and K+, but not Mg++ and Na+, decreased. Conversely, in blood serum Ca++, but not Mg++ or Na+, increased. Conclusion: In rat liver, GH: (a) binds to plasma membranes and nuclei; (b) causes significant metal ion changes in nuclei and whole cells. (Supported by USPHS Grants HD 03782 and NS 03743.)

EFFECT OF PROSTAGLANDIN $F_{2\alpha}$ ON OVARIAN BLOOD FLOW IN THE RABBIT AS MEASURED BY HYDROGEN DESATURATION. G. D. Gutknecht*, G. W. Duncan and L. J. Wyngarden*. The Upjohn Company, Kalamazoo, Michigan.

Administration of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) induces luteolysis in the hamster, rat, rabbit and monkey. It has been hypothesized that $PGF_{2\alpha}$ acts as a venoconstrictor retarding ovarian or utero-ovarian blood flow, resulting in altered luteal steroidogenesis and in luteal regression. Intravenous administration of $PGF_{2\alpha}$ (200-400 µg/kg) reduced ovarian blood flow, as measured by hydrogen gas clearance, in estrous and nine day pseudopregnant rabbits initially by 50%; the flow volume returned to 25% of control values fifteen minutes later and to nearly normal values at thirty minutes post treatment. Luteolysis, as determined by peripheral plasma progestin levels, corpora lutea progestin content and corpora lutea weights, occurred when this treatment was continued twice a day on days nine through twelve of pseudopregnancy. Subcutaneous administration of $PGF_{2\alpha}$ required a higher dose to induce a similar decline in blood flow, but the response was of longer duration. Comparable intravenous or subcutaneous administration of $PGF_{2\alpha}$ showed only a nominal reduction of kidney blood flow in the rabbit. The simultaneous induction by $PGF_{2\alpha}$ of luteolysis and reduced ovarian blood flow supports the concept that a relationship exists between the ovarian vascular system and luteal regulation.

DIFFERENTIAL EFFECTS OF STIMULATION OF BARO AND CHEMORECEPTORS ON MUSCULAR AND CUTANEOUS VESSELS. James G. Hackett*, Francois M. Abboud, and Dennis R. Ballard*. CV. Res. Labs., Univ. of Iowa College of Med., Iowa City, Iowa.

Dogs were anesthetized with choloralose and urethane, paralyzed with decamethonium and ventilated artificially. The right carotid sinus nerve was stimulated electrically close to its origin to activate baroreceptor reflexes. Nicotine (10-40 ug) and cyanide (0.1-0.4 mg/kg) were injected into the right carotid artery or the root of the aorta to activate chemoreceptor reflexes. Observations were made on changes in systemic arterial pressure (SAP), heart rate (HR) and perfusion pressures in the isolated perfused gracilis muscle (PP mus) and hindpaw (PP paw). Stimulation of the baroreceptor nerve decreased SAP (average -51 + SE 8.1 mm Hg), HR (-34 $\pm$ 7.5 beats/min), PP mus (-21 $\pm$ 15.3) and PP paw (-11 $\pm$ 3.7). Corresponding values after stimulation of chemoreceptors were: -29 $\pm$ 9.3 (SAP), -44 $\pm$ 9.4 (HR), +120 $\pm$ 31.5 (PP mus) and -35 $\pm$ 9.2 (PP paw). The results indicate that vascular responses to stimulation of baro and chemoreceptors are not reciprocal as might be expected from simple withdrawal of sympathetic vasoconstrictor tone during stimulation of baroreceptor reflexes or activation of sympathetic vasoconstrictor pathways during stimulation of chemoreceptors. A more selective effect on various components of the sympathetic system may explain the differential responses that were observed.

ACTION OF SONICATION-MODIFIED TOXIC GLYCOPROTEIN ON ATP-INDUCED MUSCULAR CONTRACTION. Anwar A. Hakim,* Yvonne Thompson,* and Sol Roy Rosenthal. Department of Preventive Medicine, University of Illinois, College of Medicine, Chicago, Illinois, U.S.A.

A glycoprotein (GP) obtained from scalded human skin has been shown to specifically inhibit the development of tension by glycerinated rabbit psoas muscle (Hakim, et al., Fed. Proc., 28, 712, 1969). Rabbits injected with GP were shown to build up antibody titers against GP (Hakim, et al., Fed. Proc., 29, 714, 1970). When administered intravenously GP proved lethal to mice, and when incorporated into the growth medium GP inhibited the growth of HeLa and HEP(2) cells.

Crude GP and GP were exposed to ultrasonic vibration for increasing time intervals at 4-10°C. Sonicated crude GP (competitin or C) or purified GP (purified competitin or PC) were found less lethal than GP when administered intravenously to mice. Mice surviving a toxic dose of C or PC survived a successive lethal dose of GP. C or PC inhibited the development of tension by the glycerinated muscle fiber. The inhibition was approximately one-tenth the inhibition caused by GP.

The magnitude of inhibition of the ATP-induced tension by fibers exposed first to C or PC for 2 min. then exposed to GP was much less than the inhibition caused by either GP or C. Preliminary studies indicate that a moiety (part) of GP molecule present in C or PC compete for the ATP binding site on the glycerinated muscle fiber and it also competes for the binding site of GP.

DIFFERENCES BETWEEN DURATIONS OF PHASES OF LEFT AND RIGHT VENTRICULAR SYSTOLE IN HEALTHY DOGS DURING SINUS ARRHYTHMIA. Robert L. Hamlin, Gregory R. Nicolosi*, and Heinz P. Pieper, The Ohio State University, Columbus, Ohio 43210

Respiratory sinus arrhythmia observed in healthy, quiet dogs consists of fluctuations in heart rate between 45 and 135 beats per minute with highest rates during inspiration. To establish mechanical correlates to these fluctuations in heart rate, catheter-tip manometers were placed in the pulmonary trunk and ascending aorta of 36 healthy dogs anesthetized so that heart rate and rhythm were identical with dogs sleeping spontaneously. Relationships between RR interval of the ECG and durations of pre-ejection (PEP), ejection (ET), and their sum (Q-i) for right (R) and left (L) ventricles (V) were determined for wide variations in RR interval. Correlations of significance and their lines of regression are: LVET= 143+0.038RR, RVET=197+0.017RR, LVPEP=86-0.016RR, RVPEP=66-0.014RR, LVQ-i=231+0.018RR. RVQ-i did not fluctuate despite fourfold changes in RR interval. For any dog, as heart rate increased during inspiration, LVQ-i shortened more than RVQ-i because RVET and RVPEP changes were equal and in opposite directions, while LVET and LVPEP changes were in opposite directions but LVET much more than LVPEP. That RVET, in dogs, shortens during inspiration whereas it prolongs in man, may be explained by the heart rate response (shortening) dominating the stroke volume response (lengthening) produced, supposedly, by augmenting venous return to the RV. This supports previous observations that physiologic splitting of the second heart sound--in the dog--results from premature closure of the aortic valve.

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VASOMOTOR BLOCKING AGENTS AND INTRAHEPATIC VASCULAR RESISTANCE. K.M. Hanson. Ohio State Univ., College of Med., Columbus, Ohio.

Effects of blocking agents on liver blood flow, resistance and vasomotor activity were studied in over 60 in situ isolated dog liver preparations. Hepatic artery (HA) and portal venous (PV) flows were measured with electromagnetic probes. Papaverine (PAP), Dibenzyline (DBZ), Dibenamine (DBA) and dichloroisoproterenol (DCI) were infused into the HA. Degree of blockade was determined by effect on initial flow decrease and resistance increase normally seen during electrical stimulation of the hepatic nerve trunk. Blocking doses were 5, 1.5 and 10 mg/kg for PAP, DBZ and DBA. Dose-response relationships for HA and PV vasculature were determined. Effects on autoregulation of HA flow, HA response to shunting of PV flow (reciprocity) and HA reactive hyperemia were studied. Results can be summarized thus:

DRUG	DOSE MG/KG	%Δ HA FLOW	%Δ HA RESISTANCE	AUTO-REGULATION	RECI-PROCITY	HYPER-EMIA	%Δ MABP
PAP	5	+40	-41	ABOLISH	ABOLISH	ABOLISH	--
DBZ	1.5	-1	-15	N.C.	DEC. OR N.C.	ABOLISH	-40
DBA	10	+20	-17	N.C.	DEC. OR N.C.	----	+2

This research was supported in part by grants from the Public Health Service (5-R01-HE11411 and HE09884), American Heart Association and Northwestern Ohio Heart Association.

DIFFERENTIAL EFFECTS OF TESTOSTERONE ON THE ACTIVITIES OF SEROTONIN SYNTHETIC AND DEGRADATIVE ENZYMES DURING THE CRITICAL PERIOD FOR MALE BRAIN DIFFERENTIATION. Carolyn M. Hardin, Meharry Medical College, Psychiatry Dept., Nashville, Tenn. 37208.

Testosterone acts in the rat during the first few postnatal days to masculinize the brain regions responsible for the regulation of the adult male pattern of gonadotropin release. Previous reports have dealt with the levels of biogenic amines (Proc.Int.Union Physiol.Sci., VII:180, 1968) and with the synthesis of serotonin (Fed.Proc.,28:278, 1969) in developing rat brain as a function of sex or testosterone treatment. The present report is concerned with sex differences in the concomitant activities of the serotonin degradative and synthetic enzymes. Monoamine oxidase (MAO) and 5-hydroxytryptophan decarboxylase (5-HTP-dec) were assayed in aliquots of homogenate from the same brains. The rats were of the Sprague-Dawley strain and were 1-2 days old. 20 male-female pairs were matched for litter and time of assay. 3×10^{-3} M iproniazid was used to inhibit MAO in the assay for 5-HTP-dec, otherwise both enzymes were assayed according to the procedure of Kuntzman et al (J.Neurochem.,6:226, 1961). Serotonin synthesis from 5-hydroxytryptophan was greater in females than in males, as previously observed. The mean paired difference of 2.02 $\pm$ 0.45 micrograms serotonin synthesized/gram brain/hour was significant at the 99.9% level of confidence. In contrast, there was no sex difference in the activity of monoamine oxidase: the mean paired difference of 5.9 $\pm$ 10.5 micrograms serotonin degraded/gram brain/hour was not statistically significant. Differential effects of testosterone on serotonin synthesis and degradation suggests that the steroid effect on the differentiating serotonergic neuron antedates functional activity of the neuron.

ELECTROMECHANICAL PROPERTIES OF FRESH WHOLE BONE.
P. G. Harms*, J. R. Neville and R. L. Peebles*. USAF School of Aerospace Medicine, Brooks AFB, Texas.

Electromechanical properties of freshly excised rat femurs were studied by determination of potentials generated across the diaphysis upon deformation of the bone with 100-2000 gm loads. The distal portion of cantilever mounted right femurs was deformed from the long axis in posterior, anterior, lateral, and medial directions. With load application, concave areas became negatively charged and then discharged exponentially to near neutrality. A similar signal of opposite polarity ensued with load removal. Peak voltages with load application, used for voltage-deformation comparisons, were 10-20% larger than those following load removal. With posterior deflection, potentials were nearly proportional to deformation at the 100-1000 gm levels; however at the 2000 gm load, voltage per unit of deformation was noticeably decreased. This decrease in voltage was associated with the occurrence of marked permanent deformation of the femur. Voltage and deformation due to a 1000 gm load were significantly less, ($P<0.01$) and ($P<0.001$) respectively, following lateral or medial as compared with posterior or anterior deflection. Regardless of the direction of deflection, voltage output was related to deformation in a manner similar to that observed with deformation resulting from varying loads. These results indicate that the magnitude of deformation-induced bone potentials is dependent upon the amplitude of deformation and may be related to the visco-elastic properties of bone.

MODIFIED SERVO-CONTROLLED SYRINGE FOR DIRECT MEASUREMENT OF MICROCIRCULATORY PRESSURES.[1]
P. D. Harris*, L. F. Hodoval[2]*, and P. A. Nicoll. Depts. of Physiology, Univ. of Missouri School of Med., Columbia, Mo. and Indiana Univ. Medical Center, Indianapolis, Ind.

A servo-controlled micropipette system for microvascular pressure measurements, similar to that of Wiederhielm, et. al. (Amer. J. Physiol. 207:173-176, 1964), has been designed according to "Bode" techniques. A change in micropipette impedance (10 micron tip-3 megs) is converted into a change in phase (0.3 degrees/10 Kohms change) of a 1000 Hertz reference. This signal is amplified, amplitude limited, and detected by phase comparator, pulse amplification, and low pass filter circuitry. After power amplification, the resulting signal excites a "voltage to pressure" driver (8 watt, 8 ohm speaker coil, magnet, and cone with a 2 inch diameter, ½ inch deep plastic housing) to regulate pipette impedance by matching micropipette and microvascular pressures. This overall system has been evaluated with variable-pressure, static-flow conditions. The v-p driver provides 450 Hertz bandwidth with 6 db resonate points at 220 and 390 Hertz. The overall system has a minimum frequency response of 40 Hertz with a maximum pressure development of 62 mm Hg for a minimum micropipette diameter of 23 microns. Thus, the current system is primarily useful for small vein (120 microns) and venule (40 microns) pressure measurements.

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[2]PHS Fellow #1-F03-GM 33,611.

RELATIONSHIP BETWEEN RAT ADIPOSE SIZE, LIPOLYTIC SENSITIVITY TO NOREPINEPHRINE AND ADENYL CYCLASE ACTIVITY. A. D. Hartman and A. I. Cohen (Intr. by Z. Hadidian). Pennwalt Corporation, Pharmaceutical Division, Rochester, New York.

A linear increase in rat epididymal fat cell size was observed as the animals grew to about 600 g when size was expressed as either the average cellular diameter or as the triglyceride content per cell. Glycerol release in vitro in response to three test doses of norepinephrine (0.038, 0.075 and 0.375 µg/ml) was observed to be inversely related to cell size when the release was expressed either on the basis of the weight of cellular triglyceride or on cell surface area. In contradistinction, however, no discernible differences could be observed in lipolytic response between cells of different sizes when glycerol release was calculated per million cells. In addition, the basal lipolytic rate was significantly increased ($p<0.05$) as the cells increased in size; this effect may be causally related to the elevation of free fatty acids observed in the plasma of fasting obese individuals. In a further attempt to understand the relationship between lipolysis and cell size, the activity of sodium fluoride-stimulated adenyl cyclase in adipocytes of different sizes was studied. Adenyl cyclase activity, like norepinephrine stimulated lipolysis, was inversely related to cell size when the results were expressed per unit surface area ($p<.05$). When enzyme activity was expressed per million cells, the activity was independent of cell size. We concluded from these observations that in the range of cell sizes studied, the lipolytic potential of the adipocyte is the same irrespective of its size. Since the catecholamine receptor at the cell surface is believed to be closely associated with adenyl cyclase, these results would indicate that there exists a fixed number of cellular receptors for norepinephrine which are distributed over a greater surface area as the cells enlarge.

ACTIVATION OF A BULBO-SPINAL SYSTEM FROM THE INFERIOR COLLICULUS Arnold H. Hassen* and Charles D. Barnes. Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

Experiments were done on 15 precollicular decerebrate cats. The animals were fixed in a rigid framework consisting of a Horsley-Clarke headholder, spinal clamp for L3 and L4, and pins through the heads of both femurs. Both hindlimbs were completely denervated peripherally and the left GS and CP nerves were placed on stimulating electrodes. The ventral root of L7 on the left side was cut and placed on a pair of electrodes for recording the MSR resulting from GS or CP stimulation. The most caudal dorsal rootlet of L6 was cut and placed on electrodes for recording the DRP. The extensor (GS) or flexor (CP) MSR was conditioned by a 50 msec train of 0.5 msec rectangular pulses delivered to the brain stem at 500/sec through concentric bipolar electrodes with a tip separation of 0.5 mm. Stimuli applied in the area of the nucleus of the left inferior colliculus and in the RF below it produced a temporal pattern of facilitation followed by inhibition of the MSR of both extensors and flexors and an accompanying DRP. Sectioning between the inferior and superior colliculi on the side of stimulation abolished the response from the inferior colliculus, leaving the RF response unaffected. Selective lesions of the brain stem indicated that more than one pathway is responsible for these spinal cord effects.
(Supported by USPHS Grants NB 07834 and NB 34986)

POTENTIATION OF THE VASOCONSTRICTOR RESPONSE TO NERVE STIMULATION BY A PROSTAGLANDIN (PGE_1). Phyllis R. Hedwall*, Francois M. Abboud, and Phillip G. Schmid*. CV. Res. Labs., Univ. of Iowa College of Med., Iowa City, Iowa.

In the vas deferens, low concentrations of PGE_1 inhibit the responsiveness to nerve stimulation (NS) whereas high concentrations of PGE_1 enhance this responsiveness. The interaction between PGE_1 and the effect of NS was tested in two vascular beds of the dog. Changes in perfusion pressure in the isolated perfused gracilis muscle and in the isolated perfused hind paw (PP paw) were measured in response to NS and to intra-arterial injection of norepinephrine (NE). PGE_1 altered responsiveness in the paw, but not in the muscle. After intra-arterial injection of a high concentration of PGE_1 (2-5 ug), the average increase in PP paw in response to NS (6Hz) was augmented from 56 $\pm$ 14 (SE) to 95 $\pm$ 22 mmHg, whereas the response to NE (0.3 ug) decreased from 65 $\pm$ 15 to 48 $\pm$ 13 mmHg. The ratio of responses to NS/NE increased from 0.86 before to 1.98 after PGE_1 ($p<0.05$). Subsequent infusion of a low concentration of PGE_1 (0.37 ug/min) reduced responsiveness to both NS and NE to 48 $\pm$ 10 and 26 $\pm$ 12 mmHg respectively, but the ratio of responses to NS/NE remained elevated. The results indicate that PGE_1 depresses vascular responsiveness to NE, but potentiates responsiveness to NS in the paw. This potentiation cannot be attributed to interference with a cholinergic component of adrenergic transmission, to inhibition of re-uptake of the neurotransmitter nor to antagonism of adrenergic beta receptors. Potentiation may be related to facilitation of release of the neurotransmitter.

ELECTRICAL RECTIFICATION IN FROG SKIN OBSERVED USING A NEW TECHNIQUE WHICH AVOIDS EDGE DAMAGE. Sandy I. Helman and David A. Miller (intr. by N.R. DiLuzio). Tulane Univ. Sch. Med., New Orleans, La.

It was recently reported that edge damage causes both open circuit voltage and skin electrical resistance to be underestimated when frog skins are studied in Ussing type chambers. (Dobson and Kidder, Am. J. Physiol. 214:719, 1968.) In order to allow study of the skin without edge damage, new techniques were developed. Instead of compressing the skin between half chambers, the tissue adhesive Isobutyl-2-cyanoacrylate (IBC-2, Ethicon, Inc.) was used to glue abdominal frog skin (Rana pipiens) to disposable lucite gaskets. The gaskets were sealed to the chambers with a high dielectric liquid, Sylgard 184 (Dow Corning). The adequacy of this method was tested by studying the same skin in large (6.4 cm^2) and small (0.64 cm^2) chambers having edge to area ratios of 0.7 and 2.2 respectively. Open circuit voltage and resistance per cm^2 were found to be identical and independent of edge to area ratio. Thus, IBC-2 provides adequate electrical seals without edge damage. In order to measure skin resistance, the steady state relationship between voltage (V) and current (I) was determined using voltage clamp pulses 600 msec in duration. The V-I plots showed that the skin rectifies current flow. In small chambers edge damage completely obscured the rectifying properties of the undamaged skin. In large chambers rectification was partially obscured, and resistance and open circuit voltage significantly reduced by edge damage. These results confirm the existence of edge damage, and the new technique provides a means of studying frog skin in its absence.

USE OF MAGNETIC TAGGING TO RECORD DOMINANT-SUBORDINATE CONFRONTATIONS IN CBA MOUSE COLONIES HOUSED IN POPULATION CAGES. James P. Henry, John A. Henry,* and Roland Rader.* Univ.of So.Calif., Dept.Physiology, School of Medicine, Los Angeles, California.

The dramatic pilomotor response of the bushy tail of the tree shrew has provided von Holst (Z. vergl, Physiol. 63:169), with a measure of the duration of sympathetic arousal and the consequences of prolonged states of excitation. His data confirms that repeated confrontation by a dominant is a powerful and potentially damaging physiological stimulus. Crowcroft, in "Mice All Over," Foulis, London '66, has observed methodical patrol activity in multiple box systems by dominant males actively searching for such confrontation with subordinates and/or intruders. The repeated ensuing stimuli can result in renal and cardio vascular pathology in mice housed in such box systems, Henry & Stephens Psychosom.Med. 31:454, '69. A new activity meter using magnetic tagging provides digital records of such patrols as well as other box to box movements. When the tagged mice pass an electronic checkpoint, a 9x2 mm magnet previously implanted in back or belly activates the appropriate dorsal or ventral Hall effect magnetic detector located in the tube and the event is recorded. Demagnetization by a high strength alternating magnetic field and reactivation by a direct current field, permit rapid selection of any two mice for observation out of the total implanted colony group. Photocells detect all mouse passages past the checkpoints. Standard 23x11x11 cm mouse boxes are arranged in an open design with long runways of 3 cm I.D. tubing in rectangular patterns. Reimer & Petras, J.Mammal. 48:188, '67. The system permits the detection of movements and identification of role players within a deme as well as beyond their territory. Potential applications include analysis of the behavioral and psychophysiological effects of early experience or drugs in a social milieu. (Supported by NASA Grant #NGL 05-018-003)

OBSERVATIONS ON TELEOST EYE MOVEMENTS. Howard T. Hermann and Martha Constantine*. McLean Hospital and Harvard Med. School, Boston, Mass.

Following conjugate saccadic eye movements in the dark adapted encephale isole goldfish, a monophasic negative potential appears over the entire surface of the optic tectum. It lags the saccadic onset by 50 to 200 msec, lasts around 180 to 200 msec and reaches peak amplitudes ranging from 100 to 500μV, but typically around 250μV. Recording at successive 62.5 depths and averaging the tectal saccadic evoked potentials (TSEP) one finds a null region around 500 to 750μ and a positive going potential at 1000 to 1250μ; however, the deep waves are not simple polarity inversions of the superficial waves. The potentials are not produced by photic or mechanical stimulation. Sudden stretch of eye muscles produces a negative wave of about 20 msec latency in the tectum. Transection of eye muscles sharply reduces the ipsilateral TSEP. In the valvula of the cerebellum, an initially positive going potential of high amplitude precedes the saccade and continues through and after the saccade in a diphasic waveform. In the mid-dorsal caudal convexity of the cerebellum at 125μdepths, single cerebellar units are silent during the positive wave. The timing of the TSEP corresponds to the onset of the slow counterslewing motion of the eye that serves to reduce slip of retinal image.

PROLONGED BED-REST IN HEALTHY HUMAN SUBJECTS: SUMMATION DIAL METHOD TO ANALYZE NON-STATIONARY BIOLOGICAL TIME-SERIES DATA. N.H. Hetherington*, L.S. Rosenblatt*, P.B. Mack*, and C.M. Winget. Geneticon, Berkeley, California, Texas Woman's University, Denton, Texas, and Environmental Biology Division, Ames Research Center, NASA, Moffett Field, California.

Previous biorhythm studies have used methods of analyses (harmonic analyses) that assume that the data are stationary in time, i.e., over successive cycles the period, amplitude and phase vary only because of random error. Data produced by 8 healthy male subjects submitted to 56 days of bed-rest and maintained on a 14L:10D regimen could not be considered stationary in time as the experiment would be expected to produce changes in amplitude and/or phase. Therefore, it was necessary to resort to other analytical methods. The sole assumption was that the period (τ = 24 hrs.) was constant. The data consisted of 6 points per day (on heart rate, body temperature and other parameters) and were fit to the following equation: $Y = a \cos \omega t + b \sin \omega t$, to produce the estimates, $\hat{a}$ and $\hat{b}$, where the amplitude, $\hat{R} = (\hat{a}^2 + \hat{b}^2)^{\frac{1}{2}}$ and $\text{Tan}^{-1}\hat{\phi} = \hat{b}/\hat{a}$. The point $(\hat{a},\hat{b})$ represents, then, the end of a vector with magnitude $\hat{R}$ and direction $\hat{\phi}$. The summation of these vectors, or train of vectors, produces the summation dial (Chapman and Bartels, Geomagnetism Vol. II, Oxford Press, 1940). The direction of the vector train is the hour of the day at which estimated peak activity occurred. Analyses of data by this method indicates that the summation dial is able to detect dynamic changes in time of peak as well as "random walks" (arhythmia); if constancy of period is assumed, a linear change of phase is also detectable. Correlations over time between physiologic parameters may be studied by use of the vector-difference dial which quantifies the angle between the summation dials of the two parameters.

INTESTINAL TRANSPORT OF SODIUM AND WATER IN SALINE-LOADED DOGS. J. T. Higgins, Jr. and N. P. Blair*, Indiana Univ. School of Medicine, Indianapolis, Indiana 46202.

The natriuretic response to saline loading is caused by decreased tubular reabsorption of sodium, and it has been suggested that this is due to the effects of a humoral inhibitor of active sodium transport. Such a substance might also inhibit active sodium transport in other tissues. Consequently we have examined total water flux, and total and unidirectional sodium flux in segments of duodenum, jejunum and colon in vivo before and during saline loading of 7 dogs. Segments of gut were cannulated and perfused at 3.8 ml/min with Ringer's solution containing Na 151, K 5, Ca 4, Cl 157, HCO_3 3 mEq/L, polyethylene glycol 100 mg% and Na^{22} 0.4 μc/L. After 3 20 min control collections, the dogs were saline loaded over 60 min with a volume of isotonic saline equal to 10% body weight, during which 3 more collections were made. During control periods duodenal net H_2O flux (F_{H2O} net) averaged +2.13 $\pm$3.45 μl/min/gm tissue and net Na flux (F_{Na} net) +0.25 $\pm$0.54 μEq/min/gm. During each 20 min saline loading period, there was a stepwise decrease in F_{H2O} net (20 min +1.41 $\pm$5.53, N.S.; 40 min -9.38 $\pm$10.72, $p<.02$; 60 min -14.44 $\pm$9.90, $p<.01$) and F_{Na} net (20 min +0.20 $\pm$0.84, N.S.; 40 min -1.36 $\pm$1.56, $p<.05$; 60 min -2.27 $\pm$1.72, $p<.02$). The influx rate of Na^{22} was unchanged during saline loading (control 0.86 $\pm$0.65 μEq/min/gm, 20 min 1.19 $\pm$0.55, 40 min 1.12 $\pm$0.53, 60 min 0.90 $\pm$0.38); hence the decrease in F_{Na} net was all due to increased Na outflux (control 0.54 $\pm$0.26 μEq/min/gm; 20 min 0.98 $\pm$0.63, N.S.; 40 min 2.22 $\pm$ 1.12, $p<.01$; 60 min 2.83 $\pm$1.63, $p<.02$). Similar directional changes were seen in the jejunum and colon. Thus the depressed net intestinal Na and H_2O flux of saline loaded dogs appears to be due to increased Na outflux and not to inhibition of absorption.

A MODEL OF PLACENTAL O_2 DIFFUSION. Esther P. Hill*, Lawrence D. Longo and Gordon G. Power. Dept. Physiol., Loma Linda Univ., Loma Linda, CA.

A forward numerical integration technique solves equations representing the diffusion of O_2 across the placenta. The relative resistances of the hemoglobin reaction rates and of the placental membrane were used to calculate the partial pressure of O_2 in maternal and fetal erythrocytes and plasma during the course of a single capillary transit. We have compared the solutions using a 4th order Runge-Kutta integration, a method similar to that of Staub, et.al. (J.Appl. Physiol. 17:21,1962) and the Bohr integration. It was assumed that the maternal and fetal blood flows were concurrent and that the total placental resistance to diffusion was due to the membrane resistance and the finite reaction rate of O_2 with hemoglobin. Based on experimental measurements in sheep, values were assumed for the diffusing capacity, the rate constants of O_2 combining with maternal and fetal bloods, maternal and fetal placental capillary blood volumes, blood flow rates, blood O_2 capacities, arterial O_2 partial pressures, fractions of maternal and fetal blood shunted and placental O_2 consumption. The dependence of O_2 transport of each of these factors was studied by observing the end capillary O_2 partial pressures resulting from varying these parameters. (Supported by USPHS 03807.)

ABSENCE OF DIRECT TOXIC ACTION OF ENDOTOXIN ON MYOCARDIAL TISSUE. L. B. Hinshaw, L. T. Archer,* J. A. Miller,* L. J. Greenfield and C. A. Guenter.* V. A. Hospital and Univ. of Oklahoma Med. School, Oklahoma City, Okla.

The effect of endotoxin on the heart is obscure and results have been controversial. The purpose of the present study was to determine if there was a direct detrimental action of endotoxin on cardiac tissue. An isolated heart and lungs removed from a donor dog were perfused with venous blood from an intact heparinized animal. Pulmonary blood flow, aortic pressure, respiration, and blood temperature were maintained constant in the isolated preparation. Cardiac output was directly measured from aortic and coronary venous outflows. Left ventricular myocardial contractile force, intraventricular and aortic pressures and oxygen uptake were determined. An LD_{90} injection of *E. coli* endotoxin was intravenously administered to the dog. Results indicate that endotoxin has no detrimental effect on the isolated heart under the conditions of these experiments. Oxygen uptake and left ventricular contractile force were maintained at pre-endotoxin values or increased above control in the presence of acidosis, pulmonary congestion, and systemic hypotension in the dog. Left ventricular end diastolic pressure was not elevated in any experiment but regularly decreased after endotoxin. Coronary blood flow progressively increased and vascular resistance significantly fell. No regular relationship between heart rate and coronary resistance was observed. In conclusion, there was no evidence to support a direct toxic action of endotoxin on myocardial tissue. Supported by V. A. Hospital, U. S. Navy Project N00014-68-A-0496 and USPHS Grant HE12302.

CENTRAL NERVOUS SYSTEM MODULATION OF BAROCEPTOR INPUT. Charles H. Hockman, Jaime Talesnik* and Kenneth E. Livingston*. Brain Res. Lab., Dept. of Pharmacology, Univ. of Toronto, Toronto, Ontario, Canada.

In adult cats with acute spinal cord transections between C-1 and C-2, electrical stimulation of the central gray substance of the midbrain induced a cardiac acceleration that was often followed by bradycardia when the stimulus was terminated. These two phenomena, however, did not always follow one another. In some animals, either effect was seen to occur alone, depending upon the stimulus parameters used. Bilateral sectioning of both the carotid sinus and aortic depressor nerves abolished these centrally-induced cardiac alterations. In earlier studies we had shown that the carotid sinus nerve sends projections to the midbrain, and that the central gray, as well as other structures forming the midbrain-forebrain limbic system, could either facilitate or inhibit reflex vagal bradycardia. In the present experiment, the tachycardia that is observed to stimulation of so-called sympathogenic regions of the brain in the cord-sectioned animal, as well as the bradycardia, appear to result from the intervention of the same central mechanisms that are involved in facilitation and inhibition of the baroceptor reflex. These data would suggest that central nervous system modulation of baroceptor reflexes is dependent upon a continuous inflow of information from baroceptors to regions of brain rostral to the medulla, and that this visceral afferent input is normally modulated to produce changes in heart rate which need not be dependent upon peripheral vascular changes. (Supported by grants from the Ontario Alcoholism and Drug Addiction Res. Fdn., and the Medical Research Council of Canada)

SHORTENING OF SECONDARY SKIN BLEEDING TIME AND DIMINUTION OF PLASMA PROTHROMBIN ACTIVITY BY PHOSPHATIDYLETHANOLAMINE AND PHOSPHATIDYLCHOLINE/PHOSPHATIDYLSERINE IN HEMOPHILIC AND NORMAL DOGS. R.R. Holburn, M. DeSipio* and M.J. Silver*. Cardeza Foundation and Depts. of Physiology and Pharmacology, Thos. Jefferson University, Philadelphia, Pa.

Phosphatidylethanolamine (PE) and mixtures of phosphatidylcholine plus phosphatidylserine (PC/PS) have been shown to have procoagulant activity in vitro (Silver et al. Thromb. Diath. Haem. X:164, 1963). We therefore studied their possible hemostatic effects in normal and hemophilic dogs. The phospholipids were suspended in 5% dextrose (pH adjusted to 7.8). Control blood samples were taken and bleeding times done prior to the IV injection of these suspensions. A large number of primary bleeding times (PBT) were done on the hemophilic dog on the day prior to the determination of the effect of PE and PC/PS on the secondary bleeding time (SBT). Control SBT was always >30 min. Twenty min after injection of PE (50 mg/kg), SBT was reduced to 14 min. The effect lasted 90 min. PC/PS (2/1) (44 mg/kg) produced 8 min SBT, 10 min postinjection. The effect lasted 60 min. PBT in normal dogs was reduced several min by PE or PC/PS (2/1). Whole blood clotting times, platelet counts, fibrinogen, factors V and VIII remained at control levels in both normal and hemophilic dogs after the injection of PE or PC/PS. Prothrombin (II) consumption in the hemophilic dog appeared to be improved. However the levels of residual II in the serum were similar to those in the corresponding plasma. PE (45 mg/kg) reduced plasma II to 20% of the control, PC/PS (45 mg/kg) to 50%. The effect lasted 4 hr. Incubation of plasma with PE in vitro resulted in a small decrease in detectable II activity. The unexpected decrease in II activity caused by PE in vivo may be related to the formation of a II-PE complex. The shortening of the bleeding time by PE and PC/PS may be due to the formation of a better platelet plug. (Supported in part by a grant from NIH)

RESPONSE PATTERNS OF "PARA-AUDITORY" CENTERS TO ACOUSTIC AND CUTANEOUS STIMULATION. Holstein, S.B.*, Humphrey, G.L.* and Buchwald, J.S. Dept. of Physiology and Brain Research Institute, UCLA, Los Angeles, California 90024

Responses to auditory and cutaneous stimuli were recorded in "para-auditory" regions of close anatomical and functional proximity to the classical auditory relay nuclei. Primary foci of these studies were the nucleus of the brachium of the inferior colliculus and the magnocellular division of the medial geniculate body. Multiple unit activity was recorded from cats with chronically implanted electrodes both in normal awake and in Flaxedil immobilized conditions. Long duration (1.5 sec) tones induced in both parabrachial and magnocellular regions a 50-100 msec onset burst of accelerated discharge which was followed by a sustained inhibition of more than 1000 msec. Trains of cutaneous stimuli (0.1 msec, 60 Hz pulses) delivered to one paw for 0.5 sec induced a sustained accelerated discharge in both parabrachi brachial and magnocellular regions. Both auditory and cutaneous responses showed progressive decrements during habituation procedures with 50-100 presentations of a single constant stimulus. During similar series of tone-shock alternations, the response habituation did not occur. Thus, these "para-auditory" pathway shows specific acoustic patterning and plasticity during habituation, sensory modality convergence, and long-lasting inter-modality interactions. (Supported by USPHS Grant NB 05427)

ALVEOLAR GAS EXCHANGES AND CARDIOVASCULAR FUNCTIONS DURING BREATH HOLDING WITH AIR. S.K. Hong, Y.C. Lin*, D.A. Lally*, B.J.B. Yim*, N. Kominami*, P.W. Hong* and T.O. Moore*. University of Hawaii, Honolulu, Hawaii.

Changes in P_{AO_2} and P_{ACO_2} during 4 min breath holding (BH) with total lung capacity were studied in 9 subjects. P_{AO_2} decreased continuously during BH, reaching 31 $\pm$ 2 mm Hg at 4 min, while P_{ACO_2} increased during the first minute after which it leveled off at approximately 50 mm Hg. During 4 min BH the lung supplied 700 ml of O_2 into the blood while it gained only 160 ml of CO_2 from the blood, indicating a significant retention of CO_2. Arterial blood gas measurements showed that O_2 content decreased by 2 vols % while CO_2 increased by 8 vols % during 2 min BH; arterial blood pH decreased by 0.10. $(A - a)O_2$ gradient was always maintained at 10-20 mm Hg. P_{aCO_2} was not different from P_{ACO_2} before BH but became lower than P_{ACO_2} at 2 min BH, the average $(a - A)CO_2$ gradient being -4.7 $\pm$ 1.3 mm Hg ($p < 0.005$). The blood lactic acid remained unchanged during 2 min BH but increased slightly 20 sec after BH ($p < 0.025$). The systolic pressure increased only slightly during 1 to 2 min of BH, after which it increased rather sharply. The pulse pressure tended to increase toward the end of BH. The heart rate decreased by 15% within 20 sec and was maintained at this level until 2 min of BH. The central venous pressure increased immediately to and was maintained at 10 to 20 mm Hg during BH. Cardiac outputs measured during 1.5 to 2 min BH by dye-dilution method were not significantly different from those measured before BH. (This investigation was supported in part by NSF Sea Grant GH-62.)

CONDUCTION IN REGENERATING UNMYELINATED FIBERS. Anthony P. Hopkins (intr. by Edward H. Lambert). Mayo Clinic, Rochester, Minn.

Regenerating myelinated fibers may at first be unmyelinated, and have a wide range of conduction velocities. Therefore, in a mixed nerve, it is not possible to examine the changes of conduction in C fibers alone. We have studied the effects of crush on the superior cervical sympathetic trunk of the rat in which less than 1% of the fibers are myelinated. The trunk was crushed about 13 mm proximal to the superior cervical ganglion. Conduction velocity was measured at 37° C in vitro at intervals after crush to 100 days. The fastest C fibers in the trunk of 12 normal rats aged ten months ranged from 1.7 to 2.5 m/sec. The very small action potential of the few myelinated fibers was not measurable at the amplifications used. Large dispersed action potentials could be regularly recorded 11 mm distal to the site of crush as soon as 10 days after injury. Conduction velocity of the fastest fibers was at first about half normal, but reached normal values within 30-40 days. The dispersion of the monophasic action potential suggested that many fibers were still conducting at less than normal velocities as late as 100 days after crush. These results show that regenerating unmyelinated fibers have rapid rates of longitudinal growth, and suggest that some of the axon sprouts have diameters near normal within 30-40 days after crush. However, maturation of the diameters of many fibers is delayed. (*Supported in part by a grant from the National Fund for Research into Crippling Diseases, London, and the Louis W. and Maud Hill Family Foundation, St. Paul, Minn.).

Changes in Myocardial Contractile Properties with Age. Sidney F. Hopkins,* Ernest P. McCutcheon,* David R. Wekstein and Roger O. Lambson,* Univ. of Ky. Med. Ctr., Lexington, Ky. 40506

The studies of Mott (Brit. Med. Bull., 1966) showed no change in circulation time with postnatal growth in rats. Since the length of the circulatory system and the cardiac output are increasing, the overall flow velocity must increase as development progresses. There is only indirect evidence that a change in peripheral resistance compensates for the added energy loss created by the increased length. We postulated that intrinsic changes in the myocardium may be associated with the rapid circulatory alterations occurring during postnatal development in the rat. Both histological and isolated perfusion techniques were used to study changes in developing myocardium. Histological studies of the left ventricle (L.V.) showed that at birth the myofibrils and mitochondria were totally disoriented but within 16 to 20 days after birth, structural organization is very similar to that found in the adult. Functional evaluation of the perfused L.V. myocardium using the variables of isometric pressure, tension, dp/dt, and integrated isometric tension revealed a significant performance decrement in the ten-day old heart compared to the adult. The 16 and 20 day old hearts were functionally similar to the adult. Changes in function were related to age rather than L.V. mass. We conclude that there is a direct relationship between functional properties and the anatomical development of rat myocardium. Studies of the postnatal circulation must include analysis of changes in myocardial structural and functional properties (in addition to changes in pressure, heart rate, flow, ventricular mass, and peripheral resistance). (Supported in Part by Human Development Studies Program, Univ. of Ky.; General Research Support Grant of Univ. of Ky., NIH 5-501-FR05374; and the Ky. Heart Assn.)

TIME-DEPENDENT P-V CHARACTERISTICS OF EXCISED CAT LUNG : EQUILIBRIUM SURFACE TENSIONS IN SITU. T. Horie* and J. Hildebrandt. Virginia Mason Research Center, Seattle, Washington 98101.

Stress relaxation during 20 min periods (static), and compliance of tidal loops during 20 min periods of ventilation (dynamic), were measured on excised cat lungs with air and with saline at various volume levels. Volume displaced (V) and transpulmonary pressure (P) were recorded on an XY plotter. Ventilation was by constant inflow and outflow. Pressure fell when V was held fixed at TLC, but rose at 85% TLC or below. Static relaxation or recovery of pressure in the saline lung were about 10% of that seen in air-filled lung. When surface tension (γ), calculated from surface energy (Physiologist 12: 162, 1969) is plotted as a function of log time, the equilibrium value approached at high V is about 20 dyn/cm. However, below 70% TLC progressively smaller equilibrium values were seen, without increased rates of rise of γ. Thus, the film behaved viscoelastically only within a certain neighborhood of a given area, and outside this region approached a different equilibrium γ. When ventilated with a tidal volume of 15% TLC at levels above 70% TLC ($\dot{V}$=5 ml/sec, after full inflation) end-expiratory pressures fell slightly and compliance of PV loops increased. At 70% TLC and below end-expiratory pressures remained almost fixed while loop compliance decreased. An unchanging loop occurred near 65% TLC, and compliance was highest at about 50% TLC. Dynamic time-dependent changes in saline lung were also small. Calculated γ at end-expiration remained almost fixed at volumes below 70% TLC, but γ at end-inspiration fell when the lung was ventilated at high volumes but rose at middle and low volumes. Airway closure could account for some of these changes, but presumably only at the very low transpulmonary pressures.

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SWEAT AND BLOOD FLOW DURING PROLONGED HEAT EXPOSURE. Donald H. Horstman* and Steven M. Horvath. Institute of Environmental Stress, University of California, Santa Barbara, California.

Sweat, blood flow, and temperature parameters were measured on nine unacclimatized men during seven hours of supine exposure to 50 C DBT, 6% relative humidity, and without water replacement. Mean water loss was 3.1 kg, 4.1% of original body weight. Total sweat rates were estimated from continuous weight loss recordings and localized sweat rates by resistance hygrometry. Limb blood flows were measured by the venous occlusion method using Whitney strain gauges. Total sweat rate reached a steady state value of 208 g/m^2 per hour at 75 min, a level which was maintained for 240 min after which a decrease to 190 g/m^2 per min occurred, this level being maintained throughout the remainder of the exposure. Thigh sweat rate peaked at 75 min (630 g/m^2 per min) after which it declined rapidly and became more variable. Trunk sweat rate reached a steady state value of 395 g/m^2 per min at 60 min and maintained this level throughout the exposure. Forearm blood flow reached a peak value of 7.6 ml/100 g per min at 60 min, declined rapidly to 6.0 ml/100 g per min at 120 min, and maintained this level until 300 min at which point a further decline occurred. Calf blood flow attained a peak value of 3.8 ml/100 g per min at 60 min after which it gradually declined reaching a value of 2.6 ml/100 g per min at 420 min of exposure. Rectal temperature, tympanic temperature, and mean skin temperature gradually increased after 75 min and continued rising until the end of exposure.

Neurohypophyseal Protein and Renal Tubular Absorption of Chloride in Dogs. R. H. House* and R. C. Herrin. Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Infusion of the "Van Dyke" protein (PP) of porcine neurohypophyses in a dosage of 0.9 to 3.9 mU oxytocic activity/min/kg, into conscious trained dogs that were loaded with saline, caused increased renal tubular absorption of chloride, with no decrease in the filtered load. No normal dog was unresponsive and this tubular response occurred in 24 tests on 8 normal dogs. Porcine neurophysin, a contribution of M. Ginsberg, in an equivalent dosage effected a similar response of lesser magnitude. In 2 dogs, adrenalectomized for 100 days and maintained with deoxycorticosterone and cortisone, PP without or with a preceding infusion of aldosterone did not reduce the excretory % of filtered chloride. In 2 other dogs, PP increased tubular absorption within 14 days post-adrenalectomy but failed at 100 days. Additional therapy of corticosterone and aldosterone or 9α fluorohydrocortisone permitted the PP to effect the tubular response. Canine PP in a dosage of 1.9 - 2.6 mU oxytocic activity/min/kg increased tubular absorption in 3 of 4 dogs. Canine PP in a dosage of 0.1 - 1.0 mU/min/kg, with less saline, in 6 of 7 trials on four dogs caused increased tubular absorption of sodium. A hyperglycemia, greater than that effected by PP did not cause anti-chloruresis. (Supported by Wisconsin Heart Association).

EFFECT OF LUMEN ACIDITY AND OSMOLARITY ON DUODENAL BLOOD FLOW AND MOTILITY. C.P. Hsieh*, J.M. Dabney, W.T. Chen*, and C.C. Chou. Dept. of Physiology, Mich. State Univ., East Lansing, Michigan 48823.

Venous outflow and luminal pressure of an in situ duodenal segment were measured while perfusing the lumen with various solutions at 4 ml/min for 16 min. Solutions studied were 5% and 50% glucose, and acidified Tyrode's solutions (pH 1.5, 2.0, 2.5, and 3.0). Tyrode's solution (pH 7.4, 300 mOsm/l) served as the pre- and post- control for the above solutions. Effects of test solutions, as per cent of the control flow, at 7, 10, and 16 min after starting perfusion were:

		Acidified Tyrode's				Glucose	
		pH 3.0	2.5	2.0	1.5	5%	50%
Control Flow (gm/min)		17.3	16.3	15.2	16.6	17.3	18.6
% Change at	7 min	-2.5	+0.1	+9.4*	+14.0*	-2.0	+10.6*
	10 min	-3.5	-0.6	+10.5*	+21.3*	-0.6	+14.5*
	16 min	-5.9	-0.1	+10.5*	+15.9*	-0.4	+14.3*

* denotes significant change from control ($P<0.05$)

Luminal perfusion with pH 2.5 and 3.0 or 5% glucose solutions did not significantly alter blood flow while pH 2.0 and 1.5 and 50% glucose solutions significantly raised blood flow. The changes in flow caused by 50% glucose, pH 1.5 or 2.0 did not differ from each other ($P>0.2$). Duodenal motility was regularly increased by pH 1.5 and occasionally by pH 2.0 or 50% glucose. The threshold pH for increased blood flow and motility was near 2.0. It is concluded that high luminal acidity and/or osmolarity increases duodenal blood flow and high acidity also increases motility. These factors may be functionally important in the duodenum when the stomach empties.

COMPARISON OF IONIC EFFECTS ON LONGITUDINAL AND CIRCULAR MUSCLE OF JEJUNUM. Jane Hu*, C. Ladd Prosser and Margaret Peterson*. Department of Physiology and Biophysics, University of Illinois, Urbana, Ill.

Previous evidence indicated that slow waves in longitudinal muscle of cat small intestine result from rhythmic active efflux of sodium and that prepotentials and spikes in both muscle layers represent calcium conductance change. Spikes increase in amplitude as external calcium concentration is raised to an optimum and then decline at higher concentrations. The concentration of calcium for maximum spike height is for longitudinal fibers 3.4 mM and for circular fibers 0.8 mM. The rise in spike height may be related to increasing calcium gradient and the decline may be due to a decrease in permeability in high calcium. The calcium concentration in longitudinal muscle is 9.86 meq/kg and in circular muscle 2.1 meq/kg, hence the concentrations for maximum spikes correlate with Ca_i levels in the two muscle layers. The ratio P_{Na}/P_K as measured from resting potential curves is high in low Ca_o and reduced in high Ca_o. After prolonged exposure to high extracellular Ca or low Na both muscle layers show bursts of high frequency spikes. The ratio of Ca to Na is critical for membrane excitability. At high Ca/Na the fibers may go into a spiking state and slow waves are suppressed; slow waves predominate when Na/Ca is high. The sodium concentration in longitudinal muscle is 144.7 meq/kg and in circular 73.4 meq/kg.

(Supported by U.S.P.H. Grant AM12768.)

ETHANOL EFFECT ON APPARENT INSULIN SECRETION RATES OF ISOLATED PERFUSED ISLETS OF LANGERHANS. Marcia Van Gemert Hudson* and Lyle V. Beck. Dept. of Pharmacology, Indiana Univ. Sch. Med., Bloomington, In. 47401

Islets of Langerhans were isolated from mouse or rat pancreas as described by Lacy (Diabetes 1967, 16, 35). Each group of 10 islets was placed in a perfusion chamber held at 37°C; loss of islets was prevented by a sintered glass disc. The Krebs bicarbonate perfusion fluids used, of pH 7.4 after aeration with 95 % O_2, 5 % CO_2, contained 2 % bovine albumin, 0.1 or 1 μg/ml of pancreatic trypsin inhibitor and either 50 or 300 mg % glucose. In nearly every experiment change from 50 to 300 mg % glucose in fluid impinging on the islets resulted almost at once in increase in concentration of immunoactive insulin present in perfusion fluid collected beyond the islets. In certain of the experiments some of the immunoactive insulin values, estimated by the method of Zaharko and Beck (Diabetes 1968, 17, 444), were apparently less than zero. This suggested that in spite of presence in perfusion fluids of pancreatic trypsin inhibitor something was being added to perfusion fluid passing pancreatic tissues placed in the chamber which was denaturing or destroying immunoactive insulin released by islets. and/or labeled ^{125}I-Insulin added during the final incubation period of the immunoassay procedure. In additional experiments, each perfusion sample collected was immediately divided into two parts, to one of which four volumes of 95 % ethanol was added. In subsequent immunoassays (in which the ethanol present was sufficiently diluted that it did not interfere) practically every sample to which ethanol had been added gave a higher value for immunoactive insulin present than did the corresponding non-ethanol sample. This finding indicates that even in presence of pancreatic trypsin inhibitor some destruction of endogenous &/or labeled insulin may occur prior to completion of its immunoassay.

IMPROVEMENT IN PHYSICAL FITNESS ASSOCIATED WITH WALKING SIX MILES PER DAY FOR TEN DAYS. W. H. Huibregtse, W. H. Doolittle, L. H. Hartley, and L. G. Jones (intr. by J. E. Hansen). Army Med Rsch Lab, Alaska, and Physiology Lab; U. S. Army Rsch Inst of Env Med, Natick, Mass.

Exercise studies (bicycle ergometer) were performed on 12 airborne infantrymen (age X = 21.5 yrs) of average size, and 4 investigators, before and after a winter field maneuver. Oxygen uptake ($\dot{V}O_2$) and heart rate (HR) were measured at a load of 100 watts (W), at approximately 70%, and at 100% of maximum $\dot{V}O_2$. Mean max $\dot{V}O_2$ was 43 ml/kg x min. Maximal values were documented by usual criteria and lactates of over 8 mM/L in blood taken 5 min post-exercise. On the 10 day maneuver an average of 6 mi/da were covered, almost one-half without packs. The maximum rate of walking was 2.5 to 3.0 mph. No high intensity work was performed. The Alaskan temperatures were mild due to unusually warm weather (0-30° F), and the subjects felt no distress. The post-maneuver data indicated a marked increase in physical fitness with an increase in max $\dot{V}O_2$ of over 6% ($P = <.01$) and a decrease ($\bar{X}$ diff = 15 beats/min) in HR response to 100 W exercise. Of the 16 subjects all improved except 3. Of these, one was in excellent condition before (max $\dot{V}O_2$ 53.1 ml/kg x min) and one was absent from the field one-half the time. Max HR was slightly ($\bar{X}$ = 3.4 beats) decreased. Activities for the soldiers, other than the walk, were similar before and during the maneuver. Rest was enforced the night before the test, whereas after the maneuver, rest on the night preceding the test was, if anything, less. This study strongly suggests that low intensity, non-fatiguing exercise of a constant nature can result in improvement of the order of magnitude observed with high intensity training, even in non-sedentary subjects.

ULTRASTRUCTURAL AND HISTOCHEMICAL STUDIES ON THE INNERVATION OF THE DUCTUS ARTERIOSUS OF THE FETAL LAMB. M. Ikeda and D.G. Silva (intr. by R.R. Sonnenschein). Departments of Physiology and Oral Medicine, UCLA Schools of Medicine and Dentistry, Los Angeles, Calif. 90024.

We previously demonstrated histochemically the existence of adrenergic nerves in the media of the ductus arteriosus of the fetal lamb (Fed. Proc. 29:320 Abs., 1970). However, with few exceptions, electronmicroscopists generally agree that nerve fibers in blood vessels are limited to the adventitio-medial zone. Therefore, ultrastructural and histochemical studies were undertaken on the innervation of the ductus. The media of the ductus was composed of alternate layers of concentrically arranged smooth muscle cells and connective tissue elements. Vasa vasorum, leucocytes and mast cells were frequently seen within the media. Large bundles of acetylcholinesterase (Ach E) positive nerve fibers and small ganglia were seen in the adventitia. Smaller nerve bundles extended into the outer third of the media where they were present in both the muscle and connective tissue lamellae. The separation between nerve fibers and muscle cells was from 2 μ to 75 Å. On the basis of their intra-axonal vesicles and their Ach E activity both cholinergic and adrenergic nerves were identified. The findings provide evidence that these vessels possess a dual innervation. (Supported by grants from USPHS FR 5304, HE 05157 and LA County Heart Association)

THE EFFECT OF TEMPERATURE ON PULMONARY VENTILATION IN THE TURTLE.
D. C. Jackson. Dept. of Physiol., Univ. of Penna., Phila., Penna.

In turtles, frogs, and toads arterial PCO_2 varies directly with temperature (Robin, Nature 195:49, 1962; Howell et al., Am. J. Physiol. 218:600, 1970) which suggests that pulmonary ventilation is higher at low temperatures in relation to metabolic rate in these poikilotherms. To test this hypothesis simultaneous measurements of respiratory minute volume (RMV) and oxygen consumption (OC) were made on turtles (Pseudemys scripta elegans) at 10C, 20C, and 30C following at least 3 days acclimation at the test temperature. To measure respiratory volumes the turtle was suspended into water from a force transducer; when the animal breathed, by raising its head into a ventilated chamber, the associated weight change was sensed and recorded. Mean values of RMV and OC were computed over periods of about an hour. The results demonstrate that ventilation varies inversely with temperature in accordance with the hypothesis. Average ratios between RMV and OC were as follows: 10C - 70; 20C - 38; 30C - 14. As a result of the increased ventilation at low temperature the RMV changed little from 10C to 30C despite large changes in OC due to Q_{10} effect; however, at any one temperature RMV varied directly with OC which indicates that respiratory control exists but that the control level is temperature dependent.
Supported by PHS Grant GM-14562 and Penna. Plan to Develop Scientists in Medical Research.

Tension Production Kinetics of Ventricular Muscle from Hibernating and Non-hibernating Mammals. H. Kurt Jacobs* and Frank E. South, Jr. Space Sciences Research Center, Univ. of Missouri, Columbia, Mo. 65201.

Temperature dependent studies of excitability, tension production, elapsed times to maximum rates of tension production and maximum rates of tension production were made on isolated trabecular strips from hibernating hamsters (HH), non-hibernating hamsters (CH), and from rats (R). The strips were driven and isometric tensions along with their first time derivatives (dP/dt) were recorded. Excitabilities of both hamster tissues were greater than that of rat tissue from 5°C to 38°C with HH>CH. Peak tension production followed the order HH>CH≥R at all temperatures below 24°C. Rats showed an optimum peak tension production at 31°C while HH and CH showed optima at 17°C to 24°C. Contraction and relaxation half-times did not appear to differ significantly, but times to maximal rates of tension rise did show significant variations. In this respect the order of sensitivity to decreasing temperature was HH>CH>R. This is indicative of a delayed onset of the active state in the hamster tissues at temperatures below 15°C. A greater intensity of the active state at temperatures below 15°C in the hamster tissues was suggested by Arrhenius plots of maximum rates of tension rise vs. 1/T which indicated that the rat tissue was more temperature sensitive than the hamster tissues.
Supported by NASA (NGR 26-004-025) and Space Sciences Research Center (University of Missouri).

Blood of Peptic Ulcer Patients Contracts Smooth Muscle. Jefferson, N.C., A. Geisel, M. Berg and H. Necheles, Michael Reese Hospital and Medical Center, Chicago, Ill.

When the central ends of the vagus nerves of dogs are stimulated, their blood contracts smooth muscle. The substance comes from the head as seen with isolated heads. The vagus nerves play a role in the pathogenesis of ulcer, and vagotomy is used widely in the treatment. For these considerations we checked one ml blood of normal persons and of persons with peptic ulcer on guinea pig ileum in vitro. In over 90% of persons with peptic ulcer a rapid strong contraction of the ileum appears. In normal persons there is no contraction or a small one with a longer latent period. In persons with peptic ulcer the factor in the blood appears to persist for a long time after complete healing of the ulcer, after sub-or even total resection of the stomach. There may be small variations, but the power of that factor appears to be high in some cases for years. In patients with other disease than peptic ulcer there were only a few instances with increased factor: 3 cases of skull fracture with brain damage, a severe burn case, and one case of pernicious anemia. In other intestinal diseases such as ulcerative colitis, diverticulitis, Chrohn's Disease, in bone fractures, hernias, etc., no increased factor was found. Results with blood from relatives of ulcer patients are promising. Isolation and chemistry of the factor is in process. A high or a low factor may predispose to or prevent appearance of ulcer.

WATER TRANSMISSION BY HOMEOTHERMIC AND POIKILOTHERMIC SKIN. Carl Jelenko, III and Jack M. Ginsburg. Medical College of Georgia, Augusta, Georgia.

Using a modified gas chromatographic system for measurement, water transmission through isolated fish and frog skins was found to closely approximate open water loss (i.e. free diffusion of water) under conditions of measurement in which mammalian skin water transmission was about 2×10^{-3} less than open water loss. From intact mammalian skins of several species we previously isolated a hexane-soluble lipid which is a major water-holding factor for these skins. This lipid was not detectable in the skins of fish or frogs when assayed by the gas-liquid chromatographic technique of Haahti. A decrement in lipid content proportional to the increase in water transmission was observed in mammalian burn eschar. These studies suggest that there is a quantitative relationship between cutaneous content of water-holding lipid and water transmission. In view of the hypothermia which is known to follow extensive burn trauma in mammals these studies suggest that evaporative thermoregulation may be related to the presence of the water holding lipid.

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POSITIVE FEEDBACK EFFECTS OF STEROIDS ON FOLLICLE STIMULATING HORMONE. Donald C. Johnson, Univ. Kan. Med. Ctr. Kansas City, Kansas.

Plasma and pituitary FSH were studied in immature female rats treated with estradiol benzoate (EB), testosterone propionate (TP) or a combination. Plasma FSH changes were evaluated by use of an endogenous augmented ovarian weight assay. A single dose of lug EB caused an increase in plasma and pituitary FSH within 24 hrs. Glandular level then fell as plasma level rose to a peak at 60 hrs. After 60 hrs plasma FSH decreased and reached a low point at 84 hrs and remained unchanged until 156 hrs. A second dose of EB at 60 hrs produced an increase in pituitary FSH, without lowering plasma FSH, within 12 hrs. After this rise, pituitary FSH fell rapidly to a low level, but plasma FSH continued to rise to another peak within 48 hrs. After this peak, plasma content fell to that of controls while pituitary content remained very low. TP(100ug) in a single dose did not cause changes in pituitary FSH. When given with lug EB the glandular FSH remained at the high control level for 96 hrs, while plasma FSH rose a moderate amount. The amount stored decreased at 120 hrs in animals receiving the double treatment. TP stimulated FSH synthesis in EB treated animals even when given 60 hrs later, but it had no effect upon plasma FSH in these animals. The results demonstrate: (1) Estrogen has a distinct positive feedback effect on both synthesis and release of FSH and (2) The amount of FSH in the pituitary is a poor indicator of the rate of synthesis or release of this hormone.

ACTIVATION AND INHIBITION OF MUSCLE POSTJUNCTIONAL MEMBRANE RECEPTORS. Ernest W. Johnson* and Rodney L. Parsons, Dept. of Physiology & Biophysics, Univ. of Vermont Coll. of Med., Burlington, Vermont.

The inhibition by d-tubocurarine and hexafluorenium of muscle postjunctional membrane receptor activation was studied in vitro on the sciatic nerve-sartorius muscle preparation of the frog (Rana pipiens). The maximum depolarization produced during microperfusion of carbamylcholine onto a single neuromuscular junction was recorded with intracellular microelectrode techniques and used as a measure of receptor activation. The slope of the carbamylcholine dose-response curve (n_H= 1.57) was greater than that predicted by the Michaelis-Menton equation (n_H=1). Following pretreatment with either d-tubocurarine or hexafluorenium, n_H decreased toward the predicted value. Whereas 1 x 10^{-5}M hexafluorenium antagonized the action of carbamylcholine to a greater extent than did 5.0 x 10^{-6}M d-tubocurarine, the latter produced a more effective neuromuscular blockade. Miniature end-plate potentials, although reduced approximately 60% in amplitude, persisted in preparations treated with 1 x 10^{-5}M hexafluorenium but rapidly disappeared in the presence of 5.0 x 10^{-6}M d-tubocurarine. Lanthanum (1 x 10^{-5}M) potentiated the effect of carbamylcholine in preparations treated with d-tubocurarine to a greater extent than in the presence of hexafluorenium. Whereas increasing the concentration of carbamylcholine surmounted the inhibition produced by d-tubocurarine, it was relatively ineffective in overcoming the antagonism produced by hexafluorenium. It is suggested that there are at least two populations of postjunctional membrane receptors for carbamycholine, one of which is competitively inhibited by d-tubocurarine and another noncompetitively inhibited by hexafluorenium. (Supported by NIH Grants: NS 07740 and Postdoctoral Fellowship GM 46027).

EFFECTS OF HEMORRHAGE AND CHRONIC SODIUM DEPLETION ON THE METABOLISM OF RENIN BY THE LIVER. J.A. Johnson*, J.O. Davis, J.S. Baumber*, and E.G. Schneider*, Dept. of Physiology, Univ. of Mo. Sch. of Med., Columbia, Mo.

It is well known that hemorrhage or sodium depletion increases renin release and increases peripheral plasma renin activity (PRA). In the present study the contribution of decreased hepatic inactivation of renin to the increased plasma renin activity was determined. Hepatic metabolism of renin was studied in conscious dogs before and following hemorrhages of 20 ml/Kg of body weight (B.W.) (6 dogs) and 30 ml/Kg B.W. (6 dogs), and in chronic sodium depletion (6 dogs). Hepatic plasma flow was determined by the bromosulfophthalein method. No significant changes in the hepatic extraction of renin or in the hepatic clearance of renin were observed following the hemorrhage of 20 ml/Kg B.W. However, hemorrhage of 30 ml/Kg B.W. resulted in a significant ($P<0.01$) decrease in hepatic plasma flow from a control of 30.8 ml/min/Kg B.W. to 16.8 ml/min/Kg B.W. The hepatic extraction of renin increased ($P<0.05$) from 33 to 104 ng/min/Kg B.W. while the hepatic clearance of renin decreased ($P<0.01$) from 6.5 to 3.4 ml/min/Kg B.W. Sodium depletion produced a decrease ($P<0.05$) in hepatic plasma flow (37.2 to 25.3 ml/min/Kg B.W.), an increase ($P<0.05$) in hepatic extraction of renin (44 to 140 ng/min/Kg B.W.) and a decrease ($P<0.01$) in hepatic clearance of renin (8.6 to 4.2 ml/min/Kg B.W.). These results indicate that following severe hemorrhage or during chronic sodium depletion a decrease in the hepatic inactivation of renin contributes to the elevated plasma renin activity.

GLUTAMATE DISTRIBUTION IN THE DORSAL SENSORY NEURON OF THE CAT. J.L. Johnson* and M.H. Aprison. Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, Indiana.

Glutamate is a good transmitter suspect in the dorsal root fibers projecting to neurons in the spinal cord and dorsal column nuclei of the medulla. Glutamate levels were therefore measured to determine the nature of its distribution in the various components of the dorsal sensory neuron, and also in other neuronal regions where glutamate is not a transmitter suspect. Several other amino acids were measured for comparison and control purposes. The order of increasing glutamate concentration was ventral root, sympathetic ganglion, and distal sensory root < dorsal root and dorsal root ganglion< dorsal medial white of cord and ventral medulla < grey of cord and dorsal column nuclei. Total free amino acids (TFAA) reflected the above glutamate differences. TFAA levels in the dorsal root ganglion were very high; the levels of several amino acids were high in the ganglion, with glutamine levels being highest. The above data indicate that there must be some differential flow mechanism in the dorsal sensory neuron directing more free glutamate towards the cord where synaptic contacts are made. The high levels of free glutamate in the regions of the cord and medulla containing dorsal root synapses suggests that there is a functional compartment for synaptic transmission in addition to a glutamate metabolic compartment. (Supported by grants MH-03225-11 (NIMH), NB-07307-3 (NIH), and Postdoctoral Training Grant MH-10695-04 (NIMH)).

INFLUENCE OF THE TESTES, OVARIES AND ADRENAL GLANDS ON GRANULATED CELLS OF THE RAT INTESTINE. S. M. Johnson* and J. E. Nellor. Endocrine Research Unit, Dept. of Physiol., Mich. State University, East Lansing, Michigan 48823.

A variety of physiological and pharmaecological conditions have been reported to modify the numbers of eosmophilic and basophilic granulocytes in gastrointestinal tissues. Subsequent to our demonstration that genital tract granulocytes numbers are markedly modified by ovarian cyclic activity or hormone treatment, the present study was designed to determine the influence of the gonads and adrenal glands on intestinal granulated cell numbers and distribution. The studies included male rats from 8 days to 2 years of age, and female rats during immaturity, at each stage of the estrous cycle, during pregnancy and lactation. Cell counts were measured on 8 random areas of duodenal lamina propria equal to .5 sq. mm. of a tissue section. After a peak at about 70 days of age eosinophilic granulated cells progressively decreased with age, whereas basophilic granulated cells increased with age. The percent basophils of total granulated cells increased with age. Eosinophilic cell counts were highest at estrus and declined to the lowest level during proestrus. Basophilic cell counts were highest during proestrus. Pregnant rats exhibited eosinophilic cell counts comparable to diestrous animals, but higher basophilic cell numbers than diestrus rats. Prolonged lactation was associated with a decline in both eosinophilic and basophilic cell counts. Eosinophilic and basophilic granulated cells were shown to vary with the hormonal state of the animal.
(Supported by NSF Grant GB-7178)

INFRARED ANALYSIS OF THE AORTA SURFACE BY KBr ABRASION METHOD, W.T.M. Johnson* and Raymond Penneys, CVP Div., Dept. Med., Univ. Penna. Sch. Med., Philadelphia, Pa.

The role of the arterial surface in cardiovascular disease has not been elucidated, partly because its chemical composition is unknown. We report an attempt to determine the composition of the first molecular layer (20.-30.Å) at the surface of the aorta. We gently and uniformly spray abrade the opened, flat, surface withfine, dry KBr powder. Surface molecules are rubbed off and collected with the KBr. This powder is pressed into a disc and analyzed by infrared. KBr is transparent in infrared, so the spectrum is of the aorta surface. Thickness of surface sample removed is calculated from density-mass-volume (area x thickness) relation. Infrared band intensity gives sample mass, area is measured directly, and density is taken as 1.0. Method was adapted from method reported by one of us (WTMJ, Official Digest, 32, 1067-78, 1960), used successfully to surface analyze 25.-50.Å of polymer films such as polyethylene, and later used on human skin surfaces. We constructed a mechanical spray abrader to surface analyze blood vessels. Uniformity and abrasion depth are controlled by angle of spray, pressure, distance, and rate of traverse of sample drum. Preliminary tests ofmethod on bovine aorta gave surface samples as thin as 57.Å. Surface samples had unique spectrum, compared to total aorta endothelium (physically removed and analyzed as intact film). Major infrared bands in surface were: NH (3300.cm^{-1}), CH (lipid) (2920.cm^{-1}), Amide I and II (1650. and 1520.cm^{-1}), and, tentatively, sulfate bands (1050.cm^{-1}). These spectra of aorta surfaces resemble chondroitin sulfate, but not heparin.

PROSTAGLANDIN $F_{2\alpha}$ MODE OF ACTION IN PREGNANT HAMSTERS. J. O. Johnston and K. K. Hunter (intr. by G. W. Duncan). The Upjohn Company, Kalamazoo, Michigan.

Administration of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) terminates pregnancy in the hamster, rat, rabbit, monkey and human. Although the mechanism of $PGF_{2\alpha}$ action is unknown, there may be alteration of ovarian and uterine functions. In the hamster, a single subcutaneous injection of 100 µg of $PGF_{2\alpha}$ on day 8 of pregnancy (day 1 = sperm positive vaginal smear) did not terminate pregnancy, while a 300 µg injection at this time did induce fetal resorption. Peripheral plasma progestin levels at 24 hours after $PGF_{2\alpha}$ treatments were determined. In 8 day pseudopregnant hysterectomized hamsters, plasma progestin values declined from 8.5 ± 2.0 (vehicle control) to 2.6 ± 1.0 and 1.1 ± 0.3 ng/ml respectively after 100 µg and 300 µg $PGF_{2\alpha}$ treatments. Similar progestin changes were seen in $PGF_{2\alpha}$ treated pregnant hamsters; the 300 µg dose lowered progestin values (2.6 ± 0.5 ng/ml). It is suggested that the primary effect of $PGF_{2\alpha}$ in pregnant hamsters is at the ovarian level, since total fetalectomy did not significantly alter 24 hour post operative progestin values. However, 300 µg of prostaglandin can induce uterine contractions, which, associated with declining progestin levels, can cause fetal disruption with subsequent resorption. The failure of 100 µg $PGF_{2\alpha}$, which is luteolytic at 4 days of pregnancy, to interrupt gestation in 8 day pregnant hamsters may be due to increased placental luteotropic support. Gonadotropins can antagonize $PGF_{2\alpha}$ action, since exogenous prolactin and FSH maintained pregnancy in the presence of luteolytic doses of prostaglandin.

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EFFECTS OF MUSCULAR LEG EXERCISE ON PLASMA LEVELS OF GROWTH HORMONE, INSULIN, EPINEPHRINE, NOREPINEPHRINE, AND CORTISOL. L. G. Jones, L. H. Hartley, and J. W. Mason (intro. by J. A. Vogel). U. S. Army Rsch Inst of Env Med, Natick, Mass. and Walter Reed Army Inst of Rsch, Washington, D. C.

Very little data is available about neuroendocrine effects on the apparent shift in energy substrate from glucose and free fatty acid to glycogen during the "anaerobic" metabolism of heavy muscular exercise. The purpose of this study was to examine neuroendocrine factors which may influence substrate utilization during exercise. Plasma levels of growth hormone (GH), insulin (IN), epinephrine (EP), norepinephrine (NE), and cortisol (CS) were measured in 16 healthy male volunteers before, during, and after exercise on a bicycle ergometer. Oxygen uptake ($\dot{V}O_2$), heart rate (HR) and blood lactates were measured during 4-10 min steady-state exercise @ 40, 70 and 100% of maximum (MAX) $\dot{V}O_2$. GH rose from 4 ± 1.3 (mean ± SEM) ug/L resting (R) to 24 ± 8.1 at 70% MAX $\dot{V}O_2$ and fell to 15 ± 3.7 @ 100%; EP from 0.09 ± .055 R to 0.41 ± .149 @ 100%; NE progressively from 2.1 ± 37 R to 4.0 ± .93 @ 100%; and CS from 7 ± 1.2 to 11 ± 1.1 @ 100% and 13 ± 1.5 30 min after MAX exercise. IN levels fell during all levels of exercise. In 8 subjects exercised @ 40% for 3 hours, plasma hormone responses were similar to those found with 10 min exercise @ 40%. In 8 subjects exercised @ 72% until ($\bar{X}$ = 106 min) pedaling rate could not be maintained (exhaustion), plasma hormone responses were similar to 100% of MAX $\dot{V}O_2$ (3-5 min). These findings suggest that: 1) The plasma hormonal response is the same for exhaustion at both submaximal and MAX exercise; and 2) The level of plasma hormones vary with the relative workload and duration; and 3) The differential utilization of muscle glycogen during high intensity exercise may be due, at least in part, to the higher levels of GH and EP and the lower levels of plasma IN.

THE SITE OF ACTION FOR HISTAMINE IN THE PULMONARY VASCULATURE.
Richard L. Jones*, Christopher A. Dawson* and Lyle H. Hamilton. Marq. School of Med., and Wood VA Ctr., Milwaukee, Wis.

There is a lack of agreement regarding the site of action for histamine in the pulmonary vascular bed. The time between appearance of a histamine-containing bolus (0.2-0.5 C below perfusate T°) at a thermistor placed in the PA cannula (TH_{PA}) and the start of the pressor response was measured during forward and retrograde perfusion at the same blood flow. This time was 2.40 sec during forward perfusion and 1.04 seconds during retrograde perfusion. Assuming an equal latent period (time taken for the response to begin after the bolus reaches the active site), $[2.40 + 1.04] / 2 = 1.72$ sec, for flow in both directions, the active site appears to be 0.68 sec (2.40 - 1.72) downstream from the TH_{PA}. The location of the active site for histamine was not affected by the dose (70 or 270 μg in 3 ml of blood). Since the capillary bed was 1.10 sec downstream from the TH_{PA}, as determined from the ether plethysmographic technique, the active site was shown to be in the arterial segment of the pulmonary vascular bed.
(Supported by the Wisconsin Heart Association.)

OBSERVATIONS ON THE FUNCTION OF THE MESINTERIC LYMPH NODE.
J. L. Jordan* (introduced by R. E. Johnson). Univ. of Illinois, Urbana, Ill. 61801

Information concerning the anatomical and functional aspects of the intestinal lymphatics is not well documented. The major objective of this report is to establish the avenues of lymph drainage from the jejunum and ileum into and thru the right and left mesenteric lymph nodes as described by Baum in 1918. It will be shown that the lymph drainage from the jejunum and ileum is not consistently departmentalized into designated parts of the lymph node. Furthermore, by collecting blood samples going to and from a specific portion of the jejunum and ileum and also collecting lymph samples from the same intestinal segments going to and from the mesenteric lymph node, one can hopefully obtain information on the filtration, secretion and metabolizing functions of these lymphatic tissues.

By using the S.M.A. 12 analyzer quantitative information was obtained from the various collected samples on the minerals and organic compounds usually determined in the clinical laboratory. Along with sodium and potassium determinations via the flame photometer a total of 13 quantitative chemical measurements were made.

The results show that small but consistent differences in such minerals as sodium, potassium and calcium can be observed between lymph leaving the intestine and that found in the blood serum. Observations on the enzyme content of blood and various lymph samples, such as alkaline phosphatase, L.D.H. and S.G.O.T. gave wide variations in concentrations suggesting that the lymph node plays a role in some type of control of certain body functions. Experiments dealing with circulatory change and its possible relation to lymph node function are contemplated

CHANGES IN RENAL NERVE ACTIVITY AND RENAL VASCULAR RESISTANCE WITH HYPOTHALAMIC STIMULATION. W. V. Judy*, I. Ninomiya* and M. F. Wilson
Dept. of Physiology and Biophysics, School of Medicine, West Virginia University, Morgantown, W. Va. 26506

The effects of posterior hypothalamic stimulation (HS) on renal nerve activity (RNA) and renal vascular resistance (RVR) were measured in the intact cat kidney preparation during constant flow perfusions from 0.4 to 44.5 ml/min. Experiments have been conducted in six cats weighing 2.5 to 4.5 kg. The HS consisted of trains of rectangular pulses; pulse duration 0.5 msec., peak current 400-500 μA, and stimulus frequencies 5-100 Hz. Immediately after HS onset RNA reached a maximum and then decayed with various time courses depending on baroceptor influences. RVR and arterial pressure (AP) changes during HS increased proportionally with mean RNA. The magnitude of change of all variables (RNA, RVR and AP) was dependent on stimulus frequency and location, and baroceptor reflexes. As the baroceptor afferent pathways were opened the secondary changes in RVR, RNA and AP became less evident. At high constant flow levels the HS effects of RVR were reduced although RNA responses remained constant. With simultaneous stimulation of two ipsi or contralateral HS locations RVR responses summed, as previously reported for RNA. An approximate linear relationship between RNA and RVR occurred during HS; however, the RNA effects on RVR were less pronounced at high renal flows. Thus, both hypothalamic stimulation and baroceptor reflexes modulate RNA which, in turn, has a proportional effect on intrarenal resistance vessels. (Supported in part by NASA Grant, NGL 49-001-001, Suppl. No. 6, and NIH Grant 10234-04.)

POST-STIMULUS K- CONDUCTANCE INCREASE IN APLYSIA GIANT NEURONS. Douglas Junge and Malcolm Brodwick*. School of Dentistry and Departments of Physiology and Anatomy, U.C.L.A., Los Angeles, California.

Stimulation of the giant (R_2) cell in the visceral ganglion of Aplysia californica, either directly via a KCl-filled electrode or antidromically, results in a 5-10 mv hyperpolarization and up to 50% increase in membrane conductance after termination of the stimulus. Both the post-tetanic hyperpolarization (PTH) and the conductance increase persist for up to 30 seconds after the end of stimulation. Action potentials are not required to produce the effects, as both occur readily in calcium-free saline containing 10^{-5} g/ml tetrodotoxin. The time-course of development of the PTH parallels that of the conductance increase. The PTH is not caused by an electrogenic pump, since it persists in the presence of 4×10^{-4} M ouabain or with cooling. A reversal potential for the PTH can be demonstrated by applying inward-directed currents immediately after the stimulus. The reversal potential varies with the external potassium concentration at about 12 mv for a 3-fold increase in $(K)_o$, and is not affected by complete replacement of external chloride with methanesulfonate. The PTH is abolished by complete replacement of external sodium with tris, and the conductance-increase is reduced to less than 20%. It thus appears that PTH may be attributed to a post-stimulus increase in K- conductance, and that it can only occur in the presence of sodium. Supported by Grant NB07794.

CORTICOFUGAL PROJECTION OF STRIATE CORTEX TO THE SUPERIOR COLLICULUS IN THE SQUIRREL MONKEY. S. Kadoya*, L. C. Massopust, Jr., and L. R. Wolin*. Neurophysiology Laboratory, Cleveland Psychiatric Institute, Cleveland, Ohio.

Cortical efferents in the superior colliculus were investigated by recording evoked potentials and unit responses following electrical stimulation. The monkeys were anesthetized with urethane-Nembutal and paralyzed with Flaxedil. Visual cortex was exposed and rectangular pulses were applied by means of fine bipolar electrodes inserted within the cortical gray matter. Photically evoked responses were also recorded. 1] A typical evoked potential following striate cortex stimulation showed both pre- and postsynaptic components. The presynaptic component was recorded in an extremely limited area of the colliculus which was related to a specific stimulating point of striate cortex. In the same area the phase reversal of the postsynaptic negative wave was also noticed. 2] These characteristic responses were mainly located in the stratum opticum of the ipsilateral side. 3] Point-to-point projection of cortical efferents to the colliculus had well-organized topographic arrangement and directly referred to the retinotopic projection of the colliculus[1] and striate cortex[2]. No interaction between photic and electrically induced evoked potentials was found. 4] Unit activity driven by striate cortex stimulation also showed topographic projection. It is suggested that the superior colliculus receives inputs from both retina and striate cortex and their terminating areas are retinotopically oriented. (Supported by grant FR-05563 from NIH.)

[1] Kadoya, S., L. R. Wolin and L. C. Massopust, Jr. The Physiologist, 1969, 12: 264.

[2] Cowey, A. J. Neurophysiol., 1964, 27: 366-393.

CAPILLARY PRESSURE (P_C), PRE- AND POSTCAPILLARY RESISTANCE, CAPILLARY FILTRATION COEFFICIENT (CFC) DURING ANGIOTENSIN INFUSION IN ISOLATED DOG HINDLIMB. R.S. Kaiser*and J.N. Diana. Dept. of Physiol. and Biophys., Univ. of Iowa, Sch. of Med., Iowa City, Iowa.

Femoral, saphenous and digital venous pressures, arterial pressure (AP), limb wt. and femoral venous outflow were measured during angiotensin (Hypertensin, Ciba) infusion in the isolated dog hindlimb perfused at constant flow (CF) or constant pressure (CP). Hemodynamically, infusion of angiotensin i.a. (1.5-2.5 μg/kg/min) produced an increase in both postcapillary (R_V) and precapillary (R_A) resistances to blood flow. For CP perfusion R_A increased during the first 3 min while R_V increased transiently and then leveled off at a value above control. P_C decreased resulting in net fluid absorption. After the first 3 min R_A decreased to control while R_V remained constant and P_C rose to control. For CF perfusion R_V and P_C increased and remained elevated while R_A and AP increased transiently but then fell to control value. After the first 2 min net filtration was observed which was persistent. CFC measured 15 min after beginning angiotensin infusion was higher than control. Since isogravimetric capillary pressure was not significantly different in the control and during drug infusion, these data indicate that surface area available for hydrodynamic flow of fluid across the capillary is increased by angiotensin infusion. (Supported by NIH Grant HE 12563)

EFFECT OF HYPOTHALAMIC AND PREOPTIC ELECTROCHEMICAL STIMULATION ON GONADOTROPIN AND PROLACTIN RELEASE IN PROESTROUS RATS. S.P. Kalra*, K. Ajika*, L. Krulich*, C.P. Fawcett*, M. Quijada* and S.M. McCann, Dept. Physiol., U. of Texas Southwestern Med. School, Dallas, Texas.

Sprague-Dawley rats with 4 day estrous cycles showed a surge of LH, FSH and prolactin release during the afternoon of proestrus. The administration of Nembutal (32.4 mg/kg i.p.) at 1:30 P.M. on the day of proestrus inhibited this surge. In order to explore the possibility of the existence of specific area(s) involved for this release of LH, FSH and prolactin various regions of the hypothalamus were electrochemically stimulated unilaterally by stainless steel bipolar concentric electrodes with D.C. current of 100 μ amp for 60 seconds. Plasma levels of LH, FSH and prolactin at different intervals following stimulation were estimated by radioimmunoassay. Electrode placements were confirmed histologically. Small stimulating lesions in the region of medial preoptic area (MPOA) (de Groot: A=7.4-8.2, L=0.5-0.8, V=-2.0) consistently stimulated the release of LH within one hour, which was associated with ovulation while FSH release was unaltered. When electrode placements were localized in more caudal regions of MPOA-anterior hypothalamic area (A=6.8-7.4, L=0.5-0.8, V=-2.0) and in the median eminence-arcuate region plasma levels of both LH and FSH were elevated one hour after stimulation and ovulation occurred. However, similar parameters of stimulation in the hypophysiotropic area failed to elevate plasma prolactin levels. Stimulations in the lateral or caudal hypothalamus were ineffective. Our results suggest the existence of two distinct but overlapping areas in the hypothalamus which control the surge of LH and FSH. Supported by grants from PHS, Ford Foundation and Texas Population Crisis Foundation.

POSSIBLE ROLE OF α-ADRENERGIC RECEPTORS IN MEDIATING THE RESPONSE OF THE HYPOTHALAMUS TO DOPAMINE. I. A. Kamberi*, R. S. Mical*, and J. C. Porter (intr. by Arthur Grollman). Dept. of Physiology, Univ. Texas Southwestern Medical School at Dallas, Dallas, Texas.

It is generally accepted that changes in the plasma FSH, LH and prolactin (LtH) concentrations of adult male rats, as determined by radioimmunoassay, are directly related to the release rate of these hormones from the anterior pituitary (AP). Dopamine hydrochloride (DA) and α- or β-adrenergic blocking agents were injected through microcannulae into the third ventricle which was exposed via a parapharyngeal approach permitting direct visualization of the AP, median eminence, stalk and the surrounding area of the basal diencephalon. Injection of 2.5 μg DA into the third ventricle caused a marked increase in the plasma concentrations of LH and FSH and a decline in the LtH level within 10 min after the time of injection. The peak concentrations for LH and FSH were achieved after 20 to 30 min and 60 to 90 min, respectively. At these respective times the concentrations of LH and FSH were more than 10-fold greater than control levels. Thirty min after intraventricular injection, the concentration of LtH was at a minimum—1/3 that of control level. Intraventricular injection of 20 μg phentolamine or phenoxybenzamine, α-adrenergic blocking agents, or pronethalol, a β-adrenergic blocking agent, did not alter LH, FSH or LtH release in peripheral plasma. Injection into the third ventricle of 20 μg phentolamine or phenoxybenzamine along with 2.5 μg DA prevented the response seen with DA alone, whereas intraventricular injection of 20 μg pronethalol with 2.5 μg DA failed to do so. These results suggest that dopaminergic neurons of the hypothalamus may have a role in the regulation of LH, FSH and LtH release secondarily to the discharge of LRF, FRF and PIF, and this effect may be mediated via α-adrenergic receptors. (Supported by NIH Research Grant AM01237 and by a grant from The Population Council.)

ACETYLCHOLINE-SENSITIVE NEURONS IN THE MIDBRAIN. H. Kawamura. Lafayette Clinic, Detroit, Mich. and Dept. of Pharmacology, Univ. of Michigan, Ann Arbor.

Many cells in the midbrain reticular formation (nucl. cuneiformis, Shute and Lewis, Brain, 90: 497-520, 1967) are believed to receive cholinergic input from hind brain reticular formation. However, no direct evidence has been provided as to the excitability change of the neurons by iontophoretically applied acetylcholine (ACh). Cats under methoxyflurane-nitrous oxide anesthesia or with rostral pontine transection were used. Cholinergic agonists (ACh, arecoline, nicotine) were applied iontophoretically on the single neurons in the midbrain reticular formation area using 5 barrel micropipettes. Many neurons in this area were excited by ACh with slower time course than by L-glutamate in the similar manner as in the cortex. Arecoline induced very long-lasting excitation (3 to 5 min). Nicotine excited some neurons with short latency (5 to 10 sec) but others with much longer latency of 30 to 60 sec. Pentobarbital (10 to 20 mg/kg, i.v.) or deep methoxyflurane anesthesia deprived sensitivity of neurons to these cholinergic agonists. Effect of 2,4-dinitrophenol, which was shown to block ACh effect selectively in the cortex, while L-glutamate excitation lasted (Kawamura and Krnjević, Pharmacologist, 11: 254, 1969), was not as selective to ACh as in the cortex. These data seem to support an idea of muscarinic as well as nicotinic sensitivity of the midbrain reticular formation neurons suggested in an earlier work (Kawamura and Domino, Int. J. Neuropharmacol., 8: 105-115, 1969).
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REFLEX INHIBITION OF SYMPATHETIC DISCHARGE BY LEFT VENTRICULAR BARORECEPTORS. Paul Kezdi , R. K. Kordenat*, A. Seeber*, K. A. Vasko* and J. W. Spickler*, Cox Heart Institute, Dayton, Ohio

The existence of cardiovascular depressor reflex from the left ventricle (LV) has previously been demonstrated and suggested that it may contribute to the total tonic action of the baroreceptors on the cardiovascular system. This study utilized sympathetic nerve recordings in dogs to quantitate the tonic action and the reflex activity in response to raising the aortic pressure by cross-clamping after successive cutting of the carotid sinus and aortic nerves and the vagi. The average sympathetic activity increased 20% of control after cutting both sinus nerves, additional 12% after cutting both aortic nerves, additional 17% after cutting both vagi trunks in the neck, indicating moderate tonic activity of the individual baroreceptor nerves during normal (control) blood pressure (cloralose + urethane anesthesia). Reflex inhibition of sympathetic activity during pressure increase due to cross-clamping the descending aorta decreased after cutting the sinus nerves by 18%, after cutting the aortic nerves by 29% and no inhibition occurred after cutting the vagi. Cross-clamping the ascending aorta (10 sec) resulting in drop of pressure in the systemic circulation and increase of LV pressure and distension markedly inhibited sympathetic activity both before and after carotid sinus and aortic deaffarentation. The reflex was eliminated by cutting the vagi. The baroreceptor nature of this reflex was demonstrated by recording of sympathetic reflex response and afferent activity in vagal fibers following inflating a ballon in the LV during cardiopulmonary bypass. The LV reflex normally exerts only small tonic activity but becomes strongly active during acute distension when it may override the attempt of the vascular baroreceptors to compensate for acute cardiac failure and hypotension.

ALTERATION OF COCHLEAR RESPONSES CORRELATED WITH PHASIC ACTIVITY IN THE PONTINE RETICULAR FORMATION. Robert E. Kingsley* and Charles D. Barnes. Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401

Previous work in other laboratories has shown that during the phasic events of REM sleep there is a presynaptic inhibition of muscle and cutaneous primary afferents as well as of the primary afferents in the dorsal column nuclei. This investigation is concerned with the effects of REM sleep upon the primary auditory pathway. Unanesthetized, decerebrate, decerebellate cats heavily paralysed with Flaxedil were used. Auditory stimulus consisted of a 10 μsec. click about 20 db. above threshold for the N1 response recorded from the round window. Activity of the pontine reticular formation (RF) was recorded with a stereotactically placed (P4,L2,H-6) bipolar concentric electrode throughout the experiment. Phasic RF episodes have been correlated with REM bouts in normal and decerebrate animals. Physostigmine (0.1 mg/kg i.v.) has been shown to induce these episodes in decerebrate animals. During the physostigmine-induced RF activity the cochlear microphonic (CM) is enhanced, while the N1 and N2 responses are diminished. These changes were not seen after physostigmine administration when the RF was quiescent, even with doses as high as 0.6 mg/kg i. v. Others, by direct ortnodromic stimulation of the olivo-cochlear bundle of Rassmussen, have shown augmentation of CM and diminution of N1 and N2 responses, thus implicating that pathway in the responses we have observed. By recording antidromic responses to stimulation of the O-C bundle, the cells of origin have been determined to be in the lateral pre-olivary nucleus and probably also in the medial pre-olivary nucleus. (Supported by USPHS Grants NB 07834 and NB 34986).

THE EFFECTS OF PHASIC PULSATION ON BARORECEPTOR RESPONSE IN ASSISTED CIRCULATION. J. S. Kirkland, Jr.* and E. C. Peirce II. Depts. of Physiology and Surgery, Emory University, Atlanta, Georgia.

This study was designed to investigate the effects of synchronous and asynchronous assisted circulation on cardiac contractility. Twenty-seven chronically instrumented dogs were perfused with a pulsatile system of veno-arterial bypass. In addition, seven of the animals were prepared for perfusion and both beta adrenergic and parasympathetic blockades were established. The animals were perfused both synchronously and asynchronously with blood being withdrawn from the superior vena cava and reinfused through a carotid artery. A decrease in external cardiac work and myocardial contractility has been demonstrated. With changes in the pulse synchronization, small but highly significant additional decreases are seen in external work and contractility as the artificial pulse is delivered in diastole rather than in systole. Following blockade, no significant decrease in contractile state could be demonstrated with changes in pulse synchronization; however, the changes in external work previously described remain present. Therefore these changes in the contractility indices may be due to a differential response of the baroreceptors to the increase in pulse frequency and change in pulse contour which occur with shifts in pulsation from systole to diastole.

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WHAT IS THE *REAL* SIGNIFICANCE OF HIPPOCAMPAL THETA RHYTHM? W. R. Klemm. Department of Biology, Texas A&M University, College Station, Texas.

The rhythmic, 4-7/sec, hippocampal activity, known as "theta rhythm", was originally thought to be correlated specifically with the "arousal response". Controversy has been created by recent reports which attribute theta rhythm to various other conditions, such as approach behavior, reward, learning and memory, processing of sensory input, and even to nonspecific voluntary movements. In the present study, electrographic recording from unanesthetized rabbits revealed a consistent association among theta rhythm, increased muscle tone or movements, and increased neuronal impulse activity in the medullary reticular formation. Theta-correlated movements were general and non-specific, including simple spinal reflexes. The increased impulse (multiple-unit) activity lasted only during phasic increases in muscle tension or movement, and was not observed in any of the 6 rostral brain areas tested. The correlations held under tranquilizer treatment, which simultaneously suppressed theta activity, muscle tone, and multiple-unit activity in the medulla (but not elsewhere). These results suggest yet another interpretation of the significance of theta rhythm, and a new theory is advanced herein to resolve the present controversy by showing that the divergent views are not mutually exclusive. (Supported by NIMH grant MH 13072).

THE KINETICS OF THE OXYGEN-HEMOGLOBIN REACTIONS: INFLUENCE OF 2,3-DIPHOSPHOGLYCERATE (2,3 DPG) AND pH. R.A. Klocke*, C. Bauer*, and R.E. Forster. Dept. of Graduate Physiology, School of Medicine, Univ. of Penna., Phila., Pa. (Intr. by G. Polgar)

We have measured the association (k') and dissociation (k) velocity constants for the reaction of O_2 with human hemoglobin at 10C in a stopped-flow rapid-reaction apparatus at a wavelength of 430 nm, pH ranging from 5.80 to 8.21, and a heme concentration of 2×10^{-5} M. At 480 nm, 37C, and a heme concentration of 10^{-3} M, we measured only k over the range pH 5.48 to 8.96. At both temperatures measurements were made with and without 5×10^{-3} M 2,3 DPG. Ionic strength was maintained at 0.2 throughout. Hb-O_2 equilibrium curves were obtained in a tonometer-cuvette, for the same conditions as in the kinetic experiments, by adding known amounts of O_2 to reduced hemoglobin solutions and measuring [HbO_2] spectrophotometrically. The P_{O_2} at half saturation (P_{50}) calculated from k'/k was 1.10 ± SD 0.17 times that obtained from the equilibrium measurements. We found that increasing [2,3 DPG] or [H+] accelerates the off-reaction and (at 10C) slows the on-reaction. At pH 7.2 for example, k=6.8 sec^{-1} without and 12.5 sec^{-1} with added 2,3 DPG, k' being 1.32×10^6 and 0.65×10^6 M^{-1} sec^{-1} respectively. The right shift of the HbO_2 equilibrium curve at 37C produced by adding 2,3 DPG (77% increase in P_{50} at pH 7.2) or by decreasing pH (64% increase in P_{50} when pH went from 7.2 to 6.8) could not be entirely explained by the increases in k (32% and 18% respectively).

INTRARENAL SODIUM REABSORPTION IN DOCA ESCAPED DOGS. Franklyn G. Knox, Edward G. Schneider,* Robert E. Lynch,* and Thomas P. Dresser.* Dept. of Physiology, Univ. of Missouri School of Med., Columbia, Missouri.

The intrarenal mechanisms associated with salt retention and subsequent escape from the salt retaining effects of mineralocorticoids have been studied by micropuncture in the dog. Two groups of dogs were given 15 mg desoxycorticosterone acetate (DOCA) daily for 4 days; 17 dogs were fed 63 mEq Na daily and 7 dogs were fed 3 mEq Na daily. Dogs on high Na diet (DOCA escaped) retained 123.6 ± SE 19 mEq Na and dogs on low Na diet (control) had a negative sodium balance of 9.4 ± 5 mEq Na. The tubule fluid to plasma inulin concentration ratio $[(TF/P)_{In}]$ from late proximal tubules of 1.75 ± .09 in DOCA escaped dogs was not significantly different from the $(TF/P)_{In}$ of 1.76 ± .10 in control dogs. Glomerular filtration and single nephron filtration rates were not significantly different between the two groups. Following infusion of hyperoncotic albumin solution, delivery from the proximal tubule was significantly and similarly increased in both groups, however, the increase in sodium excretion in DOCA escaped dogs of 217.2 ± 57.6 uEq/min was significantly greater than the increase of 61.3 ± 13.5 uEq/min in control dogs. The results indicate that some distal nephron segment is the principle site of altered sodium reabsorption in escape from the salt retaining effects of mineralocorticoids. (Supported by NIH FR 5387, HE 12580, and HE 18518).

SYMPATHETIC REACTIVE LOCI OF THE NICTITATING MEMBRANE AND PUPIL IN THE BRAINSTEM OF CATS. Michael C. Koss* and S.C. Wang. Dept. of Pharmacology, Col. of P & S., Columbia U., New York, N.Y. 10032.

CNS stimulation has long been known to produce sympathetic excitation. This investigation was undertaken to determine the specific reactive sites producing dilation of the parasympathectomized pupil and contraction of the nictitating membrane. An area extending from the hypothalamus to the caudal medulla was stimulated with coaxial electrodes in anesthetized and decerebrate cats. Pupillary responses were recorded by means of an electronic pupillometer. Bilateral responses of the nictitating membrane and pupil were obtained in the posterior hypothalamus and the entire ventrolateral reticular area. In these, the ipsilateral component is predominant and becomes increasingly evident in the lower medulla. Responsive points for the nictitating membrane without pupillary dilation were obtained: 1) in the midline regions at the level of the posterior commisure, extending caudally within and adjacent to the central grey of the midbrain, and 2) in a limited dorsal region of the lower medulla. Marked bilateral responses of both effectors were obtained from a ventral midline area in the lower brain stem. Thus, there are several distinct areas, stimulation of which consistently produces efferent cervical sympathetic excitation. In certain areas, however, responses can be elicited without a corresponding dilation of the parasympathectomized pupil. (Supported by PHS GM00438 & NS00031).

EFFECT OF DENTATE COOLING ON MOTOR PERFORMANCE DURING AFFERENT DEPRIVATION. I. Kozlovskaya,* F. Horvath,* A. Atkin,* and V. B. Brooks. Dept. of Physiology, New York Medical College, New York, N.Y. 10029.

The effect of cooling the dentate nucleus on feedback control of voluntary movement was studied in two Cebus monkeys that were trained to move a handle between two target zones on a horizontal arc centered at the elbow. Vision of the task was blocked and the only external indicator of the target was a tone sounded whenever the handle was within the correct target. Occasional withholding of the target tone decreased accuracy of target achievement in control experiments, increasing the amplitudes of the test and subsequent movements. However, when the tone was omitted for an increasing number of successive movements, the monkeys learned to work without it, and yet with the original degree of accuracy. Withholding of the target tone at this stage of training no longer altered movement amplitudes. However, it did alter amplitudes, sometimes to complete disruption of performance, when the dentate nucleus was cooled; or when afferent information from the arm was blocked by pressure. In contrast to tone withdrawal, unexpected presentations of the target tone in unusual positions failed to change significantly amplitudes of test movements. During cooling of the dentate nucleus, however, insertion of the tone significantly altered movement amplitudes in almost any position. Conclusions: In these experiments movements seemed to be guided primarily by internal and secondarily by external cues. When the external cue was withdrawn, movements could be guided accurately by internal cues. Cooling of the dentate nucleus increased the dependence on external cues, implying that the use of internal cues had been interfered with.

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THE BLADDER EXPLANTATION PREPARATION AS A MODEL FOR URETERAL PHYSIOLOGY Peregrina Labay* and Saul Boyarsky. Washington University School of Medicine and Allied Hospitals, Department of Surgery, Genitourinary Division, St. Louis, Missouri.

The surgically explanted bladder, clinically analogous to the congenital extrophy of the bladder, is feasible as a model for ureteral study. It allows easy passage of sensing devices, differential urine collection and visual observation of urinary efflux. The operative mortality and postoperative morbidity have been followed by urograms, urinalysis, pressure studies and autopsies. The animals survived surgical exteriorization of the bladder onto the anterior abdominal wall without deterioration of renal function in over 95% of the cases. Fish-hooking of the lower ureter, ureteral stenosis, urinary tract infections and skin excrescences are complications which can be minimized by external cleanliness, sterile technique and urinary antiseptics. The split bladder preparation showed a higher incidence of ureteral orifice stenosis than the bladder explant. Frequent urograms depict caliber and normalcy of the ureter. Over 9 years, more than 500 animals with bladder explants were studied for 2-6 months each. In the absence of urinary infection, differential urine collections and renal clearances were within normal limits; the ureteral peristaltic pressures and ureteral caliber, by IVU, and peristaltic pressure criteria remained normal. Peristaltic pressures recorded in conscious dogs and in dogs with intact bladders catheterized by cystoscopic means showed comparable pressure recordings to the bladder explant model. Correlated cine and pressure studies confirm these findings and responses of the ureter to drugs show the presence of adrenergic and other receptors. Contractile characteristics were confirmed by the in vitro method.

REPRESENTATION OF THE VISUAL FIELD IN THE SUPERIOR COLLICULUS OF THE GREY SQUIRREL (Sciurus carolinesis) AND THE TREE SHREW (Tupaia glis).
R. H. Lane, J. M. Allman and J. H. Kaas (intro. by R. M. Benjamin). Laboratory of Neurophysiology, Univ. of Wis., Madison, Wis.

Microelectrodes were used to map the representation of the visual field in the superior colliculus in two arboreal diurnal mammals, the grey squirrel and the tree shrew, in which the superior colliculus is extremely well developed. For comparison, portions of lateral striate cortex of both hemispheres were mapped in the same animals. The projection to the superior colliculus both in tree shrew and squirrel differed from that to striate cortex in two ways: (1) the complete visual field of one eye of close to 180° was represented in the contralateral superior colliculus, while the most nasal 30° of the visual field of that eye were represented in ipsilateral striate cortex; and, (2) neurons in the superior colliculus were activated only by stimuli to the contralateral eye while the lateral striate cortex received input from both the ipsilateral eye and the contralateral eye. The projection to the superior colliculus in tree shrew and squirrel resembled that to striate cortex in that a portion of the visual field was disproportionately represented. The region of the visual field corresponding to the intersection of the line of decussation and the horizontal midline of the retina was represented in a larger area of the superior colliculus than other portions of the visual field. (Supported by NIH Grants NS-06225 and NS-05326).

CHANGES IN HUMAN HEMATOLOGIC PARAMETERS UPON BREATHING 100% O_2 AT 760 MM HC
Edward C. Larkin*, William T. Williams* and Frode Ulvedal (intr. by Frode Ulvedal). USAF School of Aerospace Medicine, Brooks AFB, Texas

Four healthy male subjects breathed 100% O_2 at 760 mm Hg for 4 hours via mask duplicating the standard prebreathing of those being exposed to long term hypobaric environments. The following studies were done on each subject 24 hours before exposure to 100% O_2, 5 minutes before exposure, 2 hours during the exposure, immediately after exposure, 2 hours after exposure and 24 hours after exposure: hemotocrit, hemoglogin, red blood cell count, white cell count, reticulocyte count, platelet count (counts X 4) plasma hemoglobin, bilirubin, red cell fragilities, red cell population density determinations, red cell glutathione levels, and red cell glutathione stabilities. Plasma hemoglobin levels changed from a control value of 3.2 mg% as follows: to 8.4 mg% during exposure, to 22.3 mg% immediately after exposure, to 25.4 mg% 2 hours after exposure, to 8.6 mg% 24 hours after exposure. Erythrocytes became more fragile upon exposure to O_2, remaining so at least 2 hours after exposure and reverting toward normal after 24 hours. Red cell densities indicated the red cells became less dense upon exposure to O_2 suggesting the preferential destruction of the older erythrocyte population. Red cell glutathione stability levels were sharply reduced during and immediately after O_2 exposure reverting to normal by 2 hours post exposure. The mean platelet count declined significantly from a control value of 228,800 to 161,900 2 hours following exposure. 24 hours following exposure the platelet count was 195,200. None of the other parameters changed significantly. Brief exposure to hyperoxia at 760 mm Hg pressure results in damage to erythrocytes and possibly platelets which persists long after the initial insult.

EFFECT OF OVARIAN AND ADRENAL HORMONES ON CYCLIC LH RELEASE. Irene E. Lawton. Dept. Physiology, Loyola Univ. Sch. Med. Maywood, Ill.

To assess the influence of ovarian and adrenal hormone secretion during proestrus on release of the ovulatory surge of LH, Sprague-Dawley derived rats exposed to light from 5AM-7PM daily were ovariectomized or adrenalectomized at 10AM proestrus under ether anesthesia. These animals, plus intact and sham (laparotomy) controls, were autopsied later that day at 3PM, 6PM, 8PM or 10PM; another group of intact controls were autopsied at 10AM. Pituitary and plasma samples were frozen for subsequent LH assay using the ovarian ascorbic acid depletion method. Plasma LH in the intact group was significantly higher than 10AM levels by 6PM, and fell to 10AM levels by 10PM. Ovariectomy did not abolish release of the surge of LH, but appeared to advance it, since plasma LH at 3PM was significantly higher than in the intact controls. The elevated LH levels were not due to withdrawal of steroidal negative feedbacks, since plasma LH was non-detectable by 10PM and similar results were obtained in the sham group. Adrenalectomy totally abolished release of the LH surge; plasma LH remained low and pituitary LH content at 8PM was as high as at 10AM, in contrast to the significant decline in pituitary LH content by 8PM in the other three groups. These findings suggest that the advancement of LH release noted in the sham operated and ovariectomized animals was effected by release of adrenal steroids or catecholamines, and that adrenal hormones may be more critical than ovarian hormones at proestrus for triggering the LH discharge. (Supported in part by NSF grant GB-8726)

COMPENSATORY CHANGES DURING ADAPTATION TO THE WEIGHTLESSNESS ENVIRONMENT. C. S. Leach*, W. C. Alexander, and C. L. Fischer*. Clinical Laboratories, Preventive Medicine Division, NASA-MSC, Houston, Texas.

Upon transition from earth's gravity into the weightlessness state, a series of changes are postulated which, when effected, depict the adaptive processes characteristic of exposure to the space flight environment. Although to date, inflight sample collection has, at best, been severely limited and essentially unrewarding, a thorough evaluation of pre and postflight body functions has yielded information upon which a hypothesis for space adaptation has been formulated. Plasma and urinary excretion values of selected endocrine and biochemical parameters have been recorded in space crews prior to and following varying exposures to weightlessness in the Project Apollo series of Manned Missions. Significant pre and postflight changes in body weight; urine and plasma electrolytes; urinary antidiuretic hormone, aldosterone and catacholamines; and in plasma angiotensin suggest an adaptation to the weightless environment with values significantly different from those considered normal in the one g state. These adaptive changes are characterized by an absolute decrease in total body water, a total body potassium deficit, and a predicted compensated intracellular acidosis. While deemed adequate for the null gravity environment, this homeostatic "set" is not without physiological cost, and could reduce the functional reserve of exposed individuals. The hypothesis and supportive data describing this adaptive process is presented and its relevance to long duration exposure to the weightless environment is discussed.

EFFECT OF CHOLERAGENIC PROTEIN ON INTRALUMINAL DISTENTION PRESSURE OF DOG JEJUNUM. Jui S. Lee. Department of Physiology, Univ. of Minnesota, Minneapolis, Minn.

The intraluminal distention pressure (IDP) due to the accumulation of secreted fluid in the presence of choleragenic protein (CP) in the upper jejunum was studied. The maximal IDP developed under a given condition is the hydrostatic pressure which prevents further secretion of fluid and must be related to the maximal secretory activity of the intestine. Dogs were anaesthetized with Nembutal. An isolated 6-8 cm segment of the upper jejunum was closed at one end and fitted with a glass cannula at the other for pressure measurement with a Statham transducer and recording system. CP, which was isolated from the crude cholera toxin of Wyeth Laboratories (Lot 001), was introduced into its lumen. When the dose of CP was 2 - 200 μg per cm length of intestine, IDP was in the range of 13 - 88 mm Hg. Further increase of the dose yielded no higher IDP. The mesenteric arterial pressure was varied by applying a snare over the mesenteric artery of a segment and its pressure was monitored from its side branch. IDP was found to be linearly related to the arterial pressure. For example, in one segment, when the mesenteric arterial pressure was 138, 100, and 75 mm Hg, IDP was 65, 50, and 38 mm Hg, respectively. These findings and other evidence seem to support the filtration hypothesis in fluid secretion in experimental cholera. Supported by NIH grants R22-AI-08692 and AM-05073.

GLYCOGEN IN TURTLE BLADDER, M. LeFevre*, L. Dox*, and W. Brodsky, Mt. Sinai School of Med. and Inst. for Med. Res., N.Y., N.Y., and Brookhaven Natl. Lab., Upton, N. Y.

To evaluate the role of endogenous substrates in transport phenomena, glycogen levels were determined for the turtle bladder under varying conditions of incubation. Glycogen, as g glucose per g wet tissue weight, in fresh whole and split bladders was as follows: whole, 1.97; mucosal (epithelial) fraction, 1.79; serosal (muscle) fraction, 2.24. Since the serosal fraction comprises 67% of whole bladder weight, only 29%, at most, of whole bladder glycogen can be attributed to epithelial cells. After 24 hrs of incubation in substrate-free Ringer (25° C) mucosal glycogen was 29% of original, serosal, 23%. Anaerobiosis caused rapid depletion of glycogen, more disappearing in 45 min under N_2 than in 6 hrs of aerobic incubation in substrate-free Ringer. Substantial resynthesis of glycogen took place on addition of substrate, occurring at about the same rate in both fractions. Short-circuit current and transmural PD of depleted bladders, starting from near-zero levels, increased 4 to 8 hrs after addition of substrate, showing good viability of depleted bladders. In agreement with the finding of Handler et al. for toad bladder (JBC 243:1376, 1968) incubation with 10^{-4} M ouabain for 3 hrs caused a slight (20%), but significant, increase in glycogen content of whole bladder.

EFFECTS OF ULTRASONIC IRRADIATION ON GANGLIONIC TRANSMISSION P.P. Lele, S. Shibata* and J. Running*. Mass. Inst. Tech., Cambridge, Ma.

Irradiation with focused ultrasound has been shown to be the method of choice for the production of trackless focal lesions deep in the brain of experimental animals for ablation studies.[1] The ability to produce reliably reversible functional effects at the focus of the beam of ultrasound in the tissue will permit not only more accurate localization of the target site[2] for ablations studies but will also make it possible to study the function of localized areas in animals with completely intact nervous systems. Experiments were performed on the III and XII cranial nerve nuclei of the cat. Subthreshold dosages of ultrasound were administered in pulsed regimens, using concurrent sonar detection technique[3] to maintain total dosage subnecrotic levels. Changes in the pupil and the tongue musculature were monitered and correlated with irradiation, After ten day survival, the irradiated regions of the brain were prepared for histological examination as serial sections to ascertain the absence of any morphological alterations in the irradiated zone. The physiological basis for the observed results was studied in isolated inferior cervical ganglia of turtles. The results will be compared with those obtained under comparable conditions in peripheral nerves.[4] (Supported by U.S.P.H.S. Grant NS08571)

[1]Basauri, L. and Lele, P.P. (1962)., J. Physiol., 160: 513-534.

[2]Lele, P. P. (1967). Ultrasonics: 105-112:5.

[3]Lele, P. P. (1966). Med. & Biol. Engng. 4: 451-456.

[4]Lele, P. P. (1963). Exper. Neurol., 8: 47-83.

TIME COURSE OF HEMATOLOGIC CHANGES IN CHRONIC LEAD POISONING. Milton A. Lessler and Edward Cardona+. Ohio State University, College of Medicine, Columbus, Ohio, 43210.

To reinvestigate the early signs of lead poisoning, 150 gm male Wistar rats were fed Purina Lab Chow containing 1% lead acetate (PbAc) for 24 weeks. An equal number of paired controls were fed food without added PbAc. Hemoglobin, hematocrit, and reticulocyte and siderocyte counts were determined tri-weekly. Then reticulocytosis was induced by injections of phenylhydrazine in 3 rats from each group. Reticulocytes were isolated for O_2 uptake studies. The cells were hemolyzed and cell membranes isolated for Na^+ plus K^+ dependent ATPase and catalase determinations. Lead-fed rats grew slower than controls, and by the 3rd week had significantly lower body weights, but there were no definite signs of anemia during the first 9 weeks. By the 11th week, the PbAc-fed rats had significantly lower hemoglobin and hematocrit values along with elevated reticulocyte counts. These signs of anemia persisted through the 15th week, but during subsequent weeks began to return toward normal. The lead-fed rats were not anemic by the 23rd week of lead exposure. Apparently as the animals gained weight and matured, the effect of lead exposure on the erythropoietic system was diminished. O_2 consumption of reticulocytes from lead-fed animals was significantly depressed by the 12th week and remained low thereafter. Red cell catalase was elevated above control values on weeks 6 through 12, but fell significantly below controls during the 15th through 24th weeks. Red cell membrane ATPase activity of lead-fed animals was significantly below control values during the entire experiment, indicating that ATPase may serve as a good index of lead exposure. (Supported in part by USPHS Grant AM 09326 and the General Research Support Grant of the USPHS.)

EXPERIMENTAL NEOSTRIATAL BRADYKINESIA ALLEVIATED BY AMANTADINE HYDROCHLORIDE (SYMMETREL ®).

G. Lignelli*, D. Zivanovic*, G.E. Kellett*, G.R. Haase* and E.G. Szekely, Depts. of Neurology and Neurosurgery, Temple Univ. School of Medicine, Philadelphia, Pa. 19140.

Improvement in Parkinson's disease with the use of Symmetrel was first reported by Schwab et al. The report underlined the marked reduction of akinesia. Since the stereotaxically placed lesions in the campus Foreli(Spiegel et al.) frequently relieved rigidity,while the bradykinesia persisted,apparently the two Parkinson's symptoms are at least partly independent of each other. We used experimental bradykinesia produced by tungstic acid gel injection (10 µl) into the neostriatum of rats to investigate the beneficial effect of Symmetrel in animals without spontaneous locomotion. Following injection of 8-10 mg of Symmetrel solution i.m. in rats spontaneous locomotion returned. The improved running often lasted for 24 hrs. or longer depending on the severity of bradykinesia. Both decrease of spontaneous locomotion on chemical stimulation of the striatum and the return of spontaneous running following Symmetrel were highly significant. According to the manufacturer,Symmetrel is well tolerated in rats with high degree of safety. Daily oral doses of 160 mg/kg have been given.

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ELECTROCORTICAL AND BEHAVIORAL EFFECTS OF HIGH-FREQUENCY ELECTRICAL STIMULATION OF SPECIFIC PARTS OF CAUDATE NUCLEUS IN UNRESTRAINED CATS.

Samuel L. Liles. Louisiana State Univ. Medical Center, New Orleans.

A previous study in anesthetized cats showed that high-frequency stimulation of the anteroventral part of the caudate nucleus head could induce rhythmic slow-waves in the ipsilateral frontal area electrocorticogram (ECoG). In this study platinum electrodes were permanently implanted in the caudate and over various cerebral cortical areas to study the effects of high-frequency caudate stimulations in unanesthetized cats. Contraversive turning with ECoG activation was readily elicited by stimulating the posterodorsal caudate area or when relatively high pulse intensities or pulse durations were used. However, high-frequency stimulation (60-200 Hz) of a highly localized area in the anteroventral region of the caudate with limited pulse parameters (0.3-0.6 ma, 0.1-0.5 msec) produced rhythmic slow-waves (RSW) in the ipsilateral frontal area ECoG. The latency of the RSW was 5-20 sec and the RSW ended immediately on cessation of stimulation. During prolonged continuous stimulation the RSW could persist up to 2 min, during which time the frequency of the RSW gradually decreased from about 3/sec to 1/sec and the voltages of the RSW increased from 50 to 150 µv. During the caudate-induced RSW the animal was very still except for deliberate searching movements of the head and eyes in all directions. The development of the RSW was preceded by generalized ECoG activation and behavioral arousal and, in some instances, slight contraversive head turning. The magnitude of these initial behavioral responses was dependent on the pre-stimulation state of arousal, and in desynchronized sleep the RSW appeared without overt behavioral signs. These findings and those of the earlier study suggest that the anteroventral caudate area may have unique functions in the control of electrocortical activity and behavior. (Supported by USPHS, NIH Grant NS08907)

CARDIAC OUTPUT OF CARDIAC HYPERTROPHIED RATS. Yu-Chong Liu* (Intr. by T. A. Rogers) University of Hawaii, Honolulu, Hawaii.

Two types of cardiac hypertrophy were induced; one by daily injections of isoproterenol (5mg/day) for 10 days (group I), and the other by forced swimming (1 hour per day) for 41 days (group II). The development of the cardiac hypertrophy of both the whole heart and the left ventricle was ascertained at autopsy after the measurements of cardiovascular functions. Cardiac outputs were determined by a thermodilution method, with the tip of the thermister in the aortic arch, and saline at room temperature injected rapidly into the right atrium via the right jugular vein. The cardiac output was measured under pentobarbital anesthesia 3-4 days after the last treatment. The cardiac output of the isoproterenol treated rats (group I) was 18% lower than that of controls, which was almost the same as the decrease in heart rate (19%). The cardiac outputs of the group II rats were not statistically different from those of the controls. However, the group II rats exhibited a heart rate lower than that of the control group, indicating a higher stroke volume. (This investigation was supported in part by the University of Hawaii intramural grant).

MAGNESIUM STIMULATION OF CALCITONIN SECRETION IN THE PIG. E. T. Littledike (intr. by R. W. Dougherty). National Animal Disease Laboratory, ARS, USDA, Ames, Iowa 50010.

Magnesium chloride (1.38 M/l) was infused intravenously into pigs and the effect on plasma calcitonin (CT) studied using radioimmunoassay techniques. Following an initial control period magnesium (Mg) was infused for 100 min. and then the plasma magnesium levels were allowed to return to normal. Mg infusion of .002 ml/kg into normal pigs increased plasma Mg from initial levels of 1.39 meq/l to peak levels of 4.1 meq/l. CT increased during this period from .5 mμg/ml to 1.4 mμg/ml. Plasma calcium decreased .8 meq/l and plasma total inorganic phosphorus (P_i) decreased .4 meq/l (during the infusion). When the magnesium infusion rate was increased to .005 ml/kg the peak Mg level was 8.1 meq/l, the peak CT level was 3.6 mμg/ml, plasma Ca decreased 1 meq/l, and plasma P_i decreased .5 meq/l. When the magnesium rate was increased to .01 ml/kg, plasma Mg increased to 11.6 meq/l (extreme narcosis), CT level increased to 8.0 mμg/ml, plasma calcium levels decreased 1.1 meq/l, and plasma P_i decreased .4 meq/l. Infusion of Mg at .0005 ml/min increased plasma Mg only to 1.89 meq/l and produced little, if any, increase in CT secretion. The CT secretion at infusion rates of .002 ml/kg or greater appeared as a double peaked curve with the first peak occurring within 10 min. of the start of the infusion. Mg infusion into thyroparathyroidectomized pigs produced no detectable CT release and an increase in plasma Ca occurred during the infusion. This study showed that CT secretion can be stimulated by Mg and that the increased secretion can occur even under conditions of decreasing plasma Ca concentrations. Mg is not as potent as calcium on a molar basis in stimulating CT secretion.

CORONARY HEMODYNAMIC RESPONSES TO POSTURAL CHANGES IN HEMORRHAGED DOGS. C. T. Liu and R. A. Huggins. Dept. of Physiology, Baylor Col. of Med., Houston, Tex.

When morphine-pentobarbital anesthetized dogs (N=20) were tilted 45° to the head-up position from horizontal for 3 min., the left coronary flow, measured with an electromagnetic flowmeter, was decreased initially and followed by a transient increase. On returning the animal to 0° from the head-up position, the increase in coronary flow was greater than that after a 45° head-up tilt, and the flow rapidly returned to the control level. The coronary flow was decreased slightly 30 min. after hemorrhage to a blood pressure of 70-80 mmHg and was not significantly altered on reinfusion of the dog's own blood. When the hemorrhaged dog was subjected to a 45° head-up tilt, the magnitude of initial drop in coronary flow compared to control dog was increased, but the flow soon rose to the pre-tilt level. After the hemorrhaged dog was returned to 0° from the head-up position, there was an increase in coronary flow similar to that of the control animal. In control dogs subjected to a 45° head-down tilt, the coronary flow showed no significant change. When dogs were hemorrhaged to a blood pressure of 70-80 mmHg and tilted to head-down 45°, the coronary flow did not change, but when the dogs were reinfused, there was a slight decrease in coronary flow. Changes in coronary resistance were opposite in those of flow. (Supported by NIH Grant HE 05435)

AN ELECTROGENIC SODIUM PUMP IN THE FOLLOWER CELLS OF THE LOBSTER CARDIAC GANGLION. David R. Livengood* and Kiyoshi Kusano. Inst. of Psychiatric Res., Ind. Univ. Med. Ctr., Indianapolis, Indiana.

The lobster cardiac ganglion is a functionally independent unit of nine cells which display spontaneous, synchronous firing. The membrane potential of the follower cell is about -52 mV at resting level. On reimmersion of the ganglion in saline containing 15 mM K^+ following a period of exposure to K^+-free saline the membrane potential exhibits a temporal hyperpolarization with a peak of 5-40 mV. Time from onset to peak of this response is about 1 min.; time constant of recovery to the new steady level is about 2.5 min. This hyperpolarization (H-response) has no reversal potential. Membrane conductance either decreased slightly or showed no observable change during the H-response. The H-response is duplicated by Na^+ injection into the cell when the ganglion is in K^+-containing saline, but not in K^+-free saline. Similar amount of K^+ injection does not cause H-response. The H-response is blocked by ouabain, DNP and low temperature. It is also blocked by the replacement of $(Na^+)_o$ with either Li^+ or choline. Tetrodotoxin blocks firing of the burst discharge and reduces the amplitude of the H-response. However, it does not reduce the H-response resulting from increasing $(Na^+)_i$ by injection, indicating that under normal conditions the H-response is activated by Na^+ which enter mainly during the burst discharge. Activation of the H-response in the entire ganglion causes a cessation of burst discharge for few minutes, while ouabain, DNP and K^+-free treatment cause a frequency increase in burst activity. The after burst potential which shows small hyperpolarization (0-5 mV) has a reversal potential that shifts with $(K^+)_o$ changes. It is concluded that the H-response is due to the activation of the $(K^+)_o$-dependent electrogenic Na^+ pump which is able to modulate the frequency of the burst activity of the cardiac ganglion. (Supported by PHS 2F01 GM33019)

EFFECT OF PERSON COMPARED WITH SHOCK ON HEART RATE (HR) AND ON DIURESIS. Andrew Livingston, Jr.*, Joan M. Starr* and W. Horsley Gantt. VA Pavlovian Lab., Perry Point, Md.

Two naive females in which both ureters had been transplanted to the surface of the abdomen were used. The two procedures were: I. For 5 days the following conditions were employed for 15' each. a) dog alone, b) person standing near dog, c) faradic shock to foot, d) person petting, e) petting with shock. Results: Urine: a) 6.8 cc., b) 7, c) 12, d) 9.8, e) 7.4. HR: a) 87, b) 98, c) 128, d) 110, e) 113. II. A second procedure after the 5 days was: the same 5 conditions for 5' each 3 times per day instead of 15'. Results of this repetition of the shorter periods: Urine: a) 11.6, b) 11.5, c) 10.8, d) 10, e) 10.7. HR: a) 106, b) 112, c) 112, d) 124, e) 122. Catecholamines showed no definite trend. Na, K, creatinine values will be presented. Interpretation: There is a marked difference in whether each of the 5 conditions continued for 15' or for only 5'. The 15' shock caused the greatest increase in both urine and HR; petting reduced effect of shock. Using the same situations for 5' repeated 3 times daily there was no change in urine secretion but a marked increase in HR from the start (106) to the end (122) of the daily experiment. The HR also increased gradually from day to day, but not the urine. There was a marked effect of person especially on HR; but the results depend upon the time arrangement of the experiment. Comparing the diuresis with HR: they are parallel in the 15' periods, but for 5' the diuresis is less fluctuating. Effect of person is greater on HR than on diuresis. This difference in action on the cardiovascular and renal systems seems related to organ responsibility.

Plasma enzyme levels in anesthetized dogs after hypoxia and muscular activity. Daniel J. Loegering* and Jerry B. Critz. The University of Western Ontario, London, Ontario. Canada.

Exercise results in increased plasma levels of several cellular enzymes. Several mechanisms have been proposed to explain this increase, among them, the development of a relative hypoxia in the active muscles. The purpose of our study was to test this latter hypothesis. Paralyzed, anesthetized dogs were ventilated with 12, 10, 8.5 7.5% O_2 (balance N_2) for 30 min. or with 5% O_2 for 15 min. Muscular activity was produced by electrical stimulation of the hind leg muscles of anesthetized dogs for 30 min. at either 5 or 10 pulses/sec. Plasma enzyme levels were determined before, at the end of, and at ½, 1, 2, 4 and 6 hours after the hypoxic episode or muscle stimulation. The threshold for release of glutamic-oxalacetic transaminase (GOT) was between the level of hypoxia produced by ventilation with 7.5 and 8.5% O_2 (arterial PO_2=11 and 17 mm Hg respectively). Creatine phosphokinase (CPK) and lactic dehydrogenase (LDH) had thresholds for release between 10 and 12% O_2 (arterial PO_2=24 and 31 mm Hg respectively). There was no change in plasma enzyme levels with muscle stimulation at a rate of 5 pulses/sec. Muscle stimulation at a rate of 10 pulses/sec. resulted in an increase in plasma GOT (PGOT) and plasma LDH (PLDH) activities. A similar femoral venous PO_2 was produced by either muscle stimulation at 10 pulses/sec. or ventilation with 10% O_2. There was, however, no increase in plasma CPK (PCPK) after muscle stimulation. PGOT and PLDH activities showed a much more transient response to muscle stimulation than to hypoxia. It was concluded that hypoxia may be a contributing factor, but is not the primary cause of the plasma enzyme response to exercise.

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REACTIVITY OF VASCULAR SMOOTH MUSCLE TO A TERTIARY DIAMINE.
M. Losada*, J.P. Buyniski, and M.E. Bierwagen*. Cardiovascular Section, Bristol Laboratories, Syracuse, N. Y. 13201.
The effects of intravenous administration of a tertiary diamine, a derivative of trimethoxybenzoic acid, N,N'-bis[3',(3",4",5"-trimethoxybenzoyloxy)-propyl]hexahydro-1,4-diazepine, was studied in dogs during measurement of organ blood flows and perfusion pressures. Cerebral blood flow was recorded by cannulating the confluence of the cerebral sinuses and, with the lateral sinuses occluded, passing the cerebral venous outflow through an electromagnetic flowmeter (EMF) probe. Renal, skeletal muscle, coronary and aortic flows were recorded by means of non-cannulating EMF probes. Intravenous doses of up to 0.3 mg/kg of the tertiary diamine produced little change in systemic pressure, heart rate, the maximum rate of rise of left ventricular pressure (dp/dt) and left ventricular oxygen consumption. However, during this time there were pronounced increases in coronary vascular conductance (up to 230 % of control vascular conductance) and increases in cerebral vascular conductance (up to 135 % of control vascular conductance). The increase in cerebral vascular conductance was reflected also by small increases in cerebral spinal fluid pressure measured by way of the cisterna magna. The increases in coronary and cerebral vascular conductance were of long duration (> 40 min.) and indicated vasodilation of the coronary and cerebral vasculature. Only minimal or no changes were observed on skeletal muscle, renal and aortic blood flows. The increased conductance responses of the heart and brain circulations to intravenous injections of the tertiary diamine may reflect modulation of similar local control mechanisms regulating blood flow in brain and heart.

EFFECT OF ARTERIAL AND VENOUS PRESSURE MANIPULATIONS ON ISOGRAVIMETRIC CAPILLARY PRESSURE AND VENOUS RESISTANCE. M.J. Lund, P.B. Dobrin and A.A. Rovick. Loyola University School of Medicine, Department of Physiology, Maywood, Illinois 60153 and the National Institutes of Health.

Capillary pressure as well as arterial and venous resistances were determined by means of the isogravimetric technique in an isolated, skinned, dog forearm preparation. In each experiment, isogravimetric capillary pressure was obtained by two sets of paired pressure alterations: 1) by first lowering arterial pressure and then elevating venous pressure (↓A, ↑V sequence) and 2) by first elevating venous pressure and then lowering arterial pressure (↑V, ↓A sequence). In 83% of the cases, isogravimetric capillary pressure determined by the ↑V, ↓A sequence was higher than the isogravimetric capillary pressure determined by the ↓A, ↑V sequence. The ↓A, ↑V sequence also showed higher venous resistence which was attributed to the activity of post capillary smooth muscle. This interpretation was supported by the observation that perfusion of the limb with potassium cyanide abolished the differences in both isogravimetric capillary pressures and venous resistances obtained by the two sequences. A radioisotope dilution technique (RISA) verified that the isogravimetric state, as determined by weight measurements, did, indeed, reflect zero net transcapillary fluid exchange. (Supported by NIH grants HE 08682 and GM 00999.)

INHIBITION OF OVARIAN COMPENSATORY HYPERTROPHY BY INTRAHYPOTHALAMIC IMPLANTATION OF METHALLIBURE. P.V. Malven, J.A. Clemens* and C.H. Sawyer. Dept. Anat. and Brain Res. Inst., UCLA, Los Angeles, Calif.

The anti-gonadotrophic compound methallibure (ICI 33828) has been shown to inhibit ovarian compensatory hypertrophy (OCH) when administered to hemiovariectomized rats (J. Endo. 30: 399, 1964). The present experiment investigated whether intrahypothalamic implantation of methallibure would produce similar results. Methallibure, contained within the lumen of 30 gauge stainless steel tubing, was implanted bilaterally into the medial basal hypothalamus of intact cyclic rats. Control females received empty implant tubes. All implanted animals showed a normal sequence of proestrous and estrous vaginal smears after implantation, and on the first day after this sequence the left ovary was removed to check for new corpora lutea (CL). Nineteen days after hemiovariectomy, the rats were killed and the weight of the right ovary was expressed as a percentage of the weight of the left ovary (OCH). Implantation of methallibure significantly reduced OCH (107 ± 9 vs 158 ± 8). The initial post-implantation ovulation was blocked in 6 out of 12 methallibure implanted animals and in 3 out of 10 controls. Ovulation was prevented for the entire experimental period in only 2 treated animals. Careful histological examination of serial sections of the right ovary combined with the vaginal smear data allowed estimation of the number of different generations of post-treatment CL. The estimate averaged 1.8 for the methallibure implanted animals and 3.8 for the controls. The average number of CL comprising the most recent generation of CL was 10.0 and 11.6 respectively for treated and control animals. These results suggest that intrahypothalamic methallibure inhibited the proestrous release of ovulation-inducing hormone in some but not all cases. Whenever ovulation did occur in treated animals, a relatively normal number of CL were formed.

CATHODOLUMINESCENCE PRODUCED IN PROTEINS BY VAPORIZED PARAFORMALDEHYDE (VP) AS SEEN WITH THE SCANNING ELECTRON MICROSCOPE (SEM). W. M. Manger and Marcel Bessis*. N.Y.U. Med. Ctr. N.Y.C. and Inst. de Path. Cellulaire, Paris, France.

Previously no satisfactory method for producing cathodoluminescence in cells and tissues had been described. Methods reported gave relatively weak luminescence which dissipated markedly or ceased after irradiation by the electron beam. We have found that exposure of cells to VP causes an intense and relatively stable cathodoluminescence. Cells were obtained by gentle centrifugation from heparinized human blood after allowing partial sedimentation for two hours, and also from fluid removed several minutes after injecting into the peritoneal cavity of the rat 10-20 ml of isotonic saline containing a small amount of heparin. Sometimes cells were fixed with 3% glutaraldehyde and washed several times with distilled water. A small drop of fluid and cells was smeared and allowed to dry on the conventional stub used for examination in the SEM. The stubs were then exposed to VP at a temperature of about 90°C for 1½ hours. Luminescence was greater in white than red blood cells. Concentrated Gamma globulin, albumin and dried plasma also became intensely luminescent and fluorescent when exposed to VP and viewed respectively with the SEM or fluorescence microscope. This latter finding should be appreciated when considering specificity in fluorescent techniques employing VP to localize biogenic amines since protein per se can react with VP to yield autofluorescence in cells and tissues. Intense luminescence induced in proteins by VP as seen with the SEM may prove valuable in detecting antibodies on cell surfaces. (Supported partly by the Manger Res. Fnd.)

CUTANEOUS SUBDIVISION OF THE DORSAL SPINOCEREBELLAR TRACT. M. D. Mann* and D. N. Tapper. Dept. of Physical Biol. & Section Neurobiol. and Behavior, Cornell Univ., Ithaca, N.Y. 14850

The composition and properties of the cutaneous subdivision of the dorsal spinocerebellar tract (DSCT) were studied by recording in the dorsolateral funiculus (DLF) from axons identified by antidromic activation from the inferior cerebellar brachium. The locations of the axons within the DLF and the exact location of the stereotaxically placed brachial stimulation electrode were determined histologically for each cat. Conduction velocities calculated from antidromic latencies ranged from 40-110 m/sec. Four classes of cutaneous DSCT cell were identified: (1) those activated by primary afferents associated with both rapidly (Type G, D, & T) and slowly adapting receptors (Type I), (2) those activated by primary afferents associated with slowly adapting receptors only, (3) those activated only by primary afferents associated with rapidly adapting receptors, and (4) those activated by primary afferents from skin and muscle or other deep structures. Because of the special properties of Type I afferents it was possible to determine for classes (1), (2) and (4): that there was extensive convergence of primary afferents upon DSCT cells, that a single presynaptic impulse can cause a spike discharge in the postsynaptic DSCT cell, and that the slowly adapting characteristic response of the afferent is maintained. Activation of DSCT from Type I cutaneous afferent fibers suggests a role for the tactile pad receptor system in the coordination of movement. (Supported by USPHS Grants NS07505 and GM00223).

THALAMIC RESPONSES TO RAPID THERMAL CUTANEOUS STIMULATION, Henry F. Martin III* and John W. Manning, Dept. of Physiology, Emory University Atlanta, Georgia 30322. We have reported the development of a thermal probe which causes a transient warming of peripheral skin fields lasting 50-20msec. without pressing or touching the skin. This form of stimulus has been shown to result in both Aδ and C fiber activity in peripheral nerve. The present study has sampled unit activity in the ventro-basal thalamus resulting from this rapid thermal stimulus. Extracellular recordings were made with NaCl filled micropipettes in Chloralose anesthetized cats. A portion of the units recorded in the ventro-basal thalamus responded to thermal probe stimulation of the skin with a burst of 2 to several spikes with a latency of from 9-20 msec. The thresholds for activation of these units ranged from a temperature change of 2°C to 4°C as measured by a subcutaneous thermocouple. The units responding to thermal stimulation also were activated by light tactile stimulation of the skin field. The receptive fields were well localized areas of one to several square centimeters limited to a portion of a single limb or body surface. Somatotopic representation for these units was comparable to other reports for the ventro-basal thalamus. The receptive field for each of the units responding to the thermal probe was also stimulated by steady radiant heat, while recording changes in ongoing unit activity. Although the changes tended to be obscured by the irregular background activity, two general patterns were observed. Some units showed an increase in firing during warming and a decline when the heat source was removed, while other units responded in an opposite manner. By means of these two types of stimulation we have demonstrated that not only the overall rate of activity but also the characteristic thalamic bursting pattern is altered by thermal stimulation. (supported by USPHS, NIH Grant NB-02645).

EFFECT OF INCREASED GAS DENSITY ON RESPIRATORY GAS EXCHANGE IN THE ANESTHETIZED DOG. R.R. Martin*, N.R. Anthonisen and M. Zutter*. Respiratory Division, Royal Victoria Hospital, McGill University. Montreal, Quebec, Canada.

If stratified inhomogeneities of gas concentration within the lung represented a potential barrier to gas exchange, then increasing the density of the inert fraction of the inspirate should hinder gas exchange. Using a constant volume respirator we ventilated anesthetized dogs with SF_6, He and air at 1 ATA, and 5% O_2 - 95% N_2 and 5% O_2 - 95% SF_6 at 4 ATA. O_2 should diffuse about 20 times as well as in He at 1 ATA as in SF_6 at 4 ATA. Arterial, mixed venous mixed expired and end-tidal PO_2 and PCO_2 were measured in each instance under steady state conditions. No significant difference in dead space-tidal volume ratios were noted under any condition. Alveolar-arterial O_2 difference and venous admixture were not influenced by gas density unless the extremes - He at 1 ATA and SF_6 at 4 ATA were compared. Most dogs showed smaller alveolar-arterial O_2 differences when breathing SF_6 at depth than breathing He at the surface. We conclude that either 1) failure of gaseous diffusion equilibrium in small air spaces does not occur, or 2) that density dependent increases in stratified inhomogeneity are cancelled by other factors such as turbulent mixing in small airways.

Supported by the Defense Research Board and the Medical Research Council of Canada.

TESTICULAR ADENYL CYCLASE IN GONADOTROPHIN- AND THYROXINE-TREATED HYPOPHYSECTOMIZED RATS. E. D. Massie*, W. R. Gomes and N. L. VanDemark, Animal Reproduction Teaching and Research Ctr., Ohio State University, Columbus, 43210.

The response of testicular adenyl cyclase to hormone treatment was measured in hypophysectomized male Wistar rats after treatment with follicle stimulating hormone (FSH), interstitial cell-stimulating hormone (ICSH), or thyroxine (T_4). Groups of 15 hypophysectomized rats were sacrificed after a 3-day treatment with 100 µg/day of FSH or ICSH, 5 µg/day of T_4, or ICSH + T_4. Testes from treated rats, hypophysectomized controls and intact controls were incubated in vitro for 10 min with 8-^{14}C-ATP, and the radioactivity in cyclic 3',5'-AMP was measured as an estimate of adenyl cyclase activity. Testes from hypophysectomized and intact rats produced 205 ± 42 (mean ± SE) and 1293 ± 80 cpm/mg tissue, respectively ($P < 0.01$). Neither FSH (199 ± 23 cpm/mg) nor T_4 (238 ± 36 cpm/mg) treatment changed enzyme activity from levels found in hypophysectomized rats, but ICSH increased ($P < 0.01$) activity to 450 ± 38 cpm/mg and ICSH + T_4 increased adenyl cyclase (1320 ± 83 cpm/mg; $P < 0.01$) to intact control levels. These data suggest that testicular adenyl cyclase is stimulated by ICSH and that T_4 enhances this effect. (Supported by USPHS Grant HD 03822.)

HYPOXIC REFLEX FAILURE AND METABOLIC CORRELATES TO NEURONAL FUNCTION IN THE ISOLATED FROG SPINAL CORD. Donald A. McAfee, Department of Physiology, University of Oregon Medical School, Portland, Oregon 97201.

Experiments designed to influence metabolism while monitoring function were performed on the isolated frog spinal cord. Quantitative estimates of motor neuron discharge, obtained by electronic integration of spinal nerve potentials, provided a means for determining the effects of metabolic alterations on reflex discharge. The pattern of monosynaptic and polysynaptic reflex failure during hypoxia was studied. On the average, monosynaptic and polysynaptic reflex activity diminished to 50% of the control level in 52 and 40 minutes, respectively. Interpretation of focal potential records indicated that the lateral column axon and its terminals were the first elements of the monosynaptic reflex path to fail, and the motor neuron was the last. The rate of hypoxic reflex failure was hypothesized to be a function of the metabolic rate of the tissue. Increasing the metabolic rate from nervous activity by increasing stimulus rate 10 times did not increase the rate of reflex failure. However, the rate of hypoxic reflex failure was seen to be directly proportional to the ambient temperature (Q_{10}=2.5). It was concluded that the energy demand of reflex activity is small compared to the demand for maintenance of excitability. Treatment of the preparation with varying doses of ouabain resulted in reflex failure quite unlike that seen during hypoxia. Reflex failure was rapid and oscillatory and failure occurred in the pre- and post-synaptic structures at about the same time. It is suggested that the vulnerability to the effect of hypoxia, though ultimately produced by failure of ion transport, may be conditioned by the availability of metabolic energy reserves which are different in the various portions of the neuron. Supported by PHS GM-00538

THE EFFECT OF α AND β ADRENERGIC SITE BLOCKING AGENTS ON CATECHOLAMINE STIMULATION OF ISOLATED FROG SKIN. R.D. McAfee and R. Menendez-Cordova*. Tulane University School of Medicine and VA Hospital, New Orleans, La.

The use of the isolated short circuited frog skin has been extended to a study of the action of the α and β adrenergic site blocking agents on epinephrine (E), norepinephrine (NE) and isopropylarterenol (IPA). We used left and right abdomen or thigh skin from the same frog in paired experiments to compare the effect of the catecholamine alone with that of the catecholamine following pretreatment with the blocking agent in 12 experiments on each drug. Phenoxybenzamine (Dibenzylene SK&F) was used at 1.6×10^{-5} M/l concentration on the inside of the frog skin and allowed to incubate for one hour before adding catecholamine. Propranolol (Inderal, Ayerst) was used at 10^{-5} M/l concentration on the inside of the frog skin and 30 minutes later catecholamine was added. This procedure was necessary to obtain effective blockade. As determined by Students t test, Dibenzylene blocked the stimulation produced by NE on the control skin half ($P < .02$) and also the stimulation produced by E ($P < .05$) and by IPA ($P < .02$). Note that this presumed α adrenergic site blocking agent also blocked a β site stimulating catecholamine (IPA). Inderal blocked the stimulation of short circuit current produced by IPA ($P < .02$) and NE ($P < .05$) but did not block the stimulation produced by E (P, N.S.). The blockade of an α site stimulating catecholamine (NE) by Inderal and the failure of Inderal to block any of the stimulation produced by E in control skins, was not expected. The blocking of IPA by phenoxybenzamine shows that its use to block the α effect of E and thereby reveal the β effect of E is not always justified. The isolated frog skin is a unique and possibly useful model for the study of the effect of catecholamines and their blocking agents.

Neurophysiological Changes Associated with Hypovolemia. Ernest P. McCutcheon,* Donald T. Frazier, and Louis L. Boyarsky. Univ. of Ky. Med. Ctr., Lexington, Ky. 40506

The effects of hypovolemia on the responsiveness of the central nervous system was examined in anesthetized cats and dogs. Cortical and cuneate evoked responses and EEG were studied during the various stages of hypovolemic shock. Shock was produced by the withdrawal of a quantity of blood into a reservoir in order to maintain mean systemic pressure between 40 and 50 mm Hg. After spontaneous uptake of approximately 30% of the withdrawn blood, all remaining blood was reinfused. In 16 out of 18 animals, a decrease in amplitude of the cortical evoked response preceded or was concomitant with the period of spontaneous uptake of blood. In two dogs, the cortical evoked response did not change before spontaneous uptake, but did decrease in the reinfusion period. In the other 6 dog experiments, the cortical evoked potential was completely abolished before spontaneous uptake of blood occurred. Similarly in 6 out of 10 cats the cortical evoked response disappeared before uptake began. In the other four cats, the cortical evoked potential began to fall prior to spontaneous uptake but did not disappear until later in the uptake period. Evoked responses from the cuneate persisted at control levels after the disappearance of the cortical evoked responses. Changes in amplitude of the EEG paralleled the changes noted in the cortical evoked response. There was no correlation between changes in systemic blood gas levels or pH and the disappearance of the electrical events. The fall in evoked cortical potential appears to provide a good indication of impending failure to maintain systemic arterial pressure. (Supported in part by Air Force Office of Scientific Research Contract FF44620-69-C-0127) and General Research Support Grant of Univ. of Ky. [NIH-5-501-FR05374].)

CARBON MONOXIDE TOLERANCE OF THE YOUNG CHICK. James J. McGrath and James J. Jaeger (Intr. by Paul D. Sturkie). Rutgers - The State University, New Brunswick, N.J. 08903.

Chicks 0-3 weeks old were exposed to a humidified flow of 1% carbon monoxide in an exposure chamber in which temperature was held constant at 35°C. Survival time as a function of age was determined and is defined as that period of exposure in minutes at which 50% of the animals lived. Body weights and hematocrit ratios were determined prior to the exposure to carbon monoxide. Body temperature was measured throughout the exposure by means of a rectal probe. Newly hatched chicks were more resistant to carbon monoxide and survived for up to 25 minutes. Chicks 3 days of age had a mean survival time of 7.5 minutes. Survival times declined to 4 minutes in birds 7-8 days of age, and thereafter remained constant. Hematocrit ratios increased slightly from 27.7% in newly hatched birds reaching levels of 31.3% by 3 weeks of age. The younger birds underwent a greater decrease in rectal temperature in response to carbon monoxide exposure.

EFFECTS OF K^+ CONCENTRATION ON Na^+ AND Cl^- TRANSPORT BY ISOLATED RAT ILEUM. J. R. McKenney, Dept. Physiol., Med. Col. Ga., Augusta, Ga.

A major objective of this study was to determine if observations of net Cl^- transport against an electrochemical difference for Cl^- across isolated rat ileum could be attributed to passive coupling between anion and cation diffusion. Everted segments were used in apparatus for P.D. and flux measurements for ^{22}Na, ^{36}Cl, and ^{3}HOH. Incubation media included 15 mM fructose and 25 mM HCO_3^-, in which mannitol and $SO_4^=$ were substituted for Na^+, Cl^- and K^+ to maintain osmolarity. With $[K^+]$, $[Na^+]$ and $[Cl^-]$ respectively 5, 48 and 20 mM, net Na^+ and Cl^- transport were nearly equal, and with $[K^+]$ = 50 mM their transport was depressed. This effect was reversible. With $[K^+]$ = 50 mM, permeabilities for ^{22}Na, ^{36}Cl and ^{3}HOH over a wide range of Na^+ and Cl^- concentrations could be equated by the relationships $P_{Cl}([Cl^-] + [HCO_3^-]) \cong P_{Na}([Na^+] + [K^+])$ and $P_{HOH} \cong \frac{P_{Na}([Na^+] + [K^+]) + P_{Cl}([Cl^-] + [HCO_3^-])}{\sqrt{([Na^+] + [K^+])([Cl^-] + [HCO_3^-])}}$. With $[K^+]$ = 5 mM, the condition $\text{Ln}\,([Na^+] + [K^+])([Cl^-] + [HCO_3^-])_s = -(2F/RT)(E_s - E_m) + \text{Ln}\,([Na^+] + [K^+])([Cl^-] + [HCO_3^-])_m$ was approached, where $_s$ and $_m$ designate the serosal and mucosal incubation media. These results support observations that rat ileum has properties similar to negatively ionizable membranes, and indicate that the Nernst and Ussing relationships for independent ion diffusion do not apply in the case of rat ileum. However, the close coupling of net Na^+ and Cl^- transport and magnitude of the $m \rightarrow s$ fluxes for ^{36}Cl required the conclusion that there was a transport mechanism for Cl^-. Work supported by U.S.A.E.C. Contract No. AT-(40-1)-3882.

GLYCOLYTIC AND GLUCONEOGENIC ENZYME LEVELS IN PRE- AND POSTNATAL PIGS. H. J. Mersmann (intr. by C. A. Privitera). Pharmacology Dept., Shell Development Company, Modesto, Ca. 95352

Piglets of various ages, both pre- and postnatal, were examined for the levels of activity of liver enzymes primarily concerned with glycolysis or gluconeogenesis. The activities of both pyruvate kinase and phosphofructokinase were minimal on the day of birth, reached maximum at 14-21 days, and then declined. Hexokinase activity did not change while glucokinase activity gradually increased during the experimental period. Pyruvate carboxylase did not change while phosphoenolpyruvate carboxykinase activity doubled by day 2 from a substantial 0 day level. Peak activity was reached by day 21. Glucose 6-phosphatase activity gradually increased during late fetal life, was abundant on the day of birth and doubled by day 2. There was a decline in activity after this time. Fructose 1,6-diphosphatase activity was low on the day of birth, had abruptly increased by day 2, reached a maximum by day 21 and then declined. This seems to be the rate-limiting enzyme involved in liver gluconeogenesis in newborn pigs. These data, when compared with similar studies in other species, illustrate species-specific patterns in the development of neonatal enzymes.

AUDITORY SPECIALIZATION IN A BURROWING RODENT, THE MOUNTAIN BEAVER (Aplodontia rufa). Michael M. Merzenich and Lindsay M. Aitkin (intr. by Jerzy E. Rose). Laboratory of Neurophysiology, University of Wisconsin, Madison, Wisconsin.

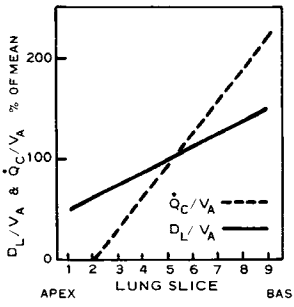
In the course of examination of the cochlear nuclear complex in a comparative series of over 100 mammalian species, striking evidence of specialization has been found in the mountain beaver. The unusual alaminar dorsal cochlear nucleus (DCN) in this species is 4-5 times as large (in relation to body weight or brain size) as in other rodents examined. The cochlear granular cell fields are also very large, comprising nearly half the volume of the cochlear complex. The cochlear nuclear complex has been explored with microelectrodes, and isolated neurons in DCN have been found to respond with great sensitivity to fluctuations in pressure at rates slower than 10 Hz. One population of neurons is driven by low frequency acoustic stimuli. An increase of pressure in the outer ear canal causes discharges of these neurons. Spontaneous activity of a second population is reduced or abolished by such stimuli. Many but not all neurons excited or inhibited by pressure are also affected by low frequency tonal stimuli (10-2000 Hz). Response to pressure is believed to originate in the cochlea. Best frequencies of a small sample of neurons of the ventral cochlear nucleus ranged from 50 to 17,000 Hz. Response properties of these neurons are similar to those described for VCN neurons in other species. Preliminary histological examination of the cochlea suggests that the scala tympani is unusually narrow toward the apex. (Supported by NIH Grants NS-06225 and NS-05326).

OXYGEN AFFINITY AND 2,3 DIPHOSPHOGLYCERATE LEVELS IN CHRONIC HYPERCAPNIA. Arthur A. Messier* and Karl E. Schaefer. Submarine Medical Research Laboratory Groton Connecticut 06340.

We have previously reported that chronic hypercapnia causes biphasic changes in oxygen affinity related to biphasic changes in pH and intraerythrocyte cation levels (Schaefer and Messier. Fed. Proc. V28, No. 2577, p720, 1969). Additional studies measuring 2,3 diphosphoglyceric acid using Lowry's fluorometric method were carried out under the same experimental conditions: exposure of guinea pigs to 15% CO_2 in 21% O_2 for periods up to seven days. Results showed biphasic changes in 2,3 diphosphoglycerate levels which exhibited a correlation of .96 with the changes in oxygen affinity (P_{50}).

VERTICAL DISTRIBUTION OF PULMONARY DIFFUSING CAPACITY (D_L) AND CAPILLARY BLOOD FLOW ($\dot{Q}_C$) RELATIVE TO ALVEOLAR VOLUME (V_A). E.D. Michaelson*, M.A. Sackner, and R.L. Johnson, Jr. Wilford Hall USAF Med. Ctr., Lackland AFB, Tex.; Mt. Sinai Hosp., Miami, Fla.; and U. Tex. (Southwestern) Med. Sch. at Dallas, Dallas, Tex.

In 5 normal upright subjects a 100-ml bolus of 1/3 each neon, carbon monoxide, and acetylene (Ne, CO, and C_2H_2) was rapidly injected into the inspirate at either residual volume (RV) or functional residual capacity (FRC) during a slow inspiration from RV to TLC; the breath was held and D_L/V_A and $\dot{Q}_C/V_A$ were calculated from the rates of CO and C_2H_2 disappearances relative to Ne. Means: D_L/V_A = 5.49 ml/min x mm Hg/L (bolus at RV), 6.88 ml/min x mm Hg/L (at FRC); $\dot{Q}_C/V_A$ = 0.579 L/min/L (bolus at RV), 1.021 L/min/L (at FRC). Similar maneuvers with boli of Xe-133 in each subject confirmed that during inspiration from RV to TLC more of the bolus goes to the upper zone if introduced at RV and more to the lower zone if introduced at FRC (Resp. Physiol. 2:234, 1967). From discrepancies in the data obtained from CO, C_2H_2, Ne boli given at RV and FRC a lung model has been constructed which describes how D_L/V_A and $\dot{Q}_C/V_A$ must be distributed to satisfy the experimental data (see figure).



RESPIRATORY RESPONSES TO INCREASED CO_2 LOADS IN EXTERNALLY CLOSED-LOOP CHICKENS. D.A. Miller*, A. L. Kunz, and R. M. Weissberg*. Department of Physiology, The Ohio State University, Columbus, Ohio 43210.

Open-loop analysis of respiratory control in the unidirectionally-ventilated chicken shows the presence of proportional and integral control and the absence of derivative control (Kunz, 1970). The experiments to be reported used a similar unidirectionally-ventilated chicken preparation. The respiratory control loop was closed, however, by having the respiratory movements control the % CO_2 in the alveolar air. A signal representing inspiratory flow computed from the output of a whole body plethysmograph was fed into an integrator with an independent forcing function input, $\dot{Q}\bar{v}CO_2$, representing CO_2 load from the venous return. The output of the integrator directly controlled alveolar PCO_2 of the chicken. Alveolar CO_2 was continuously increased by $\dot{Q}\bar{v}CO_2$ and decreased by each V_I. Analog computer simulations derived from our open-loop data successfully describe the following closed-loop behavior under CO_2 load: 1) steady state alveolar PCO_2 was maintained at a constant value without offset error over a wide range of CO_2 loads ($\dot{Q}\bar{v}CO_2$), 2) ventilation was linearly proportional to CO_2 load ($\dot{Q}\bar{v}CO_2$) and 3) the ventilatory response to a transitory disturbance in alveolar CO_2 in this system may be characterized as second order, although the damping ratio appears not to be fixed. (Supported in part by O. N. R. Grant N. R. 101-733).

FEEDING INDUCED BY 2-DEOXY-D-GLUCOSE INJECTIONS INTO THE LATERAL VENTRICLE OF THE RAT. Richard R. Miselis* and Alan N. Epstein, Dept. of Biology & Sch. of Vet. Medicine, Univ. of Penna., Philadelphia, Pa.

Ten rats (5 ♂ and 5 ♀) weighing 270-421 g were prepared with a single cerebral intraventricular cannula and were tested in a counterbalanced experimental design with 3.05 osmolal solutions of 2-deoxy-D-glucose (2-DG, an intracellular competitive inhibitor of glucose metabolism), glucose and sucrose. Each rat was tested twice with 2-DG and once with both glucose and sucrose. They were maintained on Purina rat pellets and water ad lib and were not deprived before testing. Feeding on an injection day was compared to spontaneous feeding during the same 4-hr. baseline period on the previous day. One week elapsed between all injection days. Each rat was given either one or two 7-ul injections (5 min. apart in the latter case), infused over a period of 60 sec. The average increase in feeding over that of the baseline in response to 2-DG was 2.6 g. All rats ate more. Average changes in feeding in response to both sucrose and glucose were small (+0.3 g) and insignificant. The average latency to feeding in response to 2-DG was 15.5 min. Initial studies in other rats indicate that intrahypothalamic injections of 2-DG do not alter food intake. There is a dose-dependent drop in core temperature with systemic injections (ip) of 2-DG. However, with central application of 2-DG there is no significant change in core temperature, demonstrating that the feeding is not mediated by hypothermia. These data are interpreted as direct evidence for the hypothesis that central neural glucoprivation (decreased intracellular glucose utilization) at an as yet unidentified locus is a stimulus for feeding and that central glucoprivation alone is sufficient to mobilize food intake. (Supported by NS 03469 and the Nutrition Foundation.)

A RE-INVESTIGATION OF THE MECHANISM OF MUSCLE PARALYSIS IN HYPERTONIC SOLUTIONS. M. D. Miyamoto* and J. I. Hubbard. Northwestern Univ., Evanston, Ill.

Controversy as to the mechanism of muscle paralysis in hypertonic solutions has resulted in two hypotheses, one centering on the excitation-contraction (E-C) link and the other on the effects of the internal ionic strength upon the contractile process itself. We have repeated the experiments which are interpreted as supporting an effect on the E-C link and in addition weighed the preparation (frog sartorius muscle) at 10 min intervals during these experiments, thus assessing quantitatively the degree of dehydration produced by the exposure to hypertonic solutions. These experiments include the "glycerol effect" — a phenomenon in which contractibility of muscle returns in hypertonic glycerol Ringer. Re-examination of this effect showed however that after the weight loss upon exposure to glycerol, there was some recovery of weight detectable after 30 min, interpreted as a rehydration. Moreover on return to a normal Ringer, there was a further large weight increase, the magnitude of which was dependent on the duration of the period in glycerol Ringer. The glycerol effect can thus be explained in terms of a rehydration and a loss of fiber cations both due to the entry of glycerol, which lowers the internal ionic strength. Another experiment re-examined was the finding that presoaking muscles in "isotonic" KCl Ringer prevented the loss of contractions in Ringer with a doubled [NaCl]. We have found that muscles swell in KCl Ringer and are thereafter significantly less dehydrated in 2X NaCl Ringer than control muscles not presoaked. The maintenance of contractibility can thus be explained by a lesser degree of dehydration. Our results thus support a mechanism involving the contractile process through changes in the internal ionic strength. (Supported by NSF Grant GB-14294.)

WATER AND ION MOVEMENTS IN BARNACLE MUSCLE: T-TUBULAR EFFECTS. Bert A. Mobley* and Ernest Page. Depts. of Physiology and Medicine, University of Chicago, Chicago, Illinois.

In single skeletal muscle cells of Balanus changes in cell water content (C_W) and membrane potential (V_M) have been measured as a function of external osmolality, or during change of external K and Cl concentrations ($[K]_o$ and $[Cl]_o$) of the type described in frog muscle by Hodgkin and Horowicz (J. Physiol. 148:127:1959). C_W was determined by microscopic monitoring of cell diameter with a precision of 0.2-0.4% (S.D.) of the diameter. $[K]_o$ was varied from 1-18 mM, concentrations which do not cause contracture. These measurements show (a) net KCl and water movements in response to an isosmolal change of $[K]_o$ at constant $[Cl]_o$ or of $[Cl]_o$ at constant $[K]_o$ are absent at pH 8.0 because of the low Cl permeability, but present at pH 4.5, corresponding to a change in the ratio (Cl conductance/K conductance) from 1/12 at pH 8.0 to 1/2 at pH 4.5; (b) a characteristically slow equilibration of cell volume in response to an osmotic gradient, and a striking delay in the initial establishment of a new membrane potential in response to a change in $[K]_o$ and/or $[Cl]_o$, even at constant external $[K]\cdot[Cl]$ product. These phenomena are attributed to a delayed equilibration by diffusion within the system of sarcolemmal invaginations and T-tubules (Selverston, Am. Zool. 7:515:1967); (c) anomalous rectification for net outward movements of K, demonstrable by both volumetric and potentiometric methods.

Supported by U.S.P.H.S. Grant HE-10503-04 and by a grant from the American Heart Association.

AGE AND ACQUISITION OF A "STEADY STATE" DURING CONTINUOUS, GRADED TREADMILL EXERCISE. Henry J. Montoye, Sharon Guber*, David A. Cunningham* and Stephen Dinka Jr.*. Department of Epidemiology, School of Public Health, University of Michigan.

Fifty males, age 10-65, taking part in the Tecumseh Community Health Study, walked continuously on a treadmill at 3 mi. per hr. The grade was increased 3% after 3 min. at each level. Heart rate, ventilation, O_2 uptake, and CO_2 production were recorded each min. The purpose of this particular analysis was to determine if a steady state were reached at various grades and if the time required for the acquisition of a steady state is related to age. There was little or no relationship between acquisition of a steady state and age. By the third min. at each level, almost all subjects had achieved a steady state in O_2 uptake. CO_2 production generally was still increasing during the third min. at each level; hence the resp. ex. ratio was also increasing. Except at the lowest work load, heart rate continued to increase throughout the 3 minutes at each level, regardless of age of subject. This is thought to be related to a continuous increase in body temperature. After the first 3 work loads, ventilation had not reached a steady state by the 3rd min., regardless of age of subject. Walking on a treadmill was a new experience for these subjects, most of whom were not conditioned for strenuous work. Therefore, the treadmill test was repeated 4 times in a 48-year old conditioned subject who had taken treadmill tests many times previously. With regard to the acquisition of a steady state, the same results were obtained in this subject. (The study was supported in part by Grant 9-R01-HE 12755, USPHS and Program Project Grant NIH HE 09814, USPHS.)

APNEIC BRADYCARDIA IN MAN: EFFECTS OF TEMPERATURE AND DEPTH OF IMMERSION. T.O. Moore*, J.A. Setliff* and S.K. Hong. University of Hawaii, Honolulu, Hawaii.

Heart rate (HR) responses to 60 second breathholds (BH) on total lung capacity were recorded under the following conditions: 1) face immersion at room temperatures of 25° and 5°C, and water temperatures of 5°, 15°, 25°, and 35°C; 2) whole body immersion in a shallow tank at water temperatures of 15°, 25°, and 35°C; and 3) ocean SCUBA dives at half-atmosphere increments to a depth of 60 feet. Ocean temperature was essentially constant from surface to 60 feet at 26.2° to 26.6°C. All measurements were done in triplicate. During condition 1) (N=12) the maximum degree of bradycardia in a 25°C room was slight and not different during BH in air and in 35°C water. In 25° and 15°C water, HR reduction was 12% and 21%, respectively, and 29% in 5°C water. In a 5°C room, the HR reduction was essentially identical in air, 35°, 25°, and 15°C water and averaged 11%, while in 5°C water, the reduction was 35%. Under condition 2) (N=6) HR reduction was 11% in 35°C water, 22% in 25°C water and 21% in 15°C water. No difference in response was found at any given water temperature whether the subject was immersed to the neck with face out of water, face in water, or totally immersed (using SCUBA) with or without a face mask. Under condition 3) (N=5) HR reduction was measured during BH at 60, 45, 30, and 15 feet and at the surface. Reduction was 16%, 19%, 20%, 20%, and 27%, respectively. The results indicate that apneic bradycardia is potentiated by face immersion in cold water, and by cold ambient air per se. Whole body immersion produces less reduction in HR, but a more rapid onset than in air. The reflex is attenuated with increasing hydrostatic pressure at constant water temperature. (This investigation was supported in part by NSF Sea Grant GH-62.)

DAILY AND SEASONAL FLUCTUATIONS IN CORNEAL DNA SYNTHESIS OF ADULT RANA PIPIENS. William W. Morgan* and Sherwin Mizell Dept. of Anatomy and Physiology, Indiana University, Bloomington, Indiana.

Eight twenty-four hour experiments were performed in which colonies of adult leopard frogs Rana pipiens were exposed to a 12:12 LD lighting regime (lights on 6A.M. to 6 P.M.) for two weeks before sacrifice. The animals were sacrificed in groups of twelve at two hour intervals during a twenty-four hour period. A total of nearly sixteen hundred animals were sacrificed. Each group of animals was injected with 0.33 microcuries (μc) per gram body weight ^{3}H thymidine two hours before sacrifice. At sacrifice both corneas were removed, dried, and ^{3}H thymidine uptake, as a measure of DNA synthesis, was determined by liquid scintillation procedures. Statistically significant (alpha= 0.005) daily and seasonal fluctuations in DNA synthesis (CPM/mgm tissue dry weight) were found utilizing the technique of analysis of variance. Power spectral analysis showed that the daily fluctuations in corneal DNA synthesis had a periodicity of approximately twenty-four hours. Light inversion experiments indicate that the daily rhythms are in part regulated by the lighting schedule. These results agree very closely with those reported previously by this group for dorsal epidermis and thus suggest the presence of some common regulatory factors in the control of daily fluctuations in DNA synthesis of various tissues of Rana pipiens. This data also suggests the importance of the lighting environment in regulating these fluctuating phenomena. (Supported by PHS GM39-131-01 and by NASA 15-003-053)

RELATIONSHIP OF BLOOD PRESSURE AND HEART RATE TO BODY TEMPERATURE IN BABOONS. M. S. Morishima* and C. C. Gale. Dept. of Physiol. and Biophys. and Reg. Prim. Res. Ctr., Univ. of Wash., Seattle, Wash.

Interrelationships among blood pressure (BP), heart rate (HR), and internal temperature (midbrain, Tmb) were studied in conscious baboons during periods of acute hypothalamic cooling or warming and during normal 24-hr intervals. Thermodes were implanted in the preoptic/anterior hypothalamus and thermocouple reentry tubes in the midbrain. BP and HR were recorded continuously on a polygraph via a catheter in the abdominal aorta. Onset of POAH cooling for 1-2 hr led to rapid persistent rise in BP from 105/70 to 120/90 mm Hg and in HR from 70 to 90/min in association with cutaneous vasoconstriction and shivering (n=5). Tmb rose gradually 1-1.2°C, and urinary free catecholamines were elevated. During central cooling correlation coefficients among BP, HR, and Tmb were significant. When the POAH was warmed for 1-2 hr, BP fell gradually from 120/75 to 100/60 mm Hg and HR from 165 to 135 in parallel with a slow 2°C decline in Tmb (n=6). Cutaneous vasodilatation was evident and urinary catecholamines were reduced. At the stop of POAH warming, BP rose abruptly to 150/105 mm Hg and HR to 210/min in association with strong shivering and gradual rise in Tmb. Studies of normal 24-hr periods for 4 consecutive days revealed a significant interdependence among BP, HR, and Tmb ($P<0.001$)(n=8). BP (mean), HR, and Tmb were lowest at 5 a.m. (98 mm Hg, 105/min, and 37.2°C) and highest at 5 p.m. (118 mm Hg, 158/min, and 38.8°C). Significant correlations persisted among these parameters during the 24-hr day. These data show that relationships exist among BP, HR, and Tmb during diurnal intervals and during acute thermal stress. They imply that thermosensitive neurons in the POAH can stimulate and inhibit cardiovascular centers in the brain stem.

Supported by N. I. H. Grants NB 06622 and FR 00166

A Study of Amylase Synthesis in Rat Pancreas. J.A. Morisset*, J.F. Agee*, and P.D. Webster, V.A. Hosp. and Med. Coll. of Ga., Augusta, Ga. 30904.

There are two dominant views concerning interrelationships between pancreatic enzyme secretion and synthesis. One embodied as the "secretory cycle" suggests that exocrine glands secrete and then synthesize new product. This view holds that both secretion and synthesis are variable processes. The second view suggests that secretion is variable but synthesis is constant. According to this view, changes in enzyme content result from changes in secretion. While pancreatic protein secretion and synthesis have been shown to be variable processes in pigeons, it has been argued that such observations do not apply to mammals. These experiments were designed to determine whether pancreatic protein synthesis might be variable in rats. Fed and fasted rats (48 or 72 hours) were used. Urecholine, 2 mg/kg, was administered SC. Pancreases were incubated in tissue culture media with ^{14}C-labeled amino acids and rates of protein and amylase synthesis studied. Pancreatic microsomes were prepared and incubated in media containing cell sap, GTP, and an energy generating system. Data of these experiments indicate that feeding was associated with increased incorporation of ^{14}C-label into protein, amylase, and microsomal protein. Urecholine administration was also associated with similar increases. These results show that protein synthesis in the rat pancreas is a variable process and that enhancement of synthesis follows administration of stimuli associated with enhancement of secretion. (Supported by VA and NIH Grant AM13131-02).

PROPERTIES OF ANTERIOR TIBIAL TENDON ORGANS. Carter G. Mosher*, Rebecca L. Gerlach*, Robert M. Reinking* and Douglas G. Stuart. Department of Physiology, University of Arizona, Tucson, Arizona.

Houk and Henneman (1967) have reported that tendon organs are very sensitive to forces developed by contraction of their "in-series" motor units but insensitive to muscle stretch within the physiological range. Most experiments were restricted to the soleus muscle. We have presented evidence (Stuart et al 1970), however, that there is pronounced soleus Ib input during stretches encountered in locomotion. Furthermore Alnaes (1967) has shown that most anterior tibial tendon organs give sustained discharge to passive stretch, some even firing spontaneously. These considerations have led us to experiments involving: analysis of the responses of anterior tibial receptors to twitch and tetanic contraction of isolated motor units; and, determination of their thresholds to dynamic stretch of the entire muscle. Our sample of motor units (45 from 7 experiments) displayed a homogenous distribution of contraction times (24 ± 4 msec) and fusion frequency 43 ± 9 p/sec). Mean twitch tension was 7 ± 6 gms and peak tetanic tension 21 ± 13 gms. Minimum Ib thresholds for forces developed during twitch of single motor units averaged 1.5 gms in contrast to 24 gms for dynamic stretch. Individual receptors were more sensitive to active than passive forces by a factor ranging from 0.2 to 40. A wide range of firing rates (2 to 90 imp/sec) was observed in the responses of single Ib afferents to tetanic contraction of their exciting motor units. This indicates that tendon organs need not be in direct line with all the motor units that excite them. We also observed receptors to be unloaded by contraction of "in-parallel" portions of the muscle even to the extent of occluding the response to an "in-series" portion. Further study is necessary to determine the functional significance of these latter phenomena. (Supported in part by USPHS Grant NB 07888).

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

Early appearance of lung stability in the fetus has been observed following injection of corticosteroids (Kotas and Avery, Fed. Proc. 29: 776, 1970). We studied further the effect of cortisol on fetal rabbits from 37 pregnant does and compared them with those from 21 controls. Viability of these animals upon premature delivery, aeration of the lungs, bubble stability (BS), surface activity of lung extracts (SA), and electronmicroscopy (EM) were examined. In control animals SA appeared on 28 days gestation (full term: 30 days). BS increased between 27 and 28 days. On EM, an abundance of osmiophilic inclusions were observed in type II cells after 28 days. Control animals were unable to sustain breathing before 28 days. In 16 does injected intramuscularly with cortisol (10-30 mgm/Kg) for 3 days, many fetuses were edematous or dead on 27 and 28 days upon cesarean section. There was no acceleration of lung maturation in the live fetuses. In 21 experiments, cortisol was injected directly into the fetus and amniotic sac (0.5-1.0 mgm) on 23 to 24 days. When delivered, some of the treated animals were able to breathe on 27 days while their untreated littermates could not. Lungs from treated animals, compared to controls, retained more air, exhibited better BS and, on EM, displayed abundant inclusions and disappearance of glycogen indicating accelerated alveolar epithelial cell maturation. Thus, direct fetal injection of cortisol promotes the synthesis of pulmonary surfactant and earlier extrauterine adaptation of premature fetuses. (Supported by USPHS HD-03119, HD-02459; Grant-in-aid, N.Y. Heart Ass.).

FUNCTIONAL ALTERATIONS OF MITOCHONDRIA FROM STRIATED SKELETAL MUSCLE DURING ATROPHY OF DENERVATION. M. Myrick* and R.B. Tobin. University of Nebraska College of Medicine and V.A. Hospital, Omaha, Nebr. 68105.

The effects of denervation upon gross and microscopic morphology as well as chemical composition of muscle are well known. Studies of muscle metabolism during atrophy have been reported but these are generally limited to whole muscles and slices. The authors have previously shown that total muscle mass atrophies faster than the mass of the mitochondria. The present study was designed to investigate changes in mitochondrial metabolism of skeletal muscle following denervation. Mitochondria were isolated from rat gastrocnemius following sciatic nerve section and from pigeon breast after section of the brachial plexis by modification of the Dow method. Preparations were made from these and contralateral intact muscles during atrophy, throughout 3 months following denervation. By 24-hours, respiratory control ratio, State III respiratory rate (Q_{O_2} III) and P/O ratios all increased significantly. Q_{O_2} III and control ratio remained elevated for 3 days while P/O ratio dropped below control values by this time. One week post-denervation, control ratio dropped to 58%; Q_{O_2} III was 74% and P/O ratios 79% of control value. Minimal additional changes occurred during the second week, and subsequently very slight alterations in mitochondrial function were observed. After 3 months, disintegration of muscle prevented the isolation of mitochondria. This study indicates that changes of mitochondrial function parallel morphological alterations of denervated muscle. (Supported by Veterans Administration).

CONTROL OF SWEATING IN THE SQUIRREL MONKEY. Ethan R. Nadel and John T. Stitt (intr. by J. A. J. Stolwijk). John B. Pierce Foundation Laboratory and Yale University Sch. of Medicine, New Haven, Conn.

The probable existence of thermoregulatory sweating in the squirrel monkey, indicated from calorimetric studies in this laboratory, presented an excellent opportunity to examine the characteristics and control of rate of sweat secretion in a primate. Sweating rate was continuously recorded from the hind foot, secured in a cylindrical copper capsule, by resistance hygrometry. Skin temperature of the foot was independently controlled by perfusing an outer chamber surrounding the capsule with water of known temperature. The pattern of sweat secretion was cyclical in nature and cycles were synchronous between the two hind feet. Sweating did not occur from the trunk and seemed to be limited to feet and hands and perhaps the face. When internal (rectal) and mean skin temperatures were constant and sweating was ongoing, sweating rate was related to local (foot skin) temperature. The sweating mechanism was highly responsive to rapid alterations in either ambient (mean skin) temperature or activity level (internal temperature). Thus, the control elements for rate of sweat secretion in the squirrel monkey were similar to those controlling sweating in man; the squirrel monkey would appear to be an excellent preparation for further studies of the sweating mechanism.

Electrophoretic Pattern of Renin Substrate. A. Nasjletti* L. A. Lewis and G.M.C. Masson, Cleveland Clinic, Cleveland, Ohio 44106

Unmodified and partially purified renin substrates (RS) of various species were studied by starch gel electrophoresis. Each sample was done in duplicate; one was used for identification of various protein fractions, and the other for elution and determination of RS activity in 5 well-defined areas corresponding to prealbumin and albumin (A), fast α_2-globulin and β-transferrin (B), haptoglobulin (C) α_2-macroglobulin (D) and to the point of application of sample and γ-globulin (E). The results showed that 1) 88% of the RS contained in dog plasma was present in fraction B and 12% in fraction A; 2) RS from hog serum was located only in fraction B; 3) when purified hog RS was added to hog serum or dissolved in saline, all the activity was in fraction B; 4) in serum from nephrectomized patients 87% of RS activity was in A and 13% in B; 5) the activity of rat serum after nephrectomy or estrogen treatment was only in fraction A. Similar results were obtained with purified rat RS. It is concluded that rat and human RS are part of the albumin fraction while dog and hog RS moves with the α_2-globulins, and that nephrectomy and estrogens do not change the electrophoretic mobility of RS, thus suggesting no change in nature. (Supported by NIH Grant HE-6835).

EFFECT OF SECRETIN AND CHOLECYSTOKININ-PANCREOZYMIN (CCK-PZ) ON INTESTINAL SECRETION IN THE RAT. E.S. Nasset and J.S. Ju, University of California, Berkeley.

In the anesthetized rat (urethane i.p.) the lumen of the small gut was perfused with isotonic galactose solution and the effluent was collected in twelve 15-minute periods. Dipeptidase, enterokinase, sucrase and alkaline phosphatase activities were determined as well as the concentrations of DNA and protein. Secretin or CCK-PZ in saline solution (0.4ml) was injected i.v. at dosages of 50-75 units/kg. The same volume of saline was injected i.v. in control experiments. Secretin had no effect on the effluent volume but it may have increased the output of alkaline phosphatase. There was no stimulatory effect on release of dipeptidase, enterokinase, sucrase, DNA, or protein. Secretin had the usual effect on volume of pancreatic juice and there was considerable "wash-out" of enzymes. CCK-PZ stimulates release of dipeptidase, sucrase, alkaline phosphatase and protein but has no effect on enterokinase, DNA or volume of effluent. CCK-PZ exerted the expected effect on pancreatic enzyme activity as exemplified by release of trypsin. These results confirm earlier work demonstrating that secretin is not responsible for increases in the volume of succus entericus (E.S. Nasset, Am. J. Physiol. 121: 481, 1938). The differential effects of CCK-PZ on the gut enzymes suggest that dipeptidase, sucrase and alkaline phosphatase are secreted at one locus and enterokinase at another, possibly the crypts of Lieberkühn. (Supported by NIH grant AM-11108.)

THE EFFECT OF ISOPROTERENOL ON VENTRICULAR ACTION POTENTIALS AND CONTRACTION. David Nathan and George W. Beeler, Jr. (intr. by J. R. Blinks). Mayo Foundation, Rochester, Minn.

Studies were performed on papillary muscles of the dog mounted across a sucrose gap. The force of contraction and the action potential were recorded and analysed with the aid of a CDC 3300 digital computer. Dose-response curves were performed with (-)-isoproterenol (ISO), before and after blockade of the beta-adrenergic receptors. Specific changes noted were: I) Increase in the spike amplitude. II) Increase in the height and duration of the plateau phase. III) Increase in the peak rate of repolarization. IV) Progressive increase in the peak tension, the peak rate of tension development, and the peak rate of relaxation; the time to peak tension was decreased. The electrical changes were interpreted as indicating that the main effect of the ISO was to increase the magnitude and duration of the inward calcium current during the plateau phase of the action potential, and secondarily, to increase the overall outward potassium current throughout the action potential. The mechanical changes were ascribed to the changes in calcium dynamics produced by the ISO. After beta-blockade with propranolol, repeat dose-response curves showed a shift to the right along the concentration axis for all the force parameters, and for those action potential parameters which had shown significant changes prior to blockade. This was interpreted as an indication that all of the changes noted in the force and the action potential were due to the action of ISO on beta-adrenergic receptors. (Supported by USPHS Grants FR00007, HE 12186-01, and FR05530.)

INCREASED SPLANCHNIC NERVE ACTIVITY ELICITED FROM FASTIGIAL NUCLEUS AND MEDULLA OBLONGATA. Marc A. Nathan (intr. by N. P. Clarke). School of Aerospace Medicine, San Antonio, Texas.

Miura and Reis (Brain Res. 13: 595, 1969) have demonstrated that stimulation of the fastigial nucleus in cats results in large pressor responses. They further demonstrated that this effect is mediated by the primarily crossed fastigio-bulbar tract. The results presented here generally support their findings. Sympathetic nerve activity was monitored by recording from the thoracic splanchnic nerve of anesthetized rhesus monkeys. Nerve activity was measured as the integral of 100 responses summated by a Computer of Average Transients. Latencies were also determined from the summated data. It was found that activity from stimulation of the fastigial nucleus contralateral to the splanchnic nerve from which recordings were made was about 67% of that from stimulation of the lateral reticular formation of the opposite side. Conditioning stimulation of the contralateral fastigial nucleus followed by test stimulation of the lateral reticular formation of the opposite side activated a largely coextensive neuronal pool. The conditioning-testing interval producing the greatest percentage decrease from control was at about 90 msec. The mean latency of increased nerve activity to stimulation of the lateral reticular formation of the ipsilateral side was about 70 msec, while that to stimulation of the contralateral fastigial nucleus was 80 msec. This evidence lends further support to the notion that the cerebellum can exert control over sympathetic vasomotor responses via the fastigial nucleus and its projections to the lateral reticular formation of the medulla oblongata.

GLOMERULAR CAPILLARY PRESSURE--60 or 90 mm. Hg? L. G. Navar*, P. G. Baer*, and A. C. Guyton. Univ. of Miss. Med. Cntr., Jackson, Miss.

Because of the inaccessibility of the mammalian glomerular capillary loops to direct measurement of hydrostatic pressure, there has been considerable doubt as to the magnitude of the glomerular capillary pressure (GP). Although it has been considered to be about 60 mm. Hg, some recent micropuncture experiments have provided evidence that has been interpreted as indicating that the normal GP is about 85 to 90 mm. Hg. To examine this discrepancy, GP was calculated by a new method based on the following generally held assumptions: (1) The autoregulatory adjustments in intrarenal vascular resistance due to changes in arterial pressure are localized at preglomerular sites. (2) Under conditions of ureteral obstruction and mannitol loading, the ureteral pressure equilibrates with proximal tubular pressure if GFR has ceased. (3) The renal reponses to ureteral obstruction include preglomerular dilation such that the intrarenal and preglomerular resistances are the same as when the arterial pressure is lowered below the autoregulatory range. By measuring the necessary parameters of renal blood flow, glomerular filtration rate, inulin extraction, renal arterial and intrarenal venous pressure, and plasma oncotic pressure in 12 dogs, it was possible to arrive at values for preglomerular and intrarenal resistances at different arterial pressures and during ureteral obstruction. Analysis of these results showed that during ureteral obstruction, preglomerular resistance decreased to a minimal level that averaged 5 $\pm$ 1.4 (S.D.) mm. Hg/ml/min/g. GP under these conditions was about 85% of renal arterial pressure. Under normal conditions the glomerular pressure was 61 $\pm$ 9.6 (S.D.) mm. Hg, and was relatively independent of changes in the arterial pressure within the autoregulatory range. (Supported by PHS Grant HE 11428)

CORRELATION BETWEEN THE INOTROPIC AND ARRHYTHMOGENIC EFFECTS OF ACETYL STROPHANTHIDIN. N.S. Nejad, F. Hagemeijer, M.D. Klein and B. Lown (intr. by M.G. Herrera). Harvard School of Public Health, Boston, Mass.

Changes in myocardial irritability and inotropy were evaluated during acetyl strophanthidin (AS) infusion in 6 dogs anesthetized lightly with pentobarbital. AS was given intravenously at 123 μg/min to a toxic end point of ventricular tachycardia (VT). Myocardial contractility was assessed from the peak isovolumic value of dp/dt/p, where dp/dt = first derivative of left ventricular pressure (LVP) and p = simultaneous LVP, measured with a fiberoptic pressure catheter. Measurements were made at 5 msec intervals. Myocardial irritability was determined by evocation of repetitive ventricular responses (RVR) with pulses of twice threshold energy delivered to the right ventricle in early diastole. Heart rate was kept constant in each animal with atrial pacing at 180/min. Peak dp/dt/p increased linearly up to 43 $\pm$ 9% (SEM) just before VT supervened. RVR was first demonstrable when 59% of the toxic dose of AS had been given and at a time when 51% of the total contractile increment had occurred. Upon termination of VT, RVR was again elicited. Peak dp/dt/p gradually declined and returned to control levels within 2 min of subsidence of RVR. These results indicate that the time course and magnitude of AS induced positive inotropy parallel that of AS evoked myocardial irritability.

TRANSPORT OF WATER, ELECTROLYTES, AND NUTRIENTS IN THIAMINE AND PANTOTHENIC ACID DEFICIENCY. R. A. Nelson and B. Fleshler.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota, and Case Western Reserve University, Cleveland, Ohio.

Studies of the effect of thiamine deficiency on transport of water, sodium, potassium, and glucose were carried out in intestinal segments of four dogs, and the effect of pantothenic acid deficiency on L-alanine absorption and its interaction with sodium during intestinal absorption was studied in jejunal segments of three dogs. Severe thiamine deficiency did not affect gut transport of the measured substances. In pantothenic acid deficiency, insorption of sodium steadily decreased and was least during the latter half of the deficiency period. Exsorption did not change until halfway through the deficiency period, when it increased to a level exceeding that of insorption. L-alanine absorption decreased significantly during pantothenic acid deficiency, and its decline was similar to that noted for the rate of decrease of sodium insorption. When alanine absorption was compared with sodium insorption, a significant direct linear correlation was found, and the slope of the regression line indicated that approximately 1 mmole of L-alanine was absorbed for every 2 mEq of sodium insorbed. No relationship was found between sodium exsorption and alanine absorption. It was concluded that thiamine deficiency does not affect gut transport of water, sodium, potassium, or glucose. Although pantothenic acid deficiency produced a decrease in insorption of L-alanine and sodium insorption, it did not appear to change the interaction between these two processes since the effect of pantothenic acid deficiency was similar on the movement of both substances across the gut mucosa. (Supported by NIH Grant AM-10269.)

THERMOREGULATORY RESPONSES OF BABOONS EXPOSED TO HEAT STRESS AND SCOPOLAMINE. **L M. Newman*, E.G. Cummings, J.L. Miller* and H. Wright* Medical Labs, Edgewood Arsenal, Md.**

The objects of this study were to determine whether the baboon's thermoregulatory response to heat stress involves evaporative heat loss through either sweating or panting; to access the effects of scopolamine on temperature regulation in the baboon and to obtain some indication of the similarity between the responses of men and baboons to heat and scopolamine. The measurements taken were: total weight loss, weight loss from head sweating and exhalation, skin temperature, rectal temperature, heart rate and respiratory rate. In control experiments at 43°C, the body temperatures and respiration remained in equilibrium for 2.5 hrs. The total weight loss amounted to about 180 mg/kg/min whereas water was collected from the respiratory tract at a rate of about 30mg/kg/min. In control experiments at 24°C the body temperature was lower and the total weight loss was only about 30 mg/kg/min. Following intramuscular injection of scopolamine and methyl scopolamine, total weight loss was reduced by amounts up to 50% within 30 minutes and respiratory rate and body temperatures increased within 60 minutes. However, there was no substantial change in water collected from the head and respiratory tract. It was concluded that the baboon responds to exposure to heat by an increase in body temperature and sweat production; the baboon obtains only a small fraction of its evaporative cooling from the respiratory tract and scopolamine and methylscopolamine are effective inhibitors of sweating in the baboon. In these respects the baboon resembles man.

APPLICATION OF CONVECTIVE DIFFUSION THEORY TO TRANSPORT IN STEADY CAPILLARY FLOW. Karl R. K. Nicholes* and J. A. Johnson. Mayo Graduate School of Medicine, Rochester, Minnesota, and University of Minnesota, Minneapolis, Minnesota, Departments of Physiology.

Rich and Goodman (Circ. Res. 17:274, 1965) experimentally verified G. Taylor's original or first criterion for convective diffusion in steady creeping flow in capillary tubes (Taylor, Proc. Roy. Soc. A. 219:186, 1953). They analyzed theoretically the possibility of applying convective diffusion theory to transport in circular tubes of the same dimensions as mammalian vascular capillaries. Their work has some minor errors in the calculation of mean velocity from other data and their main equation blows up for some parameter configurations. Their work fails to take into account a check on Taylor's second criterion (Proc. Roy. Soc. A. 225:473, 1954) or the mathematical resolution of the second Taylor criterion by Aris (Proc. Roy. Soc. A. 235:67, 1956). We have expanded their work to include recalculation of all their data using their mathematical approach and an alternate one which is stable for all parameter configurations. We include consideration of Taylor's second criterion and the work of Aris cited above. Without this latter analysis, the conclusions of Rich and Goodman about the applicability of convective diffusion theory to solute transport in mammalian capillaries are not valid.

ANTIDROMIC AND AUTONOMIC RESPONSES OF SUPRAOPTIC NEURONS. R. A. Nicoll, J. W. Crayton and J. L. Barker (intr. by F. E. Bloom). Natl. Inst. of Mental Health, St. Elizabeths Hosp., Washington, D.C.

Neurosecretory cells in the supraoptic nucleus of anesthetized cats were antidromically-identified by electrical stimulation of the posterior pituitary. The latency for antidromic invasion occurred in discrete jumps suggesting that the axons of neurosecretory cells branch. The responses of identified supraoptic units to afferent vagal and carotid sinus nerve volleys and neurohypopheseal stimuli were examined with a computer of average transients. Neurohypopheseal stimuli, at strengths below threshold for antidromic invasion, interrupted the spontaneous activity of neurosecretory cells. In addition to this synaptic inhibition following antidromic volleys in neurosecretory cell axons, identified neurosecretory cells were also synaptically excited by stimulation of vagal and carotid sinus nerve afferents. Since these pathways are known to be involved in the release of antidiuretic hormone (ADH), the results support the hypothesis that ADH release is related to an increase in discharge frequency of supraoptic neurons.

IONIC AND MORPHOLOGIC CHANGES IN CARDIAC MITOCHONDRIA OF ISOPROTERENOL-TREATED RATS. E.L.Nirdlinger* and P.O.Bramante, Dept.of Physiology, University of Illinois College of Medicine, Chicago, Illinois.

Several pathogenetic aspects of the myocardial necrosis which follows isoproterenol administration in experimental animals are still unclear. The hypothesis of a relative ischemia produced by increased myocardial O_2 demand due to the drug does not adequately explain the role of ionic changes participating in this syndrome. Ion concentrations (Ca,Mg,K,Na) of whole tissue homogenate and subcellular fractions (debris,mitochondria,supernatant fluid) were measured in hearts of control rats and others sacrificed at different times (1/2,1,3,11,24,48 hrs) following a single s.c.injection of isoproterenol (40mg/Kg). Mitochondrial pellets were E.M. examined in the controls and 24-hrs groups. While the controls confirmed accepted concentration values in the mitochondria (Ca,11.7 ± 2.7 nMoles/mg protein ± S.E.;Mg,48.9 ± 4.8;K,198.4 ± 18.4), the ion content and distribution in the experimental series followed a pattern of early (1st hour) and delayed (3-24 hrs) changes. In the early phase [corresponding to the immediate calorigenic effects of the drug (Bramante and Nirdlinger,this issue)] a mitochondrial Mg decrease was accompanied by an increase in Ca content,with return of both to normal after one hr. During the delayed phase,mitochondrial Ca concentration rose steadily,peaking at 24 hrs and returning to control levels at 48 hrs. Except for a Na increase at 11 hrs, other mitochondrial ions remained constant.Most mitochondria of the experimental hearts were of orthodox configuration as compared to the condensed control organelles. Increased mitochondrial Ca concentration and resulting orthodox transformation may impair the ability of cardiac cells to produce needed high-energy phosphate compounds.

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ADENOSINE AND ISOLATED CORONARY VASCULAR SMOOTH MUSCLE. James M. Norton* and Reed Detar. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Isolated helical vascular strips cut from rabbit coronary vessels (280-800μ O.D.) were suspended isometrically in a physiological salt solution at 37°C, pH 7.4, and a P_{O_2} of 100 mm Hg. Adenosine, at concentrations as high as 100 μM, has little or no effect on the resting tension of these strips. In strips from small coronaries (<600μ), active tension produced by acetylcholine (1μM) is usually only partially (<50%) relaxed by adenosine at concentrations greater than 1 μM; active tension of strips from larger coronaries (>600μ) is usually relaxed only slightly (<10%) and transiently, although occasionally active tension of large vessels exhibiting spontaneous activity is often relaxed abruptly and completely by adenosine. Strips from small coronaries exposed to relatively low concentrations of adenosine (0.1-1.0 μM) contract only transiently or not at all in response to the subsequent administration of acetylcholine. In strips from larger coronaries preexposed to concentrations of adenosine as high as 100 μM, contractile responses to acetylcholine are similar to control responses except that the rate of tension development is somewhat diminished. These data suggest that adenosine could play a role in the regulation of coronary blood flow by contributing to the local control of smooth muscle tone of the small coronary vasculature. (Supported by NIH grant # 12846-01.)

CAROTID SINUS BAROCEPTOR FUNCTIONS IN THE SPONTANEOUSLY HYPERTENSIVE RAT. S. Nosaka*, & S.C. Wang. Dept. of Pharmacology, Col. of P & S., Columbia U., New York, N.Y. 10032

Carotid sinus baroceptor reflex was investigated in the spontaneous hypertensive rat (SHR). Both sinuses were isolated and perfused with oxygenated Tyrode's solution, and the perfusion pressure was raised stepwise from 100 mmHg at 20 mmHg increments. In controls the systemic BP dropped with the first increment of 20 mmHg and showed a maximum fall at 60 to 80 mmHg increments, while in the SHR the systemic BP did not drop until the increment was 40 mmHg, and maximum fall was seen at 100-140 mmHg increments. However, when the initial perfusion pressure was 160 mmHg instead of 100 mmHg, SHR showed the same response pattern as that of controls at 100 mmHg: systemic BP dropped at 20 mmHg increment and reached a maximum fall at 80 mmHg. In addition, the steady state relation was evaluated by staircase-wise loading of perfusion pressures. In controls maximum hypotensive level was reached with perfusion pressure around 160 to 180 mmHg, while in SHR around 200 to 240 mmHg. Recording of the carotid sinus nerve activities yielded the same general relationship as shown by systemic BP in response to a variety of perfusion pressures. It was concluded that carotid baroceptors in SHR were altered in such a way as to respond to the high systemic BP, and it was suggested that an altered distensibility of the arterial wall of the carotid sinus area might be responsible for these characteristic changes in response patterns. (Supported by China Medical Board, Perkins Fund & NIH NS00031).

EFFECTS OF KIDNEY EXTRACTS AND MAMMALIAN ACTH ON ADRENAL STEROID SECRETION IN THE TURTLE (PSEUDEMYS SUEANNIENSIS) AND THE CROCODILIAN (CAIMAN SP.) Sue A. Nothstine*, James O. Davis, Daniel H. Gist*, and Roger M. deRoos*, Depts. of Physiology and Zoology, Univ. of Mo., Columbia, Mo.

Steroids were measured in postcaval vein plasma in a species of turtle and in a species of crocodilian by the double-isotope derivative method. Only corticosterone was detected in turtle plasma, but measurable levels of aldosterone, corticosterone and cortisol were found in the crocodilian plasma. Corticosterone was the major secretory product in the crocodilian. Intravenous infusion of a saline extract of turtle kidneys into turtles given dexamethasone to suppress pituitary function produced a significant increase in corticosterone secretion. The active agent in the turtle kidney extract was nondialyzable and heat labile, and when the kidney extract was incubated with turtle plasma an increase in pressor activity resulted. Infusion of a crocodilian preparation made by incubation of kidney extracts and plasma into animals given dexamethasone produced no change in steroid secretion. Both infusions increased mean arterial pressure significantly in the experimental animals. An intravenous infusion of mammalian ACTH failed to increase either steroid secretion or arterial pressure in both species. These data provide evidence for the existence of a renal pressor agent in the turtle (Pseudemys) and the kidney extracts influenced adrenal steroid secretion. No evidence was obtained for such a system with steroidogenic activity in the crocodilian (Caiman sp.).

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AMINO ACID OXIDATION BY RAT SKELETAL MUSCLE. R. Odessey* and A. L. Goldberg, Department of Physiology, Harvard Medical School, Boston, Mass.

Oxidation has been found to be a major metabolic pathway for certain amino acids in the rat diaphragm. The excised diaphragm was incubated with ^{14}C-amino acids (0.1 mM) in Krebs-Ringer bicarbonate buffer in the absence of additional energy sources. At varying times, the amount of ^{14}C recoverable as CO_2, in protein, and in the acid soluble pool was measured. After 90 min. 40% of labelled leucine was found as CO_2, 46% as protein, and 14% as acid-soluble components. Approximately 40% of the alanine and glutamic acid entering muscle was also converted to CO_2. By contrast, CO_2 production from serine and glycine was not significant. Addition of glucose (10 mM) depressed leucine oxidation by only 15%, while β-hydroxybutyrate, acetate, and pyruvate did not significantly affect CO_2 production. Cyclohexamide in doses which completely inhibit incorporation into protein, increased leucine oxidation by 56%, while 2,4-DNP (1.8 mM) inhibited CO_2 production 50%.

Oxidation of leucine and alanine increased above control levels in diaphragms from hypophysectomized or starved rats, although incorporation into protein was reduced. Electrical stimulation of the diaphragm in vitro under isometric conditions also promoted CO_2 production from leucine without affecting incorporation. Comparison with values in the literature indicate that muscle catabolizes leucine more rapidly than liver or kidney and that muscle accounts for 99% of the oxidation of this amino acid by the whole animal.

LOCAL EFFECT OF SKIN TEMPERATURE ON THE RESPONSE OF THE SWEAT GLANDS TO INTRADERMALLY ADMINISTERED SUDORIFIC AGENTS. Tokuo Ogawa* and Robert W. Bullard, Indiana University, Bloomington, Indiana 47401.

In a cool environment, the rate of local sweating induced by an intradermal injection of pilocarpine, methacholine or acetylcholine was increased when the test area was heated. The increase was greater with a higher initial sweat rate and with a greater rise in the skin temperature. The rate of drug-induced sweating was also affected by the room temperature: sweating response was greater at a higher room temperature, although it tended to last shorter. This effect of the room temperature persisted even after nerve block. These observations indicate that skin temperature directly affects the activity of the sweat glands devoid of sudomotor innervation, and are in accord with our previous observations (J. Appl. Physiol. 28:18-22, 1970) that threshold concentration of a cholinergic sudorific agent for inducing local sweating was reduced by local heating in a cool environment. Furthermore, the localized increase in the rate of spontaneous sweating by local heating was comparable with that of drug-induced sweating in an area under nerve block. It is concluded that the local effect of skin temperature on sweat gland activity is exerted predominantly by changes in glandular sensitivity to cholinergic secretagogues, including the natural transmitter substance. On the other hand, ineffectiveness of local heating on epinephrine- or norepinephrine-induced sweating suggests that the receptor mechanism of the glandular cells for adrenergic agents may be different from that for cholinergic ones. (Supported by U.S. Air Force C-001^{4} and Army MD 17-68-C-8066).

RADIATION-INDUCED CHANGES IN THE GRANULE CELL COMPONENT OF THE CEREBELLAR EVOKED POTENTIAL. Karin E. Olson* and Charles D. Barnes, Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

The granular cell component of the cerebellar evoked potential changes with radiation in experiments performed on acutely decerebrated mature cats. Cerebellar field potentials were monitored extracortically with a glass microelectrode. The sural and superficial radial peripheral nerves, as well as the juxtafastigial nuclear area, were stimulated at 1/sec in order to potentiate mossy fiber input. The effects of 200 R and higher exposures up to 25000 R, given at 100 R/min, were studied in each animal. The granular cell component of the evoked potential was consistently decreased in size as radiation increased, although there was in some cats an increase or decrease inconsistent with early exposures. When the x-ray was operating with a closed shutter in mock experiments, there were no changes in the granular cell component of the cerebellar potentials in animals in which marked changes were observed with radiation. Two year-old cats, irradiated between 24 hour prenatal and postnatal with 150 R. whole body, were studied. These animals had cerebellar potentials grossly different from nonchronically irradiated cats. Furthermore, their evoked potentials were markedly unchanged with radiation.
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ANALYSIS OF ALVEOLAR GAS EXCHANGE IN THE PRESENCE OF CARBON MONOXIDE IN THE NON-HOMOGENEOUS LUNG. **Albert J. Olszowka, Solbert Permutt, and Leon E. Farhi. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N.Y. 14214, and School of Hygiene and Public Health, The Johns Hopkins Univ., Baltimore, Md. 21205.**

The effects of carbon monoxide on O_2 content of the pulmonary capillary blood can be expected to be more pronounced in alveoli where a low ratio of ventilation to perfusion ($\dot{V}A/\dot{Q}$) causes a decrease in P_{O_2} and therefore in the P_{O_2}/P_{CO} ratio. In order to study the relationship between $\dot{V}A/\dot{Q}$ distribution, CO, and gas exchange, we have modified a computer program described previously (J. Appl. Physiol. 26: 141, 1969), where the variables are inspired gas tensions, hemoglobin concentration, and P_{50}, blood buffer base concentration, $\dot{V}O_2$, $\dot{V}CO_2$, total ventilation and perfusion and their distribution. The analysis yields in return the gas tensions in the various lung elements, in the alveolar gas, and in the arterial blood. Addition of carbon monoxide to the inspired mixture produces the expected hypoxia but in the steady state has little effect on the $(Aa)DO_2$ regardless of whether the $\dot{V}A/\dot{Q}$ distribution is fairly homogeneous or not. Similarly, at any FICO between 0 and 70 ppm the carboxihemoglobin level is not affected by $\dot{V}A/\dot{Q}$ inhomogeneity. (Supported by AF Contract F-41609-70-C-0019, & ONR Contract N00014-A-0216(NR 102-722),)

CARDIOVASCULAR REFLEXES EVOKED BY CHANGES IN TIDAL VOLUME AND BY HYPERCAPNIA IN RABBITS. Norbert Ott* and John T. Shepherd, Mayo Clinic and Mayo Foundation, Rochester, Minn. 55901.

Rabbits (2.9-4.2 kg) were anesthetized with pentobarbital, artificially ventilated and both carotid sinus and aortic depressor nerves cut. The left kidney and one vascularly isolated hindlimb were separately perfused at constant flow by roller pumps. In 5 rabbits tidal volume (V_T) was varied (5-20 ml/kg) and end expiratory pCO_2 held constant (6%). In 7 rabbits V_T was held constant and end expiratory CO_2 increased in steps from 4 up to 10%. In control conditions cold block of afferent vagal impulses (VCB) increased aortic and hindlimb pressures. A greater rise in these pressures was seen during VCB both when V_T or when end expiratory CO_2 were increased. In contrast VCB caused little change in renal perfusion pressure with increasing V_T. When the CO_2 tension was raised from 4 to 8% the response in renal perfusion pressure to VCB was increased by an average of 60.5 mmHg above the response to VCB in normocapnia.

The effect of aortic depressor nerve block was determined in 5 rabbits with carotid sinus and vagus nerves cut. V_T was held constant and the end expiratory CO_2 varied. Block during hypercapnia increased aortic, hindlimb and renal pressure by 6.0, 15.2, 30.2 mmHg respectively above the values obtained with block during normocapnia.

These studies suggest (1) that in normocapnia alterations in the discharge from receptors situated in the lung or the heart which are activated by changes in tidal volume affect mainly muscle blood vessels and (2) that hypercapnia potentiates the responses from pulmonary or cardiac receptors more than those from receptors in the aortic arch, and that the kidney circulation is predominently affected by this potentiation. Supported in part by NIH Grant HE5883.

SYMPATHETIC CONTROL OF PULMONARY VASCULAR IMPEDANCE. John B. Pace. Bockus Research Institute, University of Pennsylvania Philadelphia, Pennsylvania 19146

The influence of sympathetic nerve stimulation on pulmonary hydraulic vascular input impedance was evaluated in dogs anesthetized with chlorolose. The impedance magnitude, plotted as a function of frequency, fell from resistance values to a minimum between 2 and 3 cycles/sec., followed by a maximum between 5 and 6 cycles/sec. Sequential increases in the frequency of left stellate ganglion stimulation caused the impedance spectrum to be shifted upward in a manner which was directly related to stimulus frequency. In the control the impedance of the fundamental averaged 257 dyne.sec. $cm.^{-5}$ ($\pm$ 60 S.D.). and occurred at a frequency of 2.55 cycles/sec. ($\pm$ 0.45 S.D.) The estimated control characteristic impedance averaged 312 dyne.sec. cm^{-5} ($\pm$ 116 S.D.). The frequency of the fundamental during stellate ganglion stimulation at 10 cps averaged 3.00 cycles/sec. ($\pm$ 0.38 S.D.) and the impedance modulus averaged 438 dyne. sec. cm^{-5} ($\pm$ 108 S.D.). The characteristic impedance at 10 cps was 534 dyne. sec. cm^{-5} ($\pm$ 85 S.D.). Pulmonary vascular resistance was not systematically altered by sympathetic nerve stimulation. It is concluded that sympathetic cardiac nerve stimulation increases the opposition to pulsatile flow and since pulmonary vascular resistance is relatively unaffected, the input impedance becomes a greater fraction of the total opposition that must be overcome in moving blood through the lungs. Supported by USPHS HE 07762 and ONR 551 (54)

PHYSIOLOGICAL EFFECTS OF LOW ENVIRONMENTAL pH ON BROOK TROUT. Randall K. Packer* and William A. Dunson. The Pennsylvania State University, University Park, Pa.

Brook trout (Salvelinus fontinales) exposed to a low environmental pH (3.0 to 3.3) showed a drop in blood pH from 7.39 to 6.97. Trout exposed to an environmental pH of 3.5 suffered a loss of 50% of their total body sodium. The loss of body sodium was caused by a depression of influx from a control level of 72.5μmoles/100 g hours to zero between pH 3.0 and 4.9, as Na efflux increased markedly over control levels (J. Exp. Zool. 174:65-72, 1970). In a field study we found no significant difference in body sodium content of wild trout from three streams ranging in pH from 6.05 to 7.10. We found brook trout living in a stream draining a bog at a pH of 5.1, but we found no trout in a stream of pH 5.0 which was polluted by mine acid drainage. Trout survived 13.1 to 14.7 hours in a 150 mM Na solution of pH 3.5 as compared to 2.5 to 4.9 hours at 100μM Na and the same pH. Body sodium contents of the two groups at death were not significantly different. It appears that oxygen consumption is significantly decreased from control levels in trout exposed to pH 3.0 to 3.5. The inability of brook trout to live in waters of pH less than about 5 seems to be related to a drop in blood pH and O_2 consumption with the loss of body sodium being of secondary importance as a cause of death.

RESPONSE OF GLIA IN CAT SENSORI-MOTOR CORTEX TO INCREASED EXTRACELLULAR POTASSIUM. Lawrence Pape* and Robert Katzman. Albert Einstein College of Medicine, Bronx, New York.

With the cortex under continuous irrigation with artificial CSF, 40 electrically silent glial cells ranging in membrane potential from -50 to -95 mv were studied in the outer 400 μ. After penetrating a cell, the normal CSF was replaced by a CSF containing 40 mM K^+ which flowed until the membrane potential appeared to plateau. The 40 mM K^+ was then replaced by normal CSF, and cell repolarization observed. The response of 10 cells in the outer 30 μ provided an accurate index of glial sensitivity to 40 mM K^+. While all 10 cells showed sensitivity to 40 mM K^+, those cells with the highest membrane potential (92 mv) showed the greatest depolarization (34 mv). Cells with the lowest membrane potential (50 mv) showed the smallest depolarization (12 mv). The depth of 10 of the glial cells was verified by fluorescein electrophoresis and ranged from 10 μ to 380 μ. Correlation of the electrophysiological response of these cells with depth revealed the time course of potassium movement through the brain. A cell 10 μ deep reached a plateau in 13 seconds, while a cell at 380 μ took upwards of 114 seconds to approximate a plateau. It is concluded that while the magnitude of the response of glial cells to 40 mM K^+ is less than that which would be predicted by the Nernst equation, the time course of the glial response is still a true indicator of K^+ movement through the cortex and can be accounted for by a diffusional model.

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EFFECT OF ALTERED LUNG MECHANICS ON V/Q INEQUALITIES, R.W. Patterson*, W. Monkcom*, and S.F. Sullivan, Coll. of Phys. & Surg., Columbia University, New York, N.Y.

The purpose of this study was to assess the ventilation-perfusion inequalities that might result from the alterations in mechanical properties of the lung consequent to airway hypocapnia. Concomittantly it was necessary to determine the level of airway hypocapnia at which changes in lung mechanics become evident in the intact animal. In anesthetized (pentobarbital) dogs, paralyzed with succinylcholine (i.v. drip), end tidal CO_2 concentration was reduced below 1% by mechanical hyperventilation with air for four hours. Minute volume was kept constant and at alternate hourly intervals CO_2 was added to the inspired mixture. Alveolar ventilation and cardiac output were determined, the mechanical properties were assessed by measuring airway resistance, compliance of the lung and the work of ventilation, the effect of their changes on pulmonary function was evident by measuring the distribution of ventilation (open circuit nitrogen washout technic) and $A\text{-}aD_{O_2}$ ($P_{A_{O_2}} - P_{a}O_2$). Respiratory mechanics appear to be optimum when the end tidal CO_2 is 2%, i.e., the compliance is highest and the resistance lowest. As the airway CO_2 is further decreased, resistance increases, compliance decreases, nitrogen washout is prolonged, and $A\text{-}aD_{O_2}$ increases. When CO_2 was added to the inspired mixture resistance decreased and compliance increased, the indices of ventilation perfusion inequality, $A\text{-}aD_{O_2}$ and time course of nitrogen washout, approached the original baseline values thus demonstrating the reversibility of the hypocapneic changes. It is concluded that hyperventilation in the intact animal can produce airway hypocapnia sufficient to alter lung mechanics, alter the distribution of ventilation and increase $A\text{-}aD_{O_2}$.
Supported by NIH grants GM 09069 and 5T1 GM 00056.

REPRESENTATION OF SLOWLY AND RAPIDLY ADAPTING MECHANORECEPTORS OF THE HAND IN BRODMANN'S AREAS 3 AND 1 OF MACACA MULATTA. R. L. Paul and H. Goodman (intro. by C. N. Woolsey). Laboratory of Neurophysiology, Medical School, Univ. of Wis., Madison, Wis., 53706.

Using penetrating tungsten microelectrodes, multiunit responses were elicited by mechanical stimulation as the cortex was explored in a half-millimeter grid of recording sites distributed over the hand area of the exposed surface of the postcentral gyrus and the caudal bank of the central sulcus. Exposure of the latter was effected by wide removal of frontal cortex after exploration of the free surface of the postcentral gyrus was completed. Special attention was paid to the separation of these cortical neuronal responses on the basis of their adaptation to static mechanical deformation of the skin. Rapidly and slowly adapting responses were readily identified. Findings not previously reported include: (1) a detailed analysis of the topographical organization of Brodmann's areas 1 and 3; (2) segregation to cytoarchitectural area 3 of slowly adapting responses to mechanoreceptor stimulation; and (3) predominance of rapidly adapting discharges in area 1. These findings provide additional evidence to that offered by Powell and Mountcastle (1959) for functional specialization of the cytoarchitectural subdivisions of the postcentral gyrus. The results suggest that it would be profitable to explore further and simultaneously the functional and topographical specializations of the whole postcentral region. The authors wish to express their deepest gratitude to Drs. Clinton N. Woolsey and Michael Merzenich without whose guidance and ideas these studies would not have been possible. (Supported by NINDS grants 5-P01-NS-06225, 5-T01-NS-05326 (H.G.) and Special Fellowship 1-F11-NS-02123 (to R.L.P.).

INTESTINAL SYNTHESIS AND TRANSPORT OF NAPHTHYL-GLUCURONIDE. Jerome C. Pekas. USDA, ARS, Metabolism and Radiation Research Laboratory, State Univ. Station, Fargo, N. Dak.

Everted intestinal sacs of the small intestine of rats were incubated 2 hours at 37° C in Ringer medium (pH 7.4-bicarbonate; Na-140 mM; glucose-1 mg/ml) containing 1-naphthol-1-^{14}C (10^{-5}M) in both the mucosal and serosal fluids. Net transport of the ^{14}C label from mucosal to serosal fluid was demonstrated; this transport occurred in opposition to a concentration gradient and was most rapid in the caudal small intestine. The average (n=9) serosal to mucosal (S/M) fluid ^{14}C concentration ratios for cranial, mid, and caudal sacs were 2.2, 3.7, and 6.8 respectively. The average net mucosal-to-serosal transfer by equal length sacs from cranial, mid, and caudal regions of intestine was 0.04, 0.08, and 0.18 micromoles naphthol-equivalents respectively. Of the ^{14}C label recovered from pooled mucosal and serosal fluids, 91 and 99 percent, respectively, could not be extracted with benzene, indicating that the naphthol-^{14}C was converted to more polar metabolites. The principal labeled metabolite was isolated by column chromatography and identified as naphthyl-glucuronide by comparison of its infrared spectrum to that of authentic naphthyl-β-D-glucuronide.

DIABETOGENIC EFFECT OF HYPOPHYSECTOMY IN THE RAT. J.C. Penhos, L. Recant,*N. Voyles*and L. Castillo.*VA Hosp and Depts. of Medicine, George Washington Univ. and Georgetown Univ., Washington, D. C.

Observations on the reduced peripheral utilization of glucose and its diminished output from the liver in hypophysectomized (hpx) animals suggested to us that the absence of the pituitary gland has a diabetogenic effect on the glucose tolerance test. Fasted hpx rats (85-110g) were utilized 3 or more weeks after the operation. Oral glucose tolerance test (OGTT) were performed using a 15, 30 or 50% glucose (G) solution (1 ml/100g b.w.). Impairment of the OGTT was observed with the 30 and 50% solutions. 176, 158 and 137 mg/100 ml G (hpx) at 60, 90 and 120 minutes contrasted with controls (C) 143, 130 and 118 mg% ($p<.001$ for all values) using the 30% solution. 185, 246, 230 and 195 mg% G (hpx) contrasted with C 156, 196, 138 and 126 mg% ($p<.001$ for all values) in 50% solution test. Neither 6, 18 or 24 hours of fasting, nor force feeding twice daily with 500 mg G in addition to the regular diet, altered the impairment in the OGTT when compared with C rats. I.V. GTT (250 mg/100g b.w.) also showed a significant impairment in the hpx rats ($p<.001$) at 15, 30, 60 and 90 minutes. Bovine growth hormone (GH), 0.1mg/rat/e.o. day, for 3 weeks produced a normalization of the OGTT in the hpx rats. Excess of GH (0.5 mg/rat/day) injected after operation for period of 2 to 7 days accelerated the onset of the impairment in the OGTT that appears regularly 3 weeks after operation. During the OGTT the levels of circulating insulin were not significantly different in control or hpx groups, however, free fatty acids were significantly lower in the hpx rats. Conclusion: The absence of the pituitary gland has diabetogenic effects on the GTT. Paradoxically an excessive amount of GH is also diabetogenic.

THE USE OF CULTURED AORTIC INTIMAL CELLS FOR THE COATING OF CARDIOVASCULAR PROSTHETIC DEVICES[1]. Carl J. Pennington*, J.P.G. Williams*, and J. B. Boatman. Battelle Memorial Institute, Columbus Laboratories, Columbus, Ohio

Improvement of the nonthrombogenic character of prosthetic materials intended for cardiovascular use may be made through the use of cell cultures derived from the linings of blood vessels. To date, there has been conflicting evidence as to whether fibroblasts, which are readily cultured, are suitable for this purpose. Controlled trypsinization of vessels such as the aorta is known to release intimal cells exclusively. Using a modification of this technique, primary cultures of adult ewe aortic intima have been prepared. The cells have been grown on borosilcate tissue culture glass and on Parylene® coated polypropylene microfiber materials from the Union Carbide Corporation, Bound Brook, New Jersey. The purpose of the "microfiber" surface is to provide a better anchor for cell attachment than a smooth polymer surface would furnish. The fiber diameter is quite small with regard to the cell diameter. To date, intimal cells derived as above have been used to produce monolayers approaching 90-100 percent surface coverings. The cells are applied to the tubular prostheses centrifugally to ensure even distribution. With an initial inoculum of approximately 500,000 cells/ml, about 7 days is required for full sheeting of 15.6 cm^2. Pretreatment of the surface with sheep plasma enhances growth. Initial attempts at the preparation of intimal cultures from the jugular have had some limited success and suggests the possibility of the experimental animal's providing cells to coat prosthetic devices for later implantation into the same animal. Preliminary evidence suggests that intimal cells increase significantly the nonthrombogenic character of surfaces.

1. This research has been supported by Contract No. PH 43-67-1404 from the Artificial Heart Program, National Institutes of Health.

HYPOXIA AND HYPERCAPNIA ALONE AND IN COMBINATION UPON CIRCULATING RED CELL VOLUME. William E. Pepelko (intr. by S.M. Cain) USAF School of Aerospace Medicine, Brooks AFB, Texas.

Recent evidence has indicated that concomitant hypercapnia may prevent the hypoxia stimulated increase in erythropoiesis. To investigate this phenomenon further, total circulating red cell volume (CRCV) was measured in rats exposed up to 24 days to either hypoxia (pO_2 = 80 torr), hypercapnia (pO_2 = 160 torr, pCO_2 = 68 torr) or hypoxia plus hypercapnia (pO_2 = 80 torr, pCO_2 = 68 torr). CRCV was estimated using dilution of 51Cr labeled red cells. CRCV of the hypoxia exposed rats increased from a control level of 2.52±0.41cc/100 gm body wt. to 2.85±0.33cc/100gm after one day of exposure then continued to increase to 5.61±1.66cc/100gm by day 24. Hypoxic-hypercapnic rats on the other hand showed a rise in CRCV after one day of exposure to 3.13±0.66cc/100gm ($P<.01$) then showed no further increase with a slight drop on the 24th day. Hypercapnia alone did not affect the number of red cells in circulation although plasma volume was increased somewhat, resulting in a decrease in hematocrit. After 24 days, only the hypoxic rats showed a significantly greater red cell volume than controls. The rapid increase in CRCV after one day of exposure to hypoxia or hypoxia plus hypercapnia was probably due to a release of stored red cells in the circulation. The lack of a further increase of CRCV in the hypoxic-hypercapnic rats suggested that erythropoiesis was not increased in these animals. At present there is insufficient evidence to determine if this effect is due to alleviation of tissue hypoxia or an active inhibition of erythropoiesis.

POSTURAL BEHAVIOR OF DOGS DURING SINUSOIDAL FORCING.
W. A. Petersen*, R. A. Talbott* and J. M. Brookhart. Dept. Physiol., University of Oregon Medical School, Portland, Oregon 97201.

Four dogs have been trained to stand quietly erect on a moving platform. The platform was driven sinusoidally at 0.5, 1.0 and 2.0 Hz and at 8.0 cm (pk-pk) amplitude along the dog's longitudinal axis. Table position, positions of head and pelvis, and the vertical forces exerted by the four feet have been recorded on FM tape. These data were sampled (128 points per cycle), digitized, and edited to eight-cycle segments of stable behavior. Each segment was subjected to Fourier analysis. Sine and cosine coefficients, power and phase spectra have been statistically analysed to determine central tendencies and variability across runs and across dogs. The analyses have enabled us to estimate the range of variability of each of the measured parameters. This information about the uniformity and predictability of behavior will be important for further studies of the postural reactions of dogs during sinusoidal forcing. (Supported in part by NIH Grants NB04744 and GM00538.)

AFFERENT ACTIVITY FROM AVIAN CO_2-SENSITIVE INTRAPULMONARY RECEPTORS.
D. F. Peterson* and M. R. Fedde. Department of Physiological Sciences, Kansas State University, Manhattan, Kansas 66502.

Single unit afferent recordings from vagal fibers whose receptors were sensitive to changes in pulmonary airway CO_2 content were obtained from 32 mature Single Comb White Leghorn male chickens. Impulse frequency of CO_2-sensitive units was inversely related to CO_2 content in the ventilating gas stream during unidirectional, artificial respiration. Maximum impulse frequency varied between 8 and 23 impulses/sec occurring at or near zero percent CO_2. Neural activity ceased at CO_2 concentrations between 5 and 13%. Abrupt elimination of CO_2 from the ventilating gas stream caused a transient burst of activity within 0.15 to 1.20 sec after CO_2-free gas reached the lungs. Acetylcholine and NaCN injected into the pulmonary artery had no apparent effect on neural output from these receptors. Veratridine caused transient reduction of output and, occasionally, disruption of discharge pattern. Changes in ventilatory O_2 concentration (5-80%) did not affect discharge frequency provided CO_2 concentration was held constant. In spontaneously breathing chickens CO_2-sensitive units were silenced by adding 10% CO_2 to the inspired gas. These units responded vigorously to inflation of the respiratory system with CO_2-free gas but remained silent during inflation with gas containing 15% CO_2. Such receptors may provide a means of detecting the rate of CO_2 production by body tissues and may be involved in the hyperpnea of exercise. (Supported by USPHS Grant GM-10362 and NSF Grant GB-3594.)

CIRCULATORY RESPONSE TO EXPERIMENTAL DIVING OF THREE SPECIES OF CROCODILIANS. Richard G. Pflanzer* and Grace E. Wertenberger. Indiana University, Bloomington, Indiana.

Cine-angiocardiographic studies of the right and left heart in A. mississippiensis and C. sclerops indicate complete separation of pulmonary and systemic circuits under aerobic conditions. Both aortic arches are perfused by the left ventricle while the right ventricle supplies blood only to the pulmonary artery. Pressure-time relationships of the aortic arches, pulmonary artery, and ventricular chambers of A. mississippiensis, C. sclerops, and P. trigonatus substantiate radiographic data and further indicate maintenance of separation during experimental diving. Right ventricular pressure was seen to increase during diving but left aortic arch pressure also increased. A right to left shunt was not seen to develop during experimental diving. Analysis of blood O_2 and CO_2 content before, during, and after diving support pressure data concerning shunting of blood. Blood of both aortic arches was observed to decrease in O_2 content in parallel and without a precipitous increase in CO_2 content as would be evident in shunting.

EFFECT OF UNILATERAL VAGAL BLOCKADE ON THE HERING-BREUER INFLATION REFLEX IN CONSCIOUS DOGS. E.A. Phillipson*, R.F. Hickey*, and J.A. Nadel. Cardiovascular Res. Inst., Depts. of Med. and Anesth., University of California, San Francisco, California

Among the possible neural pathways involved in the control of breathing are a number of bronchopulmonary receptors whose afferent pathways are in the vagus nerves. The vast majority of studies of the reflexes initiated by these receptors have been acute experiments on anesthetized animals. We studied the Hering-Breuer inflation reflex in conscious, trained, tracheostomized dogs at rest and during treadmill exercise. The reflex was elicited by occluding the trachea following inspiration of a normal tidal volume, or by inflating the lungs with airway pressures of 5-25 cm H_2O. The duration of apnea produced by the reflex (10-40 sec at rest) varied directly with the inflating pressure. For a given inflation pressure and oxygen consumption, the duration of apnea was found to be highly reproducible over a period of 12-15 months. Blockade of either cervical vagus nerve by local anesthetic abolished the reflex, but did not affect respiratory frequency or tidal volume at rest or during exercise. This observation argues against the classic theories on the role of the pulmonary inflation receptors in regulating tidal volume and respiratory frequency.

(Supported in part by Program Project Grant HE-06285 from the NHLI.)

CHANGE IN ACETYLCHOLINE CONTENT IN POSTGANGLIONIC CELLS OF ADULT PIGEON CILIARY GANGLION AFTER DENERVATION. G. Pilar, D. Jenden*, and B. Campbell*. Department of Physiology, University of Utah and Department of Pharmacology, University of California, Los Angeles 90024.

Transmission failure occurs in the pigeon ciliary ganglion 46 hr after presynaptic section (2mm prox. to ganglion) and continues for a 10 day period (Landmesser & Pilar, 1970). The Acetylcholine (ACh) content of the ganglion and ciliary nerves was estimated by gas chromatography (Hanin & Jenden, 1969. Biochem. Pharmacol. 18, 837) at different times after nerve section. The control values were 39.4 ± 4.9 (Mean ± SD) ng/ganglion and 26.2 ± 2ng for the nerves of each ganglion (approx. wet wt. of ganglion = 0.2 - 0.5 mg, nerves 1 - 1.5 mg). The tissues were isolated approximately 60 sec after decapitation. No modification in ACh content was observed in tissue isolated in 3 min or after superfusion in Tyrode for 1 hr. The ACh content of the denervated ganglia decreased to 10 ng in 2 days and progressively decreased to nil by 4 days. The ACh content in the ciliary nerves also decreased after 6 days and could not be detected after 10 days with the present method (sensitivity of method = 1ng). No changes in the ultrastructure of the postsynaptic cells were observed at this time and the nerve cells continued to be excited by applied ACh and the ciliary nerves conducted impulses. The decrease in the ACh content may indicate that the presynaptic cells exert a control essential to the metabolic synthesis of ACh in the postsynaptic elements of this parasympathetic ganglion. (Supported by USPH NS 07047, NS 07938, RCDA (GP) NS 35993, MH 13737, MH 17691.)

Landmesser & Pilar, (1970). Selective reinnervation of two cell populations in the adult ciliary ganglion. Sent for Publication.

ESTIMATION OF MYOFIBRILLAR MASS FROM Mg-BINDING OF RAT HEART. Philip I. Polimeni* and Ernest Page. Depts. of Physiology and Medicine, University of Chicago, Chicago, Illinois.

During embryonic development, postnatal growth, hypertrophy, and atrophy myofibrillar mass of striated muscle may change disproportionately to the mass of other constituents of the muscle cell or of non-muscular components like connective tissue. Because it is difficult to extract myofibrillar proteins quantitatively from heart muscle, we have developed a technique for estimating myofibrillar mass from the Mg bound to isolated myofibrils and to rat hearts treated so as to extract almost all Mg except that bound to myofibrils (Fed. Proc. 29:322Abs.:1970). Mg was determined by atomic absorption spectrophotometry. The Mg content of myofibrils fractionated from ventricular homogenates and treated with KCl, deoxycholate, and EDTA was 4.2 mmoles/kg protein. The Mg content of glycerinated ventricles extracted with 150 mM KCl was 2.0 + 0.2 mmoles/kg dry weight, the dry weight used as the unit of reference being the weight before glycerination. These data yield a figure of 470 kg myofibrillar protein/kg dry weight of ventricle. The figure is high by ∿ 25% due to a contribution of residual Mg bound to mitochondrial membranes, whose magnitude can be estimated by appropriate methods.

QUANTIFICATION OF PARKINSONIAN RIGIDITY. R. S. Pozos and R. N. Stiles (intr. by D. A. Brody). University of Tennessee, Memphis, Tenn.

This report presents a possible method for dynamically quantifying Parkinson rigidity. The phase angle between the surface electromyograms (EMGs) of antagonistic forearm muscles during voluntary extension and flexion of the hand was determined at the frequency of motion. Motion was detected by an AVR-250 accelerometer. The raw EMG records (16 seconds) were digitized, full-wave rectified, and smoothed for cross-spectral analysis by a PDP-12 computer. In general, the rigid Parkinsonian patient is unable to oscillate his hand voluntarily for a prolonged period of time even at low frequencies (1-2 hz). During voluntary oscillation, EMG records taken from rigid patients show a somewhat continuous activity with considerable irregularity in amplitude contrasted with the regular bursts of activity and inactivity recorded from normals. Cross-spectral analysis of EMG records taken from normals during voluntary oscillation shows that the antagonistic muscles consistently fire at approximately 180 degrees relative to each other. However, phase angles for Parkinsonian patients with rigidity range from 18 to 109 degrees (6 patients). Three patients on L-DOPA for approximately 10 months show changes in the phase angles between EMGs from 20, 75, and 109 degrees, respectively, to approximately 180 degrees. In addition to the changes in phase angles, after 10 months on L-DOPA these patients could oscillate their hands voluntarily at a higher frequency and for a longer period of time.
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INTRACELLULAR RESPONSES OF DORSAL HORN CELLS TO SURAL NERVE A AND C FIBER STIMULI. Price, D.D.*, Hull, C.D. and Buchwald, N.A. Depts. of Anatomy and Psychiatry and Mental Retardation Center, NPI, UCLA.

Intracellular recordings were made in 65 L-7 dorsal horn cells in spinal cats. Units in layers IV-VI responding to single shocks to the sural nerve were studied. Four types of short latency (5-10 msecs) PSPs and spike responses occured in response to A fiber stimulation: (1) Initial 10-50 msec EPSP followed by a 50-250 msec IPSP (30 cells); (2) 20-275 msec EPSP only (15 cells); (3) spikes from baseline followed by a 100-300 msec depolarizing or hyperpolarizing potential (12 cells); and (4) spikes from baseline only (8 cells). Increasing the stimulus intensity to excite both A and C fibers elicited both short and long (200-550 msec) latency PSP sequences and spikes in 16 cells. Long latency PSP and spike responses included the 4 types described above with EPSP-IPSP sequences being most common. The PSP sequences with the long latency responses were qualitatively similar to those with short latency responses. The long latency responses often lasted several hundred milliseconds. Recruiting of additional spikes per stimulus were evoked by stimulation rates greater than 0.3/sec ("windup"). In most cells this phenomenon was related to a progressive diminution of IPSPs in PSP sequences. In a few cells it was associated with a progressive membrane depolarization. These long term postsynaptic facilitatory mechanisms activated by C fiber inputs may be relevant to the understanding of pain mechanisms.

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THE EFFECT OF SYMPATHETIC NERVE STIMULATION AND BETA-ADRENERGIC BLOCKING AGENTS ON THE A-V NODE AND BUNDLE BRANCHES OF THE CANINE HEART. D.V. Priola. University of New Mexico School of Medicine, Albuquerque, New Mexico.

This study was designed to evaluate the effects of cardiac sympathetic nerve stimulation on conduction velocity through the canine specialized conduction system and to determine whether differential effects are produced in the right versus the left bundle branch. 15 mongrel dogs were anesthetized with sodium pentobarbital and placed on total cardiopulmonary bypass. Surface recording electrodes were attached over the regions of the bundle of His, right bundle branch (RBB) and left bundle branch (LBB). After vagotomy, right and left stellate ganglia were stimulated (SS) at constant heart rate and the effects on conduction velocity in the three areas were simultaneously recorded. SS evoked the expected decrease in A-V nodal delay (avg. 35%). In no case was RBB or LBB conduction velocity influenced by SS. Beta-receptor blocking doses of AY-21,011 (2-4 mg/kg) produced a prolongation of A-V nodal delay as did equieffective doses of propranolol (PPL-0.5-1 mg/kg). Despite prolongation of A-V nodal conduction with PPL to the point of complete block, RBB and LBB conduction velocities remained essentially unaffected. The data show that the cardiac sympathetic nerves have little influence on bundle branch conduction velocity. In addition, both the bundle branches, unlike the A-V node, are quite insensitive to the direct electrical depressant effects of PPL.(Supported in part by NIH Grant #HE-10869 and LIMRF Grant #G-68-32)

EFFECT OF TRAINING ON THE ALACTACID ANAEROBIC ENERGY RELEASE MECHANISM IN MEN OF DIFFERENT AGES. F.S. Pyke*, S. Robinson, S.P. Tzankoff* and C.A. Brawn*. Indiana University, Bloomington, Indiana.

The effect of vigorous training on the capacity of both young men (20-22 years) and older men (44-66 years) to release energy from alactacid anaerobic sources was evaluated. Oxygen debts and levels of blood lactate were measured during the first five minutes of recovery following each of three 10 second bouts of treadmill work ranging in intensity from moderate to near the maximum rate at which each man could perform. Regression analysis of the data for each group showed that the more intensively trained younger men made greater improvements than the older men in both the treadmill speed attained and the oxygen debt incurred with a 0.10 g/kg rise in total body lactate. Both age groups also made significant improvements in a stairclimbing test that assessed the ability to release energy rapidly. However, within the trained older group, performance in this test, together with that in a 15 yard sprint and a vertical jump, was more retarded by age than was the capacity to release energy either from oxidative processes or from the alactacid oxygen debt mechanism. Varsity distance runners, with high aerobic work capacities, could develop greater alactacid oxygen debts than champion sprinters capable of generating exceptional muscular power. This relationship between aerobic capacity and the alactacid oxygen debt was substantiated by comparing individuals within the young and older age groups. (This research was supported by United States Public Health Service Grant No. R01 HD 04056-01.)

Cephalexin Penetration of the Surviving Rat Intestine
J. F. Quay and Laura Foster (intr. by W. McD. Armstrong)
Eli Lilly and Company, Indianapolis, Indiana

Cephalexin, a new antibiotic of the cephalosporin family, is well absorbed following oral dosage yielding high peak serum concentrations of antibiotic. (Wick, W.E., Appl. Microbiol. 15, 765-769, 1967). Under short circuit conditions in a modified Ussing chamber, cephalexin penetrates isolated rat jejunum more rapidly from mucosa to serosa (m→s) than from serosa to mucosa (s→m). At a cephalexin concentration of 16.3 mM in the solution bathing one side of the intestine, the unidirectional permeabilities, m→s and s→m respectively, are: 3.00 ± 0.25 and 2.08 ± 0.22 X 10^{-6} cm/sec. for eight experiments in each direction. 11 mM glucose in the bathing solution increases the short circuit current, and presumably water flow, without affecting cephalexin permeabilities, indicating independence of cephalexin fluxes and water flow. In contrast 30 mM glycine inhibits the m→s flow of cephalexin suggesting competition for a mediated step. In the presence of glucose, 0.2 mM 2-4 DNP inhibits both the short circuit current and the m→s penetration of cephalexin. The mucosa to serosa permeation of the small intestine of the rat by cephalexin is presumed to consist in part of passive diffusion and in part of a metabolically dependent mediated transfer process.

THE EFFECT OF GONADECTOMY ON STEROID BINDING TO SERUM PROTEINS IN IMMATURE RATS. Judith Ramaley. Anatomy-Physiology, Indiana University, Bloomington, Ind. 47401

Binding of steroids to serum proteins was determined by equilibrium dialysis. Ovariectomy at 22 days of age increased progesterone binding, decreased estradiol binding and had no effect on testosterone binding at 26 days, 30 days, 35 days, 39 days and 46 days of age. Castration at weaning increased the binding of estradiol slightly in males. These changes were associated with a reduction in the amount of total serum protein and a depression of the alpha and beta globulin peaks obtained by polyacrylamide gel electrophoresis. Ovariectomy after puberty decreased the binding of estradiol without affecting the serum protein pattern. Competitive binding studies suggest that both the albumin and globulin fractions participate in the changes in steroid binding after gonadectomy. The results suggest that the changes in binding of steroids to serum proteins in maturing rats are due to puberal changes in gonadal secretion. Changes in the binding of steroids to serum proteins may be a factor in the onset of puberty. Supported by NSF Grant BG 17438

DYNAMIC RESPONSES TO CARDIAC NERVE STIMULATION IN THE BABOON. David C. Randall and J. Andrew Armour (intr. by Orville A. Smith). Regional Primate Res. Ctr. & Dept. of Physiol. & Biophys., Univ. of Wash., Seattle, and Dept. of Physiol. Stritch School of Med., Loyola Univ., Chicago.

Cardiovascular responses were elicited by stimulating various components of the sympathetic and parasympathetic nerves and ganglia supplying the heart of the baboon. Myocardial activity was measured via strain gauge arches sutured at various locations on the four heart chambers and on one or two papillary muscles of the left ventricle. Arterial and left ventricular pressures were recorded. In the cervical regions sympathetic and parasympathetic trunks are contained within a common neurilemmal sheath. Whereas stimulation of these major components separately, as well as of the stellate ganglion, evoked the classically described responses, stimulation of smaller cardiac nerves elicited changes in contractile force from localized myocardial regions. Vagal stimulation in paced and non-paced hearts showed negative inotropic action on ventricular myocardium. The right ventricle was generally more responsive to nerve stimulation than the left. The phrenic nerve was shown to contain fibers which influence the heart. Post-mortem examination supported the stimulation studies; whereas the sympathetic and parasympathetic systems have some connections at higher cervical levels, these systems are so intermingled at and below the middle cervical ganglion that any functional or anatomic distinction between them is virtually meaningless. (Supported by NIH Grants FR00166 and HE08682.)

PLASMA CATECHOLAMINES AND CARDIOVASCULAR RESPONSES TO SYMPATHETIC STIMULATION. W.C. Randall, J.A. Armour,* D.C. Randall,* O.A. Smith, Loyola University, Maywood, and Washington University, Seattle.

In a series of seven baboon experiments the heart was repetitively stimulated by reflex, humoral, or electrical excitation of the sympathetic cardiac nerves; progressively decreasing responsiveness of cardiac musculature became apparent. Vagal excitation exerted profound effects. Blood pressure, myocardial contractility and heart rates remained within or above normal control limits. In eight subsequent experiments, the adrenal veins were cross-clamped with relatively rapid deterioration in cardiovascular status, but vigorous responsiveness to sympathetic stimulation and catecholamine injections was retained. Plasma levels of catecholamine (CA) (average 0.15 and 0.40 μg/liter for epinephrine and norepinephrine (NE) respectively) were monitored in a third series in which the adrenal veins were initially clamped and subsequently released, with neural and humoral testing of functional responses throughout. Vigorous sympathetic responses marked the periods of low plasma CA concentration. Upon release of the adrenal vein clamp, CA levels became greatly elevated with marked increases in systemic arterial and intraventricular blood pressure, myocardial segment contractile force, and heart rate. NE and supramaximal stimulation of the stellate ganglia now failed to augment any of these parameters. Again, vagal stimulation was profoundly effective. It is concluded that levels of circulating catecholamines from the adrenal medulla exert important influences upon general cardiovascular responsiveness to sympathomimetic and vagal excitation. (Supported by NIH Grant HE08682, and NIH Grant FR00166)

INVOLVEMENT OF ADRENERGIC RECEPTORS IN THE OVULATION AND IMPLANTATION PROCESSES IN THE RAT. Albert Ratner (intr. by S. Solomon). Univ. of New Mexico Sch. of Med., Albuquerque, N.M. 87106.

Alpha adrenergic blockade with phenoxybenzamine (25 mg/kg) effectively blocked ovulation in the rat when administered prior to the "critical period" on the day of proestrus (1:00 PM), but failed to block ovulation if administered at 5:00 PM. The blocking effect of phenoxybenzamine was overcome by injecting 20 i.u. of HCG at 3:00 PM. Beta adrenergic blockade with propranolol or MJ-1999 (25 mg/kg) had no effect upon ovulation. Administration of phenoxybenzamine (20 mg/kg) on days 4 and 5 of pregnancy prevented implantation in 70% of the rats studied, as judged by the examination for implantation sites on day 11 of pregnancy. In those rats that implanted, the number and size of the implants were normal. Propranolol (25 mg/kg) had no effect on implantation. Alpha receptor blockade is not thought to suppress prolactin secretion, since a single injection of phenoxybenzamine was shown to induce pseudopregnancy in cycling rats. These data indicate that alpha adrenergic receptors play a role in ovulation and implantation processes. It is possible that such occurs by influencing the release or action of luteinizing hormone. (Supported by a grant from the National Science Foundation, GB 8084.)

MECHANISM OF SOUND PRODUCTION IN THE 17-YEAR CICADA. Kenneth H. Reid (intr. by S. M. Walker). Department of Physiology and Biophysics, University of Louisville, Louisville, Kentucky.

The adult male cicada, Magicicada septendecim, "sings" by vibrating two tymbals situated on the flanks of the rostral part of its abdomen. Each tymbal is driven by a separate muscle. The mechanism of sound production was analyzed by recording the sounds, the muscle tensions and movements, and the electrical activity of the tymbal muscles. The sound consists of a series of chirps, each lasting about 5 msec, which increase in tempo to a continuous sound composed of chirps produced at a rate of about 100/sec. After 2-5 sec the chirp rate decreases rapidly, ending the pattern. During the main burst of sound the two tymbal muscles are excited alternately about 50 times per second. A single twitch of the tymbal muscle is completed in 20 msec; the peak tension is reached in 7 msec. The excitation-contraction latency is 2.5 msec. The working end of the tymbal muscle terminates on a flat plate, which is connected to the tymbal by a short tendon-like apodeme. When the muscle contracts, tension is exerted on the tymbal and it buckles inwards. The tymbal consists of a thin sheet of chitinous tissue containing a series of stiff ribs. As the tension increases the ribs buckle successively, emitting a series of 7-8 KHz pulses; on relaxation they jump back, producing a (weaker) out-chirp. No evidence was found for any "release-deactivation" of these tymbal muscles, despite a careful search using natural, quick-stretch, and resonant stimulation. This mechanism, as described by Pringle for several species of Ceylonese cicadas, permits the muscle to contract several times for each activation; it is replaced in this species by the ribbing of the tymbal, which has the same effect.

CATABOLISM OF ENDOGENOUS HISTAMINE IN THE MOUSE. Margaret A. Reilly* and Richard W. Schayer, Research Center, Rockland State Hospital, Orangeburg, New York. 10962

The problem of identifying by in vivo methods, the tissues and enzymes participating in catabolism of endogenous histamine, has been approached as follows: aminoguanidine (AG) and 1,4-methylhistamine (MeH), inhibitors of the major histamine-catabolizing pathways, oxidation via diamine oxidase (DAO), and methylation, respectively, (Brit. J. Pharmacol. 38, 478, 1970), were first shown not to affect histamine formation in vitro or in vivo. Mice were then pretreated either with saline, AG, MeH, or AG & MeH, injected i.v. with ^{14}C-L-histidine, sacrificed 10 minutes later, and tissues assayed for ^{14}C-histamine and total ^{14}C. In all tested tissues, levels of ^{14}C-histamine in AG-treated mice did not differ significantly from controls; however, MeH-treatment definitely increased ^{14}C-histamine levels in blood, brain, liver, heart, lymph node and stomach, but not in muscle or intestine. Results were similar to those for injected ^{14}C-histamine with a major exception: the DAO of intestine, highly active in destroying blood-borne ^{14}C-histamine, did not catabolize endogenous ^{14}C-histamine. The findings suggest that (a) endogenous histamine is inactivated almost entirely by methylation, (b) intestinal DAO functions mainly to destroy amines formed by bacteria in the lumen, and (c) ^{14}C-histamine in the tissues is mainly formed locally. (Supported by N.I.H. Grant AM-10155)

EFFECT OF INHALATION OF O_2 AND CO_2 GAS MIXTURES ON SPONTANEOUS GASPS AND APNEA IN UNANESTHETIZED DOG. Edward J. Reininger and Peter Segall*. McGill University, Montreal, Canada.

Episodes of spontaneous gasps and apnea, with associated cardiovascular changes, occur in the dog regularly with a rate characteristic of each animal. To determine if there is any chemical influence on gasp frequency, the dog fitted with a face mask is permitted to inspire various gas mixtures to change its Pa CO_2 or Pa O_2. Dogs breathing gas mixtures containing 40%, 20.9% (air), and 10% O_2 exhibit an average of 7.0, 7.5, and 18.1 gasps per hour, respectively. The addition of 3% CO_2 to each of the above mixtures shifts the response curve upwards, resulting in 14.9, 17.3, and 24.2 gasps per hour, respectively. The presence of CO_2 is found to reduce or eliminate the post-gasp apneic period; this apnea is considered chemically mediated and is caused by the Pa CO_2 falling below the CO_2 apneic threshold. Although only minor changes occur in respiratory and heart rate, the composition of a gas significantly influences the gasp frequency. The origin of a gasp cannot be explained on a chemical basis, as reaching gasp threshold values of Pa CO_2 or Pa O_2 since, e.g., inhalation of a 40% O_2 gas mixture probably does not permit the Pa O_2 to fall to the lower values found when the animal breathes room air. The spontaneous gasp in the dog probably functions to reopen collapsed alveoli.
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INPUT IMPEDANCE AS AN INDEX TO REFLECTION SITES. J. W. Remington and W. L. Powers*, Dept. Of Physiology, Medical College of Ga., Augusta, Ga.

A series of conceptual models was used to describe the effect of reflection sites in series with a terminal resistance, building towards the aortic model used to derive a flow pulse from a pressure pulse. Input impedance was derived by Fourier analysis. Five pulses, varying only in cycle length, were analyzed for each model. A uniform tube with a terminal resistance showed an impedance peak near the expected frequency (f_1) and again at $2f_1$. Phase difference became 0 at f/2, f, 3f/2 and 2f. Changes in both above 12 Hz were variable from pulse to pulse, laid to the small P and Q modulus values. When a 2nd reflection was placed central to the resistance, impedance no longer peaked at f_1, or even at the frequency expected for the shorter length (f_2), but at an intermediary value, and phase and moduli curves were no longer clearly related. Use of 3 reflection sites in series accentuated the impedance peak at f_1 and another peak developed at f_2. Phase difference agreed with neither in either location of 0 or in curve inflection. More complicated models could give either slurring of low frequency impedance peaks or more commonly augmentation. Because of the limitation to low frequencies, the Fourier technique can neither prove nor disprove the aortic model, but impedance changes resulting from use of this model show many points of similarity with those obtained by an analysis of aortic pulses. Because of amplitude and timing changes produced by serial reflections, it is concluded that either modulus peaks or phase difference inflections may be of limited use in assigning reflection sites. (Supported by Grant HE-10602-04.)

INHIBITION OF INSPIRATION BY ELASTIC RESPIRATORY LOADING. J. E. Remmers, J. F. O'Donnell*, S. H. Loring* and D. Bartlett, Jr.*. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

The effect of elastic loading of the respiratory system on tidal volume, duration of inspiration and diaphragmatic motor discharge was studied in four healthy, awake subjects, while they sat upright in a whole-body volumetric plethsymograph sealed around the neck. Light, single-breath loads (3.5 cm H_2O/l) were produced by closing the plethysmograph for the duration of one breath, thus converting it to a constant volume chamber. Diaphragmatic potentials were recorded from a bi-polar, esophageal catheter electrode positioned at the level of the diaphragm by a balloon inflated in the stomach. A smoothed electromyogram (EMG) and the total discharge per breath were recorded.

Elastic loading decreased tidal volume, duration of inspiration and diaphragmatic discharge in all subjects. EMG and total discharge per breath decreased 43% and 54%, respectively. The reduction in tidal volume was less than that expected from the reduction in diaphragmatic discharge. This finding implies preferential inhibition of diaphragmatic motor units, whereas the decrease in inspiratory duration indicates supra-spinal inhibition of inspiration. These responses to elastic loading can be ascribed to reflex inhibition of inspiratory activity by intercostal afferents (Remmers & Tenney, Physiologist 12:338, 1969), but the participation of conscious factors in particular cannot be excluded. The responses manifest differential recruitment of inspiratory muscles and increased respiratory frequency, both of which may increase the mechanical efficiency of breathing for a decreased compliance. (Supported by NIH grant # HE 02888-14.)

ADRENERGIC MECHANISMS IN THE CANINE MESENTERIC CIRCULATION. D. G. Reynolds* and K. G. Swan. Walter Reed Army Inst. Research, Wash., D. C.

The effects of alpha (α) and beta (β) adrenergic stimulation and blockade upon mesenteric hemodynamics were studied in anesthetized dogs. Mesenteric arterial blood flow (MBF) was measured electromagnetically. Arterial (AP) and portal (PP) pressures were recorded from intravascular catheters. Resistance was calculated from these data. With intraarterial injections of 0.1 μGm Kg^{-1}: norepinephrine ("$\alpha > \beta$") reduced MBF from 322 ± 40 (S.E.) to 93 ± 8 ml min^{-1} ($p < .01$) within 15 sec. At 45 sec MBF (433 ± 71 ml min^{-1}) exceeded control ($p < .01$). AP and PP were unchanged from control values (150 ± 2 and 6.5 ± 0.5 mm Hg). Epinephrine ("$\beta > \alpha$") caused a similar response, marked vasoconstriction followed by vasodilation. Isoproterenol ("pure β") effected slight vasoconstriction, 320 ± 27 (control) to 259 ± 33 ml min^{-1} ($p < .01$), followed by marked vasodilation, 623 ± 65 ml min^{-1} ($p < .001$) at the same time intervals. Phenylephrine ("pure α") evoked less vasoconstriction and no dilation. α adrenergic blockade (phenoxybenzamine, 1.5 mg Kg^{-1}, I.V.) did not alter these responses to norepinephrine; whereas "epinephrine reversal" did occur, mimicking isoproterenol responses, which lacked significant vasoconstriction preceding dilation. "Phenylephrine reversal" (vasodilation) followed α blockade. β blockade (propranolol, 0.5 mg Kg^{-1}, I.V.) then restored vasoconstrictor dominance to epinephrine and caused "isoproterenol reversal" (predominant vasoconstriction). Thus both endogenous catecholamines are vasoconstrictors in the dog gut. Epinephrine, but not norepinephrine, can be "reversed" by α blockade. The presumed "pure" agonists can also be reversed by adrenergic blockade, leaving norepinephrine the only "classical" agonist eliciting a pure adrenergic mechanism in this vascular bed.

PROPORTION OF CARDIAC OUTPUT AND OF TOTAL BODY OXYGEN CONSUMPTION WHICH IS USED BY THE MAMMARY GLANDS. Monica Reynolds. Laboratory of Physiology, Dept. of Animal Biology, School of Veterinary Medicine, Univ. of Penn., Phila., Pa.

In each of six goats, cardiac outputs and mammary blood flows were measured simultaneously at various times during the prepartum periods and the lactation cycles. Values for the former were obtained by the direct Fick (O_2 consumption) method and for the latter by the continuous thermodilution method. There was considerable variation in the results. Cardiac output values ranged from 6 to 26 l/min. In general, they followed the milk production, increasing after parturition and declining to a relatively steady state at mid-lactation. The proportion of cardiac output distributed to the udder ranged from 3 to 13%. In most of the goats there was a small increase in the proportion following parturition after which there was a decline to a steady state. Total body O_2 consumption ranged from 400 to 800 cc/min. In any one goat there was little variation between the prepartum and lactation periods. Mammary O_2 consumption, however, varied with the milk production, i.e., it increased during the first part of the lactation period and remained constant or declined slightly during mid-lactation. The proportion of mammary O_2 consumption to total body O_2 consumption, thus, increased at first and thereafter either remained constant or declined slightly. Overall this proportion ranged from 4 to 14%.

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LEFT VENTRICULAR VOLUMES AND HEART AND BODY WEIGHT IN UNANESTHETIZED MAMMALS. E. A. Rhode,* H. Kines,* and J. P. Holt. Univ. of Calif., Sch. of Vet. Med., Davis, Calif., and Heart Research Lab., Div. Exp. Med., Univ. of Louisville, Louisville, Ky.

Left end-diastolic (EDV), end-systolic (ESV), and stroke volumes (S), heart rates (R), cardiac output (CO), total peripheral resistance (TPR), and stroke work (SW) have been measured in the control and unanesthetized state in 40 mammals of four species; horses, cattle, sheep, and goats, varying 20 fold in body weight (BW) and 35 fold in heart weight (HW). The log-log relationships between these variables and body and heart weight have been determined. The coefficients for the power functions relating these cardiovascular variables to heart and body weight are not greatly different from those previously reported in anesthetized animals. Relationships for the left ventricle are described by equations relating ventricular volumes to $BW^{1.0}$, heart rate to $BW^{-0.25}$, cardiac output to $BW^{0.75}$, and TPR to $BW^{-0.75}$. These are: $EDV = 2.71\ BW^{1.0}$; $S = 1.15\ BW^{1.0}$; $HR = 237\ BW^{-0.25}$; $CO = 293\ BW^{0.75}$; $TPR = 34831\ BW^{-0.75}$; $SW = 2.15\ BW^{1.0}$, where EDV and S are in ml, HR is in beats/min., CO is in ml/min., TPR is in dynes-sec. cm^{-5}, SW is in gram meters, and BW is in Kg. It appears that unanesthetized animals have, on the average, a slightly greater EDV, stroke volume, stroke work, and cardiac output than when anesthetized. (Supported by USPHS Grant HE 05622.)

COMPARISON OF TECHNIQUES FOR MEASURING MEAN CAPILLARY PRESSURE IN PERFUSED ORGANS. D. R. Richardson*, J. W. Prather *, and B. W. Zweifach. University of Kentucky, Lexington, Ky., and University of California, San Diego, La Jolla, California.

The purpose of this study was to compare estimates of mean functional capillary pressure (Pc) in the isolated dog limb as obtained by three different techniques: 1) measurement of isogravimetric venous pressure under zero flow conditions; 2) extrapolation of isogravimetric venous pressures to zero flow, and 3) calculation of Pc from steady state measurements of plasma and tissue fluid colloid osmotic pressures, and tissue fluid hydrostatic pressure. The tissue fluid osmotic and hydrostatic pressures were obtained from chronically implanted capsules. Method 3 was applied before and after isolation of the limb and the respective values for Pc averaged 10.7 and 13.2 mm. Hg. In the isolated limb the gravimetric techniques (1&2) yielded average values for Pc of 15.0 and 13.9 mm. Hg. respectively. The higher value of method 1 was probably due to shifts in the Starling equilibrium since in many instances, the capsular fluid hydrostatic pressure during the zero flow isogravimetric state rose above control. In two experiments similar elevations in the capsular fluid pressure were also noted with method 2. Our conclusions are: a) that Pc is lower in the intact than in the isolated limb, and b) that calculation of Pc from capsular fluid variables (method 3) is a reliable method of determining mean functional capillary pressure in both in-situ and isolated organs as evidenced by the close proximity of Pc when determined by all three methods in the isolated limb.

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DELAYED METABOLIC RESPONSES OF THE RAT DIAPHRAGM TO GROWTH HORMONE IN VITRO. J.A. Rillema* and J.L. Kostyo. Emory Univ., Atlanta, Ga.30322

A study was made of the early time-course of the in vitro stimulatory actions of bovine growth hormone (BGH) on leucine incorporation into protein, AIB transport and glucose oxidation to CO_2 by isolated diaphragms of hypophysectomized rats. Diaphragms were preincubated for 1-4 hr at 2 C with BGH to distribute the hormone throughout the tissue in the absence of metabolism. Then ^{14}C-leucine, ^{14}C-AIB or ^{14}C-glucose was added to the medium and incubation continued for various brief periods at 37 C. Stimulatory effects of BGH on the above parameters of metabolism were not detectable when incubation at 37 C was for periods of 15 min or less. A similar delayed response was seen in vivo when rats were injected with BGH i.v. and then given an i.v. injection of ^{14}C-leucine to pulse-label diaphragm protein. Attempts were made to shorten the time required to produce an in vitro effect of BGH on protein synthesis by increasing the permeability of the diaphragm to large molecules such as the hormone. Diaphragms were sliced into thin strips dorso-ventrally or treated with phospholipase C, trypsin, crude or purified collagenase or dimethylsulfoxide. The two former treatments produced marked changes in the permeability of the tissue to ^{125}I-albumin. However, none of the treatments shortened the delay in the action of BGH on leucine incorporation into protein. Interestingly, treatment of the diaphragms with trypsin or crude collagenase destroyed their ability to respond to BGH, perhaps suggesting that certain proteins are involved in the primary interaction of the hormone with the cell. In any case, the above results indicate that the rapid effects of BGH studied are not immediate but have a brief but definite inductive phase which is dependent upon metabolism. Hence, these effects may be secondary to more primary metabolic events induced by the hormone.

COMPARISON OF VOLUME OF CANINE LEFT VENTRICULAR CASTS AND ANGIOGRAMS USING BIPLANE AND MONOPLANE ROENTGEN VIDEOMETRY. E. L. Ritman*, R. E. Sturm*, and E. H. Wood, Mayo Graduate Schl. of Med., Rochester, Minn.

Silastic casts of canine left ventricles supplied by H. Sandler were impaled on thin rods along the longitudinal axis and mounted at an adjustable angle from the plane of the x-ray beams of the biplane video system (JAP 24:724, 1968) and centered at the intersection of these beams. Biplane roentgen images of the cast and its angular position about its longitudinal axis were recorded on videotape (every video field 60 times/second) as the cast was rotated 360° in two seconds. This procedure was repeated at different angles of the longitudinal axis and for casts made at different stages of cardiac contraction. Orthogonal diameters of the ventricle were measured in real time by videometry at 50 to 80 positions along its longitudinal axis for each video field and its volume and shape calculated by a time-shared digital computer (CDC 3300) 60 times each second (Fed Proc 26:72,1970). Ventricle volumes were calculated from: 1) biplane (a) on the assumption that each of the up to 80 pairs of diameters of the silhouettes measured were the major and minor diameters of an elliptical disc, and (b) when the "disc" shape was reconstructed from the sequence of video fields recorded while the cast rotated; 2) monoplane: volumes were calculated according to an empirical relationship of the area and a cross-section of one silhouette. The considerable variation in the calculated volume of any one cast depended on its orientation and position relative to the biplane system. In general, the calculated volume was an overestimate. Biplane angiograms of the left ventricle in anesthetized dogs were also analyzed and the stroke volume (difference of the end-diastolic and end-systolic volumes) was generally an underestimate relative to the stroke volume calculated with indocyanine green dilution technique. (Supported in part by NIH grants HE4664, HE3532, and AHA grants CI 10, and 69,073.)

PARAMETRIC ANALYSIS OF PRESSURE AND FLOW PULSES IN ARTERIAL CONDUITS. R. L. Rockwell*, M. Anliker, and E. Ogden. Naval Weapons Center, China Lake, Calif. 93555; Dept. of Aeron. and Astron., Stanford Univ., Stanford, Calif. 94305, and Environmental Biology Div., NASA, Ames Research Center, Moffett Field, Calif. 94035.

A nonlinear analysis of large amplitude pressure waves was made for a theoretical model of the canine aorta and its continuation beyond the saphenous artery. Pressure and flow pulses were predicted by prescribing the ejection pattern of the heart and the physical and geometric features of the system. The effects of branches and bifurcations were modeled by a continuous outflow pattern which varies with location and pressure. At the distal end of the vessel, the terminal condition was specified either in the form of a peripheral resistance or in terms of a constant end pressure. The basic geometry was defined by an exponential decrease of the arterial diameter with distance from the heart. The elastic properties of the vessel wall were given through the wave speed and its dependence on location and pressure. This information was also used to determine the cross-sectional area variation with pressure and distance by integrating the wave speed-distensibility relation. The nonlinear equations for one-dimensional incompressible fluid flow were solved on the digital computer for parameters corresponding to a hypothetical 30 kg dog. In the numerical solutions the effects of reflections arising from the boundary conditions, taper and changes in the local wave velocity were included by employing the method of characteristics. Many familiar features of the natural pulse induced by the heart are predicted by the mathematical model, including the incisura, the growth and subsequent decay of the pulse pressure, and the gradual development of the dicrotic wave. As the pulse wave propagates down the aorta, we know that there is a marked steepening of the wave front. This is also predicted by the theory if the basic equations are not linearized.

OXYGEN CONSUMPTION OF NORMAL AND HEMOLYZED RABBIT RETICULOCYTES. Harold C. Rohrs. Department of Zoology, Drew University, Madison, N. J. 07940

Oxygen consumption of rabbit reticulocytes was decreased following exposure of these cells to hypotonic solutions. Reticulocytes obtained from animals made to be anemic by repeated injections of phenylhydrazine were incubated at 38.5° C in a modified Kreb's Ringer Phosphate Glucose (KRPG) solution that was 122.6mM in NaCl; 6.0mM in KCl; 2.5mM in $CaCl_2$; 1.2mM in $MgCl_2$; 1.2mM in Na_2SO_4; 6.0mM in Na_2HPO_4; 3.0mM in NaH_2PO_4 and contained 1.5 mg glucose/ml. Cells were hemolyzed by placing them in hypotonic KRPG solution that had one-fifth the concentration of dissolved salts as the incubating fluid. Restoration was effected by adding concentrated KRPG solution. Oxygen consumption was measured with a YSI Model 55 Oxygen Monitor. Reticulocytes consumed little or no oxygen immediately following hemolysis. As time passed, oxygen consumption increased until a maximum was reached after approximately five hours. Maximal respiration of hemolyzed cells was approximately one-half that of untreated reticulocytes. Resumption of oxygen consumption was not affected by storage at 4° C. These experiments indicate that the return of oxygen consumption following hemolysis by osmotic shock may depend upon re-establishment of certain processes or relationships within the cells; such re-establishment is not directly dependent upon the expenditure of metabolic energy.

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THE METABOLIC RESPONSE TO DIRECT STIMULATION OF THE INTACT CEREBRAL CORTEX. M. Rosenthal* and F.F. Jöbsis. Dept. of Physiology and Pharmacology, Duke University

Direct cortical stimulation has been used to evoke electrical potentials and changes in the metabolic activity of the intact cat cerebral cortex. Metabolic activity at the stimulated surface of the cortex is measured by the intensity of a fluorescence signal at about 450 mu when the tissue is illuminated by light of 366 mu. The fluorescence changes have been interpreted as changes in the oxidation-reduction level of intramitochondrial NADH. The electrical potentials consist of a negative spike followed by a positive after-potential and a negative wave or negative after-potential. These after-potentials evoked by serial stimulation summate and appear as transient changes in the DC or steady potential of the cortex. The fluorometric changes consist of an initial decrease in the fluorescence signal followed by a return of the signal to the steady-state level within 20 sec. The technique of fluorometrically monitoring the metabolic activity associated with cortical activity is seen as a valuable means of obtaining information on the energetics of cortical activity and as a possible test system to determine the cortical effects of various pharmaceuticals. (Supported by N.I.H. NS06729 and 2T01-GM-00929).

LUNG IRRITATION AND GASTRIC MOTILITY. Roland P. Roth* and Martin F. Tansy. Dept. of Physiology, Temple University, School of Dentistry, Philadelphia, Pa.

The effects of gaseous air pollutants on gastric motility in the conscious unrestrained rat were investigated. Twenty-four rats were exposed in a dynamic air-flow chamber to varying concentrations of NO_2, SO_2, CO and O_3 with gastric motility measured by indwelling balloons. Rats exposed to 1 ppm SO_2 for 5 days or 0.25 ppm O_3 for 2 days showed no change while there was gastric inhibition at 300 ppm SO_2 for 12 hours and 1.5 ppm O_3 for 2 hours. In all instances following chamber flushing recovery was complete within minutes. To evaluate the site and nature of stimulation rats also were exposed to oil of mustard, benzaldehyde and amyl acetate. Saturated dental paper points were introduced without obstruction into tracheal and retro-nasal cannulae. Oil of mustard but not benzaldehyde or amyl acetate inhibited gastric motility only when applied to the trachea. In general, the drop in activity was immediate and proportional to the degree of exposure. Nasal irritation was ineffective in eliciting the response. The results of these experiments suggest that gastric inhibition is not produced by either odor or nasal irritation but rather by irritation of the lower air passages. (Supported by NIH Fellowship No. 5F01-ES38728-03)

ARTIFACT DUE TO THE STAGNANT LAYER ON ELECTRODE SURFACE IN A CONTINUOUS-FLOW REACTION APPARATUS. H.H. Rotman*, R.A. Klocke* and R.E. Forster. (intr. by S.Winegrad) Dept. Grad. Physiology, Sch. of Med., Univ. of Penna., Phila., Pa.

Analytical electrodes with a relatively slow response time (10-15 sec) can be used to measure rapid kinetic processes in a Hartridge-Roughton continuous-flow apparatus since steady state conditions prevail. Theoretically, a stagnant layer of reacting fluid exists on the electrode membrane and, if sufficiently thick, will produce an overestimate of the extent of the reaction as indicated by the electrode. We have assessed this error in a continuous-flow apparatus at a linear reactant velocity of 280 cm/sec in two ways: (A) The rate of dehydration of carbonic acid was measured with a CO_2 electrode over the initial linear portion (40 msec) of the reaction. In 31 experiments the average extrapolated time intercept was -5.5 ± SD 3.4 msec, representing an equivalent underestimate of the correct reaction time. (B) P_{O_2} of water and of a saturated solution of $CaCl_2$, both equilibrated with air and neither undergoing reaction, was measured with a teflon-covered platinum electrode 0.0127 cm in diameter. Because the electrode consumes O_2, the measured P_{O_2} will be decreased in solutions with a low O_2 solubility and diffusion coefficient if an appreciable stagnant layer of fluid is present. In five experiments the apparent P_{O_2} in the $CaCl_2$ as measured by the electrode was only 21% that in water. Knowing the O_2 consumption of the electrode (calculated from the electrode current), and measuring the viscosity and O_2 solubility of the $CaCl_2$ solution, we calculated an effective stagnant layer of 5 on the electrode.

ENTRANCE OF COLLOIDAL ThO_2 INTO THE T TUBULES AND LONGITUDINAL TUBULES OF GUINEA PIG VENTRICULAR MYOCARDIUM. R. Rubio and N. Sperelakis. Univ. of Virginia School of Med., Charlottesville.

Colloidal ThO_2 particles were used as electron-opaque markers to trace "intracellular" compartments continuous with the bulk interstitial fluid (ISF) of guinea pig heart. Guinea pig ventricular muscle was selected because the transverse (T) tubules are very large. Isolated beating hearts (Langendorff) were perfused for 30 min with oxygenated Ringer solution containing 1% ThO_2, and then immediately fixed with glutaraldehyde. The ThO_2 particles, which had a mean diameter of 61 ± 1 Å, entered into many T tubules and into what is generally considered longitudinal sarcoplasmic reticulum, including lateral cisternae; tracer did not penetrate into the intercalated disk clefts. No differences in distribution of ThO_2 were observed in a heart made electrically and mechanically quiescent by elevating the K^+ concentration to 16 mM or in a heart not exposed to ThO_2 until after fixation. In frog heart, ThO_2 also failed to enter the clefts at intercalated disks and desmosomes, although it entered into the narrow intercellular clefts between the thin cells: no tubular profiles filled with ThO_2 were seen. It is concluded that in mammalian cardiac muscle the lumens of longitudinal (L) tubules are continuous with the T tubules. Direct observations of morphological continuity between the lumens of T and L tubules were also observed in the absence of ThO_2. Thus, the T-L tubular system forms an interconnected orderly network lined with basement membrane and open to the bulk ISF; the volume occupied by this lattice is estimated to be 8 to 16% of cell volume. Hence, the myofibrils and mitochondria have close access to a space that is continuous with the ISF and which may be of similar cationic composition; such an arrangement should facilitate excitation-contraction coupling.

EVIDENCE FOR THE IMPORTANCE OF VERY LOW DENSITY LIPOPROTEINS (PRE-β) IN THE TRANSPORT OF EXOGENOUS CHOLESTEROL IN THE RABBIT. L.L. Rudel, M.D. Morris*, and J.M. Felts, Banting and Best Dept. of Med. Research, U. of Toronto, Toronto, Canada, and Depts. of Biochem. and Ped., U. of Arkansas Medical Center, Little Rock, Arkansas

Rabbits were trained to ingest meals containing 6% fat and 0.08% cholesterol (C). Thoracic duct lymph was obtained in sequential time samples after an intraduodenal injection of a tracer dose of ^{3}H-C. The ^{3}H-C appeared in both chylomicrons (chylo, S_f>400) and a pre-β fraction (S_f 20-400) and at early time intervals had a ratio (pre-β:chylo) near 1. Collections from 7 to 10 hours had a ratio from 2 - 3, and at 19 to 22 hours, the ratio had increased to 4 - 5. Over 50% of the ^{3}H-C recovered in lymph was in the pre-β obtained from 10 to 22 hours after the dose was given. C ester specific activity (CESA) of the lymph chylo and pre-β were highest at these later times, and were 3 to 4 times higher than corresponding free C specific activity (FCSA). In other experiments, the time course of appearance of exogenous ^{3}H-C was measured in sequentially collected plasma lipoproteins obtained from unanesthetized rabbits. Each lipoprotein fraction (chylo, pre-β, α, and β) had a CESA which was higher at all times than the corresponding FCSA. CESA of pre-β increased more rapidly than any of the other lipoprotein fractions reaching peaks at 6 and 12 hours after feeding, suggesting a possible dual origin for the plasma pre-β particles. Thus, it appeared that the major transport form of exogenous C in the low C-fed rabbit is ester C, of which the larger fraction is transported into lymph and plasma in a pre-β lipoprotein. Supported by the Medical Research Council of Canada, the Ontario Heart Foundation, and NIH Grant GM-37, 164-01.

RESPONSE PATTERNS OF SINGLE MOTONEURONS DURING MONOSYNAPTIC REFLEX STABILIZATION BY AFFERENT VOLLEYS. P. Rudomin and J. Madrid*
Centro de Investigación y de Estudios Avanzados, I.P.N., México 14, D.F.

It has been shown (J.Neurophysiol.32:140,1969) that in the spinal cat variability of monosynaptic reflexes (MR) can be reduced by conditioning volleys to cutaneous and muscle afferents. This could result either from a decrease of correlated excitability fluctuations simultaneously affecting many members of the population and/or from a reduction of uncorrelated fluctuations. To evaluate changes of these two variability sources we studied the monosynaptic responses of single motoneurons during MR stabilization. Since at short conditioning-testing (CT) stimulus intervals cutaneous volleys inhibited and at longer intervals facilited MR and monosynaptic responses of gastrocnemius motoneurons, for each series the CT interval was adjusted (range 25 to 40 msec) to balance excitation and inhibition. In those conditions mean MR were unchanged and there was a marked reduction of MR variability. However, monosynaptic response patterns of single motoneurons and conditional probabilities of cell firing relative to a given MR size were unchanged. When CT intervals were varied (from 15 to 200 msec), MR stabilization was paralleled by a reduction of the coefficient of correlation between the monosynaptic responses of pairs of motoneurons belonging to the same motor nucleus. Assuming no correlation between the monosynaptic responses of both units, the relation between population variance and composite unit variance was rather poor. This relation improved when the observed coefficient of correlation was considered in composite unit variance computations. It is concluded that stabilization of MR produced by afferent stimulation is mainly due to a reduction of correlated influences impinging onto the monosynaptic path.

THE ACTION OF IODOACETIC ACID ON GLYCERALDEHYDE 3-PHOSPHATE DEHYDROGENASE (GAPD) IN MAMMALIAN NERVE. M. I. Sabri* and S. Ochs, Indiana University School of Medicine, Indianapolis, Indiana.

A study of the axoplasmic transport of materials in the sciatic nerve fibers of cat following the injection of ^{3}H-leucine into the lumbar 7th ganglion and incorporation by the cell bodies has shown a fast transport at a rate close to 400 mm/day (Ochs, Sabri & Johnson, Science 163: 686, 1969). In an in vitro study of fast transport and its relation to metabolism, asphyxiation by N_2 or NaCN and uncoupling by DNP were all found to produce block of transport within 15 min (Ochs, et al, Fed. Proc. 29: 264a, 1970). Iodoacetic acid (IAA) block of glycolysis was found to cause a decrease in the amount of fast transport and eventual failure in 1-2 hrs (Ochs & Smith). To eliminate the possibility of a slow entry of IAA causing the declining pattern of downflow rather than resulting from a block of glycolysis, the effect of IAA on GAPD was studied. Cat sciatic nerves were exposed to various concentration of IAA for short intervals of 5-15 min at 38°C. The protein fraction containing GAPD was isolated from the high speed supernatant by acetone precipitation and enzyme activity was determined by the change in absorbance at 340 mμ in the presence of arsenate. IAA in concentrations as low as 0.5mM inhibited 90% of the GAPD in the nerve after a 10 min exposure. With 5mM IAA a 5 min exposure caused a 80-90% inhibition. At 10mM IAA an exposure of 10 min brought about complete inhibition of GAPD. Lactate dehydrogenase of the nerve was not affected by such a treatment with IAA. Replacing the NAD with NADP resulted in complete loss of GAPD activity. Supported by PHS Grant NB 08706-01, NSF Grant GB 7234X1 and The Hartford Foundation.

RED CELL VASCULAR VOLUME CHANGES DURING IRREVERSIBLE HEMORRHAGIC SHOCK. Paul R. Sale* and Carleton H. Baker. University of Louisville School of Medicine Louisville, Kentucky 40202.

The blood of anesthetized, splenectomized dogs was labeled with red cells-^{32}P. Following control determinations the animals were hemorrhaged to 30 mm Hg mean pressure and maintained until 50% of the shed blood was taken up and then the remainder was reinfused. Cardiac output and central blood volume (dye) were periodically determined and changes in radioactivity of muscle, skin, paw, intestinal wall and liver were monitored by Geiger-Mueller tubes. Cardiac output and central blood volume decreased markedly during hemorrhagic hypotension, increased to levels less than control values following reinfusion and progressively fell until death. All peripheral beds studied showed marked decreases in vascular volume (to 65 to 75% of control) following hemorrhage. Muscle volume rose rapidly to levels above control (130% of control) during the hypotensive period and continued increasing even after reinfusion to nearly twice the control level (180% of control). Cutaneous, intestinal and liver volumes increased to levels close to the control levels by the end of the hypotensive period and then increased to levels significantly above the control following reinfusion (120-150% of control). Paw vascular volume declined until after reinfusion when it increased somewhat, never actually reaching the control level (85% of control). Although pooling of blood occurs in most all peripheral tissues except the paw, muscle is the largest mass and, therefore, would contain the largest volume of pooled blood during the irreversible stage of shock. (Supported by USPHS grant HE-11,966 and the Kentucky Heart Association.)

PULMONARY GAS EXCHANGE, HEART RATE, AND BLOOD PRESSURE WHEN BREATHING DENSE GASES. J. V. Salzano, G. D. Blenkarn*, H. A. Saltzman and J. A. Kylstra. Duke Univ. Med. Center, Durham, N. C., and Univ. of N. C., Chapel Hill, N. C.

Pulmonary gas exchange, heart rate and blood pressure were measured in three resting subjects, in a dry hyperbaric chamber, at one to 8.6 atmospheres absolute (Ata), during exposure to breathing gases of differing density (0.384-7.73 gm/L), kinematic viscosity (52.9-2.4 centistokes) and inert gaseous composition (helium, nitrogen and neon), but with a similar PI_{O_2} of approximately 150 mm Hg. No significant deviation from control values at one Ata of air occurred for $(A-a)D_{O_2}$, $(I-a)D_{O_2}$, heart rate or blood pressure at any density of breathing gas encountered in this experiment. It is concluded that a significant impedance to diffusion of oxygen in the terminal airway due to the physical characteristics of the breathing gas does not occur within the range of inspired densities studied or is blunted by compensatory mechanisms. (Supported by NIH Grant HE07896 and ONR contract.)

PROTON CONDUCTANCE OF SUBMUCOSAL MEMBRANE OF FROG GASTRIC MUCOSA. S. S. Sanders* and W. S. Rehm. Dept. of Physiology and Biophysics. University of Alabama in Birmingham, Birmingham, Alabama.

Much evidence indicates that the relative proton conductance (PC) of biological membranes is very low but Champion et al. (Clin. Res. 14:107, 1966) present evidence for a high relative PC of striated muscle plasma membrane. They observe that step changes in external pH produce transient changes in potential difference (PD) and interpret this to mean that the large amount of intracellular K^+ poises the system. Studies with a 4-electrode in vitro technique on the submucosal-facing plasma membrane (M_s) of the mucosal cell layer of frog gastric mucosa have indicated that total conductance of M_s = sum of K^+ and Cl^- conductances. Effect of changes of external $[HCO_3^-]$ on PD of M_s is negligible but it is possible that relative PC of M_s is high and a short-lasting transient ΔPD was overlooked. Changing CO_2 (5% → 1% → 5%) stepwise without changing HCO_3^- caused a pH change and showed no transient change in PD; but the diffusion barrier present between bathing fluid and M_s (with time constant about 1 min) negates significance of no transient ΔPD. Changes in $[HCO_3^-]$ (25 ⇄ 5 → 25 mM) of submucosal bathing media in either Cl^- or Cl^--free ($SO_4^=$ for Cl^- plus sucrose) solutions without changing CO_2 (gas = 95% O_2 - 5% CO_2) results in ΔpH of 0.6 and no transient ΔPD. First reading was obtained within 10 sec. following ΔHCO_3^-. If M_s has very high relative PC then predicted transient would depend on conductance of return circuit in M_s (i.e., conductance of $K^+ + Cl^-$) and amount of buffer in cells. Calculations reveal that transient should last longer than 10 sec and since no transient was seen we conclude that the relative proton conductance of M_s is negligible. (NIH and NSF support.)

IDENTIFICATION OF A CALCIUM BINDING COMPONENT IN DOG KIDNEY CORTEX.

Howard Sands and Richard H. Kessler. Northwestern University, Chicago, Illinois.

Using a modification of the chelex-chelating resin method to assay calcium binding activity, a calcium binding component of the cortex of dog kidney has been identified. It is a protein as determined by the following criteria: Binding activity is not lost on dialysis; the component loses 70% of it's activity when incubated at 60°C for 10 min. and 88% of its activity after 4 hr. incubation with 20%pronase. It is further characterized by the facts that 20% trypsin or phospholipase C do not affect the binding activity. Specific activity of the binding component of cortex is about 5 fold greater than that found in kidney medulla or spleen. Thirty percent of the activity is associated with particles that sediment at 30,000 xg for 20 min. Almost no activity is found in the 105,000 xg supernatant. The possibility that calcium binding is associated with membranes is indicated by loss of activity upon treatment of the 16,000 xg supernatant with Triton X-100 or sonication. In ten experiments, the specific activity of the component from cortex and medulla was related to plasma calcium concentration. Plasma calcium levels were altered by parathyroidectomy in 6 of these experiments. As plasma calcium decreased, the ratio of specific activity cortex:medulla increased [correlation coefficient 0.819±0.109]. The specific activity of cortex and medulla are reciprocally related.

MODIFICATION OF THE CARDIOPULMONARY EFFECTS OF ACCELERATION BY WATER IMMERSION AND LIQUID BREATHING. D. J. Sass*, E. L. Ritman*, P. E. Caskey*, N. Banchero and E. H. Wood, Mayo Grad. School of Med., Rochester, Minn.

The effects of G_y acceleration on cardiovascular and respiratory function in dogs were compared under three conditions: 1) normal respiration in air; 2) totally immersed in a saline-filled chamber providing control of respiratory rate, tidal and residual volumes when breathing air or oxygen; and, 3) when respired in the same manner with oxygenated liquid fluorocarbon (FC 80). Pressures in the aorta, pulmonary artery, right and left atria, left pulmonary vein, and right and left pleural spaces were recorded. Oxygen saturations of aortic, pulmonary arterial and left pulmonary vein blood were recorded continuously by cuvette oximetry. The results indicate that: 1) arterial hypoxemia due to dependent pulmonary arteriovenous shunting caused by acceleration is not minimized by water immersion alone; 2) dogs can be respired with liquid fluorocarbon for 4 hours or longer at 37.5°C without clinical signs of respiratory distress with arterial PCO_2 values controlled between 16 and 40 mm Hg and with arterial blood 100% saturated at breathing rates between 4 and 8 per minute; 3) liquid respiration prevented dependent pulmonary arteriovenous shunting at $+6G_y$; 4) in air-breathing dogs vertical gradients in pleural pressure were approximately 0.7 cm H_2O/cm vertical distance between pleural catheter tips in contrast to 1.6 cm H_2O/cm vertical distance in fluid-breathing experiments. The specific gravity of the fluorocarbon was 1.7. Theoretically liquid breathing can protect against pulmonary arteriovenous shunting and injury due to acceleration, injury to the thoracic contents due to transient or sustained extreme changes in environmental pressure, and can minimize decompression problems associated with such changes (e.g., deep sea diving). (Supported in part by grants USAF F41609-69-C-0058, AHA CI 10, NIH HE3532, NASA NGR 24-003-001, and U. S. Navy.)

VASOPRESSIN-DEPENDENT REFLECTION COEFFICIENTS IN ISOLATED COLLECTING TUBULES. J. A. Schafer and T. E. Andreoli. Duke Med. Ctr., Durham, N. C., (presently at U. of Ala. Med. Ctr., B'ham, Ala.)

Isolated rabbit cortical collecting tubule segments were perfused with Krebs-Ringer buffer (KR), 125 mOsm L^{-1}, containing ^{3}H-inulin. The bathing medium contained either 290 mOsm L^{-1} KR or ~170 mOsm L^{-1} KR with ~120 mOsm L^{-1} of either urea, sucrose or n-butanol. P_f, the osmotic water coefficient ($\mu L\ min^{-1}cm^{-2}Osm^{-1}$), was computed from the net water flux, lumen to bath. Without vasopressin (ADH), P_f was ca. zero at 3 hours. When ADH (0.2 - 1.0 mU ml^{-1}) was added to the bathing medium, tubular cells and intercellular spaces swelled, indicating that ADH increased the water permeability of the luminal membrane (Grantham et al, J. Cell Biol., 36: 355, 1968). Under these conditions, P_f rose uniformly, and was 20.5 ± 8.6 (SD) for KR bathing medium. The ratios of the ADH-dependent P_f values for the different bathing media were: urea-KR: KR, 0.99 ± 0.10 (14); urea-KR: sucrose-KR, 0.96 ± 0.08 (7); KR: sucrose-KR, 1.07 ± 0.19 (5); butanol-KR: KR, 0.22 (1). Thus, the ADH-dependent reflection coefficients were unity for NaCl, urea and sucrose, while that of butanol approached zero. In thermodynamic terms, these reflection coefficients do not exclude the possibility that, in the presence of ADH, the resistance of the tubular epithelium to water flow includes both a diffusion barrier and a barrier containing pores having relatively large radii. Although ADH increases the water permeability of the luminal membrane, the latter may still contribute significantly to the total resistance to water flow. (Supported by: NIH AM-13239, NSF GB-8479, Amer. Ht. 68659 and NIH RCDA GM-18161.)

EXTRARENAL WATER LOSS & ADH. **E. Schlein,* G. Spooner,* M. Pickering* and R. Cade. Department of Medicine, University of Florida.**

Clinical evidence of decreased insensible water loss in anephric patients undergoing chronic hemodialysis led us to measure the rate of extrarenal water loss in eight normal volunteers, and in ten anephric patients. Water loss occured at a rate of 35 ml/hour in the normal controls and 21 ml/hour in the anephrics. The effect of Ethanol on extrarenal loss was studied. In the normal it increased to 48 ml/hour while in the anephrics it increased to 45 ml/hour. To ascertain if this was an ADH effect each group was then studied by giving both Ethanol and ADH. Water loss in these experiments was 18 ml/hour in the anephric and 21 ml/hour in the normal subjects. In another set of experiments water loss following administration of ADH was 18 ml/hour in both groups. When rate of insensible loss in anephrics was considered as a function of serum urea concentration an almost linear relation was found. Our data shows a defect in extrarenal water loss exists in anephric patients and that it can be abolished by administration of Ethanol. The ethanol effect can in turn be blocked by administration of ADH. The most likely explanation for the defect in extrarenal water loss is that a high serum osmotic pressure causes release of ADH.

EFFECT OF SALINE INFUSION ON SUPERFICIAL NEPHRON FILTRATION RATE IN THE DOG. Edward G. Schneider*, Robert E. Lynch*, Thomas P. Dresser*, and Franklyn G. Knox, Dept. of Physiology, Univ. of Mo. Sch. of Medicine, Columbia, Missouri.

It has been reported that saline infusions in the dog cause disproportionate increases in superficial nephron filtration rate (snfr) in comparison to glomerular filtration rate (GFR). However, recently this observation has been attributed to recollection artifact. To examine this point, micropuncture studies were performed in 7 dogs during hydropenia and following saline loading (62.5 ml/Kg). Sodium excretion by the micropunctured kidney was increased 165 ± SE 50 μEq/min. following saline infusion ($P<.025$) and GFR was unchanged. During hydropenia fractional sodium reabsorption from 34 late proximal tubule sites was 46 ± 3.5%, snfr was 0.71 ± .05 nl/sec and the ratio snfr/GFR was $2.2 \pm 0.2 \times 10^{-6}$. Following saline infusion, fractional sodium reabsorption was decreased to 24 ± 4.1% in 27 recollected proximal tubules ($P<.005$) and to 29 ± 4.1% in 33 late random proximal tubules which were not previously punctured ($P<.005$). The snfr in recollected tubules (0.88 ± .09 nl/sec) or random tubules (0.84 ± .10 nl/sec) were not significantly different or increased. Furthermore the snfr/GFR for recollected tubules ($2.4 \pm 0.3 \times 10^{-6}$) and for random tubules ($2.3 \pm 0.3 \times 10^{-6}$) were not significantly different or increased. In conclusion, in the presence of a significant natriuresis in the dog, the superficial nephron filtration rate and the ratio snfr/GFR were not significantly altered using either recollection or random micropuncture techniques.

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GONADAL INVOLUTION IN DEVELOPING HAMSTERS: A NECESSARY NEURAL PATHWAY. L.P. Schramm, D.K. Pomerantz*, C.E. McMahon* Dept. of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland 21205. Dept. of Physiology, University of Rochester, Rochester, N.Y. 14627.

Evidence suggests that the gonadal involution resulting from bilateral orbital enucleation of developing male hamsters is mediated by a pathway including the inferior accessory optic tract (IOT), superior cervical ganglion (SCG) and pineal gland. However, the central neural pathway between the IOT and the SCG has not previously been sought. Previous studies in our laboratory demonstrated efferent sympathetic systems in close proximity to mesencephalic accessory optic nuclei and the medullary lateral spinothalamic tract (LST) of cats and monkeys. The present study tested the hypothesis that the region of the LST also contains systems necessary for gonadal involution. 25 day old hamsters were subjected to enucleation, enucleation and bilateral LST lesions, enucleation and sham lesions and lesions alone. 50 days after surgery the hamsters were sacrificed. The gonads were weighed and the brains were studied histologically. The marked gonadal involution induced by enucleation was prevented when enucleation was accompanied by LST lesions. Electrode tracks which did not destroy the LST did not prevent involution. These data are consistent with the hypothesis that the LST contains a descending pathway between the IOT and the SCG. However, the importance of ascending sensory systems has not yet been disproved.

MOTONEURON-LIKE BEHAVIOR IN A RELAXATION OSCILLATOR. *Peter C. Schwindt** and *William H. Calvin*. Departments of Physiology & Biophysics and of Neurological Surgery, University of Washington, Seattle, Washington.

Many features of motoneuron accommodation and rhythmic firing studies can be reproduced without difficulty in a relaxation oscillator model. This oscillator (a *multivibrator*) produces "spikes" separated by a voltage trajectory similar in form to those of cat spinal motoneurons. Many phenomena seen in the subthreshold region of their membrane potential trajectory are not unique, but are strikingly similar to common relaxation oscillator behavior. The prespike "local response" seen in motoneurons is also observed in the relaxation oscillator under analogous conditions, such as during repetitive firing at the minimum rate, and during linearly rising stimuli. "Accommodation" and linear frequency-current curves are also observed in the model; noise added to the oscillator input produces effects quite similar to synaptic noise in motoneurons. Phase plane analysis demonstrates that subthreshold nonlinearities are critical in determining these motoneuron-like properties of the model: A voltage-dependent conductance was used in the relaxation oscillator model, analogous to *anomalous rectification* in motoneurons. Post-spike-time-dependent conductances were not used and were not necessary to produce the motoneuron-like features of the ramp trajectory (see Calvin, *supra*) nor the threshold phenomena. The usefulness of the model lies not in a correspondence with motoneuron circuitry, but rather that it provides a motoneuron-like behavior ameanable to analytic methods. Thus, the role of "anomalous rectification" can be determined in analogous situations involving "accommodation" and "rhythmic firing".

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CARBONIC ANHYDRASE CONTENT OF MUCOSAL CELLS OF THE URINARY BLADDER OF THE TURTLE. Walter N. Scott and Yousif E. Shamoo*. Institute for Medical Research and Mount Sinai Medical and Graduate Schools of The City University of New York, New York, N.Y.

In the isolated urinary bladder of Pseudemys scripta, both the active acidification of the mucosal fluid and the active transport of chloride are inhibited by Diamox. Attempts to relate these effects to the inhibition by Diamox of carbonic anhydrase (CA) have been frustrated by the failure to demonstrate the enzyme in the mucosal cells. Suspensions of mucosal cells were prepared from exsanguinated turtles in a manner designed to minimize the possibility of contamination by RBC's. The cell suspensions were sonicated, centrifuged at 100,000 xg for 60 min., and the hemoglobin content and CA activity of the supernatant fraction measured. Carbonic anhydrase activity, assayed by the method of T. Maren, amounted to 24.4 $\pm$ 1.7 E.U. per gram mucosal cell, or 1.0 $\pm$ 0.1 E.U. per mgm soluble protein. By measuring the hemoglobin content and CA activity of turtle RBC's as well as the mucosal cells, we determined that no more than 2% of the CA activity in the mucosal cell extracts could be accounted for by contaminating RBC's. By titration of the CA activity with 2-o-chlorphenylthiadiazole-5-sulfonamide (Cl 13,580) the enzyme content of the mucosal cells was 2.32×10^{-9} moles per gm wet weight and of the RBS's, 22.8×10^{-9} moles per gm wet weight. Preparations from the mucosal cells and the RBC's hydrolyzed both o- and p-nitrophenylacetate. While the esterase activity of the RBC's was inhibited by sulfonamides, the esterase activity of the mucosal cell preparation was not demonstrably inhibited by either Diamox or Cl 13,580. Similar observations have been reported for the human kidney (Tashian, BBRC 14, 256) and for the rat prostate (McIntosh, Biochem J. 114, 463). (Supported by USPHS grant AM 13135).

RESPIRATORY AND BARORECEPTOR INFLUENCES ON SOMATO-SYMPATHETIC REFLEXES. H. Seller*, A. Kaufman* and K. Koizumi. Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

In chloralose-urethane anaesthetized and vagotomized cats, immobilized with flaxedil, sympathetic efferent nerve activities were compared at various spinal levels and pre- and postganglionic sites (white rami T_1-T_2, T_{10}-T_{11}, L_1-L_2; cervical sympathetic trunk, splanchnic n., cardiac n., renal n.). Three simultaneous recordings were made from various combinations of sympathetic nerves. Reflexes were evoked by stimulation of sciatic or spinal nerve (L_1-3) A-fibers. The influence of central respiratory activity (phrenic n. discharge) and that of baroreceptor excitation (bilateral carotid sinus distension) upon the sympathetic reflexes was tested. Spontaneous activity of all recorded sympathetic nerves increased synchroneously with phrenic n. discharge. This modulation of sympathetic activity was well correlated with the strength of the phrenic activity and disappeared with loss of phrenic discharge in hyperventilation. The supraspinal sympathetic reflex was enhanced during phrenic activity and the silent period was markedly reduced but there was no clear change in the spinal sympathetic reflex. Baroreceptor activity completely abolished the supraspinal reflex without producing any significant change in the spinal reflex. During low frequency somatic stimulation (below 5/sec) baroreceptor activity reinforced the usual depressor reaction and strongly counteracted the usual pressor reaction to high frequency stimulation. All baroreceptor reactions showed adaptation within 3-4 sec. Contrary to other reports (Coote and Downman, J. Physiol. 202:147,161, 1969) it was found that the effects of baroreceptor activation on supraspinal somato-sympathetic reflexes, as recorded at various spinal levels and pre- and postganglionic fibers, were the same. (Supported by USPHS grant NB-847-15)

THE IMPORTANCE OF THE PENTOSE PHOSPHATE SHUNT TO ACID SECRETION IN THE ISOLATED GASTRIC MUCOSA OF THE RAT. Thomas J. Sernka* and John B. Harris. University of California at San Francisco, San Francisco, California.

In the presence of 25mM glucose the acid secretion of the isolated gastric mucosa of the rat averaged 1.8±0.3 μEq/cm2/hr during a 4 hr period. After a 90 min exposure to 25mM pyruvate acid secretion fell to 0.2±0.1 μEq/cm^2/hr. This decline was similar to that encountered in paired mucosae without substrate. The low concentration of endogenous glycogen, 29% that of the mucosa of the bullfrog, did not maintain acid secretion. Since both pyruvate and glucose stimulated oxygen consumption by 18±3 and 22±2%, respectively, it is unlikely that a permeability barrier accounted for the failure of pyruvate to support acid secretion. Lactic acid production was equivalent to 0.36±0.04 μmoles/cm^2/hr during a 4 hr incubation of mucosal slices with 25mM glucose. Thus lactic acid production could account for no more than 20% of the total acid secreted. Pentose phosphate shunt activity was evaluated by the ratio of labelled CO_2 evolved from glucose-1-C14 as compared to that from glucose -6-C14 in paired mucosae. In contrast to an expected ratio of unity in the absence of the shunt, the ratio for mucosal slices incubated 4 hr with 25mM glucose was 4.5±0.4. Hence a major fraction of the glucose utilized to support acid secretion is oxidized directly through the pentose phosphate shunt. Presumably any glucose or pyruvate that is oxidized via the citric acid cycle supports mucosal functions other than acid secretion. (Supported by NIH Grant AM 12606.)

EFFECTS OF p-NITROPHENYL PHOSPHATE ON THE SHORT-CIRCUITING CURRENT IN THE TURTLE BLADDER. Yousif E. Shamoo*, Herman R. Wyssbrod*, and Walter N. Scott. Institute for Medical Research and Mount Sinai Medical and Graduate Schools of The City University of New York, New York.

Isolated hemibladders of the fresh-water turtle, Pseudemys scripta, bathed on both sides by oxygenated Na^+-Ringer solutions containing 17 mM HCO_3^- and maintained in the short-circuited state, were exposed to p-nitrophenyl phosphate (p-NPP), p-nitrophenol (p-NPOH), and 2,4-dinitrophenol (DNP). Addition of p-NPP (4 mM) to the serosal bathing fluid resulted in a 50% inhibition of the short-circuiting current (I_{sc}) after a mean time of 42 minutes. p-NPOH, the hydrolytic product of p-NPP, reached concentrations of 30-60 µM after 45 to 60 minutes. The rate of decline of I_{sc} appeared to follow the progressive accumulation of p-NPOH in the serosal fluid. When p-NPP was added to the mucosal fluid, there was neither inhibition of I_{sc} nor hydrolysis of p-NPP. The direct addition of p-NPOH (1 mM) to the serosal or to the mucosal bathing solution resulted in a 50% inhibition of I_{sc} after a mean time of 58 minutes. Lower concentrations of p-NPOH had no effect. Addition of DNP to the serosal or mucosal bathing fluid (1 mM) resulted in a 50% inhibition of I_{sc} after a mean time of 44 minutes. The mean times required for 50% inhibition of I_{sc} by p-NPP, p-NPOH and DNP, 42, 58, and 44 min. respectively, were not significantly different from one another ($P > 0.1$), suggesting that p-NPOH, rather than p-NPP, was the transport inhibitor and that the mechanism of action of p-NPOH and DNP were similar. (Supported by USPHS grants AM13037 and AM13135, by NSF GB 7764 and by NASA NGR33-171-001).

FIRST-BREATH RESPONSES OF THE INSPIRATORY MUSCLES TO AN INCREASE IN AIRFLOW RESISTANCE AND THE ROLE OF THE REFLEX AFFERENT PATHWAYS. R. Shannon* and F.W. Zechman, Jr. Dept. of Physiology and Biophysics, Univ. of Ky. Med. School, Lexington, Ky. 40506

Single motor unit EMG's of the diaphragm and external intercostals were monitored in anesthetized-intact, vagotomized, rhizotomized (T_1-T_{12} and C_4-C_7), and vagotomized-rhizotomized cats to determine the role of afferent information from, respectively, the lungs, chest wall, and diaphragm in the reflex response to an increase in airflow resistance. V_T, $\dot{V}$, P_{esop}, and inspiratory work on the lungs and airways were simultaneously monitored. The responses of the external intercostals to the loading were (1) an increase in the rate of unit activity, (2) earlier firing time, (3) extended firing time, and (4) recruitment of new units. Afferent information over the vagus contributes to (1) and (4) and is responsible for (3). Afferent information via the thoracic dorsal roots contributes to (1) and (3) and is responsible for (2). All components of the loading response were eliminated after both the vagi and thoracic dorsal roots were sectioned. The response of the diaphragm to loading was a small increase in the rate of unit activity and extended firing time; both were eliminated by vagotomy. Cervical dorsal root sections had no effect on spontaneous activity of the diaphragm or it's loading response. There was an increase in dP_e/dt during the loaded breath which was sufficient to maintain the inspiratory work rate, even though dV/dt was decreased. With all afferent pathways sectioned (loading reflex absent), the inspiratory work rate was still maintained during the loaded breath. This suggests that a major portion of the increase in force developed during the loaded breath (intact animal) is related to the intrincic force-velocity relationship of the respiratory muscles. (Supported by NIH grants HE 10628 and GM 00800 and USAF contract F33615-67C-1370.)

PLASTICITY IN THE RESTORATION OF RETINO-TECTAL PROJECTION IN ADULT GOLDFISH: A GRADIENT HYPOTHESIS. S. C. Sharma (Intr. by H. Davis). Biology Department, Washington University, St. Louis, Mo.

In surgically formed compound eyes in xenopus embryos the retino-tectal projection, when recorded later in life, revealed that each half of the compound eye appeared to spread its fibers across the whole rostro-caudal extent of the tectum (Gaze et. al, J. Physiol. 165:484, 1963). It was suggested that the apparent spreading was the result of a form of gradient chemospecification of the retina as a result of which each half compound eye might be expected to spread its connexions to the entire rostro-caudal axis of the tectum. Gaze & Sharma (Exp. Brain Res. 10:171, 1970) reported evidence for a comparable spreading of connexions in adult goldfish by allowing the whole eye to regenerate into a half rostral tectum. These experiments revealed a sign of compression of the visual field, thus suggesting that a strict place specificity does not exist in the rostro-caudal axis of the adult tectum.

In the present study the whole optic nerve was allowed to regenerate into (a) the caudal half tectum after removal of the rostral half and, (b) the rostral and caudal 1/3 of the tectum after the removal of a central 1/3 strip lying between them and extending along the medio-lateral axis. There may be a partial restoration of the retino-tectal projection which in (a) should have gone to the extripated tectum. Actually this projection was found in correct sequence of positions on the residual caudal tectum. Moreover, a partial restoration of field positions was observed in (b), in correct sequence of positions, but it was confined to the rostral tectum. These results suggest that the recognition mechanisms of optic nerve fibers in the tectum show gradient qualities on which place specificity is based. (Supported by USPHS Grant NB-0571 to Dr. V. Hamburger.)

LUMPED APPROXIMATION IN SERIAL TRACER-KINETIC SYSTEMS. C.W. Sheppard, Dept. of Physiology, Univ. of Tennessee, Memphis, Tenn.

In tracer-kinetic systems with a central compartment communicating with many peripheral ones (mamillary case), theory shows that events in the central compartment may be approximated by lumping the periphery into a few equivalent compartments (Sheppard and Householder, J. Appl. Physics 22, 150). For continuous systems, particularly serial, lumping permits the use of electrical analogs. Serial (catenary) systems have been empirically lumped (Newman et al Circulation 4, 735), but without theoretical justification which comes from the theory of Markoff processes with a discrete space and continuous time parameter. In an exchanging system with turnover and with upstream compartment initially labeled, the label concentration in the terminal compartment resembles a typical indicator-dilution(ID) curve. The kinetic parameters of the system yield a matrix with a characteristic polynomial p(S). The Laplace transform of the ID curve seen at the outflow is proportional to 1/p(S) whose power-series expansion in the region S→0 permits the approximate system to be matched with the transform of any other theoretically more appropriate system. Expansion also yields the relevant statistical moments including variance skew, etc. In general, competing models must all have transforms which agree in the region S→0. This must include simple or generalized random-walk models where the discrete Markoff system merges into the case of a continuous space parameter. Approximate success of lumped models may explain why in some cases compartmental tracer-kinetic models have succeeded in physiological systems where the existence of actual discrete compartments would seem to be in doubt. Clearly, in mamillary, catenary or other systems, the agreement between the predictions from a lumped model and actual experimental results does not necessarily imply the basic validity of the lumped model.

THE RELATIONSHIP OF DIETS WITH AND WITHOUT SOYBEAN MEAL TO CHANGES IN THE PROPERTIES OF BACTERIAL FLORA IN FECAL SAMPLES FROM THE DOG. T. Shimizu*, F. R. Steggerda and J. J. Rackis*. Univ. of Illinois, Urbana, Illinois 61801.

It has been suggested that the gas production in the intestine following the consumption of soybean products is due mainly to a fermentation by the gram positive spore forming clostridia bacteria. To test whether other groups of bacteria can contribute to the gas production, the following series of experiments were performed. Dogs were kept on meat diet for 2 weeks and on the 7, 10 and 14th days, fecal samples were collected and processed for the presence of a number of anaerobic and aerobic bacterial groups as well as their gas producing ability. The succeeding 2 week period diet was changed to contain 10% meat plus dehulled, defatted soybean meal. The two diets were isocaloric, and no change in the weight or health of the animal was observed. The results show that the fecal samples collected on the soybean diet gave significantly greater amounts of gas than those on the meat diet. Also the count number of the specially treated clostridia, bacteriodes and facultative gram negative Enteric Bacillus were higher on the soybean than on the meat diet. Likewise the aerobic streptococcus and lactobacillus bacteria colony count was higher on the soybean diet. The gas producing ability of the anaerobic facultative streptococcus and bacteroides bacteria appears to be nearly as effective as that of the clostridia. The role of different bacteria on gas production in man is also being studied.

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EFFECTS OF ACTINOMYCIN D AND ACTH ON HAMSTER ADRENAL RHYTHMS. R. Shiotsuka* and R. V. Andrews. Creighton Univ., Omaha, Nebr.

A circadian rhythm in RNA concentration was observed in organ-cultured hamster adrenals. Preincubation with Actinomycin D and postincubation with ACTH decreased ^{3}H-uracil and ^{3}H-glycine incorporation rates in all four time-quadrants of a day (24 hrs). A circadian rhythm has also been reported in hamster adrenal steroidogenesis *in vitro* (Andrews & Folk, 1964). Peaks, indicating maximum secretory activity, occur at about 24:00. Similar long term organ-culture studies showed the effects of a pulsed dose of Actinomycin D and ACTH to be time dependent. The first expected peak in the adrenal secretory pattern was blocked by Actinomycin D alone, and with ACTH when administered at 12:00 and 24:00. A pulsed dose of Actinomycin D and ACTH administered at 24:00 led to arrhythmicity in the steroid secretory pattern.

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EFFECTS OF OZONE ON THE LUNG. F.Silverman*, G.M.Bell*, C.D.Burnham*, M.Hazucha*, J.Mantha*, L.D.Pengelly*, and D.V. Bates. Departments of Physiology and Medicine, McGill University, Montreal, Canada.

Each of ten normal male subjects was exposed to ozone in the concentration range of 0.6-0.8 ppm for 2 hours while seated in a large well-ventilated environmental chamber. Parameters of pulmonary mechanics; Cst, Cdyn, R_L, and F/V curves were obtained from measurements of airflow, pressure at the mouth and esophageal pressure. Volume was derived from electronic integration of the flow signal. Fractional uptake of carbon monoxide as an indication of pulmonary diffusion was measured. Tests were performed immediately before and after ozone exposure, as well as at intervals of 4 and 24 hours post-exposure. Preliminary data from the group indicate that although most of the subjects noted cough and substernal soreness, indicating irritation of upper airway, the earliest measurable change was a reduction in compliance at a respiratory frequency of 60 breaths per minute and a decrease in CO extraction; airway resistance and static compliance were not changed. In some subjects a change in the shape of the maximal expiratory flow/volume curve was noted. One subject showed more severe symptoms and effects when ventilation was doubled by light bicycle exercise in the chamber with ozone at 0.75 ppm.

(Supported by the Medical Research Council of Canada.)

TIME AND SPACE CORRELATIONS OF HUMAN SMALL BOWEL CONTRACTIONS: METHODS OF DETECTION AND COMPUTER ANALYSIS. R. B. Singerman*, N. W. Weisbrodt*, J. R. Glover*, E. O. Macagno*, and J. Christensen. Dept. of Int. Med., Coll. of Med., and the Hydraulics Inst., Coll. of Engineering, U. of Iowa, Iowa City, Iowa and the Iowa City VAH.

We studied small-bowel contractions in healthy volunteers who had swallowed a bundle of four polyvinyl tubes after a 16-18 hour fast. Each water-filled tube had a closed tip and a distal lateral hole. The four holes were placed one cm. apart. Each was covered by a latex rubber sleeve. The tubes were positioned with flouroscopy in the third part of the duodenum. The proximal ends of the tubes were connected to low-volume-displacement pressure transducers. The transducer outputs were monitored with a polygraph and stored on magnetic tape. After a 10-30 minute control period, the subject drank 16 oz. of skimmed milk and a 1-2 hour record was made. The four outputs showed transient pressure peaks independent of each other. These transients were roughly triangular in form, consistent in duration, but varying in amplitude. They were assumed to be due to localized contractions of the circular muscle of the small bowel. An IBM Data Acquisition and Control System was used to analyze the data. Peaks were identified by the computer using a time-averaging technique. Two programs were used to identify contractions and to determine time intervals between contractions. The first computed time intervals between successive contractions on one channel; the second computed time intervals between sequential contractions among the four channels.

SWEAT SECRETION DURING POSITIVE AND NEGATIVE WORK. Kenneth A. Smiles* and Sid Robinson. Indiana University, Bloomington, Indiana.

The purpose of this study was to evaluate the possible role of neuromuscular drive in the regulation of sweating during positive and negative work. Speed of walking was partially separated from work rate by having the two subjects carry two loads (2 and 12.5 kg) on a packboard at each of three speeds upgrade (+10%) and downgrade (-10%) walking on a treadmill in a cool environment (21°C db, 13°C wb). After reaching a nearly steady thermal state during the initial 25 min of each experiment, the subjects walked for an additional 45 min during which measurements of metabolic rate, skin temperatures, rectal temperature, and sweat rate were made. At similar metabolic rates sweating was much greater during negative work. Sweat rate correlated well with the total heat production (THP) in the men ($r = 0.939$), where THP = $\dot{V}O_2 \pm$ Work. Sweat rate could be predicted just as accurately from metabolic heat production and speed of walking ($r = 0.954$) as from metabolic heat production and external work ($r = 0.961$) done by the men (upgrade), or done on the men (downgrade). The increase in sweating observed at a particular speed by carrying the 12.5-kg load could be explained solely on the resulting increase in metabolic heat production and seemed largely independent of the change in the external work caused by the load. Linear combinations of mean skin and rectal temperature could not accurately predict sweat rate ($r = 0.558$), although rectal temperature did correlate significantly with sweat rate ($r = 0.537$) and skin temperatures were higher during negative work ($p < 0.01$). It was concluded that neuromuscular reflexes and/or possibly temperature receptors in the area of the working muscles are an essential part of the system which regulates sweat secretion during work. (Supported by US-AMRDC Contract MD-2449.)

INFLUENCE OF ALTITUDE ACCLIMATIZATION ON BLOOD FLOW IN THE ISOLATED HINDLIMB. Elvin E. Smith and A. P. Shepherd, Jr.*. Dept. of Physiology and Biophysics, Univ. of Miss. School of Med., Jackson, Miss.

Many previous investigations have shown that the blood volume and vascular capacity of the cardiovascular system increases upon continued exposure to altitude. This study was begun to investigate the effect of these changes upon the pressure:flow relationship in the isolated dog hindlimb. Ten dogs were exposed to a simulated altitude of 20,000 ft. for a period of 16 weeks. The average hematocrit increased from 35.6% to 55%. The average hemaglobin rose from 12.5 gms % to 18.2 gms %. After acclimatization pressure:flow curves were run on the isolated, maximally vasodilated hindlimb. Three curves were run on each hindlimb using blood with hematocrit of 20, 40, and 60. No difference of statistical significance was observed in the pressure-flow relationship at any of the tested hematocrits, when compared to control hindlimbs passing through the same test sequence. We believe that these results show that changes in capillary density do not influence significantly the vascularly flow patterns in altitude acclimatization. Rather they show that normal vasodilation of the existing vessels is responsible for the maintenance of normal pressure and flows irrespective of the increased in vitro blood viscosity. The net result is an increase in oxygen transport with no increase in the cardiac work load.
Supported by NIH Grant HE 09160 and NIH Predoctoral Fellow Grant GM00316

Single Glomerular Filtration Rates of Superficial Nephrons in Varying Physiological States. Sidney Solomon. Univ. New Mexico Sch. of Med., Albuquerque, N.M. 87106

Single nephron glomerular filtration rates (SNGFR) and total kidney GFR has been measured in rat kidneys in different physiological states. By assuming that there are 30,000 nephrons per kidney, the relationship of superficial SNGFR found to that expected has been used to make inferences about distribution of SNGFR. By using animals of different sizes, it has been possible to further control these studies. As animals age, superficial nephrons account for a larger fraction of overall GFR. With Ringer loading (5.3 and 30 ml/hr as compared to 1 ml/hr infusion rate), SNGFR increases in all nephrons, seemingly moreso in juxtamedullary nephrons of older animals. Chronic volume expansion produced by administration of ACTH has the same effect as acute volume expansion. Reduction of GFR by reducing body temperature also results in preferential filtration by juxtamedullary nephrons even though GFR and SNGFR is reduced. Certain aspects of these results may be explained by plasma skimming and reduction of filtration in juxtamedullary nephrons as animals age. (Supported by a grant from the National Science Foundation, GB 7844.)

VOLUNTARY MARCH RATE AS A MEASURE OF WORK OUTPUT IN THE HEAT. Roger G. Soule* and Ralph F. Goldman. US Army Rsch Inst of Env Med, Natick, MA.

Industrial work output, particularly for hard physical work decreases under environmental heat stress, although any increase in energy cost in the heat is almost imperceptible. Preliminary studies on work by a soldier, viz: marching, indicated that his voluntary, but unknown, march rate selected on a self paced, "servo-titrating" treadmill was not reduced in the heat, even under conditions leading to heat exhaustion. Six subjects were then trained to pace themselves on such a mill so they could complete 5 miles in 120 min or less at 40C, 50% RH; the men "learned" to speed or slow their pace to cover this distance in 120 min or less without suffering heat exhaustion or reaching a heart rate of 180 bpm or a T_R of 40C. After several trial exposures, during which they monitored their speed, heart rate and T_R, they were able to "hunt" a pace on the continuously accelerating or decelerating treadmill which allowed them to work without reaching such limits. Then, in controlled sequence, a 25%, 50% or 75% relative humidity was presented on a given day at the constant 40C temperature. March rate was not increased at the 25% RH condition but was roughly the same as at the 50% condition, with almost all men completing the 5 miles in 120 minutes or less. At the 75% RH condition, the voluntary rate "learned for walking in heat" again did not change and the men were unable to complete the task because of symptomatic and/or physiological limits specified above. Thus, although the rate of march appears to be established by habit and not to be reduced by heat stress, men can be conditioned to march at a slower pace in the heat. However, such reduction in pace after training is not cued by impending heat exhaustion or titrated to physiological cues of rising heart rate or body temperature but is merely an arbitrary reset of the march rate to a generalized "hot" condition.

CORONARY BLOOD FLOW OF DOGS WITH EXPERIMENTAL CORONARY ARTERY DISEASE. H. V. Sparks, E. L. Carlson*, and J. R. Cant.* University of Michigan, Ann Arbor, Mich. 48104.

Coronary blood flow (CBF) of four unanesthetized dogs was measured before and during development of experimental coronary artery disease (CAD). Polyvinyl catheters were implanted in a major branch of the left coronary artery and in the thoracic aorta. CBF was determined by monitoring the clearance of ^{85}Kr from the myocardium during rest and the intracoronary infusion of ATP. Administration of allylamine and an egg yolk emulsion produced large and small artery disease with areas of medial necrosis, intimal proliferation, intracellular lipid deposits, vascular inflammation and thrombosis. CBF measurements were made repeatedly for 2-6 weeks as the disease progressed. Resting CBF of a representative dog decreased from 90±13 (N=13) to 65 ml/100 g min (N=15). Maximum ATP induced CBF fell from 244±37 (N=13) to 164±30 ml/100 g min (N=15). CBF decreased steadily as CAD developed. On the first day after allylamine and egg yolk administration maximum ATP induced CBF was 200 ml/100 g min; 30 days later it was 152 ml/100 g min. Human CAD usually results in low maximum CBF but normal resting CBF. The low resting CBF observed in this study may be a result of small vessel involvement which could prevent adjustment of CBF to meet metabolic demand. (Supported by USPHS, NIH Grant HE-09874.)

^{90}Sr-CALCIUM INTERRELATIONSHIPS IN MAN. Herta Spencer, Joseph Samachson*, Edward P. Hardy, Jr.*, and Joseph Rivera*+. Metabolic Section, VA Hospital, Hines, Illinois and Health and Safety Laboratory, U.S. Atomic Energy Commission, New York, New York.

^{90}Sr and calcium balance studies were performed in man under strictly controlled dietary conditions during the intake of different levels of ^{90}Sr and of calcium. The dietary intake of ^{90}Sr and calcium and the excretions of the two elements in urine and stool were determined in each 6-day metabolic period. ^{90}Sr analyses were determined by low level β-counting. The intake of ^{90}Sr ranged from 3.3 to 20.1 pCi/day and the intake of calcium ranged from 120 to 1700 mg/day. Calcium supplements were given either as milk or as calcium gluconate tablets. The urinary and fecal ^{90}Sr excretions increased with increasing ^{90}Sr intake; the average urinary ^{90}Sr excretion corresponded to 12% of the ^{90}Sr intake while the fecal ^{90}Sr excretion averaged 85% of the intake on the different ^{90}Sr intake levels. The ^{90}Sr balances were in equilibrium on the low ^{90}Sr intake and the balances increased with increasing intake. The $^{90}Sr/Ca$ ratios of the stool were similar to those of the diet while the $^{90}Sr/Ca$ ratios of urine were either lower or higher than the $^{90}Sr/Ca$ ratio of the diet. The Observed Ratio (O.R.) urine/diet, was somewhat greater than 1 on a calcium intake of about 800-1200 mg/day given as milk while this ratio was very variable on low calcium intake and on a high calcium intake given as calcium gluconate. In contrast the O.R. stool/diet was about 1 on either low or on high calcium intake whether calcium was given as either milk or as calcium gluconate. (Supported by AEC Contract AT(11-1)-1231-57.)

+ Deceased

COMPARATIVE EVIDENCE FOR THE FUNCTION OF THE CAROTID AND ORBITAL RETIA. M. P. Spencer, J. R. Howard*, R. R. Gonzalez*, Virginia Mason Research Center, Seattle, Wash., and B. Sheridan*, Inst. of Comparative Biol., San Diego, Calif.

By means of corrosion casts and dissections, we examined the arterial supply to the brain of 63 species of mammals in 25 families and 9 orders. Of the 2 major types of rete mirabile that supply the Circle of Willis, Type 1 is extracranial with subtypes orbital and ophthalmic. The orbital extracranial rete sends rami intracranially through the orbital foramen. Type 2, the carotid or intracranial rete, lies on either side of the sella tursica and was found in all of the Artiodactyls examined as well as vestigial in certain Canidae. The orbital extracranial rete was found in 3 Felidae and in 1 Hyaenidae. No rete supplying the brain was found in the Florida otter, the American brown bear, the kinkajou, nor in the Tasmanian kangaroo, jack rabbit, Indian elephant, rock hyrax, horse and 5 primates. Four Cetaceans disclosed a basi-cranial rete supplied through the foramen magnum from the spinal rete. Considering defensive behavior, there seems to be a general correlation between the presence of rete supplying the brain and habits of animals which impose strong headward decelerations. Possible exceptions may be in the rhinoceros, hippopotamus, and the camels. The Cetaceans are well known to defend themselves by means of ramming, but their additional need for a cerebral spinal rete may correlate with the need for an arterial oxygen reservoir during long dives in supplying the central nervous system.

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HYPOTHALAMIC CONTROL OF RESPIRATORY PATTERNS. H.A. Spurgeon* and C.N. Peiss. Loyola University School of Medicine, Maywood, Illinois.

Although hypothalamic effects on respiration have been known for many years, little definitive evidence exists regarding the importance of this center in the tonic control of respiratory rate and airflow patterns. The present study was designed to investigate these influences and to determine the central sites for experimentally driving respiration in the cat. Utilizing bipolar electrodes in cats anesthetized with sodium pentothal, crescendo trains of appropriately timed stimuli were delivered to the periventricular gray of the hypothalamus. Airflow was measured with a Fleisch penumotachograph, phrenic discharge with bipolar electrodes, and blood pressure was monitored. Results indicate that by varying the number of stimuli delivered in a specific train, the degree and rate of onset of phrenic activation may be varied proportionally. Maximum airflow velocity and rate of development of the inspiratory phase are likewise increased. By increasing the number of trains per minute, the respiratory rate may be increased. Post-stimulus inhibition indicative of hyperventilation does not occur, and the animal returns to control respiratory patterns within 1-3 cycles. At the onset of stimulation, response is immediate in the first evoked respiratory cycle, but maximum effect occurs after two or three cycles have been paced by the stimulus. Lesions in the descending pathways indicate the evoked response is extremely difficult to block, and is therefore presumed to travel via diffuse pathways. These studies are not consistent with the concept that normal respiratory patterns are wholly determined in lower brainstem centers. Analysis of transfer function between hypothalamus and final motor pathway (phrenic) may provide meaningful evidence for the role of the hypothalamus. *Supported by NIH Grant HE08682 and Fellowship GM39561 (H.S.).*

STEADY STATE PULMONARY TRANSVASCULAR WATER FILTRATION COEFFICIENT, k, IN UNANESTHETIZED SHEEP. N.C. Staub. Univ. of Calif., San Francisco, and Curtin Sch. Med. Res., Canberra, Australia.

The sheep is a large, gentle and patient animal with an extensive pulmonary lymphatic system that suggested it would be a good model for studies of normal and abnormal pulmonary transvascular water flow. I used unanesthetized sheep with chronically draining pulmonary lymph cannulas to measure net steady state lung water filtration over periods of two hours, while simultaneously measuring pulmonary artery (Ppa) and left atrial (Pla) pressures to calculate capillary pressure (Pcap = Pla + 0.4 (Ppa - Pla)) and sampling blood and lymph for protein concentration and colloid osmotic pressure determinations. For pericapillary interstitial fluid, I assumed its hydrostatic pressure equaled zero (alveolar pressure) and assumed the lymph represented its protein content. In seven experiments on four sheep lymph flow averaged 4-6 ml/hr which represents about 50% of total lung net water flow since the sheep has two other smaller efferent lymphatics. Pcap averaged 14.8 cm H_2O at left atrial level; plasma proteins averaged 5.65 g/100 ml (37% albumin) and lymph proteins averaged 3.90 g/100 ml (48% albumin) giving 6.3 cm H_2O net effective osmotic pressure. Calculated k for 5-10 ml/hr total water flow averaged 0.15-0.30 ml/hr x cm H_2O x 100 g (wet lung). This is about one-tenth the value reported in acute edemogenic experiments in anesthetized dogs or isolated dog lungs.

(Supported in part by PHS Grant HE-06285 and PHS Fellowship 1-F03-HE-06383-01.)

MOTOR UNITS AND ACTION OF THE PLANTARIS MUSCLE OF THE CAT. Edward K. Stauffer*, William C. Nemeth*, George E. Goslow, Jr.* and Douglas G. Stuart. Department of Physiology, University of Arizona, Tucson, Ariz.

While vestigial in man the plantaris muscle, PL, is as developed as the triceps surae in the cat. The action of PL is bivalent, although its relative contribution to ankle extension and digit flexion remains uncertain. This report is concerned with the relation between the role of PL in locomotion and the mechanical properties of its motor units. Deeply anesthetized cats were held to a sturdy metal frame with clamps. Temperatures at the rectum, spinal cord oil pool and PL oil pool were independently maintained at 37 ± 1°C by thermistor controlled heaters. Initial muscle length was set to give a peak of active tension during an isometric twitch. We followed the techniques outlined by McPhedran et al (1965) for functional isolation of single PL axons. Under these rigid conditions, our present sample (64 motor units from 3 experiments) displays: fast contraction times (10 to 30 msec) and high fusion frequencies; and, twitch tensions ranging from 0.5 to 17 gm and peak tetanic tensions of 7 to 110 gm. These data reveal that PL units resemble fast gastrocnemius, G, units (Burke 1967) in the high speed and large force of their contraction. PL inserts onto and assists flexor digitorium brevis (FDB) in digit flexion. Also contributing to digit flexion are flexor digitorium longus, FDL, and flexor hallucis longus, FHL, with high speed but low force motor units (Swett and Olson 1966). Average conduction velocity for PL, FHL and FDL is faster than FDB by a magnitude as great as that separating G from soleus, S, (Boyd and Davey 1968). Thus it remains to determine the speed and force of motor unit contraction for FDB to assess the division of labor for digit flexion in fashion similar to that between G and S for ankle extension (Henneman and Olson 1965). (Supported in part by USPHS Grant NB 07888).

ARTERIAL TONOMETRY FOR THE ATRAUMATIC, CONTINUOUS AND INSTANTANEOUS MEASUREMENT OF ARTERIAL BLOOD PRESSURE. Paul D. Stein and Edward F. Blick (intr.by E.D. Frohlich) Univ.of Okla. and VA Hosp.,Okla.City,Okla.

There is a need for a non-invasive method for the measurement of arterial blood pressure(BP)that not only can give systolic and diastolic pressures, but also can give wave forms, continuous measurements, and beat-to-beat variations. For this reason, a new method of arterial tonometry was developed. It is based upon the principle that displacement of a mechanical force sensing device located over a superficial artery can be made to be proportional to BP within the artery. Since tonometric BP measurement is in a sense direct, though non-invasive, it has many of the advantages of intra-arterial BP measurement. Instantaneous and transient variations of BP can be observed and the configuration of wave forms can be recorded. In this regard, the method has an advantage over phonoarteriographic and Doppler ultrasonic sphygmomanometry. Measurements must be calibrated in each patient by a single BP taken by any other convenient means. Sixty-five simultaneous comparisons were made in 20 normotensive patients of the effects of various interventions upon intra-arterially and tonometrically recorded BP. Wave forms of tonometric BP were strikingly similar to intra-arterial BP. When peak systolic or diastolic BP was raised or lowered by as much as 30% from control values, tonometric BP correlated linearly with intra-arterial BP ($P<.001$). Increments of greater magnitude were indicated by prominent changes, but did not show this linear correlation. A curvolinear calibration curve may be required for higher BP increments. Obviously, care must be taken to affix the transducer directly over the artery (usually radial or dorsalis pedis) to avoid artifacts. The instrument seems particularly suited for the atraumatic measurement of transient effects of drugs or physiological interventions, or for the continuous monitoring of arterial BP during surgery.

CARDIAC ARRHYTHMIAS DURING GRADED HYPERCARBIA. Joseph M. Stinson and Joel L. Mattsson*. 6571st Aeromedical Research Laboratory, Holloman AFB, New Mexico 88330.

Abrupt exposure of conscious men and dogs to high levels of CO_2 have reportedly increased or decreased heart rate, and produced various cardiac arrhythmias. In order to determine ECG changes produced by more gradual increment in CO_2, as might occur in an enclosed environment with malfunctioning CO_2 removal systems, three rhesus monkeys and three chimpanzees were exposed to CO_2 increased at 30%/hr in an environmental chamber with ambient atmospheric pressure (4300 ft elevation), oxygen tension and temperature. Non-cyclical sinus arrhythmia occurred in all animals with onset at 24-28% CO_2 in rhesus, and at 30-50% CO_2 in chimpanzees. Premature ventricular contractions were observed in all chimpanzees. One chimpanzee had atrial fibrillation starting at 55% CO_2. Heart rate decreased progressively above CO_2 concentrations of 10% to maximal bradycardia (30-40% of control) at 35% CO_2. Similar arrhythmias in five rhesus exposed to graded hypercarbia at 1/2 atmosphere total pressure demonstrate that these cardiac changes are PCO_2 dependent. Reversal of CO_2-induced bradycardia and sinus arrhythmia by atropine sulfate suggests that these changes are mediated by the vagus nerves.

THERMOREGULATION IN THE SQUIRREL MONKEY. J. T. Stitt* and J. D. Hardy. John B. Pierce Foundation Laboratory and Yale University Medical School, New Haven, Conn. 06519

A heat balance study was carried out on five adult male squirrel monkeys, (Saimiri sciureus) weighing between 900 and 1000 g, over a range of temperatures from 10°C to 35°C. Indirect and partitional calorimetry were employed; mean skin and rectal temperatures, oxygen consumption, respiratory heat loss and total evaporative heat loss were measured in each animal in the steady state at 5°C intervals over the range studied. Heat losses were partitioned accordingly. From these observations the following conclusions were drawn: - 1) The thermoneutral range for squirrel monkeys is small and is located around 30°C. 2) Below ambient temperatures of 30°C metabolic rate increases rapidly with reducing ambient temperatures at a rate of 0.35 W k_g^{-1} $°C^{-1}$. 3) At temperatures above 30°C evaporative heat loss was an increasingly important factor in maintaining thermal balance. The major route of evaporative heat loss was sweating; respiratory heat loss increased very little. 4) The combined coefficient of cooling in still air was 60 W m^{-2} $°C^{-1}$ for the seated monkey. 5) Below 25°C conductance was 9-12 W m^{-2} $°C^{-1}$ but increased to 45.0 W m^{-2} $°C^{-1}$ at an ambient temperature of 35°C. The upper limit of heat tolerance in the squirrel monkey appears to be in the region of 35°C - 40°C. Animals which were trained to remain docile in the restraining chair could maintain thermal balance at temperatures up to 39°C but in many cases the animals started to struggle at ambients above 35°C and were unable to maintain equilibrium. (Fellowship support to J. T. Stitt was provided by the Medical Research Council of Canada.)

RIGHT ATRIAL FUNCTION DURING A VOLUME LOAD. **H. L. Stone, R. M. Payne,* and E. J. Engelken,* Biodynamics Branch and Data Processing Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.**

In previous work left atrial function has been described using a volume load to increase left atrial diameter and pressure. The dynamics of the right atrium under the same conditions are described in the present study. Under sterile surgical conditions, ultrasonic dimension gages were placed across the right atrium and a catheter was positioned in the right atrial chamber through the appendage in 6 mongrel dogs. The animals were allowed to recover for 2 weeks before further experimentation. Right atrial dimension and right atrial pressure were recorded during a volume load. At rest, the right atrial diameter decreased with systole and rapid ventricular filling which was similar to that found for the left atrium. At the peak of the volume loading curve the results for the right atrium were also similar to those found in the left atrium, namely, a fusion of the two decreases in diameter into a single shortening. The average resting mean right atrial pressure of 1.4 mm Hg increased to an average of 12 mm Hg during the volume load, while the right atrial end-diastolic diameter increased an average of 18% over this pressure range. The shortening of diameter with right atrial systole increased with increasing pressure, but then declined as right atrial pressure was raised further. The point of decline of right atrial systolic shortening occurred at an average change in pressure of 1.4 mm Hg above the control level. Thus the functional characteristics of the right atrium are similar to those reported for the left atrium, but are different in terms of distensibility and the point at which systolic shortening declines. The right atrium appears to be approximately twice as distensible as the left atrium meaning that in the normal atrial pressure range a given change in volume in the right atrium produces less change in pressure than the same volume change in the left atrium.

CALORIMETRIC DETERMINATION OF ENERGY EXCHANGE DURING AROUSAL FROM COLD TORPOR IN THE BAT. Robert C. Stones (intr. by Roy F. Burlington). Department of Biological Sciences, Michigan Technological University, Houghton, Michigan.

Limited information on energy exchange in hibernators prompted the measurement of total heat loss (THL) and oxidative heat production (OHP) in the bat Myotis lucifugus, during arousal. A calorimeter system was used to determine the balance between THL and OHP. Heat loss (HL) was measured directly and partitioned into radiation (Qr), convection (Qc), and evaporation (Qe) fractions. Concurrently, body temp. (Tb), O_2 consumption, and CO_2 production were measured. At Ta = 15°C, Qr, Qe, and Qc, HL rates throughout arousal accounted for an average of 97, 2, and .6% of the THL, respectively. The proportion of each partitioned HL rate to the THL rate did not change significantly throughout arousal, or by season. Seasonal variation, however, existed in the O_2, fasting respiratory quotient (RQ), and Tb patterns. Tb and O_2 usually peaked simultaneously at the peak of arousal. The RQ was at or above 1.0 at the onset and about .75 at the end of arousal, with the overall RQ averaging .81. OHP exceeded THL during the initial rise of Tb, eventually peaking out higher (in winter) or lower (in fall) than the THL. When Tb leveled out at the end of arousal, the OHP also reached its peak and then fell abruptly while the THL continued to rise. In calculating energy balance, OHP did not account for the Tb rise or total heat production (THP) of the bat. The energy balance (OHP/THP ratio) varied throughout arousal with the OHP for all bats ranging from 29% (Oct) to 57% (Nov) of the THP. The OHP/THP ranged from 1.6% (Oct) to 64.5% (Feb) at the onset of arousal and 100% (Nov) to 41% (Jan) at the peak of arousal. In general, OHP accounted for more of the THP in winter and early spring than in late summer and fall. (Supported by NSF Grants GB-6302 and GB-11983).

SEASONAL CHANGES IN PITUITARY-ADRENAL FUNCTION OF WILD LEMMINGS. R. Strohbehn* and R. V. Andrews. Creighton Univ., Omaha, Nebr.

Endocrine changes were monitored for a population of brown lemmings at Point Barrow, Alaska during the summer of 1969. Seasonal endocrine changes were observed for the population. Adrenal secretory rates for corticosterone, hydroxycorticosterone, and progesterone were higher during the initial trapping period when the animals had been exposed to a history of winter temperatures, to snow, to the spring melt, to predation, and to population density pockets. When these factors disappeared with the coming of the Arctic summer, secretory rates dropped. The coming of fall or beginning of winter resulted in increased secretory rates. Measurement of pituitary ACTH for the lemming population supported adrenal secretory data. ACTH levels were high during the initial trapping period and then fell during subsequent trapping periods. Male pituitary ACTH levels, however, remained high all summer, indicating possible prolonged effects on the male population segment. When adrenal glands were incubated with exogenous ACTH, it was found that glands taken from animals caught during the initial trapping period were more refractory to ACTH stimulation than glands from animals captured during subsequent trapping periods. It was also noted that pregnant females collected during all trapping periods remained more refractory to exogenous ACTH. Hence, possible protection may be afforded to the female population segment by pregnancy. Supported by the Arctic Institute of North America.

FREQUENCY CODING DURING TWO-TONE INHIBITION IN CAT'S PRIMARY AUDITORY NEURONS. N. Suga, R.M. Arthur* and R.R. Pfeiffer*. Depts. of Biol. & Ele. Eng., Washington University, St. Louis, Mo.

The discharge rate of a primary neuron for a continuous tone at its best frequency is often reduced by the simultaneous delivery of a tone burst. This reduction is called two-tone inhibition. In order to explore the properties of this inhibition, particularly frequency coding during the inhibition, the discharge pattern of primary neurons was analyzed with a computer which plotted the compound period (CP) and post-stimulus-time histograms. The CP histogram, representing the probability of discharge as a function of time for one or a few cycles of a periodic stimulus, resembles the waveform of sound below 4 kcps. The CP histogram of discharges during inhibition showed that single neurons carry information about the combined waveform of the two tones. The information about each tone is, however, modified by the inhibition in both amplitude and phase from that indicated by the CP histograms for the individual tones. Since the excitation transmission from the hair cells to afferent nerve terminals appears to be chemical, the generator current is probably half-wave rectified, unlike the receptor current. The CP histograms of activity during inhibition are matched by adding together the waveforms of two tones, without half-wave rectifying them. This suggests that two-tone inhibition is associated with a mechanism more peripheral than the point of rectification. (Supported by NSF, GB-13904 & NIH, FR-504, FR-07054 & NS-07498).

LENGTH-TENSION PROPERTIES OF THE ALVEOLAR WALL OF MAN. T. Sugihara* and C. J. Martin. Virginia Mason Research Center, Firland Hospital, and University of Washington, Seattle, Washington.

Lung tissue was obtained from patients undergoing surgery or at postmortem. Several small pieces of lung were removed from the parenchyma and dissected in a saline bath to dimensions approximating 30 x 30 x 250 μ. The tissue was resuspended in a saline bath between force and length transducers, the outputs of which were fed into an XY plotter. The length-tension relationship formed an area of hysteresis that was measured with a planimeter. The hysteresis ratio (HR) was calculated from $\left[\int_{l_o}^{l_f} F_{ex}dl - \int_{l_o}^{l_f} F_{rel}dl\right] \Big/ \left[\int_{l_o}^{l_f} F_{ex}dl\right]$ where F_{ex} is the force on extension, F_{rel} is that on relaxation, l_o the resting length and l_f the final length. HR diminishes with repeated cycling and becomes stable after three to four cycles. The average value for a "stable" HR is 0.32. This value is relatively unchanged over a wide range of strain and at frequencies varying from 2 to 30 cycles per minute. It has no distinct relationship with age, nor with the patient's expiratory flow rate. The maximum extensibility of the tissue predicted from length-tension curves was unrelated to HR. Stress relaxation (SR) of lung tissue following a sudden change in strain does not follow a single exponential decay of force versus time. SR correlates well with the HR showing it to be related to dynamic hysteresis.

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LACK OF SUPPORTIVE EVIDENCE FOR EXISTENCE OF A SPECIFIC IRON BINDER IN THE HUMAN GASTRIC JUICE (HGJ) Charles H.J. Swan* and G.B. Jerzy Glass
Gastroenterol. Research Lab. New York Med. Coll. N.Y., N.Y.

This investigation aims at evaluation of the role of HGJ and its glycoprotein (GP) components in protecting Fe salts from precipitation at an alkaline pH, and in specific Fe binding. We confirmed the protective action at pH 8 of HGJ, chondroitin sulfate A and fractions of non-sulfated GP separated as described in Digestion 2:124, 1969 and followed by DEAE-cellulose salt fractionation, yet found it to be non-specific. The amount of Fe retained in solution ranged from 5.5 to 10.7 μg/ml dry wt. and therefore 5-10x less than claimed by others for HGJ. The comparison of the amount of Fe kept in solution by HGJ at pH 8 and claimed to represent Fe bound to GP was at least 10x higher (6.6 μg/ml vs 0.14-0.67 μg/ml) than that precipitated from the same supernatant by 10 vol. acetone at pH 2, known to precipitate the total GP of HGJ. Equilibration dialysis of HGJ and H_2O vs. $^{59}FeCl_3$ sol. at pH 2 revealed no significant difference in distribution of Fe which would have been expected from Donnan's equilibrium. Paper electrophoresis of $^{59}FeCl_3$ "bound" to conc. HGJ at pH 2 and $^{59}FeCl_3$ alone in Teorell-Stenhagen (TS) buffer pH 4-11, acetate buffer pH 4, and borate buffer pH 8-10 revealed no consistent Fe binding component in HGJ with the electrophoretic mobility of its macromolecular components. Fe-buffer complexing has been also noted at some pHs independent of the presence or absence of a "protein binder." Elution of $^{59}FeCl_3$ "bound" in the pH 8 supernatant fraction of HGJ-^{59}Fe yielded radioactivity in the excluded volume from Sephadex G-150 which after concentration was electrophoresed at various pHs in acetate and borate buffers. No evidence was obtained as to the consistent movement of Fe with protein bands. The title of the abstract expresses our conclusions. (Supp. by AM-09701 grant from NIAMD)

LONGTIME EFFECTS OF ASPIRIN AND CORTISONE ON THE MUCIN COMPONENTS OF SALIVA EVOKED BY NERVE AND PILOCARPINE STIMULATION. T. Takeuchi*, E. R. Ensrud*, and F. R. Steggerda. Univ. of Illinois, Urbana, Illinois 61801.

In mongrel dogs, by sterile technique, saliva was collected from the right submandibular salivary duct using nerve and pilocarpine stimulation. After 1 month's recovery antiarthritic drugs (commercial aspirin tablets 5 grain/kg/body weight/day or cortisone acetate tablets 100 mg/day) were force fed daily for an average of 30 days. Then saliva was similarly collected from the left submandibular duct. After each collection period the salivary gland was removed for future histological studies. A routine dietary regimen was followed throughout the entire experimental period. The results showed that the rate of salivary secretion evoked by pilocarpine stimulation was much faster than that by nerve stimulation when compared on the basis of similar protein content. The composition of the protein-bound carbohydrate was different in pilocarpine stimulation compared with nerve stimulation. Five components of mucin (protein and four different protein-bound carbohydrate fractions) increased in their concentration with increased frequency of stimulation. Longtime effects of aspirin or cortisone on protein and protein-bound carbohydrate of salivary mucin showed that the amounts of all four components of protein-bound carbohydrate decreased after aspirin ingestion. No significant change in the amount of protein was observed in the case of feeding with aspirin. Cortisone feeding resulted in the same effect on the concentration of protein and the three carbohydrate components (fucose, hexose and hexosamine), but not so in sialic acid. Histological studies show no appreciable change in structure of the gland.

Supported by Carle Foundation, Urbana, Illinois.

EFFECT OF HYPERTHERMIA ON HEAT BALANCE DURING RUNNING IN THE AFRICAN HUNTING DOG. C.R. Taylor, Knut Schmidt-Nielsen, Razi Dmi'el* and Michael Fedak*. Duke Univ., Durham, N. C.

The tricolored Cape Hunting Dog (Lycaon pictus), a dog-like African carnivore, hunts in running packs. To maintain body temperature at 37-38°C while running across the African savannah would require high rates of evaporation. In the laboratory we found that the hunting dog while running had relatively low rates of evaporation and a high rectal temperature (T_R). At 26°C, the running hunting dog had a higher T_R than the domestic dog and lost less water by respiratory evaporation. At 15 km hr^{-1} and 26°C the hunting dog's T_R was 41.2°C ± 0.05 and it lost 25.1% ± 0.5 of its heat production by respiratory evaporation; corresponding figures for domestic dog were 39.2°C ± 0.03 and 49.7% ± 3.0. At rest, however, the hunting dog increased respiratory evaporation and maintained nearly constant T_R at air temperatures (T_A) up to 41°C. The advantage of a high body temperature while running would be reduced if evaporation were increased to pull body temperature back to normal resting levels when the animal stops. We therefore measured the effect of 20 min running plus 40 min recovery on heat production and evaporation. In the hunting dog, even at T_A = 41°C, 40% of the additional heat generated by the run was lost without evaporation. The hunting dog's low evaporation while running might increase the distance it can pursue its prey. (Supported by NIH Research Grant HE 02228 and NIH Research Career Award 1-K6-GM-21,522 to KSN.)

VASCULAR REACTIVITY AND TISSUE CADMIUM CONCENTRATIONS IN CADMIUM HYPERTENSION. Gurdarshan S. Thind*, Grace M. Fischer* and William S. Blakemore. Bockus Research Institute and Graduate Hospital, University of Pennsylvania, Philadelphia, Pennsylvania.

Six to eight weekly IP injections of 2 mg/kg Cd^{++} acetate produced a sustained elevation of 131.0 ± 10.5 mmHg in the ear blood pressure of nine rabbits. In comparison with the control normotensive (N) aortic strips, hypertensive (H) strips were found to be less stiff ($P < 0.005$) and developed significantly lower active tension with angiotensin ($P < 0.001$). All H tissues had significantly higher Cd^{++} than did N tissues ($P < 0.01$). Within the N group, kidney had a significantly

Tissue	Mean Cd^{++} ± SE (µg/g of tissue)	
	Normal	Hypertensive
Kidney	0.290 ± 0.055	35.641 ± 5.876
Liver	0.077 ± 0.011	33.360 ± 7.261
Aorta	0.063 ± 0.010	0.931 ± 0.145
Mesenter. Art.	0.075 ± 0.029	1.861 ± 0.272
Pulmon. Art.	0.139 ± 0.043	1.188 ± 0.184
Heart	0.021 ± 0.002	0.641 ± 0.190

higher Cd^{++} than other tissues. Differences in the water content of N & H tissues were not significant. In view of the selective renal Cd^{++} accumulation and altered vascular reactivity to angiotensin, the kidney may have a role in the pathophysiology of Cd^{++} induced hypertension.
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CONTRALATERAL CONDITIONING OF LUMBAR MSRs AS A PARADIGM OF A GENERALIZED AFFERENT "ON RESPONSE". J. Steven Thomas* and Charles D. Barnes. Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

A sequence of lumbar DR/VR MSR amplitude changes in decerebrate cats to contralateral DR stimulation has been described and been found to involve a supraspinal relay. The response pattern consists of an initial facilitation (20-25 msec. through 50-60 msec.), a period of reflex inhibition (50-60 msec. through 100-120 msec.) and occasionally a second period of facilitation lasting out to 170-190 msec. after the onset of the conditioning stimulus. This pattern of MSR changes is now shown to be distributed to both flexors and extensors and to arise from stimulation of low threshold afferents from flexor, extensor and cutaneous nerves. This conditioning sequence can also be identified with ipsilateral conditioning stimulation although complicated by a greater segmental reflex contamination. Similar patterns of MSR changes have been reported by this laboratory following auditory and visual stimulation. Audio and contralateral conditioning of lumbar MSR show occlusive interaction and respond in parallel to drug administration, surgical procedures and to variations in the condition of the animal. A survey of the literature has found descriptions of similar MSR response patterns in facial and lumbar motor pools following stimulation of forelimb afferents and in lumbar and thoracic reflex activity after visceral afferent stimulation. It is argued that the pattern of MSR excitability changes seen in lumbar motoneurones after contralateral stimulation offers a convenient paradigm of a generalized brainstem "on response" to any increase in the level of afferent activity. (Supported by USPHS Grants NB 07834 and NB 34986).

EFFECTS OF IMPULSES FROM ELECTRICALLY EXCITED VENOUS AFFERENTS ON SPINAL CORD REFLEXES. Floyd J. Thompson* and Charles D. Barnes. Dept. of Anatomy and Physiology, Indiana Univ., Bloomington, Ind. 47401

The purpose of this study is to describe the central interactions of impulses from those afferent fibers innervating the femoral vein of the cat. Midcollicular decerebrate cats were used in a series of conditioning -testing experiments. The popliteal fossa was opened and the peripheral nerves common peroneal and gastroc-soleus exposes in an oil pool. The femoral vein was exposed in an oil pool and electrically insulated with silastic from the adjacent saphenous nerve. L_4-L_7 lumbar lamenectomy exposed the required spinal cord roots. Stimulating electrodes were placed under the femoral vein and impulses from the exvenous afferents served as the conditioning reflex. Stimulating electrodes were placed on lumbar 6 ventral root. In the decerebrate cat, conditioned venous afferents produced a monosymaptic flexor facilitation on the common peroneal test reflex. The polysynaptic flexor reflex was inhibited. No effect was observed on the extensor monosynaptic, but the polysynaptic demonstrated slight inhibition (10% of control). In the decerebrate cat, spinal at mid-thoracic level, conditioning the venous afferents produced inhibition of both flexor and extensor mono and polysynaptic reflexes. Time sequence conditioning-testing experiments indicate that the time course of the inhibition is 30-200 msec., with the maximum effect appearing 35-65 msec. following the conditioning stimulus, amplitude decreased to about 40% of the control. It is apparent that the spinal cord interneurons mediating the impulses from the venous afferents receive input from supraspinal nuclei. (Supported by USPHS Grant NB-34986 and USAF Grant F-44620-68-C-0014)

CHANGES IN CALCIUM STATUS ELICITED BY ADRENOCORTICOTROPIN (ACTH). Paul A. Thornton. VA Hosp., Lexington, Ky. 40507 and Dept. of Phys. & Biophys., Univ. of Ky., Lexington, Ky.

Earlier work (Stoerk et al., P.S.E.B.M. 114:690, 1963, and Canas et al., Metab. Clin. Exptl. 16:670, 1967) indicated that adrenal activity was associated with serum calcium change in parathyroidectomized animals. Other work (P.S.E.B.M. 127:1096, 1968) illustrated that ascorbic acid increased bone ^{45}Ca mobilization in prelabeled chicks. Since the adrenal characteristically releases ascorbate following ACTH stimulus, the effect of ACTH on blood calcium status was studied. Intact chicks and rats, prelabeled with ^{45}Ca, were given ACTH (iv). Response criteria included changes in blood calcium and ^{45}Ca activity. Both species exhibited hypocalcemia within 10 minutes following ACTH and an elevation of plasma ^{45}Ca almost immediately thereafter. Each parameter has essentially returned to normal by 60 minutes. These results are interpreted as indicating an initial hypocalcemic effect followed by an increased bone salt mobilization. Adrenalectomized rats and those given inactivated ACTH failed to exhibit either response, suggesting that the changes were mediated via the adrenal. These results suggest that products from the adrenal gland may participate in regulation of blood-bone relationships.

A DISCREPANCY BETWEEN DEPLETION AND RELEASE OF PITUITARY LH AND FSH. P.V. Tigchelaar*, N.D. Diebel*, T.R. Kingsley*, and E.M. Bogdanove. Department of Anatomy and Physiology, and Medical Sciences Program, Indiana University, Bloomington, Indiana, 47401.

The post-partum (PP) rat pituitary discharges LH and FSH shortly after delivery. Since the PP LH and FSH depletions — about 20 and 60 μg eq., respectively, by radioimmunoassay (RIA) — exceed comparable preovulatory pituitary depletions in proestrus cycling females by more than ten-fold, they have been used in an attempt to analyze LH and FSH secretory (transfer) kinetics. Treating observed pituitary depletion rates as constant infusion rates, we generated the serum LH and FSH curves which would be expected if the half-life ($t\frac{1}{2}$) and distribution volume (V) for each of these hormones were as previously estimated for non-PP rats by bioassay (Endocrinology 84: 1118, 1969). Observed serum LH and FSH curves never equaled or exceeded predicted curves. Ergo, either 1) less hormone enters the blood than disappears from the gland, or 2) available values for V and/or $t\frac{1}{2}$ were grossly inapplicable in the PP rat. RIA studies of $t\frac{1}{2}$ and V for rat LH and FSH have therefore been undertaken in PP and other types of rats. The rat LH and FSH half-lives in PP rats agreed with previous estimates, from which we conclude that our $t\frac{1}{2}$ assumptions cannot account for the failure of predicted serum LH and FSH curves to coincide with observed curves. However, V is harder to assess than $t\frac{1}{2}$. The finding that at least 80% of the hormone which disappears from the gland cannot be accounted for may thus reflect one, or both, of two possibilities: 1) an error in our understanding of the extrapituitary consequences of hormone release (distribution, binding, or altered immunoreactivity); 2) a hitherto unsuspected intrapituitary component of the secretory process, which we might term "negative synthesis".

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INFLUENCE OF PHYSICAL TRAINING OF ADRENALECTOMIZED RATS. C.M. Tipton, P.J. Struck*, K.W. Baldwin*, R.T. Dowell* and R.D. Matthes*. Exercise Physiology Laboratory, Univ. of Iowa, Iowa City, Iowa.

Saline maintained adrenalectomized (ADX) male rats participated in a modified exercise training study for 80 days. There were 15 non-trained (NT) and 16 trained (T) animals. Water tests conducted before (4%) and after (7%) the investigation plus 11-OCHS levels at time of sacrifice (5 µg%) verified the surgical procedures. At the termination of the study, rats were capable of running 1 hr/day at speeds which increased HR by 100 beats/min. and RT by 1.2°C. After 40 days the T rats had gained less weight (43±6 grams) than the NT rats (58±6) and this relationship prevailed throughout the study. There was no evidence for the resting bradycardia of training; but T rats did exhibit less cardiac acceleration than NT rats after an IP injection of atropine (1 mg/kg). T animals also exhibited less cardiac acceleration during a 9 minute sub-maximal treadmill exercise test. An in situ muscle work test was conducted and the average work time for T and NT ADX animals was 1/10th that of the non-ADX animals. T rats did not have higher muscle glycogen levels than NT rats nor did they have stronger knee ligaments. When isolated hearts were perfused with isoproternol (.2 µg/ml) the rates from the T group were greater than from NT group. It was concluded that ADX rats could and would perform increasing periods of exercise and that it was possible to produce some training effects in these animals. (Supported by funds from Iowa Heart Assoc and NIH Grant AM-08893-05)

(H^+) ON REDOX STATE OF NAD^+ LINKED SUBSTRATES. R.B. Tobin, M.A. Mehlman*, K. Chaperon*, and V. DeVore*. V.A. Hospital and University of Nebraska College of Medicine, Omaha, Nebraska 68105.

The redox state of Nicotinamide Adenine Dinucleotide (NAD^+) is a major factor in the regulation of metabolic pathways. Since reduction of NAD^+ involves dissociation of a proton, changes in (H^+) may have significant effects on NAD^+ linked metabolic processes. Prior work by Tobin (Am. J. Physiol. 207:601, 1964; The Physiologist 12:376, 1969) showed that biological lactate (L) to pyruvate (P) ratios (L/P) do not follow theoretical predictions. Work being presented is a continuation of in vitro studies of (H^+) effect on NAD^+-linked substrates. Utilizing slices and homogenates of normal rat liver we have studied the intramitochondrial redox state of NADH/NAD by assay of substrates of the enzyme B-Hydroxybutyrate dehydrogenase. This enzyme catalyzes the reaction Acetoacetate (AcAc) + NAD + $H^+ \rightleftharpoons$ B-Hydroxybutyrate (B-OH) + NAD^+ and is located exclusively in mitochondria (Williamson, Lund and Krebs, Biochem. J. 103:514, 1967). Work with L and P as cytoplasmic NAD linked substrates has been extended. AcAc, B-OH, L and P were all measured enzymatically after incubations. L/P of homogenates tended to follow theoretical values over the pH range from 5 to 9. This is quite different from liver slices. (B-OH), (AcAc), and B-OH/AcAc of slices, plus (AcAc) of homogenate all increased as pH of media increased from 4 to 7, but at pH's from 7 to 10, values remained constant. Homogenates showed constant B-OH and a fall in B-OH/AcAc as pH increased from 5 to 7, with constant ratio at pH's 7 to 10. Data indicate that although intramitochondrial NADH/NAD^+ of liver slices is sensitive to acid media, the redox ratio is not directly related to extracellular (H^+). Disruption of cell architecture by homogenization permits cytoplasmic and mitochondrial NADH/NAD^+ to be closer to equilibrium with pH of the media.

RELATIONSHIPS OF VOLUME, FLOW AND PRESSURE IN THE CORONARY VASCULAR BED. Richard J. Traystman* and Baruch Bromberger-Barnea. Dept. of Environmental Medicine, The Johns Hopkins University, Baltimore, Md.

In 32 isolated perfused dog hearts with empty chambers, the relationships between coronary arterial pressure (Pa), coronary flow (Q), and coronary vascular volume (V) were studied. V was measured with a weight gauge from which the preparation was suspended. Steady state measurements of change in V with change in $\dot{Q}$ ($\Delta V/\Delta\dot{Q}$) at constant coronary sinus pressure (Pcs) and transient measurements of change in V with time following a step change in either $\dot{Q}$ or Pcs were made. Transient ΔV's with time were single exponentials and the time required for ΔV to reach 63% of its final value was considered the time constant (T). These measurements were analyzed in terms of a theoretical model of the coronary circulation which contained a compliant area located between an upstream resistance and a downstream resistance. If the model were a realistic one, $\Delta V/\Delta\dot{Q}$ and the transient T measured by either step change in $\dot{Q}$ or Pcs should all be the same, and should equal the product of the downstream resistance and the compliance. The compliance (C) of the system was considered to be $\Delta V/\Delta Pa$ produced by a change in Pcs at constant flow. With epinephrine administration $\Delta V/\Delta\dot{Q}$ decreased from .081 to .058 min, the transient T following a step change in $\dot{Q}$ decreased from .095 to .050 min, and the transient T following a step change in Pcs decreased from .055 to .044 min. C increased from .830 to 1.001 ml/mm Hg and the total vascular resistance decreased from .715 to .377 mm Hg/ml/min. Knowing the compliance and time constant we calculated the downstream resistance. Knowing the total resistance and the downstream resistance, we calculated the upstream resistance. With epinephrine administration both downstream and upstream resistance decreased considerably. (Supported by USPHS Grants 5 T01 HE 05453 and 5 P01 HE 10342.)

EARLY CHANGES IN LUMINAL VELOCITY AND GFR AFTER UNILATERAL NEPHRECTOMY. M.E. Trimble and R.J. Goss*, Brown University, Providence, R.I.

The present study was undertaken in an attempt to demonstrate that functional overload may be a causative factor in the initiation of compensatory renal growth. Luminal velocity in superficial (S), middle (M) and juxtamedullary (JM) nephrons was measured according to a modification of Hanssen's technique (Baines et al, Pflüg. Arch. 308:244, 1969). Male rats were anesthetized (160 mg/Kg Inactin) and measurements were made during control periods and following unilateral nephrectomy (UN) at 1 hour (UN+1 hr.) and 24 hours (UN+24 hr.).

		Luminal Velocity (mm/sec)		
	N	S	M	JM
Control	7	0.70 ± 0.01(123)	0.77 ± 0.01 (92)	0.95 ± 0.02 (86)
UN+1 hr.	6	0.75 ± 0.02*(99)	0.83 ± 0.02*(87)	0.97 ± 0.02 (78)
UN+24 hr.	6	0.74 ± 0.01*(98)	0.78 ± 0.01 (96)	0.87 ± 0.02*(77)

*significantly different from control, $p<0.05$

N= No. of animals ( )= No. of tubules

By 1 hour after nephrectomy, luminal velocity in S and M nephrons had increased. At 24 hours, S velocity remained elevated while JM velocity was depressed. In parallel experiments, GFR/left kidney was determined prior to and following right nephrectomy. Thirty min. collection periods were begun 10 min. after nephrectomy and continued for 150 min. GFR was also measured 24 hrs. after nephrectomy. A transient rise in GFR was noted. Peak values 20-30% above control GFR occurred between 10-70 min. post-nephrectomy. Thereafter, GFR declined gradually to control levels by 160 min. post-nephrectomy. The present findings are consistent with observations of a positive correlation between luminal velocity and GFR and suggest that S nephrons are subjected to functional overload prior to or concomitant with compensatory increases in renal protein. (Supported by PHS Grant # 5-T01-HD-00019-09)

VISCO-ELASTIC RELAXATION TIME SPECTRUM AND WAVE PROPAGATION IN SKELETAL MUSCLE. X. T. Truong. Veterans Administration Hospital and Baylor College of Medicine, Houston, Texas.

A method was developed to derive the relaxation time spectrum of skeletal muscle from measurements of visco-elastic wave propagation constants. Continuous longitudinal sinusoidal mechanical waves of 20 to 10,000 Hz were propagated through whole sartorius frog muscle along its longitudinal axis, and the phase velocity and attenuation coefficient were measured. Measurements were made with various degrees of stretching of the resting muscle, and during the contracting state.

The velocity-frequency curve showed velocity limits at both the low and high frequency ends, while the attenuation-frequency curve had an upper limit. These findings appeared to be compatible with the analog Maxwell mechanical model, composed of a continuous spectrum of Maxwell elements and an auxiliary elastic element, all connected in parallel. The relaxation time spectrum for the resting muscle showed that the majority of the relaxation times were less than one millisecond. There was an increase in wave velocity with passive stretching and active contraction, and a resulting rise in the spectrum amplitude. The total elastic modulus of the analog Maxwell model, and the modulus of the auxiliary elastic element of the model were estimated from the wave propagation data.

SEQUENTIAL EMPTYING OF LUNG COMPARTMENTS. S. Tsunoda* and A. C. Young. Firland Hospital, Virginia Mason Research Center, and University of Washington, Seattle, Washington.

The alveolar dilution ratio (ADR) varies within the lungs. For our study geographically distinct regions with the same ADR are lumped together and the continuous range of ADR's is represented by four discrete values, one of which is set to be zero to correspond to the series dead space.

The determination of the ADR's and their relative contribution to the end tidal expired gas is made by comparing the end tidal values of F_{N_2} during a N_2 washout with the predicted results from a four compartment analog model of the lungs. Using these same ADR's their relative contribution at any phase of expiration can be similarly determined. A plot of the contribution of each ADR as a function of expired volume then gives a direct determination of the relative importance of sequencing of the different compartments and the mixing of dead space gas on the slope of the expired F_{N_2} curve.

Continuous tracings of F_{N_2} at mouth level with expired volume and flow have been obtained on 20 seated subjects ranging in age from 16 to 64. Dead space volume appears in the first part of expiration and contributes less than 6% to the tidal expiration beyond 250 cc in young subjects. In older subjects the dead space extends further into the expired volume. A well ventilated compartment contributes large volumes to early expiration and little after 300 cc is expired, a finding more marked in youth than age. There are one or more poorly ventilated compartments that contribute increasingly to expiration in all subjects. The lung compartments do not empty simultaneously.

Supported in part by NIH grant HE 01892.

THE EFFECTS OF VIGOROUS PHYSICAL TRAINING ON METABOLIC, RESPIRATORY, AND CIRCULATORY RESPONSES OF MIDDLE-AGED AND OLDER MEN. S.P. Tzankoff*, S. Robinson, F.S. Pyke*, and C.A. Brawn*. Indiana University, Bloomington, Indiana.

Fifteen sedentary men, ages 44-66, spent 60-90 minutes, 3-4 times a week for 6 months in vigorous physical training. Activities included tennis, handball, swimming, jogging, and walking. Before, and at the middle and end of the activity period, their adjustments to a standard walk (5.6 km/hr, 9% grade for ten minutes) and to exhausting work on the treadmill were determined. Maximal work was attained at 5.6 km/hr by increasing the grade every minute until the subjects reached exhaustion. The energy cost in the 10-min walk was unchanged, but $\dot{V}_E$, blood lactate, and heart rate in this work decreased on the average by 8.7, 36.0, and 8.6% respectively with training. In exhausting work average values of maximal work capacity, $\dot{V}o_2$, $\dot{V}_E$, and blood lactate increased by 21.6, 17.1, 16.6, and 13.0% respectively with training. Maximal heart rate did not change. The younger men (ages 44 to 53) had generally higher maximal $\dot{V}o_2$, $\dot{V}_E$, and blood lactate than the older men (ages 54 to 66). The older men had lower initial maximal work capacities and blood lactates in exhausting work and on the average the percentages of increase in these parameters with training were greater. Although no dietary restrictions were either imposed or encouraged, the subjects lost an average of 1.8 kg of body mass and their basal blood cholesterol decreased by 12.3%. Basal $\dot{V}o_2$, $\dot{V}_E$, heart rate, and arterial pressure were unchanged. These effects of training are similar to previous results obtained in this laboratory on young men, except the latter showed a significant decrease in maximal heart rate. (Supported by PHS-R01-HD-04056-01.)

MEAN AND PULSATILE OPTICAL DENSITY (O.D.) CHANGES IN BONE. Daniel D. Upthegrove, Gunter N. Franz, and Kenneth C. Weber, (intr. by J. C. Stickney) ALFORD, EHS, USPHS, HEW, and Dept. Physiology & Biophysics, West Virginia University Med. Ctr., Morgantown, West Virginia 26506

Circuitry which linearizes the output of a photocell was developed and tested so that total and accurate pulsatile O.D. changes could be measured over a wide range of O.D. In an in vitro setup, the system was checked using non-rigid and rigid tubing. Pulsatile O.D. changes were found in the non-rigid tubing using both blood and indocyanine green dye. In the rigid tubing, pulsatile O.D. activity was found with blood but not with dye. The O.D. of intact tibias of dogs was examined and the results showed pulsatile O.D. changes with the same basic frequency as the heart rate. The bone was successively perfused at a constant rate (set to maintain equivalent blood pressure) through the femoral artery with blood, saline and indocyanine green dye. In 13 trials in 9 dogs the mean pulsatile O.D. activity during blood perfusion was 0.21 $\pm$ .03% of the total O.D. change which occurred when the vascular system of the bone was perfused with saline. In the same dogs the mean pulsatile O.D. activity during indocyanine green dye perfusion was 0.15 $\pm$ .04% indicating that a considerable amount of the pulsatile activity was due to volume changes within the vascular system and not due to flow related phenomena. Twenty-four injections of acetylcholine (60-90 μgm) were made into the femoral artery under constant flow conditions and the mean O.D. decreased by 20 $\pm$ 1.3% of the maximum O.D. change. In 26 similar injections of norepinephrine (8-10 μgm) the mean O.D. decreased by 23 $\pm$ 2.4%. It is concluded that the volume of the vascular system within bone can change appreciably. Supported in part by PHS Grant #5501 FR 05347-08 and 5501 FR 05433-08 from West Virginia University School of Medicine and Dentistry.

UNIT FIRING PATTERNS IN CAUDATE AND PALLIDUM DURING A DELAYED RESPONSE PARADIGM IN THE MONKEY. A.A. Uyeda, C.D. Hull and N.A. Buchwald, Departments of Anatomy and Psychiatry and Mental Retardation Program, NPI, UCLA

A behavioral paradigm was designed to probe the relationship of the activity of caudate nucleus cells to those of the globus pallidum. Monkeys were trained to suppress lever-pressing for 10 secs. after the presentation of a light in order to receive a liquid reinforcement (grape juice). Unit activity of the caudate nucleus, the overlying cortex and white matter and the globus pallidum were recorded extracellularly from trained animals during performance. The spontaneous activity recorded from these different neuroanatomical regions shows striking differences. Caudate cells fire slowly (0.5-2/sec.) in contrast to discharge rates in the pallidum (15-20/sec.). Prior to and during the lever-pressing response, increases in mean spike rate occurred in all recorded regions. These rates increased gradually to a peak and then abruptly return to "spontaneous" firing level. Analysis of firing rates were made for two 6 sec. epochs. The first epoch extended from 2 secs. prior to the onset of the light to 4 secs. afterward. The second epoch was similarly timed with relation to the animal's lever-press. The onset of the light had no obvious effect on the mean firing rate of caudate units, but was associated with a 1 sec. increase in rate of firing in the pallidum. Associated with the lever-press a sharp peak in unit firing rate which lasted for 1.0-1.5 secs. occurred in both caudate and pallidum. Unit activity associated with correct (reward) and incorrect (failure to delay lever-press for 10 secs.) responses were compared. A clear difference in the unit firing pattern following rewarded and nonrewarded responses occurred. This difference was greater for pallidal than for caudate neurons. These smaller variations in mean firing rates of caudate units during the response epoch appear to be amplified in pallidal neurons; that is, the variations in firing are correlated even though the mean frequencies differ.

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FECAL IODINE AS A MEASURE OF THYROID HORMONE SECRETION RATE. L. Van Middlesworth, Univ. of Tenn. Medical Units, Dept. of Physiology and Biophysics, Memphis, Tennessee.

Rats were fed a Remington low iodine, low residue diet for 8 months. They developed large thyroids which contained 0.3 to 0.8 µg iodine. The thyroidal iodine was 4 to 5 percent triiodothyronine (T_3) and 2 to 4 percent thyroxine (T_4). To determine the excretion pattern of iodine for T_3 and T_4 in such rats, 0.01 µg of T_4 labeled with ^{125}I and 0.01 µg of T_3 labeled with ^{131}I were injected intraperitoneally with 10 mg $KClO_4$ (to prevent recycling of radioiodine through the thyroid). Within 4 days the urinary excretion of ^{131}I from T_3 had accumulated 78% of the dose and the ^{125}I from T_4 had accumulated 55% of the T_4 dose. The accumulated fecal excretion approached 24% of each isotope by 6 days. Therefore, the daily fecal excretion of both T_3 and T_4 may approach 24% of the quantity of hormonal iodine secreted per day under equilibrium conditions in rats fed Remington diet.

INPUTS TO EARLY AND LATE HAIR-S AND TOUCH-S NEURONS IN THE CONTRALATERAL FOREPAW FOCUS IN SOMATOSENSORY AREA II OF THE CAT.
R. A. Vargo*, J. J. Dallman* and R. W. Morse Med. College of Ga., Augusta, Ga. 30902

In cat anesthetized with α-chlorolose 128 hair-s and 101 touch-s neurons have been isolated in the contralateral forepaw focus in Somatosensory Area II, SII(CFP), by conventional extracellular microelectrode techniques. Their first spike activity was analyzed in depth sectioned time-depth spike density maps. The maps depict the hair-s subset displaced significantly earlier in time than the touch-s subset. Hair-s neurons tend to follow higher iterative stimuli than touch-s neurons, but their difference in thresholds is negligible. From 0.6 to 1.2 mm in depth below the pial surface temporally distinct subsets of 55 hair-s (7.0 - 12.5 msec.), 20 late hair-s (13.5 - 20.0 msec.), 39 early touch-s (8.0 - 13.5 msec.) and 18 late touch-s (14.5 - 22.0 msec.) neurons were observed. The early s neurons followed significantly higher iterative stimuli than the late s neurons, while their threshold differences were not prominent. Perhaps the early hair-s and touch-s neurons, 0.6 - 1.2 mm in depth in SII(CFP), are excited by a faster afferent system than the late hair-s and touch-s neurons, but each system conducts information concerning hair sensitivity faster than information concerning touch sensitivity. (This investigation was supported by U. S. Public Health Service Grants ME1001, CH1001, NB07184 and NDEA Title IV Graduate Fellowship Program.

VISCERAL CIRCULATORY ADJUSTMENTS TO SEVERE FREE-RANGING EXERCISE IN DOGS BEFORE AND AFTER HEART BLOCK.
S.F. Vatner*, C.B. Higgins*, T. Patrick*, and D. Franklin. Dept. of Med., Univ. of Calif. San Diego, and Scripps Clin. &Res. Fdn., LaJolla

Severe exercise is traditionally believed to cause a compensatory shunting of blood flow (BF) from the mesenteric (M) and renal (R) beds. This adjustment is not a significant feature of the response to severe exercise in dogs. This potent mechanism might be utilized when alternate compensatory mechanisms, such as heart rate (HR), are limited. Dogs were instrumented with Doppler ultrasonic flow probes on the R and M arteries and miniature pressure gauges in the aorta. To determine the visceral response to severe exercise in normal dogs and those with limited ability to increase HR, measurements of BF and arterial pressure (AP) were telemetered from 10 normal, untethered dogs running 15-25 m.p.h. behind a mobile recording unit in the field and in 5 dogs with induced complete heart block (HB). In normal dogs exercise increased HR from 82 to 256/min. and AP from 89 to 140mmHg, while MBF and RBF remained constant. In HB dogs during exercise HR increased only from 49 to 80/min. and AP from 80 to 91mmHg, while MBF and RBF decreased to 37% of pre-exercise control. The HB response was not altered by ventricular pacing at 100/min. but at 200/min a more normal response resulted. Thus, the response to severe exercise in normal dogs does not involve a compensatory shunting of visceral flow, but in heart block when the increase in heart rate during exercise is limited mesenteric and renal blood flow are severely compromised.

IN-VITRO SPONTANEOUS MOTILITY OF THE HUMAN VAS DEFERENS. W. P. Ventura*, M. Freund, J. E. Davis*, and C. Pannuti*. New York Med. Coll., New York, 10029.

The presence of spontaneous motility of the human vas deferens in an organ bath with perfusion system has been demonstrated. One hundred and sixty 3-cm pieces of vas were used to record the spontaneous motility for 4 hours in an isotonic system; 50-ml. organ bath, transducer, polygraph (Fertil. Steril. 14:416, 1963). In-vitro studies on the vas were made from different source material: 20 cadavers, 30 vasectomies under local anesthesia, 15 vasectomies under general anesthesia, and 15 vasectomies under spinal anesthesia. It was noted that vas from cadavers displayed spontaneous motility (up to 24 hours after death). No spontaneous motility was observed in vas taken at vasectomy under local anesthesia. The apparent irreversibility of local anesthetics on the subsequent in-vitro motility of the vas is an interesting point. All vasa from vasectomies under general anesthesia were spontaneously motile in vitro and showed contractile responses to norepinephrine but not to acetylcholine or oxytocin. This confirms the hypothesis that the motility of the vas in vivo is under the control of sympathetic fibers which release norepinephrine. The presence of spontaneous motility in vitro leads to the working hypothesis that there is spontaneous motility of the human vas in vivo. Quite unexpectedly, the vasa from vasectomies under spinal anesthesia showed no spontaneous motility in vitro. This observation suggests the hypothesis that the tone in the sympathetic fibers innervating the vas (and, therefore, the amount of norepinephrine released and the amount of motility induced) is dependent on the integrity of a spinal center.

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PROLONGED BED-REST IN HEALTHY HUMAN SUBJECTS: DIURNAL VARIATION IN ADRENOCORTICAL AND THYROID FUNCTION. Joan Vernikos-Danellis, Carolyn S. Leach*, Paul C. Rambaut*, and Pauline B. Mack*. Environmental Biology Division, Ames Research Center, NASA, Moffett Field, Calif., Preventive Medicine Division, Manned Spacecraft Center, NASA, Houston, Texas, and Texas Woman's University, Denton, Texas.

Eight healthy males, aged 20-40, were submitted to bed-rest for 56 days on a 14L:10D regimen (lights-on 9:00 a.m.) and fed on Apollo diet. Four of these subjects exercised with an exergenie three times daily throughout the experiment. Urinary cortisol was determined for each subject in six hourly pools collected for several days before, ten days post and throughout the bed-rest. Circulating cortisol, triiodothyronine (T_3) and thyroxine (T_4) concentrations were determined in blood samples drawn at four hourly intervals for 48 hour periods before, 10, 20, 30, 42, and 54 days during, and 10 days post-bed-rest. A significant fluctuation in plasma and urinary cortisol occurred with peak levels occurring around 7:30 a.m. throughout the experiment. However, bed-rest markedly reduced the amplitude of the steroid rhythm resulting in decreased mean 24 hour steroid outputs. Neither exercise nor the 10 days post-bed-rest ambulatory period prevented or corrected this effect. In contrast, the amplitude of the T_4 rhythm appeared to increase as bed-rest progressed and the total serum T_3 concentration increased during the latter part of the bed-rest. The data indicate that bed-rest affects the amplitude of the diurnal rhythm of adrenal and thyroid secretions thereby altering the total 24 hour hormonal output. Furthermore, neither exercise nor the 10 day post-bed-rest ambulatory period prevents or corrects these effects.

EVANS BLUE DYE AND THE DEVELOPMENT OF "MYOGENIC TONE" IN ISOLATED RESISTANCE VESSELS. R.L.Verrier* and D.F.Bohr. Dept of Physiol., Univ. of Mich., Ann Arbor, Mich. 48104.

Previous studies in this laboratory have shown that isolated resistance vessels (80-350μ o.d.) from rat skeletal muscle, but not from mesentery, develop myogenic tone when perfused with physiological salt solution. In the current study, the extent to which the dye, Evans Blue, used in the dissection procedure, affects the development of tone was evaluated. In all vessels studied, when dissection was performed without dye little or no tone developed in either vessel type over an 8 to 10 hr period. When Evans Blue (3ml of 10^{-3}g/ml) was injected into the perfusate, tone developed in skeletal muscle vessels, within 5 to 10 min, but required considerably longer in mesenteric vessels. Although the presence of Evans Blue appears to be necessary for the induction of tone in isolated perfused segments, this phenomenon also depends on the individual characteristic of the vascular smooth muscle. Because the dye increases responsiveness to bolus injections of calcium chloride in parallel with the development of tone, it is thought that the induction of tone by Evans Blue results from a persistent increase in cell membrane permeability to extracellular calcium and/or a decreased extrusion or trapping of this ion.

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SODIUM FLUXES IN FRESH AND STORED HUMAN ERYTHROCYTES. Roger W. Voight and R. E. Taylor, Jr., Department of Physiology and Biophysics, University of Alabama Medical Center, Birmingham, Alabama 35233.

The sodium concentration ($(Na)_i$) in fresh human erythrocytes was elevated by incubation at 37° C in 150 mM NaCl to approximately the same level as in red cells stored for 4 weeks at 6° C in ACD plasma. Both groups of cells were then stored at 6° C in a solution containing initially 146 mM Choline, 4 mM K^+, Na^+< 0.05 mM (mostly $^{22}Na^+$, 0.1 μC/ml), pH 7.5. At 48 hour intervals, samples were taken from each group, washed free of extracellular choline and ^{22}Na, and incubated at 37° C in bicarbonate Ringer's containing 10 mM glucose and 4 mM adenosine. The sodium flux in the presence (M_p) and absence (M_t) of ouabain was then measured by determining the rate of loss of radioactivity. There was a progressive decline in $(Na)_i$ and a corresponding decrease in active sodium flux (M_t-M_p); at comparable sodium levels there was no significant difference in the active component between fresh and old cells. The ouabain insensitive (passive) flux in fresh cells showed a small but insignificant decrease for 5 days but was significantly increased by day 7; in sharp contrast, however, the passive component in old cells was more than twice that of the fresh cells after 2 days, and increased progressively and markedly during further storage. It is possible that this increased "leakiness" in ACD-stored erythrocytes may be related to their decreased viability as determined by post-transfusion survival.

MODE OF CATECHOLAMINE ANTAGONISM OF OXYTOCIN-INDUCED MILK-EJECTION. Helmuth Vorherr and Robert A. Munsick* University of New Mexico School of Medicine, Albuquerque, N.M.

In lactating ethanol or barbiturate anesthetized rats or rabbits we have further investigated the mechanisms by which Epinephrine (E), Isoproterenol (IP), Norepinephrine (NE), Phenylephrine (PE) and Angiotensin II (A) inhibit the milk-ejection response to oxytocin. The above substances were injected intravenously or intra-arterially with or 30 sec. before oxytocin, in the absence and presence of α and/or β blockers, and mammary intraductal pressures were recorded.

Agents & Dosage		INHIBITION OF OXYTOCIN-INDUCED MILK-EJECTION		
Rats	Rabbits	Alpha-Blockade	Beta-Blockade	Alpha & Beta-Blockade
E 2.5-500ng	0.5-1µg	+++	++ - +++	∅
IP 1-500ng	0.5-2µg	++++	∅	∅
NE 2.5-500ng	0.5-2µg	+ - ++	+++	∅
PE 1-2µg	10-20µg	∅	++++	∅
A 50-100ng	0.5-1µg	++++	++++	++++

+ = Oxytocin inhibitory effect of 25%, as compared to controls without blocker (++++ = 100%). ∅ = No oxytocin inhibition.

We conclude that the inhibition by E, IP and NE is mediated respectively by 50-75%, 100% and 25-50% stimulation of myoepithelial β receptors. PE inhibition is mediated by vasoconstriction via vascular α receptors; E and NE also inhibit in this way to the extent of about 25% and 50-75% respectively. Myoepithelial α receptors are absent or silent. The inhibition caused by A is probably due to non-adrenergically induced vasoconstriction. Supported by NIH Grant R01 HD04028-02 and by Damon Runyon Memorial Fund, Grant DRG-1002A.

PURIFICATION AND PROPERTIES OF UTERINE MYOSIN A (MyA)[1] Phyllis Wachsberger* and George Kaldor[2], Department of Physiology and Biophysics, Woman's Medical College of Pennsylvania, Phila., Pa.

MyA has been prepared from rabbit uteri by a 15 min. extraction with 1 M LiCl and 1.5 mM ATP. The extract was further purified by precipitation at 0.25 M and at 0.05 M KCl concentration. The last precipitate was dissolved in 0.6 M KCl and centrifuged at 30.000 RPM for three hours. The uterine MyA obtained by this method appeared to be homogenous in the ultracentrifuge. The S_{20} of this protein was 6.4×10^{-13} and its diffusion constant was 1.68×10^{-7}. The M.W. of the uterine MyA was estimated at 530.000. The helical content of this protein was measured by optical rotary dispersion between 589 and 365 mµ. The b_o was calculated to be 260 which gave a helical content of 41.9%. The ATPase activity of this uterine MyA at pH 7.5 in the presence of 10 mM Ca^{2+} and 0.6 M KCl was 0.10 µM/min./mg prot. at 26°C. Under similar conditions but at pH 5.3 (optimal pH) the ATPase activity was 0.52 µM/min./mg prot. The energy of activation was 16.200 at pH 7.5 and it was lowered to 13000at pH 5.3. Mg^{2+} in 1 mM concentration inhibited 50% of activity of the Ca^{2+} activated enzyme. 5 mM dinitrophenol caused 75% activation at pH 7.5 but almost completely inhibited the ATPase activity at pH 5.3. PCMB in 10^{-5}M range strongly inhibited the enzyme at both pH's. Uterine MyA appears to have a similar M.W. and helical content to skeletal MyA. The pH optimum and Mg^{2+} sensitivity of the Ca^{2+} activated uterine MyA ATPase is lower than that of the skeletal enzyme.

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2. Recipient of Res. Career Dev. Award K03 NS 33196

THE EFFECT OF PHYSICAL ACTIVITY ON CREATINE PHOSPHOKINASE AND GLUTAMIC-OXALACETIC TRANSAMINASE LEVELS IN MUSCLE AND BLOOD PLASMA OF RATS. J.A. Wagner*and J.B. Critz. Univ. of Western Ontario, London, Canada.

Creatine phosphokinase (CPK) and glutamic-oxalacetic transaminase (GOT) levels were measured in plasma and cardiac, soleus and gastrocnemius muscles in order to study metabolic adaptations and mechanisms for alterations in enzyme levels occurring during physical training. Rats were subjected to one of five levels of physical conditioning: control rats (standard cage; 3 weeks), spontaneously active rats (standard activity cage; 3 weeks) and trained rats (enforced swimming on alternate days for two, four and six weeks). At the end of each conditioning period the appropriate rats were sacrificed in either the resting condition or immediately following a single sixty minute swim. Six weeks was the minimum duration of training needed to produce elevated enzyme levels in all three types of muscle. The resting myocardial CPK level increased from 31.1 International milliunits per microgram nitrogen ($mU/\mu gN_2$) in control rats to 35.9 $mU/\mu gN_2$ in rats trained for six weeks, and the resting soleus CPK level increased from 68.0 to 80.5 $mU/\mu gN_2$. Training rats for six weeks resulted in an elevation in the resting myocardial GOT level from 22.6 to 27.6 $mU/\mu gN_2$, soleus GOT level from 12.0 to 15.5 $mU/\mu gN_2$ and gastrocnemius GOT level from 4.07 to 5.68 $mU/\mu gN_2$. Rats trained for six weeks had post-exercise muscle enzyme levels that were similarly elevated above the post-exercise levels of controls. Cardiac muscle showed an earlier enzyme adaptation to training than did either type of skeletal muscle. Post-exercise muscle enzyme levels showed a training effect earlier than did the resting enzyme levels. Plasma GOT levels, but not plasma CPK levels, increased as training progressed and appeared to be dependent upon a muscle to plasma gradient. (Supported by Def. Res. Bd. Canada.)

EFFECT OF ADRENOCORTICAL HORMONES ON PLASMA RADIOIMMUNOASSAYABLE GROWTH HORMONE (RIA-GH) IN RATS. **I. Wakabayashi, M.D.*, A. Arimura, M.D. and A.V. Schally, Ph. D. Department of Medicine, Tulane University School of Medicine and Endocrine and Polypeptide Laboratories, Veterans Administration Hospital, New Orleans, La.**

It has been reported that plasma RIA-GH in rats is decreased by stress and increased by gentling the animals. It is possible that these responses of plasma RIA-GH might depend on or be influenced by activation of the pituitary-adrenal axis. In the present study, the influence of adrenocortical steroids on plasma RIA-GH was investigated in rats. Female Sprague Dawley rats were used throughout the experiment. Plasma GH was determined by radioimmunoassay using NIAMD-RAT-GH RIA KIT. Three hrs after an i.p. injection of dexamethasone (Dex) (400 µg/100 g body weight) GH levels in the plasma were considerably suppressed. But if Dex was injected 30 min before, it did not alter the plasma RIA-GH. On the other hand, Nembutal injection (3.5 mg/100 g body weight, i.p.) increased plasma RIA-GH levels. Fifteen min after Nembutal injection into rats which were also given Dex 3 hrs previously, plasma RIA-GH levels were significantly higher than those in rats pretreated with Dex only. Five days after adrenalectomy the plasma RIA-GH showed a tendency to rise, but at longer intervals after adrenalectomy the RIA-GH levels were lower than those in corresponding controls. Both in intact and adrenalectomized rats, application of either stress, or administration of Dex 3 hrs before suppressed plasma RIA-GH to the same extent. The combination of stress and Dex injection did not further depress the plasma RIA-GH as compared to stress alone. These data indicate that the decrease of plasma RIA-GH under the conditions of stress is independent of adrenocortical activation.

PASSIVE ROLE OF THE BILE DUCT SYSTEM IN THE DELIVERY OF BILE INTO THE INTESTINE. K. G. Wakim, Mayo Clinic and Foundation, Rochester, Minn.

Our recent studies on human and canine biliary systems revealed that smooth muscle fibers were scattered sparsely among the connective tissues in the duct wall of only 12% of the cases and that the duct wall did not have a complete muscular layer. Consequently we became interested in determining whether spontaneous or drug-induced peristaltic activity can be demonstrated in segments from various levels of the bile ducts. The biliary duct system, including a segment of duodenum, was freshly removed and immediately placed in oxygenated Tyrode's solution. Each segment from the cystic, hepatic, extramural, and intramural duct portions was suspended for bio-assay in warm (35 C) oxygenated Tyrode's solution. Spontaneous and drug-induced activities were exhibited only by the intramural duct segment while it was intimately surrounded by the duodenal muscle layers but not after it was deprived of all the surrounding duodenal muscles. After the effects of histamine, acetylcholine, methacholine (Mecholyl), and other drugs were recorded for each duct segment, a portion of each segment was put in formalin; histologic sections were made and stained specifically for muscle; the muscle content was correlated with the biologic activity recorded by the bio-assay from the same fresh segment. The conclusion that the biliary duct system per se functions as a passive conduit and not as an active peristaltic organ in the delivery of bile into the intestine is justified by (1) the presence of only sparsely scattered smooth muscle fibers in the fibroelastic wall of the bile duct; (2) the total absence of a complete encircling muscle layer; and (3) the failure to demonstrate any significant spontaneous or drug-induced activity in any of the isolated perfused fresh segments of the bile duct, including the intramural segment when deprived of the duodenal muscles surrounding it.

DEPRESSION OF SPONTANEOUS NEURONAL ACTIVITY IN EXPLANTS FROM MAMMALIAN BRAIN IN TISSUE CULTURE. F. Walker and W. Hild. (intr. by K. Kusano). Inst. of Psych. Res., Ind. Univ. Med. Ctr., Indianapolis, Ind. and Dept. Anat., Univ. Texas Med. Br., Galveston, Texas.

Explants from the cerebellum and midbrain of newborn rats were maintained on cover slips in roller tubes by the "flying cover slip" method of culturing mammalian neural tissue. Each cover slip used for this study had a hole 100 to 250 μ in diameter drilled through its center over which the tissue was explanted and maintained for 4 to 6 weeks before measurements were taken. At the end of that time the cells had migrated into the hole and recordings could be taken of the spontaneous activity without the perturbation of introducing an electrode into the tissue. Impedance measurements and d.c. recordings were also taken from these explants containing neuroglia and neurons. Brief electric shocks in the msec range of less than 10^{-8} amp/μ^2 evoked bursts of activity but no clear alteration in the impedance. Increasing the current density or duration of electric shock produced a depression of the recorded spontaneous neuronal activity for a duration measured in minutes accompanied by a d.c. shift. The same shock produced an impedance change: first a brief drop measured in seconds followed by an elevation of the same duration as the depression of spontaneous neuronal activity. A d.c. shift and impedance change could be obtained from cultures evidencing no spontaneous activity or from corpus callosum known to contain only neuroglia. The results are similar to those that characterize the phenomenon of spreading depression in other preparations in vivo. The presence of neurons are not necessary for the observations of impedance change or d.c. shift. (Supported by PHS grant NB 03114 and F.W. by special fellowship 1-F3-MH-37,569-01 (APA) and Eli Lilly and Co. grant-in-aid).

EVIDENCE FOR FUNCTION OF THE SARCOPLASMIC RETICULUM IN Z LINE FORMATION AND THIN FILAMENT AGGREGATION IN SKELETAL MUSCLE FIBERS OF FETAL RATS. S. M. Walker and M. B. Edge*. Dept. of Physiology and Biophysics, University of Louisville, Louisville, Kentucky.

A characteristic structural relationship between tubules of the sarcoplasmic reticulum (SR) and the Z line has been observed in fully developed fibrils of skeletal (J. Cell Biol. 39: 469, 1968) and cardiac (Anat. Rec. 166: 51, 1970) muscle fibers. The purpose of the present study is to look for the earliest stage in Z line formation showing close association with the SR tubule. Cross-sections of fibrils varying in thickness from 0.06 to 0.8 μ were examined at the Z line level in leg muscles of 15 to 20 day fetal rats. Electron micrographs revealed tubules of SR encircling the fibril at the Z line level from the smallest to the largest fibril size. The space between the SR tubule and the Z line is about 100 Å wide and it is traversed by electron-opaque strands which appear to be connections of the SR tubule and the Z line. This close approximation and apparent connection of the SR tubule with the Z line from the beginning to the completion of Z line formation seems to warrant the conclusion that the SR tubule plays a role in Z line development and thin filament aggregation. It is suggested that the SR tubule and the electron-opaque strands at the Z line level provide precursors for structural material required for aggregation of thin filaments to form the thin filament component of the fibril. (Supported by NSF grant GB-8538, NIH grant 5 RO1 NS07930-02 and grants from the American Heart Association and the Kentucky Heart Association.)

STABLE STRONTIUM BALANCES IN MAN. Janet M. Warren* and Herta Spencer. Metabolic Section, VA Hospital, Hines, Illinois.

Stable strontium balances were determined in man under strictly controlled dietary conditions in control studies and during both oral and intravenous administration of stable strontium. The diet contained about 1 mg strontium per day. Most of the ingested strontium was passed in stool and the balance was either slightly negative or in equilibrium. During the oral intake of 1536 mg stable strontium per day given as the lactate for 30 days the urinary stable strontium excretion increased markedly, the stable strontium balance became strongly positive but the percent net absorption was similar in stable strontium study and in the control study, 30.5% and 29.2%, respectively. The intravenous dose of 612 mg stable strontium as the gluconate was infused daily on 6 days. During the 6 days of intravenous stable strontium infusions, 30-40% of the dose was excreted in urine and 5-10% in stool. By 30 days after the infusions of stable strontium a total of 60% had been excreted in urine and about 30% in stool. Strontium continued to be excreted in both urine and stool following the 6 intravenous stable strontium infusions for over 100 days in amounts which were about 6-10 times greater than the baseline excretions. (Supported by AEC Contract AT(11-1)-1231-52.)

EFFECT OF PITUITARY EXTRACT ON THE GONADOTROPIN AND PROLACTIN RESPONSE TO CRUDE RAT HYPOTHALAMIC EXTRACT IN VIVO IN MALE RATS. J.T. Watson*, K. Wakabayashi*, L. Krulich*, P. Illner*, C.P. Fawcett* and S.M. McCann. Dept. of Physiol., Univ. of Texas Southwestern Med. Sch., Dallas, Texas.

The effect of repeated intravenous injections of crude rat stalk-median eminence (SME) extract (1 SME/injection) on serum FSH, LH and prolactin was evaluated. A control sample of serum was obtained from etherized rats immediately prior to the iv injection of SME extract. Another blood sample was collected 8 min later. Immediately thereafter a 0.1 ml/min infusion of crude pituitary extract was continued for ½ hr at concentrations varying from 200-1200 ng LH/ml. The initial procedure of sampling and injection of SME was then repeated 1½ and 3½ hr after pituitary infusion. A significant decrease in prolactin levels occurred after each injection with hypothalamic extract in normals ($P<.05$, $P<.005$, $P<.02$) while the results in castrates were equivocal. There was a significant increase in LH in both normal ($P<.001$ after first and third injection) and castrates ($P<.01$, $P<.005$, $P<.02$). When the plasma level of LH was increased by approximately 25-40 ng/ml by the pituitary extract infusion, the LH response was ameliorated or abolished in normal animals but not in castrates. Prolactin levels were only slightly raised by the infusion and no effect was observed on the response to SME. Cortex extract at the same dose by weight of tissue or saline failed to modify LH or prolactin levels significantly. SME extract produced little or no change in serum FSH . It is concluded that hypothalamic extract can rapdily increase serum LH and decrease serum prolactin and that the LH response is reduced in intact males by infusion of pituitary extract. (supported by grants from NIH, Ford Foundation, and Texas Population Crisis Foundation).

INDIRECT MECHANISM OF ANTINATRIURESIS BY BETA ADRENERGIC STIMULATION. William H. Waugh. Dept. Med., Univ. of Ky. Col. of Med., Lexington, Ky.

Classical beta adrenergic stimulating agents (e.g. isoproterenol and metaproterenol) are known to induce antinatriuresis in whole animals, although the mechanism is unclear (e.g. Heidenreich et al. Arch. Pharmak. Exptl. Pathol. 263:439, 1969) and it can occur in the chronically denervated kidney (Botting et al. Arch. Internat. Physiol. Biochim. 69:203, 1961). To study the mechanism, saline diuresis was sustained in DOCA-primed anesthetized dogs by constant iv infusions of isotonic saline-1.5% mannitol solution, at 0.4 ml/kg/min (after 60 ml/kg as prime). Then, dl-isoproterenol, at 0.08-0.10 ug/kg/min, was infused iv for 40 min. In innervated kidneys, isoproterenol reversed sodium diuresis by about 80%, with average reductions in C_{Cr} and C_{PAH} of less than 15% and in mean arterial pressure of less than 10%; in contralateral acutely denervated kidneys, sodium excretion was reduced by about 37%, with no significant change in C_{Cr} and C_{PAH}. In dogs with prior unilateral nephrectomy and a similar degree of saline diuresis in the remaining acutely denervated kidney, identical isoproterenol infusions reduced sodium excretion by less than 25%, despite similar average reductions in mean arterial pressure of less than 10% and similar increases in heart rate. It, therefore, appears that slightly hypotensive infusions of isoproterenol normally provoke antinatriuresis during volume expansion mainly by reflexly induced renal sympathetic tone and by release of an agent from the innervated kidney, which causes antinatriuresis even in the acutely denervated kidney. The residual mild antinatriuretic effect of isoproterenol, seen in the denervated kidney after contralateral nephrectomy, likely results from reduced renal perfusion pressure and/or circulating alpha adrenergic hormone. (Supported by NIH grant HE 06092 and Ky. Heart Assn. Chair Cardiovascular Res.)

REGIONAL REDISTRIBUTION OF BLOOD FLOW IN LIZARDS DURING HEATING. W.W. Weathers*, L.A. Baker* and F.N. White. Department of Physiology, UCLA School of Medicine, Los Angeles, California.

The capacity of some lizards to alter their thermal conductance has been related to increases in cutaneous blood flow during heating as determined by the clearance rate of ^{133}Xe (Morgareidge and White, 1969. Nature 223:587). Iguana iguana and Tupinambis nigropunctatus were used to determine the effect of heating on skin and muscle blood flow and peripheral resistance of the posterior portion of the body. Muscle and skin blood flow in the hind legs and tail was estimated by the ^{133}Xe clearance technique. Posterior peripheral resistance was calculated from dorsal aorta blood flow ($\dot{Q}_{da}$), measured with a chronically implanted electromagnetic flow probe, and the difference between femoral arterial and venous pressures. Heating the hind legs and tail with an incandescent heat lamp resulted in an increase in $\dot{Q}_{da}$ and skin blood flow while muscle blood flow decreased or remained unchanged and posterior peripheral resistance decreased. Increases in $\dot{Q}_{da}$ and skin blood flow occurred before any change in deep body temperature was observed. After systemic infusion of a dose of dibenzyline (4.5 mg/kg) which blocked the pressor response to norepinephrine, muscle blood flow increased in response to heating. We conclude that in response to heating a sympathetically mediated vasoconstriction occurs in muscle which results in a preferential shunting of the observed increase in $\dot{Q}_{da}$ to the skin. We postulate that this is a mechanism for increasing the rate of heat gain. (Supported by USPHS grant HE 5696 and NSF grant GB-8523)

AFFERENT NEURAL ACTIVITY OF CARDIOVASCULAR ORIGIN IN THE CANINE ANTERIOR AND POSTERIOR ANSAE SUBCLAVIA. J. S. Wechsler*, J. R. Dorchak* and J. P. Kampine* (intr. by J.J. Smith). Departments of Physiology, Anesthesiology and Cardiology, Marquette School of Medicine, Milwaukee, Wis.

Brown (J. Physiol. 1967, 190, pp.35-53) demonstrated the presence of A-delta afferent fibers in the cardiac sympathetic fibers of the cat which were involved in the response to myocardial ischemia. Mongrel dogs were anesthetized with Sodium Pentobarbital (30 mg/kg), intubated, placed on positive pressure respiration by means of a Harvard pump connected to an oxygen line and a left lateral thoracotomy was performed with the removal of the second, third, and fourth ribs. Blood from the left femoral artery was pumped by a Sarns roller pump into a catheter placed in the left common coronary artery after first passing through a heat exchanger maintained at 37°C. Placement of the left coronary arterial catheter was verified during the course of the experiment as well as at the conclusion of the experiment. Impulse traffic was recorded by means of silver- silver chloride wick electrodes. The output of the electrodes, one on the nerve trunk and one placed on or near the sheath of the nerve was amplified by a Tektronix 3A3 differential amplifier and displayed on a Tektronix 564 cathode ray oscilloscope. Left ventricular pressure was simultaneously recorded by a Statham P23dB pressure transducer and displayed on the oscilloscope screen. The oscilloscope was triggered by left ventricular pressure and a Polaroid camera was used to photograph the observed responses. The animal was placed in a copper screen shielded cage which was grounded. Increases in impulse traffic from the anterior and posterior ansaw subclavia were recorded with increases in coronary flow and perfusion pressure. (Supported in part by the Wisconsin Heart Association).

THE DISTRIBUTION AND REGULATION OF SODIUM IONS IN THE VENTRAL NERVE CORD OF PERIPLANETA AMERICANA. D.J. Weidler and P.J. Gardner (intr. by A.L. Bennett), Departments of Physiology and Anatomy, University of Nebraska College of Medicine, Omaha, Nebraska.

A previously reported study on Periplaneta nerve cord with radiosodium by another investigator indicated that there were two efflux components, a fast one thought to be extracellular in origin and a slow one of intracellular origin. On the basis of anatomical and electrophysiological studies, this description appears inadequate. In the present study, compartmental analysis of radiosodium movement was correlated with anatomical studies. Desaturation of nerve cords saturated with sodium-22 yielded the following six components characterized by their respective half-times: first component, 6 sec; second, 17 sec; third, 85 sec; fourth, 30.6 min; fifth, 1.46 hr; sixth, 23.8 hr. The size of the fourth component is significantly larger in females than in males. Since the fat-body is correspondingly larger in females than males, it follows that the fourth component originates in the fat-body. Furthermore, the fifth component is greatly reduced in the presence of 5 mM sodium azide. Since a potential difference of 15 mV across the neural sheath has been reported, we hypothesize that the fifth component originates in the extracellular portion of the neural space (i.e., within the neural sheath) and that sodium ions are actively absorbed by the neural sheath. Given the probable origins of two components, the probable sources of the other components is as follows: first, second and third, series of exponentials of diffusion from the nerve cord surface; sixth, intracellular space of neurons and glia. Calculations of sodium concentrations based on anatomical compartment sizes determined from photomicrographs are consistent with this hypothesis.

THE EFFECTS OF CARBONIC ANHYDRASE INHIBITION ON PERFORMANCE, BLOOD GASES AND ACID BASE BALANCE. Stephen A. Weinstein and Z. Annau, * Dept. of Environmental Medicine, The Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Maryland.

The investigations which we report in this paper were undertaken to obtain simultaneous behavioral and physiological measurements in a single species in 8% oxygen with and without carbonic anhydrase inhibition. Maren and Travis described a new carbonic anhydrase inhibitor (Benzolamide), which, in low doses or one hour after a higher dose has a selective renal action. Eight rats, with implanted hypothalamic electrodes and with indwelling catheters in the abdominal aorta, were trained to self-stimulate. After stable behavioral and physiological base lines were obtained, the rats were exposed to 8% oxygen for 110 minutes and continuous measures of self-stimulation, pH, pCO_2 and pO_2 were taken. Performance, as measured by self-stimulation rate was improved in those rats receiving 20 mg/kg i.p. benzolamide one hour prior to testing. There was a decreased pH in the drug recipients, but no increase in pO_2 or pCO_2. This supports our earlier findings which indicated that C.A. inhibitions sufficient to act upon renal mechanisms, but not severe enough to cause erythrocytic inhibition is capable of attenuating the deleterious effects of hypoxia upon neural function.

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TIME AND SPACE CORRELATIONS OF HUMAN SMALL BOWEL CONTRACTIONS: RESULTS OF COMPUTER ANALYSIS. N. W. Weisbrodt*, R. B. Singerman*, E. O. Macagno*, J. R. Glover*, and J. Christensen. Dept. of Int. Med., Coll. of Med., and the Hydraulics Inst., Coll. of Engineering, U. of Iowa, Iowa City, Iowa and the Iowa City VAH.

Miniature-balloon manometric records, taken from 4 loci 1 cm. apart in the human distal duodenum after feeding, were analyzed by computer for temporal and spatial relationships of contractions. For each transducer output, analysis of the frequency distribution of times between contractions and the joint frequency distribution of contractions and times between contractions showed the following temporal relationships: 1) the frequency distribution of times between contractions has repetitive peaks. This suggests that each intercontractile period is a multiple of one slow wave cycle. One slow wave cycle without contraction is called a rest cycle (RC); 2) the frequency distribution of contractions and RC at one locus is extremely skewed: contractions and rest cycles occur most often in groups of one to three. 3) The joint frequency distribution of contractions and RC shows that most contractions occur in groups of one to three followed by one to three RC. 4) the locus of the gut monitored by a single tube is active 20-40% of the recorded time. Study of the four loci one cm. apart yielded the following conclusions about spatial relationships: 1) contraction length may be as small as one cm; 2) about 20% of contractions at any one locus are part of a group occurring in a proximal-to-distal sequence with an apparent velocity of less than 1.25 cm./sec., over three or more adjacent loci. The remainder of the contractions appear to be random; 3) the sequential contractions often occur over all four loci with a proximal-to-distal phase lag of about three seconds.

GAS EXCHANGE WHEN ONE LUNG REGION INSPIRES FROM ANOTHER. John B. West. Departments of Medicine and Bioengineering, University of California, San Diego, La Jolla, California.

Pulmonary gas exchange has been studied in computer models of the lung containing compartments which received part or all of their inspired gas from adjacent compartments. Such behavior is likely to occur with collateral ventilation, or when lung units located distally on the airways inspire gas from alveoli more proximally situated (series inequality of ventilation). It was found that a lung region which inspired gas from an adjacent region ("parasitic lung") usually had a high alveolar P_{CO_2} and a grossly impaired CO_2 output. By contrast, its O_2 uptake was much less affected, and its respiratory exchange ratio was therefore low. The gas exchange of a whole lung containing a parasitic compartment generally had its CO_2 output reduced more than its O_2 uptake except when the ventilation-perfusion ratio of the parasitic compartment was very low. In models in which the O_2 and CO_2 transfer were held constant, increasing series inequality of ventilation caused a rapid rise in arterial P_{CO_2} but a slow fall in mixed venous P The arterial P_{O_2} rose quickly when overall ventilation was increased. When the inspired oxygen was raised, alveolar-arterial P_{O_2} differences were generally small. This behavior differed markedly from that found with parallel inequality of ventilation and a log normal distribution of ventilation-perfusion ratios.

SEASONAL CHANGES IN HEPATIC RIBOSOME AGGREGATION AND PROTEIN SYNTHESIS IN THE HIBERNATOR. B. K. Whitten, M. A. Posiviata* and W. D. Bowers*. U. S. Army Research Institute of Environmental Medicine, Kansas St., Natick, MA 01760.

Hibernating mammals undergo prolonged periods of winter hypothermia and fasting during which time they lose weight. In the spring and summer they rapidly gain weight. Hepatic protein synthesis is apparently decreased during hibernation (Am.J.Physiol. 214:1360-62, 1968). To substantiate and explain this finding, hepatic ribosomes were isolated from hibernating and normothermic thirteen-lined and golden-mantled ground squirrels. Seasonal variations in hepatic ribosome aggregation were investigated by sucrose density gradient and electron microscopic techniques. Changes in ribosome aggregation were correlated with protein synthetic capacity using a highly purified in vitro preparation. Hepatic ribosomes isolated from spring, summer or fall normothermic animals were characterized by a large number of high molecular weight aggregates and a rapid rate of protein synthesis. Ribosomes from winter normothermic animals had a greater percentage of lower molecular weight aggregates and a decreased rate of protein synthesis. Ribosomes isolated from winter hibernating animals had few aggregates, a majority of monomer or single ribosome units and a very low rate of protein synthesis. Crossing experiments with normal rat preparations indicated that the decreased protein synthetic capacity in hibernating animals was primarily due to ribosome disaggregation.

RESPONSES OF THE CALIFORNIA SEA LION TO DIFFERENT ENVIRONMENTAL TEMPERATURES. G.C. Whittow, D. Matsuura*, and Y.C. Lin*. Department of Physiology, School of Medicine, University of Hawaii, Honolulu, Hawaii.

Although the California Sea Lion encounters high air temperatures under natural conditions, it is not known whether it is physiologically equipped to deal with these, or whether it relies entirely on behavioral mechanisms of temperature regulation. In order to throw some light on this problem, three sea lions were exposed to air temperatures of 36°C, 30°C, 18°C and 10°C. None of the animals was able to achieve thermal equilibrium at an air temperature of 36°C or 30°C, the rectal temperature reaching 40°C after an exposure of 140 min to the former temperature. Skin temperature changes over the range of environmental temperature studied, suggested that both the flippers and the skin on the trunk participate actively in the regulation of heat loss. There was little evidence that either respiratory or cutaneous evaporative cooling mechanisms were important in the regulation of body temperature. Sweating could not be detected by the starch-iodide technique and the maximal respiratory rate recorded was 11 resp./min. One animal shivered at an air temperature of 9°C, when its rectal temperature was 36.7°C and the skin temperature on the trunk was 19.9°C. (Supported by NSF Grant GB 8393 and the U.S. Naval Undersea Research and Development Center, Hawaii.)

CARDIOVASCULAR FUNCTION IN RESPONSE TO SELECTIVE BRAIN HYPOTHERMIA IN THE DOG. A.J. Whitty,Ph.D.,* R. Blau,M.D.* M. Freedman, M.D.,* and P.P. Foa, M.D., Ph.D. Dept. of Research, Sinai Hosp. Detroit, Michigan

Selective brain hypothermia by perfusion of the ventriculocisternal system did not result in the hypotensive levels that have been reported when other methods of hypothermia are used. To determine what cardiovascular changes occurred, cardiac output by dye dilution and mean transit time was measured in 1) normothermia, 2) hypothermia, 3) hypothermia associated with ligation of the brachiocephalic and left subclavian arteries at the arch of the aorta, and 4) after hypothermia followed by rewarming. Lifting ligatures were positioned one week prior to the experiment. Measurements of mean blood pressure, pulse rate, cortical and rectal temperatures and ECG were recorded. Cardiac output, central blood volume, and total peripheral resistance were calculated. In the ligated dogs the following results were obtained:

	Control	Hypothermia	Ligated Hypothermia	Rewarmed
Mean C.O. L/min	1.93 (11)	1.43 (10)	1.55 (10)	1.56 (11)
Mean Diff.L/min		0.50	0.38	0.37
S.E. of Diff.		0.36	0.32	0.23
'T' Value		1.396	1.191	1.635

No difficulty was experienced in maintaining adequate peripheral circulation and adequate cardiac output when cortical temperatures were kept at 20-23°C. for one hour or more. Aided by General Support Grant FR-05641, N.I.H.

EFFECT OF SEROTONIN, MORPHINE, OUABAIN, AND GANGLIONIC STIMULANTS ON THE CAT COLON SLOW WAVE. Martin Wienbeck* and James Christensen, Gastrointestinal Research Lab., Univ. of Iowa College of Medicine and Veterans Administration Hosp., Iowa City, Iowa 52240

Cat colon circular muscle shows rhythmic depolarizations (slow waves, SW). We studied drug effects on slow wave rate (SWR) and duration (SWD) in whole colon everted over a mandrel, in Krebs' solution aerated with carbogen at 36-37°C. Glass pore electrodes (pore=50 μ) were put on exposed circular muscle of ascending colon, right flexure, mid transverse, left flexure, mid descending, and sigmoid colon. Mean SWR were (from proximal to distal): 2.8 ± 1.0, 3.2 ± 1.1, 3.8 ± 1.0, 5.1 ± 1.6, 5.5 ± 1.1, 5.2 ± 0.7 (SD) cycles/min. Mean SWD were: 5.9 ± 4.5, 7.4 ± 5.3, 6.9 ± 4.5, 5.9 ± 2.1, 4.9 ± 1.2, 4.7 ± 1.0 (SD) sec. Serotonin, morphine and ouabain had little effect on SWR. They all reduced SWD and increased spike activity. The excitatory effect on spikes was most pronounced with serotonin. Ouabain 3 μM and higher reduced SW amplitude and finally eliminated SW. Nicotine and dimethylphenylpiperazinium did not change SWR or SWD. SWD is labile and affected by a variety of drugs with action on smooth muscle. SWR is more stable and less affected. Ganglionic stimulants do not interfere with SW mechanism.

ASSAY OF LUTEINIZING HORMONE IN ANIMALS TREATED WITH ANTI-OVULATORY SUBSTANCES. Donald L. Wilbur (intr. by Wilburn J. Eversole) Indiana State University, Terre Haute, Indiana 47809.

The purpose of this study was to determine the effects of aminoglutethimide (AG), estrone, and progesterone on blood plasma and anterior pituitary concentrations of luteinizing hormone (LH) activity in mature female rats. Each experimental animal in group 1 received 50 mg/kg AG in 0.5 ml of buffered saline. Each animal in group 2 was injected with 1 μg of estrone in sesame oil per 100 gm of body weight (BW), and each rat in group 3 was administered 1 mg of progesterone in oil per 100 gm BW. The following morning vaginal smears were taken immediately before sacrifice. The effects of aminoglutethimide on blood plasma and anterior pituitary levels of LH activity were determined by the ovarian ascorbic acid depletion bioassay of Parlow. Blood plasma was concentrated by cold acetone fractionation. Other investigations included comparisons of progesterone and estrone effects upon LH activity in the blood plasma and anterior pituitary. The effects of AG, estrone, and progesterone upon the estrus smear were noted. Animals receiving progesterone showed the highest pituitary LH levels and the lowest plasma LH levels. Aminoglutethimide and estrone acted similarly upon the LH activity levels of the pituitary and plasma. Animals injected with AG or estrone had elevated pituitary LH activity and lower plasma LH activity than controls. All three substances acted similarly upon the estrus smear.

EFFECT OF AMILORIDE AND FUROSEMIDE ON Na REABSORPTION IN PROXIMAL TUBULES IN RATS. T. W. Wilczewski*, G. Carrasquer and D. R. Gelbart*. University of Louisville School of Medicine, Louisville, Kentucky.

Experiments were performed to test the effect of amiloride and furosemide on Na reabsorption in the proximal tubule. Sprague-Dawley rats were infused with saline or Ringer's solution at a rate of 6 ml/hr or higher, depending on the urine flow. Proximal tubules were perfused with rat Ringer's containing ^{3}H-inulin and ^{22}Na, following the technique of Sonnenberg and Deetjen (Pfluger's Arch 278:669, 1964). Fourteen tubules were perfused as control; 12 tubules following i.v. injection of 10 mg/kg of amiloride; and 6 tubules following i.v. injection of 100 mg/kg of furosemide. The log. of the ratio (collected fluid)/(perfused fluid) concentration was plotted versus length of perfused tubule. The calculated slopes of the regression lines were: 7.25×10^{-2}; 8.51×10^{-2} and -5×10^{-2} mm^{-1} for ^{3}H-inulin in control, in amiloride, and in furosemide treated rats respectively; and -29.8×10^{-2}, -21.3×10^{-2} and -11.9×10^{-2} mm^{-1} for ^{22}Na in control, in amiloride, and in furosemide treated rats respectively. The unidirectional permeability to ^{22}Na was calculated taking into account the change in inulin concentration, and the values were: 61.1×10^{-4}, 44.7×10^{-4} and 43.6×10^{-4} mm/sec in control, in amiloride, and in furosemide treated rats respectively. Amiloride, apparently, did not affect the net reabsorption of sodium as suggested by the fact that its effect on inulin concentration was not different from control; on the other hand it decreased the unidirectional flux of sodium perhaps due to a decrease in the passive permeability. Furosemide decreased both the net and the unidirectional flux of sodium, apparently affecting both the active and passive components of sodium transport. Supported by USPHS.

THE PERFORMANCE OF ISOLATED HEARTS MAINTAINED FOR PROLONGED PERIODS IN VITRO. K. Wildenthal (intr. by J. H. Mitchell). Univ. of Texas SW Med. Sch., Dallas, Texas.

To provide a system in which functioning hearts could be studied in vitro for longer than is possible with conventional methods, a technique has been developed for maintaining mouse hearts in organ culture. Under appropriate conditions the hearts survived and beat for a week in chemically-defined "Medium 199" and for 2-4 weeks when the medium was supplemented with serum, insulin and cortisol. Acetylcholine caused bradycardia and norepinephrine caused tachycardia in all hearts, at all stages of culture. In contrast, tyramine caused tachycardia in hearts maintained in culture for less than a day, but had no effect on hearts cultured for longer than two days. Low doses of ouabain had no effect on cardiac rate, but they increased the vigor of contraction; high doses (10^{-4} M) often induced arrhythmias, including atrial flutter or fibrillation and ventricular bigeminy. The results demonstrate that isolated hearts function in organ culture for prolonged periods and retain normal responsiveness to a variety of agents that affect the myocardial cells directly; responsiveness to indirectly-acting sympathomimetic agents, however, are rapidly lost in culture, presumably as a consequence of cardiac denervation and depletion of endogenous norepinephrine. (Supported by USPHS HE31967 and the Dallas Heart Asso.)

THE VISUALIZATION OF PROSTHETIC SURFACES ENDOTHELIZED WITH AORTIC INTIMAL CELLS[1]. J.P.G. Williams*, C.J. Pennington*, and J.B. Boatman. Battelle Memorial Institute, Columbus Laboratories, Columbus, Ohio.

Lining of an arterial vascular prosthesis by the body's own cells may improve the surface nonthrombogenicity. To achieve this objective of cell coated prosthetic devices, a number of surface configurations have been derived to facilitate cellular adhesion. The surface structure thought to be most advantageous is composed of many polypropylene fibers forming a three dimensional lattice ranging between 10 and 50μ in depth. The fibers are coated with 200 Å layer of Parylene® (Union Carbide). The cells thus are only in contact with Parylene®. Intimal cells obtained from the thoracic aorta of sheep have been grown on the surfaces. The surfaces and the adherent cells have been examined by light microscopy and by both scanning and conventional transmission electron microscopy. The cells grow out from multiple points of attachment to the surface forming individual plaques. When cells from different plaques meet they do not overgrow one another and an extensive covering can be obtained. Scanning electron microscope examination of cell attachment to these complex surfaces has indicated that the cells are extremely flattened and demonstrate filamentous projections. The transmission electron microscope also indicates that the cells are flattened. Microvilli can be seen on the surface and while there appear to be points of attachment to the fibers, the presence of certain electron dense structures within some cells suggests the possibility that the cells envelop the fibers.

1. This research has been supported by Contract No. PH 43-67-1404 from the Artificial Heart Program, National Institutes of Health.

INTRAVENTRICULAR PROPAGATION TIME: EFFECTS OF EPINEPHRINE, K^+ AND PROPRANOLOL. R. L. Williams*, R. L. Vick, D. A. Riopel*, and D. G. McNamara.* Depts. of Physiology and Pediatrics, Baylor College of Medicine, and Dept. of Pediatric Cardiology, Texas Children's Hospital, Houston, Texas.

Several investigators have reported decreased intraventricular propagation time (↓T) in the dog when plasma [K] is elevated moderately, and the ↓T caused by epinephrine (E) is attributed to hyperkalemia (↑[K]). Recent studies have shown that the ↑[K] caused by E is transient, and that ↓[K] is the persistent effect. When E is administered by continuous infusion, arterial [K] reaches a peak in 3-4 minutes, returns to control by 10-15 minutes, falls and remains below control for the duration of the infusion. We have used this technique to provide a more rigorous and quantitative test of the role of plasma [K] in the effects of E on T. The SA node was crushed and the heart was driven in open-chest, anesthetized dogs. Two T's were measured, T_1 from the appearance of the stimulus artifact to the electrogram recorded from near the stimulus (conus) and T_2, from the stimulus artifact to the electrogram from a distal electrode. Arterial [K] was altered biphasically by infusing E, 2 μg/kg/min, and increased by infusing KCl alone, or concurrently with E. Change in both T_1 and T_2 correlated inversely with change in [K]. These data support the hypothesis that E alters T indirectly through changes in arterial plasma [K]. In addition, E was infused after the administration of propranolol, 2 mg/kg, causing only a small, sustained ↑[K] and a small, sustained ↑T. These results indicate that the effects of E on [K] are mediated at least in part through stimulation of β-adrenergic receptors, and that propranolol directly or indirectly nullifies the usual effects of increased plasma [K] on intraventricular propagation time. (Supported by USPHS T12-HE 05752, HE 08372, and 5-K3-HE 05421).

RENAL TUBULAR TRANSPORT OF TRYPTOPHAN CONGENERS IN DOG. W.M. Williams* and K.C. Huang. Univ. Louisville, School of Med., Louisville, Ky.40202

Studies with an isolated renal tubules and cells preparation have shown that L-tryptophan and its N-acetyl derivative are accumulated against a concentration gradient, but its D-isomer is not. L-Tryptophan uptake was blocked both by L-phenylalanine and DNP. L-Tryptophan efflux from proloaded tubules and cells was temperature dependent, enhanced by L-phenylalanine and relatively unaffected by DNP. Clearance experiments were performed in dogs to determine the renal handling of these amino acids in vivo. The compounds were administered to pentobarbitalized dogs in a priming dose and sustaining infusion. Negative T values were obtained with L-tryptophan, indicating a net tubular reabsorption, while D-tryptophan and N-acetyl-L-tryptophan gave positive values, indicating net secretion. The reabsorption of L-tryptophan was partially blocked by intrarenal arterially infused L-phenylalanine but was unaffected by DNP at a dose which decreased the Tm of p-aminohippuric acid. Stop-flow experiments revealed that L-tryptophan is both reabsorbed and secreted by the proximal tubules, with the former process predominating. The ratio $(U/P_{L\text{-try}})/(U/P_{in})$ was below 0.3 in all samples but increased by almost 100% in the portion corresponding to the proximal tubule. The secretory component of L-tryptophan transport was completely blocked by probenecid. In studies with the same technique D-tryptophan and N-acetyl-L-tryptophan gave ratios above two, suggesting secretion. The secretion of these compounds was completely blocked by probenecid. It was concluded that the three tryptophan congeners are transported in the direction of secretion by an organic acid secretory mechanism and that L-tryptophan is reabsorbed by a mechanism shared by L-phenylalanine. (Supported by grants NIAMD AM2217-12 and NSF GB-8435).

CHANGES IN TISSUE K DURING HIBERNATION. J. S. Willis. Department of Physiology and Biophysics, University of Illinois, Urbana, Ill.

Despite the fact that maintenance of high cellular K and low Na is an essential requirement for survival at the low body temperature (5°C) experienced by hibernating mammals, few studies have attempted to determine K concentrations of cells during hibernation. Two independent but cursory studies have shown that there is little if any decrease in tissue K of a limited number of tissues during hibernation. One of the studies reported that kidney cortical K rose spectacularly in hibernation of hamsters and ground squirrels. A more recent investigation of red blood cells, however, indicated that despite a clear cold adaptation, red blood cells of ground squirrels do lose K gradually over several days of hibernation, but are able to reaccumulate it upon arousal. In the present study a wider variety of tissues were selected for analysis in hibernating hamsters and ground squirrels. Four new results were obtained: (1) Leg skeletal muscle (in contrast to diaphragm) loses K during hibernation in both species; (2) K content of liver of ground squirrel increases during hibernation (3) As observed before, K in kidney cortex increases in both species, but in addition the increase in ground squirrels was observed to be correlated with days in hibernation; and (4) The K content of kidney cortex declines to nearly normal within a few hours after the initiation of arousal. These results seem to show that some tissues, notably kidney cortex, may serve as "sinks" for K lost from less perfectly adapted cells such as erythrocytes and some skeletal muscle fibers. This interpretation in turn suggests the possibility that progressive loss of K may limit the period of a single "bout" of hibernation and may also serve as a trigger for arousal. (Supported by NIH Grant GM11494).

PROLONGED BED-REST IN HEALTHY HUMAN SUBJECTS: CIRCADIAN FREQUENCIES OF HEART RATE AND BODY TEMPERATURE. C.M. Winget, S.E. Cronin*, P.C. Rambaut*, and P.B. Mack*. Environmental Biology Division, Ames Research Center, NASA, Moffett Field, California, Preventive Medicine Division, Manned Spacecraft Center, NASA, Houston, Texas, and Texas Woman's University, Denton, Texas.

The synchronization of physiologic rhythms may depend upon several environmental factors. Although light is usually accepted as the primary Zeitgeber, the effect of posture and exercise on rhythm synchronization was investigated. Eight healthy male subjects were maintained in a defined environment with a photoperiod of 14L:10D for a 6 day ambulatory, pre-bed-rest equilibration period, 56 days of bed-rest, and a 10 day post-bed-rest recovery period. Four of the subjects exercised during bed-rest. Body temperature (BT) data were obtained using ear thermistors (Yellow Spring, Model 402) and heart rate (HR) was measured from pulse rates and by Beckman EKG sensors connected to a cardiotachometer. During bed-rest mean HR increased while BT decreased. These changes were less marked in the exercised group. Following the recovery period mean HR continued to rise while mean BT continued to be depressed. HR rhythms remained stable throughout bed-rest (peak~1600 h.). During the equilibration period BT rhythms showed little variation between subjects (peak~1800 h.). During bed-rest more variation was noted: 3 subjects continued to exhibit stable rhythms; in 3 subjects aberrant rhythms were recorded periodically; 1 subject exhibited a 180° phase shift while the last showed a linear shift in phase. An "uncoupling" between HR and BT was thus noted for 5 of the 8 subjects. The results indicate that the mechanisms regulating the circadian rhythmicity of the cardiovascular system may be less susceptible to postural changes than those affecting general metabolism.

INCREASED RBC IRON UPTAKE AFTER INTRASPLENIC INJECTION OF N^6-2'-O-DIBUTYRYL 3'5'-CYCLIC ADENOSINE MONOPHOSPHATE (DCAMP). J. Winkert and C. Birchette* Meharry Med. Col., Nashville, Tenn.

DCAMP when administered by i.v. and s.c. routes was shown previously to stimulate iron incorporation into erythrocytes of post-hypoxic mice.(Winkert and Birchette, Fed. Proc. 29: 843, 1970). The present study was undertaken to determine the effectiveness of DCAMP when injected directly into an erythropoietic organ. Twelve mature female CF1 mice were exposed to altitudes ranging from 18,000 to 23,500 ft for 7 hrs. daily over a 30 day period. On the 2nd day following the last exposure the mice were anesthetized with nembutal, shaved over the abdomen, and scrubbed with zephiran. Each spleen was extruded through a left abdominal incision, clamped off from the circulation at the hilus and infiltrated through a 30 gauge needle with 0.1 ml 0.16M NaCl or 1.25 mg DCAMP in 0.1 ml 0.16M NaCl. The clamp was removed 2 minutes after it was applied and the circulation was restored. The incisions were closed with wound clips. On the 4th day 0.02 microcuries Fe^{59} citrate/g was given i.v. and the % RBC uptake determined 20 hrs. later. RBC Fe^{59} uptake in 5 saline injected mice was 4.2 $\pm$ 0.17 % (Mean $\pm$ S.E.) and in 7 DCAMP mice was 8.9 $\pm$ 1.4 %. The difference was significant (P = 0.02). Terminal hematocrits were 58.1 $\pm$ 1.7 in the saline group and 55.1 $\pm$ 2.4 in the DCAMP group. (No significant difference). Thus DCAMP given intrasplenically as well as parenterally augments iron uptake by post-hypoxic mouse erythrocytes. Supported by NIH grants 5R01CA02080 and 5S01FR05422.

Iron Movement into Rabbit Reticulocytes: Effects of Ethacrynic Acid and Cysteine. W. C. Wise. Department of Physiology, Medical University of South Carolina, Charleston, S. C., 29401.

Recent reports have indicated the possible involvement of sulf - hydral groups in iron movement into the maturing red blood cell. The effects of the sulfhydral inhibitor, ethacrynic acid, on iron movement are under investigation. Reticulocytes obtained from phenylhydrazine treated rabbits were incubated at 37°C in MEM with added serum and $^{59}FeCl_3$, or were incubated in a medium containing Na^+, K^+, Mg^{++}, phosphate buffers, glucose, serum and $^{59}FeCl_3$. The iron and serum were mixed first so that the iron was bound to the serum transferrin. Ethacrynic acid was found to inhibit iron uptake in rabbit reticulocytes at concentrations of 10^{-5} moles/liter and higher. The concentration which produces 50% inhibition in uptake after 2 hours was found to be 1.5×10^{-4} moles/liter. Ethacrynic acid seems to affect the movement of iron from the media to the cell membrane more than from the cell membrane to the cell interior. Analogs of ethacrynic acid which have less sulfhydral binding power have less effect on iron uptake. Ethacrynic acid's inhibition can be partially removed if cells are incubated with cysteine after pre-incubation with ethacrynic acid. Cysteine at 10^{-3} moles/liter stimulates a four-fold increase in iron uptake by the cell stroma. This work supports the hypothesis that iron movement on to the cell membrane involves sulfhydral group binding. (Supported by National Institutes of Health GRSG-RR05420).

SPONTANEOUS REWARMING AFTER COLD WATER IMMERSION. J. M. Witherspoon* and R.F. Goldman. US Army Rsch Inst of Env Med., Natick, MA 01760

Rewarming aspects of human thermoregulation were studied following acute cold water immersion. Male test subjects were exposed to 20°C unstirred water for 15 minutes and then removed, to "rewarm" in air at 25°C. Thin subjects, i.e. defined as having less than 10% body fat, have mean surface temperatures (10 sites) which are warmer than those of normal subjects in cold water and which increase more rapidly on coming out. The asymptotic mean surface temperature toward which an individual rewarms has an inverse linear relationship to his body fat thickness; the rate of rise has a direct linear relationship with his rate of oxygen consumption during immersion. Exercise immediately after cold water exposure tends to increase both the asymptotic level and the rate of rise of surface temperatures, whereas even mild hypoxia (12% O_2) appears to reduce the asymptote and the rate of rise. There is considerable variability in the regional pattern of rewarming. Distal surface areas exhibit a continuing fall in surface temperatures due to evaporative cooling, large surface to mass ratios and persisting vasoconstriction, while proximal surfaces, especially over the torso, show the most rapid rewarming. Deep body temperature also continues to fall after the end of immersion, due to redistribution of body heat. Thin subjects show the greatest fall in rectal temperature, in association with the most rapid surface rewarming. Moderate exercise usually prevents this rectal temperature fall when breathing room air but appears to be less effective in maintaining body temperature when breathing hypoxic gas mixtures. In the resting subject, hypoxia does not appear to alter the fall of deep body temperature during the rewarming period.

EFFECT OF HYPERTHERMIA ON RABBIT KIDNEY CELLS IN CULTURE. Alida Withrow* and Irving Gray. Dept. of Biology, Georgetown Univ., Washington, D.C.

Mammalian tissue culture cells show an altered growth rate at hyperthermic temperatures. An investigation of the monolayer growth of a rabbit kidney cell line, RK-1, has been performed at 37.5°C (control) and 41.5°C (hyperthermic). All cells were grown initially at the control temperature for 48 hours (zero time period). One-half of the cells were then moved to the hyperthermic temperature for 24, 48 or 72 hours. The growth of the cells was measured by determining the total protein of each culture. Growth of the hyperthermic cultures appears to remain static as the total protein per culture did not change significantly from that of zero time. During the same period, however, the control cultures continued to grow. At each time period, growth of the control cultures was significantly increased over the hyperthermic cultures. The hyperthermic cells were still viable. Cells maintained at 41.5°C for up to 5 days were returned to the control temperature and resumed growth. Protein turnover studies were performed using L-leucine-C^{14}. The hyperthermic cultures showed a slightly higher turnover rate at 24 hours, but by 72 hours this rate had fallen to half that of the control cultures ($p<0.02$). We are currently investigating nuclear ribonucleic acid turnover in order to determine the steps involved in the altered cell growth in hyperthermic cells. Preliminary results of RNA turnover studies have shown decreased turnover in both the hyperthermic and control cultures, with the hyperthermic cultures showing a slower turnover than the control. Electron microscopic examination of the cultured cells is underway.

NON-RECOVERY OF DEPRESSED PRESSURE-VOLUME CURVES WITH NEBULIZED LECITHIN. S. W. Woo*, U. Büch*, D. Gail*, and J. Hedley-Whyte. Department of Anaesthesia, Harvard Medical School and Beth Israel Hospital, Boston, Mass. 02215.

A rapid method for depressing deflation pressure-volume (PV) curves in excised dogs' lungs at 23 C is the use of halothane in addition to repeated hyperinflation (J.Appl.Physiol. 26:571,1969). We attempted to restore the PV relationships to control by administration of a fog of DL-dipalmitoyl lecithin (DPL) as suggested by Merrill et al (Science 164:1167,1969). Seven lungs were ventilated with 2.3% halothane in air to an end-inspiratory pressure 28-32 cm H_2O (V_T 59 ml/kg body wt (bw) f 20) for 30 min. 2% DPL was dispersed in 0.9% saline (Branson 75-W ultrasonic generator S-75, 20 kHz) before delivery to the lungs by an ultrasonic generator (Ultramist III, 800 kHz, Rahway, N.J.) for 30 min at V_T 56 ml/kg bw, f 20, each ventilation at 24 C. Percent maximum lung volume (MLV) was further depressed 15% by DPL ($P<.01$ at P_{TP} from 20-5 cm H_2O). To rule out halothane's role in our results, 4 other lungs were ventilated at 24 C with air (V_T 29 ml/kg bw) to an end-insp. pressure 20 cm H_2O for 2 hr followed by ventilation with DPL at 24 C for 2 hr with further depression (mean % MLV 79→73→68 at P_{TP} 10 cm H_2O, $P<.02$, $<.01$, $<.05$). Three more lungs were identically treated but at 37 C, % MLV, 84→77→69 at P_{TP} 10 cm H_2O (P=NS, $<.05$, $<.05$). Finally, 5 lungs were ventilated for 2 hr with O_2 at 37 C (V_T 51 ml/kg bw, end-insp. pressure 30 cm H_2O), followed by DPL for 90 min at 37 C but V_T half previous level and end-insp pressure 20 cm H_2O, end-exp. pressure 3 cm H_2O. Under these conditions the loops were not improved. We are unable to explain the discrepancy between our results and those of Shannon et al. (J.Appl.Physiol. 28:470,1970).

EFFECTS OF ATROPINE AND LOCAL ANESTHETICS ON MECHANICAL AND ELECTRICAL ACTIVITY OF CIRCULAR MUSCLE IN THE SMALL BOWEL OF CAT AND GUINEA PIG. J.D. Wood. Thompson Biological Lab., Williams College, Williamstown, Ma.

Circular muscle of jejunal segments from both species was mechanically and electrically quiescent when equilibrated at 37 C in Tyrode or Krebs solution. Procaine HCl (10^{-4} g/ml), lidocaine HCl ($5X10^{-5}$ g/ml) and l-hyoscyamine HBr ($8X10^{-5}$ g/ml) elicited electrical spikes and rhythmic, phasic contractions of the circular muscle. Electrical and mechanical activity which appeared after atropine was inhibited by trasnmural electrical stimulation. This inhibitory effect was not antagonized by guanethidine but was abolished by procaine and lidocaine. Transmural electrical stimulation of quiescent preparations by repeatitive 0.25 msec square pulses at 10 ma and 10/sec was followed by large amplitude contractions and electrical spikes. The duration of the poststimulus response and the number of electrical spikes of the response progressively increased as a function of increased concentration of l-hyoscyamine in the organ bath over a range of $5X10^{-6}$ to 10^{-4} g/ml. The latent period for the poststimulus response was unaffected by atropine. Procaine and lidocaine closely resembled atropine in effect on poststimulus response, except that the latent period for the response was prolonged by increased concentration. Excitation by atropine and local anesthetics may be attributed to either a direct action on the muscle or to an indirect effect from an action on intramural neurons. The second alternative will be considered. Atropine and local anesthetics might interrupt nervous transmission in spontaneously active, nonadrenergic, inhibitory pathways within Auerbach's plexus. Spontaneously active inhibitory innervation may hyperpolarize and clamp the muscle membrane in a continuous state of inhibition. Disinhibition would allow myogenic excitation and conduction.

RESPIRATORY SENSITIVITY TO CO_2 AT INCREASED AMBIENT PRESSURE. L.D.H. Wood* and A.C. Bryan, Canadian Forces Institute of Environmental Medicine, and Department of Anaesthesia, Toronto General Hospital, Toronto, Canada.

CO_2 retention in healthy men at increased ambient pressure has been reported previously. This suggests decreased sensitivity of the respiratory system to CO_2 which could be due to depression of the respiratory centre or to altered ventilatory mechanics. We measured CO_2 sensitivity at 1.0, 4.0 and 7.0 Ata in two ways: (1) the rebreathing CO_2 breath-hold time curve of Godfrey and Campbell (Quart.J. Exp. Physiol. 54:117, 1969); (2) the rebreathing CO_2 ventilatory response curve of Read (Aust. Ann.Med. 16:20, 1967). During the latter procedure, eosphageal pressure-volume loops were measured to derive inspiratory work. The slope of the ventilatory CO_2 response curve decreased as ambient pressure increased. For a given PCO_2, inspiratory work and tidal volume did not change with ambient pressure but respiratory frequency and air flow rates decreased at depth. There was no change in the slope of the breath-holding CO_2 response curve. We interpret the constant relationships of PCO_2 with inspiratory work and breath-hold time to show unaltered respiratory centre sensitivity to PCO_2. Because the same inspiratory work performs less ventilation at depth, the ventilatory response to CO_2 is diminished. These observations offer an explanation for the alveolar hypoventilation in healthy men at depth, which is consistent with similar observations reported previously in patients with obstructive lung disease at 1.0 Ata.

PATTERNS OF LOCALIZATION IN THE "MOTOR" CORTEX OF THE DOG. C. N. Woolsey, T. Gorska, A. Wetzel, T. C. Erickson and J. Allman. Laboratory of Neurophysiology, Medical School, Univ. of Wis., Madison, Wis., 53706.

The motor region of the cerebral cortex was first demonstrated by Fritsch and Hitzig in 1870 in the dog. In spite of the century which has passed since then, there does not yet exist an adequate map of the somatic motor region of the dog s cerebral cortex. In the present study we have undertaken to provide such a map in the figurine style "to which we have become accustomed." The region defined includes the "postcentral" sensory field, the "precentral" and "supplementary", motor areas and, to a lesser extent, the "second" somatic sensory-motor area. Sixty-cycle A.C. stimuli of controlled duration and amperage were applied monopolarly in 2 mm. steps over the exposed cortex of the dorsolateral and medial aspects of the hemisphere. Most of the cortex in the relevant fissures was also examined after exposing the bank to be stimulated by removing the opposing bank. In addition to mapping the normal brain, the effects on the map of chronic section of the medullary pyramid were also studied. Results will be presented as figurine maps and as stimulation threshold charts (Supported by NINDS grants 5-P01-NS-06225 (T.G.), 5-T01-NS-05326 (A.W.), Special Fellowship, 1-F11-NB-2064 (A.W.) and NSF predoctoral fellowship (J.A.).

MODULATION OF LUMBAR CORD REFLEX ACTIVITY BY AUDITORY STIMULATION IN THE DECEREBRATE AND CHLORALOSE ANESTHETIZED CAT. Charles G. Wright* and Charles D. Barnes, Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana 47401.

Previous investigation in this laboratory has shown auditory stimulation produces a pattern of facilitation followed by inhibition of the lumbar cord test monosynaptic reflex (MSR) in both decerebrate and chloralose anesthetized cats, and that pathways coursing in the medullary MLF are involved in mediating the spinal cord influence. Further study of the audio-spinal reflex mechanism in which brain stem and spinal cord responses were recorded to tonal stimuli before and after various surgical lesions has yielded additional data.

Although the latency of onset (20-30 msec) and pattern of MSR influence are similar in decerebrate and chloralose animals, the facilitation inhibition sequence is of longer duration in the chloralose preparation (about 100 msec in decerebrate vs. 400 msec or more with chloralose).

Brain stem lesions demonstrate that a medially descending pathway (probably medial reticulo-spinal) is largely responsible for production of the MSR inhibition. The facilitation of lumbar MSR is apparently mediated by pathways coursing in both the medial and lateral aspects of the lower medulla since MLF lesions eliminate the sound-evoked potential recorded in ventral roots and hindlimb nerves but fail to abolish the MSR facilitation.

A dorsal root potential (DRP) often showing two distinct peaks is associated with the lumbar cord audio-spinal influence. The DRP varies in latency between 20 and 40 msec and lasts 40 to 100 msec. It is reduced in amplitude but not abolished by medial medullary lesions. (Supported by NIH Grants NB 07834, NB 34986 and GM 36642)

OPPOSING EFFECTS OF CHRONIC ARTIFICIAL GRAVITY UPON URINE OUTPUT OF DEVELOPING SWISS WEBSTER MICE AT 4 AND 7 G'S. Charles C. Wunder, Frederic N. Meyer* and Mary E. Mason*. Univ. of Iowa, Iowa City, Iowa.

Our laboratory has previously established that, although various animals can survive and grow and mice can even breed throughout chronic centrifugation, growth and longevity of mice decreases progressively with g. In contrast to those progressive decrements, changes of urine flow with increasing g are more complex. No change was measureable at 2 G's, as tabulated (after 3, 11, and 24 days) in cumulative ml of urine/mouse minus baseline projection ± S.E. (# surviving mice/# original mice, # separate cage measurements). In contrast to the increased flow reported from this laboratory for 1.7-G and 3-G rats under similar conditions (Bengele, A.J.P. 216:659, 1969), 4-G mice demonstrated decreased flow. Flow increased at 7 G's. Although 1-G, pair-fed, control mice (pfc) exhibited 3 weeks of growth comparable to that of their high-g counterparts, the reduced food intake alone can not explain the urinary results, as pair-feeding resulted in greater flow than with either ad lib-feeding or high-g exposure. Baseline values (bl) are tabulated in ml/mouse/day ± S.E.

G's	RPM	bl	3 Days	11 Days	24 Days
1	0	2.1±.2	0.8±.6(47/48,4)	4±3(47/48,4)	14 (6/6,1)
2.2	44	1.9±.1	1.2±.3(90/90,7)	5±2(88/90,7)	20±21(11/12,2)
pfc	0	1.9	10.9 (18/18,1)	21 (17/18,1)	
4	44	2.1±.2	-1.3±.2(90/90,7)	-7±1(86/90,7)	-11±4 (9/12,2)
pfc	0	2.5±1.0	9.0±3.2(30/30,2)	16±10(28/30,2)	-22 (4/6,1)
7	57	1.8±.3	6.2±.1(12/12,2)		
pfc	0	1.8	13.4 (6/6,1)		

INCREASED LIVER ATPASE ACTIVITIES WITH HEMORRHAGIC SHOCK. M.A. Wurth*, M.M. Sayeed and A.E. Baue. Dept. of Surgery, Washington Univ. Sch. of Medicine and Jewish Hospital of St. Louis, Missouri, 63110.

An alteration of membrane transport functions is postulated as a possible cellular defect in hemorrhagic shock. However, there is no conclusive evidence to support this hypothesis. In this study we have determined (Na+K)-ATPase activity in hemorrhagic shock. This enzyme system has been implicated in active ion transport across cell membranes. Hemorrhagic shock was produced in Holtzman albino rats by bleeding animals through the femoral artery to a mean arterial pressure of 40 mm Hg for varying periods of time. Liver, lungs and brain were obtained from shocked and from unbled control animals and homogenized. The microsomal fraction, isolated from deoxycholate-treated homogenates by differential centrifugation, was the source of enzyme. Mg-ATPase and (Na+K)+Mg-ATPase were measured by titration of H^+ released during ATP hydrolysis using a pH-stat. (Na+K)-ATPase activity was calculated as the difference between (Na+K)+Mg-ATPase and Mg-ATPase. Increased ATPase activities were found in the livers of animals with prolonged shock. Mg-ATPase was 98.6 nmoles H^+ liberated/(mg protein x min) ± 5.28 (SEM) in 10 control animals and 123.2 nmoles H^+ liberated/(mg protein x min) ± 8.50 (SEM) in 10 shock animals ($P < 0.05$). (Na+K)-ATPase was 27.6 ± 2.04 (SEM) in controls and 41.3 ± 2.14 (SEM) in shock ($P < 0.005$). Brain and lung ATPase levels were not changed. The increased ATPase activities may be related to an altered ionic environment produced by hemorrhagic shock.

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Effects of Ergocornine on Prolactin and LH Secretion in Rats. **Wolfgang O. Wuttke*, E.E. Cassell* and J. Meites. Dept. of Physiology, Michigan State University, East Lansing, Mich.**

Daily injections of ergocornine (EC)(.4 mg/100 g/day) for 20 days or implantation of 200 ug EC in the median eminence, suppressed any serum prolactin (P) increase and depressed pituitary P content in cycling rats. All rats continued to cycle normally. Injection of various doses of EC (5, 50 or 200 ug/100 g) in the early afternoon of proestrus before the critical period inhibited the late afternoon rise in serum P and produced a dose-dependent depression of serum LH values. All animals ovulated the following night, indicating that relatively low serum LH levels may be sufficient to induce ovulation and that P is not directly involved in ovulation. Incubation of male pituitary halves with hypothalamic extract from EC treated proestrous rats resulted in decreased P release, suggesting that hypothalamic PIF content was increased. This does not exclude the possibility that small amounts of EC remain in the hypothalamic extract and may directly inhibit pituitary P release. The mechanism by which the larger doses of EC inhibited pituitary LH release remains to be clarified. (Dr. Wuttke is a postdoctoral fellow of the Max Kade Foundation, New York, N.Y. This work was supported by NIH grants AM 07484 and CA 10771).

EFFECT OF VALINOMYCIN ON TRANSPORT OF SODIUM, CHLORIDE AND BICARBONATE IN ISOLATED URINARY BLADDER OF PSEUDEMYS SCRIPTA. H. R. Wyssbrod* and W. A. Brodsky. Institute for Medical Research & Studies and Mount Sinai Medical and Graduate Schools of The City Univ. of N.Y., New York, N.Y.

Turtle bladders, bathed on both sides by solutions containing various combinations of Na, Cl and HCO_3, were maintained in the short-circuited state. Effects on transport of Na, Cl or HCO_3 were inferred from changes in electrical parameters, namely in short-circuiting current, spontaneous potential difference (PD), and resistance. Valinomycin in ethanol was added to a final concentration of 1 μM to either the mucosal or serosal surface of one hemibladder, while the paired hemibladder served as a time control for addition of ethanol. In the aerobic state, addition of valinomycin to the serosa had no effect on electrical parameters, while regardless of the combination of ions bathing the mucosa, addition of valinomycin to the mucosa resulted in an increase in resistance and a decrease in the magnitude of both PD and short-circuiting current. Anion transport was inhibited more rapidly than Na transport. In the anaerobic state, addition of valinomycin did not result in any change in electrical parameters. However, upon switching from the anaerobic to the aerobic state, transport in control hemibladders increased more than that in valinomycin-treated hemibladders; hence, addition of valinomycin (to a final concentration of 1 μM) in the aerobic state results in the establishment of a metabolic state intermediate between the aerobic and anaerobic states. (Supported by NIH Grant AM 13037, NSF Grant GB-7764 and NASA Grant 33-171-(001).)

EXCITATION AND INHIBITION OF MAMMALIAN NEUROSECRETORY NEURONS. Hiroshi Yamashita* and Kiyomi Koizumi. Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

In Nembutal anesthetized (30 mg/kg) and hemispherectomized dogs intra- and extracellular recordings were made from supraoptic (SON) and paraventricular nuclei (PVN) of the hypothalamus by glass capillary electrodes. Neurosecretory neurons were identified by antidromic excitation of the cells following stimulation of the posterior lobe of the pituitary. Antidromic potentials often showed complete separation of two components: a first small and a second large (SD spike) spike. Intervals between these two spikes could be as long as 10 msec. In "spontaneously" firing neurosecretory cells these two spikes sometimes discharged at different rates. Intracellularly recorded action potentials had longer duration than seen in most mammalian neurons. In these intracellular recordings large excitatory synaptic potentials (EPSP) were observed. Inhibitory synaptic potentials (IPSP) were occasionally recorded following orthodromic stimulations which inhibited the neurosecretory cells. Antidromic excitation of neurosecretory cells was also followed by an inhibition of "spontaneous" discharges lasting for 100 to 200 msec. Intracellular recordings in such instances showed an IPSP. Depolarizing current applied intracellularly through a microelectrode could excite neurosecretory neurons. Some characteristics of action potentials recorded from neurosecretory neurons can be explained by the anatomical finding that many synapses are found on axons as well as on the cell body. (Supported by USPHS grants NB-06537-04 and NB-847-15)

Thrombocyte Metabolism in Intact and Bursaless Birds. James Yarbrough*, M. Wells*, and Bruce Glick. Departments of Zoology and Poultry Science, State College, Mississippi.

Our objectives were to collect pure samples of chicken thrombocytes which are known to be phagocytic in the chicken and to compare the O_2 uptake of these cells from Bursectomized (BSX) and control birds. A cell suspension containing 98% thrombocytes was collected by allowing whole blood to clot in conical centrifuge tubes maintained in an ice bath for 15-20 minutes. The average O_2 uptake/hr/10^8 cells over a 3 week period was 20 ul for controls and 18.6 ul for BSX birds. Addition of carbon to the *in vitro* procedure significantly increased the O_2 uptake, but did not change the relative difference between the control and BSX birds. Therefore, BSX may not influence the postengulfment phase of phagocytosis. (Supported, in part, by PHS grant 03398)

THE EFFECTS OF ADAPTATION ON THE NEURAL CODE FOR TASTE QUALITY. U. Yinon* and R. P. Erickson, Departments of Ophthalmology and Psychology, Duke University, Durham, North Carolina 27706.

Using pentobarbital anesthetized hamsters, the responses of individual chorda tympani taste neurons to "primary" taste stimuli (NaCl, HCl, QHCl, sucrose) and water were examined. Each stimulus was preceded by 40 sec. adaptation to each of these 5 stimuli. After adaptation to water, 50% of the neurons were "specific," responding strongly to only 1 of these stimuli; the rest responded to several or all stimuli. Following adaptation to other stimuli, the "specific" types were seen to be responsive to several stimuli. Both enhancement and depression of responsiveness could occur in the same neuron following adaptation to different stimuli. The direction of this effect is not easily predictable from the similarity of the adapting and test stimuli; i.e., a strong response may follow adaptation to the same stimulus. This finding is not common to all mammals. Since the taste quality of a stimulus is influenced by prior stimuli, the effects of adaptation on the neural code for taste quality (across-fiber pattern, AFP) were investigated. The AFP for HCl and QHCl were not greatly influenced by these adapting stimuli, but the AFP for sucrose, NaCl and water were very dependent on the state of adaptation; e.g., water elicited a variety of taste messages following other stimuli, as would be expected from psychophysical data.

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EFFECT OF HYPOTHALAMIC-STALK-MEDIAN EMINENCE EXTRACT (HSME) ON TRANSMEMBRANE POTENTIALS OF CELLS IN RAT ADENOHYPOPHYSIS. D. H. York*, F. L. Baker* and J. Kraicer. Dept. of Physiology, Queen's University, Kingston, Ontario, Canada.

The "stimulus-secretion coupling" hypothesis proposes that hormone release is initiated by a depolarization of the plasma membrane. HSME, an extract which has been shown to be rich in releasing factors was injected into the carotid artery of anaesthetized rats and the consequent changes in transmembrane potential (TMP) of adenohypophysial cells followed. Four hundred and ninety cells were impaled with potassium citrate filled micropipettes. All cells had negative TMP's (Avg. 21.8 ± S.E. 0.5 mV). The injection of a volume of extract containing 1 HSME was studied on 63 cells, of which 36 were sufficiently stable for the effects to be evaluated. From these experiments it is clear that a hyperpolarization is the most commonly observed membrane effect (38% of cells) in the adenohypophysis and the depolarization predicted by the stimulus-secretion coupling theory is seen in only a small minority (5%) of cells. In control experiments on 57 cells, extracts from cerebellum, cerebral cortex or brain stem were injected. These injections produced no detectable change in TMP.
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A Quantitative Study of Primary Potentiation of the Frog Neuromuscular Junction. S. G. Younkin* and S. D. Erulkar, Univ. of Pennsylvania Med. School, Philadelphia, Pa. 19104

Mallart and Martin[1] have shown that primary potentiation at the frog neuromuscular junction has two distinct components. They showed that the potentiation following short trains (five impulses) may be described by assuming linear summation of the potentiation that follows a single impulse. The usefulness of the linear summation model is that it provides a quantitative description of primary potentiation at any time during or after any tetanus. It is important to determine whether linear summation continues to occur after longer tetanic trains. We have investigated this using intracellular recording from single endplates of the frog sciatic nerve-sartorius preparation. In all experiments, isotonic Ringer's solution containing 10.0 mM Mg^{++} and 1.0 mM Ca^{++} was used. Our experiments confirm the presence of two components in primary potentiation. The relevant values obtained were: f_1 (amplitude of first component) = 0.66; 1/b (time constant of first component) = 35 msec; f_2 (amplitude of second component) = 0.054; 1/g (time constant of second component) = 310 msec; t_{max} (time to peak of second component) = 120 msec. Furthermore primary potentiation after a variety of trains containing up to forty-five impulses (150/sec for 50 msec; 50, 100, 130, and 150/sec for 300 msec) continues to fit curves predicted by assuming linear summation; this demonstrates validity for the linear summation model for these longer trains. Even longer trains (100/sec for 600 or 1000 msec) have been examined. After these, a third component of potentiation - "post-tetanic potentiation" (PTP) develops. With this number of impulses, the presence of the PTP as well as the possibility of concomitant depression makes precise assessment of primary potentiation uncertain in our system. Supported by USPHS NB-02941.

[1] (Mallart, A. and Martin, A.R., J. Physiol 193: 679-694, 1967.

REINNERVATION OF DENERVATED SKELETAL MUSCLE BY AXONS OF MOTOR, SENSORY, AND SYMPATHETIC NEURONS. Andrew A. Zalewski (intr. by Lloyd Guth). Natl. Insts. of Health, Bethesda, Md.

Denervation atrophy of skeletal muscle is reversed after reinnervation of the muscle by axons of any somatic motor neuron, but not after reinnervation by dendrites of sensory neurons. In order to determine whether the trophic function of nerve on muscle was specific to axons of motor neurons, the sternomastoid muscle of adult rats was studied from 1 - 5 months after denervation and after reinnervation by the following axons: its original motor nerve, the motor hypoglossal nerve, the central fibers of the sensory neurons of the vagal nodose ganglion, and preganglionic cervical sympathetic nerve fibers. Functional reinnervation (as indicated by muscle appearance, contraction, weight, fiber size, enzyme activity, and by the formation of new motor-end-plates) was successful only after reinnervation by the axons of the sternomastoid (original nerve) and hypoglossal nerve neurons. Muscles reinnervated by axons of sensory or sympathetic neurons remained chronically denervated in all respects The results demonstrate that only axons of motor neurons can reverse denervation atrophy of muscle. It is concluded that this trophic influence of nerve on muscle is a property that is unique to motor neurons.

EFFECTS OF CHRONIC MITRAL STENOSIS ON ADH RELEASE IN DOGS. J. E. Zehr, A. Hawe, A. Tsakiris, D. C. McGoon and W. E. Segar, (intr. by R. Nelson)
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Simultaneous observations of blood antidiuretic hormone (ADH) and cardiovascular responses resulting from small non-hypotensive hemorrhage were studied in 7 dogs with surgically created chronic mitral stenosis and in a control group of 4 animals. The stenotic dogs exhibited pronounced histologic alterations of atrial endocardial and myocardial tissue secondary to long-term (15-23 months) left atrial and pulmonary bed hypertension. Simultaneous measurement of left atrial pressure (LAP) by transseptal puncture, and of left ventricular end diastolic pressure indicated that in the stenotic dogs a mean LAP of 26.1 + 9.8 (SE) cm water and a mean diastolic gradient of 21.3 + 5.3 (SE) cm water across the mitral valve was present in the control state. Control blood ADH levels were comparable in the normal and stenotic groups. Small non-hypotensive hemorrhage resulted in increased blood ADH levels in both the normal and stenotic groups, however a marked attenuation in the rise in blood ADH levels was present in the stenotic group despite a two-fold greater fall in LAP when compared to normals. It is concluded that extensive histologic alterations, secondary to long-term left atrial and pulmonary bed hypertension, has resulted in a decreased operating gain in the low-pressure hypothalamic posterior pituitary axis. (Supported by NIH Grants HE-3532 and HE-12776.)