CONTENTS

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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 authors.

MULTIPLE PASSIVE TRANSFER OF TARIF. V.J. Adamkiewicz and P.J. Sacra*. University of Montreal, Montreal, Que., Canada.

The shock-injection of dextran (12 mg/100 g. i.v.) into dextran sensitived (30 mg/rat i.p., 8 days previously), genetically susceptible Sprague-Dawley rats (150-180 g. b.w.) caused within one hour the appearance in the serum of a hyperergic factor, the "Transferable Anaphylactoid Reaction Inducing Factor" (TARIF), as well as an allergy. Hypoglycemic rats (Insulin-Zn, 2 units/100 g. s.c.) produced enough TARIF so that it could be transfered passively with the serum (0.5 ml/100 g. i.v.), every hour, through three consecutive lots of other hypoglycemic rats, causing each time an allergy. Hyperglycemic rats (8 millimoles D-glucose/100 g. per os; alloxan diabetes) produced less TARIF, so that it could be transfered only to one lot of hypoglycemic rats. Therefore, D-glucose inhibited the production of TARIF by dextran. TARIF transfered to hyperglycemic rats produced no allergy. But transfered further into hypoglycemic rats again produced the allergy. Therefore, the production of allergy by TARIF was also reversibly inhibited by D-glucose (Grants: U.S. Department of Health, Education and Welfare A-184; Medical Research Council of Canada MT-640.

NON-LINEAR RELATIONSHIP OF SPIKES AND WAVES IN CORTICAL NEURONS. W. R. Adey and R. Elul*. Dept. of Anatomy and Space Biology Laboratory, Brain Research Institute, University of California, Los Angeles, Calif.

Spontaneous wave activity was observed in intracellular recordings from cortical neurons in unanesthetized, pretrigeminal cats. The waves reached 15-20 per cent of the average resting potential, which was 45-70 mV. Firing of the cell always occurred on a depolarizing wave, but often not at the peak of depolarization. In a large portion of the cell population, waves were frequently observed with depolarizing peaks exceeding the triggering level, but without spike initiation. No significant difference in slope and time course of waves of the two groups was found. In some cells, consecutive spikes were triggered at a different triggering level; 5 mV threshold fluctuations over brief periods were common. No signs of damage were detected in cells that exhibited the behavior described here. Two alternative explanations are offered for the apparent non-linearity in spike-wave relationships: (1) Cortical cells may have several spike triggering zones of different thresholds. The required interplay of triggering zones is difficult to explain in terms of refractory periods, however, since the interspike interval is around 50 msec, and some "switching mechanism" must be postulated. (2) A more likely assumption may be that of high coupling resistance between the electrode and spike triggering zone. In this case the potential at the electrode tip may not reflect events at the triggering zone; synapses in vicinity of the electrode may then produce a large recordable potential change while having only minor effect on spike generation, and conversely with synapses close to the triggering zone. Following this explanation, intracellular recording may only give an indication of local membrane potential changes.

TEMPERATURE CHANGES IN THE HEART MUSCLE DURING THE CARDIAC CYCLE IN DOGS. S. Afonso*, J. A. Will*, and G. S. O'Brien. Cardiovascular Research Laboratory, University of Wisconsin, Madison, Wisconsin.

Studies of the thermal topography of the left ventricular myocardium in dogs have shown that the temperature is not uniform at different sites in the myocardium. In the current study it has been observed that small temperature variations $< .01$ of a degree C. are also present at any single site. These variations occur within the cardiac cycle. Temperatures were obtained with needle thermistors inserted in the left ventricular myocardium through a left thoracotomy. The pericardium was opened, sutured to the intercostal and thoracic musculature and the surface insulated from the environment with glass wool. Experiments performed to elucidate the cause of these variations suggest that they represent heat redistribution in the myocardium during the cardiac cycle. (Supported in part by grants from the Wisconsin Heart Association.)

DETERMINATION OF STROKE VOLUME BY MEASUREMENT OF ISOVOLUMETRIC CONTRACTION AND EJECTION TIMES - Clarence M. Agress, Stanley Wegner*, Shigeo Nakakura*, Cedars of Lebanon Hospital, Los Angeles, California

The ejection interval (ET), isovolumetric contraction interval (ICT) and arterial pressure (MSP) each have shown relationships to the stroke volume index (SVI) but have proved reliable for its estimation only in limited circumstance. This investigation was undertaken to examine the usefulness of these parameters in combination for the estimation of the SVI in dogs at rest and after stress. In the resting animal ICT and ICT^2 provided the most reliable means of estimating the SVI. Inclusion of ET and MSP did not add to the correlation. The equation at rest was:

$$SVI(\pm.28)\ ml/Kg = 706 - 15.7\ ICT + 0.101\ ICT^2$$

The addition of stress and recovery data demonstrated that ET and ET^2 were also important factors. Again MSP did not improve the estimate of SVI. The highest correlation was obtained with the equation:

$$SVI(\pm.28)\ ml/Kg = -184 - 1.91\ ICT + 4.33\ ET - 0.00672\ ET^2 + 0.0429\ ICT^2 - 0.0276\ ET \cdot ICT$$

It was concluded that measurement of the isovolumetric contraction and ejection phases of left ventricular systole provides a reliable estimation of the stroke volume index in dogs at rest or after stress.

ROLE OF SINOAORTIC NERVES IN THE DEVELOPMENT OF EARLY RENAL HYPERTENSION. N. Alexander and M. DeCuir.* Univ. of So. Calif. School of Med., Los Angeles, Calif.

The arterial baroreflex mechanism minimizes acute pressor responses and might function similarly to reduce the rate of increase of MAP in experimental renal hypertension. If a direct relationship exists between rise of MAP and the renal stimulus used to initiate and maintain the rise, and if the same degree of stimulus were applied to kidneys of animals without sinoaortic nerves, an increased rate of MAP rise could reasonably be attributed to absence of the nerves. Renal hypertension was produced in rabbits by unilateral nephrectomy and enclosure of the opposite kidney in a latex capsule. Semiliquid material collected inside the latex capsule to produce a measurable counter pressure around the kidney termed "extrarenal counter pressure" (ERCP). Simultaneous measurements of ERCP and MAP were made during the first 8 postoperative days in 38 normal (N) and 11 sinoaortic denervated (SD) conscious rabbits. Data from N and SD rabbits were divided according to preoperative MAPs: Group A, 60 to 79 mm Hg; Group B, 80 to 100 mm Hg. Only ERCP values of N rabbits that matched those of SD rabbits were selected (range, 16 to 77 mm Hg) and plotted against increase in MAP. There was a linear relationship between ERCP and MAP rise in both N groups and extrapolation of regression lines showed ERCP reached 13 mm Hg in Group A and 24 mm Hg in Group B before MAP increased. These values subtracted from measured ERCP values in the respective groups gave an "effective" ERCP. The average ratios of increase in MAP to effective ERCP were: Grp. A: N, 1.27 ± 0.63; SD, 1.68 ± 1.35 ($t=1.72$, $p > 0.1$); Grp. B: N, 1.40 ± 3.6; SD, 1.62 ± 2.23 ($t=0.2$, $p > 0.9$). Conclusion: Absence of sinoaortic nerves did not significantly increase the rate at which MAP rose in early renal hypertension.

THE EFFECT OF AGE ON THE BIOCHEMICAL AND MECHANICAL PROPERTIES OF RAT MYOCARDIUM. Norman R. Alpert, Henry H. Gale* and Natsu Taylor*. University of Illinois College of Medicine, Chicago, Illinois.

The decrease of cardiac reserve with age raises the question whether these changes result from primary alterations in the myocardium. To answer this question biochemical and mechanical properties of rat myocardium were measured in 75 rats ranging in age from 100 to 1000 days. In 55 animals these studies were carried out on the same hearts. Myofibrils were isolated and the ATPase activity measured at various ATP, Ca^{++}, and Mg^{++} concentrations. Both Ca^{++} and Mg^{++} activated myofibrillar ATPase activity decreased as a function of age. Actomyosin was prepared from the left ventricle of these hearts and ATPase activity measured at low and high ionic strength and in the presence of Ca^{++} and Mg^{++}. Ca^{++} activated ATPase activity was reduced as a function of age. ATP sensitivity of the actomyosin was measured and this also decreased as a function of age. Mechanical studies were carried out on columnar carnae and papillary muscles. The velocity of shortening at all loads decreased as a function of age as did the velocity-time curve when considered without the latent period. Active and passive length tension, series elasticity, latent period and velocity-time relationship with latent period were unaltered by age.
(Supported in part by Grant HE 2766.

THE EFFECT OF PERSON ON CARDIAC AND MOTOR RESPONSIVITY TO SHOCK IN DOGS. Sandra L. Anderson* and W. Horsley Gantt. Pavlovian Labs., Johns Hopkins Univ. and V.A. Hosp., Perry Point, Md.

Faradic shock applied to the leg of a dog produces flexion of the leg and increased heart rate. Petting the dog, on the other hand, causes generally a decrease in heart rate. The present study investigates the interaction between petting and shock by petting the dog while he is being shocked. What is the balance between increase due to shock and the decrease due to petting? In dogs in which the effect of shock and the effect of petting were previously determined, motor and cardiac responses were recorded in two control situations (petting alone, shock alone) and one experimental situation (petting during shock) for 10 days, 12 trials a day, 4 of each of the above categories. The results showed peaks of heart rate (average of 40 trials) of, e.g.: Control-62, Petting-43, Shock-96, Petting and Shock-79. Thus, petting during shock significantly suppressed the cardiac reaction to shock ($p<.001$); however, petting did not inhibit the motor response to shock. Instead, it appeared that the petting came to be a conditional stimulus for the motor response, while it suppressed the cardiac response to shock. The fact that the responses of these two systems were dissimilar illustrates the usefulness of the concept of "schizokinesis". This experiment gives a quantitative indication of reduction of the cardiac reaction to a painful stimulus by petting, showing that the effect of person markedly decreases the autonomic components of the unconditional responses to a powerful unconditional stimulus.

AN ISOLATED PERFUSED RAT BRAIN PREPARATION. R. K. Andjus, K. Suhara and H. A. Sloviter (intr. by W. M. Parkins). Univ. of Pennsylvania School of Medicine, Philadelphia, Pa.

In order to perform metabolic and tracer experiments in an intact, isolated and unanesthetized brain, a relatively simple preparation which consists of the skull and its contents has been developed. Prior to surgery, the unanesthetized rat was made hypothermic by the closed vessel technique(combined hypoxia and hypercapnia). With the body temperature at 16°, both internal carotid arteries were cannulated with plastic catheters after tying the external carotid and pterygopalatine arteries. Perfusion was started and then the mandible and all facial and neck muscles were removed. A tourniquet was tightened around the vertebral column which was then transected. The vertebral canal was then packed with bone wax. The entire operative procedure can be completed in one hour by one person. Perfusion was carried out with a small roller type pump in series with a simple bubble oxygenator, which was made entirely from disposable plastic transfusion sets. The "blood" used for perfusion was a suspension of thoroughly washed dog erythrocytes in a Krebs-Ringer bicarbonate buffer containing bovine serum albumin and glucose. The total volume of blood which was recirculated was about 10 ml and the rate of perfusion was 1-2 ml/min. The electroencephalogram(EEG) was recorded from 4 electrodes on the top of the skull. Most preparations showed EEG activity for about 2 hours and some as long as 5 hours. Addition of pentylenetetrazol(Metrazol) to the blood invariably produced typical high voltage activity in the EEG, even after spontaneous activity had ceased. This action of Metrazol occurred even after a 5 hour perfusion when the blood glucose concentration was below 10 mg/100 ml. The activity induced by Metrazol was accompanied by a marked increase in the rate of lactate production.

USE OF ELECTRICAL STIMULATION TO ELICIT DCR IN PSEUDOPREGNANT RATS. John F. Ansbro* and Neena B. Schwartz, Dept. of Physiol, Univ. of Ill., Coll. of Med., Chicago.

For the purpose of quantifying uterine sensitivity to a deciduomal eliciting stimulus, varying amounts of electrical current were applied to the uterus on day 4 of pseudopregnancy. An electrical stimulus ranging from 1 to 100 mamps. intensity and 1 to 100 msec. duration at a frequency of 5/sec. and stimulus train of 10 sec. was applied to the ovarian and cervical ends of each cornu. On day 9 the animals were sacrificed and each cornu divided into ovarian and cervical halves (quadrants). A subjective evaluation of the presence or absence of DCR was consistently confirmed by wet weights and % water determinations. The wet weights of the sections subjectively designated positive (+) were 0.535g $\pm$ 0.318 (S.D.) and 0.523g $\pm$ 0.358 for ovarian and cervical sections respectively, and 0.093g $\pm$ 0.016 and 0.097g $\pm$ 0.020 in the negative (-) ovarian and cervical quadrants. The % H_2O data showed 84.8% $\pm$ 1.5 and 84.8% $\pm$ 1.1 in the + ovarian and cervical areas, and 81.0% $\pm$ 3.8 and 80.7% $\pm$ 3.9 in the - ovarian and cervical sections. There was no significant difference between the ovarian and cervical quadrants in the wet weights or % H_2O. Similarly, ovarian and cervical quadrants did not differ in the % of + responses at the same voltage and duration of stimulation (χ^2 analysis). Although there was no significant increase in quadrant size with increasing intensity and duration of stimulus, a relationship was found between the intensity and duration of stimulus and effectiveness of deciduoma elicitation: as current intensity increased from 1 to 100 mamps. and duration from 1 to 100 msec. the % of + responses rose significantly from 0 to essentially 100%. However, no clearly demonstrable threshold stimulus was seen. (Supported by PHS B-3801)

DIRECT STEADY STATE MEASUREMENT OF $\dot{V}_A/\dot{Q}$ RATIO DISTRIBUTION.
N. R. Anthonisen* and D. V. Bates, Joint Cardiorespiratory Service, Royal Victoria Hospital and McGill University, Montreal, P.Q.
When saline containing Xe^{133} in solution is infused intravenously at a constant rate, and minute ventilation is steady, a state will be reached in which a constant fraction of the intravenous input of Xe^{133} is matched by expired gas elimination. In this steady state, the regional $\dot{V}_A/\dot{Q}$ will be related to regional alveolar concentration (F_A) and pulmonary artery concentration ($C\bar{v}$), and may be directly computed provided that (1) cardiac output is known or assumed, and (2) the effect of reinspired dead space gas is ignored. After the infusion is discontinued, the subject breathes into a closed circuit in which Xe^{133} is monitored and regional count rates are recorded until constant. Simultaneous end tidal Xe^{133} concentrations and total Xe^{133} elimination were measured and used to confirm the existence of steady state conditions while the infusion was proceeding. In four normal subjects seated upright, a steady state was achieved within 3 minutes of starting the infusion. Twelve scintillation counters positioned posteriorly over right and left lungs provided data permitting direct calculation of $\dot{V}_A/\dot{Q}$ ratios for each counter field during a normal resting ventilation and cardiac output condition. This new technique permits calculation of $\dot{V}_A/\dot{Q}$ ratio distribution without treating ventilation and perfusion as if they were unrelated phenomena.

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DYNAMICS OF HEPATIC THYROXINE METABOLISM IN MAN. William G. Appleton, Jr.* and J. Thomas Dowling. King County Hosp. and Univ. of Wash. School of Med., Seattle, Wash.

Kinetic studies employing serial forearm plasma and external hepatic counting of injected, labeled thyroxine (T_4) shows a rapid incorporation of tracer by the liver reaching a maximum at 3 hours and comprising 30% or more of the extrathyroidal T_4 pool. Double isotope studies employing I^{125} and I^{131} T_4 reveal a coinciding peak in urinary iodide I^{125}/I^{131} ratios indicating active deiodination in vivo during hepatic sequestration. Ten to 30 minutes after injection of I^{131} T_4, brachial arterial and hepatic venous bloods were serially sampled for 2-3 hours in healthy volunteers. Plasma and TCA precipitable radioactivity were determined as well as hepatic blood flow. Without demonstrable change in specific activity, the A-V difference (4.4%) accounted for a mean hepatic clearance rate of 28.6 ml/min of plasma. Chromatography of hepatic venous samples reveals labeled I^- and a compound with the mobility of tetraiodothyroacetic acid (T_4A) in amounts comprising a progressively greater proportion of plasma radioactivity. The hepatic clearance rate for T_4 greatly exceeds previously determined biliary clearance rates in man. Thus the hepatic parenchyma in man actively clears and transiently stores a significant amount of circulating thyroid hormone, transforming a portion and delivering I^- and presumably T_4A to hepatic venous blood. Further direct kinetic measurements in vivo should aid in defining the physiological significance of this central role of the liver in T_4 metabolism.

DISTRIBUTION OF γ-AMINOBUTYRIC ACID IN CAT SPINAL CORD AND ROOTS. M. H. Aprison, L. T. Graham, Jr.*, C. F. Baxter* and R. Werman, The Institute of Psychiatric Research, Indiana Univ. Med. Center, Indianapolis, Ind. and V. A. Hospital, Sepulveda, Calif.

The inhibitory action of iontophoresed γ-aminobutyric acid (GABA) on central nervous system neurons is well established and has been confirmed by us. Moreover, strong evidence exists for the role of GABA as an inhibitory transmitter at arthropod synapses. Central nervous system inhibitory transmitters appear to be exclusively manufactured by and released from interneurons with short processes. Thus a postsynaptic inhibitory transmitter would be expected to be concentrated in spinal grey matter. Experimental data show a consistent pattern of distribution of GABA in cat spinal cord and roots. The order of decreasing concentrations is dorsal grey > ventral grey > dorsal white = ventral white > dorsal root = ventral root. This concentration sequence persists when calculated as percent of total free amino acids in each part. The distribution of GABA is thus compatible with that of an inhibitory transmitter. This pattern is distinctly different from that of glutamic acid. Glutamic acid is distributed in a pattern compatible with that of the major somatic noncholinergic postsynaptic spinal cord excitatory transmitter (Fed. Proc. 24, 462, 1965). Determination of the equilibrium potential for GABA action is now in preparation. Supported in part by grants from NSF (GB2692) U. S. P. H. S. (NB-04405-03, MH-03225-06, NB 3743), and United Cerebral Palsy (R-174-64).

ACTION POTENTIALS OF ESOPHAGUS AND GASTROESOPHAGEAL SPHINCTER IN DOGS: Masaki Arimori,* Jerry F. Schlegel and Charles F. Code, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Bi-polar silver-silver chloride electrodes for implantation in the wall of the esophagus were placed on the esophagus of 8 dogs. They provided recordings of the electrical activity in the muscle layers of the wall of the esophagus for 15 to 45 postoperative days. Simultaneous electrical pressure and cineradiographic observations were made. In the body of the esophagus, no electrical activity was detected in the resting state. During deglutition, bursts of very fast electrical potentials occurred which corresponded to the peristaltic contraction. Conduction velocity of the electrical activity was 3.6 ± 0.2 cm/sec (mean of 4 dogs). Continuous, slow, rather rhythmic electrical activity occurred in the gastroesophageal sphincter in the resting state. Slight reduction of this activity occurred during the relaxation associated with deglutition. A burst of fast mixed with slow activity accompanied the contractile phase of the deglutitive response of the sphincter. Repetitive swallowing inhibited the deglutitive electrical activity in the body of the esophagus, lowered sphincteric pressure, and reduced somewhat the slow activity in the sphincter. (Supported in part by NIH Grant AM-2015.)

BRAIN WAVE PATTERN DURING THE RAPID EYE MOVEMENT PERIOD OF SLEEP. Eugene Aserinsky. Dept. of Physiology, Jefferson Med. Coll., Phila., Pa.

By means of an LGP-30 computer, a Fourier analysis of the EEG was performed on 7 adult subjects during the "ascending stage 1" or REMP of sleep. Four-second epochs, manually digitized to yield 100 pts/sec., were selected from records showing either definite ocular motility or unmistakable ocular quiescence. The eye movements themselves generated potentials which had 66.5% of their energy in the 1-3 cps range; these potentials were reflected as artifacts on the occipital as well as on the frontal leads, and had to be accounted for in evaluating the brain wave data. Concurrent with the rapid eye movements, the occipital EEG showed a marked increase in the 7-12 cps (alpha) range and a decrease for 5-6 cps (theta) as compared to the EEG pattern during ocular quiescence. The frontal EEG showed only the decrease in theta when the eyes moved. These results suggest that the so-called "stage 1" is neither physiologically nor psychologically homogeneous. Simple visual scrutiny of the low voltage EEG does not clearly distinguish any difference in the brain wave pattern during ocular quiescence as compared to motility However, the computer analysis suggests that there may be justification for subdividing "stage 1" into two categories designated "stage 1Q" and "stage 1M". The "stage 1Q" would represent a low amplitude, alpha-poor EEG with some 5-6 cps present and would be found within the ocular quiescent portions of the rapid eye movement period; the "stage 1M" would coincide with the bursts of eye movements and would have significant alpha activity, especially in the occipital leads. Since in the waking state, at least, visual imagery is associated with a suppression of alpha amplitude, the increase of alpha in "stage 1M" does not readily support the notion that REM represents scanning motions of visual imagery. (Supported by a grant from NIMH).

OSMOLALITY EFFECTS ON APLYSIA NEURONS. G. Austin, M. Sato*, H. Yai*, J. Maruhashi* and H. C. Longuet-Higgins*. Div. of Neurosurgery, Univ. of Oregon Medical School and Dept. of Theoretical Chemistry, Cambridge, England.

Rate of swelling in hypo osmolal solutions was measured in 52 neurons of Aplysia giving $P_W = 0.35 \times 10^{-5}$ cm./sec. per osmole/l. difference across the cell membrane. A theoretical expression was derived for single file flow of molecules of water (M_W), through a membrane 'pore' ~ 100 Å long, containing ~ 100 'sites'. $J = F(P_{LR} N_W^L - P_{RL} N_W^R)$, where J = net flux in molecules/sec. per unit difference in osmolality across the membrane; F = collision frequency with end sites of 'pore', P_{LR} = probability that a molecule entering from the left, emerges from the right, and P_{RL} vice versa. N_W^L and N_W^R = mole fractions of H_2O at external ends of 'pore'. J was calculated to be approximately 4×10^7 M_W per second. From P_W/J we calculate approximately 2×10^9 'pores'/cm.^{2} of membrane. Hyperosmolal solutions caused a decrease in membrane resistance (M.R.) and hyperpolarization, measured by use of 2 intracellular microelectrodes. Hypo osmolal solutions caused an increase in M.R., and minimal change in resting potential in either direction, depending on the initial value.

RENAL EXCRETION OF DINITROPHENOL AND ITS ANALOGUES. K. L. Bailey* and K. C. Huang, Univ. of Louisville, Sch. of Medicine Louisville, Ky.

The inhibitory effect of 2, 4-dinitrophenol (DNP) and 2, 4, 6-trinitrophenol on renal tubular transport of PAH and other organic acids has been known for many years, but the mechanism of their action has not been explored. Studies with isolated renal tubules and cells in this laboratory have shown that DNP accumulates in renal tubules and inhibits the PAH uptake competitively, indicating that DNP probably shares the same transport mechanism as PAH and other organic acids. Radioactive C^{14}-labelled nitrophenol compounds were synthesized and administered to pentobarbitalized and bicarbonate infused dogs in a primer dose and then with continuous infusion. Inulin was given simultaneously to measure the GFR. Radioactivity of the urinary samples, plasma and its ultrafiltrate were determined. The T value (=UV -F) was then calculated. It was found that DNP at a dose of 2.5 μmol/kg. gave a positive T value, suggesting tubular secretion. When the dose was increased, the T value of DNP became negative. The nitrophenol analogues, o-, p-nitrophenol and 2, 4, 6-trinitrophenol at doses of 5 μmol/kg. up to 10-15 μmol/kg. showed a positive T value, but the last compound, at a dose of 40 μmol/kg., yielded a negative T value. The data support our early conclusion that the inhibitory effect of DNP and its analogues on PAH transport is due to a competition on transport system. (Supported by a Training Grant (PHS 2G-461) and Research Grant (A 2217-07) of U. S. P. H. S. NIH).

MODIFICATION OF NITROUS OXIDE METHOD FOR DETERMINING THE CORONARY BLOOD FLOW WITH GREAT ADVANTAGES. Theodore A. Balourdas (intr. by E.M.K. Geiling), Howard U., Coll. of Med., Dept. of Pharmacology, Washington, D. C.

Using the nitrous oxide method with application of the Fick principle for determining the coronary blood flow and other hemodynamic factors under normal and various pathophysiological conditions in hundreds of experiments on dogs (Balourdas, T.A. et al., Fed. Proc. 15:7, 1956; Ibid. 17:8, 1958; Ibid. 18:7, 1959; Circulation 20:981, 1959; etc.), I experienced the disadvantages of the original method (Kety and Schmidt), required 12 to 15 arterial and venous (Cor.S.) blood samples for each experiment. Given that in all experiments we performed two runs using the desaturation phase, by 150 ml. of blood were withdrawn. The advantageous modification requires: (1) The zero saturation time N_2O arterial-venous values taken during the last 15 seconds preceding the first minute of desaturation period (A-V-myocardial N_2O Equilibrium=Nominator). (2) Continuous integrated blood sampling withdrawal during the first 4 minutes (2 ml/min). (3) The last fifth minute or last minutes continuous blood sampling withdrawal. N_2O values are added to the previous values. Sum of V-A N_2O difference in time of minutes is the denominator of Fick equation. Advantages: (a) Saving time and avoiding laboratory difficulties determining only 6 bl. samples by Van Slyke apparatus. (b) Saving considerable amount of blood. (c) Blood samples are integrated more accurately in N_2O content by the organism rather than by integration of individual per minute N_2O determinations. (d) Avoidance of errors in determinations.

REGIONAL DIFFERENCES IN PLEURAL AND ESOPHAGEAL PRESSURES IN DOGS IN THE UPRIGHT BODY POSITION STUDIED WITHOUT THORACOTOMY. N. Banchero*, A. G. Tsakiris* and E. H. Wood. Mayo Clinic, Mayo Graduate School of Medicine, Rochester, Minnesota.

Intrathoracic pressures were measured simultaneously via saline-filled catheters from four different sites in the right pleural space and esophagus of dogs under morphine-pentobarbital anesthesia while supported in the supine and upright body positions by a half-body cast. Radiopaque teflon catheters (O.D. and I.D.: 1.3 and 0.7 mm.) were inserted percutaneously into the pleural space by an air-tight technic while connected to P23D Statham gauges. Intraesophageal pressure was measured via a catheter 3 mm. in diameter. Mean end-expiratory pleural and esophageal pressures were corrected to the level of the respective catheter tips using biplane x-rays. Pressures were also recorded in the right atrium, pulmonary artery and aorta as well as proximal to a flowmeter at the oral end of an endotracheal tube. In the supine body position pressures were higher at superior sites in the thorax as compared to pressures recorded at dependent sites. In the upright body position pleural pressures were about -18 cm. H_2O in superior parts of the lung about 8 cm. above vertebra T6 while values of about - 4 cm. H_2O were recorded at dependent sites about 10 cm. below T6 giving a pressure gradient in the cephalo-caudad direction of about 0.8 cm. H_2O/cm. vertical distance. These vertical pressure differences were closely followed during step-wise withdrawal of one of the catheters from the apex towards the base. Esophageal exceeded pleural pressures interpolated to similar heights in the thorax by about 3 cm. H_2O. Step-wise withdrawal of the esophageal catheter revealed a pressure gradient similar to that observed in the pleural space. These differences in pleural and esophageal pressures appear to be related to the weight of the thoracic contents. (Supported by Research Grants NASA NsG-327, AHA CI 10, AHA CF 13 and NIH HE-03532.)

Antidiuretic Hormone Not Necessary for Renal Response to Changes in Blood Volume. J. D. Bargainer* and J. W. Woods. Dept. Physiol., The Johns Hopkins Med. Sch., Baltimore. Urine output and other renal parameters were studied in unanesthetized dogs following complete transection of the midbrain thereby depriving the hypothalamus of afferents of vagal origin. Surgery was performed under ether anesthesia and aseptic conditions and the animals studied during the subsequent 48-72 hours. Water diuresis was induced by duodenal infusion of water. Urine was collected from bladder or ureteral catheters. Arterial pressure was monitored with a strain gauge manometer. Hypertonic saline and appropriate control injections were made through a non-occluding carotid catheter;other injections were made through a venous catheter. (1)The function of the supraoptic system was tested in all dogs by intracarotid infusion of 0.5M NaCl. The expected transient antidiuresis was observed in all but one dog. Injection of 0.5M NaCl intravenously produced no change or an increase in urine production. Antidiuresis was also produced in all but one dog by intravenous ADH(2.0 mu).(2) Constriction of the vena cava below the kidneys was followed, in every case, by a prompt antidiuresis.(3) Hemorrhage (10 ml/kg) was followed, in each instance, by a prompt antidiuresis.(4)Infusion of whole blood or dextran was always followed by a prompt diuresis.(5) The one dog which failed to respond to intracarotid 0.5M NaCl and to ADH did respond to caval constriction and to hemorrhage. Autopsy revealed cystic, edematous kidneys.(6) In one experiment one kidney was "denervated" by stripping the arteries and veins. Results described in 1-4, above, were duplicated by the individual kidneys. These results are interpreted to mean that acute changes in circulating blood volume must affect urine output by some mechanism other than altered ADH secretion.

CYCLIC DEGENERATION AND RENEWAL OF MOTOR END-PLATES IN MAMMALIAN SKELETAL MUSCLE. D. Barker and M. C. Ip (intr. by J. P. Segundo). Dept. of Zoology, Univ. of Durham, England.

Studies of teased, silver preparations of normal and de-afferented cat and rabbit hindlimb muscles show that motor endings do not maintain a fixed morphological identity as has generally been assumed, but periodically degenerate and are renewed. The collateral and ultraterminal sprouting of motor axons that effects the renewal is shown by between 30 and 40% of fusimotor plate-ending axons; and by about 20% of skeletomotor axons. Sprouting and end-plate renewal are more obvious inside than outside the spindle owing to the multiple and polyneuronal nature of fusimotor innervation. The duration of the life-span of an end-plate remains to be determined. In view of the existence of this process certain revisions will be necessary of the assessments made of neuromuscular disease, and new interpretations will be required regarding the re-innervation of motor end-plates after nerve injury.

Experimental Alteration in Gastric Mast Cell Population. Ami Barzilai, M. D. *, John P. Delaney, M. D. *, Wallace Ritchie, M. D. *, Arnold Lande, M. D. *, Owen H. Wangensteen, M. D. Dept. of Surgery, Univ. of Minn. Med. School, Minneapolis, Minnesota.

A full thickness gastric biopsy, from a constant location in the mid-anterior body of the stomach wall, was obtained from 25-control dogs and stained, using the Giemsa-Trichrome technique. The mast cells were counted in 12 fields of lamina propria immediately below the surface epithelium. Biopsies were also done on 50 more dogs who had the following operative procedures or secretory stimuli: Chronic vagal stimulation (insulin, mechanical and electrical), chronic pilocarpine administration, chronic cortisone administration, antrectomy, antral exclusion, antral diverticulum to the colon, inferior-mesenteric-caval transposition and vagotomy plus pyloroplasty.

Average differences from the controls were as follows: Insulin hypoglycemia -43%, mechanical vagal stimulation -62%, electrical vagal stimulation -62%, pilocarpine -43%, cortisone -62%, antral exclusion -81%, antral diverticulum to the colon -53%, mesenteric-caval transposition -53%, antrectomy -23%, vagotomy and pyloroplasty -14%. The differences for the antrectomy and for the vagotomy and pyloroplasty groups were not statistically significant. It is concluded that procedures or stimuli associated with hypersecretion are accompanied by a reduction in the gastric mucosal mast cell content. (Supported by a USPHS Grant, the John A. Hartford Foundation and the Donald J. Cowling Fund for Surgical Research.)

CONTINUOUS MEASUREMENT OF CLEARANCE OF INDOCYANINE GREEN FROM THE CIRCULATION. J. B. Bassingthwaighte and J. H. Reed*, Mayo Graduate School of Medicine, Rochester, Minnesota.

Indocyanine green (ICG) is removed from the blood solely by hepatic clearance. A servo system has been devised to control ICG concentration in the blood of humans at steady or slowly varying (sinusoidal) levels. Concentration was detected via a Waters dichromatic earpiece densitometer (Physiologist, 7:234, 1964). The infusion rate for ICG solution was adjusted via a combination of integral, proportional and derivative control using either a digital or analog computer. After the two minutes required to attain constant ICG levels of 1-2 mg./L there was a gradual, moderate diminution of the pump rate over the next 15 to 30 minutes. Under these circumstances infusion rate divided by concentration equals hepatic clearance; decrease in clearance reflects decreased hepatic extraction. A model of the circulatory system plus the liver has been used to simulate the experiments and suggests that the liver can be considered as having two or more compartments. (Supported by grants from the Minnesota Heart Association and U.S.P.H.S., HE-09791)

RECOVERY OF ERYTHROCYTE STEM CELLS IN THE POST-RADIATION RAT. S. J. Baum. Armed Forces Radiobiology Research Institute, Bethesda, Md.

Earlier research has demonstrated that rats exposed to 300 R X-rays show a decrease in ^{59}Fe uptake which attains its lowest point at 48 hours post-radiation. From then on an exponential increase is noted and on the sixth post-radiation day ^{59}Fe incorporation returns to pre-radiation normalcy. The initial decrease has been ascribed to destruction of erythrocyte precursors and the rate of return to normalcy to an increased release of stem cells for the proliferation of erythrocytes. The present experiment has been designed to test this hypothesis. Adult male Sprague-Dawley rats were made polycythemic by the intravenous injection of washed homologous erythrocytes until their hematocrits were increased to 65 percent. Maximum ^{59}Fe incorporation decreased in such animals from approximately 65 percent to 18 percent. Upon the administration of erythrocyte stimulating factor (ESF) rich rat plasma, iron uptake returned to 65 percent when measured two days after ESF injection. In ESF administered irradiated (300 R X-rays) polycythemic male rats, iron uptake diminished to below 10 percent of normal values during the first 48 post-radiation hours. Recovery commenced two days after radiation and ^{59}Fe uptake approached 70 percent of control values on the 4th post-radiation day. Thereafter, maximum iron incorporation fluctuated for the next 11 days and at no time during this period did it return to normal values. Since the amount of ^{59}Fe incorporated into newly formed erythrocytes may be correlated with the number of stem cells released due to stimulation by the exogenous ESF, it must be concluded that the ESF administered to irradiated polycythemic rats stimulated the release of fewer stem cells or that there were fewer stem cells capable of stimulation.

ELECTRICAL POTENTIALS OF ISOLATED ADIPOSE TISSUE CELLS. Paul M. Beigelman, Gerald H. Schlosser* and Leona V. Miller*. U.S.C. School of Medicine, Los Angeles, California.

It is possible to prepare isolated adipose tissue cells with normal physiological and biochemical attributes. The technique (method of Rodbell) utilizes incubation of rat epididymal adipose tissue with collagenase, followed by repeated washing. The isolated adipose tissue cells are then suspended in warm 1% agar in Krebs-Ringer bicarbonate solution. This suspension is permitted to harden in a 0.5 x 1.0 mm. plastic container. Krebs-Ringer bicarbonate is layered on the surface. Penetrations of this preparation with KCl-filled glass micro-electrodes, of 15-30 megohm resistance, are recorded utilizing a Dynagraph with electrometer coupler modified so that micro-electrode tip potentials and resistance may be monitored. Various control preparations evoke no DC electrical potentials. Preparations of the adipose tissue suspension repeatedly have demonstrated 20-40 millivolt DC electrical potentials, presumed to be resting membrane potentials.

CRITICAL OXYGEN TENSIONS IN TURTLES. Daniel A. Belkin (intr. by W. N. Stainsby. Physiol. Dept., Univ. Fla. Coll. Med., Gainesville, Florida.

Oxygen uptake and animal chamber effluent P_{O_2} were continuously measured by means of a constant-temperature circulating volumetric respirometer and a Pauling O_2 analyzer while P_{IO_2} was reduced. The critical P_{IO_2} (t_c, below which $\dot{V}_{O_2}$ depended on P_{IO_2}) for several kinosternid and testudinid species varied from 8 to 12 mm Hg; terrestrial and aquatic species did not differ. t_c appeared independent of rate of P_{IO_2} reduction at the rates used (<10 mm Hg/hr). Turtles were resting, unrestrained, body temp. 22°C (restraint, particularly of the head, elevated t_c). When $\dot{V}_{O_2}$ was plotted as a function of P_{IO_2} below t_c, the resulting linear regression had an extrapolated intercept near $P_{IO_2} = 0$. The slope of this regression line (termed the critical oxygen gradient, G_c, and given by $d\dot{V}_{O_2}/dP_{IO_2}$, $P_{IO_2} < t_c$) reflects the maximum overall O_2 transport capacity for that animal. If the turtle was active and O_2 uptake was thereby increased, t_c was directly proportional to $\dot{V}_{O_2}$ at any given activity level, while G_c remained constant. G_c may be a more reliable measure of an animal's maximum O_2 transport capability than is t_c, as the following comparison illustrates.

ANIMAL	a. resting $\dot{V}_{O_2}$ (mM/kg hr)	b. t_c (mm Hg)	G_c (a/b)
turtle (Sternothaerus minor, 22°C)	0.9	8	0.11
snake (Farancia abacura, 22°C)	1.2	40	0.03
mammal (Mus musculus, thermoneutral)	68.0	40	1.70

The differences between snake and turtle may be related to the latter's greater respiratory and cardiac response to hypoxia. Together with its relatively small normal O_2 requirement, this allows the turtle to maintain normal rates of oxidative metabolism at lower ambient P_{O_2} than can other amniotes, without needing the much more efficient O_2 transport mechanisms imposed on endotherms such as Mus by their high metabolic rates. (Supported by NSFG 9817 and U.S.A.F. Contract AF 41(609)-2421)

THE EFFECT OF RENAL LYMPHATIC OBSTRUCTION ON THE RENAL LYMPH CONCENTRATIONS OF Na^+, K^+, AND UREA. Richard D. Bell* and M. Jack Keyl, Dept. of Physiol., Univ. of Okla. Med. Ctr., Oklahoma City, Oklahoma.

The effect of obstruction of renal lymph drainage on concentrations of three renal lymph constituents was studied in 11 dogs. A comparison of these data with those derived from experiments in which there was minimal lymphatic obstruction suggests several conclusions. Ligation of renal lymphatics leads to a significant elevation in Na^+ concentration in renal lymph. This procedure also appears to increase the concentration of urea in the lymph whereas K^+ concentration is not affected. (Supported by a grant from NIH.)

Cardiovascular Effects of Weightlessness
Evaluation of Preventive and Corrective Procedures

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Summary: When an unprotected astronaut is exposed to prolonged weightlessness we expect to find loss of vascular tonus, change of blood distribution with a shift from the legs towards head and trunk, and a decrease of the total blood volume. Of the various possible protective procedures the combination of exercise and Graveline's venous occlusion cuff applied intermittently to the legs has been adopted by the NASA for research and will now be tested in actual space flight. If preventive measures are not adequate, the astronaut can be protected during re-entry by means of antigravity suit or similar device. The main problems at present are:

1. Lack of suitable monitoring procedure for cardiovascular responsiveness.

2. Lack of adequate protection against orthostatic hypotension during the post-landing phase.

Evidence for Electrical Transmission of Action Potentials in Vertebrate Visceral Smooth Muscle. W.Berger* and L.Barr Dept. of Physiol. Univ. of Mich., Ann Arbor.

Recent studies have shown that transmission of action potentials in frog atrial bundles is electrical (Barr and Berger. Pflug. Archiv. 279:191, 1964) and that the necessary connections between cell interiors are specialized regions of contact between plasma membranes, i.e., nexuses (Barr, Dewey, and Berger. J. Gen. Physiol. 48:797, 1965). Nexuses have been found also between the cells of guinea pig taenia coli muscle. Experimental evidence for electrical transmission in preparations of guinea pig taenia coli was obtained using a sucrose gap technique similar to that used on frog atrial bundles. A narrow sucrose gap blocks propagation of action potentials, evoked here by ACh, by increasing the extracellular resistance, thereby decreasing electrotonic current flow. When the sucrose gap was shunted with a variable resistor biphasic action potentials were recorded. The resistor acted as an artificial extracellular current pathway between active and inactive cells. Since addition of a shunt resistor only allows attenuated electrotonic current flow across the gap, it is concluded that in vivo electrical transmission of action potentials occurs with a large safety factor. (Supported by the Deutsche Forschungsgemeinschaft and USPHS Grant AM-03819.)

STUDIES ON THE GASTRIC INHIBITORY SUBSTANCE (GIS) IN HUMAN SALIVA. Michel Berlinski* and René Menguy. Department of Surgery, University of Kentucky Medical Center, Lexington, Kentucky.

Previous studies have shown that whole human saliva contains a gastric inhibitory substance (GIS) responsible for inhibition of gastric HCl secretion when lyophilized saliva is injected intravenously to laboratory animals. The purpose of this study was to determine the origin of the GIS in saliva and to find out more about its mode of action on HCl secretion. Samples of saliva—whole—parotid—submaxillary—sublingual—were collected from 8 normal subjects under an identical stimulus. Individual samples were dialyzed in the cold and freeze dried. Inhibitory activity of individual samples of dry saliva were tested on gastric secretion of pylorus ligated rats. In addition, the inhibitory effect of whole saliva on histamine and insulin stimulated HCl secretion of gastric fistula dogs was studied and compared with the inhibitory effect of whole canine antral mucus. Data led to the following conclusions: (1) GIS in whole saliva is elaborated mainly by the sublingual glands. Submaxillary saliva had only moderate inhibitory activity and parotid saliva had none. (2) Whole saliva inhibited both histamine and insulin stimulated HCl secretion of dogs to a far greater degree than identical doses of canine antral mucus.

ORIGIN OF THE PRIMARY EVOKED POTENTIAL IN A SIMPLE CORTEX. M. A. Biedenbach and Charles F. Stevens (intr. by H. D. Patton). Physiology and Biophysics, Univ. of Wash. School of Med., Seattle, Wash.

The simple structure of the frontal olfactory cortex makes it a favorable region in which to study the origin of a cortical primary response. Cell counts reveal that most of the neuron cell bodies lie in a densely packed 300 μ thick lamina, and Nauta studies indicate that lateral olfactory tract (LOT) axons synapse directly on the superficially directed dendrites of these cells. Brief electrical stimuli to the LOT evoke a large surface negative wave (latency < 1 msec. after arrival of the LOT volley) followed by a longer lasting surface positive wave. The turnover point of this evoked potential is, according to marking experiments, superficial to the dense cell body lamina. Fine glass microelectrodes driven through the cortex encounter single units in numbers proportional to the neuron soma density at each cortical depth. Most units discharge during the surface negative wave and are silent during the surface positive wave, although some discharge Renshaw cell-like on the declining phase of the first wave and during the early part of the second wave. Intracellular recording from the first variety of cell reveals an EPSP with a monosynaptic latency (coincident with the surface negative wave) and a large IPSP corresponding in time to the positive wave of the primary. Varying the magnitude of the LOT stimulus results in parallel changes in intracellular PSP and extracellular gross wave amplitude. We conclude that, for the frontal olfactory cortex, the primary evoked potential is mainly the extracellular sign of an EPSP-IPSP sequence occurring simultaneously in cells of the densely packed superficial pyramidal layer.

TOLERANCE OF TWO MAMMALIAN HIBERNATORS TO WATER DEPRIVATION. G.L. Bintz* and M.L. Riedesel. Univ. of New Mexico, Albuquerque, N.M.

Regarding water and electrolyte metabolism of mammalian hibernators previous reports include: 1) environmental stresses, such as, water and food deprivation and cold exposure, increase frequency of hibernation; 2) changes in water and electrolyte concentrations, particularly Mg, occur during hibernation; 3) there is no water intake during hibernation. The present study investigated tolerance of golden mantled ground squirrels, 13-lined squirrels, and laboratory rats to deprivation of drinking water. Criteria for comparing responses to water deprivation were: 1) time required for 30% weight loss and 2) water content of tissues. Experimental conditions included animals caged at least two months prior to tests, 22 ±1 C air temperature, and rat pellets ad lib. Animals were sacrificed when weight loss was equal to 30% of initial body weight. Time required for 30% weight loss was 5-6 days for six rats and 10-24 days for ten ground squirrels. Duplicate samples of blood, liver, skeletal muscle, kidney, lung, heart, and small intestine were dried to constant weight, 60 C. After 30% weight loss all tissues of the rat were dehydrated whereas only the blood of the hibernator was dehydrated and the water content of the liver increased. Mean values and standard deviations include:

	Lab rat		C. lateralis		C. tridecemlineatus	
	Control	30%Wt.Loss	Control	30% Wt.Loss	Control	30% Wt.Loss
blood		74.57	77.69	75.74	76.59	74.83
s.d.		(1.10)	(0.65)	(0.56)	(1.94)	(0.83)
liver	73.88	70.99	66.64	68.06	65.07	68.67
s.d.	(0.78)	(0.65)	(0.63)	(0.68)	(1.39)	(1.51)
skel. muscle	75.11	72.58	71.76	70.56	71.53	71.68
s.d.	(0.49)	(1.00)	(1.68)	(0.12)	(2.34)	(1.75)

(Supported by National Science Foundation Grant GB 216.)

DETERMINATION OF VENTRICULAR FUNCTION FOLLOWING IRRADIATION OF THE RIGHT VENTRICLE. Vernon S. Bishop[2], H. L. Stone[3], and A. C. Guyton[4].

Experimental progressive heart failure was produced in ten dogs by exposing the right ventricle to 20,000r of Co-60. The visible myocardial lesion was from 65-90% of the wet weight of the right ventricle. By using ventricular function curves to quantitate the ability of the heart to pump maximum quantities of blood, the functional status of the ventricles was determined in conscious dogs prior to and following irradiation. The maximum ability of the ventricles to pump blood as quantitated by ventricular output curves remained normal during the first 14 days post-irradiation. Following this period the plateau of the ventricular output curve became progressively depressed and the curves shifted to the right along the pressure axis. The average reduction in the plateau of the ventricular output was 43%. Peak heart rate and peak arterial pressure recorded during the plateau of the ventricular output were variable, and no systematic changes were seen until just prior to death. Left ventricular minute work and stroke work displayed descending limbs prior to and following irradiation. Cardiac output was variable from day to day and was maintained in the normal range when the plateau of the ventricular output curves had fallen to one-half of the normal. The cardiac reserve (maximum ventricular output minus control cardiac output) decreased during the last 10-20 days of the experiment.

[1]Supported by grants in aid from NIH and AEC. [2]Department of Nuclear Engineering; Texas A&M University; College Station, Texas. [3]Biodynamics Branch; School of Aerospace Medicine; Brook AFB, Texas. [4]Department of Physiology and Biophysics; University of Mississippi; Medical Center; Jackson 6, Mississippi.

CHANGES IN THE ORTHODROMIC AND ANTIDROMIC RESPONSE OF OPTIC TRACT DURING THE EYE MOVEMENTS OF SLEEP. E. Bizzi (intr. by E. V. Evarts). NIH, Bethesda, Md.

Previous studies have shown that monophasic waves of 100-140 msec duration appear in the lateral geniculate (LG) of the cat in synchrony with the rapid eye movements (REM's) of sleep. Following retinal photocoagulation these LG waves persist unmodified for 3 days, grow smaller from 3-6 days, and disappear after the 6th day though the REM's persist. The time course of wave disappearance corresponds to the time course of optic nerve degeneration. This suggests that optic tract (OT) terminals are involved in the genesis of the LG waves. To test the excitability of OT terminals during the LG wave and the concomitant REM, electrodes were chronically implanted in the LG and OT of the cat. Recordings were made in darkness. The LG wave triggered a train of 3 pulses (0.1 msec, 300/sec) to OT, giving rise to presynaptic and postsynaptic responses in LG. For control, identical stimuli were delivered during the intervals between REM's. The presynaptic spikes showed a maximum decrease of 10% 20-30 msec after the beginning of the LG wave, and some reduction persisted up to 60 msec. The postsynaptic response to the first of the 3 pulses showed a slight increase or no change. The second decreased by 15-20% and the third by 20-45%. The excitability of OT terminations in LG was tested by recording the antidromic response to LG stimulation during REM's, the stimulus being triggered by the LG wave. This antidromic response in the chiasma revealed a facilitation lasting 65 msec from the start of the LG wave and reaching a peak of 14-18%. When LG waves were used to trigger a flash, the evoked response was reduced in LG and visual cortex but unchanged in OT. The reduction of OT orthodromic and increase of OT antidromic responses together with the changes in the flash-evoked responses are consistent with the occurrence of presynaptic inhibition at OT terminals during the REM.

Radioisotopic Radiodensitometric Renograms for Kidney Function Testing by Continuous Monochromatic Radiodensography. William T. Blessum*, Alfred W. Brody, and J. Raymond Johnson, Creighton University School of Medicine, Omaha, Nebraska.

Standard renographic contrast agents (Conray*, Hypaque*, Diodrast*; Dose: 90 mg. I_2/Kg.) were injected intravenously in nembutal-anesthetized dogs. A collimated, constant-intensity 47 KEV x-ray beam from 200 mc PB-210, directed through the kidney at a scintillation detector, measured the changing radiodensity during excretion (5 and 50 sec. time constants). The resulting curves were morphologically similar to Radio-Hippuran renograms and were subjected to the same type of analysis. For 50 control curves in 9 dogs, average excretory half-time was 7.83 min. (S.D.-2.53 min.) and average peak time was 3.78 min. (S.D.-1.11 min.). Acute graded ureteral back-pressures resulted in graded increases in excretory half-times, peak times, and peak heights. Acute renal artery stenosis caused increased half-times and peak times and decreased peak heights. Acute venous stenosis caused increased half-times and peak times and irregular changes in peak heights. Curves preceded by hippurate loading injections (10-15 gm.) showed no regular changes in peak time or excretory half-time, and suggestive but not conclusive diminutions in peak height. (Supported in part by USPHS Research Grant HE 09099; Conray* courtesy Mallinckrodt Pharmaceuticals; Hypaque* and Diodrast* courtesy Winthrop Laboratories.)

FIELD STIMULATION AS A MEANS OF EFFECTING THE GRADED RELEASE OF AUTONOMIC TRANSMITTERS IN ISOLATED HEART MUSCLE. John R. Blinks*(intr. by J.M. Marshall). Harvard Medical School, Boston, Mass.

Electrical stimuli are known to cause the release of acetylcholine and norepinephrine in preparations of isolated heart muscle, presumably by exciting intrinsic autonomic nerve fibers. Field stimuli, applied through large electrodes on opposite sides of the preparation, may be used to produce pronounced and reproducibly graded sympathomimetic and parasympathomimetic effects without disturbing rate or rhythm. The preparation is driven at constant frequency with threshold pulses applied through a punctate cathode in contact with the tissue. Such stimuli release negligible amounts of the transmitters. Field pulses are applied at various overall frequencies, all pulses timed either to coincide with a threshold pulse or to fall in the refractory period of the myocardium. The adrenergic component of the response can be studied without interference from the cholinergic in atrial or ventricular muscle exposed to 10^{-6} M atropine. The cholinergic component can be studied alone in atrial muscle from kittens pretreated with reserpine. There is a slight, but definite, cholinergic response in the cat papillary muscle. Field stimuli used to ensure synchronous excitation in preparations of isolated heart muscle exert substantial sympathomimetic and parasympathomimetic effects at all but very low frequencies of contraction. The maximal sympathomimetic effect of field stimulation can normally be achieved with two pulses per second; the inotropic effect is equal to the greatest achievable by the addition of norepinephrine. Field stimulation cannot be used in studying the interval-strength relationship in heart muscle unless release of endogenous transmitters is taken into account. (Supported by USPHS grants HE-03738 and HE-02205.)

FORCE FREQUENCY RELATIONSHIPS AFTER DEPLETION AND REPLACEMENT OF ATRIAL NOREPINEPHRINE BY EPINEPHRINE. E. I. Bloomquist* and E. T. Angelakos. Dept. of Physiol. Boston Univ. Sch. of Med., Boston, Mass.

Guinea pig atria were perfused for 60 min. with 10 mcg/g epinephrine (E) and subsequently washed for 90 min. with Locke's. Controls were perfused for 150 min. with Locke's. Chemical analysis showed that in atria treated with E, the norepinephrine (NE) stores were almost completely depleted, having a mean of 0.20 mcg/g as compared with 1.77 mcg/g in the controls. The mean content of E in treated preparations was roughly equal to that of NE in the controls (1.80 mcg/g). Histochemically, the trihydroxyindole method which is specific for E showed that the E was taken up into the adrenergic nerve fibers; the formaldehyde condensation method which does not differentiate NE from E showed no change in nerve fiber content of total catecholamines. No difference in background fluorescence was detected with either method indicating that non-specifically bound E had been washed from the tissue. Force frequency curves done on left atria before treatment and after NE-E exchange showed differences in the frequency at which the peak tension occurred and in the magnitude of the tension, the direction of change in magnitude being dependent on driving frequency. (Supported by the Council for Tobacco Research and USPHS HE-09616 and K3-15,457.)

CARBOHYDRATE METABOLISM AT ALTITUDE. F. Duane Blume* and Nello Pace. Dept. of Physiology, University of California, Berkeley.

Liver glycogen and blood sugar values were measured in mice exposed for various periods of time to an altitude of 3,800 meters. Chronic exposures of two weeks or more resulted in a 50 per cent reduction in liver glycogen values. The blood sugar values were more variable, but were in the direction of significantly lower circulating levels. In order to determine possible alterations in the glycolytic pathway, the conversion in vivo of several carbon-14 labelled intermediate compounds to labelled CO_2 was measured at sea level and after a four week exposure to altitude. The altitude animals were found to have markedly slower conversion rates for uniformly labelled glucose at 10 AM than the sea level animals. However, the utilization rates at 10 PM were found to be nearly the same for both groups. No differences were observed between sea level and altitude mice in the daytime conversion of glycerol-1-3-C14, acetate-2-C14, pyruvate-3-C14 and succinate-2-C14. The alteration is clearly noted when the animal depends largely upon endogenous sources for glucose (10 AM); however, the alteration is not observed during the feeding period (10 PM) when body demands are being supplied from exogenous sources. The conversion rate of D-glucose-1-C14 was compared to that of D-glucose-6-C14 at sea level and altitude. In sea level mice, the C-1 label was recovered more rapidly than the C-6 label, indicating conversion via the hexosemonophosphate shunt. At altitude, a discernible difference did not occur between C-1 and C-6 labelled glucose; in addition, the total yield of labelled CO_2 was much lower than at sea level for both compounds. It is suggested that hexosemonophosphate shunt activity is reduced at altitude. (Supported by ONR Contract Nonr-222(38).)

NON-UNIFORMITY OF LUNG COMPLIANCE IN NORMAL SUBJECTS

W.S. Blumenthal* and L. Cander, Hahnemann Medical College and Hospital, Philadelphia, Pa.

Distribution of ventilation was measured in normal subjects with the breath by breath N_2 washout technique of Fowler et al. Peak-to-peak intraesophageal pressures (Δ P) were monitored simultaneously. Measurements were made at slow f at large tidal volumes and rapid f at smaller tidal volumes. The data allowed the computation of the volumes of the well and poorly ventilated lung spaces (V_{L_1} and V_{L_2} respectively), and the volumes ventilating the well and poorly ventilated spaces (V_{A_1} and V_{A_2} respectively). From these values and the intraesophageal pressures we computed the "minimal specific compliance" of each space where $C_{min} = V_A/V_L \times \Delta P$. In 4 normal subjects, the average volume and average C_{min} of V_{L_1} at slow f were 412 ml and .177 L/cm x L respectively. Similar values for V_{L_2} were 2158 ml and .041 L/cm x L respectively. At more rapid f the volume, but not the C_{min} of V_{L_1} decreased. The data revealed that more than 50% of the effective alveolar ventilating volume is utilized by V_{L_1} which is only about 1/5 of the alveolar volume. The data documented the presence of uneven distribution of compliances in normal lungs and suggest that the distribution of compliances may be a more important determinant of distribution of ventilation in normal people than the distribution of resistances. (Supported by USPHS Grant HE 05569).

COMPARISON OF NORMAL AND POST-ECTOPIC CARDIAC CYCLES DURING CINE-ANGIOGRAPHIC STUDIES.

Clorinda S. -S. Bohler*, Mark Brown*, Robert L. Rainey*, and Philip Dow. Departments of Physiology, Radiology, Medicine, and the Hemodynamic Center, Medical College of Georgia, Augusta.

Cineangiographic studies of patients with mitral and/or aortic valve disease presented an opportunity to study the effects of post-ectopic diastolic filling upon the subsequent beat, with previous "normal" beats serving as controls for each patient. Monoplane films taken at 30 frames per second were reviewed and critical frames were chosen for time and area measurements. Arvidsson formulas were adapted to these data, with gravimetric planimetry of irregular shapes. Changes in ejection time and stroke volume were correlated with the large changes in LVEDV. In some hearts the ejection fraction of the large and small beats remained constant as in the cases reported by Miller and Swan. In other hearts the end-systolic volume was the more nearly constant figure between the large and small beats, over a considerable range of EDV. Exceptions are found to both these relationships, which may have prognostic significance.
Supported by grants from the Life Insurance Medical Research Fund and USPHS #HE-07266.

A PLASMA FACTOR THAT CAUSES CONTRACTION OF VASCULAR SMOOTH MUSCLE. David F. Bohr, Borje Johansson* and George Henry*. Department of Physiology, University of Michigan, Ann Arbor.

Isolated vascular smooth muscle, mounted in a bath of physiologic salt solution, contracts in response to the addition of homologous plasma. The heparinized dog plasma is collected in cold siliconized equipment and separated from its platelets by immediate centrifugation. There is marked individuality in the sensitivity of vascular smooth muscle from different sites, to the stimulating action of this factor. Of the vascular smooth muscles studied, that from small subcutaneous resistance vessels (300 to 400μ diameter) is most responsive, that from coronaries least responsive. The factor responsible is evidently not a commonly recognized plasma component: 1) Not catecholamines - Alpha adrenergic blockade with dibenamine fails to block the action of plasma. Both norepinephrine and epinephrine cause relaxation of coronary resistance vessels; the plasma factor causes constriction. 2) Not 5-hydroxytryptamine - Concentrations of dibenamine which block the action of 5-hydroxytryptamine do not block that of the plasma factor. 3) Not angiotensin - The response of most isolated vascular smooth muscle to angiotensin exhibits rapid tachyphylaxis; the response to the plasma factor does not. Although the chemical nature of this factor that causes constriction of isolated vascular smooth muscle has not been characterized, the evidence indicates that it may be an important determinant of non-neurogenic vascular tone. (These studies were supported by a grant from the American Heart Association).

HALF-LIFE OF Ca-45 IN VARIOUS SUBCELLULAR STRUCTURES OF SKELETAL AND CARDIAC MUSCLE. Augusto Bondani* and Ralph Karler. Dept. of Pharmacol., Univ. of Utah Coll. Med., Salt Lake City, Utah.

The present work represents a study of the half-life of Ca-45 in the nuclear, mitochondrial, and microsomal fractions of skeletal and cardiac muscle labelled in vivo. The experiments were performed on rats administered Ca-45 intravenously and sacrificed at various time intervals from 15 min to 8 hr after administration. Muscles were homogenized in a sucrose-tris buffer medium and the homogenates were fractionated by standard differential centrifugation technics. The results indicate that the Ca-45 activity disappears exponentially. The decrease in Ca-45 in skeletal muscle nuclei follows a single function with a half-life of 5.2 hr. The decay of Ca-45 activity in skeletal muscle microsomes involves two functions, a rapid component with a half-life of about 30 min and a slower component with a half-life of 8.9 hr. Skeletal muscle mitochondria initially show an increase in Ca-45 activity, but there is a decrease in activity after one hour with a characteristic half-life of 4.2 hr. The decrease in Ca-45 activity in skeletal muscle homogenates appears to follow a single exponential function, masking the early changes seen in mitochondria and microsomes. For all cardiac muscle fractions, including the homogenate, the decrease in Ca-45 activity can be resolved into two exponential functions, a fast component with a half-life of about 30 min and a slower component. The slower component half-life for cardiac nuclei is 3.0 hr; for cardiac mitochondria, 6.9 hr; for cardiac microsomes, 3.8 hr. The half-life data for Ca-45 demonstrate some striking differences between cardiac and skeletal muscle. (Supported by NIH grants NB-04553, 5-K3-NB-864.)

DISAPPEARANCE OF SALT AND SWEET PREFERENCES IN RATS DRINKING WITHOUT TASTE AND SMELL. Katarina T. Borer* and Alan N. Epstein. Dept. of Biology, Univ. of Penna., Philadelphia, Penna. and Dept. of Anatomy, Univ. of California, Los Angeles, California.

Rats prefer sweet solutions to water across a broad range of concentrations (2-40%). Sodium chloride solutions are preferred well into the hypertonic range (ca. 1.5%) but are avoided at higher concentrations. In this study, the dependence of such choice behavior on taste is demonstrated with a technique (Epstein, Science, 1960, 131, 497) that permits the study of drinking in the absence of oropharyngeal sensations. The rat is equipped with a chronic gastric tube and is given constant access to a bar that activates a pump that delivers fluid through the tube directly into the animal's stomach. Choice behavior was studied with two bars on opposite walls of the chamber, one delivering water and the other delivering a test solution. Oral preferences were studied by requiring the animal to press the bars to deliver fluids into a cup or spout beside the appropriate bar. Test solutions were alternated between bars. When the animals were drinking by mouth typical "two-bottle" preference curves were generated for sucrose (2.5-40%, N=1) and glucose (5-40%, N=5). And a preference for saccharin (0.05%, N=2) and a normal preference-aversion curve for NaCl (0.3-3%, N=8) were obtained. In the absence of oropharyngeal sensations all preferences were abolished and the aversion for the highest salt concentrations did not appear. Choices between bars were not determined by the nature of the solutes being delivered. The animals worked at the bars as if both were delivering water. Taste is therefore the sole determinant of the preferences for sweet and salty solutions exhibited by rats having constant access to the test solutions and water.

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CHRONOTROPIC AND INOTROPIC CARDIAC EFFECTS IN POST TOURNIQUET HYPEREMIA. J. T. Botticelli and R. L. Lange*. Dept. of Med., Marquette Univ. Sch. of Med., Milwaukee, Wisc.

Hemodynamic responses to reactive hyperemia induced by arterial tourniquets may be related to variation in vascular resistance (SVR). Changes in venous pressure (VP) and central blood volume (CBV) have not been observed, however information is lacking on the possible inotropic response to metabolites from the ischemic area. Right heart and aortic catheterization allowed measurement of heart rate (HR), VP, aortic (AP), pulmonary artery wedge (PAW) pressures. Indicator dilution methods were used for cardiac output (CO) and CBV. Stroke volume (SV), SVR, and stroke work (SW) were derived. Parameters were calculated at intervals: A, during 15 minute tourniquet application; B, during brief release and reapplication intended to return SVR to prerelease levels and isolate the ischemic area and; C, at intervals for 20 minutes after release. Ten normal subjects showed a drop in CO with A, and a transient rise in B and C. After blockade with TEAC in six subjects, maneuver A produced a % change in: CO (-18), HR (+1), SVR (+24), SW (-20). Transient release in maneuver B yielded CO (+9), HR (-2), SVR (-12), SW (-18). Momentarily after reapplication: CO (-11), HR (-18), SVR (+21), SW (+12) but by 10 minutes conditions of A were present. With C the CO quickly approached normal (-1), however HR progressively decreased to (-24) for 20 minutes. Since SVR returned to and slightly exceeded control (+10), SW rose significantly (+26) and was sustained. CBV, VP and PAW showed slight random variation. Reflex activity prevents significant alteration in hemodynamic parameters in the unblocked state. Results after TEAC and maneuver B suggest the release of substances resembling bradykinin with negative chronotropic and positive inotropic effects since the time course of changes was shortened by reapplication.

AIRWAY RESISTANCE AND LUNG VOLUME DURING PHYSIOLOGICAL BREATHING PATTERNS IN MAN. A.Bouhuys and B.Jonson*. Dept. Physiol., Emory Univ. Sch. Med., Atlanta, Ga., and J.B. Pierce Fndn., New Haven, Conn.

We used Jaeger and Otis' method (JAP,19:813,1964) to obtain recordings of alveolar pressure (Palv), air flow ($\dot{V}$) and lung volume changes ($\int\dot{V}$) during mouth breathing at normal and increased tidals and flow rates. Thoracic gas volume (TGV) was obtained several times in each run, using Boyle's law; these data were used to calibrate the $\int\dot{V}$ record in terms of TGV. Static recoil curves (Pst(1)) were obtained separately with the esophageal balloon method. Graphs of Palv vs. $\dot{V}$ were obtained at 20, 50 and 80% of vital capacity (VC) in 4 subjects. Average values for K and K' in $Palv = K.\dot{V} + K'.\dot{V}^2$ were:

INSP.:	20%	50%	80% VC	EXP.:	20%	50%	80% VC
K	1.89	0.89	0.60	K	2.38	0.80	0.45
K'	0.44	0.47	0.51	K'	0.47	0.50	0.40

At low $\dot{V}$ (½-1 LPS) the data on the relations between airway resistance, lung volume and Pst(1) agree with those of Briscoe et al. (JCI,37:1279, 1958) and of Butler et al. (JCI,39:584,1960). In most subjects airway resistance depended on the volume history of the lungs. This was most evident when resistances during inspiration from different endexpiratory levels were compared: inspiratory resistance at the same TGV was the higher, the lower the preceding endexpiratory level. Closure of small bronchi near RA may lead to irregular lung expansion during the next inspiration; for equal $\dot{V}$ at the mouth volume flow per small bronchus may then increase compared to regular expansion with all bronchi patent. This increased $\dot{V}$ in small bronchi would require higher Palv for equal $\dot{V}$ at the mouth. This may at least partially explain the hysteresis-like behavior of airway resistance in this study.
Supported by USPHS grants OH00160 (OH00207), and HE08326.

THE EFFECT OF CARNOSINE AND CATION EXCHANGE RESIN ON ATP-INDUCED CONTRACTION OF GLYCERINATED MUSCLE FIBERS. W. J. Bowen, National Institutes of Health, NIAMD, Bethesda, Maryland.

Carnosine and its constituent amino acids (β-alanine and histidine) accelerate ATP-induced isotonic shortening of glycerinated rabbit muscle. To investigate whether these were specific or ionic effects and whether pH was involved a variety of experiments was done. It was found that pH 8 was optimal so all experiments were done at that value. Contraction was induced by 5mM ATP purified by passage over cation exchange resin, H-cycle. With only the sodium present which is necessary to neutralize ATP-acid, shortening was slow with varying rates and extents. 5mM $MgCl_2$ was more effective than 0.1M KCl. Carnosine (0.1M) was more effective than 0.1M KCl with or without Mg++ so the augmentation of contraction was not an ionic strength phenomenon. In the presence of KCl, $MgCl_2$ and carnosine as much as 69% shortening occurred in 2 sec. compared to less than 10% with KCl or $MgCl_2$ only and about 30% with KCl and $MgCl_2$ together. Histidine was about as effective as carnosine, but β-alanine was less so. Contraction was also augmented by imidazole.

The above results were obtained with normal glycerinated fibers. When fibers were put into 50% glycerol with an excess of cation exchange resin (H or Na cycle) resin-treated Na_4 ATP induced little contraction unless Mg++ was added. Ca++ had a small effect. Contraction was better in the presence of carnosine than with KCl. Fibers treated with resin in Na cycle contracted better than those treated with resin in H-cycle. Also, $(NH_4)_4$ ATP produced faster and more contraction than Na_4ATP.

DETERMINATION OF FLOW IN A MULTICOMPARTMENT MODEL BY EXTERNAL DETECTION OF GAMMA RADIATION. D.L. Boyd* and S.H. Steiner. Medical Service, VA Hosp. and Indiana Univ. School of Medicine, Indianapolis.

An eight-compartment recirculating flow model was connected in series to a 150 ml compartment which served as a cardiac mixing chamber. All other compartments were in parallel. Total volume of the system was 14 L and compartment volumes ranged from 0.5 to 3 L. Compartment flow rates were varied from 120 to 2140 ml/min. Total system flow was maintained at 5.12 L/min by a calibrated flowmeter. Inflow to each chamber was measured without disturbing the system. Each compartment was observed in turn by a collimated scintillation probe which led to a linear ratemeter with a 1-second time constant. Rates of change of indicator (Cs^{137}) input and washout were recorded. The difference between these mono-exponential functions was extrapolated to T_0 semi-logarithmically. Counts per minute at T_0 were converted to a fraction of the injected tracer by counting a known amount of injectate using identical volume and geometry. Systemic flow was calculated by the Stewart-Hamilton indicator dilution method. Three methods were used to calculate compartment flow: (1) Extrapolation to T_0 of indicator input and net rate of redistribution; (2) Extrapolation to T_0 of change in organ indicator content in the absence of recirculation; and (3) Using the "$t_{\frac{1}{2}}$" of change in organ indicator content in the absence of recirculation. The T_0 of the injected fraction (Methods 1 & 2) was multiplied by calculated systemic flow to determine compartment flow. Comparing actual and calculated flows gave the following mean percent errors and standard deviations: Method 1 (-0.15±6.86); Method 2 (-0.65±11.11); Method 3 (-2.07±11.69). The correlation coefficient for each method was greater than +0.98. There was no correlation between the calculated flows and cardiac output, compartment volumes or compartment distance from the cardiac chamber. (USPHS H07398, H6308; AMA-ERF Contr. Tobacco & Health)

REPRODUCTION AND FOOD HABITS IN MERRIAM'S KANGAROO RAT. W. Glen Bradley and Roger A. Mauer (intr. by D. B. Dill). Biol. Dept., Nevada Southern University, Las Vegas, Nevada.

Collections of Merriam's kangaroo rat (Dipodomys merriami) were made from a creosote bush community near Las Vegas, Nevada for the period 30 May 1962 until 31 January 1965. All months of the year were represented and 895 animals were examined. The reproductive condition of all animals was determined. Some males were found to be in reproductive condition, as evidenced by scrotal testes or abdominal testes 5 mm or longer, during all months of the year. Approximately 50 percent or more males were in reproductive condition during the period February through September. Some females were reproductively active for the period January through August. Visible embryos, recent placental scars, and lactation were the criteria for determining reproductively active females. Our findings indicate that two or more litters may not be uncommon. The stomachs of 740 kangaroo rats were examined and food items determined as seeds, greens, and insects. These are expressed as percent by volume of the total stomach contents. The diet is primarily made up of seeds. Greens become important as a food source for the period February through May and again in August. Greens make up over 30 percent of the stomach contents during these months. We suggest that greens are utilized primarily as a water supplement during the period of active reproduction in both males and females.

ACTIVATION OF THE METIN-ACTOMYOSIN SYSTEM BY CALCIUM. F. Norman Briggs and Franklin Fuchs*. Dept. of Physiol. University of Pittsburgh School of Med., Pittsburgh, Pa.

Although the ATPase activity of myosin B is subject to control by calcium that of purified actomyosin is not. Ebashi has suggested that tropomyosin may be the protein which confers calcium sensitivity to purified actomyosin preparations although he found that tropomyosin prepared by the method of Bailey did not so act. Szent-Gyorgyi and Kaminer have described a tropomyosin-like protein which they called metin and which we have examined for calcium sensitizing activity when mixed with purified actomyosin preparations. Metin was found to convert actomyosin preparations previously insensitive to calcium into a calcium sensitive system. Metin has also been found to possess strong calcium binding properties and may, therefore, represent the site of action of calcium in the activation of myofibril ATPase activity.

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VARIATIONS IN THE CHLORIDE CONTENT OF ISOLATED SQUID AXONS F.J. Brinley Jr. and L.J.Mullins, Dept. of Physiology, Johns Hopkins University School of Medicine; and Dept. of Biophysics, University of Maryland School of Medicine, Baltimore, Maryland.

The internal chloride concentration in squid axons was determined in samples of axoplasm extruded from 30 axons obtained from live squid brought to Baltimore from Ocean City,Maryland during May-June,1964 and March-May,1965. The analyzed axons showed a bimodal distribution of chloride concentrations. The mean lower value was 51.9±2.5(17)mM/Kg (mean ± SEM,n). The mean higher value was 96.5±5.5(13) mM/Kg. The lower values were obtained during the earlier trials in both years. The equilibrium potential for the low chloride axons was 52 mv and 41 mv for the high chloride axons. The mean diameter of the axons was 548 microns (395-1010). Sample preparation methods included: 9 hr ash with added NaOH at 450°C; 2 hr digestion with NaOH at 100°C;1-20 hrs leeching in distilled H_2O plus NaOH; 1-7 days leeching with 1 N acid. KCl standards run in parallel with the analyses showed mean recoveries of 98-102%. Chloride was determined by coulometric titration. These results indicate that the wide range of internal chloride concentrations found by other investigators may depend upon more than differences in experimental technique. The variation observed in the present series may be due to changes in the temperature of the water from which the squid were taken. Supported by NSF grant GB-1765 and NIH grant GM-08427.

EFFECT OF DIURETICS ON RENAL CALCIUM CLEARANCE AND URINE CALCIUM-47 SPECIFIC ACTIVITY. Anne M. Briscoe,* Felix E. Demartini,* and Charles Ragan. First (Columbia University) Medical Division, Bellevue Hospital. New York, N.Y.

The effect of intravenously administered chlorothiazide, ethacrynic acid, and mercuhydrin on the excretion of calcium-40 and of calcium-47 was studied in normal human subjects. A tracer dose of calcium-47 was injected 24 hours previously. Classical renal clearance techniques were employed with appropriate control prior to the administration of the diuretic. The renal clearance of calcium-40 was increased by all three diuretics during the one-and-a-half hour study period. The percentage of the dose of calcium-47 excreted per ml and the urine specific activity were greatly increased by ethacrynic acid, significantly increased by chlorothiazide, and slightly and less consistently by mercuhydrin. Estimates were made of the amount of ionized and bound urine calcium-40 and calcium-47. A greater percentage of non-ionized (bound or complexed) atoms of both isotopes was found in the urine during diuresis. There was a greater loss of recently administered calcium-47 atoms than of the calcium-40 atoms in diuresis. These observations are compatible with the hypothesis of a delayed exchange of new atoms with one or more bound serum calcium fractions. It may be inferred that the transport of the bound or complexed calcium is modified by the diuretic to a greater extent than that of the ionized calcium.

OBSERVATIONS ON THE ROLE OF THE CARBOXYL GROUP IN AMINO ACID TRANSPORT. Kenneth R. Brody,* Richard P. Spencer, Francia E. Vishno.* Department Radiology, Yale University School of Medicine, New Haven, Connecticut.

No transport against a concentration gradient occurred using the hamster everted small intestine in vitro if the COOH group of an α-amino acid was replaced by CH_2OH, CH_3, $CO.C_6H_5$, or CO-NHOH. Transport apparently occurred when the replacing group was $CO.NH_2$. Evidence is presented that in these cases deamination or transamination (producing the free amino acid) likely preceded transintestinal transport of the compound. Glycine-2-C^{14} methyl ester hydrochloride, purified to free it of glycine, was not transported by everted intestinal sacs from hamster, rat or chinchilla. There was thus no appreciable esterase activity under these conditions. A phosphonic acid analogue ($R\text{-}CHNH_2.PO_3H_2$) was not transported against a concentration gradient and did not inhibit amino acid movement ($-PO_3H_2$ cannot replace -COOH). A sulfonic acid analogue ($R\text{-}CHNH_2.SO_3H$) was not completely stable under these conditions (pH 7.4 Krebs-Bicarbonate, 37°C, 95% O_2 + 5% CO_2, 1 hr) It was not transported, and was not a transport inhibiter. Aminoiminomethane sulfinic acid also did not inhibit transport. Carboxylic acids alone, and amines plus carboxylic acids, were not effective inhibiters of amino acid transport. A second COO^- or SO_3^- group on the amino acid converted a transported molecule into a nontransported one. These compounds were also not inhibiters of amino acid transport.
(Supported by grants from the U.S. Public Health Service.)

DIFFUSABILITY OF CIRCULATING ANTIDIURETIC HORMONE IN THE DOG. A. H. Brook* and L. Share. C.S.I.R.O., Australia, and Western Reserve Univ., School of Med., Cleveland, Ohio.

The question whether antidiuretic hormone (ADH) in plasma exists as the free octapeptide or is bound to some large molecule was investigated by circulating blood of an anesthetized dog through a dialysis chamber, and assaying the dialysate and plasma for ADH. The rate of dialysis of endogenous ADH was compared with the rate of the in vitro dialysis of highly purified arginine vasopressin. In both cases the diffusion rate was dependent on the concentration gradient of ADH across the membrane. The percent equilibrium attained after one hour of dialysis was found to be the same in vivo and in vitro. Information on the diffusability of ADH across capillaries was obtained by introducing a physiological salt solution containing 6% Dextran into the thoracic and peritoneal cavities. Subsequently samples from these sites were assayed for ADH. Lymph was collected from the thoracic duct and from the cervical lymphatic duct, and assayed for ADH. ADH was present in lymph and in fluid withdrawn from the thoracic and peritoneal cavities. It is concluded that in the dog ADH exists in plasma essentially as the free octapeptide which can diffuse across capillary membranes into the extravascular space.

DEPRESSOR REFLEX ARISING FROM THE LEFT CORONARY ARTERY OF THE CAT. A. M. Brown (intr. by J. H. Comroe, Jr.). Cardiovascular Res. Inst., University of California Medical Center, San Francisco, California.

Ten cats were anesthetized by the intraperitoneal injection of pentobarbitol. The main left coronary artery was perfused from a common carotid artery. Sudden, brief (5 sec) changes in perfusion pressure (PP) were produced from a pressurized reservoir containing 2 ml arterial blood at 37°C. Similar volumes injected into the right atrium or aorta had no effect. PP, aortic and right atrial pressures were registered using strain gauge manometers. An electroneurogram was recorded from the cut central end of a branch of the inferior cardiac nerve. Sudden increases in PP always caused a striking decrease of sympathetic nervous discharge. In 8 cats blood pressure fell without bradycardia; in 2 there was neither hypotension nor bradycardia. Veratridine (1µg intracoronary) produced hypotension. Vagotomy abolished these changes. Brief cessation of coronary flow or intracoronary injection (10 µg) NaCN had no effect. Three of five cats anesthetized using chloralose showed only bradycardia when PP was increased. The threshold at which the reflex could be elicited varied from 20 to 100 mm Hg above the control PP. It seems likely that coronary mechanoreceptors with afferent vagal nerve fibers form the sensory limb of this reflex. (Supported in part by USPHS HE-5251.)

SOME CHARACTERISTICS OF ELECTRICAL ACTIVITY EVOKED IN THE EYECUP OF THE PLANARIAN DUGESIA TIGRINA. H. Mack Brown* and T.E. Ogden, VA Hospital, Div. of Neurology and Dept. of Physiology, University of Utah College of Medicine, Salt Lake City, Utah.

The planarian ocellus consists of two cell types. Darkly pigmented epithelial cells form a pigment cup containing the distal portions of the retinular or light sensitive cells. Electrical activity evoked by light in the ocellus of the unanesthetized planarian was recorded with KCl or sodium citrate filled glass capillary micropipettes (20 megohms). The form of the ocellar potential (O.P.) elicited by intense illumination (10 μsec electronic flash) was a simple wave of long duration (.7-1 sec.) and consisted of three components: (a) a small amplitude early negative wave with minimum latency of 35 msec.; (b) a larger negative component with latencies ranging from 70-100 msec.; (c) a slow positive wave. No unitary discharges were recorded in the eyecup. Components of the O.P. were found to be temperature sensitive. The response latency and peak delay of the second negative component varied inversely with temperature within the range of 10-40°C. The amplitude of all components increased as temperature was raised from 12°C. to 27°C. From 27-43°C. the amplitude of the components progressively decreased. The Q_{10} of the physiological processes represented by the O.P. was 1.25 for the range of 12-25°C. This is in the range of values obtained for rate limited photobiological reactions. Supported by VA Research Associate Program and USPHS Grant NB-04135.

RESPONSE OF LIMB VEINS TO AORTIC AND CAROTID CHEMORECEPTOR STIMULATION, Norman L. Browse* and John T. Shepherd, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The responses of the limb veins to separate stimulation of aortic and carotid body chemoreceptors have not been defined. The occluded-limb technique, in which the venous pressure in a dog's hind limb was monitored below a pneumatic cuff inflated to 300 mm Hg, gave a direct measure of reflexly mediated changes of venous tone. The technique of Comroe and Mortimer (J. Pharmacol., 146, 33, 1964), whereby the arrival of a drug at the carotid bodies is delayed by inserting long tubes in the carotid arteries, allowed the effects of separate stimulation of these two chemoreceptors to be determined. Sodium cyanide was injected at the aortic valve, and the resultant venous response to aortic and carotid chemoreceptor stimulation was studied. Responses from both bodies were similar and were not dependent on the ventilatory changes. Initially, there was a modest venoconstriction. As stimulation was repeated, the responses became strongly dilator in 6 of 10 dogs. The aortic and carotid responses were abolished by vagotomy and division of the sinus nerves, respectively. Both the constrictor and the dilator responses were due to changes in activity of sympathetic vasoconstrictor fibers. Reflex venodilatation could also be produced with other drugs and by lowering blood pressure in the aorta or in a carotid sinus preparation. (Supported by NIH Grant HE-05883.)

A STUDY OF CONDITIONING IN CHRONICALLY SPINALIZED KITTENS. Jennifer S. Buchwald and Sharon G. Schramm*, Depts. of Pediatrics and Anatomy and the Brain Research Inst., Univ. of California, Los Angeles, Calif.

The capacity of the spinal cord isolated from higher centers to mediate the development of a conditioned response has been studied in a group of 21 kittens 1 to 21 days of age. After low thoracic transection, kittens were trained with a light brush stroke to the skin overlying the hamstring muscles (CS) paired with a 0.5 sec duration shock to the hindpaw of the same leg (US). Sessions of 35 trials were run four times daily and observations were confined to the 420 trials of three consecutive days. Initially, no response was evoked by the CS but a brisk flexion was produced by the US. After 4-5 sessions, however, the brush stroke began to elicit a distinct forward movement of the hindleg and responses to the CS increased on subsequent sessions. If the US were then withheld, the CS response declined; subsequent US reinforcement reestablished the CS response. Other spinalized kittens were not subjected to the complete conditioning paradigm but only to repeated presentations of the CS. After 4-5 sessions the brush stroke began to evoke responses similar to those of the kittens trained with US reinforcement. There was not, however, a decrease in performance equivalent to that observed in the preceding group when the shock was withheld. Non-spinalized litter mates subjected to these same training procedures developed no responses to the brush stroke. This data suggests that spinal cord transection, per se, leads to the appearance of new reflex responses, presumably due to progressive hypersensitization of spinal cord neurons following a central lesion. However, the disappearance of the response to brushing when shock is withheld and its reappearance when shock is reinstated suggests that reversible changes in the reflex responsiveness of the isolated cord can be imposed upon the ongoing pattern of excitability.

SYNAPTIC ACTIVITY IN MOTONEURONS DURING NATURAL ACTIVATION OF MUSCLE RECEPTORS. R. E. Burke* and P. G. Nelson. Spinal Cord Section, NINDB, NIH, Bethesda, Md.

Intracellular recordings of synaptic events in gastrocnemius motoneurons have been obtained during tonic and phasic passive stretch, and during active twitch, of the gastroc-soleus muscle in cats. Passive gastroc-soleus stretch always results in the appearance of "synaptic noise" in intracellular records, the individual components of which are often small. However, in a number of cells, unitary-appearing miniature EPSPs were elicited by small tonic stretches (25-50gm loads), with amplitudes up to 2.5 mv, and with some showing evidence of rhythmic occurrence. The frequency and amplitude of the rhythmic unitary EPSPs often tend to decline during maintained stretch. With increasing stretch more unitary miniature EPSPs are recruited, and those rhythmically active increase in frequency. These changes parallel those in muscle spindle afferent discharge simultaneously monitored in dorsal rootlets. With sufficient stretch the unitary EPSPs summate into a steady depolarizing potential shift. When an active twitch is superimposed on varying levels of steady stretch, spindle discharge and the miniature EPSPs cease simultaneously, with return of the depolarizing shift to baseline. During the falling phase of twitch tension there is an accelerated burst of spindle firing with a concomitant burst of miniature EPSPs. The unitary miniature EPSPs, particularly those rhythmically active, are inferred to be due to firing in single muscle afferent fibers.

EFFECT OF EPINEPHRINE ON THE PERIPHERAL CIRCULATION. P. Caldini*, S. Permutt, and J.A. Waddell* The Johns Hopkins University, Baltimore, Maryland.

The effect of epinephrine on the peripheral circulation was studied in anesthetized open-chest dogs where blood flow and right atrial pressure (P_{RA}) were independently controlled by a right heart bypass. This preparation allowed us to measure changes in blood volume from the bypass reservoir and to construct P-V curves of the systemic vascular bed over a wide range of P_{RA} at constant blood flow. Portal pressure was recorded, and the relationship between change in portal pressure and change in P_{RA} was also studied. At constant blood flow and P_{RA}, infusion of epinephrine in amounts sufficient to produce an approximate 50% increase in systemic arterial blood pressures (2-5 μg/kg/min) caused a consistent decrease in blood volume and increase in portal pressure. The systemic P-V curve was shifted to the right along the pressure axis in a manner suggesting the development of a critical opening pressure in the systemic veins of approximately 1-3 cm H_2O. The slope was moderately decreased. Before epinephrine, changes in P_{RA} at constant flow brought about comparable changes in portal pressure, whereas during epinephrine infusion portal pressure did not change at all following moderate changes in P_{RA}. These findings suggest that epinephrine causes constriction of veins. In the portal system, the venoconstriction is enough to make the portal pressure insensitive to changes in downstream pressure, presumably because of the presence of a vascular waterall between the portal system and the right atrium.

RELATION BETWEEN ARTERIAL PRESSURE AND BLOOD AND INTERSTITIAL VOLUMES IN ISOLATED, PERFUSED DOG KIDNEYS. M. H. Caley,* W. G. Kerrick,* and A. R. Koch. Dept. of Physiol. and Biophys., Univ. of Washington, Seattle.

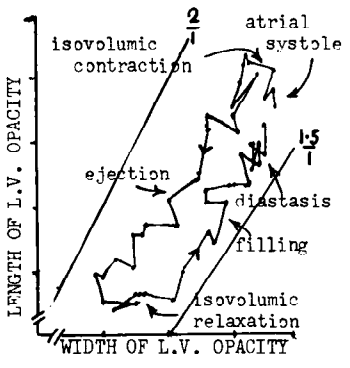
Renal blood flow remains relatively constant as arterial pressure rises above 80 mm Hg. The increased resistance to blood flow implies a decreased vascular volume at the location of resistance change. As arterial pressure rises, large decreases in total vascular volume accompanied by interstitial volume increases would indicate that resistance changed in the high capacity, high compliance venous portion of the vasculature. An adjustable constant pressure pump was used to perfuse isolated dog kidneys with arterial blood. At a given pressure, I^{131}-labeled albumin was injected into the arterial perfusate at a constant rate; venous blood was then monitored for radioactivity. After the I^{131} in venous blood had reached a plateau, injection was stopped. Steady-state vascular volume was calculated from total counts of I^{131} from the instant injection had ceased until the fall-off was complete, the plateau level of radioactivity, and steady-state blood flows. Interstitial volume changes were obtained by subtracting vascular volumes from steady-state kidney weights. Both volumes were determined at several pressure levels above 80 mm Hg in each experiment. In the autoregulatory range, vascular volume was found to decrease significantly as arterial pressures were increased, sometimes by amounts in excess of the estimated arterial volume. Interstitial volume was found to increase markedly as arterial pressures were raised above 80 mm Hg. These results indicate that the observed resistance change was not exclusively preglomerular in origin, and that a significant part of the change occurred in the venous vasculature. (Supported by grants from the American Heart Association (63653), National Heart Institute (HE 04469) and U.S. Public Health Service Grant (FR-5432).)

PREDICTION OF INTERSPIKE INTERVAL HISTOGRAM FROM SYNAPTIC NOISE.
William H. Calvin and Charles F. Stevens (intr. by T. C. Ruch).
Physiology & Biophysics, University of Washington, Seattle, Wash.

Intracellular recordings from repetitively firing motoneurons suggest that observed variability in the interspike interval might arise from synaptic noise superimposed upon the approximately linear rise of membrane potential to the firi g level. If this is correct, it should be possible to predict a neuron's interspike interval histogram (IIH) from the statistical properties of its synaptic noise. Large noise standard deviation (SD), by allowing earlier threshold crossings, should produce a large SD of the IIH. The rapidity of the noise fluctuations, however, determines how often the potential might reach an amplitude sufficient to cross threshold, and thus has a strong effect on the IIH shape. After the IIH of a cat spinal motoneuron was compiled, spikes were eliminated so synaptic noise could be measured in isolation. The noise had an approximately Gaussian amplitude distribution, and shot noise theory adequately predicted the motoneuron PSP shape from the noise autocorrelogram. A LINC computer then simulated the neuron behavior by adding filtered Gaussian noise to a ramp, and compiled IIH's for threshold crossing times. The first three central moments of the simulated and observed motoneuron IIH's were in good agreement only when the SD and autocorrelogram of the simulator noise corresponded to measured motoneuron values; systematic deviations from motoneuron IIH skewness and SD were observed for other values of noise SD and autocorrelation. It would appear that the statistical properties of synaptic noise, in this case, are adequate to predict the motoneuron IIH.
(Supported by NIH grants FR 00150-01 and NB 05934-01)

LENGTH-WIDTH DIAGRAMS OF THE HUMAN LEFT VENTRICLE. R.Carlisle*, D.G. Greene and I.L.Bunnell. Dept. of Med., State Univ. of N.Y. at Buffalo and the Buffalo General Hosp., Buffalo, N.Y.

The length and width of the left ventricular opacity are measured, from cineangiograms taken in the right anterior oblique projection, in the course of calculating left ventricular volumes, as previously described. These measurements can also be compared directly by plotting the one against the other for each 1/60 sec of the cardiac cycle. The resulting length-width diagram takes the form of a loop, as shown in this instance:



Loops have been constructed from the data obtained for patients undergoing routine cardiac catheterization where cineangiography was employed for pressure-volume studies. Conclusions drawn so far are (1) During the 2 isovolumic phases of each cycle, contraction and expansion of the width precede that of the length, for the majority of subjects. (2) The ejection and filling limbs generally lie along isopleths, indicating a constant length/width ratio. (3) Occasionally the loop is more horizontal and intersects isopleths. This effect was related to elevation of systolic pressure. (4) Uncoordinated contractions are manifested as a distortion of the normal configuration. (Supported in part by PHS grants 5T1 HE 5508-03 and HE 07539-03.)

RENAL TUBULAR IMPERMEABILITY TO UREA IN RATS. G. Carrasquer, S. Solomon and H. Sonnenberg. Univ. of Louisville School of Medicine, Louisville, Kentucky and Univ. of New Mexico School of Medicine, Albuquerque, New Mexico.

Accumulation of urea in obstructed kidneys of dogs in sodium chloride diuresis has been attributed to persistent filtration and intraluminal trapping, due to poor impermeability of the nephron wall to urea (G. Carrasquer and A. L. Baldwin, Fed. Proc. 23:363, 1964). To test intraluminal trapping of urea the following experiments were performed. Sprague-Dawley rats were dehydrated and starved for 24 hours, after which H^3-methoxy-inulin and C^{14}-urea were injected intravenously or intramuscularly. Diuresis was induced by i.v. infusion of 1.0 M mannitol or 0.5 M NaCl. After 40-60 minutes the ureter was connected to a manometer and the flow was stopped. Samples were obtained by micropuncture from distal tubules preceding and following obstruction of the ureter. Preliminary results show that ureteral obstruction induced a 10-fold increase in the U/P ratio of H^3-inulin and a 5-fold increase in the U/P ratio of C^{14}-urea in the distal tubules of NaCl loaded rats. No significant changes in the U/P ratio of H^3-inulin or C^{14}-urea were observed during the period of obstruction in mannitol diuresis. These findings demonstrate restricted permeability of the distal tubule to urea and are in accord with the hypothesis of restricted permeability of the loop of Henle, since a large fraction of the filtered urea remained trapped in the lumen during the period of obstruction. Accumulation by secretion of urea may be ruled out from the findings in mannitol diuresis. (NIH and AHA support)

SMOOTH MUSCLE RESPONSES IN AN ISOLATED VESSEL PREPARATION. Oliver Carrier, Jr. and William C. Govier*. Univ. Miss. Med. Ctr. Jackson, Miss.

An isolated perfused vessel technique is being used to investigate the physiological and pharmacological properties of vascular smooth muscle. Typical responses to tyramine, norepinephrine, epinephrine and high potassium solutions are obtained. Supersensitivity in vessels from dogs pretreated with reserpine has been obtained. Vessels from reserpinized animals reacted to l-norepinephrine at a concentration ten times less than that required for controls. *In vitro* reserpine perfusion results in complete loss of vascular tone and some indications of supersensitivity. Dibenzyline perfusion results in blockage of the responses to norepinephrine and epinephrine. Perfusion with MAO inhibitors prevents norepinephrine responses but not high potassium contracture. Tissue electrolytes and tissue dependence upon perfusate electrolytes are being investigated. Preliminary work has resulted in values of 149.1 ± 27.1 meq Na/kg dry weight and 49.9 ± 5.3 meq K/kg dry weight for vessels placed directly into drying tubes from the animal upon dissection and 66.9 ± 11.4 meq Na/kg dry weight and 20.0 ± 4.1 meq K/kg dry weight for vessels bathed for 1 minute in oxygenated sucrose solution. At the present time only femoral arteries and branches there of have been used in these studies. (This work has been supported by USPHS Grants No. HE 09391-01 and HE 08678-02).

ON "MUSCLE SENSE" IN MAN. Sylvester J. Carter* and Samuel Gelfan. New York Medical College, New York City 29.

An attempt was made to answer the question whether impulses from muscle spindles, if they do reach the cerebral cortex in unanesthetized man, are consciously interpreted as signalling changes in muscle length and tension. The tendons available at the wrist, and Achilles tendons, were exposed under local anesthesia restricted to the skin of this area in suitable surgical cases. Such tendons were pulled slowly or briskly so as to stretch only the muscles with varying degrees of force, or pulled in the opposite direction so as to flex the fingers or whole hand. Pressure, squeezing or pinching of muscles percutaneously before, during and after tendon pulling were readily recognized and accurately localized, as was also joint movement. But at no time did any of such patients experience any sensation of muscle pulling or stretching. If any of the Group I or Group II spindle afferents of forearm and triceps surae muscles in man do project to the somatosensory area, as has been reported for some Group I muscle-spindle afferents of cat forelimbs (Oscarsson & Rosén, 1963), the transmitted signals from the stretch receptors are not consciously perceived or appreciated as such. (Supported by PHS grant: NB-04417)

Carbonic Anhydrase Inhibition And Exercise Tolerance. S. Cassin, Dept. of Physiol., College of Medicine, Univ. of Fla., Gainesville, Florida.

Rats trained to run on a treadmill were able to run in excess of two hours at 0.4-0.5 miles per hour in room air whether carbonic anhydrase was inhibited or not. When subjected to an hypoxic environment (6-7% O_2 in N_2), animals in which erythrocytic and renal carbonic anhydrase were inhibited by acetazolamide (100 mg/kg) ran approximately 30% longer than did controls. Other rats given 2-3 mg/kg of an analogue of acetazolamide (2-benzenesulfonamido 1,3, 4, thiadiazole-5-sulfonamide or Cl 11,366) with a selective renal inhibition and no respiratory effect were unable to run longer than controls in the same hypoxic environment. Animals treated with acetazolamide showed an elevation in subcutaneous gas pouch carbon dioxide and carotid arterial oxygen tension during the hypoxic stress in contrast to controls and animals treated with Cl 11,366. These data support the view that generalized carbonic anhydrase inhibition permits exercising rats to run longer in an hypoxic environment than animals without this inhibition. The enhanced exercise tolerance under these conditions is associated with an elevated tissue oxygen tension which results from an increased ventilation subsequent to tissue retention of carbon dioxide. (Supported by Contract AF 41 (609)-2421 with the USAF School of Aerospace Medicine.)

DETERMINATION OF MIXED VENOUS O_2 AND CO_2 TENSIONS BY A RE-BREATHING METHOD. P. Cerretelli*, J. Cruz*, and H. Rahn. Dept. of Physiology, State University of New York at Buffalo, Buffalo, N. Y.

By means of a mass spectrometer it is possible to follow the kinetics of equilibration of O_2 and CO_2 tensions between mixed venous blood and lung gases when a gas mixture of 7% CO_2 in N_2 is rebreathed. Starting from the end of a normal expiration the subject rebreathes every 2 seconds 2.5 - 3 liters of the mixture in an anesthesia bag. Within 4 - 8 seconds a plateau is reached for both CO_2 and O_2. The plateau for CO_2 is a measure of true $P\bar{v}CO_2$. The O_2 plateau is assumed to be a measure of $P\bar{v}O_2$. Under the conditions of our experiments calculations show a possible maximum error for $P\bar{v}O_2$ of 3 mm Hg. In six subjects the $P\bar{v}O_2$ ranged from 35 to 52.
(Supported by the Buswell Fellowship Fund, the U. S. Public Health Service, and the U. S. Air Force.)

SOME NEUROPHYSIOLOGICAL ASPECTS OF MENTAL RETARDATION: CORTICAL EVOKED RESPONSES TO VISUAL AND AUDITORY STIMULI. Loring Chapman, Harvey Dingman* and Richard Morris* Dept. Psychiatry, Center for the Health Sciences, University of California, Los Angeles, and California Dept. Mental Hygiene, Pacific State Hospital, Pomona, California.

Cortical evoked responses were averaged with a special purpose digital computer in 50 patients with mongolism, 50 with a diagnosis of undifferentiated mental deficiency, 10 with childhood autism, and 50 normal controls matched for age. The patients were carefully selected to be free of gross neurological disorders or major EEG abnormalitites. Responses to photic and auditory stimuli (clicks) were studies in the waking state and during various levels of sleep, with and without sleep inducing medication. The method shows promise of demonstrating abnormalities not apparent from simple visual inspection of the EEG, and the results (a reduced difference between responses recorded in the waking state as contrasted with those during sleep) suggest that the functioning of the reticular activating system is impaired in many retarded patients, even in the absence of gross structural brain damage.
Supported in part by NIMH grant MH-08667 and Career Program Award K3-MH-22,553-01.

THE INFLUENCE OF AFFERENT VAGAL STIMULATION UPON CORTICAL AND SUBCORTICAL ACTIVITY. M. H. Chase and M. B. Sterman (intr. by C. D. Clemente). Depts. of Anatomy, Physiology, and the Brain Research Inst., Univ. of Calif., Los Angeles, and VA Hosp., Sepulveda, Calif.

High-frequency, low-voltage stimulation was delivered to the cut central end of the cervical vagus nerve in the acute, locally anesthetized cat while cortical and subcortical CNS sites were being monitored. At the cortical level vagal stimulation resulted in bilateral EEG synchronization which occurred after a latency of 10 to 40 seconds. Subcortical sites such as the hippocampus, amygdala and centralis lateralis displayed patterns of activity similar to those typically seen correlated with EEG synchronization during behavioral sleep. Hippocampal theta activity was immediately abolished upon the onset of vagal stimulation. This occurred irrespective of concomitant cortical synchronization, however, hippocampal theta was never observed during cortical spindling. These responses have also been induced in encéphale isolé preparations with cervically severed vagal and sympathetic trunks, lending credence to the belief that they are of neurogenic rather than peripheral humoral in origin. These experiments emphasize the influence of visceral afferents on cortical and subcortical patterns of wakefulness and sleep. (Supported by USPHS grants MH-10083 and MH-07037.)

ADAPTATION OF THE CAROTID BODY TO A RAPID CHANGE IN PCO_2. V. Chernick† W. A. Hodson* and R. E. Dutton, The Johns Hopkins University, Baltimore, Md.

If the peripheral chemoreceptors exhibit rapid accommodation to a given increment in P_aCO_2, this could account for the finding that an oscillating P_aCO_2 produces a greater ventilation than a non-oscillating P_aCO_2 of the same mean level (Dutton et al., Fed. Proc. 24: 272, 1965). This hypothesis was tested in the anesthetized dog using three stimulus levels (ΔPCO_2 of + 15, 31, and 49 mm Hg). Stopcocks were positioned in each carotid artery so that the carotid body could be perfused by the dog's own blood or quickly changed to manual perfusion of hypercapneic, normoxic blood for periods of 20-30 seconds. Infusions were made from syringes kept at body temperature, without altering carotid artery pressures. All levels of ΔPCO_2 produced an abrupt rise in breath-by-breath ventilation ratio (VR). The peak VR was higher and was reached more quickly with the largest ΔPCO_2. Adaptation occurred rapidly at all three levels within seconds after the peak VR was attained, but VR remained above control values. VR adapted /VR peak was .89, .74, and .67 for ΔPCO_2 of 15, 31, and 49 mm Hg respectively. The possibility that apparent adaptation was caused by a fall in the PCO_2 of the blood perfusing the aortic bodies was ruled out by experiments in which end-tidal PCO_2 was held constant by suitable adjustment of inspired CO_2. It is concluded that stimulation of the carotid body results in a peak ventilatory response proportional to P_aCO_2. With maintenance of a given carotid artery PCO_2 rapid adaptation occurs, the degree of which is proportional to the ΔPCO_2.

METABOLIC RATE AND BODY TEMPERATURE IN POCKET MICE (PEROGNATHUS SPP.). Robert M. Chew, Robert G. Lindberg* and Page Hayden*. Northrop Space Laboratories, Hawthorne, Calif.

Six species were studied at ambient temperatures of 0-37°C: P. flavus (7.5g), longimembris (8.2), amplus (12.8), intermedius (13.0), formosus (18.3) and baileyi (30.6). These are all desert-inhabiting species which become hypometabolic at low temperatures or when denied food; flavus and longimembris are among the smallest of mammals. Longimembris can maintain a stable core temperature at T_a 0-34°C, but variations of 1.5°C in an hour and 5° in a day are common in normally metabolic mice. At T_a 10°C, core temperature is a function of metabolic rate. Longimembris seems to have four zones of temperature regulation. Metabolic rates of the six species form a family of curves. Average maintenance rate over 12-24 hr varies from $Y = 15.01 - 0.41X$ for flavus to $Y = 7.27 - 0.19X$ for baileyi (Y = ml O_2/g hr, X = T_a °C). Total conductance ranges from 0.40 ml O_2/g hr for flavus to 0.18 for baileyi. Physical conductance in dead mice was 0.014 cal/cm^2 min °C for longimembris and 0.012 for formosus. Lower critical temperatures vary from T_a 29.5°C for baileyi and formosus to 35°C for longimembris. There is a sharp increase in metabolic rate at a body wt of about 10.0 g; extrapolation suggests a theoretical limit to body wt of Perognathus of 2.5-3.5 g. These pocket mice have metabolic rates only half those predicted by metabolic formulae developed for nondesert-inhabiting mammals. The insulative values of their pelages may be higher than other temperate zone mammals. Both characteristics are adaptive to habitats such as deserts where there are chronically limited food supplies. (Work supported by NASr91).

CONTENT AND DISTRIBUTION OF POTASSIUM AND CREATINE IN RATS. K. S. K. Chinn (intr. by G. J. Klain). U.S. Army Med. Rsch. and Nutr. Lab., Denver, Colorado.

Only limited information is available on the content and distribution of potassium and creatine between the muscles and remaining tissues of the body. Consequently, the quantities of potassium and creatine as well as protein in the muscles, and the remaining body tissues were determined in each of 40 male (39 to 247 days old) and 12 female (45 to 108 days old) rats. Muscle potassium averaged 0.405±0.028 mEq/g protein with no age or sex differences being apparent. The potassium content of the remaining tissues, however, was highly age dependent, ranging from 0.342±0.038 mEq/g protein in young rats (39 to 69 days old) to 0.301±0.028 mEq/g protein in adult rats (70 days and older). The creatine content of muscle was age dependent, ranging from 22.18±3.57 mg/g protein in young rats to 25.49±2.21 mg/g protein in adult rats. The creatine content of the remaining tissues was independent of age and averaged 6.33±1.33 mg/g protein. No significant sex differences were obtained. In all adult rats, an average of 55.58±2.32% of total body potassium and 78.81±3.64% of the total body creatine were found in muscle.

Neurogenic Control of Thrombolysis - M. H. Cho and B.K. Kim *
Upstate Medical Center, Syracuse, New York

The effect of innervation on thrombolysis was examined in the marginal ear vein of rabbits by denervating one ear and then inducing thrombi in both ears. Transection of the auricularis magnus nerve produced a more rapid thrombolysis in the operated ear up to 3 weeks postoperatively as compared to the control ear. After 4 weeks, this difference between ears disappeared and a reversal occurred. Simultaneous transection of the auricularis magnus and a superior cervical sympathetic ganglion showed essentially similar results, although the accelerating effect on thrombolysis remained after 4 weeks. Ganglionectomy alone had relatively little effect on thrombolysis as compared to section of the auricularis magnus. When denervation via transection, or crushing, or alcohol or dibucaine injection followed thrombi induction, the lysis of the treated side was markedly accelerated as compared to the control. It was concluded that there is neurogenic control of thrombolysis in the rabbit ear vein which is mediated predominantly by the sensory nerve auricularis magnus.

EFFECTS OF EPINEPHRINE, ACETYLCHOLINE, Ca^{++}, Mg^{++}, and K^{+} ON INTESTINAL COMPLIANCE AND VASCULAR RESISTANCE. C. C. Chou*, J. B. Scott*, F. J. Haddy and J. M. Dabney*. Univ. of Okla. Med. Center, Okla. City, Okla.

The effects of epinephrine (Epi.), acetylcholine (Ach.), Ca^{++}, Mg^{++}, and K^{+} on the compliance (C) of the ileum were studied simultaneously with their effects on ileal vascular resistance (R), in 18 dogs. A segment of ileum containing a flaccid rubber balloon was perfused at a constant flow (Circulation Res. 14:234, 1964). Perfusion pressure and ileal intraluminal pressure were measured at balloon volumes of 0, 5, 10, 15, 20 and 30 ml of water. Ileal compliance (ml/mm Hg) and vascular resistance (mm Hg/ml/min) were calculated before, during, and after I.A. infusion of isotonic solutions of Epi. (0.2 µg/min), Ach. (10 µg/min), $CaCl_2$ (0.5 ml/min), $MgCl_2$ (0.5 ml/min), and KCl (1 ml/min).

		Before		During		After		
	N	C	R*	C	R	C	R	
Epi.	10	0.88	7.81	2.15**	7.73	1.24	8.17	* at 0
Ach.	4	1.03	8.24	1.79	6.43	1.51	9.08	balloon
$CaCl_2$	10	1.12	8.45	2.10**	8.09	0.97	8.19	volume.
$MgCl_2$	10	1.07	8.37	1.65**	6.03**	1.12	8.74	
KCl	10	1.00	7.96	1.04	9.16	1.04	8.53	**$p < 0.05$.

Epi. and Ca^{++} increased C without affecting R while Mg^{++} increased C and decreased R. At the infusion rates used the changes with K^{+} and Ach. were equivocal.

We suggest that these changes in ileal compliance reflect changes in ileal smooth muscle tension and thus changes in extravascular and transmural pressure. Thus a fall in extravascular pressure may have attenuated the effect of Epi. and Ca^{++} but supplemented the effect of Mg^{++} on vessel caliber. The total effect on blood flow through the ileum produced by a particular agent may be determined by its effect on both visceral and vascular smooth muscle.

A Microelectrode Study of the Effect of Pitressin on Electrical Properties of Toad Bladder, Tushar K. Chowdhury* and Fred M. Snell, Dept. of Biophysics, State Univ. of N.Y., Buffalo, N. Y.

It is well recognized that in normal Ringer's solution, addition of pitressin to the serosal bathing fluid causes a large increase in the short-circuit current exhibited by the toad bladder but a proportionately smaller increase in the transbladder electrical potential difference. The net result in resistance is that of a decrease. This has been hypothesized by several investigators to be due to an increase in the permeability of a passive barrier near the mucosal surface. We have undertaken a study utilizing microelectrodes which have been inserted to different depths within the active region (that region associated with the origin of electrical potential) of this tissue and held in position. The electrical properties have been then measured, first in the absence and then in the presence of pitressin. The results clearly indicate that there is a decrease in the resistance not only in the region between the mucosal surface and the tip of the microelectrode but also in the region between the tip of the microelectrode and the serosal surface.

(Supported by USPHS Research Grant No. GM 06730)

A TECHNIQUE FOR THE QUANTITATIVE STUDY OF CAROTID SINUS BEHAVIOR. B.N. Christensen*, T.A.Pryor* and H.R.Warner, Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S.Hosp., Salt Lake City, Utah. Supported by a grant from NIH #FR 00012.

A 3-stage computer program has been written to facilitate the quantitative study of input/output relationships of the carotid sinus. The input to this organ is the time course of pressure in the artery and the output is defined as the time course of frequency of firing of a single fiber of carotid sinus nerve. The first stage of the program generates an amplitude histogram from direct input of action potentials from the animal to determine the presence of a single fiber preparation. If the histogram indicates more than one fiber, the computer system can often be used to discriminate a single fiber. Phase two samples pressure at a rate of 100 samples/second and measures the time interval between successive action potentials. The time course of firing rate is then determined from these intervals over each heart cycle and averaged with the time course of all preceding cycles. These frequency and pressure waveforms are continuously displayed on a scope. When the average time course of frequency of firing becomes stable the waveforms can then be stored on digital tape for further analysis. Many such records can be calculated from a single experiment and later used for analysis by phase three of the program. This phase is designed to test mathematical models which predict the firing rate from arterial pressure and rate of change of pressure. Parameters for a model can be entered from a typewriter and modified to optimize the agreement between predicted and recorded frequency. When parameters for one wave have been found the model using these parameters is tested by predicting subsequent curves in the same and other experiments. In this way parameter variation and correlation can be investigated.

THE MECHANISM OF PYRAMIDAL TRACT EXCITATION IN MOTOR CORTEX STIMULATION. M. H. Clare, G. H. Bishop and W. M. Landau. Dept. of Neurology, School of Medicine, Washington University, St. Louis, Mo. 63110.

In adult cats the pyramidal tract response to stimulation of motor cortex at the surface and at various depths, using gross and fine electrode combinations, is analyzed, with particular emphasis upon threshold and latency determinations. The effects of polarization upon the responses of units recorded locally in motor cortex are also determined.

When the motor cortex is stimulated by the usual monopolar or bipolar electrodes applied to the pial surface, the D-wave results from primary excitation of PT axons in the deep cortex or subcortical white matter. Some slower conducting axons that are also directly stimulated probably underlie the I-waves. The I-wave complex is predominantly the result of excitation of cortical afferent fibers in the deep cortex or subcortical white matter. The cortical response associated with projected PT volleys is therefore analogous to the evoked cortical response of specific thalamocortical radiation excitation.

The implications of these conclusions for motor cortex and other central nervous system stimulation are discussed.

SPINAL PATHWAY FOR SHIVERING. George Clark, Margaret M. Powers* and Gorman H. Daron*. Civil Aeromedical Research Institute and University of Oklahoma Medical School.

Although recent reviews stress reticulo-spinal, rubrospinal and tectospinal tracts as possible pathways for shivering little experimental work has been done. In four cats large midline lesions designed to destroy any crossing fibers in the region of the red nucleus were made. Shivering as a result of exposure to cold occurred in all of these. Thus neither the tectospinal nor rubrospinal tracts are essential for shivering. In another series of cats various portions of the spinal cord were destroyed in the upper thoracic region. These animals were exposed to 5°C and checked to determine presence of shivering above and below the lesion. Study of the lesions indicated that the pathway must lie in the medial half of the dorsal half of the lateral columns. Normal bladder function and voluntary motion may occur when shivering is lost below the lesion.

EFFECT OF TEMPERATURE AND IONIC COMPOSITION ON TRANSIENT POTENTIAL RESPONSES TO STEP CURRENTS IN FROG SKIN. J.S.Clark (intr. by H.R.Warner) Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S. Hosp., Salt Lake City, Utah. Supported by a grant from the Utah Heart Assoc.

Transient potential responses across frog skin (Rana Pipiens) to step currents were studied by substitution of the outside bathing solution cation from the alkali series and by varying temperature. An Ussing frog skin preparation was used. Step changes in current were achieved by electrodes in outside and inside solutions connected to a constant current source. Sulphate ringer was used on the inside of the skin.

Following a step change in current density (ΔJ) through the skin, the potential change (ΔE) across the skin obeyed

$$\Delta E = \Delta J \{A+B(1-EXP(-t/BC))\} \qquad \text{Equation (1)}$$

for a time equal to 2 to 5 time constants. The extent to which equation (1) was obeyed was apparently determined by the time constant and magnitude of longer term transients. C was constant for a given skin, varying over all experiments from 2.3 to 4.6 $\mu fd/cm^2$. On the other hand, B normally varied in a given skin with changes in outside cation and temperature by a factor of 4. Compared to B, A was small and more than half of its value was due to the resistivity of free solution between the recording electrodes.

Equation (1) suggests that the potential changes result mainly from a single diffusion barrier. Cations of the alkali series fall into two definite classes in regard to their effects (temperature included) on B and on the smaller amplitude but slower transients. The first class contains Na^+ and Li^+, while K^+, Rb^+ and Cs^+ constitute the second. The effects of temperature on B provides a basis for analysis of diffusion differences between the two classes.

AN EARLY ACTION OF THYROTROPHIC HORMONE ON THYROID SEROTONIN LEVELS. Judith A. Clayton* and Clara M. Szego, Dept. of Zoology, Univ. of Calif., Los Angeles.

As part of a continuing investigation of the stimulatory influence of trophic hormones on their target organs through altered metabolism of endogenous vasoactive amines, the response of serotonin to TSH was studied in the rat thyroid. At autopsy, each thyroid was divided between two pools of tissue from identically treated animals. Two sets of 8- to 15-lobe pools, one set from saline- and one from TSH-injected animals, were analyzed simultaneously. Serotonin was extracted, partially purified and analyzed by bioassay on Venus mercenaria heart. Four hr after IV administration of 1 to 2 IU TSH per 100 g BW to intact, 1 month old male rats sensitized by 8 days' thyroxine pretreatment, serotonin declined significantly from saline-injected control levels of 3.937 ± 0.246 to 3.043 ± 0.260 $\mu g/g$ fresh wt; $P < 0.025$. Duplicate pool values agreed to 7.3% (avg). Concomitantly, thyroid water increased significantly ($P < 0.005$). A dose of ACTH 20 to 40 times in excess of that calculated as maximum contaminant in the TSH preparation administered failed to elicit a thyroid serotonin response. The results are consistent with the suggestion that serotonin, possibly in concert with other vasoactive substances, may participate in the early hyperemic response to TSH. (TSH was a generous gift of the Endocrinology Study Section, NIH. Supported by USPHS predoctoral fellowship 5 F1 GM-18,989 and by grant CA-01488 from the NIH.)

MUCOSAL AND TOTAL BLOOD FLOW IN HOLLOW ORGANS. R.F. Coburn*, M.Swerdlow*, K. Luomanmaki* and R.E. Forster. University of Pennsylvania, Phila., Pa.

Theoretically it should be possible to calculate the superficial blood flow in the wall of a hollow viscus from the rate of disappearance of CO from the lumen, provided the Pco in the lumen gas (Pco_b) is great enough so that end-capillary blood in the superficial vessels is saturated with CO. The use of CO should have the advantage over an inert soluble gas, in that it is bound to hemoglobin and not likely to leave the blood or diffuse down into deeper tissues. We have investigated CO uptake in the urinary bladder in twenty 12 to 15 Kg anesthetized dogs. The ureters were ligated, the abdomen closed, a polyethylene urethral catheter inserted, and varying concentrations of CO in N_2 or O_2 injected into the bladder. Gas was sampled every 5 minutes and analyzed with a gas chromatograph, and fluxes of the various gases determined from the product of the change in gas percentage with time and the gas volume which was measured by Ne dilution. The rate of CO uptake ($\dot{V}co$), with bladder volumes of 60 to 80 ml, varied from 0.022 to 0.230 ml/min STPD. $\dot{V}co$ was proportional to Pco_b in the range 3 to approximately 480 mmHg suggesting that CO uptake in this range was limited by diffusion. In the range Pco_b 480 to 704 mmHg, $\dot{V}co$ (a) remained constant; (b) decreased significantly during epinephrine infusion and following ligation of 2 of the 4 vesicular veins; (c) was stopped by circulatory arrest; (d) did not change significantly when the mean capillary Po_2 in the gas exchange vessels was increased an average of 90 mmHg by oxygen breathing; and (e) did not change as a result of varying bladder volume from 35 to 100 ml. These results are evidence that CO uptake is limited by blood flow over this range of Pco_b. "Mucosal" blood flow, calculated from $\dot{V}co$ at Pco_b equal to 600 mmHg and the blood CO capacity, averaged 0.94± SD 0.08 ml/min. Total vesicular blood flow, calculated in 5 experiments from $\dot{V}co$ and the venous-arterial CO difference using the Fick Principle, averaged 4.4± SD 0.5 ml/min.

THE USE OF POSITRON EMITTER IN THE DETERMINATION OF CORONARY BLOOD FLOW IN MAN. A. Cohen,* E. Zaleski,* E-D Luebs,* and Richard J. Bing. Wayne State University School of Medicine, Detroit, Michigan.

The measurement of coronary blood flow using a positron emitter, Rubidium-84, and a coincidence counting system has been carried out on individuals with and without arteriosclerotic heart disease. The effect of nitroglycerin on coronary flow has also been studied. With this method the activity of the heart muscle alone is measured. The coronary sinus is not catheterized, and the coronary flow is measured in absolute units. The accuracy of the method has been established by comparing the results with those obtained on the isolated dog heart. All calculations are performed by a digital computer.

Fifty-six patients without and 23 with arteriosclerotic heart disease were studied. Individuals without arteriosclerotic heart disease were divided according to age (above and below 40 years) and sex. The coronary flow in individuals below 40 was 258 ± 14 ml/min. and above was 242 ± 16 ml/min. ($P>.90$). The coronary flow in males was 236 ± 14 ml/min. and in females 262 ± 17 ml/min. ($P>.90$). The coronary flow in arteriosclerotic heart disease patients was 222 ± 16 ml/min. and in normals 250 ± 15 ml/min. ($P>.90$).

Nitroglycerin was administered sublingually to 14 patients with and 22 patients without arteriosclerotic heart disease. In individuals without arteriosclerotic heart disease, nitroglycerin increased the coronary flow 41 percent during the first 7 minutes ($P<.001$) and 62 percent during the remaining 7 minutes ($P<.005$). In arteriosclerotic patients the drug failed to raise the coronary flow; the average decline was 17 percent ($P<.05$). Papavarine failed to alter the coronary flow. Isoptin was effective in increasing the coronary flow in normals, while the effect of Intensain was less consistent.

INTRATHORACIC IMPEDANCE CHANGES DURING HEAT EXPOSURE. Bernell Coleman, Alrick B. Hertzman and Louis S. D'Agrosa*. St. Louis University School of Medicine, St. Louis, Missouri.

Intrathoracic impedance pulses were determined in 6 normal, semi-nude subjects exposed to elevated ambient temperature (43° C). The plethysmograph arrangement was a four electrode system. Two electrodes were placed around the base of the neck and a single electrode was placed around the lower thorax approximately two centimeters below the xiphosternal joint. The fourth electrode was positioned around the abdomen between the subcostal and intertubercular planes. The two outer electrodes were excited by a 100 kc constant current source and the impedance changes due to cardiac activity between the two inner electrodes were recorded. Comparison of results obtained before (28° C) and during heat exposure showed the following changes: Impedance pulse amplitude (Δz) increased by 40 percent; impedance changes (Δz) during the cardiac cycle were 0.1 and 0.18 ohms, respectively. A slight increase was also noted in total intrathoracic impedance (Z). These impedance changes showed a close temporal relationship with increases in cutaneous opacity pulses, skin temperature and onset of sweating. Increases in cardiac output, calculated from the relation, stroke volume/total thorax volume = impedance pulse/total impedance, were due almost entirely to the increase in stroke volume. Supported by AF contract and USPHS Grants HE-04939 and HE-07070.

INTRACELLULAR RECORDING FROM CAT SPINAL MOTONEURONS IN POST-ASPHYXIAL RIGIDITY. H. Collewijn* and A. Van Harreveld. California Institute of Technology, Pasadena, California.

After asphyxiation of the lumbosacral spinal cord in cats for 30-35 minutes, permanent extensor rigidity of the hindlimbs may develop in the ensuing weeks. Intracellular recordings were made from motoneurons in such preparations. Neither the membrane potential nor the appearance, threshold and latency of the spikes elicited by orthodromic, antidromic and direct stimulation were different from those in motoneurons of normal cats investigated with the same method. There was, however, evidence of increased excitability of the motoneurons. Stimulation of the dorsal root was often followed by two soma spikes. The second one may have been elicited by multisynaptic activity. Also "spontaneous" repetitive activity was observed. The "spontaneous" spikes were elicited by small irregular transitory depolarizations with the appearance of EPSP's. Membrane potentials declined after circulatory arrest at a rate of 3-4 mV per minute; complete recovery after reoxygenation was observed. The excitability was greatly enhanced after the soma had depolarized moderately. The complete sequence of events during acute asphyxiation and the recovery therefrom was observed in a few cases in which the intracellular position of the electrode was maintained throughout the whole period. In contrast to observations on normal cords, it was found that in rigid animals the orthodromic excitation was unusually resistant to asphyxia, and survived at least as long as antidromic and direct excitation. EPSP's had not completely disappeared after 20 minutes of oxygen deprivation. These findings agree with earlier observations on the asphyxial survival of spinal reflex activity. (Supported by grants from the Office of Naval Research, Nonr-220-34, and from the Netherlands Organization for the Advancement of Pure Research.)

DYE DILUTION CARDIAC OUTPUT MEASUREMENTS IN DOGS WITH DENSITOMETER, RECORDER AND COMPUTOR. W.D. Collings and R.A. Wolthuis.* Department of Physiology, Michigan State University, East Lansing, Michigan.

Dogs were prepared with in-dwelling polyethylene catheters in a jugular vein and a carotid artery. The tip of the venous (injection) catheter lay in the right atrium or right ventricle. The arterial (collection) catheter tip was in the aortic arch or close to it. Dye (indocyanine green) dilution curves were produced with a densitometer (Gilson, DTL) and servo-recorder (Gilson) combination. Curves were analyzed by Hamilton's method. These data are compared with cardiac output values obtained on the same dogs using a Sanborn Model 130 cardiac output computer. It was immaterial whether recorder and computer were connected in series or used independently. Computer cardiac output values ranged from 5% above to 3% below results from the densitometer-recorder combination. When all determinations were averaged, computer cardiac output values were 1% higher than densitometer results. This is based on an average minute volume output of about two liters in dogs weighing 10.5 to 14 kg. The advantage of the computer is in its capacity for repeated heart output measurements in a relatively short time. (Supported by NASA Grant N_8G 516.)

ELECTROLYTES IN GASTRIC JUICE AFTER ADRENALECTOMY AND GLUCOCORTICOID ADMINISTRATION. A. R. Cooke* and M. I. Grossman. Vet. Adm. Center, Los Angeles, Calif. U.S.A.

Using histamine and gastrin as secretory stimulants studies were made on the electrolyte composition of gastric juice from dogs with Heidenhain pouches. It was found that $[H^+]$ was related to $[Na^+]$ in an inverse rectilinear manner but unrelated to $[Cl^-]$ or $[K^+]$. The $[Cl^-]$ tended to have relatively fixed values in the presence of varying $[H^+]$. After bilateral adrenalectomy (DOCA or saline maintenance therapy) the electrolyte concentration and relationships were virtually unchanged but volume rate of secretion was markedly reduced with histamine stimulation. When small doses of glucocorticoids were given to the adrenalectomized animal the volume, $[H^+]$, $[Cl^-]$, $[K^+]$ rose to values significantly higher than those obtained in the intact animal and the $[Na^+]$ fell. In a further series of Heidenhain pouch dogs with intact adrenals, glucocorticoids in large doses were given. Electrolyte values were not significantly altered. These results suggest that mineralocorticoids have no effect on the electrolyte composition of gastric juice of adrenalectomized dogs and that glucocorticoids have an effect only in the adrenalectomized animal.

EFFECT OF TRAUMA AND LOW VISCOSITY DEXTRAN (LVD) ON RED CELL CHARGE. Richard Corley and Norman R. Joseph, (Intr. by W.C. Shoemaker), Dept. of Surg. Res., Cook County Hospital and Dept. of Chemistry, College of Pharmacy, U. of Illinois.

The density of negative colloidal charge of erythrocytes was measured using electrometric techniques of Joseph et al. (Biochimica Biophysica Acta 8:575, 1952). An electrical potential (E) was established at a boundary between .15 M NaCl and 2 ml. of packed red cells buffered at pH 7.4. It was measured in millivolts. The 0.15 M NaCl was then replaced by 0.015 M NaCl, and the displaced potential reading (E') determined. The difference between (E) and (E') is termed the "dilution potential" (E_d). The density of the negative colloidal charge or (x), expressed as equivalents of negative colloidal charge per/kg blood may be calculated from the observed values of the dilution potential using the approximation formula $E_d = - 11.8 + 197x$. The constant -11.8 represents the calculated value of the dilution potential at an aqueous boundary at 25°C, and the proportionality factor 197 represents the standard mobilities of Na and Cl. The average red cell dilution potential measured in cells from 11 normal patients was -1.7 mV; this increased to +0.3 mV after the administration of low viscosity dextran (mean molecular weight 40,000) 1.4 gm/kg. Dilution potentials were obtained in using red cells of 14 postoperative surgical patients, the average being +1.8 mV; this increased to +4.4 mV after administration of LVD. The administration of LVD to the normal subject resulted in an average increase of 30% in the calculated density of the negative colloidal charge. LVD produced a 20% increase in the colloidal charge of erythrocytes of posttraumatic patients. The latter was proportionally less, since the baseline potential of the traumatized patient was higher than the normal subject.

The Cause of Death in Parabiosis Intoxication. E.A. Cornelius* and C. Martinez, Dept. of Physiology, Univ. of Minnesota, Mpls., Minn.

Evidence has been presented previously that both anemia and homologous disease are etiologic factors in parabiosis intoxication. (Cornelius, E.A., et al., The Physiologist, 7, No. 3, Aug., 1964) This report deals with further investigations of this syndrome. Mice of the A strain were placed in parabiosis with ($AxC_{57}Bl/1$) F_1 hybrids (group I). Similar pairs were separated 6 and 10 days after union (II). The following controls were used: F_1 hybrids suffering from homologous disease (III), F_1 hybrids subjected to daily bleeding (IV), F_1 hybrids in parabiosis with F_1 hybrids (V), and normal F_1 hybrids (VI). The hybrid partners in group I showed a bimodal mortality curve, most of the deaths occurring one week or two weeks after parabiosis. Separation at 6 days (group II) eliminated the first mortality peak. Separation at both 6 and 10 days shifted the second peak slightly in the direction of longer survival. Temperature and weight studies in the homologous disease controls (III) showed cyclic changes: the initial decrease in these parameters corresponded temporally to the first mortality peak of the hybrid parabionts, and the second decline ended in death of the animals at a time corresponding to the second peak. It is suggested that the same cyclic phenomenon occurs in parabiosis intoxication - the second mortality peak being due primarily to homologous disease, and the first to the initial immunologic attack of the parental strain cells on a hybrid mouse greatly weakened by blood shunting to the parental strain partner.

COMPARATIVE ELECTROLYTE EXCRETION PATTERNS DURING CONDITIONED ANTIDIURESIS AND IN RESPONSE TO EXOGENOUS VASOPRESSIN. S. A. Corson, E. O'L. Corson,* J. S. Fleming,* and S. Vanecko.* Lab. of Cerebro-visceral Physiology, Department of Psychiatry, Ohio State University College of Medicine and College of Pharmacy, Columbus, Ohio. Conditioned antidiuretic responses (CAR) were developed in hydrated dogs be reinforcing tones with electrocutaneous stimuli to a foreleg. The urine during the CAR had an osmolality of 1200-2200 mOs/L and a high urea concentration, but low concentrations of electrolytes (particularly Na and Cl) that could not be accounted for by changes in glomerular filtration rate (GFR). In contrast, injections of 8-arginine vasopressin Sandoz or of USP posterior pituitary reference standard (0.6-1.2 mU/kg) in unanesthetized trained dogs led to an antidiuresis accompanied by high concentrations and high minute outputs of Na, Cl, and K. This would suggest that in CAR, in addition to vasopressin release, other factors may be involved, e.g., catecholamines. Berne et al. (Am. J. Physiol. 171:564, 1952) reported Na retention in response to catecholamine injections in dogs even in the presence of elevated GFR. Nickel et al. (J. Clin. Invest. 33:1687, 1954) reported diminished electrolyte excretion without change in urine flow when l-norepinephrine was given to human subjects during an antidiuresis produced by pitressin infusions. The participation of these factors in CAR is being investigated. (Supported by grants from the National Institutes of Health, Central Ohio Heart Association, and Hoyt Foundation.)

DISTRIBUTION OF TRANSIT TIMES THROUGH CORONARY AND RENAL CIRCULATION. C.M.Coulam* and H.R.Warner, Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S.Hosp., Salt Lake City, Utah; E.H.Wood, and J.B. Bassingsthwaighte, Dept. of Physiology, Mayo Clinic and Univ. of Minn., Rochester, Minn. Supported by a grant from NIH, #HE 04664.

A mathematical model of the circulation has been developed which allows for calculation of the fraction of cardiac output traversing an organ from a knowledge of the distribution of transit times of an indicator through that pathway (Annals of N.Y.Acad. of Sciences, 115:721, 1964). In the present study, a technique is described which allows for the determination of these transit time distributions from simultaneously recorded upstream (aorta) and downstream (coronary sinus or renal vein) time course of cardio green dye. Each curve is first converted to a Fourier series and the transfer function H(n) determined as the ratio of downstream amplitude to upstream amplitude for each harmonic component. H(n) is then converted back to the time domain to obtain the unit impulse response function h(t) which by definition is the desired distribution of transit times. Comparison of the downstream curve with the convolution of h(t) and the upstream curve provides a test of the accuracy of h(t). Mean transit times of a dog anesthetized with morphine and nembutal were 8.2 seconds and 6.76 seconds for the coronary (TC) and renal (TR) circulation. During infusion of acetylcholine into descending thoracic aorta, TC increased to 9.41 seconds while TR fell to 6.01 seconds. With infusion of adenosinetriphosphate TC was 8.13 seconds and TR was 5.67 seconds. Attempts were also made to measure distribution of transit times from aorta to pulmonary artery during these maneuvers.

DEHYDRATION AND MUSCULAR WORK. F.N.Craig and E.G.Cummings. US Army EA Chemical Research and Development Laboratories, Edgewood Arsenal, Md.

Maximal oxygen intake and endurance in grade walking in a warm environment (46 C dry bulb, 23 C wet bulb) were compared before and after six hours of sweating at rest with and without restriction of water intake. In nine men the average dehydration was 4.3 per cent of the body weight with restricted water intake and 1.9 per cent on a second day with unrestricted water intake. Walking time was reduced by 48 per cent on the first and 22 per cent on the second day. Maximal oxygen intake was reduced by 27 per cent on the first day and 10 per cent on the second. Oxygen intake and heart rate increased progressively during the walks. Final heart rates averaged 197 on the first morning (AM1), 202 on the first afternoon (PM1) and 198 on the second afternoon (PM2). The following comparisons were made at the time of the end of the PM1 walk: respiratory exchange ratio was 0.99 (AM1), 0.98 (PM1) and 0.99 (PM2); oxygen intake (l/min) was 2.72 (AM1), 2.81 (PM1) and 2.81 (PM2). Reduction in walking time was better correlated with increase in rectal temperature (0.84), decrease in fraction of carbon dioxide in mixed expired air during work (0.82) and increase in heart rate in standing before work (0.82), than with dehydration (0.63). Reduction in maximal oxygen intake is considered to be secondary to reduction in walking time; the latter was greater than the former because of the shape of the curve relating time and oxygen intake. Attainment of the same final heart rates validates the voluntary endpoints for walking, and suggests that the limitation on walking time is related to the circulation. Since the respiratory data provide no evidence of increased lactic acid production or decreased capacity for oxygen intake, they appear to rule out the working muscles as the site of the limitation.

EXAMINATION OF SINGLE CELLS WITHIN CAT BRAIN STEM FOR ADAPTATION TO ANGULAR ACCELERATION. George H. Crampton (intr. by A. D. Keller). US Army Medical Research Laboratory, Fort Knox, Kentucky.

Vestibular nystagmus of cat and man does not show a decline during prolonged constant angular acceleration. A decided decline or adaptation is found, however, in human psychophysical intensity judgments of the same stimulus. In this experiment, the electrical activity of cells within the vestibular nuclei in anesthetized cats was examined to determine if adaptation is evident at that level. The head was centered over the vertical axis of rotation, and a microelectrode advanced according to stereotaxic coordinates into the region of the vestibular nuclei. Small electrode adjustments were made to locate and isolate a single cell which responded to gentle hand driven horizontal oscillations of the turntable. Then, repeated long duration constant angular accelerations separated by five minute intervals were employed during a recording period of more than one hour. Each electrode tip location was subsequently confirmed histologically. Thirty-five units from 34 animals were studied. One cell response was too variable to classify. The discharges from 15 cells showed no adaptation whatsoever during accelerations of up to 45 seconds duration, and in this respect correlate well with nystagmic functions. The remaining 19 units displayed a limited adaptation and more nearly agree with the time course of the human psychophysical response.

Color Vision in the Antelope Ground Squirrel

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This squirrel has a yellow lens and pure cone retina. The spectral sensitivity curve based on the b-wave of the ERG is complex with a peak in the region of 480 nm and another at about 526 nm. Behavior studies in which different animals are conditioned to go to a blue light, a green light or an orange light and to press a bar indicate that some form of color vision is present in this ground squirrel. Certainly blue is discriminated from green, yellow, and orange. Luminosity is not the factor involved, since lights of equal luminosity were used. Smell is not the factor, since the reward (a sunflower seed) was given at a central feeding station removed from the light ports. The spectral sensitivity curve based on the off-effects of the ERG lack the peak at 480 nm. Cortical evoked potentials to colored light flashes show responses with large on- and little or no off-effects to blue light and responses with large off-effects to flashes at longer wavelengths. An on-off color mechanism is suggested by the results.

UNITARY RESPONSES OF THE LATERAL RETICULAR NUCLEUS.

E. C. Crichlow* and T. T. Kennedy. Dept. of Physiology and Biophysics, Univ. of Washington School of Medicine, Seattle.

Forepaw stimulation, during barbiturate anesthesia in cats, evokes potentials in (a) the posterolateral part of the ipsilateral anterior lobe, (b) the ipsilateral paramedian lobule and (c) the contralateral paramedian lobule of the cerebellar cortex. This somatotopic localization reportedly is mediated via the lateral reticular nucleus (LRN). Cells within this nucleus were studied with 3M. KCl. filled micropipettes to determine the relationship between the nucleus and the cerebellum. Cells isolated in LRN were found to have small peripheral excitatory fields ipsilateral to the recording site. Surround inhibition was observed. Stimulus modality of these cells encompassed both cutaneous and deep sensibilities; however, each cell exhibited definite modality specificity. With bipolar or concentric stimulating electrodes on cerebellar areas (a) and (b), antidromic stimulation was used to determine the site of termination of the axons of these LRN cells. Direct cerebellar termination was evident only within (a) the posterolateral part of the ipsilateral anterior lobe. Stimulation of (b) the ipsilateral paramedian lobule resulted in orthodromic activation. With paramedian stimulation as the conditioning stimulus and peripheral stimulation as the test stimulus, inhibition of the test response was evident with C-T intervals up to 400 msec. Reversal of the order of stimulation produced no such effect.

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ROLE OF VENTILATION IN MAINTAINING CARDIAC OUTPUT DURING POSITIVE PRESSURE BREATHING IN MAN. J. Cruz*, P. Cerretelli*, and L. E. Farhi. Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, N. Y.

It has been shown that continuous positive pressure breathing (PPB) causes a decrease in cardiac output ($\dot{Q}$) in the anesthetized animal, but the results in erect, awake man have not been adequately described. In five subjects $\dot{Q}$ was determined repeatedly (by indirect methods) at different levels of PPB. A steady state is achieved within 5 minutes and $\dot{Q}$ decreases to 60% of control values at a pressure of 25 cm H_2O. However, this decrease is not constant but is related to ventilation, an increase in the latter tending to restore $\dot{Q}$ to normal levels. Changes in $\dot{Q}$ after 5 minutes of exposure to PPB are believed to be due to changes in ventilation.

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UNIT ACTIVITY IN THE PREOPTIC REGION FOLLOWING INTRAVENTRICULAR INJECTION OF SEROTONIN AND EPINEPHRINE. D. Cunningham* and J. D. Hardy. John B. Pierce Foundation Laboratory and Dept. of Physiology, Yale University, School of Med., New Haven, Conn.

The activity level of single units in the preoptic area of the dog maintained under urethane/chloralose anesthesia have been recorded prior to and following the introduction of serotonin and epinephrine into the ventricular system. Before the injection of an agent, units were studied for their responsiveness to local temperature change by circulating water 36-41° through implanted thermodes in adjacent tissue which permitted controlled variations in hypothalamic temperature within a physiological range. "Warm" sensitive units showing a marked increase in firing rate corresponding to increase in hypothalamic temperature, were generally observed to significantly decrease their level of activity upon the intraventricular injection of both epinephrine (50μg) and serotonin (200 μg). Similar results were also obtained when these agents were studied with insensitive units in the preoptic region whose firing rates remained unchanged during hypothalamic heating or cooling. The changes in firing rates of the single units after intraventricular injection of epinephrine were similar to those previously reported for systemic injection. Small changes in body temperature were observed following both intraventricular and systemic injections. Supported in part by USPHS Grant No. NB-04655.

INFLUENCE OF X-IRRADIATION ON FUNCTIONAL DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM. J.J. Curry, G.J. Maletta, and A. Vernadakis (intr. by P.S. Timiras). Dept. of Physiology, Univ. of Calif., Berkeley.

Functional development of the central nervous system (CNS), as assessed by responses to electroshock stimulation (100 ma), was determined in rats X-irradiated in utero. Pregnant rats were exposed to 100 r (19r/min), whole-body X-irradiation at 14 days of gestation. The brain of rats reaches maturity between the third and fourth week after birth. During this period of development, the rat responds to electroshock with distinct consecutive seizure patterns. The time of appearance of the full flexor-extensor seizure pattern coincides with morphological and biochemical brain maturation. The day of appearance of the flexor-extensor seizure pattern was determined in control and irradiated progeny. Also, the duration of the flexor, extensor, and clonic components of the seizure were measured up to 45 days of age. Irradiated rats exhibited the flexor-extensor seizure at 16 (16.5-15.1) days, two days earlier than controls. Acceleration of the appearance of the maximal seizure pattern suggests altered functional development of the CNS after prenatal irradiation. After these animals became adult, hind-limb tonic extension was always longer, and tonic flexion, clonus, and total seizure were shorter in irradiated rats than in controls. After 43 days of age until the termination of the experiment at 80 days, a current of 100 ma elicited hind-limb extension in a higher percentage of irradiated animals than in controls. These data indicate that the intensity of the seizure was greater in the irradiated animals, and that prenatal exposure to X-irradiation has long-lasting effects on brain activity. (Supported by NIH and AEC.)

EVIDENCE FOR TWO FUNCTIONALLY-DISTINCT PATHWAYS FOR ACTH RELEASE: A CORTICOSTEROID-SENSITIVE AND A CORTICOSTEROID-RESISTANT PATH. —M.F. Dallman*, G.A.Hedge*, W. Halpern*, and F.E.Yates, Dept. of Physiology, Stanford Univ., Stanford, Calif.

To determine whether the adrenal cortical response to ACTH-releasing stimuli invokes open-loop or closed-loop (negative-feedback) control, we assessed the response to various stimuli in female rats in the absence and presence of very large corticosteroid feedback signals (Dexamethasone 25 ug/100 gm. B.W. S.Q. 2-4 hours before stimulation). The responses observed (increases in plasma corticosterone concentration) were of two classes. Class I consisted of complete suppression of ACTH release by Dexamethasone, and was observed following ether exposure (60 seconds), I.V. epinephrine, rupture of the tympanic membranes, burn of a hind foot, electric shock to a hind foot, or abdominal incision. Class II revealed a large corticosteroid-resistant component and was observed following hemorrhage (2% B.W.), hypoxia, laparotomy plus intestinal traction, deep neck dissection, or I.V. vasopressin. Increasing the dose of Dexamethasone to 600 μg/100 gm. B.W. did not change the frequency or magnitude of the corticosteroid-resistant component of Class II stimuli (laparotomy plus intestinal traction; hemorrhage). Hypophysectomy abolished the responses to both Classes of stimuli. All rats except those exposed to ether or hypoxia were anesthetized before stimulation. Analog computer analysis showed that a single, restricted signal, closed-loop controller with a variable setpoint input, and a separate median eminence input can account for all the responses observed. Supported by USPHS grant No. AM-04612.

Renal Response to Acute Osmotic Load in Chickens. William H. Dantzler (intr. by W.H. Sawyer). Dept. of Pharmacology. Columbia Univ., College of Physicians & Surgeons. New York, N. Y.

Chickens can produce urine only twice the osmolality of the blood. Thus, they are limited in their ability to reduce plasma osmolality by renal excretion of salt in excess of water. How, then, do chicken kidneys respond to acute osmotic loads? Following 2.5% mannitol infusion, 6% NaCl infusion was started at the same rate. Tm_{PAH}, Tm_G or both were measured during control and experimental periods. PAH was given through renal portal system (via leg vein) or through general venous system (via wing vein). GFR decreased following infusion of 20 mEq NaCl/kg and continued to fall with continued NaCl infusion while plasma osmolality and Na rose. Urine flow increased initially and did not fall below control levels until about 40 mEq NaCl/kg had been given. Uosm increased, but urine did not become hyperosmotic. Tm_{PAH} and Tm_G decreased proportionally to GFR, suggesting that changes in GFR, result from changes in the number of functioning nephrons. Infusion of PAH via renal portal system did not change the relationship between Tm_{PAH} and GFR. Tm_{PAH} decreased more than Tm_G with small decreases in GFR. This suggests that 1) decreased portal circulation to tubules precedes decrease in GFR; 2) decreased tubular flow caused increased intraluminal PAH concentration and depression of secretion or increased back diffusion. Like reptilian and amphibian kidneys, which cannot produce hyperosmotic urine, and unlike mammalian kidneys, which can, avian kidneys respond to an acute osmotic load with a decreased number of functioning nephrons. Thus, in absence of ability to excrete excess salt, they reduce GFR, conserving water and tending to reduce plasma osmolality at the expense of excretion of waste.

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LOCAL EFFECTS OF O_2 AND CO_2 ON RESISTANCE TO BLOOD FLOW THROUGH DOG LIMB AND KIDNEY. R. Daugherty*, J. Scott*, J.Dabney*, and F. Haddy, Depts. of Med. and Physiol., Univ. of Okla. Med. Center, Okla. City, Okla.

The effect of local changes in O_2 and CO_2 on the forelimb and renal vascular beds was examined with a reservoir-free system in 31 intact dogs. The animal's arterial or venous blood was passed through an isolated lung from another dog and perfused into the right brachial or left renal artery at a constant rate. Using venous blood as the perfusate, systemic arterial pressure (P_S mm Hg), brachial or renal perfusion pressure (P_p mm Hg) and P_{O2} (mm Hg), O_2 content (vol.%) and pH of the perfusing blood were measured during ventilation of the isolated lung (the ventilation to perfusion ratio was purposely set high) with 5% CO_2 - 20% O_2 - 75% N_2 (control), 5% CO_2-95% N_2 (hypoxia), 5% CO_2-20% O_2-75% N_2 (control) and with ambient air(hypocapnia). Using arterial blood as the perfusate, P_S, P_p, P_{O2}, and pH were again measured during ventilation of the lung with ambient air(control) and 20% CO_2-20% O_2-60%N_2(hypercapnia).

	Limb (flow = 103 ml/min)					Kidney (flow = 104 ml/min)					
	N	P_S	P_p	P_{O2}	pH	O_2	N	P_S	P_p	P_{O2}	pH	O_2
Control	7	105	100	114	7.35	16.0	8	91	110	129	7.28	13.5
Hypoxia	7	106	66*	2	7.37	0.9	8	88	115	6	7.31	0.7
Control	7	106	101	112	7.35		8	87	124	123	7.26	
Hypocapnia	7	99	176*	122	7.90	16.2	8	80	208*	113	7.96	11.0
	Limb (flow = 128 ml/min**)						Kidney (flow = 104 ml/min**)					
Control	10	128	116	106	7.59		6	108	108	93	7.57	
Hypercapnia	10	127	95*	118	7.18		6	107	84*	122	7.16	

*P = <0.01 relative to control; ** arterial blood.

Ventilation of the lung with 100% O_2 ($P_{O2} \simeq 650$ mm Hg) produced equivocal changes in P_p. Thus severe hypoxia decreased limb vascular resistance but had little effect on renal resistance. Limb and kidney resistances were decreased by marked hypercapnia and increased by hypocapnia.

OBSERVATIONS RELATED TO DRUG-INDUCED ALTERATIONS OF BEHAVIOR IN FIGHTING MICE. J.P. DaVanzo, M. Daugherty *, R. Ruckart * and K. Oliver *. A.H. Robins Research Laboratories, Richmond, Va.

Isolation-induced fighting behavior is commonly employed as a screening method for uncovering potential major tranquilizers. Both short term and long term isolation has been described for such purposes. This necessitates dealing with large numbers of animals. A screening method is described in which isolation and training are combined so as to increase the number of fighters produced. Once fighting behavior is established, the same animals are continuously re-used. The relative importance of training as opposed to length of isolation is demonstrated and a definite seasonal effect on the development of fighting behavior is shown. Ablation of vision does not affect fighting behavior, nor does it alter the ED50 of drugs which suppress this behavior. No difference could be demonstrated in the plasma corticosterone levels and brain biogenic amine content of fighters and their aggregated counterparts. A variety of agents, in addition to those reported by others, was shown to suppress fighting behavior.

LUNG ELASTIC RECOIL AND THE EFFECT OF POSTURE ON FUNCTIONAL RESIDUAL CAPACITY. J.T. Davidson,* G.A. Lillington,* L.B. Beilin* and K. Wasserman. Stanford University School of Medicine and Palo Alto Medical Research Foundation, Palo Alto, California.

In a study of the effects of aging on lung function in the rabbit, it was noted that the difference between the Functional Residual Capacity (FRC) in the young and old animals was narrowed when this lung volume was measured with the animals in the prone position and widened in the head-up position. As a significantly higher mean lung compliance was noted in the old animals relative to the young, the relationship between FRC and body posture was examined in rabbits with different static lung compliances. The pressure-volume curve was obtained by inflating the lungs with known volumes of air and recording the transpulmonary pressure. FRC was measured by the body plethysmograph method, values being obtained in the horizontal, 20 degrees head-up, and 20 degrees head-down positions. The results indicate that there exists a close association between loss of elastic recoil and the quantitative effect of posture on FRC. (Supported in part by the California Tuberculosis & Health Assoc. and NIH Grant No: TW 754-01)

EFFECTS OF INTRACEREBRAL DEXAMETHASONE (D) AND RESERPINE (R) ON COMPENSATORY ADRENAL HYPERTROPHY (CAH). Julian M. Davidson and Shaul Feldman*. Stanford Univ., Stanford, Cal. and Hadassah Univ. Hosp., Jerusalem, Israel.

Adrenal weight maintenance and CAH were studied in male rats following the systemic or intracranial implantation of crystalline cortisol (F), D or R. When implanted in the median eminence region of the hypothalamus, D was significantly more effective than F in inhibiting CAH, but pituitary implants of D exerted only a slight inhibition. Complete CAH inhibition and adrenal atrophy resulted from implantation of D in the posterior "septum complex" (de Groot) and neighboring thalamic and hypothalamic regions. Implants remote from this area were generally ineffective. Double subcutaneous implantation of R resulted in adrenal hypertrophy in most of the experiments performed. Bilateral implants of R in the basal hypothalamus or in the midbrain reticular formation had no significant effects on adrenal weight maintenance or CAH. It was concluded that: (1) the relative potencies of F and D as inhibitors of ACTH secretion is due, at least in part, to the relative potencies of their effects on the central nervous system; (2) the effects of intracranial implantation of crystalline corticoids cannot be explained on the basis of release of the steroids into the systemic circulation; (3) R has not been shown to affect "feedback" sensitive structures in the hypothalamus; and (4) forebrain areas remote from the median eminence are distinctly sensitive to the "feedback" action of corticoids.

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TIME-DOSE RESPONSES TO GASTRIN AND HISTAMINE IN AUTOGENOUS AND HOMOTRANSPLANTED CANINE GASTRIC POUCHES. W.D. Davidson*, I.A. Daves*, C.A.E. Lemmi*, J.H. Miller* & J.C. Thompson. Depts Surg & Med, Harbor Gen Hosp, Torrance, Cal., and UCLA Sch of Med.

Gastrin is the hormonal link in the neuro-humoral stimulation of gastric secretion, while the physiologic role of histamine is unknown. The time-dose acid and pepsin response to gastrin and to histamine was studied in 25 gastric pouch dogs divided into 4 groups: Group I (7 Heidenhain pouch (HP) dogs); II (6 HP-antrectomized); III (5 HP-denervated antral pouch); IV (7 dogs with heterotopic homotransplant of antral and fundic pouches). Pure gastrin (Gregory & Tracy, 1964) and histamine were infused on consecutive days; the rate was doubled each hour until peak gastric acid secretory response reached. Results: Ratio of maximal acid response to gastrin compared with maximal response to histamine (G_{max}/H_{max}) in different groups was as follows: I-.64, II-.46, III-.55, and IV-.96. There was no significant difference in the maximal acid response to gastrin or to histamine between any of the groups tested, although antrectomy rendered the fundic pouch more sensitive to small amounts of gastrin. Supramaximal doses of gastrin routinely inhibited acid output, a finding also noted in one-half of the histamine infusions. Gastrin, on a molecular basis, was 140-1900x (mean 650x) more potent an acid stimulant than histamine. Although pepsin output remained at high levels for long duration with both gastrin and histamine, this plateau persisted longer with gastrin. Conclusion: Histamine provoked a greater maximal acid secretory response than gastrin in 4 groups of denervated fundic pouch dogs, although gastrin was much more potent on a molar basis. Fundic pouch maximal response to gastrin was not altered by antrectomy or homotransplantation. (Supported by John A. Hartford Foundation, Inc., and by USPHS Grants # 07961 & 07962)

AUDITORY CORTICAL RESPONSES TO TONE BURSTS

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Central Institute for the Deaf, St. Louis, Missouri

For 6 normal-hearing young adults, the following relations of the slow cortical evoked response (vertex to mastoid) to certain parameters of auditory stimuli were established. The stimuli were trapezoidal bursts of a 1000 Hz tone at about 90 dB re 0.0002 μbar.

1. An "on" response is evoked by the onset of a tone burst and, if the burst is long enough, a smaller but otherwise similar "off" response by its termination. The on and the off responses interact with one another according to the intervals between them like successive responses to clicks or tone pips.

2. At both on and off the latency of the steep slope between the N_1 and the P_2 peaks, measured from the beginning of the rise (or fall) of the tone burst, is constant at about 145 msec, at least for linear rises or falls up to 100 msec.

3. For a rise-time of 6 msec the amplitude (N_1-P_2) of the response shows no clear relation to the duration of the plateau although the subjective loudness increases considerably as the plateau is increased from 0 (a tone pip) to 100 msec. (NINDB Grant B-3856)

EFFECTS OF AUTOLOGOUS AND HOMOLOGOUS BLOOD AND DEXTRAN EXCHANGE ON THE BLEEDING VOLUME OF DOGS.

S. Deavers, R. A. Huggins and E. L. Smith. Baylor Univ. Col. of Med., Houston, Texas.

Three groups of morphine-pentobarbitalized dogs were used for the experiments. One group was bled from a femoral artery, and the blood was simultaneously reinfused through a femoral vein (autologous). The second and third groups were bled and simultaneously infused with homologous blood and dextran, respectively. The volume of exchange was 500 ml for each group. Then the dogs were bled to a mean arterial pressure of 35 mm Hg. Measurements of cell and plasma volumes, venous hematocrit, protein concentration and mean arterial pressure were done before and 20 minutes after the exchange and immediately after hemorrhage. Autologous group: the only effect of the exchange was a significant rise in venous hematocrit. The bleeding volume was 34.5% of the blood volume. After hemorrhage, cell volume, total protein and concentration decreased significantly from that expected. Homologous group: no significant changes were observed after the exchange. However, these dogs bled only 26% of their blood volume to reach 35 mm Hg arterial pressure. Following hemorrhage there was a significant loss of plasma, while venous and circulatory hematocrits were above expected values. Dextran group: mean arterial pressure and cell and plasma volumes increased significantly after the exchange. The bleeding volume was 36% of the blood volume. Cells mobilized remained in the circulation; however, of the 13.3 ml/kg of fluid gained during the exchange transfusion, 9.4 ml/kg was lost after the hemorrhage. The bleeding volumes for all three groups were significantly less than a mean bleeding volume of 49% for dogs not receiving an exchange before hemorrhage.

(Supported by research grants from NIH and the Army.)

A Simplified Geometric Calculation of the Area and Mean Time of Indicator-Dilution Curves. Thomas H. Dee*, John G. Langdon*, Alfred W. Brody, and J. Raymond Johnson. Nebr. Heart Assn. Chair of Cardiovascular Research, Creighton Univ. School of Medicine, Omaha, Nebraska.

During the measurement of cardiac output by triple indicator bolus injection techniques (Fed. Proc. 21:137, '62), simultaneous calculation of the volumes of specified segments of the circulation demands accurate knowledge of the mean time for each indicator curve. Acceptable, rapid methods for calculation of the mean time by hand are needed. In addition, judgment is needed for selection of acceptable curves; such judgment may be obtained during hand calculation or planimetry of the records of the indicator-dilution curves but is not easily obtained by relegating all calculations to the more or less remote programs used by computing machinery. Rapid methods of hand calculations are therefore also needed for the area under the indicator curve and for the cardiac output, which retain and reinforce the development of judgment. Close approximation of computer results was possible by reduction of the curve to a leading triangle, a median rectangle, and a final semilogarithmic component. Readout involves measurement of only 4 values; the peak height (H_{Pk}), initial and final peak times (T_{IPk}, T_{FPk}) and the semilog half-time ($T_{\frac{1}{2}}$)(appearance time = 0). The area (A) under the curve, summing in order the triangle, rectangle, and semilog area, is: $A = H_{Pk}\left\{\frac{1}{2}T_{IPk} + (T_{FPk} - T_{IPk}) + 1.443\,T_{\frac{1}{2}}\right\}$. The mean time is expressed by:

$$H_{PK}\left\{1/3(T_{IPk})^2 + \tfrac{1}{2}(T_{IPk} + T_{FPk})(T_{FPk} - T_{IPk}) + (T_{FPk} + 1.443T_{\frac{1}{2}})(1.443T_{\frac{1}{2}})\right\}\Big/A.$$

In another field, examination of the records from chromatographic gas analysis suggests a similar good fit by this approximation, especially in curves with tailing. (Supported in part by USPHS Research Grant 09099, and Training Grant HE 5506).

Duration of Achlorhydria and Mortality Following Experimental Gastric Freezing. J. P. Delaney, M. D. *, W. P. Ritchie, Jr., M. D. *, Arnold Lande, M. D. *, Ami Barzilai, M. D. *, O. H. Wangensteen, M. D. Dept. of Surg., Univ. of Minn. Med. School, Minneapolis, Minnesota.

Controlled temperature canine gastric freezing was carried out employing;(1) perfusion rates of 3000-4000 cc/min, (2) thermocouples affixed to but insulated from the balloon, to provide a measure of mucosal temperature, (3) variable coolant temperatures, (4) 30 minute perfusion times. Factors evaluated were pitressin administration, rapid rewarming, balloon shape, and inflow dispersion device.

The use of pitressin apparently increased the incidence of fatal gastric injury. Rewarming provided a very significant protection, but the duration of histamine and insulin achlorhydria was somewhat less. A round balloon frequently caused fatal gastric injury, almost uniformly when a simple end hole inflow tube was used.

Duration and incidence of achlorhydria after stomach shaped balloon freeze.

			Mean days of achlorhydria		Incidence of initial achlorhydria	
temp. °C	rewarm	pitressin	Histalog	Insulin	Histalog	Insulin
-4(30min)	-	+	7.4	23.0	52%	57%
-4(30min)	+	-	5.0	17.8	30%	60%
-20(5min)	+	-	2.9	7.7+	31%	84%

The observation that insulin achlorhydria was more prolonged than histalog achlorhydria suggests that gastric freezing injures intramural vagal nerve endings. (Supported by a USPHS Grant, the John A. Hartford Foundation and the Donald J. Cowling Fund for Surg. Res.)

VENOLYMPHATIC REFLUX IN CHRONIC ARTERIOVENOUS FISTULA. M. K. Denney* and R. C. Read, Wayne State Univ. Coll. of Med., Detroit, Michigan

We have previously reported that chronic abdominal arteriovenous fistulae produce hematochylia. The purpose of the present study was to investigate the mechanism of this contamination of the lymph by blood. Cannulation of peripheral lymphatics in 40 dogs with variously situated AV fistulae demonstrated that the passage of red cells into lymph originates in the immediate area of the AV shunt. Lymphangiograms performed on 20 of these animals revealed networks of enlarged lymphatic channels and hypertrophic lymph nodes congested with blood. Thoracic duct side pressures were elevated up to 10 cm H_2O above normal, and lymph flow was increased 2-5 times in these animals. Higher hematocrits (1-20%) were found in the thoracic duct lymph of those animals minimally dissected during construction of the fistula. Stripping of the adventitia and ligation of all branches of the vein resulted in a decrease in the number of red cells (0-.5%). If the dissection included excision of regional lymph nodes thoracic duct lymph remained normal. Lymph from 10 normal dogs and from 10 dogs receiving sham operations contained practically no red cells. These findings indicate that greatly elevated venous pressures promote reflux of blood through preexisting lymphaticovenous communications, causing congestion of lymphatics with increased flow and elevation of thoracic duct pressure. It is suggested that this phenomenon may have a pathophysiological role in diseases in which arteriovenous shunting occurs.

CONGRUENCE OF EXCRETORY FUNCTIONS IN LIVER AND KIDNEY: SULFONAMIDES. A. Despopoulos and H. Sonnenberg.* Univ. of New Mexico School of Medicine, Albuquerque, New Mexico.

The thesis that liver and kidney possess qualitatively similar mechanisms for excretion of organic acids was tested in the isolated perfused rat liver. It was anticipated that sulfonamides which are actively excreted by renal tubules would be concentrated in the bile and that their biliary excretion would be inhibited by probenecid. Sulfonamides were identified as diazotizable amines both before and after hydrolysis, and their bile to perfusate concentration ratios were recorded. Three categories of compounds were established: (1) Compounds not concentrated in the bile and also not actively excreted by renal tubules: sulfanilic acid, sulfanilamide, N^4-acetylsulfanilamide, and N^1-benzoylsulfanilamide. (2) Compounds concentrated in the bile and actively excreted by renal tubules: N^4-acetylsulfamerazine, N^4-acetylsulfamethazine, N^4-acetylsulfathiazole, sulfisoxazole, N^4-acetylsulfisoxazole, and sulfamethylthiadiazole. (3) Compounds concentrated in the bile but not actively excreted by renal tubules: sulfadiazine, N^4-acetylsulfadiazine, sulfamerazine, sulfamethazine, sulfathiazole, metahexamide, and carbutamide. Biliary excretion of compounds in categories (2) and (3) was sensitive to inhibition by probenecid; excretion of compounds in category (1) was not influenced by probenecid. The discordant responses of liver and kidney to compounds in category (3) could be accounted for by metabolic biotransformation of the test substances; compounds which appeared in the bile were not the compounds which had been introduced into the system. Paper chromatography established that in several instances as much as 95 per cent of diazotizable amine appearing in bile represented metabolites of the original compound.

HYPOXIA ON VASCULAR SMOOTH MUSCLE CONTRACTION. Reed L. Detar* and David F. Bohr. Department of Physiology, University of Michigan, Ann Arbor.

The contractile response of helical strips of rabbit aorta to epinephrine (10^{-9}) is diminished at oxygen tensions below control levels of 100 mmHg pO_2. At 70 mmHg, contraction is 80 to 100% of control; at 30 mmHg, 40 to 70%; and at 2 to 3 mmHg, less than 10%. Decreased contraction becomes evident within 1 minute after lowering pO_2, and the time for development of half-maximal effect is less than 5 minutes. The time required for recovery is dependent on the degree and duration of hypoxia. Upon return of the tissues to 100 mmHg, 50% recovery occurs within 1 minute after a 3-minute exposure at 30 mmHg; within 5 minutes after a 3-minute exposure at 2 to 3 mmHg. Increasing the duration of hypoxia (2 to 3 mmHg pO_2) to 15 and 60 minutes, increases the time for 50% recovery to 10 and 30 minutes, respectively. These effects of hypoxia are less pronounced at high concentrations of epinephrine (10^{-5}). These results indicate that oxygen plays an important and immediate role in the processes necessary for contraction of vascular smooth muscle (Supported by NIH Grant HE 03756).

HISTOLOGICAL AND ELECTROPHYSIOLOGICAL CHANGES IN LATERAL GENICULATE FOLLOWING LESIONS OF VISUAL CORTEX.
James H. Dewson,III*, K. L. Chow, and Karl H. Pribram
Stanford University School of Medicine, Palo Alto, California

Alterations in both flash-evoked electrical activity and gliosis during retrograde degeneration in the dorsal nucleus of the lateral geniculate body were studied over 50 weeks in 32 rabbits. Six animals were prepared for chronic electrophysiological investigation and evoked potentials were obtained from both lateral geniculates through indwelling bipolar electrodes prior to and following unilateral visual cortex ablations. The remaining 26 rabbits were killed at various intervals after similar cortical removals. Results show that (1) the amplitudes of the early components of the evoked potential decrease drastically immediately following the lesioning, tending to recover within 1-2 weeks, with a further gradual decline to zero over the succeeding 3-5 weeks. (2) The number of neurons measured in areas of .0002 cu. mm (when compared with the lateral geniculates of the normal side) decreases 80% within 3 days and 95% within 4 weeks. (3) Similar measurements show that glial cell reactions are complex and differential: astrocytes show rapid proliferation with gradual return to normal, while oligodendrocytes and microglia increase more slowly, maintaining a high level over 50 weeks.
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PERMEABILITY OF MYELINATED NERVE FIBERS TO NON-ELECTROLYTE MOLECULES. F.P.J. Diecke, Department of Physiology, Univ. of Iowa, Iowa City, Iowa.

An estimate of effective pore size in myelinated axons was obtained by measuring the permeability of uncharged lipid-insoluble molecules of graded size. Small desheathed branches of sciatic nerve of frogs containing mainly large motor fibers were used because of their relatively uniform fiber population. The test molecules were: tritiated water and C-14 labeled ethanol, ethyleneglycol, urea, malonamide, glycerol, arabinose, galactose, sucrose and inulin. The rate coefficients for saturation and desaturation were determined for each test molecule to exclude transfer other than passive diffusion. The permeability coefficients and the diffusion area per unit path length ($A/\Delta x$) were then calculated from the rate coefficients. Sucrose and inulin are nonpermeable and distribute only in the extracellular spaces while the permeability of the other molecules is a function of molecular radius. If diffusion area per unit path length ($A/\Delta x$) is plotted against the molecular radius the data can be best fitted by the theoretical curves for steric hindrance in membranes with a mean pore radius of 4-4.5 A. Ethanol with a much higher oil-water partition coefficient than the other test molecules shows a significant deviation from this theoretical curve.
(Supported by USPHS Grant NB-05188.)

SWEAT CHLORIDE CONCENTRATION IN RELATION TO AGE. D. B. Dill, F. G. Hall and W. van Beaumont*. Indiana University, Bloomington, Indiana.

Chloride concentration in body sweat, (Cl), was measured in 12 men and 31 boys walking at 100 m/min in desert heat. Ages of the men ranged from 20 to 73 and of the boys, 10 to 19. Environmental temperature ranged from about 30°C in the evening at Boulder City, Nevada to 47.2°C one afternoon in Death Valley, California. Sweat rate, SR, measured in ml per min and per m^2 of body surface varied enough to permit estimating (Cl) at a common SR of 7 $ml/min \cdot m^2$, SR 7. The results prove that (Cl) increases with age: the lowest concentration was 7 mEq/liter in a boy of 16 with an SR of 8 $ml/min \cdot m^2$ and the highest was 106 mEq/liter in Dill at age 73 at an SR of 13 $ml/min \cdot m^2$. Other evidence supporting the age dependence of (Cl) consists of measurements on Dill, F. G. Hall and C. F. Consolazio made under similar conditions in 1937 and in 1964. The increases in (Cl) at SR 7 over the 27-year period were, respectively, from 39 to 59, 16 to 27.5, and 29 to 32.5. Apart from the dependence of (Cl) on age there are large individual differences at any age. These as well as the age-dependent relation may reflect variations from one person to another in the activity of the adrenal cortex and a declining adrenocortical activity in a given person with age. (Supported by PHS grant CD-00056.)

CHARACTERISTICS OF CENTRAL VISUAL PATHWAYS IN MACAQUES. Robert W. Doty, Center for Brain Research, University of Rochester, Rochester, N.Y.

Data were accumulated from 13 Macaca nemestrina, mostly using unanesthetized animals with chronically implanted electrodes. Conduction velocities in optic tract (OT) are, roughly, 15 and 6 m/sec, and at least double this in the optic radiation. Synaptic delay at the lateral geniculate nucleus (LGN) is 1.0 msec or less, but for the earliest and fastest response at area striata is 2.5 - 3.5 msec! In the alert state these synapses can sometimes respond fully to a second volley within less than 10 msec, with recovery proceeding in the order: primary synapses in area striata, parvocellular, then magnocellular components of LGN. Barbiturates greatly prolong recovery times and, for area striata at full anesthetic levels, may abolish early responses. In alert animals latency for response in OT following a high-intensity, strobotron flash is usually 13 msec. Given the above figures and known distances a response should begin in area striata within 20 msec. However, the minimal latency here is usually 30 msec; yet by interaction of photically and electrically elicited responses it can be shown that some components of the photic response traverse the fastest OT-LGN systems. This paradox is not fully understood, but is probably related to differences in synaptic operation under the two conditions. The fastest fibers of OT predominate in the magnocellular layers of LGN. The function subserved by the magnocellular layers must be poorly represented in the fovea since extirpation of the "foveal projection" in area striata (one monkey) produces less than half the magnocellular degeneration expected on the basis of parvocellular degeneration and per cent area striata removed. The centrencephalic system exerts a powerful control over transmission at LGN for both electrically and photically elicited responses. (Supported by USPHS Grant NB 03606)

THE CRITICAL EFFECT OF A "DELAYED" MYOCARDIAL CONTRACTION ON THE FORCE OF THE SUBSEQUENT CONTRACTION. R. A. Doughty*, L. A. Hasher*, C. E. Schott*, and G. N. French

It is well established that frequency of contractions influences their force, that early extra-systole potentiates the next contraction, and that the delayed contraction is potentiated, depending on the previous rate.

Using the isometrically contracting cat papillary muscle, we have shown that a delayed contraction reaches a maximum force which is the same from 5 to 50 seconds after the previous one. Present studies show the delayed contraction to be markedly diminished by a single interpolated delayed contraction. The time-force relationships of this phenomenon are presented. The results do not appear consistent with the PIEA - NIEA theory.

THE COURSE OF PREGNANCY IN RATS FED A VITAMIN E DEFICIENT DIET. Ben H. Douglas*, H. G. Langford, and R. B. Arhelger* Dept. of Medicine, Univ. of Miss. Med. Center, Jackson, Miss.

It has been suggested that a diet which contains oxidized lipids and is low in vitamin E will produce toxemia in the pregnant rat. Controls were established for arterial pressure, proteinuria, and urine volume on 15 female rats. Following this, Group I, 10 rats, was exposed to males for a period of 5 days and Group II, 5 rats, served as controls. All the animals were then fed a vitamin E deficient diet which contained oxidized lipids. The arterial pressure of Group I changed from 128 mmHg±2 S.E.M. during the control period to 122 mmHg±4 S.E.M. at delivery while the arterial pressure of Group II rose from 129 mmHg±1.5 S.E.M. to 141 mmHg±8 S.E.M. during the same period. The urine volume of Group I was 0.59 cc/hr±0.04 S.E.M. during the control period and 0.70 cc/hr±0.08 S.E.M. at delivery. The urine volume of Group II changed from 0.58 cc/hr±0.05 S.E.M. to 0.73 cc/hr± 0.1 S.E.M. during the same period but it was more variable following initiation of the diet. There was no significant change in proteinuria in either group. Two of the animals in Group II died prior to delivery. Autopsy revealed renal glomerular capillary thrombosis, adrenal hemorrhage, and extensive hemorrhage and necrosis of the placenta. The remaining animals were continued on the diet and autopsied two weeks following delivery but none showed lesions such as these. Two possibilities appear: (1) these animals had the lesions but recovered following delivery, and (2) the diet did not produce the lesions in these animals. Conclusion: The above diet in our hands has failed to produce 2 major components of toxemia, hypertension and proteinuria.

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OXYGEN CONSUMPTION RELATED TO BODY TEMPERATURE CHANGE IN QUADRIPLEGIC SUBJECTS. **J.A. Downey *, H.P. Chiodi, R.C. Darling and J.A. Sarno *. Dept. Physical Medicine and Rehabilitation, Columbia University and New York State Rehabilitation Hospital, West Haverstraw, New York.**

Studies were performed to determine whether a fall in central temperature alone would cause an increase of O_2 consumption. Seven subjects with functional C 5-7 cord transection were studied 8-24 months after the onset of paralysis. Central cooling was induced by placing the insensitive part of the body in cool water or in a surgical cooling blanket. Skin and central (rectal and external auditory canal) temperatures were monitored. Oxygen consumption was measured by open circuit method. With a fall in central temperature, there was no increase in oxygen consumption until approximately 35.6° C. Below 35.6° C. oxygen consumption increased in all but one patient. This increase in O_2 consumption occurred even when the sentient skin temperature was maintained at greater than 34.5° C.

This investigation was supported in part by Public Health Research Grant GM-11624, from the National Institutes of Health.

EFFECT OF ALLOXAN ON PANCREATIC ELECTROLYTE SECRETION. David A. Dreiling and Oswaldo Tiscornia*. Dept. of Surg., Mt. Sinai Hospital, New York, N.Y.

This study attempts to evaluate the effect of alloxan upon external pancreatic secretion and to elucidate whether or not the ductular system of the gland has a secretory function. The maximum pancreatic secretory capacity of 11 Thomas cannula dogs was determined with secretin and pancreozymin before and sequentially after the rapid administration of 50 mg. of alloxan intravenously. Pancreatic flow, bicarbonate secretion, enzyme elaboration, blood sugar and blood amylase were determined serially. Pancreatic biopsies were taken at sacrifice or autopsy. The 11 dogs became diabetic within 24 hours - 7 remained severely diabetic, 4 showed mild diabetes and 2 reverted to normal glucose tolerance. Pancreatic biopsies, though grossly normal, all showed varying degrees of tubular necrosis. There were definite alterations of the external pancreatic secretion in all dogs, changes evident even in those whose diabetic state reverted to normal. In general there was an initial suppression of all parameters with a gradual return to normal secretion by the end of a month. The mean bicarbonate concentrations were significantly depressed whereas the mean enzyme concentrations were significantly elevated at the height of secretory suppression. These data, correlated with the histologic findings i.e. first tubular necrosis and then ductular reduplication, suggest a different cellular origin for enzyme elaboration and fluid-electrolyte secretion and indicate a secretory function for the pancreatic ductules.

STUDIES ON THE RENAL ACTIVITY OF THE NEUROHYPOPHYSEAL OCTAPEPTIDES, (1) EXPERIMENTS WITH VASOPRESSIN INFUSIONS IN THE RAT. Willard M. Duff*, Edward H. Grinnell*, and Jenő Kramár. Creighton Medical School, Omaha, Nebraska.

Former studies reported in the last fall meeting of this Society on the renal activity of vasopressin were continued. Alcoholized, hydrated rats with previously prepared ureteral fistula were used. Water balance was maintained by combined intravascular and oral routes. Arginine vasopressin was infused at a constant rate in concentrations yielding between 0.03-0.40 mμU/min. and urine changes were observed by means of a two minute sampling technique. Observations in 48 experiments confirm previous findings concerning the dual nature of the renal activity of vasopressin: the hormone is able to produce diuresis as well as antidiuresis. For the demonstration of the diuretic effect the infusion technique proved to be superior to single injections. The type of response whether diuretic or antidiuretic, was found to depend on the vasopressin concentration in the infusion fluid, low concentrations being diuretic, high concentrations antidiuretic. Creatinine excretion regularly decreased during antidiuresis and increased during diuresis. Chloride concentration and excretion regularly increased during antidiuresis, the respective changes were variable during diuresis. Comparison of the results of the present infusion study with those obtained by the single injection technique and reported previously, showed many similarities indicating that, under the prevailing conditions and in the rat, both glomerular and tubular systems are involved in the dual action of vasopressin.

EFFECT OF VOLUME HYPERTROPHY ON VENTRICULAR FUNCTION IN UNANESTHETIZED DOGS. John P. Duffy,* Paul R. David,* and H. J. C. Swan, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Right and left ventricular function was studied in 7 normal unanesthetized dogs (Group 1) and again 2 weeks after closure of bilateral femoral arteriovenous fistulas (AVF) which had been present for 2 months (Group 2). Four animals in Group 2 had a residual volume overload, as judged by ventricular end diastolic pressures (VEDP) that were higher than those in Group 1; these were restudied after bleeding to their normal VEDP. Eight unanesthetized dogs were studied with open AVF of 2 months' duration (Group 3). All animals were killed after the experiments and separate ventricular weights were recorded. Biventricular hypertrophy was present in Group 3 (RV+37.5%:LV+37.8%) and significant hypertrophy persisted in Group 2 (RV+33.3%:LV+18.9%). Mean values for ventricular function indices were:

GP	Heart rate/min	Stroke vol, ml	RV stroke work, gmM	RVEDP, mm Hg	RVdp/dt, mm Hg/sec	LV stroke work, gmM	LVEDP, mm Hg	LVdp/dt, mm Hg/sec
1	114	22.6	5.2	1.6	634	31.5	6.4	3,457
2 Normal VEDP	116	24.2	7.1	1.7	711	33.5	7.6	3,402
	124	20.4	5.2	1.3	644	25.3	6.3	3,377
3	154*	49.7*	17.0*	9.4*	908	71.0*	18.0*	2,831

*Significant differences.

Ventricles subjected to chronic volume overload have a greater increase in work capacity than in muscle mass; in contrast to pressure overload, on removal of a volume overload the work capacity is subnormal in relation to the muscle mass. (Supported by NIH Grant HE-09374.)

BIOCHEMICAL ASPECTS OF RAT DECIDUOMATA AND THEIR ALTERATION BY TREATMENT WITH AN OXAZOLIDINETHIONE. G. W. Duncan, L. J. Wyngarden* and J. C. Cornette*. Research Labs., The Upjohn Co., Kalamazoo, Michigan.

Deciduomata formation in pseudopregnant intact and steroid treated ovariectomized rats was used to provide a first approximation of the uterine response at nidation. One and four days following unilateral uterine traumatization, RNA, DNA, protein and glycogen content, uterine weight, tritiated estradiol and progesterone uptake and P^{32} incorporation were determined. The results obtained in these animals were concurrently compared with those obtained in rats treated in addition with an oxazolidinethione derivative. This latter compound effectively inhibited deciduomata formation. In steroid treated rats, it reversed the progestational effect on each of the above biochemical constituents. The effects did not resemble those associated with dihydronaphthalene, ergocornine, clomiphene or steroid-induced deciduomata inhibition. The compound did not exhibit uterotropic, anti-estrogenic, androgenic, gonadotropin inhibiting or blastolytic activities but did, however, effectively inhibit pregnancy in rats.

STUDIES ON THE EFFECTS OF SECRETIN ON THE VISCOSITY OF PANCREATIC SECRETION IN CHILDREN WITH CYSTIC FIBROSIS.
Barry Dworkin*, Peter Lott, Jr.* and H. Necheles.
Micheal Reese Hosp. and Medical Center, Chicago, Ill.

Duodenal fluid and pancreatic secretion was aspirated by duodenal intubation in children with cystic fibrosis, and the effects of intravenous injection of secretin on the viscosity of the secretions were assayed. Viscosity was determined with a recording viscometer for non-homogeneous fluids of our own design (Dworkin, Wolach, and Necheles, J. Appl. Physiol. 1964, 19:798). It was found that secretin diminishes the viscosity of pancreatic secretion in these patients considerably; no untoward effects of secretin were observed. A table with our results will be presented. Experiments on dogs indicate diminution in viscosity in pancreatic and in other glandular secretions following i.v. secretin.

Supported by Hartford Foundation Grant.

Thermosensitivity of septal and preoptic neurons in cats.
J. S. Eisenman. Dept. of Physiology, Univ. of Penn., Phila., Pa.

Responses of single neurons to local heating and cooling were recorded in the septal and preoptic areas of Urethan anesthetized cats, using steel microelectrodes. Tissue temperature (T) was varied by perfusing four thermodes which bracketed the area studied. The perfusate temperature was controlled by passing it through a semiconductor Peltier device. T was recorded by a thermistor probe placed in a contralateral position, symmetrical with the microelectrode. Units were found which were thermally insensitive or truly thermosensitive. The Q_{10}'s of the thermosensitive cells, derived from the slopes of linear regressions fitted to plots of log firing rate vs. T, ranged from 1.7 to 8.5. Since thermosensitivity with a Q_{10} of about 2 is characteristic of rhythmic biological activity, only those units showing greater sensitivity were considered to be specialized thermodetectors. A third group consisted of thermosensitive units whose response curves showed sharp changes in slope. Several of these had high firing rates in the cool portion of the temperature range and decreased their rate as T was raised above a particular, threshold level. The majority increased their activity when heated above threshold T. The former responses were found only in the septal nuclei, while the latter were more widely distributed. These responses are thought to originate from interneurons in thermoregulatory pathways. Thus, types of activity that could be related to heat loss and heat conservation mechanisms have been recorded from the septum. The finding of thermally insensitive cells may result from the artificial form of thermal stimulation.

Supported by USPHS grant NB-04301.

EFFECT OF SOME ANTI-ANGINAL DRUGS ON VENTRICULAR REACTIVE HYPEREMIA IN DOGS. C. H. Ellis and Carole Snarski*. The Wellcome Research Labs., Burroughs Wellcome & Co. (USA) Inc., Tuckahoe, New York.

The mechanism of action of drugs currently used in treating angina is not yet understood. Some relationship of pain to myocardial anoxia or ischemia probably exists. In open-chest dogs the heart responds with a marked reactive hyperemia to transient occlusion of the anterior descending branch of the left coronary artery. We have studied the action of several clinically used anti-anginal drugs on this response. Occlusion periods of 10 sec. were used. Flow was recorded via electromagnetic flowmeter. Drugs were given i.v. Results: nitroglycerin, erythrityl tetranitrate, pentaerythritol tetranitrate, theophylline, visammin, dipyridamole, and three β-adrenergic blockers (pronethalol, propranalol, DCI) reduced or abolished the hyperemic response. The actions of nitroglycerin and visammin were transient; those of the long lasting nitrates, theophylline, dipyridamole and the β-adrenergic blockers persisted longer. The adrenergic blockers usually did not cause increased coronary flow directly; the nitrates and theophylline caused an increase for several minutes; nitroglycerin's effect was transient. Dipyridamole increased coronary flow more markedly than the nitrates, but did not depress the hyperemic response as much. Tolazoline increased coronary flow and enhanced the reactive hyperemia induced by brief coronary occlusion. Reactive hyperemia can be reduced by severe hemorrhage and enhanced by transfusion, but the response does not seem to be directly related to systemic arterial pressure. The response is not altered by increasing coronary flow by respiratory arrest, so depression of the hyperemic response by drugs that increase coronary flow probably indicates independence from pre-occlusion flow rate.

ELECTROKINETIC EFFECT IN LIVING CELLS AND THE CAPACITANCE OF THE CELLULAR MEMBRANE. R. Elul (intr. by W. R. Adey). Space Biology Laboratory, Brain Research Institute and Dept. of Anatomy, University of California, Los Angeles, and The Pasadena Foundation for Medical Research, Pasadena, Calif.

Living cells exhibit movement in an electric field. The mechanism of this effect was investigated by the use of a focal electric field. Cultured neurons and connective cells move to the positive pole of the field. When these cells are dissected, membrane fragments still show a qualitatively similar movement. It is concluded that electrophoresis of living cells does not depend upon presence of volume charge in the cytoplasm, and most likely the electrokinetic effect results from interaction of the electric field with polarized ionic layers at the interphase between the membrane and the solution on each side. Selective adsorption of ions into the membrane matrix, or attraction to fixed charges embedded in it, would give rise to a double ionic layer on each side of the membrane. These double ionic layers, irrespective of their origin, would act as capacitors in series with the membrane. The present results suggest the existence of such ionic layers on both sides of the membrane, and it is proposed that they may contribute significantly to cellular capacitance. The values of capacitance found *in situ* for Aplysia cells are of the same order as those found for mercury drops in a solution of comparable ionic strength. In neurons of other species, however, the capacitance is 5-10 times lower, suggesting existence of an additional, smaller series capacity. Inasmuch as the capacitance of the ionic layer depends upon the ionic strength of the solution, experimental verification of these conclusions may be possible by direct measurement of input capacity of cells in solutions of different ionic composition.

CARBONIC ANHYDRASE BINDING AND TRANSPORT OF CARBON DIOXIDE. T. Enns and S. McGowan*. Physiol. Res. Lab., Scripps Inst. of Ocean., U.C.S.D., La Jolla, California.

Experiments with bovine red cell carbonic anhydrase have shown that the enzyme increases diffusive CO_2 transport in aqueous solutions both by increased utilization of bicarbonate diffusion and by direct enzyme action. Transport rate increases of as much as 50-fold have been demonstrated with enzyme and bicarbonate and 3-fold with enzyme alone. These studies have also given support to the concept that the enzyme binds CO_2 and OH^-. Measurement of $C^{14}O_2$ diffusion through millipore filters containing solutions in which carbon dioxide tension, bicarbonate concentration, enzyme concentration, and pH were varied systematically have been made. They give information regarding the relationship between enzyme binding of CO_2 and carbon dioxide tension, and the relationship between enzyme binding of hydroxide ions and hydroxide ion concentration.

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ROLE OF HISTAMINE IN SECRETION AND VASODILATATION IN CAT SUBMAXILLARY GLAND F. Erjavec, M.A. Beaven, B.B. Brodie, (intr. by E. Costa)
National Heart Institute, Bethesda, Maryland

In previous studies of cat submaxillary gland we have demonstrated a close relationship between cholinergic stimulation and release of non-mast cell histamine. The glandular histamine, labeled by intravenous injection of H^3-histamine, is liberated mostly as metabolites into saliva and venous blood during parasympathetic stimulation. Increased cholinergic stimulation is always accompanied by increased blood flow. Atropine blocks the salivation, but not the increased blood flow nor the release of labeled histamine into venous blood. Therefore, this amine might play an important role not only in salivation, but also in functional vasodilatation in submaxillary gland during parasympathetic stimulation.

A STUDY OF THE ULTRASTRUCTURE OF THE RABBIT GRAAFIAN FOLLICLE AS IT APPROACHES RUPTURE. Lawrence L. Espey*, Carol Slagter*, Robert Weymouth*, and Paul Rondell. Univ. of Mich., Ann Arbor.

The fine structure of the wall of the rabbit Graafian follicle has been examined in an attempt to elucidate some of the physical changes which occur in the follicle during the ovulatory process. Whole ovaries from both mated and unmated estrous rabbits were fixed in Palade's buffered osmium tetroxide. The protruding apexes of the larger follicles were cut from the ovaries while in 100% EtOH and subsequently embedded in an epon mixture. The tissue was oriented so that the sections were cut perpendicular to the layers of the tunica albuginea, thecae, and granulosa and thus showed full wall thickness in the region of expected rupture. The tunica albuginea and theca externa were predominately composed of fibroblastic-like cells enmeshed in an extensive network of collagen. Except for the occasional blood vessels and collagen fibrils in the theca interna, this layer and the granulosa were each dominated by a stratum of cells containing numerous mitochondria and lipid-like granules. Approximately 8 hr after mating (about 2 hr before rupture) the tissue began a progressive phase of disintegration in the general area where the stigma normally develops. Follicles estimated to be within minutes of rupture had, at most, only fragmentary remnants of the granulosa, and the fibrous outer layers of the wall had thinned to less than 1/5 their width in follicles from unmated estrous rabbits. Not only was there a separation of cells, but also the collagen fibrils of the preruptured follicles appeared appreciably sparse in comparison to precoital control follicles. The cells dissociated in a manner which supports the idea that there is an active deterioration of the connective tissue elements in the wall of the Graafian follicle as it approaches rupture.

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THE EFFECTS OF AMINO-GLUTETHIMIDE ON THE RAT OVARY. W.J. EVERSOLE and D.J. Thompson.* Indiana State University, Terre Haute, Indiana

Amino-glutethimide, a central nervous system depressant and anticonvulsant, was injected subcutaneously daily in a dose of 25 mg/Kg or 50 mg/Kg for two weeks into Charles River CD strain immature female rats. One set of rats was 21 days and another 28 days of age at initiation of the injections. Control rats were injected with either physiological saline or water. At autopsy the ovaries were dissected free of fallopian tube and extraneous fat, weighed on a torsion balance, and fixed for histological study. During the two-week treatment period the animals exhibited normal body weight gain and appeared to tolerate the drug without showing obvious symptoms of decline in general activity. The ovaries of the "21 day-old" treated groups were heavier than their controls, whereas the ovaries of the "28 day-old" treated groups were approximately the same weight as their controls. Histological studies of the gonads in the latter groups of treated rats showed an increase in number of vesicular follicles and a decline in number of corpora lutea. Studies are in progress on the histological structure of the ovaries from the "21 day-old" groups and further plans are being made to study the effects of amino-glutethimide on reproductive processes.

Frictional Forces in Rabbit Knee Joints In Vivo. J. Job Faber and Gary R. Williamson*. Department of Physical Medicine and Rehabilitation, University of Washington, Seattle, Washington.

Retarding forces in joints were measured at rotational velocities and loads approximating those in life in anesthetized New Zealand White Rabbits. Skin and musculature of the knee and tibia were removed. Blood supply to the knee was left intact. The femur was fixed with respect to the board supporting the animal. The tibia was attached to a pendulum system with the knee joints as axis of rotation and springs to provide the restoring force. Loads in excess of 30 kg could be applied to the knee by means of two springs in the instrument. The rotational amplitude was ± 10 deg and the frequency about 5 cycles per second. A photokymograph recorded the motion of a light bulb on top of the instrument. All moving joints in the instrument were made with ball bearings or ball bushings. Energy consumption due to flexion and extension of the knee were calculated from the decrease in amplitude of the oscillations when the limb was released from a deflected position. The recordings were analyzed on the assumption that two kinds of retarding forces exist in joints: 1) a constant, velocity independent, friction and 2) a viscous friction, linearly proportional to velocity. The frictions of the instrument alone were measured and subtracted from the values obtained on animal joints. In contrast to findings reported in the literature, the velocity proportional friction at normal loads and velocities accounts for more energy consumption than may be justifiably neglected in considering total joint friction. Supported by an interim grant from the Western Washington Chapter of Arthritis and Rheumatism Foundation. PHS grant AM#08894, and OVR grant, R&T 3.

ROLE OF RNA SYNTHESIS IN MINERALOCORTICOID ACTION IN THE RAT. D. D. Fanestil*, G. Fimognari*, and I. S. Edelman. University of California School of Medicine, San Francisco, California.

Earlier studies have indicated that RNA and protein synthesis mediate the action of aldosterone on sodium transport across isolated anuran skin and bladder. This report concerns the role of steroid stimulation of RNA synthesis in mineralocorticoid action in rats. Unanesthetized, adrenalectomized rats maintained on saline drinking water were injected subcutaneously with 2 µg of steroid hormone or the diluent, urine was collected at two hour intervals and the rates of Na^+ and K^+ excretion were determined. The hierarchy of mineralocorticoid effectiveness was aldosterone > cortisone ≅ progesterone > estradiol. Actinomycin D (50 µg/100 g rat) blocked the anti-natriuretic response to aldosterone but had a complex effect on the kaliuretic response. Incorporation of H^3-orotate into RNA was measured in homogenates of kidneys taken from adrenalectomized rats 90 minutes after subcutaneous injection of 2 µg of aldosterone or diluent (n = 11). Aldosterone significantly enhanced the incorporation of orotate into RNA in the 600 x g sediment and the 100,000 x g supernatant fractions. In a separate set of experiments (n = 6), actinomycin D (20 µg/ml) added to the incubation medium, *in vitro*, inhibited orotate incorporation into RNA by 65 ± 2.5 % in the 600 x g sediment, 19 ± 4.6 % in the 100,000 x g supernatant and 14 ± 1.0 % in the 100,000 x g sediment. These results are consistent with the postulate that an early step in steroid regulation of sodium transport involves stimulation of synthesis of nuclear RNA.
(Supported by a grant from USPHS, No. HE-06285.)

THE EFFECT OF BILE SALTS ON THE ATP-ASE ACTIVITY OF MUCOSAL HOMOGENATES FROM RAT JEJUNUM AND ILEUM. Robert G. Faust and Shih-min Liu Wu*. Univ. of North Carolina, School of Med., Chapel Hill, N. C.

Mucosal homogenates of rat jejunum and ileum (0.4 to 1 mg dry wgt of tissue) were incubated in a medium containing various concentrations of sodium taurocholate, sodium glycocholate, Na^+ and K^+, 50 mM Tris-HCl (pH 7.45), 0.4 mM $MgCl_2$ and 0.4 mM ATP at 37° C for 3 minutes. The Na^+-K^+ stimulated ATP-ase activity of both the jejunal and ileal homogenates was inhibited by 1 mM ouabain. Mucosal ATP-ase activity of jejunum was approximately 3 times greater than that observed with ileum. Bile salts (1 and 2 mM) increased the ATP-ase activity of jejunal homogenates in the presence of Na^+ and K^+. The Na^+-K^+ stimulated ATP-ase of mucosal homogenates from ileum was increased by 1 mM sodium glycocholate and 2 mM sodium taurocholate. However, the ATP-ase activity of ileal homogenates was inhibited when the sodium glycocholate concentration was raised to 2 mM. These bile salts at low concentrations have been shown by Faust and Wu (Fed. Proc. 24: 652, 1965) to uncouple oxidative phosphorylation and to reduce ATP levels in rat jejunum. (Supported by USPHS Grant No. AM-07998).

ISOVOLUMIC WORK PERFORMANCE IN A RINGER-PERFUSED RABBIT HEART. H. Feinberg and E. Boyd*, Col. of Med., Univ. of Ill., Chicago, Ill.

Ringer solution (32°C) containing 0.0275, 0.055, 0.0825 or 0.11 mM Ca^{++} was perfused in a retrograde fashion though a rabbit heart. Isovolumic pressure (20-140 mm Hg) (VP) was recorded from a water-filled balloon (0.5-1.0 ml) placed in the empty left ventricle. Coronary venous fluid, drained from the right ventricle under negative pressure, was continuously analysed for oxygen with a platinum electrode. At a flow rate of 2-6 ml per gram, a range of oxygen consumption (O_2C) of 2.4-8.3 cc/100 gm/min was observed. At heart rates of 80-120 moderate to high VP was maintained over 2-3 hours without evidence of hypoxia. Increasing Ca^{++} led to an increase in both HR and VP and an increase in end-diastolic pressure (EDP). At each Ca^{++} concentration VP was a direct function of balloon volume (BV). BV in excess of 1.5-2.0 ml led to an increase in EDP. EDP decreased and VP increased following epinephrine or paired pulse stimulation of the ventricle. A linear relationship between O_2C and HR x VP was observed ($O_2C = 2.51 + 2.41 \times 10^{-4}$ HR x VP) despite variation of Ca^{++} or the administration of epinephrine. (Supported by grants from the American Heart Association and PHS HE-08921).

AGE AND DIETARY FACTORS INFLUENCING ANTIBODY ABSORPTION IN NEWBORN PUPPIES. Mylon E. Filkins and D. Dale Gillette, (intro. by Melvin J. Swenson). Dept. of Physiology and Pharmacology, College of Vet. Med., Iowa State University, Ames, Iowa.

Colostrum-free newborn puppies maintained on either starvation, saline-dextrose, or milk-replacer diets for various lengths of time were fed serum from dogs hyperimmunized against Salmonella pullorum and bled fifteen hours after feeding of hyperimmune serum. Serum was titrated by tube agglutination. Intestinal proteolytic activity was measured by the digestion of casein. The absorption of immune globulins from the intestinal tract of the puppy occurred primarily during the first 24 hours after birth. Nursing puppies had the shortest period of absorption followed in order by those on milk-replacer, saline-dextrose, and starvation diets. There was an increase in proteolytic activity from birth to 72 hours which was slightly accelerated by milk-replacer diet as compared to saline-dextrose diet. Inhibition of tryptic activity by the feeding of trypsin inhibitor or an increase in tryptic activity by the addition of trypsin to the diet did not significantly alter the period of antibody absorption. The absorption of intact globulins from the intestinal tract seems more dependent on age than on diet or intestinal proteolytic activity.

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SENSITIVITY OF UREMIC RED BLOOD CELLS TO DIGOXIN. Felisa Fisch*, C. R. Kleeman and Louis H. Miller*. Departments of Medicine, Cedars-Sinai Medical Center, Mount Sinai Hospital Division, and UCLA Medical Center, Los Angeles, California.

The sensitivity of uremic tissues to cardiac glycosides was studied. The "binding" of digoxin to human RBC after increasing periods of incubation in normal and uremic blood was measured based on the action of cardiac glycosides on sodium efflux from erythrocytes. The rate constant was determined measuring the appearance of Na^{24} in the medium from red blood cells previously loaded with the radioisotope. The "binding" of digoxin increased exponentially with time and reached a maximal value of 2½ hours after the glycoside was added. There was a significant difference in the maximal action obtained with the same digoxin concentration added to normal and uremic RBCs. After 3 hours incubation with 1.3×10^{-7} M digoxin, the per cent of inhibition of the rate constant for Na efflux was 61± 3.2 in 5 normal bloods and 38±2.3 in 6 uremic bloods. The control rate constant before addition of digoxin was also significantly different; the average was $5.80 \pm 0.5 \times 10^{-3}$ min.$^{-1}$ in normal RBCs and $3.75 \pm 0.46 \times 10^{-3}$ min.$^{-1}$ in uremic RBCs. When the erythrocytes of the uremic patient were incubated with normal plasma the "defect" of glycoside action could be partially reversed. Conversely, when normal RBCs were incubated with uremic plasma, the per cent inhibition by digoxin of the Na^{24} efflux was lower than the inhibition obtained with the same RBCs in normal plasma. In experiments performed with uremic patients after hemo- and peritoneal dialysis, the sensitivity to digoxin returned to levels seen in normal blood.

Some factor (or factors) primarily present in uremic plasma are responsible for the diminished sensitivity of RBCs to digoxin action and possibly for the Na^{24} transport defect seen in uremic blood.

VENTILATORY RESPONSES TO TRANSIENT ACIDIC AND ISOHYDRIC VERTEBRAL INFUSIONS DURING AIR AND CO_2 BREATHING. R.S. Fitzgerald*, N. Gross*, and R.E. Dutton, Jr. The Johns Hopkins University, Baltimore, Maryland.

Domizi and Perkins (The Physiolgist, Vol.7, No.3) have shown that ventilatory responses to the infusion of acidified normocapnic blood into the carotid arteries were essentially as prompt as those to hypercapnic blood or to cyanide. In seven infusions of acidified normocapnic blood (mean pH 7.21 and Pco_2 = 35 mm. Hg) into the vertebral arteries of four animals (mean pH = 7.42 and $PaCO_2$= 36) we observed no significant change in ventilatory ratio (VR). Eleven infusions of hypercapnic blood (mean Pco_2 = 64 mm. Hg) with varying pH (7.11 to 7.66) produced a mean VR = 1.49 (1.03 to 2.70). The responses to the hypercapnic infusions were delayed by 15-35 (mean 24) seconds, whereas the response time following infusion of 0.2 to 0.4 ml of 25 or 50 per cent alcohol (a medullary depressant) was only 3 to 5 seconds. Vertebral infusion of normal blood failed to prevent prompt hyperventilation when 9% CO_2 was breathed. If the animal's own vertebral blood flow was restored while the dog continued to breathe CO_2, there was a further increase in V_E after 18-31 seconds. These results suggest: 1) that the central arterial stimulus in the physiolgical pH range is CO_2; 2) that, under physiological conditions the sudden transitory changes in arterial Pco_2-pH exert their effect at the periphery and not centrally; and 3) that, compared to the peripheral chemoreceptors, the medullary receptors are relatively inaccessible to blood-borne stimuli.

DAILY PHYSIOLOGICAL RHYTHMS OF UNRESTRAINED MONKEYS. G. E. Folk, Jr., W. Ashlock, and M. Baker. Arctic Aeromedical Laboratory and University of Iowa, Fort Wainwright, Alaska, and Iowa City, Iowa.

Four circadian (daily) physiological rhythms of two unrestrained stump-tailed macaques were studied for 9 months. They were maintained in large cages in a sound-proof air-conditioned chamber (25 ± 1° C); results were compared with colony macaques. Variables included: lights on 8A-8P; continuous light; feeding at 9A; automatic feeding once an hour; one animal alone; one with mirror; two animals in adjoining cages. Containers for urine were automatically presented each hour, giving time of voiding and urine volume; urine electrolytes have been analyzed but are not reported here; heartrates, EKG, and core temperatures were recorded at 15 minute intervals from implanted radio capsules. Rhythms were demonstrated by Schuster periodogram. Body temperatures showed abrupt day-night resettings from about 38.4° C to 37.5° C; heartrates varied from 104 b/m to 182 b/m with a peak at about 9A and a daily low at about 12:30A. The kidneys partially or entirely shut down most of the night: Monkey A produced 262-640 ml per day, none at night, and voided 4-6 times per day; Monkey B produced 480-575 ml per day, 4-31% of this at night, and voided 6-10 times over 24 hours. Interrelationships include: body temperature drops (resets) rapidly when the light goes out, followed by a gradual drop in heartrate. Both animals invariably voided the accumulated night-urine during the last part of the low body-temperature setting and before the light went on. (Supported by N.S.F.).

PHOSPHOLIPID INVOLVEMENT IN GASTRIC MICROSOMAL ATPase. J.G. Forte, G.M. Forte* and P.D. Saltman*. Graduate Program of Biochemistry. University of Southern California, Los Angeles, California

Light microsomes isolated from rabbit and frog gastric mucosal homogenates by differential centrifugation between 17,500 x g x hr and 120,000 x g x hr appear morphologically derived from elements of the smooth-surfaced endoplasmic reticulum of acid-secreting cells. (Fed. Proc. 24: 714, 1965). These membraneous preparations exhibited high ATPase activity which was reduced by lecithinase C down to 15% of the control. Addition of exogenous lecithin to the preparation treated with lecithinase C restored ATPase activity up to 65% of the original level. No significant alteration of ATPase activity was induced by lecithinase A, lecithinase D, phosphodiesterase, lipase, or neuraminidase. Diethyl ether extraction of the microsomal pellet at -20°C reduced activity to about 50% of the control. This residual activity was further inhibited (40%) by lecithinase C. Chromatographic analysis of the ethereal extract showed mainly cholesterol and neutral fats with relatively small amounts of phospholipid. Phospholipids were readily extracted from the microsomes with chloroform-methanol, which abolished enzymic activity. Examination of negatively stained microsomes showed a general deterioration after incubation with lecithinase C. The normally smooth surface of the tubular structures became irregular and lobular elements often protruded from the membrane fragments. These results show that phospholipids are essential (1) for optimal activity of microsomal ATPase, and (2) for structural integrity of the membranes. It appears that phosphate groups of the phospholipids involved are specific for the maintenance of enzymatic action. (Supported by the U.S. Public Health Service and the Hartford Fndn.)

A Comparison of $S^{35}O_2$ Absorption by the Nose and Mouth under Conditions of Varying Concentration and Flow. R. Frank, R. Yoder, E. Yokoyama, and J. Brain, Department of Physiology, Harvard School of Public Health, Boston, Mass.

Dogs were anesthetized, paralyzed (gallamine triethiodide) and ventilated artificially through a tracheal cannula; $S^{35}O_2$ was pumped through the surgically isolated upper airways (head, larynx, uppermost trachea) via a lucite mask that had separate connections to the nose and mouth. The concentrations of $S^{35}O_2$ entering and leaving the upper airways were monitored continuously with a 0.5 liter ionization chamber coupled to a vibrating reed electrometer. Nearly complete removal-rates could be determined with a precision of several hundredths of a percent. Results: Nasal absorption of $S^{35}O_2$, at a flow of 3.5 L/minute for 5 minutes, exceeded 99% for all concentrations of incoming gas (1-50 ppm). Uptake of $S^{35}O_2$ by the nose remained greater than 99% when flow was increased to 35 L/minute (concentrations: 1, 10 ppm). The mouth provided equally efficient absorption when the concentration of $S^{35}O_2$ was only 1 ppm and flow was 3.5 L/minute. However, significant fractions of the gas penetrated beyond the mouth when either the concentration or, more importantly, the rate of administration was increased. Once penetration of the upper airways by $S^{35}O_2$ occurred, it was possible to demonstrate desorption of the gas from the mucous lining for periods lasting 20-30 minutes after the end of exposure. (Supported by U.S. Public Health Service Grant No. OH00100.)

PERMEATION CHARACTERISTICS OF PERFUSED PIGEON CROP MUCOSA. William L. Frantz. Dept. of Physiology, Michigan State University, East Lansing.

Mucosal membranes are prepared by clamping the ventral wall of the pigeon crop between two interlocking plastic rings at constant tension and area. The serosa and muscle are scraped from the underlying mucosa. Inspection under a dissecting microscope is made to ascertain the integrity of the mucosa and the completeness of the separation. Mucosa perfused on both surfaces (2.54 cm^2) with identical solutions of stirred, oxygenated (95% oxygen, 5% CO_2) M 199 (Grand Island Biological Co.) or bird Ringer are alternately monitored for transmembrane potentials and short-circuit current. When steady states are achieved Na^{22} or H^3 is pipetted into one side of the perfusion chamber and samples are taken from the other chamber at fixed intervals and counted according to standard procedures. Sodium has a transfer constant of 0.03 hr^{-1} in either direction with negligible amounts of tracer recoverable from the membrane. Tritium has a transfer constant of 0.18 hr^{-1} in the direction mucosal to serosal surface. These membranes retain tritium in a ratio of 1/50 of the count which passes through. The transfer constant in the direction serosal to mucosal surface is 0.058 hr-1. This suggests that water moves through the mucosa of the pigeon crop independent of Na^+ but more readily from the mucosal to the serosal surface than in the opposite direction.

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TWO MECHANISMS FOR DISINHIBITION IN IDENTIFIABLE NEURONS IN APLYSIA. W. Frazier*, R. Waziri* and E. R. Kandel (intr. by E. Henneman). Harvard Med. Sch., Boston, Mass.

Among the identifiable cells on the left side of the abd. gangl., certain neurons generate large elementary IPSPs attributable to the action of a single inhibitory interneuron (IN-I) (Frazier, et. al., 1965). One of these identifiable "follower" neurons (FN) generates an IPSP in response to spike activity in an identifiable IN-I. In the isolated ganglion, this IN-I provides the major demonstrable inhibitory input to this FN. By recording from and passing current into IN-I and FN concurrently, it is possible to record changes in IN-I at its own synaptic input, and to infer changes at its axonal termination on FN. This technique permits study of inhibition and disinhibition of FN by changes in frequency and/or amplitude of the elementary IPSP produced in FN by IN-I. Maintained synaptic or directly initiated increases in firing frequency of IN-I produces maintained inhibition of FN. Maintained postsynaptic inhibition of IN-I, spontaneously or in response to nerve stim. decreases its spike frequency and produces disinhibition in FN. Nerve stim. can also produce a 30-50% decrease in the amplitude of a test IPSP generated in FN by direct stim. of IN-I at a constant rate. This second type of disinhibition can occur without a change in the slope resistance of FN suggesting a possible presynaptic mechanism of disinhibition. Postsynaptic and presynaptic disinhibition have different integrative consequences. The former exerts its effect by producing changes in firing frequency of IN-I; the latter modulates IPSP amplitude without effecting IN-I firing frequency.

POST-COLD EXPOSURE DRINKING PHENOMENON IN RATS. Melvin J. Fregly and Irving W. Waters*, Dept. of Physiol., Univ. of Fla., Coll. of Med., Gainesville, Fla.

Male albino rats were maintained in individual metabolism cages and exposed continuously to air at 6°C. for 1, 3, 6, 10 and 12 days. Food and water were available ad libitum. Measurements of daily food and water intakes both prior to and during exposure to cold for either 1 or 3 days revealed that food intake increased immediately upon exposure to cold while water intake either remained unchanged or decreased compared with pre-cold exposure values. The relationship between simultaneous daily food intake and water intake was altered significantly by cold such that less water was ingested for a given food intake during exposure to cold than prior to it. Upon return to air at 26°C., water ingestion began within one-half hour and persisted for at least one day. Water intakes at 1/2, 1, 2, 3 and 24 hours after removal from cold were significantly greater than those of controls maintained for similar periods of time at 26°C. The magnitude of the water intake during the first 2 hours after removal from cold air was approximately 3 times the urinary output measured during the first 2 hours after entrance into cold. The relationship between the initial diuresis on entrance into cold and the drink observed after removal from cold remains to be established. The results suggest, but do not prove, that rats exposed to cold may be dehydrated relative to controls. The drink following removal from cold may be a manifestation of the relative dehydration. (Supported by Contract DA-49-193-MD-2549 with The Office Of The Surgeon General).

DEPRESSION OF INSULIN EFFECTS ON I^{131} CONCENTRATION BY STOMACH. M.H.F. Friedman and Lionel W. Rosen.* Department of Physiology, Jefferson Medical College, Philadelphia, Pa.

Under pentobarbital anaesthesia dogs were provided with total stomach pouches or separate pouches of the antrum and corpus. NaI^{131} was administered intravenously and activities of plasma, gastric juice, gastric mucosa and skeletal muscle were determined by well scintillation counter for the ensuing 6 hours. The I^{131} concentration capacity of antral mucosa was higher than that of corpus mucosa and neither areas were influenced by vagectomy or elevation of blood sugar levels. Administration of crystalline insulin increased both the gastric mucosa: plasma and the gastric juice: plasma ratios from control values of 30 to 40 to values of 150 to 400. Peak concentrations were in the fourth hour. Skeletal muscle I^{131} was not affected. The augmenting effects of insulin on I^{131} concentration were on both antrum and corpus. The increased concentrating capacity of the stomach following insulin administration was not influenced by concomittant intravenous administration of glucose but was abolished by thyroidectomy performed prior to I^{131} and insulin administration. The augmenting effects of insulin on gastric connentration of I^{131} were found only in the dog and could not be demonstrated in the guinea pig, hamster, and rat.

ALTERATIONS IN FLUID, ELECTROLYTE AND ENERGY BALANCE IN RATS WITH MEDIAN EMINENCE LESIONS. Madeline Fusco and Richard L. Malvin. Department of Physiology, University of Michigan.

Complete metabolic balance studies were made on rats rendered permanently D.I. by electrolytic lesions in the median eminence of the tuber cinereum. Daily water, food, Na and K intakes; urine volume and osmolality; and Na and K excretion were measured for periods up to six months. Following lesion, the rats showed the characteristic signs of diabetes insipidus, i.e., polyuria and polydipsia. Among the additional observations made in this study, four were most striking. 1) Food intake also increased significantly above the control value. This increased food consumption was due in part to the marked increase in water exchange. 2) Although these rats continuously excreted hypotonic urine, when challenged by water deprivation, they were able to concentrate their urine to nearly control levels. 3) The animals appeared to be in negative potassium balance. 4) These animals altered water intake and urine volume, but not urine osmolality when food deprived or fed sucrose. This is in contrast to control rats which showed marked reductions in urine osmolality and no change in water intake or urine volume.

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SUBTHALAMIC INFLUENCE UPON THE VENTRAL TEGMENTAL AREA OF THE MIDBRAIN Norman H. Gahm* and Jerome Sutin. Yale U. School of Med., New Haven, Conn.

In cats anesthetized with barbiturate, bilaterally synchronous rhythmical activity occurs in the ventral tegmental area (VTA) adjacent to the interpeduncular nucleus. This activity slows from 12 to 6 per second as the depth of anesthesia is increased. Similar activity, phase related to that of the VTA is seen in the lateral habenular, entopeduncular and subthalamic nuclei. Exploration of the diencephalon with single pulse stimuli indicates a pathway from the subthalamus which ascends through the entopeduncular nucleus, ventralis anterior and reticular nucleus, where it passes dorso-caudally to reach a position near the habenula. It then descends to the VTA in or about the habenulo-interpeduncular tract. The latency of the VTA response following stimulation of the subthalamus is 13 msec.; entopeduncular nucleus, 9 msec.; ventralis anterior, 8 msec.; and habenula, 6 msec. The slow wave activity recorded from the habenular, entopeduncular and subthalamic nuclei leads that of the VTA by 6, 9, and 13 msec. respectively. Small lesions just lateral to the habenular nuclei, or of the habenulo-interpeduncular tract abolish both VTA rhythmic slow wave activity and evoked responses. However, slow wave activity continues in the entopeduncular and subthalamic nuclei. Single pulse stimulation of the globus pallidus suppresses the slow wave activity at all sites for 200 - 500 msec. Pallidal stimulation also blocks responses evoked in VTA by subthalamic or entopeduncular stimulation but not those produced by ventralis anterior or habenula stimulation, indicating that the inhibition occurs in the pathway below the level of the ventralis anterior. Aided by a United Cerebral Palsy Foundation Postdoctoral Fellowship to NHG.

BACKGROUND AND EVOKED ACTIVITY IN THE AUDITORY PATHWAY: EFFECTS OF PAIRING NOISE WITH SHOCKS IN UNANESTHETIZED CATS. David Galin* (Spon: I. Tasaki). NIH, Bethesda, Md.

Sustained "white" noise was presented alone and then paired with subcutaneous electric shocks. Recordings were made from chronically implanted electrodes in round window (RW), cochlear nucleus (CN), trapezoid body (TRZ), inferior colliculus (IC), medial geniculate (MG), and auditory cortex (AI). Three variables were studied in CRO and "integrator" records: i) absolute level of background activity between noise presentations, ii) absolute level of sustained noise-evoked activity, iii) evoked response amplitude [difference between i) and ii)]. After noise-shock pairing, background activity in IC decreased up to 50%, and noise evoked little or no response. The cat's behavior was reflected more clearly by absolute levels of background and evoked activity than by response amplitude. When noise was again presented without shocks, background activity returned to control levels more slowly than evoked activity. Background must be considered in evaluating evoked activity and also as a significant physiological variable in itself. These effects at IC did not depend on level of arousal, middle-ear muscle actions, or changes in medullary auditory areas. Decreases in activity were also seen at RW, CN, TRZ in some animals which showed decreases in IC. Each cat showed a characteristic pattern of response to noise-shock pairing. These individual differences were seen even in RW recordings where they could not be attributed to differences in electrode positions, tissue damage, or gliosis. It is concluded that experience affects sensory processes early in the auditory pathway.

ORIGIN OF PRESYNAPTIC COMPONENTS OF THE CORD DORSUM POTENTIAL. Edgar L. Gasteiger and Alexander K. Florov*. Dept. of Physical Biology, N. Y. State Vet. Coll., Cornell U., Ithaca, N. Y.

The most likely explanation of the early components (A_1, A_2, etc.) of the cord dorsum potential (CDP) is that they represent a presynaptic intra-medullary compound action potential which enters by way of the dorsal root (Tarlov and Gelfan, J. Neuroph. 1955; Austin and McCouch, ibid.). During a study of CDP in cats, earlier investigations upon which this interpretation is based were repeated with modern oscillographic techniques which permit cross comparisons with high resolution. The presynaptic components were analyzed by stimulating the tibial, gastrocnemius, or sural nerves and recording simultaneously the incoming biphasic and monophasic action potentials from the dorsal root, the cord dorsum potential from a ball electrode close to the entry point, and the ventral root potential. The central terminations of the incoming volleys were explored by mapping. Components of the CDP presynaptic potentials and the dorsal root incoming volley were compared for relative latency of components, build-up of stimulus and synaptic blockage by conditioning, repetitive stimulation, asphyxia and drugs. With all the experimental methods, a direct positive correlation could be made between the several components of the presynaptic potentials and those of the compound action potential recorded monophasically from the dorsal root. This correlation was best seen and most completely examined for responses to tibial nerve stimulation. Our results confirm the interpretation that the prepotentials arise from intra-medullary compound action potentials as indicated by Tarlov and Gelfan.
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RELIABILITY OF RESPIRATORY REVERSAL BETWEEN ESOPHAGUS AND STOMACH. Anthony Geisel*, Toyohisa Arai*, Nelson C. Jefferson and Heinrich Necheles. Michael Reese Hosp. Chicago.

It is taken for granted that, when recording tubes pass through the esophago-gastric junction, the negative inspiratory waves reverse into positive waves. An explanation for this is that the reversal is caused by relatively negative respiratory pressure changes in the esophagus, and by positive respiratory changes in the stomach. However, in extensive studies on dogs we find that there are exceptions in all parts of the stomach. The relatively negative respiratory pattern was frequently observed 1-5 cm below the gastro-esophageal junction, and in still other instances, several or all tubes showed negative respiratory deflections. Thus, judging by the respiratory pattern alone, one would consider all tubes to be in the esophagus. It is possible that the passage of tubes through esophageal sphincters and the cardia makes these sphincters incompetent so that air enters esophagus and stomach, and that movements of air in and out of the stomach or air pockets with respiration, may produce relative negative pressures in the stomach. The openings of the tygon tubes used were radiopaque, and on x-ray films these markers as well as silver clips attached at the cardia confirmed location of openings.

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UPTAKE OF AMINO ACIDS BY RAT SMALL INTESTINE: PATTERNS ALONG INTESTINE FOR DIFFERENT TRANSPORT GROUPS. Mary Jean George* and R. David Baker. Univ. of Texas Medical Branch, Galveston, Texas.

Classification of amino acids into different transport groups has been based mainly on studies of competitive inhibition and of human genetic defects. We have been able to detect differences in uptake pattern along the small intestine among certain amino acids; these differences help to assign these amino acids to particular transport systems. If the uptake patterns for two amino acids are different, there must be some difference in the transport system or systems utilized. Each small intestine was slit open and incubated for 1 hr in medium containing a C^{14}-labeled L-amino acid. After incubation it was divided into 8 equal segments which were extracted and uptake of radioactivity measured. All amino acids studied were transported better by the mid intestine than by either end, but certain definite differences were observed. Among the neutral amino acids the patterns for L-leucine, L-alanine, and L-methionine were quite similar, but transport of betaine was relatively more deficient at each end of the intestine and the site of maximum uptake was more proximal. The patterns for L-proline, glycine, and AIB were intermediate between the methionine and betaine patterns. When participation of proline in the methionine system was inhibited by the addition of equimolar methionine, the proline pattern became identical to that of betaine. This evidence supports the idea that there are at least two different transport systems for neutral amino acids, one for N-substituted amino acids and one for the other neutral amino acids, both of which may be utilized by L-proline (and probably by glycine and AIB). The basic amino acids L-arginine and L-lysine followed patterns quite similar to those of alanine and leucine. (Supported by USPHS Grant No. AM-05778).

ESSENTIAL FATTY ACIDS EFFECTS IN GROWTH RATE AND OXIDATIVE PHOSPHORYLATION OF HELA S_3 CELLS. L. E. Gerschenson, J. F. Mead, I Harary and D. F. Haggerty (intr. by M. Seraydarian). Laboratory of Nuclear Medicine and Radiation Biology, University of California at Los Angeles.

The metabolism and function of essential fatty acids have been studied in tissues from whole animals. Mammalian cells in culture provide a more simple and direct approach to the problem. Hela S_3 cells were cultured on glass. The growth rate was measured by determining total protein; respiratory control and P:O ratio were measured using polarographic techniques in whole homogenates. Total fatty acid analysis of the cell lipids was performed using gas-liquid-chromatography. Addition of albumin-bound linoleic or arachidonic acids enhanced the growth of the cells. The cells grown in essential fatty acid-deficient medium showed a loss of respiratory control, uncoupling of the oxidative phosphorylation, and a pattern of fatty acid deficiency in the lipid analysis. Therefore, linoleic and arachidonic acids are growth factors for Hela S_3 cells in culture and are found to be necessary for the physiological integrity of the mitochondria of these cells. (Supported by grants from the AEC, NIH and C.N.I.C.T.A.)

DIFFERENCES IN LEVELS OF ATP AND ADP IN NORMAL AND FAILING GUINEA PIG HEART MITOCHONDRIA. Menard M. Gertler, Miroslav Plechaty* and Robert G. Guthrie*. IPM&R, New York University School of Medicine, New York, New York.

There appears to be complete agreement that adenosinetriphosphate (ATP) is intimately associated with myocardial contractility. The source of ATP for these processes has not been adequately explained and forms the basis for this presentation. Studies were made on fluctuations in the incorporation of P-32 in ATP and ADP (adenosinediphosphate) nucleotides in mitochondria derived from failing and normal guinea pig hearts. There appeared to be a striking decrease in P-32 incorporation into ADP of the failing heart mitochondria, whereas there was no change in the P-32 incorporation of ATP in the failing heart mitochondria. Further differences were shown when specific activities of the nucleotides were studied. The ATP/ADP ratio is 1.4 in the mitochondrial preparations derived from the experimentally produced heart failure guinea pigs. The ATP/ADP ratio in the mitochondrial preparations derived from the normal guinea pig heart is 1.75. It is reasonable to conclude that ADP level is decreased in mitochondria derived from experimentally produced failing guinea pig hearts. Theoretically, there are several reasons for this: (a) increased utilization of ADP to form ATP, and (b) increased utilization of ATP in failure mitochondria.

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HEAT PRODUCTION OF RABBIT PAPILLARY MUSCLE. C.L. Gibbs*, N.V. Ricchiuti* and A.J. Brady. Cardiovascular Research Laboratory, Univ. of Calif., Los Angeles.

The present myothermic technique makes certain demands as regards the size, shape and structure of the muscles used. By choosing a small preparation that contains parallel fibers, tension and work can be accurately measured and oxygenation is not a problem. A special thermopile was constructed which contained a groove at the bottom of which were the active junctions. The preparation was positioned in the groove such that there was always close contact between it and the junctions. A major problem is the large heat capacity of the thermopile relative to that of the muscle. It is therefore necessary to calibrate the apparatus by liberating a known amount of energy into the muscle. At 18-22°C the resting heat was about 30 mcals/gm muscle/minute and the twitch heat/beat ranged between 1.5 and 2.5 mcals/gm at 30 beats/minute. Except for the higher resting heat rate, cardiac muscle seems to resemble skeletal muscle in the relationship between total heat produced and the isometric tension. Under isotonic conditions it appears that the heat correlates better with the load than with the work.

Lipid Accumulation in the Livers of Partially Hepatectomized Rats Anik Girard* and Paul S Roheim. Albert Einstein College of Medicine, New York

In the rat partial hepatectomy produces a fatty liver. Thus, in 12 to 24 hours after removal of 60% of the liver, the triglyceride concentration of the remaining liver increased 5 to 10 fold. During this period there were no consistent changes in plasma lipid concentrations. While the fatty acids accumulating in the liver are derived largely from adipose tissue, experiments utilizing the technique of Stein and Stein (Biochem. Biophys. Acta 60:58, 1962) for labeling of epididymal fat pads with fatty acids suggested that increased mobilization of fatty acids was no greater than in sham operated animals. Lipoprotein synthesis was measured following administration of ^{14}C-labeled amino acids 24 hours after hepatectomy. In these animals the total incorporation of ^{14}C into plasma proteins other than lipoproteins was markedly reduced as was their specific activity. However, the total incorporation and specific activities of very low and low density lipoproteins were not decreased. These findings may be related to the fact that the fat content of the livers of hepatectomized animals decreases at about 24 hours and suggest that if impairment of lipoprotein synthesis is responsible for fat accumulation in these animals it must occur at an earlier time.

SYNTHESIS OF PHOSPHOLIPIDS IN THE LUNG OF THE DEVELOPING RABBIT FETUS. Louis Gluck and Michael Sribney (intr. by S.E.Downing). Depts. of Peds. and Biochem., Yale Univ. Sch. of Med., New Haven, Conn.

Although the importance of phospholipids, especially lecithin, in pulmonary surface activity and alveolar stability is well established, the pathways for their synthesis have not been studied previously in developing mammalian fetal lung. The reactions below were studied in lung homogenates of rabbit fetuses from 21 to 30 days (term) gestation; * indicates ^{14}C-labelled compounds introduced and recovered; compounds underlined were used in reaction mixtures:

A. CDP-*choline + D-α,β-diglyceride $\longrightarrow$ *lecithin

B. CDP-*ethanolamine + D-α,β-diglyceride $\longrightarrow$ *phosphatidylethanolamine (PE) $\xrightarrow{+3CH_3}$ *lecithin.

C. (*CH_3)-S-adenosyl-L-methionine + PE $\longrightarrow$ *lecithin

D. *Serine + PE $\longrightarrow$ *phosphatidylserine (PS) $\xrightarrow{-CO_2}$ *PE $\xrightarrow{+3CH_3}$ *lecithin

Incorporation in reaction A is greatest at 21 days and declines during gestation. Reaction B shows a high incorporation throughout gestation, with a sharp rise on day 24-25, and a sharp drop after day 26. Reaction C increases steadily during gestation to peak incorporation on day 28, and then declines. Reaction D has peak incorporation on day 26. These findings suggest reaction A is the major early pathway for lecithin synthesis. The other reactions increase in activity after day 24, producing precursor PE, by reaction B and by decarboxylation of PS (reaction D). The methylation of PE to form lecithin by reaction C appears especially important prior to term to produce the concurrent sharp drop in PE and rise in lecithin concentrations observed.

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CORTICAL MIDLINE LATE RESPONSES DURING EEG SYNCHRONY IN THE CAT. W. R. Goff, M. B. Sterman and T. Allison (intr. by Victor E. Hall). VA Hosps., West Haven, Conn. and Sepulveda, Calif.; Yale Univ. School of Med., New Haven, Conn., and Dept. of Anatomy, Univ. of Calif., Los Angeles, Calif.

Long latency averaged cortical evoked responses which differ from previously reported late potentials were evoked by ulnar nerve shocks in chronic and acute, locally anesthetized cats. Recorded from dural and pial monopolar electrodes, the response is negative-positive with peak latencies at about 50 and 125 msec respectively. It is localized to middle and posterior midline and immediately adjacent bilateral cortical areas. This midline late response (MLR) has the following properties: In chronic animals it appears only during the synchronized EEG characteristic of slow wave sleep. It is absent during the desynchronized pattern of alert waking or REM sleep. In acute animals, comparable results correlate with similar EEG changes. Mesencephalic reticular formation stimulation abolishes the MLR; basal forebrain stimulation enhances it. The correlation between evoked and spontaneous activity is not absolute, however. MLR enhancement and suppression can be produced without concomitant EEG effects. The ascending pathway for the MLR is apparently extralemniscal; single shock stimulation of mesencephalic reticular formation evokes it, while stimulation of VPL nucleus is ineffective. Auditory and visual stimuli evoke responses comparable to the somesthetic MLR. The waveform, latency, and distribution of the MLR differentiate it from late responses recorded maximally at contralateral somatosensory I and from "association" areas. Its properties suggest its homology to late somatic evoked responses which we have reported in man during slow-wave sleep, and which are similar to the "K-complex."

MUSCLE HYPERTROPHY IN HYPOPHYSECTOMIZED RATS. Alfred L. Goldberg (intr. by H. M. Goodman), Department of Physiology, Harvard Medical School, Boston, Mass.

Compensatory hypertrophy was induced in the rat Soleus and Plantaris muscles by cutting the connections of their synergist, the Gastrocnemius, to the Achilles tendon of one limb. The contralateral limb received only a sham operation and served as a control. Within a week, the wet weight of the Plantaris of the operated limb was 25% greater and that of the Soleus 40% greater than their controls. This growth was evident within 24 hours and reached its maximal extent by five days. Histological evidence showed that this weight increase was correlated with increased diameters of the muscle cells. The extent of muscle hypertrophy was similar in hypophysectomized and normal animals. Treatment with growth hormone did not increase the extent of hypertrophy but did significantly increase the muscle mass on both limbs. These studies support the conclusion that pituitary growth hormone is not essential for skeletal muscle hypertrophy, and that two types of muscle growth can be distinguished: 1) growth hormone-dependent type, and 2) work-induced hypertrophy.

HUMAN TOOTH SURFACE TEMPERATURE. M. P. Goldberg* and A. C. Brown. University of Washington, Seattle, Wash.

The object of this work was to evaluate the factors determining surface temperature in isolated teeth. In 15 human subjects (ages 11 to 23), the six maxillary anterior teeth were isolated using a square rubber dental dam which was large enough to cover the nose. The dam eliminated radient and convective interchange of heat with mouth and prevented warming by the breath; the teeth were kept dry to eliminate evaporative cooling. Ambient air temperature was 21°C. Most of the measured teeth were normal, but one tooth from each subject had been endodontically treated, due to pulpal disease, by having all the pulp tissue removed and replaced by inert material. Surface temperatures were measured at several points on each tooth using fine (40 gage) thermocouples. The mean temperatures were central incisors: 30.0°C; lateral incisors 30.7°C; cuspids 31.1°C. Similar teeth showed little variation between various subjects (standard deviation: 1.0°C). The temperatures of the endodontically prepared teeth did not differ significantly from the normal teeth. Thus it was concluded that (1) the major source of heat of isolated teeth is passive conduction from surrounding tissue, since the pulp metabolism and blood flow in the normal teeth did not increase their surface temperatures above that of the nonvital teeth; and (2) the total equivalent conductance from body core to tooth surface is approximately equal to the equivalent conductance from surface to environment, since the isolated tooth surface temperature was about halfway between ambient temperature and deep body temperature. (Support by NIDR Grant 5T1 DE 71).

HEMODYNAMIC EFFECTS OF PRESSURE INJECTION OF RADIO-OPAQUE MEDIA. S. J. Goldberg*, L. M. Linde, D. Desilets and S. Berens*. Department of Pediatrics, Physiology and Radiology. School of Medicine, University of California, Los Angeles, California.

This study was designed to determine the hemodynamic effects of pressure injection of radio-opaque medium into the pulmonary artery (pulmonary angiocardiography). Dogs were prepared as follows: At operation, vinyl catheters were sewn into the left atrium (LA), Pulmonary artery (PA) and aorta. An electromagnetic flow probe was placed around the ascending aorta to measure cardiac output (CO). Several weeks later, a catheter was passed into the PA for solution injection (1cc/kg). An R-wave triggered injector was used to inject 80% Na Iodothalamate (NI), 0.9% NaCl and a dextran solution prepared to be isoviscous with respect to NI. Vascular pressures, CO and the EKG were monitored during and for at least 90 seconds following injection. Seventy-three experiments were performed. Very significant increases in LA, PA and systemic pressure occurred almost immediately following injection of all solutions, then all tended to return toward control. No further significant changes occurred for control solutions. In the NI group, a secondary increase occurred in PA and LA pressures at approximately 10 seconds postinjection. EKG T-wave changes and decreases in CO and systemic pressure also occurred at this time. As CO increased during the next ten seconds, all pressures tended to return toward normal. Approximately 30 seconds postinjection, a tertiary rise in CO, LA, PA and systemic pressure began and always persisted for 90 seconds and sometimes as long as 5 minutes. These timed hemodynamic events may have significant implications for interpretation of cineangiograms.

EXOGENOUS CREATININE EXCRETION IN MAN. Ralph Goldman, Richard A. Yadley and David S. Nourok (intr. by John Field). Department of Medicine, University of California Center for the Health Sciences, Los Angeles.

The administration of exogenous creatinine causes a marked increase in renal tubular secretion of creatinine in man. There is little quantitative documentation of this response, despite its relevance to the interpretation of creatinine clearances. Nine normal individuals and six patients with varying levels of renal insufficiency were given intravenous infusions of creatinine at a rate of 20 mg/min. The endogenous creatinine clearance to inulin clearance ratio in the normal subjects was 1.11. The ratio of the exogenous creatinine clearance to inulin clearance ratio was 1.35 as soon as the creatinine infusion was started, rose quickly to 1.73, then gradually fell to 1.40 after ninety minutes of infusion. The patients with renal insufficiency had an initial ratio of 1.50 and showed no abrupt rise when exogenous creatinine was infused. A late rise to 1.71 after ninety minutes is probably not significant. It seems most likely that a small increment in the serum creatinine concentration can cause an increased effectiveness of the tubular mechanism for creatinine secretion. An alteration in the serum creatinine resulting in enhanced tubular transport, or reducing apparent serum creatinine concentration without affecting filtration, is less probable. The high pre-infusion ratio in patients with renal insufficiency, and their failure to respond to exogenous creatinine, suggests that once activated, the mechanism for increased tubular excretion may continue as long as the stimulus of an elevated serum creatinine persists.

VALIDATION OF FINGER COOLING PREDICTIONS; THE ROLE OF BODY HEAT STORE AND COLD INDUCED VASO-DILATATION (CIVD). R. F. Goldman and J. J. Powers*, U.S. Army Research Institute of Environmental Medicine, Natick, Massachusetts.

Frequently studies attempt to formulate finger cooling either by empiric fit of data or by theoretical formulation under such restricted cooling conditions that validation is difficult. The present formulation, to be presented elsewhere, simultaneously considers initial finger temperature, ambient temperature and wind velocity, amount of insulation and circulatory heat input and has been validated at +40°F and -70°F and also at -40°F with initial finger temperature held constant at 60°F or 80°F by thermostated auxiliary heat. Two physiologic factors must be considered, body heat content and cyclic cold induced vasodilatation (CIVD). In the presence of an initial body heat surplus, while slight variable cooling may occur, onset of significant cooling is delayed but once initiated follows the predicted curve. The precision of the relation between amount of heat surplus and delay in onset of cooling requires further study. During CIVD, calculated increases in circulatory heat input from the 7 kcal/m^2/hour of maximum constriction to up to 450 kcal/m^2/hour occur. However, the elevation of temperature is transient with no residual benefit, finger temperature falling along the initial cooling curve as if in fact no CIVD had occurred. Thus, CIVD episodes although preventing cooling during their occurrences, do not otherwise alter predicted cooling.

Use of Thermal Analysis in Gastric Freezing. R. L. Goodale, Jr.*, J. P. Delaney,* B. Zimmerman,* W. P. Ritchie,*Jr., O. H. Wangensteen, (intr. by J. T. King). Dept. of Surg., Univ. Minn. Med. School, Mpls. Minn.

It was shown previously that round canine Heidenhain pouches are rendered achlorhydric for 16 wks. average when tissue temp. is kept at -4°C for 40 min. using a 100 to 200 ml round freezing balloon(Physiologist 7:145, 1964). Only 2 to 3 wks. of achlorhydria result from freezing the intact canine stomach with a 1000 ml stomach-shaped balloon. Despite attempts to duplicate the uniform temperatures obtained with the round balloon, discrepancies of several °C occur on the surface of the larger balloon.

Dye studies show perfusion patterns in small round glass flasks are different from those in stomach shaped flasks. The coefficients of heat transfer for the 200 ml and large balloons are 0.25 and 0.1 calories/cm^2. -min. -°C respectively at identical flow rates and thickness. This is due to the higher fluid turnover rate and thinner fluid boundary layer in the small balloon. Even in this balloon the boundary layer imposes the major (84 to 64%) resistance to total heat transfer. Yet, as the coolant flow increases tenfold, the thermal resistance of this layer decreases and the boundary layer heat coefficient, (and Nusselt number) rises by 280% and 60% in small and large balloons respectively. Since these increases are non-linear, there is a practical optimal flow for each balloon. Such studies should aid in the design and evaluation of gastric balloon freezing systems. (Supported by a USPHS Grant, the John A. Hartford Foundation and the Donald J. Cowling Fund for Surgical Research.)

EFFECT OF CHRONIC ACIDOSIS AND ALKALOSIS ON RAT CSF-BLOOD POTENTIAL. Cecilie Goodrich (intr. by J. R. Pappenheimer). Dept. of Physiology, Harvard Medical School, Boston, Mass.

Changes in blood pH are associated with changes in the electrical potential between cerebrospinal fluid (CSF) and blood. It has been suggested by Mitchell et al. (Physiologist 7:208) that these changes are transient, the P.D. returning to its control value at steady-state. The present experiments compare the relationship of P.D. and pH during acute and chronic changes in blood pH. Rats were made acidotic or alkalotic by administration of 20 mM/kg NH_4Cl or $NaHCO_3$ twice daily. After 3 days the animals were anesthetized and the P.D. between blood and cisternal fluid was measured with glass capillary electrodes and saturated KCl-agar bridges. In control animals the mean values for standard bicarbonate and P.D. were 30 meq/kg H_2O and 4.5 mV respectively. In acidotic animals the corresponding values were 11 meq/kg H_2O and 11.0 mV. In alkalotic animals the values were 37 meq/kg H_2O and 4.6 mV. When chronically treated rats were acutely infused with HCl and $NaHCO_3$, potential varied with blood pH as it did in the untreated rats. There was no significant difference between the slopes or intercepts of the least squares regression lines of the P.D.-pH plot for acute rats, chronically acidotic or alkalotic rats. These results indicate that the relationship between CSF-blood potential and blood pH in the rat is not transient; changes in acid-base balance produce changes in P.D. which are maintained chronically and which reflect sustained alterations in distribution of ions between CSF and blood.

Effects of Metabolic Acidosis on Susceptibility of Mice to Oxygen Toxicity. Sheldon F. Gottlieb and Allen Cymerman.* Jefferson Medical College, Philadelphia, Pa.

Recently Walker (Canad. J. Biochem & Physiol 39:1803, 1961) showed that mice, adapted to living in environments containing high concentrations of CO_2, were more resistant to the convulsive manifestations of oxygen toxicity than unadapted animals. In order to ascertain whether this CO_2 protective effect was possibly due to the acidosis or to the adaption to CO_2, it was thought that studying the effects of another acidifying agent would help clarify the mechanism of the CO_2-caused oxygen resistance and provide additional insight into the mechanism of oxygen toxicity.

In acute experiments, NH_4Cl (400 mg/kg) was administered I.P. to Swiss mice. In paired experiments it was found that NH_4Cl induced metabolic acidosis provided a 60% increase in protection against the convulsive effects of 100% O_2 at 5 ata. Similar results were obtained with animals chronically adapted to NH_4Cl. NH_4Cl (100-350 mg/kg) exerted no protective effects against 5 ata. O_2 toxicity.

NH_4Cl treated animals exhibited marked ventilatory responses. The mechanism of the protective action of NH_4Cl in mice to 5 ata O_2, in part, appears to be related to the respiratory stimulating action of the acidosis. Other possible mechanisms for the O_2-protective action of NH_4Cl may be ascribed to NH_4Cl induced metabolic changes.

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PROBABILITIES ASSOCIATED WITH SPIKE DISCHARGES IN AUDITORY NERVE FIBERS. P. R. Gray,* N. Y. S. Kiang, and J. W. Shipley,* Center for Communication Sciences, Research Laboratory of Electronics, Massachusetts Institute of Technology, and Eaton-Peabody Laboratory of Auditory Physiology, Massachusetts Eye and Ear Infirmary.

The time patterns of spike discharges in auditory nerve fibers are influenced by both stimulus characteristics and refractory properties of the neurons. Conventional post stimulus-time (PST) histograms reflect the combined influence of these two factors, but these factors can be studied separately by appropriate processing of the data. Statistical analyses of spontaneous activity suggest that one may consider a neuron to be "recovered" when it has not discharged during the previous 20 msec. The effect of the stimulus on a fiber that has apparently recovered can be studied by estimating the conditional probability of a spike in a particular interval of time, given some minimum time since the last firing. Analysis of these "recovered probabilities" helps to explain certain otherwise puzzling features of the conventional PST histograms and leads to a more complete understanding of the relation between discharge probabilities of these fibers and the mechanical motion of cochlear structures. (Supported in part by the Joint Services Electronics Program (Contract DA36-039-AMC-03200 (E)); NSF (Grant GP-2495), NIH (Grant MH-04737-05), NASA (Grant NsG-496); and in part by research grant NB-01344, NINDB of the NIH Public Health Service.)

THE SITE OF INCREASED VASCULAR RESISTANCE DURING ISOMETRIC MUSCLE CONTRACTION. Sarah D. Gray* and Norman C. Staub. Cardiovasc. Res. Inst. and Dept. Physiol., Univ. Calif. Med. Ctr., San Francisco, Calif.

Various investigators have shown that strong isometric contraction causes a reduction in blood flow to skeletal muscle. According to Barcroft, the increased resistance to blood flow during sustained contraction of the calf muscles may be due to a nipping of the main artery or vein by taut muscle fibers. Pearson believes that the capillaries are emptied by a squeezing action of the contracting fibers; other reviewers make general statements about compression of intramuscular vessels. We have attempted to localize the site of increased flow resistance. In anesthetized rats we rapidly froze relaxed (n=10) or isometrically contracted (n=10) gastrocnemius muscles to study the capillary bed. Qualitatively, the capillaries in contracted muscles (av. max. T=2.1 kg/cm^2) contain as many or more red cells as resting muscle. Quantitation of the number of open capillaries per muscle fiber is in progress. Electromagnetic flowmeter studies in 17 anesthetized dogs showed a rapid decrease in arterial inflow with the onset of isometric contraction of the lower leg muscles (av. max. T=3.4 kg/cm^2), but only minor flow changes with passive tension of the same degree. The state of vascular tone in the muscle (reduced by bradykinin infusion or reactive hyperemia; increased by norepinephrine infusion) had no significant effect on the results. Rapid angiography (2/sec) in 5 additional dogs gave reproducible evidence for compression and focal defects in the larger supplying arteries. On 3 more dogs, venous as well as arterial angiograms showed obstruction at comparable points. Our results indicate "nipping" and compression of larger vessels as they enter contracted muscle or pass between muscle bundles. We have found no evidence of squeezing or obstruction of capillaries. (Supported by USPHS grants HE-06285 and 5-F1-GM-16,376.)

ACTIVE ION TRANSPORT IN THE RABBIT CORNEA. K. Green. (intr. by M.E. Langham.). Wilmer Institute, Johns Hopkins Hosp., Baltimore, Md.

The mechanism by which the thickness of the cornea is maintained at a steady value remains to be elucidated. When mounted in an appropriate chamber the rabbit cornea shows a potential (P.D.) of 5-6mv with the aqueous side positive. This P.D. increases with time after 60 mins. Sodium and chloride fluxes were determined under short-circuit conditions and it was found that, during the first hour after excision from the eye, the cornea showed active inward transport of both sodium and chloride ions. After this hour the chloride movement became a purely passive movement whilst sodium transport accounted for all the measured current. Isolated epithelia exhibit about 2/3 rds the activity of the whole cornea whereas isolated endothelia show no electrical characteristics. These results have been further confirmed using microelectrode techniques. The transport 'pump' is therefore assumed to reside in the epithelium, and determinations of the epithelial electrolyte content indicate that the location is at the most anterior surface of the cornea. The actual location of the transport 'pump' has been the subject of much conjecture in the past, and the present findings enable a precise location to be made for the transport system. It remains to be shown whether this 'pump' controls corneal thickness through effects on the concentration of the stromal bathing fluid and hence controlling the swelling of the stromal mucopolysaccharide by maintaining a constant level of hydration.

A STUDY OF MOTONEURON SPONTANEOUS ACTIVITY AND REFLEX HABITUATION UNDER CONDITIONS OF DECREASED INHIBITION OR INCREASED EXCITATION. Kathryn T. Green* and Jennifer S. Buchwald, Depts. of Anatomy and Pediatrics and Brain Research Inst., Univ. of California, Los Angeles, Calif.

Repeated stimulation of the hindpaw has been shown to result in a progressive decline in the reflex discharge of motoneurons, even with intervals of 15-45 sec between stimulations. This progressive decrease, or habituation, of response was recorded most frequently from ventral root units discharging phasically to the stimulus with large potential amplitudes. In an attempt to determine the mechanism underlying this reflex habituation, the present experiments were carried out. A constant current, 60 cps, 0.5 sec duration shock train was delivered to the hindpaw of cats spinalized with a low thoracic section. Each stimulus series consisted of 20 cutaneous stimulations delivered at 15 sec intervals. Strychnine was used to diminish post-synaptic inhibition and physiological stimulation was used to increase excitation. Interval time histograms of the motoneuron responses were obtained from an IBM 7094 computer for periods prior to and subsequent to each 0.5 sec stimulation. With diminished inhibition (0.01-0.05 mg/kgm strych), silent units which discharged phasically to the stimulus with high amplitude potentials and which showed marked habituation to repeated stimulation became increasingly tonic and, concurrently, showed a diminishing amount of habituation. Tonically discharging units with smaller potential amplitudes showed little habituation prior to strychnine and changed relatively little following strychnine. The effects of increased excitatory input are currently being evaluated. Data analyzed thus far indicate that tonic activity may depend significantly upon the amount of post-synaptic inhibition and that habituation of reflex responses may develop by potentiation of this inhibition through repeated stimulation.

DIRECT CURRENT COUNTERSHOCK IN THE TREATMENT OF DIGITALIS INDUCED VENTRICULAR TACHYCARDIA.

Kalman Greenspan, Edward F. Steinmetz*, Thomas J. Lord* and Charles Fisch. Krannert Heart Research Institute, Indianapolis, Indiana.

Many forms of cardiac arrhythmias have been successfully treated with application of closed chest countershock. However, it is reasonable to assume that temporary total cardiac depolarization may not permanently eliminate ectopic ventricular tachycardias induced by toxic amounts of drug (s). It is only when the drug is sufficiently dissipated that countershock by depolarizing the ectopic ventricular pacemaker (s), affords the sinoatrial cells an opportunity to drive the heart. The purpose of this study was to determine the effect of external direct current countershock in dogs with ventricular tachycardia induced by acetyl strophanthidin (A S). Repeated countershocks ranging from 50 to 300 joules in intensity was attempted in 15 dogs intoxicated with A S. In all cases the countershock failed to terminate or even interrupt the ventricular tachycardias. However, in the same A S intoxicated animals, the intravenous injection of 40 to 80 mgm of xylocaine was efficacious in restoring the heart to a regular sinus or supraventricular rhythm. It is concluded from the study that direct current countershock is not of value in terminating a digitalis induced ventricular tachycardia. (Supported by Krannert Fund, and in part by USPH Grant H-6308 and Training Grant 5363).

STUDIES ON THE RENAL ACTIVITY OF THE NEUROHYPOPHYSEAL OCTAPEPTIDES, (3) COMPARISON OF THE RENAL ACTIVITY OF OXYTOCIN AND VASOPRESSIN.

Edward H. Grinnell*, Jenő Kramár and Willard M. Duff*. Creighton Medical School, Omaha, Nebraska.

Analysis of the data obtained in 347 experiments on rats with the two octapeptides revealed many similarities and some dissimilarities. (1) In principle, both hormones influence urine flow in a parallel manner: low doses cause diuresis, high doses antidiuresis. The basic difference is in the absolute doses. The oxytocin/vasopressin dose ratio with relation to diuresis was approx. 1500, to antidiuresis 40,000. (2) Both hormones increase creatinine clearance and excretion during diuresis and both exhibit a biphasic response (decrease followed by increase) during antidiuresis. However, with oxytocin the second phase is less conspicuous. (3) During diuresis chloride excretion is increased by both hormones. During vasopressin-antidiuresis a similar increase is noted, however, during oxytocin-antidiuresis chloride excretion decreases. (4) During vasopressin-antidiuresis chloride concentration increases, whereas oxytocin results in an irregular renal response. (5) The reported experimental data suggest that the dual actions of these two hormones must necessarily involve both, the tubular and glomerular parts of the nephron. Nevertheless, in the case of oxytocin the glomerular effect is so preponderant that the tubular manifestations are not easily discerned.

SENSITIVITY AND RESPONSIVENESS OF THE MYOEPITHELIUM OF INVOLUTING RAT MAMMARY GLAND TO INTRAVENOUS OXYTOCIN. Clark E. Grosvenor. Univ. of Tennessee, Memphis, Tenn.

We have previously demonstrated the presence and contractibility of myoepithelial cells in the involuting rat mammary gland. In the present study we have investigated the sensitivity of these cells to oxytocin and their contractile response over a range of oxytocin dosage. Myoepithelial cell contraction was measured in groups of 7 rats undergoing mammary gland involution for 1, 5 or 9 days by first inserting a cannula intraductally and allowing milk to fill the ducts and alveoli by gravity flow. The milk-filled cannula was connected to a pressure transducer and intramammary gland pressure in response to intravenous oxytocin was recorded as cm. water.

	Threshold sensitivity (mU)			Slope of response		
	Day 1	5	9	1	5	9
	.01	.09	.13	30	35	27
	.02	.14	.40	30	32	8
	.06	.22	.40	20	25	6
	.11	.35	.43	11	17	5
	.13	.47	1.00	8	16	5
	.22	.53	2.10	8	15	5
	.22	.94	6.50	8	10	4
Mean	0.11	0.39	1.57	16	21	9

These data suggest that the sensitivity of the myoepithelium to oxytocin decreases as the mammary gland involutes whereas their contractility diminishes only from the 5th to 9th day during which time mammary gland involution accelerates and becomes complete. Supported by a grant and Career Development Award from the USPHS.

THE DEPENDENCE OF CAPILLARY FLOW ON FIBRINOLYTIC ACTIVITY. M. M. Guest, T. P. Bond* and J. R. Derrick*. Departments of Physiology and Surgery, University of Texas Medical Branch, Galveston, Texas.

Fibrin clots do not form in capillaries even when clotting is overtly manifest in the remainder of the circulation. Furthermore, erythrocytes do not adhere to other erythrocytes while in capillaries, even though they may travel through larger vessels in aggregates of various types. Based in part upon the presence in capillary endothelium of a potent activator of the precursor of the fibrinolytic enzyme and other evidence to be presented it is hypothesized that sufficient fibrinolytic activation occurs in capillaries to block coagulation and to alter fibrinogen in such a manner that microthrombosis does not occur in these vessels. Additional support for this concept is supplied through recording the behavior of the microcirculation in a number of experimental conditions by high speed cinephotography. Some of this cinefilm will be presented.

EFFECTS OF THE DURATION OF CHLORALOSE OR BARBITURATE ANAESTHESIA ON THE MAINTENANCE OF BLOOD PRESSURE FOLLOWING HEMORRHAGE. P.D.Gupta,* J.P.Henry and J.P.Meehan, Dept. Physiol. USC School of Medicine, Los Angeles, California.

Up to 30% estimated blood volume can be drawn from dogs 1-4 hrs. after anaesthesia with 30 mg sodium pentobarbital/kg without a significant fall of mean arterial pressure. However, mean pulse rate rises from 130/min to 200/min. With chloralose the blood pressure is also sustained and the initial pulse rate is only 70/min, rising to 180/min with 30% loss. Repetition of the bleeding with reinfusion once every 4 hrs. reveals progressive deterioration with the pentobarbital. Thus at a second hemorrhage at 8 hrs. the mean pressure (5 animals) fell to 60% of the initial resting value with 30% loss and the pulse rose from 145 to 180/min. Under chloralose the pressure remained unchanged; the pulse rose from 94/min to 170/min. At the third sequence at 12 hrs. the pentobarbital pressure fell to 45% of control with 30% loss; with chloralose (5 animals) it remained at 95%. Pulse changes at this stage were still more sharply differentiated. With pentobarbitone at 8 hrs. constancy or even a rise in venous pressure suggests increased venomotor tone after a 20% hemorrhage. At the 12 hr. period this occurs after only 10% loss. With chloralose a progressive fall in venous pressure with blood loss on all occasions suggests little change in venomotor tone. All changes in the conscious animal approximated those with chloralose.
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THE NEURAL CONTROL OVER CHOLINESTERASE ACTIVITY OF SKELETAL MUSCLE. Lloyd Guth and William C. Brown*. Laboratory of Neuroanatomical Sciences, N.I.N.D.B., N.I.H., Bethesda, Maryland

In previous experiments we have found that denervated rat skeletal muscle loses about 50% of its cholinesterase (ChE) activity within three days, whereas tenotomized muscle retains a normal ChE activity. Following reinnervation, several weeks are required for the normal level of ChE to be restored. The present study was performed to determine the effects of partial denervation, collateral reinnervation, and hyperneurotization on the ChE activity of muscle. The soleus and plantaris were partially denervated by transecting spinal nerves L4 or L5. ChE activity of muscle homogenates was determined at one week (i.e., before collateral reinnervation) and at 8 weeks (i.e., after collateral reinnervation). In another group L4 was crushed and ChE determined 4 months postoperatively (at which time the muscles had become hyperinnervated by the collateral sprouts from L5 plus the regenerated axons from L4). Partial denervation produced a decrease in ChE that was proportional to the number of muscle fibers that had been denervated. Following collateral reinnervation the ChE was restored to normal levels. The ChE of the hyperneurotized muscle was not above normal. It is concluded that a decreased neuronal pool can, by virtue of collateral branching, maintain a normal level of ChE in the muscles it innervates. Furthermore, it appears that the upper and lower limits of ChE activity are established by factors intrinsic to the muscle, but that within these limits the enzymatic activity is proportional to the number of innervated muscle fibers.

SURFACTANT ALTERATION IN KEROSENE PNEUMONITIS. J. D. Hackney and C. R. Collier. Rancho Los Amigos Hospital, Downey, Calif. and Loma Linda University, Loma Linda, Calif.

Kerosene pneumonitis is important in clinical toxicology and has been used as an experimental model of pneumonitis in animals. Because of the gross pathological features of atelectasis and pulmonary transudation, we postulated that changes in surfactant activity might be important in the pathologic physiology of this condition. We have studied the effect of instilling kerosene into the airway of tracheostomized rabbits and excised rabbit lungs. Surface tension was measured during cyclic compression and expansion of the film on a modified Langmuir trough. Minimum surface tension of saline extracts of rabbit lungs after 3 hours: 7 controls, mean 8.6 dynes per cm. (S.D. 2.2); 23 kerosene-poisoned, mean 22 (S.D. 5.1). These changes were highly significant ($p < 0.001$). In the anesthetized open chest mechanically ventilated rabbits, localized areas of decreased aeration were detectable as early as 5 minutes after intratracheal instillation of kerosene. With time these areas became progressively more apparent. When kerosene was added to normal lung extract in various ways, surfactant activity was not significantly affected. These findings suggest that change in surfactant is important in the pathogenesis of kerosene pneumonitis. They also suggest that in this model the major effect on surfactant is not related to direct interreaction with kerosene. The change in surfactant could be due to a decrease in production, but this would imply that the turnover rate must be very rapid. This aspect and the role of possible inhibitors are being investigated. Because of the rapid time course, this model should be especially valuable in the further study of surfactant pathophysiology. (Supported by USPHS Research Grant OH-00155)

EFFICACY OF HYDROCHLOROTHIAZIDE IN PREVENTION AND REVERSAL OF ADRENAL-REGENERATION HYPERTENSION*. C. E. Hall, O. B. Holland* and O. Hall*. University of Texas Medical Branch, Galveston, Texas.

It has been reported that 5 mg/kg/day of hydrochlorothiazide failed to prevent acute adrenal-regeneration hypertension, but reduced blood pressure and salt intake when given chronically (Tox. and Appl. Pharmacol. 1, 406, 1959), if treatment is begun after onset of hypertension. The finding that many rats on a normal salt intake develop adrenal-regeneration hypertension, as reported at this meeting, suggested that this might indicate an undue, hormonally-induced sensitivity to normal levels of dietary Na. This was tested. Uninephroadrenalectomized, contralaterally adrenal enucleated rats were divided into two groups: one received 1% NaCl to drink, the other a 1% NaCl + 0.03% hydrochlorothiazide solution. On the 22nd day hypertension was common in the first group which was subdivided into two subgroups each having the same mean blood pressure and about equal numbers of normotensive, mildly hypertensive and severely hypertensive members. Each received one of the above solutions. All rats receiving 1% NaCl continuously became hypertensive, and the mean blood pressure rose throughout the experiment. None given saline and diuretic from the outset did so. Mean blood pressure of those given hydrochlorothiazide from the 22nd day declined thereafter. Three mildly hypertensive animals became normotensive and two with moderately high pressures became mildly hypertensive, but one animal which had a pressure of 192 mm Hg at the start ultimately reached 238 mm Hg. It is concluded that the diuretic prevents adrenal-regeneration hypertension if given from the outset and ameliorates mild to moderate established hypertension. In either case salt intake is reduced. It appears not to reverse severe hypertension, or to reduce the salt intake of animals so affected.
Study supported by grants He 02703 and He 08054 from USPHS.

THE MINIMAL UTILIZABLE OXYGEN AND THE OXYGEN DISSOCIATION CURVES OF BLOOD OF RODENTS. F. G. Hall, Department of Physiology and Pharmacology, Duke University Medical Center, Durham, N. C.

Determinations were made of the minimal utilizable oxygen and the hemoglobin oxygen affinities of blood of 16 species of rodents and 2 lagomorphs. These species varied in size, metabolic rates, and environment habitats. There is a correlation between the ability of certain animals to extract oxygen to a minimal oxygen tension and the position of their blood oxygen dissociation curve. Smaller rodents have a relatively higher critical oxygen tension and a higher hemoglobin loading tension for oxygen while larger rodents have a lower critical oxygen tension and a lower hemoglobin-oxygen loading tension. Superimposed on this, however, is that animals adapted to a lower environmental oxygen environment have a lower critical oxygen tension and a hemoglobin with a higher oxygen affinity.

FACILITATED OXYGEN FLUX - ITS POSSIBLE RELATION TO DIFFUSION OF OXYHEMOGLOBIN. H. T. Hammel. John B. Pierce Foundation Laboratory, New Haven, Connecticut.

Scholander discovered that the steady state flux of oxygen through a thin film of water could be enhanced many times by adding hemoglobin to the water. Several authors have ascribed this facilitated flux of oxygen to the diffusion of oxyhemoglobin down its gradient although the details of their formulations have not been rigorously supported by experimental evidence. A series of measurements of $\dot{Q}_{O2}$ and $\dot{Q}_{N2}$ through a film of hemoglobin solution were made for which the pO_2 and pN_2 on one side were always 16.5 and 62.5 mm Hg respectively while the pO_2 on the other side was increased from 0.5 to 14 mm Hg by adding increasing thicknesses of teflon film to this side. When the facilitated oxygen flux was small, it was found to equal the calculated flux assuming that the oxygen was carried by the diffusing oxyhemoglobin and that Henry's law and the equilibrium dissociation curve for oxyhemoglobin apply at the two surfaces of the hemoglobin film. When the facilitated oxygen flux was greatest, it was found to be only one half the calculated flux, presumably because the oxyhemoglobin was not in equilibrium with the dissolved oxygen at the surfaces.

DIENCEPHALIC AND MESENCEPHALIC REGULATION OF PLASMA ANTIHEMOPHILIC FACTOR (FACTOR VIII). James W. Hampton and C. G. Gunn (intr. by R.A. Schneider). Univ. of Okla. Med. Center, Okla. City, Okla.

Neurohumoral regulation of blood clotting was first suggested by Cannon. Recently catecholamines have been shown to raise and hibernation to lower plasma clotting Factor VIII levels. The present study explores the effect of brain stimulation on plasma Factor VIII activity. Twelve dogs had permanent electrodes stereotaxically placed in their brains. At 3 week intervals each dog received either 10 minutes of interrupted stimulation or an equivalent sham period with no stimulation. Factor VIII activity was measured before, during and after experimental procedures using a modification of the thromboplastin generation test with mixtures of canine and human hemophilic plasma. The assay for Factor VIII activity was very reproducible both with repeated determinations on the same sample and with samples drawn only a few minutes apart. No changes in Factor VIII were encountered in 40 sham procedures. Brain areas in which stimulation induced an increase in Factor VIII included hypothalamic, mesencephalic and thalamic sites. Stimulation of limbic, and other hypothalamic areas produced decreases in Factor VIII activity. These areas possess recognized autonomic influences. Other brain areas such as hippocampus, preoptic area, spinothalamic tract and superior colliculus produced no Factor VIII changes when stimulated. Factor VIII changes were independent of changes in hematocrit, fibrinolytic activity, or prothrombin times. It is concluded that central neural mechanisms exist which may increase or decrease plasma Factor VIII activity.
(Supported in part by USPHS Grants HE-06286, HE-07453 and HE-03111)

A POPULATION STUDY OF NEURONS IN NUCLEUS VENTRALIS POSTERIOR OF THE CAT THALAMUS. Fredric Harris (intr. by A. L. Towe). Univ. of Washington School of Medicine, Seattle, Wash.

Extracellular microelectrode recording techniques were employed to study neurons in nucleus ventralis posterolateralis of thalamus in cats anesthetized with chloralose and paralyzed with Syncurine. Tracks were stereotaxically oriented on a 1 mm grid covering a 3x4x5 mm block of tissue which included all of VPL. Neurons were isolated through electrical stimulation of the contralateral forepaw and were then tested for response to natural and electrical stimulation of other appendages. Classification was made on the basis of natural stimulus and characteristics of response to electrical stimulation of the contralateral forepaw (latency, spikes per discharge, threshold, and frequency-following). Modifiability of response to peripheral stimulation by prior stimulation of postcruciate, postdimple, and coronal cortex was studied. Data from individual animals were pooled, with unit stereotaxic locus as a basis. Within the total population, neurons in VPL appear to be segregated into two groups, a dorsal one responsive to hair deflection and a ventral one responsive to touch stimulation. At the border between, the same neuron may be responsive to both hair and touch stimulation. These subgroups differ in response characteristics to electrical stimulation of contralateral forepaw and manner in which their response to peripheral input is modified by cortical stimulation. Early-firing, touch-responsive neurons may activate a cortical loop, via coronal tissue, which feeds back onto and modifies the excitability of both touch- and hair-sensitive neurons in VPL. Both facilitatory and inhibitory influences have been observed. Unit response data are used in interpretation of gross wave records from VPL. (Supported by Research Grant NB 396 and Training Grant PHS TI-GM-260 from the National Institute for Neurological Diseases and Blindness.)

In Situ Blood Perfusion of the Rabbit Placenta. Frederick M. Hart* and J. Job Faber. Department of Physical Medicine and Rehabilitation, University of Washington, Seattle, Washington.

Umbilical vessels of rabbit fetuses near term were cannulated in situ to allow artificial perfusion of the placenta. The fetus was removed and replaced with an adjustable flow pump and a rotating disc tonometer in which rabbit blood was equilibrated with ca. 50 mm pCO_2 in N_2. Oxygen and carbon dioxide tensions and hydrostatic pressures in the arterial and venous catheters were continuously recorded. Blood flow was controlled by the pump, and measured at the venous catheter outlet. Periodic samples of blood were taken for pH determination. All measurements were made at the temperature of the saline bath (39.1°C) in which the maternal animal was partially immersed. Oxygen content was calculated from pO_2, pH, and temperature by the use of published oxygen dissociation curves for this species. Oxygen uptake was measured at umbilical flow rates comparable to those in rabbit fetuses in situ, and at higher flow rates. Properly functioning preparations were obtained only by following certain precautions; including: (1) premedication of pregnant animal with reserpine (0.25 mg/kg/day) for 3 days prior to experiment; (2) prevention of contraction of uterus under the placenta; (3) continuous filtering of perfusion blood; (4) use of rabbit blood. In the above preparation at normal flow rates, oxygen uptakes and driving pressures were equal to those in intact fetuses and losses of blood to the maternal circulation were negligible. Placental oxygen consumptions were measured by clamping of uterine circulation and perfusion of umbilical circulation with oxygenated blood.

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Effects of Acetylcholine on Cortico-medullary Osmotic Difference. Rodney B. Harvey, Dept. of Physiology, University of Minn., Mpls., Minn.

Acetylcholine (Ach) infused at 0.25 mg/min. into one renal artery of anesthetized dogs produces a homolateral diuresis, increased solute excretion and doubles renal blood flow. Comparison of changes in medullary tissue and urinary solute concentrations was made to investigate the mechanism of action of Ach on urinary changes. Three control periods of urine collection from both renal pelves of hydropenic dogs were made. Following the controls Ach was infused into one renal artery for 5-12 min. Both kidneys were then rapidly removed and sectioned. Analyses were performed on boiled slices for Na, K, urea, inulin, and PAH. The results indicate: 1. The control urines were highly concentrated with urea and K salts being the major solutes; there were large cortico-medullary solute differences, and medullary tip and urine concentrations of all solutes were markedly different although total osmolalities were comparable. 2. Ach infusion markedly reduced tissue and urine urea concentrations and total osmolality. The increased excretion of H_2O, Na, and urea was accompanied by a rapid reduction in cortico-medullary concentration difference. The medullary tip concentration of urea, Na, and K approached urine concentration during 10 min. of Ach infusion. These data are consistant with an increase in collecting duct permeability to Na, K, and urea during Ach infusion in a preparation that previously showed large concentration differences of solute; but not water, across the collecting duct. It is suggested that the medullary solutes are washed out into the urine during Ach infusion. (Supported by USPHS Grant HE 07002).

TEMPERATURE OF THE BRAIN AND BLOOD IN THE UNANESTHETIZED MONKEY. J.N. Hayward, E. Smith*, and D.G. Stuart, Dept. Anatomy, U.C.L.A., Dept. Physiol. Sciences, U. Calif., Davis and V.A. Hospital, Long Beach, California.

Experiments were performed on monkeys (Macaca mulatta) to determine the relationship between temperature of the hypothalamus and the arterial blood. Thermocouples were surgically implanted in intracranial and extracranial sites and in the venous and arterial vasculature. Temperatures of cerebrospinal fluid, brain and blood were measured in monkeys at rest in a primate restraining chair in a lighted, sound attenuated environmental chamber at neutral ambient temperature (23-28C). Cortical EEG and orbicularis oculi EMG activity were recorded. Brain temperatures were higher than intra-aortic and intra-carotid arterial blood temperatures by 0.2-0.6C. Anterior hypothalamic temperatures were generally closer to arterial blood than posterior hypothalamic and rostral midbrain temperatures. The highest brain temperatures found above arterial blood were in the subcortical white matter of the parieto-occipital lobe. Temperatures of the cerebrospinal fluid in the cortical subarachnoid space varied considerably but were generally above arterial blood temperature. Rapid rises and slower falls in anterior hypothalamic temperature, observed during changing EEG, EMG and motor activity, were associated with simultaneous shifts of similar magnitude and direction in blood and other brain sites. The increment of temperature difference blood:brain was usually maintained.
(Supported in part by USPHS Grants NB-05638 and NB-05199)

ISOLATION AND CHARACTERIZATION OF THE HETEROSACCHARIDE MOIETY OF THE HUMAN TAMM AND HORSFALL URINARY GLYCOPROTEIN. Robert Heath° and Myles Maxfield, Biophysics Program, University of Southern California, L.A., California.

The fibrous glycoprotein of Tamm and Horsfall which inhibits myxoviral hemagglutination of molecular weight 7×10^6 has previously been shown to be a polymer of glycoprotein units of molecular weight 28×10^3. About 25% of the glycoprotein monomer unit is heterosaccharide. Digestion of the glycoprotein with alkali or papain releases the heterosaccharide. The heterosaccharide shows a sedimentation velocity of 0.67 svedbergs. Assuming a spherical molecule (with 30% water of hydration), this corresponds to a molecular weight of 3.5×10^3 or approximately the minimum molecular weight from carbohydrate analysis. It is concluded that the Tamm and Horsfall glycoprotein monomer is composed of a protein unit with two heterosaccharides of MW 3.5×10^3 attached.

FACTORS AFFECTING UPTAKE OF SUGARS IN THE COLON.
J. W. Heaton, Jr.*, Stanford Univ., Palo Alto, Calif. and D. S. Parsons*, Oxford Univ., Oxford, England, (intr. by G. A. Feigen).

The colon has been shown to possess a mechanism for the active transport of sodium; the mode of sugar transport in the colon requires further clarification. We studied the tissue uptake of 2 actively transported hexoses and a pentose under a variety of conditions. Everted sacs were made from the terminal 10 cm. of the rat colon from which the muscular layers had been removed; these were incubated for one hour. The sugar concentration in the tissue water was then compared with that in the medium and expressed as the fraction of tissue water accessible to the sugar. The partition coefficients (alpha) were approximately equal for 3-methylglucose, galactose, and l-arabinose (0.70), whether the sugar was on both sides of the membrane or on the serosal side only. Colonic mucosa was practically impermeable to galactose when present on the mucosal side only. When there was no sugar in the serosal fluid, the partial replacement of sodium on the mucosal side by lithium, potassium, or choline had no effect on the mucosal penetration of 3-methylglucose. It was increased by incubation in an atmosphere of nitrogen. Phlorizin, 1×10^{-4}M, in the mucosal solution caused a slight increase in the permeability to galactose. Comparable studies with inulin showed a space of 0.04 (alpha) when inulin was present only on the mucosal side and 0.38 when present on the serosal or both sides. Comparison of the values obtained with the various sugars with the inulin spaces shows that the sugars are able to penetrate the cellular water. No evidence of accumulation of sugar against a concentration gradient was found.
(This study was carried out during the tenure of a Special Postdoctoral Fellowship of the National Institute of Arthritis and Metabolic Diseases).

PASSIVE CALCIUM TRANSPORT IN RAT INTESTINE. Harold Helbock and Paul Saltman (intr. by John G. Forte). Graduate Program of Biochemistry. University of Southern California. Los Angeles, California 90007

The short circuit technique of Ussing was applied to calcium transport across intestinal mucosa from rats previously starved 24 hr. Unidirectional flux rates, S → M and M → S, were measured at 15 min intervals in a large series of membranes. Throughout a 2 hr period, the flux ratio was unity under short circuit conditions. No evidence for active transport of calcium was seen for Ca at 10^{-5} M. Further confirmation for the passive nature of Ca movement was the comparison of Na^{22} and Ca^{45} flux in the same membrane aerobically and anaerobically. Sodium was inhibited approximately 35%, while Ca movement was slightly enhanced due to increased permeability of the membrane. The rate of Ca transport was directly proportional to its concentration in the range of 10^{-6} to 10^{-3} M. No evidence for a membrane bound facilitating carrier was evident. The interaction of Ca and phosphate was studied. As phosphate concentration increased at a constant Ca, there was an initial increase of transport followed by inhibition due to the formation of insoluble calcium phosphate complexes. The ability of a variety of chelating agents to enhance calcium transport was observed. Parallel *in vivo* experiments using intact animals with ligated intestinal segments yielded similar results. It is concluded that both *in vitro* and *in vivo* there is no evidence for active transport of Ca. Calcium ion either free or bound to ligands moves passively across the intestinal membrane where it is ultimately bound to a variety of carriers in the blood stream. Regulation and control of calcium transport is a function of the competition of the calcium ion with low molecular weight soluble chelates which are transportable, and insoluble ligands which prevent its utilization, and permeability properties of the membrane. (Supported by grants from the Hartford Foundation and the U.S. Public Health Service.)

OBSERVATIONS CONCERNING TEMPERATURE REGULATORY MECHANISMS IN THE OSTRICH STRUTHIO CAMELUS. Roger H. Helmendach, Harold D. Dent* and Edward P. Brown*. Department of Physiology and Biophysics, Loma Linda University, Loma Linda, California.

Observations and multiple temperature measurements were made on ostriches deprived of water and exposed to hot environments. Deep cloacal temperatures remained relatively constant around 40°C. throughout most of a 50 hour experiment but became labile near the end.

In contrast to feather erection as seen in most birds to increase insulation against cold, the ostrich raised its feathers in order to shade the skin under hot ambient conditions and lay its feathers down to increase insulation in the cold. This shading effect in the heat is accomplished due to the fact that the feather shafts are largely bare with tufts of filaments and down concentrated near the tips.

Under conditions of extreme radiant heat load the temperature gradient from the underlying skin to the outside of the feathers was observed to be as high as 17°C. Heat loss is also increased by wing fanning.

Resting respiratory rates were noted to be as low as 4 per minute and tended to increase with standing. Thermal polypnea has been observed to a maximum rate of 55 breaths per minute. Resting heart rates (sitting) were as low as 11/minute. Increases to 40/minute were observed due to standing and tended to be higher at high environmental temperatures. (This research was supported in part by the General Research Support Grant to Loma Linda University and by HTS 5171.)

RESPIRATION AND ENERGY METABOLISM OF THE SHEEP AS RELATED TO SKIN, RECTAL AND BRAIN TEMPERATURES. Allan Hemingway, Department of Physiology, Medical Sch., Univ. of Calif. at Los Angeles and Dept. of Physiology, Medical Sch., Univ. of Otago, Dunedin, New Zealand.

Experiments were conducted to determine the physiological characteristics of the sheep as a homeotherm and to evaluate the usefulness of this animal in studies of physiological temperature regulation. Sheep were immersed in a water bath of controlled temperature varied through a range which incited shivering with cold and thermal tachypnea when warm. Respiration was measured by collection of expired air in a spirometer from a tightly fitting mask. Measurements were made of ventilation rate (minute volume of respiration), tidal volume, respiratory rate, oxygen consumption rate and respiratory quotient. Electromyographic potentials were obtained from intercostal and masseter muscles. The animals were tested before and after operation for insertion of thermistors in the brain. It was found that the neutral skin temperature, where ventilation rate was a minimum, was 34-35°C. Brain temperatures in an air environment, 18-22°C, were 0.2 to 0.5°C lower than rectal temperatures. In some experiments shivering occurred at a higher brain temperature than in a neutral environment and increased after the onset of shivering. In one sheep there was a sharp critical rectal temperature, with oxygen consumption rate being elevated for all rectal temperatures below this threshold. The sheep is an excellent laboratory animal for temperature regulation investigation being apparently less excitable than dogs or cats.

Homeokinetic Theory and Remote Experimental Cybernetic Analysis of Delayed Feedback of Oral Breath Pressure. John Henry*, Richard Junas*, & Karl U. Smith. Dartmouth Medical School and University of Wisconsin

A first remote feedback analysis of respiratory control in normal individuals and emphysema patients has been completed by means of a long-distance computer-controlled feedback loop between Madison, Wisconsin, and subjects located in Hines Memorial Veterans Hospital, Chicago. Ten normal subjects and ten patients were trained and tested in synchronous and delayed visual feedback of oral breath pressure control. The transduced breath pressure signal of the subject was transmitted over analog data lines from the Hines hospital experimental station to the hybrid computer station at Madison, where it was converted to digital form and programed for feedback delays and other types of experimental control. After deconversion, the programed signal was transmitted back to Chicago over another analog data line and displayed to the subjects on an oscilloscope as a computer-controlled visual feedback of their own breath pressure movements. Patients were inferior to normal subjects in learning and performance in synchronous and delayed breath-pressure feedback control. Differences between normal subjects and patients were evident namely at low delay magnitudes between 0.1 and 1.0 seconds. The experiment demonstrates the feasibility of our methods of remote experimental cybernetic analysis of respiration in training and testing respiratory patients. Results confirm in some detail the assumption that real-time kinetic factors in external skeletal muscle systems determine the dynamic pattern of oral breath pressure regulation and possibly other levels of respiratory behavior. The methods also have direct implications for space science.

CELL POPULATION KINETICS IN TAIL SKIN EPIDERMIS OF RATS. O. Heroux, National Research Council, Ottawa, Ont., Canada.

H^3-thymidine, 0.5 μc H^3 per g. B.wt. was given by subcutaneous injection to two groups of adult rats kept at 30°C. The specific activity level of the H^3-thymidine was such that one group received 0.06 μg and the other 0.018 μg of thymidine per g. B.wt. The maximum number of DNA-labelled cells in tail epidermis as seen on autoradiographs was obtained after 5 hrs in the 1st group and within one hour in the 2nd. In both cases, however, the maximum average number of grains per labelled cells was attained within one hour. The calculated duration of synthesis of DNA was 7 hrs in the 1st group and 14 hrs in the 2nd. Possible explanations for such a lack of agreement in the results are discussed.

EXTINCTION OF AVOIDANCE-CONDITIONED BEHAVIOR BY ACTH OR CORTISOL. G. Heuser, E. Endroczi and R. Koelling (intr. by D. H. Solomon). Depts. of Medicine and Anatomy and Brain Research Institute, UCLA, and VA Research Programs, Long Beach.

11 cats were trained in an avoidance-conditioning situation in which a shock to the feet was the unconditioned and a tone the conditioned stimulus. First, the cats were taught to escape to a safe platform in response to the tone and allowed to reach a 100% response level. Then extinction was started, i.e. no more reinforcing shocks were delivered when the cat did not respond to tone. While most animals began to extinguish their response spontaneously only after about 5-7 days (25 trials each day), a single injection of ACTH (4 I.U./kg. i.m.) or cortisol succinate (8-100 mg/kg. i.m.) on the third day led to an immediate drop in performance, with early extinction, in 8 cats. These hormones thus appear to induce early forgetting of, or less concern over, a previously experienced anxiety-inducing situation.

BIDIMENSIONAL STATISTICAL ANALYSIS OF THE OXYGEN CONSUMPTION AND BODY WEIGHT IN RATS. A. Heusner and P. Jolicoeur* (intr. by R. E. Smith) Dept. of Physiol. UCLA Sch. of Med., Los Angeles, Calif. and Dept. of Biology, University of Montreal.

The weight exponent of the relation between O_2 consumption and body weight as estimated in rats is smaller than the Kleiber-Brody interspecific weight exponent (Heusner & Harmelin, C.R. Soc. Biol. 157:376, 1963). This difference becomes statistically significant if the size of the sample is sufficiently large, i.e., ($0.58 \leq b \leq 0.68$, $p=0.05$, $N=252$). The difference is introduced through the assumption of the regression analysis that the random variations in body weight (fat, water, fur) can be neglected as being small, relative to the weight range. However, this is not true if the weight range itself is small. In this case, the principal axis of the covariance matrix becomes a better description of the most probable relationship between O_2 consumption and body weight than is that given by the least-squares regression line. This is because the former estimate takes into account random variations in both body weight and O_2 consumption. The confidence interval (Jolicoeur, Biometrie, 1965, in press) of the weight exponent estimated in this way includes the Kleiber-Brody interspecific weight exponent of mammals, i.e., ($0.65 \leq b \leq 0.75$, $p=0.05$, $N=252$). Supported by a Postdoctoral Fellowship from the National Research Council of Canada.

SOME PHYSIOLOGICAL ASPECTS OF EXPOSURE TO HIGH HEAT, HIGH HUMIDITY IN DOGS. E. Arnold Higgins* and P. F. Iampietro. Physiology Laboratory, Civil Aeromedical Research Institute, Oklahoma City, Oklahoma.

Thermal panting is recognized as a temperature regulating mechanism but its physiological consequences outside of biothermal control are seldom evaluated. Forty-five unanesthetized dogs were used with five animals each exposed to nine different environmental conditions consisting of three ambient temperatures (TA) [100°F (37.8°C), 110°F (43.3°C) and 120°F (48.9°C)] and relative humidities (RH) (30%, 60% and 90%). Animals were exposed for two hours or until rectal temperature (TR) reached 42.0°C. Responses were evaluated after an initial thirty minute exposure (control) to 24°C and near 50% RH. The more severe the heat load (combined TA and RH) the greater the rate of elevation of TR over control levels (i.e. less successful the biothermal defense). In the later stages of heat loading respiratory rate (RR) declined while a high negative correlation between blood CO_2 and TR was maintained throughout the exposure indicating an increase in alveolar ventilation. Under combined conditions of high TA and RH (large thermal load) the non-biothermally involved physiological consequences of panting became evidenced by the increased pH and decreased blood CO_2 (as a result of the thermally forced hyperventilation) and an increase in blood O_2 attributed to the reflex maximum peripheral vasodilation (increased peripheral blood flow, cardiac output, and consequent reduced percentage O_2 extraction by the tissues) These data indicate that the phenomenon of panting should be evaluated more completely in terms of homeostatic mechanisms other than body temperature control. Also, physiological correlates of effective respiratory heat exchange other than RR measures need to be developed. Further, respiratory patterns during hyperthermia in relation to respiratory control limits influenced by blood CO_2 levels require additional attention.

LUNG TISSUE RESISTANCE (Rlt) AND DYNAMIC COMPLIANCE (Cdyn). J. Hildebrandt, (intr. by A. C. Brown). Dept. of Physiol. and Biophys., Univ. of Wash., Seattle, Wash.

Dynamic p-v loops of excised cat lungs were measured by a method in which gas flow is not present: a fixed amount of gas in the lung was compressed and expanded in an oil-filled plethysmograph. The transpulmonary pressure, i.e., the pressure at the airway opening minus the pleural pressure (Pao-Ppl) was recorded on the Y-axis of an oscilloscope, and volume change, V, on the X-axis. Since the airway was closed by the pressure gauge, Pao=Palv. Sinusoidal volume changes of different frequencies (0.01-20 cps) and of different amplitudes (tidal volumes, V_T, from 5 to 40 ml) were imposed on the lung, and the resulting p-v loops photographed. RESULTS. [1] Pressure-volume curves were open loops at all frequencies. Loop areas, representing energy loss per cycle, were not directly proportional to frequency as would be the case if Rlt were a linear resistance. Instead, loop area was nearly independent of frequency over the range 0.01 to 2.0 cps. At higher frequencies the area increased sharply. This suggests that in our preparation losses due to pendelluft become important only above 2 cps. Because of the inertance of the surrounding oil, resonance was reached at fairly low frequencies (8 to 19 cps), complicating the analysis. Loop area is approximately proportional to the square of V_T. [2] Lung elastance (1/Cdyn) rose nearly linearly with the log of frequency. Since, by the above argument, unequal local compliances do not affect the measurements below about 2 cps, the fall in compliance must be due solely to the mechanical properties of the tissue. Thus the decrease in Cdyn in the intact lung as frequency increases is partly due to tissue plastic properties, as well as to unequal time constants. (Supported by Training Grant PHS TI-GM 739-08 from the National Institutes of Health.)

INTRACELLULAR POTENTIALS AND FREQUENCY PATTERNS OF BULBAR RESPIRATORY NEURONS. J. R. Hildebrandt and C. F. Stevens (intr. by A. C. Young) Dept. of Physiology and Biophysics, Univ. of Wash., Seattle, Wash.

Intracellular action potentials were recorded from respiratory neurons in the region of nucleus ambiguus in the cat. The animals were decerebrated while under light Nembutal anesthesia and vagotomized; carotid sinus nerves were cut and, in some cases, the spinal cord was cut at C_8. Membrane and action potentials in both inspiratory and expiratory neurons varied from 10 to 60 mV. Overshoot of the action potential was never observed. In most of those cells in which a slow potential change underlying the spikes could be observed, the frequency of discharge depended on the magnitude of the slow depolarization. However, in some cells frequency decreased even though there was a depolarizing drift in membrane potential. This latter agrees with a previous report by Salmoiraghi and von Baumgarten (J. Neurophysiol. 24, 1961). Hyperpolarizing drifts in membrane potential were occasionally seen immediately following spontaneous discharge. More frequently, hyperpolarizing shifts in an expiratory cell were found to coincide with inspiration and vice versa. If the cell fired throughout the respiratory cycle, the action potentials were larger but at a lower frequency during the hyperpolarization. No IPSP-like potentials could be observed during the hyperpolarizing shift. Our description of cells whose frequency appears to be dependent on input (slow potential changes) indicates that at least two types of cells exist in the deafferented medullary respiratory centers. These types may play different roles in respiratory control. (Supported by PHS TI-6M-26-06).

A COMPARATIVE STUDY OF SHOCK (HYPOTENSION) ELICITED BY ENDOTOXIN, HEMORRHAGE AND LIMB OCCLUSION.
Lerner B. Hinshaw, Lura A. Solomon*, and Dale A. Reins*. Dept. of Physiology, Univ. of Okla. Med. Ctr. and Dept. of Surgery, V.A. Hosp., Okla. City, Okla.

Little information is available concerning the relationships between the various forms of shock. The present study was primarily designed to contrast vascular changes occurring in the dog foreleg as a result of systemic hypotension produced by endotoxin (LD_{80}, E. Coli), hemorrhage (4 1/2 % dog weight) and limb occlusion (tourniquet placed on upper hind limb 7 hours and released at zero time). Forelimbs were surgically removed from anesthetized dogs with the exception of the brachial artery. Large veins were severed to drain at atmospheric pressure. Small artery and vein pressures in the paw were continuously recorded during the two hour course of experiments. Results show marked increases in total limb resistance in all instances due primarily to changes in the segment from small artery to small vein. Large vessel and venous segment resistances showed increases in all experiments to varying degrees. Early marked elevations of limb resistance occurred with hemorrhage and endotoxin which later declined, while resistances during the post-limb occlusion period progressively rose during the two hour period. Limb blood flow and pH significantly decreased, heart rate decreased early but rose later in hemorrhage and limb occlusion experiments, and hematocrit increased to varying degrees in the three forms of stress. Although findings reveal similarities in these kinds of shock, significant differences are also evident. Results support the view that each form of shock (hypotension) may employ its own unique mechanisms.
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K+ EFFECT ON INSULIN INHIBITION OF GASTRIC SECRETION IN THE DOG. Basil I. Hirschowitz and George Sachs*. Department of Medicine, Division of Gastroenterology, University of Alabama Medical Center, Birmingham, Alabama.

Insulin inhibits histamine stimulated gastric secretion by an unknown mechanism, independent of hypoglycemia or the vagus, but presumably by a direct action on the gastric mucosa. This inhibition is reversed by an intravenous injection of 1 mEq/Kg KCl, and the reversal is maintained for 1 - 1 1/2 hours. The fall-off of secretion after the injection of insulin alone is also reversed by KCl injection. The continuous infusion of KCl after insulin prevented any change in $[H^+]$, $[Cl^-]$ and $[Na^+]$, but there was partial inhibition of volume and K^+ secretion. NaCl was without effect on insulin inhibition and KCl alone had no stimulating action on the mucosa. K^{42} flux data suggest a rapid small and slow large cellular K^+ compartment not appreciably altered during insulin inhibition. It is suggested that insulin inhibition may occur via a redistribution of cell K^+ with depletion of K^+ sites essential for secretion, and the injected K^+ repletes those sites with restoration of secretion.

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BROWN FAT AND THERMOREGULATION IN DEER MICE AT ALTITUDE. R. J. Hock, J. C. Roberts* and R. E. Smith. White Mountain Research Station, University of California, and Department of Physiology, UCLA.

Deer mice, Peromyscus maniculatus sonoriensis, from the sea level colony at UCLA were translocated to Barcroft Lab. (3800 m., P_B 485 mm Hg) for 100 days, during which metabolic rate (MR)(at T_A 10, 20 and 32C), colonic temperature (T_B) and interscapular brown fat weight were determined at selected intervals and compared with similar data on sea level and high altitude native controls. After 100 days a group of these mice was returned to sea level and studied for another 50 days. The data show that: 1) Immediately on exposure to hypoxia, T_B decreased 0.76C, MR increased from 3.03 to 3.65 ml O_2/gm/hr and brown fat wt/body wt increased 40%. 2) By 7 days T_B returned to pre-translocation level, from which it did not vary significantly during the remaining period at altitude. 3) With the restoration of T_B to control levels, MR and brown fat ratio decreased, reaching pre-translocation values by 15 days. 4) On return to sea level, T_B of translocated mice was significantly below that of colony controls. Simultaneously there was an increase in brown fat mass until T_B reached control level, at which time brown fat weight again decreased. 5) Initially, on exposure to altitude, both absolute and relative brown fat weights rose to levels found in native Barcroft mice. Thus it appears that body cooling, whether induced by hypoxia or cold, gives rise to compensatory thermoregulatory responses in brown fat.

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THE PREFERENTIALLY RAPID INTESTINAL ABSORPTION OF FATS ADMINISTERED IN MICELLAR FORM TO DOGS AFTER ACUTE EXCLUSION OF PANCREATIC JUICE. Frank J. Hohenleitner and John R. Senior (intr. by T.G. Schnabel Jr.) Philadelphia General Hospital, Philadelphia, Pennsylvania.

Rapid uptake of micellar monoolein and oleic acid has been shown to occur in slices and sacs of proximal small gut, supporting the concept that this form of lipid is preferentially absorbed under physiologic conditions. To compare the rates of absorption of lipid as triglyceride suspensions and as micellar solutions, lipids in these forms were infused into the distal duodenum of fasted, anesthetized dogs beyond ligatures which excluded further entry of pancreatic juice and bile during the test period. Micellar mixtures of fatty acids from corn oil and 1-monoolein in a molar ratio of 2:1 were prepared using 13-18 ml of native canine gall bladder bile per 100 ml of final solution, made up to volume with physiologic saline, and pH adjusted to 6.8. The mixtures contained a total of 5-10 g of lipids per 100 ml and showed no gross turbidity or precipitate. Thoracic duct lymph was collected for a 30 minute period before infusion of 6-7 ml of micellar solution per kg body weight, and for a total of 2 hours afterward. Alternatively, triglycerides as corn oil were substituted for the fatty acid-monoglyceride and administered as a fat emulsion. In contrast to no increase in lymph triglycerides after infusion of the triglyceride emulsion, the administration of the micellar lipids resulted in an immediate and marked rise in lymph triglycerides and gross lactescence. From fasting levels of 0.9-1.2 mg of lymph triglyceride per kg body weight per 30 minutes, the micellar solutions induced 3 to 7-fold rises to 3.2 to 6.8 in 1.5-2 hours. This pronounced difference in the rate of fat absorption in the intact, anesthetized animal provides further evidence that the monoglyceride-fatty acid-bile salt complexes (micelles) are the preferred physiochemical form for absorption.

THE ROLE OF DIETARY SODIUM CHLORIDE EXCESS IN ADRENAL-REGENERATION HYPERTENSION. O. B. Holland*, O. Hall* and C. E. Hall. University of Texas Medical Branch, Galveston, Texas.

It has been averred that hypertensive vascular disease develops in adrenal enucleated rats only if a kidney is removed and salt intake is increased. Recently we have reported that the disorder does develop in rats having both kidneys if the salt intake is increased sufficiently. The present study is concerned with the presumed necessity of increasing the sodium chloride consumption. Uninephroadrenalectomized and contralaterally adrenal enucleated rats were given 1% NaCl solution to drink for 45 days and the response in them compared with that of rats either allowed to drink the solution for 1, 2 or 3 weeks postoperatively and given tap water thereafter, or given tap water exclusively. Severe hypertension developed in almost all animals exposed to any period of augmented NaCl intake and in half of those which had received only water. In a second experiment of 52 days duration, similarly operated animals were given saline throughout, or for 2, 4 or 6 days postoperatively, receiving distilled water thereafter, and their response compared with that of rats given water only. Moderate to severe hypertension developed in all rats on continuous saline and mild to moderate hypertension in 63% of each of the groups with limited periods of excess and in 50% of those given only distilled water. It is concluded that salt in addition to that contained in normal commercial rations is not essential to the development of adrenal-regeneration hypertension in susceptible animals, although such supplementation does increase the incidence and severity of the condition and may be essential to the response in highly resistant animals.

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EFFECT OF RESPIRATORY OSCILLATION OF ARTERIAL P_{O_2} AND P_{CO_2} ON CAROTID CHEMORECEPTOR ACTIVITY AND PHRENIC NERVE ACTIVITY. Thomas F. Hornbein. University of Washington School of Medicine, Seattle, Washington.

The effect of respiratory oscillation of arterial P_{O_2} and P_{CO_2} on carotid chemoreceptor activity and phrenic nerve activity has been studied in cats under pentobarbital-gallamine anesthesia. The animals were ventilated mechanically at large tidal volume and slow rate to enhance the magnitude of blood-gas oscillations. The common carotid arteries were perfused alternately either with arterial blood possessing respiratory oscillations of P_{O_2} and P_{CO_2} or with the same blood after oscillations had been removed by passage through a mixing chamber implanted in the abdominal cavity. Rhythmical oscillations of carotid chemoreceptor nerve activity resulted from perfusion with oscillating blood-gas stimuli, but mean integrated nerve activity was identical to that observed in response to the non-oscillatory stimulus. Integrated phrenic nerve activity was likewise not influenced by the presence or absence of oscillating blood-gas stimuli. Observations at different P_{aO_2} suggest that ventilation is not affected either by amplitude or rate of change of stimulus (O_2 - CO_2 interaction) to the peripheral chemoreceptors. Electrical stimulation of the sympathetic nerve supply to the carotid body did not alter this relationship. (Supported by USPHS Grant HE-08866-02.)

EVOKED POTENTIALS ARISING FROM NEURAL POPULATION ELEMENTS EXCITED AT DIFFERENT TIMES ON A WARPED SURFACE

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Certain types of cortical electrical events are non-propagated, so that the associated electric fields must have standing wave characteristics. However, cortical electric events typically are generated by neurone populations which cannot be activated simultaneously on impulse driving. Hence the sum of the standing wave fields due to asynchronous activation of adjoining regions of cortical neurones must give the appearance of a traveling wave. Analysis of cortical wave forms is further complicated by curvature in cortical surfaces. A model is presented that shows the effects of curvature and time lag in activation on the waveform of potential generated at points in space around a laminar array of elements simulating a population of cortical neurones. In the examples considered a single population element is a dipole with a separation between positive and negative point charges that is very small in comparison to the dimensions of the population as a whole. These elements are oriented normal to a curved surface to form a dipole sheath. The time-variance of each element in response to an impulse is assumed to have the form of a damped sinusoid. The calculated results are compared with waveforms evoked by single-shock stimulation of the prepyriform cortex in cats. The calculated results show possible mechanisms for disparity of peak amplitudes on opposite sides of the approximate zero isopotential for failure of a true isopotential to occur, and for a brief positive wave often preceding initial negativity.

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ELECTROLYTES IN BODY AND HAND SWEAT OF MALES WORKING IN THE HEAT. Steven M. Horvath and W. van Beaumont.* Institute of Environmental Stress, Univ. of Calif., Santa Barbara, Calif. and Dept. of Physiol., Indiana Univ., Bloomington, Indiana.

The concentrations of solutes, Na, K and Cl in body and hand sweat were measured on 9 adult males (31-73 years) and 31 young boys (10-17 years) while performing a standard walk. The walks were for a period of 60-70 minutes at 100 m/min. They were conducted on a quarter mile track at Boulder City, Nevada. The mean maximum temperatures at Boulder City ranged from 34-42 C with a relative humidity of approximately 25 per cent. Rectal temperatures were obtained before and after the work period and mean skin temperatures calculated from 5 areas were secured at 15 or 30 minute intervals during the walk. Relationships between sweat rates, body and surface temperatures and electrolyte concernatives in both body and hand sweat will be presented in respect to age and heat acclimation.

THE EFFECT OF HYPOPHYSECTOMY AND GROWTH HORMONE ON THE INCORPORATION OF LABELLED LEUCINE INTO GUINEA PIG DIAPHRAGM PROTEIN IN VITRO. J. Hotchkiss (intr. by E. Knobil). Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

Chronic administration of purified preparations of bovine, porcine and simian growth hormone failed to stimulate weight gain or nitrogen retention in hypophysectomized guinea pigs. Since the known antibody production occurring during growth hormone treatment might have obscured the possible growth-promoting effectiveness of these preparations, experiments were performed to test the effectiveness of purified growth hormone preparations added in vitro on the incorporation of labelled leucine into the diaphragm protein of normal and hypophysectomized guinea pigs. Our results show that (1) unlike the rat, hypophysectomy in the guinea pig did not depress the incorporation of radioleucine into diaphragm protein; (2) the addition of bovine, ovine, porcine and simian growth hormone in vitro (50 µg/ml) failed to stimulate an increase in leucine incorporation into the protein of normal, hypophysectomized or sham-operated guinea pigs; (3) insulin added in vitro (0.1 U/Ml) was highly effective in stimulating leucine incorporation ($p<0.001$). A purified guinea pig growth hormone preparation is currently being tested for amino acid incorporating ability in the guinea pig.

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THE EFFECT OF ACIDS ON GASTRIC EMPTYING. J.N. Hunt and M.T. Knox (intr. by Morton I. Grossman). Guy's Hospital Medical School, London, England.

A series of experiments were performed to measure the relative effectiveness of several acids in slowing gastric emptying in man. The acids used were hydrochloric, acetic, lactic, citric, tartaric and phosphoric. Test meals of 750 ml of different concentrations of these acids were given to 17 subjects. The volume of meal recovered at 20 min was plotted against the concentration of acid in the given meal. The effectiveness of the acids tested, as measured by their ability to slow gastric emptying, was found to be directly proportional to the square roots of the molecular weights, and not related to either fat solubility or pK values. This is consistent with the view that it is necessary for the acids to diffuse through a barrier before activating the duodenal receptors which are responsible for the slowing of emptying.

DISTRIBUTION OF PULMONARY DIFFUSING CAPACITY (D_L) IN RELATION TO PULMONARY CAPILLARY BLOOD FLOW ($\dot{Q}_c$). R.W. Hyde*, R.E. Forster, J. Nairn* G.G. Power*, and R. Rynes*. Dept. of Physiology (Grad. Div.) and Dept. of Medicine, School of Med., Univ. of Penna., Philadelphia, Penna.

We have used two techniques to measure distribution of $D_L/\dot{Q}_c$ in normal human subjects. (1) We simultaneously measured by breathholding methods D_L with 0.4% CO ($D_{L,CO}$), D_L with labelled O_2 of mass 34 ($D_{L,O_2^{34}}$), and $\dot{Q}_c$ by the acetylene technique. Membrane diffusing capacity for CO ($D_{M,CO}$) and pulmonary capillary blood volume (V_c) were calculated by measuring $D_{L,CO}$ at different P_{A,O_2}. Because the hemoglobin in V_c acts like a huge sponge for CO, $D_{L,CO}$ is barely affected by uneven distribution of $D_L/\dot{Q}_c$. On the other hand in the measurement of $D_{L,O_2^{34}}$ mean end capillary $P_{O_2^{34}}$ is about 70% of $P_{A,O_2^{34}}$ so that if uneven $D_L/\dot{Q}_c$ ratios are present in the lungs, total O_2^{34} uptake at the same $P_{A,O_2^{34}}$ will be less, producing a decrease in measured $D_{L,O_2^{34}}$. In 3 sitting subjects measured $D_{L,O_2^{34}}$ was 54% of $D_{L,O_2^{34}}$ calculated from the relationship: $1/(D_{L,O_2^{34}}) = 1/(V_c \times \theta) + 1/(1.19 \times D_{M,CO})$. This difference between measured and calculated $D_{L,O_2^{34}}$ could be explained if 67% of $\dot{Q}_c$ went to a volume of the lung having only 25% of total D_L. (2) We measured $D_{L,CO}$ during 5 sec breathholding periods with an average $P_{A,CO}$ of 27 mm Hg and compared these results to control measurements performed in the same way except that $P_{A,CO}$ was 1.8 mm Hg. If $D_L/\dot{Q}_c$ is uneven, in those capillaries with a high $D_L/\dot{Q}_c$ blood may become fully saturated with CO before leaving the alveolus resulting in a significant rise in blood P_{CO} in those capillaries and a fall in observed overall $D_{L,CO}$. In 2 subjects at $P_{A,CO}$ of 27 mm Hg observed $D_{L,CO}$ was 16% lower than at a $P_{A,CO}$ of 1.8 mm Hg. This finding could be explained if 67% of $\dot{Q}_c$ went to a volume of the lung having only 20% of D_L.

MOTONEURON RESPONSES TO STIMULATION OF THERMOREGULATORY REGIONS OF THE HYPOTHALAMUS. Koichi Ishikawa*, Kenneth Ott*, Douglas Stuart and Earl Eldred. University of California at Davis and Los Angeles and VA Hospital, Long Beach, California.

In 35 lightly anesthetized cats, the firing patterns of L_7 and S_1 alpha and gamma motoneurons were analyzed during electrical stimulation of hypothalamic, striatal and thalamic structures. While local warming of the preoptic-anterior hypothalamic (PAH) region supresses shivering, its electrical stimulation and that of the other structures, had no clear-cut suppressive effect on gamma discharges. The dorsal posterior hypothalamic (PH) region most effective in augmenting gamma discharges included, but was not restricted to that dorsomedial PH region whose stimulation had previously been shown to evoke shivering. A greater intensity of electrical stimulation was necessary to produce later and less pronounced effect on gamma discharges during PAH, striatal and thalamic stimulation than during PH stimulation. Gamma motoneurons responded rhythmically or "followed" PH stimulation of 50 msec trains up to 10 trains/sec. Each train consisted of 100/sec 1 msec square wave pulses. Some alpha motoneurons "followed" these trains up to 20/sec, others only to 5-10/sec. The results suggested that: 1) gamma motoneuron discharges during hypothalamic stimulation are not intimately related to the activation and suppression of shivering; and 2) rhythmic motor activity can be initiated by rhythmic hypothalamic activity as evoked by electrical stimulation. Our previous results would caution that such rhythmicity is probably unrelated to the rhythmicity of shivering.

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EFFECTS OF AMBIENT ALKALINE EARTH CONCENTRATIONS ON FROG GASTRIC SECRETION. A. Jacobson,* M. Schwartz,* and W. S. Rehm, Departments of Radiology and Engineering Physics, University of Louisville, Louisville, Kentucky and Department of Physiology and Biophysics, University of Alabama Medical Center, Birmingham, Alabama.

Mucosae were mounted between chambers with Cl^- Ringers (Ca^{++} = 1 mM) on the nutrient side and a Ca^{++}-free solution on the secretory side. The PD, resistance (ΔPD/applied current) and H^+ rate (pH stat method) were measured. It has been reported (Am. J. Physiol., in press) that the removal of Ca^{++} from the bathing solutions results in an initial rise in resistance of about 40% (1st phase) followed by a decrease in resistance (2nd phase) to values much lower than the control values. During the 1st phase the secretory rate decreases by about 40% and the PD by about 10%. During the 2nd phase the PD decreases to near zero and the H^+ rate to zero. In the present experiments, the threshold nutrient Ca^{++} concentration for reversal of 2nd phase (increase in resistance) was about 0.03 mM. Maximal resistance levels (2nd phase $\longrightarrow$ 1st phase) were reached with Ca^{++} concentrations in the range of 0.07 to 0.15 mM. Increasing the nutrient Ca^{++} concentration to 0.6 mM (or lower) reversed completely the 1st phase (reduction in resistance to control level). Addition of Mg^{++} to either side or both sides up to concentrations of 67 mM failed to reverse the 2nd phase (resistance remained at the very low level of the 2nd phase). After the 2nd phase was reversed by the addition of Ca^{++} to a concentration of 0.1 mM addition of Mg^{++} failed to reverse the 1st phase. Both Sr^{++} and Ba^{++} temporarily reversed the H^+ rate in both phases. (NIH and NSF support.)

EFFECT OF GASTROSTOMY AND ESOPHAGOSTOMY ON GASTRIC EMPTYING TIMES. Nelson C. Jefferson, Toyohisa Arai*, Anthony Geisel* and Heinrich Necheles. Michael Reese Hosp. Chicago.

We have demonstrated previously that installation of a metal gastric fistula in the dog or adhesions of the stomach to the abdominal wall is followed by considerable shortening of gastric emptying time (E.T.) as demonstrated by barium meals and fluoroscopy. This result was not due to a foreign body reaction, because washers attached at various sites of the stomach did not change gastric E.T. The reduction of E.T. was so considerable, that previous studies with the use of gastric fistulas may be incorrect in certain aspect. For this reason, in order to study gastric mechanisms without gastric fistulas, we have used esophageal fistulas. In view of results obtained with gastric fistulas and in view of the nerve connections in the intrinsic plexuses which are continuous between esophagus and stomach, and in view of the autonomic innervation of both organs, we thought it necessary to study E.T. before and after installation of an esophageal fistula, prepared according to the method of Komarow. We found that such fistulas did not change gastric E.T. We present these findings in order to propose the use of esophageal fistulas rather than gastrostomies for certain observations on gastric mechanisms.

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TEMPORAL ASPECTS OF PITUITARY LUTEINIZING HORMONE(LH) SYNTHESIS IN THE RAT RECEIVING SHEEP HYPOTHALAMIC EXTRACT. Donald C. Johnson and Darren M. Nelson*, Kansas University School of Medicine, Kansas City, Kansas.

Immature female rats were treated with gonadotropins in preparation for the ovarian ascorbic acid depletion (OAAD) assay of LH. Groups of 6 animals received either 0.5, 1.0 or 2.0 pieces of sheep hypothalamus (purified extract, 400ug/piece, which is equivalent to 145mg of hypothalamic tissue) and killed at precise intervals from 0 to 300 minutes later. Plasma and pituitary LH were measured by the OAAD method, using NIH-LH-S5 as the standard. The plasma level rose quickly, but after 15 minutes began to fall toward the zero time control levels. The amount of LH in the pituitary either remained the same, or fell slightly during the first 15 minutes, but was at or above control level at 30 minutes post injection. In contrast, pituitary LH content fell drastically 10 minutes after a single injection of 20ug NIH-LH. The quantity of LH present in the plasma was directly proportional to the dose of extract given, but the amount leaving the pituitary was not. The ratio of rise in plasma LH to the fall in hypophyseal LH at 7.5 minutes was 1.85 with 0.5 pieces and 6.32 with 2 pieces of hypothalamus. With one piece, the hypophyseal LH level did not fall, even though the plasma concentration rose. The results are interpreted as indicating that hypothalamic extract causes a synthesis as well as a release of pituitary LH and further that the ratio of one function over the other is related to the dose of extract given.

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THE PYLORIC ANTRUM AS A MEDIATOR OF INSULIN INDUCED CHOLERISIS.
R. S. Jones* and F. P. Brooks. Dept. of Physiol. and Harrison Dept. of Surg. Res., School of Med., Univ. of Pa., Phila., Pa.

Since insulin-induced hypoglycemia produces a choleresis in conscious dogs (Am. J. Physiol. 204:825, 1963) but sham feeding had little effect (Proc. Soc. Exper. Biol. & Med. 118:481, 1965), we attempted to determine the role of the pyloric antrum by comparing bile flow before and after antrectomy. Three mongrel dogs weighing 22-23 Kg were prepared with chronic gastric and duodenal fistulae (Thomas) after removing the gall bladder and severing the lesser pancreatic duct. Bile was collected in 4 hourly periods following transduodenal catheterization of the common bile duct after an 18-24 hr fast. Insulin 1.5 u/Kg I.V. induced a choleresis similar to that previously reported. Output of total solids increased also. The pyloric antrum was removed and completeness of antrectomy was confirmed by histologic examination. Two dogs had complete studies after antrectomy consisting of 3 expts. under control conditions and 3 after insulin in each dog. Before antrectomy the mean volume of bile collected during 3 hrs (excluding the first hr after catheterization) was 12.4 ml ± 6.7 s.d. in control expts. and 26.2 ± 5.2 after insulin. Total solid output increased from 1046 mg ± 367 to 1624 ± 534. These differences are significant ($p < .01$, $< .05$). Following antrectomy control flow was 10 ml ± 5.6 and after insulin 14.4 ± 10.1. Values for total solids were 870 mg ± 301 and 999 ± 405 respectively. These increases were not significant ($p > .1$, $> .2$). We conclude that the pyloric antrum is necessary for the normal response to insulin and possibly the source of a choleretic agent released by vagal stimulation.
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THE RESPONSE OF THE BLOOD VESSELS IN THE SKIN AND MUSCLE OF THE HUMAN FOREARM TO HYPERCAPNIA. Ralph Jung* and Chester Hyman. The Los Angeles County General Hospital and U.S.C. School of Medicine, Los Angeles, California.

Measurement of peripheral blood flow in the human forearm by electrocapacitance plethysmography and differentiation of flow in the skin from that in muscle tissue by use of a counterpressurization cuff under the plethysmograph has shown that 5% CO_2 breathing leads to vasodilatation of the vessels of the skin without affecting the vessels in muscular tissue. Post-Hypercapneic vasodilatation also occurs in the vasculature of the skin of the intact and nerve-blocked forearm. Arterial occlusion of one leg during the hypercapneic period followed by release of the blood in the leg during the post-hypercapneic period also leads to vasodilatation of the vasculature of the skin. These findings, currently under further investigation, indicate that CO_2 may have a local effect on vasculature of skin without exerting any influence on the vessels of muscle tissue.

ACOUSTICAL DETECTION OF OSTEOPOROSIS. J. M. Jurist* and W. A. Selle. Department of Biophysics and Nuclear Medicine, UCLA School of Medicine, Los Angeles, California.

Routine radiographic techniques under optimal conditions cannot detect osteoporosis until at least 30% demineralization of trabecular bone occurs. Osteoporosis this far advanced usually cannot be successfully reversed. Since the so-called senile or post-menopausal osteoporosis (which is usually observed first in the pelvis and lumbar spine) is a phenomenon occuring throughout the skeletal system, a detection scheme utilizing the ulna would be useful in detecting incipient osteoporosis. The method of detection under investigation makes use of the observation that the product of resonant frequency and length of a bar in a damped medium is a function of density ($FL=\Phi(\rho)$). The function of density ($\Phi(\rho)$) was determined with 6 excised ulnas, and a study of FL as a function of age, nutritional status, and activity was made on a group of 50 normal subjects and 50 known osteoporotic and diabetic subjects. The mean FL for the osteoporotic subjects was $\sim$ 50% of the mean FL for the normal subjects. These results show that the acoustical method of detection is from 3 to 5 times more sensitive than the present radiographic method and has potential value in the management of geriatric patients.

MECHANISM OF HIND LIMB TOURNIQUET REPLACEMENT* ON SURVIVAL OF NORMAL AND ADRENALECTOMIZED RATS. John Kabal and Estelle R. Ramey. Dept. of Physiol. and Biophysics, Georgetown Univ. Med. Center, Washington, D. C.

Maintenance of a bilateral hind limb tourniquet for 5 hrs. followed by removal of the tourniquet results in 100% mortality within 12 hrs. in intact rats and in 2 hrs. in adrenalectomized rats. If the tourniquet is left in place for periods up to 24 hrs. the rats show limb necrosis but all survive. If the tourniquet is removed after 5 hrs. and then is replaced bilaterally within a critical 4 hr. period in intact rats or a critical 10 min. period in adrenalectomized rats, all the animals survive. If the tourniquet is replaced unilaterally within a critical 2 hr. period in intact rats and within a period of less than 10 min. in adrenalectomized rats we found that 100% of the intact and 80% of the adrenalectomized rats survived. Plasma obtained from tourniquet shocked rats had no effect on the survival of any recipient animals. Since the first 2-4 hrs. after tourniquet removal is the period of maximal extravasation of plasma into the ischemic limbs these experiments support the concept that plasma loss is a primary factor in the development of tourniquet shock. Adrenalectomy itself increases capillary permeability and susceptibility to additional vascular leakage.

ROLE OF MITOCHONDRIAL ORGANIZATION IN THYRONINE-INDUCED STIMULATION OF PROTEIN SYNTHESIS. N.Kandemir*, E.Eich*, J.Alfano*, and R. L. Greif. Cornell University Medical College, New York, New York.

Added thyronines increase incorporation of C-14 labeled amino acids into mitochondrial protein (Bronk, J.R. Proc. Nat. Acad. Sci. U.S. 50,524-6,1963). We report here that if mitochondria are allowed to swell by incubating them in buffered sucrose prior to the addition of an incorporation mixture containing C-14 leucine, the hormone-induced increase in incorporation is abolished. Such pre-swollen mitochondria still incorporate C-14 leucine, but at a reduced level.

Ultrasonic disruption of rat liver mitochondria for 30 seconds at $0^{\circ}C$ also abolishes the increment in leucine incorporation produced by added l-thyroxine or triiodothyroacetic acid. Mitochondria disrupted by ultrasound also incorporate reduced but significant amounts of C-14 labeled leucine. They are capable of showing a small degree of swelling on incubation with thyronines, but respiratory control is absent. These experiments suggest that a tightly-coupled system is needed only for that portion of incorporation that is hormone sensitive. (This research supported by grants from the USPHS and the National Science Foundation).

EFFECTS OF STIMULATION OF THE REGION OF RED NUCLEUS UPON MUSCLE SPINDLE ACTIVITY. M. Kano* and E. Eldred. Dept. of Anatomy, Univ. of California, Los Angeles, Calif.

The effects on muscle spindle activity of stimulation of the red nucleus and adjoining regions has been carried out in acute cat preparations under chloralose and urethane anesthesia. Spindle activity from the triceps surae or anterior tibial muscles of the otherwise denervated hindleg was monitored from the S1 dorsal root, the multiunit activity being integrated. Effects from stimulation of the posterior part of the red nucleus are stronger than at other sites in this general area. The most commonly encountered effect seems to be one of modulation, rather than simple facilitation or inhibition. Thus one animal may yield a different result than another, depending upon background levels of activity; or the sign of effect may be reversed in the same animal during pinna-reflex induced activation of spindles. In all instances effects seem to be exerted bilaterally.

THE EFFECTS OF OUABAIN, CO_2, EDTA AND HYPERCALCEMIA ON CSF CALCIUM. R. Kaplan*, L. Graziani*, A. Escriva* and R. Katzman. Albert Einstein College of Medicine, Bronx, New York.

In acute experiments the Ca influx and efflux from CSF was determined in anesthetized cats. During continuous ventriculo-cisternal perfusion with synthetic CSF, Ca^{45} was given I.V. The flux coefficient into CSF averaged 0.011 ml of serum effectively cleared of isotope. When the serum Ca was decreased by I.V. EDTA, the influx coefficient increased, tending to maintain the total CSF Ca influx at its previous level. When ouabain was added to the perfusate in these hypocalcemic animals, the influx coefficient decreased from the high value to below normal values, suggesting an ouabain sensitive active component to the influx mechanism. When the serum Ca was increased to above normal values by I.V. calcium-gluconate, the influx coefficient reciprocally decreased to below normal values. Adding ouabain to the perfusate does not change the influx coefficient in these hypercalcemic animals. A plot of the serum Ca levels against the CSF Ca influx discloses a diffusion component of increasing importance in the hypercalcemic animals. The efflux of Ca from CSF was measured by adding Ca^{47} or Ca^{45} to the perfusate. This efflux coefficient remained within the normal range when EDTA or calcium-gluconate was given I.V., also when ouabain was added to the perfusate. The electrical potential between CSF and blood was measured during ventriculo-cisternal perfusions. The potential was manipulated by the induction of respiratory acidosis. The Ca^{45} influx coefficient was independent of CSF-blood electrical potential gradient when using normal synthetic CSF. When ouabain 10^{-4} M was added to CSF, Ca^{45} influx coefficient became inversely related to the electrical potential gradient. This is further evidence for an ouabain sensitive, active component to the Ca transport mechanism.

THE PREOPTIC AREA-A POSSIBLE TRIGGERING MECHANISM FOR POLYPNEIC PANTING IN CATS. Soichi Katayama* and S. C. Wang. Department of Pharmacology, College of Physicians & Surgeons, Columbia University, New York City.

In cats lightly anesthetized with intraperitoneal chloralose (40 mg/kg) or urethane (1 gm/kg), polypneic responses (respiratory rate more than 100/min) were observed during electrical stimulation of the posterior hypothalamic area and the medial tegmental area of the midbrain. These areas were not thermosensitive. Local diathermy evoked marked panting only when applied to the preoptic area. The thermosensitive panting pathways in the diencephalon as reported by Magoun et al. (J. Neurophysiol. 1:101, 1938) could not be confirmed. On the other hand, electrical stimulation of the preoptic area produced post-stimulatory polypnea (P-SP), which outlasted the stimulation period by several min, with maximal increase in the respiratory rate occurring 1-3 min after termination of the stimulus. Ablation of the frontal pole or decortication did not prevent the responses, and indeed, enhanced the responses. Further, the P-SP responses, once elicited by preoptic stimulation, were not abolished by a subsequent section between the anterior hypothalamus and the preoptic area, or by a subsequent local microinjection of procaine hydrochloride (0.03 ml, 10% solution), or pentobarbital sodium (0.005 mg, 6% solution) in the preoptic area. These results appear to suggest that in the posterior hypothalamus and midbrain there is a polypneic center which could be triggered into prolonged activity by preoptic stimulation. There also may be an inhibitory mechanism in the forebrain. (Supported by 5T1NB-5173 and NB-00031)

FACTORS AFFECTING EXTRAOCULAR MUSCLE TENSION. Ronald L. Katz and Kenneth E. Eakins (intr. by S.H. Ngai). Departments of Anesthesiol., Ophthalmol. and Pharmacol., Columbia Univ., College of P & S., New York, N. Y.

This study concerns the effects of succinylcholine, epinephrine, isoproterenol, and cervical sympathetic stimulation on the tension of extraocular muscles of the pentobarbital anesthetized cat. The intravenous injection of 1-128 μg/kg succinylcholine produced a dose-dependent increase in tension in all of the extraocular muscles studied. The response often appeared to have two components, an initial fast phase and a later slower phase. Atropine (1-4 mg/kg) did not inhibit the response of the extraocular muscles to succinylcholine. The intravenous injection of d-tubocurarine (25-500 μg/kg) markedly reduced the response of the extraocular muscles to succinylcholine. Hexamethonium (5-10 mg/kg) depressed the initial phase of the response to succinylcholine, but markedly increased the second slower phase. The effect of succinylcholine on the extraocular muscles was markedly reduced by the sympathetic beta-receptor blocking agent pronethalol (2.5-10 mg/kg), but was not inhibited by the sympathetic alpha-receptor blocking agent dibenzyline (5 mg/kg). In some animals, dibenzyline potentiated the response to succinylcholine. Intravenous injections of both epinephrine (2-15 μg/kg) and isoproterenol (5-10 μg/kg) increased extraocular muscle tension. These agents inhibited the response to subsequent doses of each other and succinylcholine. Cervical sympathetic stimulation also increased extraocular muscle tension. It is concluded that an adrenergic mechanism may be involved in the control of extraocular muscle tension. (Supported in part by USPHS grant GM 09069-03 and by Fight-for-Sight Grant-in-Aid (G 303) of the National Council to Combat Blindness, Inc., New York.)

CEREBRAL D.C. POTENTIAL CHANGES IN THE RABBIT DURING EATING AND DRINKING. H. Kawamura* and C.H. Sawyer, Department of Anatomy and Brain Research Institute, UCLA, Los Angeles, California.

D.C. potential changes recorded from the frontal cortex and hypothalamus in unrestrained rabbits with chronically implanted electrodes (reference electrode on occipital bone) are of two types: one reflecting conditions associated with characteristic EEG patterns and evoked potentials (e.g. arousal, slow wave sleep, paradoxical sleep) and the other lacking in typical EEG correlates (e.g., after eating dry alfalfa pellets or drinking water). Rabbits deprived of food and water for 12 to 24 hours show marked negative D.C. shifts (1-2 mV) during and after eating dry alfalfa pellets and equally impressive positive shifts after drinking water (1-3 mV). In either case recovery to the previous D.C. level takes about 40 to 90 minutes depending on the period of deprivation and to some extent on the amount of food or water taken by the animals. These phenomena do not appear to result directly from changes in blood osmolality or brain temperature but seem to reflect a more or less sustained alteration in blood-brain barrier potential difference which occurs immediately after intake of food or water.

ARGININE UPTAKE BY DOG RENAL CORTEX MITOCHONDRIA IN VITRO. Daniel M. Keller. Dept. of Physiol., Univ. of Tenn., Memphis, Tennessee.

Experiments were performed to determine whether dog renal cortex mitochondria take up Arg in vitro and whether or not the uptake may be related to Arg reabsorption in vivo. Mitochondria were isolated by the method of Schneider and Hogeboom, incubated at 0° or 30° in a medium suitable for oxidative phosphorylation, with [Arg] at 0.1 to 50 uM. Arg uptake was stopped by cooling to 0° and mitochondria promptly separated by centrifugation for analysis. The ratio of [Arg] in the mitochondrial pellet water to [Arg] in the supernatant (Arg "space") was 0.7 at time zero and slowly increased to 0.9 at 40 min when incubated at 0°. At 30° Arg space increased rapidly, approaching a maximum in 10 to 25 min of 3 to 6 depending on [Arg]. After some uptake had occurred at 30°, cooling to 0° stopped further uptake but did not cause release of Arg, whereas reducing the [Arg] in the medium to zero caused rapid release of Arg. The Arg taken up by the pellet at 30° in excess of the product of pellet water and supernatant [Arg] obeyed the Langmuir adsorption isotherm over the range 0.1 to 20 uM. Other natural amino acids at 25 uM were tested for ability to inhibit the initial rate of Arg uptake ([Arg] = 1 uM.) In the presence of a second amino acid, the rate of Arg uptake was the following % of control: Orn 43, Lys 66, Gly 75, Cys 77, Leu 88, Glu 91, Ala 94, Try 100, Asp 101, His 102. It is concluded that Arg is concentrated within or on mitochondria and the process may be relevant to tubular reabsorption of Arg. (Supported by USPHS Grant AM 04871-04)

BEHAVIORAL AND NEURAL RESPONSES OF CATS TO NOCICEPTIVE THERMAL STIMULI. Dan R. Kenshalo. Florida State University, Tallahassee, Florida.

Behavioral measurements of the threshold for warm stimuli applied to the inner thigh show that cats cannot use mild warm stimuli as cues to avoid receiving a mild electric shock. They successfully avoid the electric shock only when the temperature of the stimulator reaches about 52° C. This is considered to be the nociceptive threshold because this is also the stimulus temperature at which untrained cats consistently make escape responses. Recordings of neural activity in small twigs of the saphenous nerve show many spontaneously active fibers. The frequency of this activity is dependent upon skin temperature. Mild warming of the skin produces a transient reduction in this neural activity. Strong warming, e.g., 52° C., causes an almost complete suppression of activity in these fibers and is accompanied by activity in fibers which showed no activity at lower temperatures.

ALVEOLAR CARBON DIOXIDE TENSION DURING MUSCULAR EXERCISE IN TRAINED AND UNTRAINED MEN. Karlheinz Kesseler (Intr. by U. C. Luft) Dept. of Physiology. The Lovelace Foundation, Albuquerque, N.M.

Considerable disagreement exists concerning the magnitude and direction of changes in alveolar CO_2 tension during exercise. A study was undertaken to ascertain whether the influence of the individual's physical condition and the work intensity, which have not received much attention in this regard, might be responsible for the observed discrepancies. Seven subjects with marked differences in physical condition performed an exercise test with stepwise increasing workloads up to the limit of their capacity on a bicycle ergometer in the supine position. Respired air was analyzed continuously for CO_2 (Infrared), ventilation and gas exchange measured with a Metabograph (Fleisch). 1. There were no significant differences in the resting values. 2. With increasing workloads, end-tidal CO_2 tensions increased initially and then dropped considerably. 3. The highest CO_2 tensions were observed in the well-trained subjects (maximum:trained, 54 mm Hg at 200 watts, untrained 40.5 mm Hg at 75 watts). Plotting the logarithm of alveolar ventilation against the work load gave straight lines the slopes of which were consistently steeper for untrained men. These relationships may explain some of the diverse results reported in the literature. Variations in both end-tidal and mid-expiratory CO_2 tensions were not closely consistent with the changes in arterial blood as shown by simultaneous determinations at different work loads. The difference between arterial and end-tidal CO_2 was generally smaller in well-trained men.

EFFECTS OF ACOUSTIC STIMULI ON SPONTANEOUS SPIKE DISCHARGES IN AUDITORY NERVE FIBERS. N. Y. S. Kiang and M. B. Sachs,* Center for Communication Sciences, Research Laboratory of Electronics, Massachusetts Institute of Technology, and Eaton-Peabody Laboratory of Auditory Physiology, Massachusetts Eye and Ear Infirmary.

Single auditory nerve fibers in anesthetized cats exhibit spike discharges even in the absence of controlled acoustic stimuli. These fibers respond to appropriate tonal stimuli by showing an increase in the rate of discharge. When spike discharges are driven by either tonal or noise stimuli the addition of certain other tones results in a reduction in the rate of driven activity. These last tones, when presented alone, do not reduce the discharge rate to a level below that of spontaneous activity. Under certain conditions, a temporary reduction of discharge rate below spontaneous level can be demonstrated but these reductions cannot be maintained. It is suggested that the generation of evoked discharges may involve mechanisms that differ from those that generate spontaneous discharges. (Supported in part by the Joint Services Electronics Program (Contract DA 36-039-AMC-03200(E); NSF (Grant GP-2495), NIH (Grant MH-04737-05), NASA (Grant NsG-496); and in part by research grant NB-01344, NINDB of the NIH Public Health Service.)

GALACTOSE-C^{14} AUTORADIOGRAPHS OF INTESTINAL TISSUE FROM A HUMAN INFANT WITH GLUCOSE-GALACTOSE MALABSORPTION. William B. Kinter, Charles E. Stirling*, and Albert J. Schneider*. Departments of Physiology and Pediatrics, State University of New York Upstate Medical Center, Syracuse, New York.

Clinical observations having suggested a genetic defect in glucose-galactose transport, we undertook to localize at the cellular level the failure of the absorptive mechanism. The in vitro incubation, frozen section autoradiographic method of Kinter and Wilson (J. Cell Biol. 25: 19-40, 1965) was modified for use with fresh samples of mucosa taken from near the duodenal-jejunal junction with an orally introduced biopsy capsule. Prior to rapid freezing for autoradiography, 10-50 mg tissue samples were incubated for 3 min at 37 C in oxygenated Krebs medium containing 15% albumin and 1-5 mM labeled galactose. Control autoradiographs of normal human, as well as hamster, mucosa showed a marked accumulation of galactose-C^{14} within columnar epithelial cells of villi, i.e., a step-up in content near the brush border and a step-down near the basal end of these cells. In contrast, autoradiographs of the infant's mucosa showed only the basal step-down, the brush border step-up being completely absent. Finally, 0.2-1 mM phlorizin in incubation medium clearly decreased the step-up of galactose-C^{14} content found in normal human mucosa. These observations suggest that the infant's otherwise normal appearing columnar absorptive cells are lacking a phlorizin sensitive, uphill transport mechanism located near the brush border. (Supported by USPHS Grants AM-06479 and FR-85.)

OXYGEN TRANSFER ACROSS THE SHEEP PLACENTA
T. Kirschbaum*, W. Lucas* and N. S. Assali
UCLA School of Medicine

Oxygen transfer across the placenta was studied in near term pregnant ewes under spinal anesthesia, with the fetus marsupialized to the abdomen to protect umbilical circulation. Uterine and umbilical vein blood flows were measured with electromagnetic flowmeters. Arterial and venous blood samples were obtained from the ewe and her fetus through catheters implanted in maternal and fetal vessels, and were analysed for pO2, pCO2, pH, percent saturation and hemoglobin content. After a control period, maternal hyperoxia or hypoxia was obtained by ventilating the lungs with appropriate gas mixtures. The results show that fetal blood pO2 remains less than 60 mm Hg, despite maternal arterial pO2 as high as 500 mm Hg. Oxygen consumption values, computed from flows and arteriovenous oxygen content differences, suggest the operation of uterine vascular shunts, opening in states of high maternal arterial pO2. Changes in uterine vein oxygen content and in uterine vascular pressure - flow characteristics support this suggestion. Although other factors may be operating, it appears that intrauterine vascular shunting may be a significant factor in maintaining low fetal blood pO2 despite high maternal pO2, so that the oxygen sensitive ductus arteriosus may remain open prior to the onset of fetal respiration.

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ACUTE AND CHRONIC EFFECTS OF STELLATE STIMULATION. *M.A. Klouda and G. Brynjolfsson**. Departments of Physiology and Pathology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago.

Prolonged stimulation of the stellate ganglion in dogs produced systolic hypertension, tachycardia, gross changes in the ECG, and pathologic lesions in the cardiac musculature. Stellate stimulation was continued for 4 hours at 5 msec pulse duration, 10 cps, and 5 volts. The systolic hypertension and the tachycardia rapidly disappeared when the stimulation was terminated. The ECG changes persisted for several hours after the stimulation ceased. They consisted mainly of a decrease in amplitude of the QRS complex, an increase in amplitude of the T wave, and sometimes an inversion of the T wave. The amplitude of the Q wave often increased and the S-T segment was elevated. The cardiac lesions initially consisted of hemorrhage, edema and neutrophilic infiltration as demonstrated by microscopic examination of hearts immediately following stimulation. Areas of frank necrosis were demonstrated in the myocardium of hearts examined several days after the stimulation. Both the histologic changes and the ECG alterations were reminiscent of those seen in ischemic necrosis. *(Supported by Public Health Service Grant HE 08682.)*

THE EFFECT OF SELECTIVE RENAL ANGIOGRAPHY ON GLOMERULAR FILTRATION RATE AND RENAL PLASMA FLOW IN MAN. F. G. Knox*, I. L. Bunnell, C. M. Elwood* and E. M. Sigman*. Depts. of Med. and Urol., State Univ. of N. Y. and Buffalo General Hosp., Buffalo, N. Y.

Previous studies of the effect of renal angiography on kidney function in the dog have given rise to the assertion that renal angiography significantly depresses renal function. For this reason, follow-up studies of renal function in the post-angiography period are commonly delayed, often necessitating a second hospital admission. To test the effect of renal angiography in man under actual clinical conditions the renal function of six patients was measured before and one day after selective renal angiography. Ten ml. of 76% methylglucamine diatrizoate (Renografin), adequate for excellent visualization, was injected into each renal artery with an automatic syringe through a catheter manipulated under fluoroscopic control. In addition, an aortogram utilizing 25 ml. of the same contrast agent was performed on each patient. The mean glomerular filtration rate (GFR), determined by standard inulin clearances, was 98 ml/min/patient before angiography and 95 ml/min/patient after angiography with a standard error about the identity regression of ±12.5 ml/min/patient. The mean renal plasma flow (RPF), determined by para amino hippurate clearance, increased from 408 to 447 ml/min/patient following angiography with a standard error about the identity regression of ±27 ml/min/patient. For both GFR and RPF, the variance about the regression was within that predicted from expected day to day change in function and error in measurement - - - indicating that this contrast material given in these doses does not significantly alter these renal functions in man.

ADENOSINE TRIPHOSPHATE INDUCED SALIVATION
Leon Kraintz and E. A. Puil* University of British Columbia, Vancouver 8, B. C., Canada.

These studies were undertaken to determine whether ATP would induce salivation in the dog anaesthetized with sodium pentobarbital. Parotid and submandibular ducts were cannulated with polyethylene tubing and the left carotid artery was catheterized through the thyroid artery for intra-arterial injections and blood pressure monitoring. Blood pressure and salivary flow were recorded using appropriate transducers with a Physiograph recorder. Intra-carotid injection of 1 mg/kg of ATP (disodium salt) induced salivation from the ipsilateral submandibular and parotid glands. A marked decrease in blood pressure also occurred and persisted for 1-2 minutes. Atropine administration prevented the salivation and blood pressure response to ATP. It is concluded that intra-carotid administered ATP directly affects the salivary glands. Since this effect can be abolished with atropine it is suggested that the ATP has a cholinomimetic action on the salivary glands.

STUDIES ON THE RENAL ACTIVITY OF THE NEUROHYPOPHYSEAL OCTAPEPTIDES, (2) RENAL ACTIVITY OF OXYTOCIN. Jenő Kramár, Willard M. Duff*, and Edward H. Grinnell*. Creighton Medical School, Omaha, Nebraska.

The renal actions of synthetic oxytocin were studied in alcoholized, hydrated rats with previously prepared ureteral fistula after single injections and during slow infusions of the hormone. Water balance was maintained by oral or by combined oral-intravascular routes. The changes in urine flow, chloride concentration, chloride and creatinine excretion were observed by the use of a two minute sampling technique. The results of 127 experiments are summarized as follows. The dual action of oxytocin on water excretion, diuresis and antidiuresis, was easily demonstrable in both types of experiments. Whether diuresis or antidiuresis was produced depended entirely upon the oxytocin dose injected or concentration of the hormone infused. Single injections of 2.0 μU or infusions yielding 0.1-0.3 μU/min. produced diuresis, whereas 50 μU and 5 μU/min. respectively caused antidiuresis. A zone of transition was noted between the two extreme levels. Diuresis was accompanied by increased and antidiuresis by decreased chloride and creatinine excretion. Creatinine excretion closely paralleled inulin and endogenous creatinine clearances. The degree of hydration of the animals and their basic urine flow rate did not influence the above findings significantly. In producing the described changes in water and electrolyte excretion, oxytocin seems to act on both glomerular and tubular parts of the nephron.

Myosin and LDH of Phasic and Tonic Chicken Muscles. R. V. Krishnamoorthy and B. C. Abbott. University of Illinois, Urbana, Illinois. A variety of biochemical differences exist between the fast and slow muscles of mammals. The difference in their speeds of contraction has been related to differences in the ATPase activities of myosin isolated from them, and also to the amount of glycolytic or oxidative enzymes, the distribution of LDH sub-units and to relaxing factor activity. The comparative biochemistry of similar muscles in birds has received little attention. We find differences in myosin ATPase activities and in properties of LDH in the fast and slow muscles of chicken. Preparations were made from anterior (ALD) and posterior (PLD) latissimus dorsi muscles which lie next to each other. The former is tonic (slow) while the latter is totally phasic (fast). The myosin ATPase from the PLD shows greater Ca^{++}, EDTA and actin-Ca^{++} activation than the ALD. This Ca^{++} activated ATPase shows a smaller increase with pH than that from the PLD, similar to myosin from mammalian cardiac muscle. The ATPase of both myosins are inhibited by excess divalent ions or substrate, and studies on the effect of substrate concentration show a common Km but different Vm values at pH 9.1 and 25°C. More myosin, more sarcoplasmic and less stroma proteins can be extracted from the fast muscle although water contents are the same. Each muscle shows a single LDH type on disc polyacrylamide gel electrophesis: that from the ALD migrates the more rapidly, demonstrates substrate inhibition and is stable up to 60°C. Coenzyme specificity studies indicate that the PLD myosin is of the M type while that of the ALD is of the H type which suggests an emphasised aerobic metabolism. Supported by USPHS Grant HE 8218-02 and Medical Life Insurance Research.

DIVING REFLEX BRADYCARDIA IN UNANESTHETIZED GEESE. J. Krog*, J.E. Cohn and R. Shannon*, Department of Medicine, University of Kentucky, Lexington, Kentucky.

Effects of head immersion on cardiovascular performance and arterial blood gas tensions were studied in domestic geese. Vascular pressures were recorded and blood samples obtained from wing artery and vein via indwelling polyethylene catheters. Anterior air sac pressure was recorded. Cardiac output was determined by indicator dilution methods. After initial (control) measurements the head was immersed in water. Thoracic wall motion ceased immediately after nares immersion, and within 15 seconds bradycardia developed. Air sac pressure stabilized at 4-6 cms H_2O, cardiac output fell to 30% of control, central venous pressure rose 5-10 mm Hg, and mean systemic arterial pressure increased slightly. Arterial P_{O2} fell 35-40 mm Hg while P_{CO2} rose 6-10 mm Hg. Three birds with low tracheotomy, breathing spontaneously through this orifice when their heads were immersed, did not develop bradycardia. The immersion-bradycardia reflex was present in these birds before tracheotomy. Two other tracheotomized birds, not breathing spontaneously after head immersion, exhibited bradycardia which was abolished by artificial respiration. Bradycardia was not induced in birds by inhalation of O_2-CO_2 mixtures causing blood gas tensions comparable to levels seen during immersion. Pretreatment with 100% O_2 inhalation did not abolish the immersion reflex. Conclusion: Immersion of the head produces stimulation of nares receptors which leads to glottis closure and cessation of thoracic movement. The bradycardia which occurs can be abolished by thoracic wall motion. Blood gases do not affect this phenomenon. (Supported by NIH Grant HE 08932-01)

METHODS OF ESTIMATING BODY COMPOSITION OF A MILITARY POPULATION. Harry J. Krzywicki (intr. by I. C. Plough) US Army Medical Research & Nutrition Laboratory, Fitzsimons GH, Denver.

The assessment of nutritional status requires clinical, biochemical and dietary study of individuals or populations. Skinfolds and standard height weight tables inadequately define gross body composition. Estimates of body density by underwater weighing or of muscle mass by K^{40} counting are time consuming and lack portability which precludes their use in the field. Measurement of body volume by water displacement in a portable human volumeter effectively estimates body density. Body volumes, whole body K^{40} counting, total body water from deuterium or tritium dilution, residual lung volumes by nitrogen dilution and selected anthropometry were obtained on 105 soldiers aged 17 to 52 years, to determine the minimal number of basic measurements permitting field predictions of body components. Body volumeter data showed body density to decrease with age from 1.073 ± 0.008 to 1.048 ± 0.008 and body fat to increase from 14.0 ± 3.2% to 24.4 ± 1.3%. Total body potassium declined with age from 2.19 ± 0.30g to 1.83 ± 0.20g K/kg body weight. Body density, and fat free mass values were consistent with reported values in the literature for 20 to 40 year olds. Body fat estimates by direct volumetry correlated (r = 0.815) with fat computed from K^{40} measurements (Forbes, 68.1 mEq K/kg lean body mass). Several reported equations for predicting body components from anthropometric measurements failed to describe the military population. Body volumetry by water displacement effectively ranks populations in terms of density and fat.

DIFFERENTIAL GASTRIC AND SALIVARY SENSITIVITY TO ANTICHOLINERGICS IN SHAM FED DOGS. R. H. Kubin; W. R. Keeler; A. P. Klotz (intr. by P. R. Schloerb). Univ. of Kansas Med. Center, Kansas City, Kansas.

Anticholinergic inhibition of the salivary and gastric secretory response of healthy esophagostomized, gastrostomized dogs was studied in 103 daily sham feedings. The weight of saliva and the volume of gastric secretion were determined for each feeding. After control periods anticholinergic drugs were given by single intravenous injection at variable intervals before sham feeding. For each interval the log dose was plotted against both responses and the dose necessary to produce 50% inhibition of each was determined by interpolation. Therapeutic ratio (TR) (salivary 50% inhibitory dose/gastric 50% inhibitory dose) was calculated for each interval. For atropine at intervals 20, 40, 100 minutes TR was greater than 1 (3.2-1.3); for interval of 160 minutes TR was less than 1(.88). Plot of TR was inversely proportional to time interval. For heteronium bromide, a quaternary ammonium anticholinergic, TR was greater than 1(2.8) only at 20 minutes; thereafter it was less than 1(.85-.93). Thus gastric secretory response to parasympathetic effector cell stimulation was more sensitive to both drugs than was the salivary secretory response; however as time interval was increased this difference disappeared. The unequal sensitivity of stomach and salivary glands to anticholinergic drugs is suggestive of preferential gastric sensitivity. The change in TR with time definitely establishes that the cholinergic receptors of stomach and salivary glands behave differently in response to some anticholinergic drugs.

LOCOMOTOR ACTIVITY PATTERNS IN APLYSIA CALIFORNICA. Irving Kupfermann* (intr. by E. R. Kandel). Harvard Med. Sch., Boston, Mass.

The abd. gangl. of Aplysia provides a relatively simple system in which certain types of circadian rhythms (Strumwasser, 1963) and neural analogues of behavioral conditioning (Kandel and Tauc, 1963; Frazier, et. al., 1965) may be studied on the cellular level. Although there has been extensive work on the isolated ganglion, the behavior of the intact animal has received little attention. In the present work, the locomotor activity of single animals, maintained in a partitioned, 50 gal., temperature regulated, filtered and aerated tank, under controlled light-dark (LD) cycles was studied by means of time-lapse cinematography. The major motility pattern is controlled by the degree to which the water is disturbed. Animals in non-perturbed water move around the periphery of the tank 70-90% of the time and travel up to one mile in 8 days. Animals in water agitated so as to simulate tidal activity are stationary 50-95% of the time. This stationary behavior is interrupted by bursts of activity which last from a few min. up to 12 hr. Preliminary work with 12 hr. on-off LD cycles indicate that activity bursts of animals in perturbed water are correlated with the LD cycle. The locomotion of animals in non-pert. water is not obviously dependent on the LD cycles. These motility patterns as well as their entrainment by water perturbation and by light are presumably neurally determined. Knowledge of and control for these cycles in the whole animal may therefore increase the ability to experimentally control and interpret certain neurophysiological data obtained in isolated ganglia. (Supported by NINDB Grant No. NB-04550-02).

TISSUE GAS TENSIONS DURING METHEMOGLOBINEMIA. T.W. Lamb (introduced by S.M. Tenney). Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Tissue gas tensions in rat subcutaneous gas pockets were studied during graded methemoglobinemia produced by the injection of p-aminopropiophenone. With increasing methemoglobinemia, tissue PO2 fell progressively. PCO2 remained constant until the oxygen carrying capacity was less than one-half normal after which a small decrease was seen. The tissue gas tension response was rapid and of approximately the same magnitude as that observed with blood loss anemia, indicating that blood viscosity was not an important controlling variable. Although mean tissue gas tensions and local venous gas tensions are nearly equal at rest under normal conditions, they differ when the oxygen carrying capacity is reduced. Calculations based on each of these values further support the view that subcutaneous gas is in equilibrium with the local venous blood. Based on this assumption, local blood flow and the minimum capillarity necessary to prevent anerobic metabolism were computed. With progressive reduction in the oxygen carrying capacity, blood flow and capillarity requirements increase in equal amount until one-half normal levels are reached. Below this point, flow requirements increase more rapidly than do the needs for more open capillaries. Throughout all ranges of reduced oxygen carrying capacity, the observed increase in blood flow was near the minimum level required to supply oxygen to cells at such a tension that oxygen would not be a rate limiting substrate.
(Supported by PHS Grant H-2888-09).

THE EXTRACELLULAR FLUID SPACE OF THE HEMORRHAGED RAT. Stanley Lang, Kenneth D. Serkes* and Morton D. Pareira*. Dept. Surgery, Jewish Hosp. St. Louis and Washington Univ. School of Med., St. Louis, Missouri.

The question of origin of water for re-expansion of the plasma volume following severe hemorrhage has been examined. There seems to be no recruitment of water into the extracellular fluid (ECF) compartment following a rapid hemorrhage in excess of 30% of the total blood volume. In spite of the fact that plasma volume is at least 100% of the control value at 2 hours following hemorrhage, the ECF is reduced by exactly the amount of water lost in the hemorrhage at this time. Both chemical and radioactive sucrose distribution spaces were used to measure the ECF of the nephrectomized rat. There is little difference in sucrose equilibration time in the control animal and one bled a volume of whole blood equivalent to 2% of its body weight. Chemical and tracer radiosucrose determinations agree very well. There seems to be a small, extrarenal utilization of sucrose with time causing apparent increases in the sucrose space.

ABSTRACT

ACUTE AND CHRONIC CENTRIFUGATION OF RODENTS by K. O. Lange, R. C. Martin, A. B. Broderson and W. K. Richardson (Intr. by- Fred W. Zechman, Jr.) Special centrifuges are used for NASA studies of the effects of gravity and rotation on behavior. Apparatus for chronic exposure to 2.65g is used for breeding and raising rats and mice for later exposure to gravity fields between 1 and 4g. Another apparatus produces the discrete levels of 1.5, 2.5, and 3.5g simultaneously, and can expose 72 rats to hyper-gravity for physiological studies. During acute exposure to fields of gravity, animals are allowed to change their weight by locomoting within the apparatus. One such centrifuge is a rotating paraboloid which simulates gravity from 1 to 3.2g. Location of the subject is continuously monitored by recording the intensity of gamma radiation from a source attached to the subject. Larger but slower centrifuges produce 1 to 2g, or 1 to 4g on subjects contained in parabolic runways. Location of the animal in these centrifuges is determined by actuation of microswitches underneath the subject, which, in turn, operate event recorders. Spiral centrifuges create gravity fields which vary in range with variation in rotational rate; the subject's location is recorded photographically. Performance of rats in these apparata has been reliable; subjects tend to prefer lower g, even after prolonged exposure to higher g.

AGREEMENT IN EXERCISING PULMONARY DIFFUSING CAPACITY DETERMINED BY DIFFERENT METHODS. W.H. Lawson (intro. by H.A. Lyons) U.S. Army Res. Inst. Environ. Med., Natick, Mass.

Diffusing capacity for CO was measured at graded work loads up to maximum on a bicycle ergometer by breath holding at total lung capacity (Dcosb) and rebreathing (Dcorb) methods in 4 men. Dcosb was always greater, mean 30%. Breath holding measurements at lower lung volume (Dcosb1), within .3 l rebreathing volume, reduced the difference to 8% but it was still significant ($P < .005$). A distinct plateau was always observed in Dcorb at the top three work loads. Mean data in one subject were:

Load (watts)	0	66	86	101	136	156	176
O_2 consump.(l/min)	.39	1.07	1.75	2.47	3.12	-	3.1
Dcosb(ml/min x mm)	40	48	50	52	56	61	63
Dcosb1(ml/min x mm)	33	41	39	42	42	49	-
Dcorb (ml/min x mm)	26	37	39	35	43	42	39

Dcorb was measured rebreathing 100% O_2 in 3 subjects to determine lung membrane diffusing capacity and capillary blood volume, and hence calculate oxygen diffusing capacity (DO_2) using a blood-O_2 reaction rate of 2.7 ml/ml x min x mm Hg. At mean O_2 consumption ($\dot{V}O_2$) 1.79 (S.D. $\pm$ .08) calculated DO_2 was 54 (S.D. $\pm$ 11, n=9) compared to 50 (S.D. $\pm$ 8, n=5) measured in exercising men by Shepard et al with the steady state O_2 method at $\dot{V}O_2$ 1.74 (S.D. $\pm$ .11)(J. Appl. Physiol. 13:205, 1958). These results indicate that differing values in exercise diffusing capacity by the above methods are largely due to differences in lung volume and/or red cell-gas reaction rates.

ORIGIN AND FLOW OF RENAL LYMPH DURING OSMOTIC DIURESIS. S. J. LeBrie and H. S. Mayerson. Dept. Physiol., Tulane Univ. School of Med., New Orleans, La.

Renal capsular lymph flow and protein concentration were measured in dogs during diuresis induced by 20 ml/kg body weight of 12.5% mannitol or 4% saline or 30% urea solution. Lymph flow increased four-fold during infusion at 10 ml/min. of mannitol or saline. Urea, infused at 5 ml/min., only slightly increased lymph flow although it produced a marked diuresis. Increment in lymph flow was directly related to the amount of infused volume retained. Qualitative changes in distribution of blood between cortex and medulla, estimated from the assumptions of Reubi (Helvet. med. acta, 25: 516, 1958), were related to changes in lymph flow. Cortical plasma flow did not correlate with lymph flow; medullary plasma flow, however, did directly correlate with lymph flow. This suggests increased capillary filtration in medullary areas during osmotic diuresis. Lymph protein flow in gm/min. increased with all 3 osmotic agents. This supports the idea of increased capillary filtration during diuresis and emphasizes the role of the lymphatics in draining protein from the interstitium. (Supported by U.S.P.H.S. Grant HE-04306 and by Research And Development Command, U.S. Army, Contract DM-49-143 MD 2012).

A CORTICAL SURVEY OF THE HEDGEHOG (Erinaceus). Richard A. Lende and Keith Sadler*, Albany Medical College, Albany, New York and Univ. Colo. Medical Center.

A member of the Insectivora, the lowest order of living placental mammals, was investigated for its comparative significance. It was considered that this primitive group might demonstrate elemental features of patterns of neocortical representation. The evoked potential technique and cortical stimulation were used in 11 Hedgehogs under barbiturate anesthesia. The entire lateral neocortical surface appeared to contain primary areas. Overlap among fields was found and this was most extensive between somatic sensory area I and somatic motor area I. However, these two areas could be distinguished on the basis of pattern and threshold, as opposed to the Marsupialia. A second somatic sensory area was found but a supplementary motor area could not be established. There was great elaboration of the sensory and motor areas concerned with the snout, undoubtedly a region of important function in the hedgehog. In several studies movements of the pinna were obtained on stimulation throughout the cortical auditory area. A visual area of moderate size was found. The disposition of cortical areas and patterning within them appeared generally typical of placentals. (Supported by PHS Research Grants, NB02600 and NB05976).

INSULIN AS A FACTOR IN THE REGULATION OF LIVER PROTEIN METABOLISM DURING ACUTE CENTRIFUGATION STRESS. H. A. Leon, M. Rowley*, E. G. Averkin*, NASA, Ames Research Center, Moffett Field, California.

In an earlier report (Leon et al., Life Sci. 4:736, 1965), it was established that liver protein synthesis as measured by the incorporation of amino acids by cell-free liver systems, is significantly stimulated within 3 hours by centrifugation at 4.7xg in fasted rats be they intact, adrenalectomized or hypophysectomized. Others have established that centrifugation stress can also lead to rapid increases in blood glucose thereby implicating insulin as a factor in the above response. To test this, fasted rats rendered diabetic by alloxan 3 weeks previously were likewise subjected to centrifugation stress for 3 hours at 4.7xg and comparisons were made to non-centrifuged diabetic controls. It was found that the amino acid incorporating ability of the liver systems subsequently prepared was greatly depressed by the stress. At the same time it was found that 2 I.U.of PZ insulin injected just prior to centrifugation, alleviated and 4 I.U.of insulin prevented the impairment of the amino-acid incorporation. On the other hand, fasted alloxan-diabetic-adrenalectomized rats showed no impairment of incorporation by the stress but instead showed a small increase possibly attributable to residual insulin release. The implications are that insulin, possibly by making glucose metabolically available is a necessary requirement for stress-induced stimulation of amino-acid incorporation in liver. Likewise, the well-known antagonism of insulin and adrenal steroids with respect to carbohydrate balance might appear to be applicable to liver-protein metabolic changes consequent to acute stress.

TRANSMURAL POTENTIAL DIFFERENCES ACROSS ISOLATED SMALL INTESTINE OF BULLFROG. Roy J. Levin* (intr. by C.A.M. Hogben) Univ. of Iowa, Iowa City.

Potential differences (P.D.) were recorded across the wall of isolated, everted proximal small intestine of the bullfrog, R. catesbeiana. In chloride saline (5.6 mM glucose), initial and subsequent P.D. were low (1.4 ± 0.2 mv) but significantly greater in sulphate saline (3.7 ± 0.7 mv), serosa positive to mucosa. Dinitrophenol, iodoacetamide, fluoride and ouabain depressed these P.D. With sulphate saline, actively transported sugars (glucose, galactose, 3-Methyl glucose) increased the P.D. when added to mucosal fluid. Mucosal phloridzin (5.10^{-4}M) blocked this increase but not the increase caused by glycine. DL-alanine, L-cysteine, L-methionine, L-glutamic and DL-aspartic acids also increased the P.D. when they were present in mucosal fluid (5.6 mM). Increases caused by 5.6 mM glucose and glycine were additive. Glucose or glycine potentiated the P.D. even in N_2 though less effectively than in O_2. Addition of 5.6 mM xylose, sorbose, fructose, sucrose, ascorbic acid, urea or sodium acetate to the mucosal fluid depressed the P.D. This is attributed to an osmotically induced or "streaming P.D." Results indicate that the isolated small intestine of bullfrog is a useful model for investigating association between solute transfer, P.D. and metabolic energy sources.

EFFECT OF HYPOXIA UPON LEFT VENTRICULAR CONTRACTILITY. Matthew N. Levy, Manuel L. Ng,* Hilaire DeGeest,* and Harrison Zieske* St. Vincent Charity Hospital, Cleveland, Ohio.

Isolated, isovolumetric, paced, canine left ventricle preparations were subjected to hypoxia under conditions of either constant perfusion pressure (increasing flow) or constant coronary blood flow (decreasing pressure). Characteristically, hypoxia elicited a biphasic response in terms of the changes in left ventricular systolic pressure. There was a significant stimulation (ave. 8% increase) of left ventricular contractile strength with mild to moderate hypoxia (60-90% O_2 saturation), and depression (10-18% reduction) with severe hypoxia (20-40% O_2 saturation). In the experiments conducted with constant pressure, there was no apparent relation between the changes in the O_2 delivery (O_2 content x coronary blood flow) and the changes in the contractility of the myocardium. The biphasic response of the ventricular contractility to hypoxia is attributed partly to the changes in pH of the perfusate and partly to the direct inotropic effect on the myocardium.

RESPONSES TO BLADDER DISTENSION IN PATIENTS WITH SPINAL TRANSECTION. *R.J. Lewin**, *R.D. Wurster** *and W.C. Randall*. VA Hospital, Long Beach and UCLA and the Department of Physiology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago.

Blood pressure, sweating, cutaneous volume pulses, skin and deep temperatures were recorded simultaneously and continuously during controlled elevation of urinary bladder pressure in patients with spinal cord transection above T_5 and in another group with a lesion below T_5. Sparse but definite sweating and distinct vasomotor activity was observed in skin supplied by the isolated spinal cord of all patients during bladder distension. Profound elevation in systolic pressure marked those patients with lesions above T_5. Lesser elevations were observed in patients with lesions below T_5. Increased amplitude of volume pulses in skin innervated by the proximal or intact portion of the cord may be related to passive response to increased intravascular pressures. The marked elevation in systolic pressure observed in patients with relatively high lesions strongly suggests the participation of sympathetic augmentor influences acting upon the ventricular musculature and resulting in increased systolic ejection. Lesions located at or below T_5 interrupt ascending impulse traffic within the spinal cord, hence eliminating a probable direct pathway between the urinary bladder and the sympathetic cardiac nerves. (Supported by Public Health Service Grant HE 08682 to Loyola University and a gift from the Spinal Cord Research Foundation to the VA Hospital, Long Beach.)

POSTSYNAPTIC NATURE AND LONG SYNAPTIC DELAYS OF SLOW RESPONSES IN SYMPATHETIC GANGLIA. B. Libet. Dept. of Physiology, Univ. of Calif. School of Med., San Francisco, Calif.

Surface positive (P) and later negative (LN) potentials with durations in seconds follow the initial EPSP (excitatory postsynaptic potential) of curarized ganglia. LN has properties of a slow EPSP (Libet, J. Physiol. 1964, 171, 1-25). All of these potentials decrement rapidly with distance along the postganglionic nerve while they are absent on the preganglionic side; all are depressed and abolished in Ringer's with low Ca/Mg ratios; and all exhibit post-tetanic potentiation. Anti-cholinesterases initially enhance the amplitude and duration of the slow EPSP, and markedly enlarge those of the P response. This evidence supports our hypothesis that the slow ganglionic potentials, like the EPSP, are postsynaptic responses, localized to the soma-dendritic regions and dependent upon presynaptic release of transmitter substance. By selectively depressing the EPSP with strong curarization, the onset of the P potential shows a net additional delay of about 35 msec. In the absence of P response, the net delay for onset of slow EPSP is seen to be 200-300 msec. These extraordinarily long synaptic delays may be explained on the basis of long diffusion times required for transmitters to reach the postsynaptic receptor sites. (Supported by U.S. Public Health Grant NB-00884).

EFFECTS OF VASOPRESSIN AND ALDACTONE ON EXCRETION OF WATER AND ELECTROLYTES BY PREGNANT RATS. I. J. Lichton and Anne P. Rasa (intr. by T. A. Rogers). Univ. of Hawaii, Honolulu. Late in gestation rats regularly exhibit diminished urinary excretion of water, sodium, and total osmotic solutes in response to oral loading with isotonic saline solution. The present work was undertaken to determine whether increased levels of vasopressin or aldosterone could account for these responses. Virgin female Fisher SPF rats were given isotonic saline, 5 ml/100 g body wt, by stomach tube and urine was collected for 6 hr. This test was repeated a week later with the administration of either a) no drugs, b) 0.5 U vasopressin tannate, or c) the same dose of vasopressin plus 5 mg of Aldactone. All rats were mated and the tests were again repeated on the 20th day of gestation with the dose of vasopressin increased to 1.0 U, and that of Aldactone to 10 or 20 mg. In all three experiments there were significant depressions in the excretion of water, sodium, potassium, and total osmols in the term pregnant rats. Excretion of water, in ml/100 g body wt, was decreased from 5.62 to 3.09 at term in control rats, from 3.75 to 1.59 in rats given vasopressin alone, and from 6.13 to 3.68 in rats given vasopressin plus 20 mg Aldactone. Excretion of total solutes, in mOsm/100 g body wt, was decreased from 3.04 to 1.66 at term in control rats, from 2.62 to 1.18 in rats given vasopressin alone, and from 2.82 to 1.66 in rats given vasopressin plus 20 mg Aldactone. Decreases in excretion of sodium and potassium were parallel to the decreases in excretion of total osmols. These data support the conclusion that the antidiuresis and antisaluresis of late pregnancy in rats are not dependent upon increased supplies of vasopressin or aldosterone. Supported by NIH grant HE-07733.

POTASSIUM INDUCED VOLUME CHANGES IN SINGLE CRUSTACEAN AXONS: ITS QUANTITATION BY INTERFERENCE MICROSCOPY. E.M. Lieberman* and E.B. Wright, Physiology Dept., University of Florida, College of Medicine, Gainesville

Crustacean axons swell when subjected to K+ rich solutions. Interference Microscopy was employed to quantitate volume and refractive index changes of axoplasm induced by K^+ rich solutions. Above a critical value of 3-5X(40-65mM/L) normal K^+ the diameter of the axon was directly related to the external K^+ concentration. The relationship was approximately linear. The refractive index change was inversely related to external K^+ concentration, also in linear fashion. In 6 cases observed to date in which note was made of a critical K^+ concentration it was seento fit within the 40-65mM/L range. K^+ induced swelling occurred in a matter of seconds, while recovery after removal of K^+ took several minutes. In high K^+, 100mM/L or above, recovery was not complete and was directly related to the severity of treatment. Axons pre-treated with 10X normal calcium (230mM/L) or procaine (1%) showed delayed onset of K^+ induced volume increase by several minutes and the rate of swelling was slowed. Veratrine (1pp1000) caused a slow swelling of the axons. Comparison of the swelling data to already existing electrophysiological data on crustacean axons suggests a positive correlation between water movement and membrane polarization. The rate of depolarization in K^+ rich solutions is very fast (seconds) compared to repolarization (minutes) when K^+ is washed away. This qualitatively parallels the course of water movement under similar conditions. Moreover K^+ in the external solutions must range 3-5X normal to record consistent depolarization of the membrane. This value approximates the critical value for swelling in axons. Finally, recovery of the electrical activity, as is recovery of axon size, is incomplete and related to severity of treatment when greater than 3-5X normal K^+ is used. Supported by Grant NSF G 24013.

EFFECTS OF DIGITALIS ON THE PULMONARY CIRCULATION. L. M. Linde, S. J. Goldberg*, R. Iverson* and P. Gaal*. Department of Pediatrics, Physiology and Surgery. School of Medicine, University of Calif., Los Angeles, California.

The effects of digitalis glycosides on the normal and abnormal pulmonary circulation of intact unanesthetized dogs were studied. At thoracotomy, an electromagnetic flow probe was placed on the ascending aorta and vinyl catheters permanently placed in the aorta, pulmonary artery and left atrium. A silastic shunt was inserted between the aorta and pulmonary artery so that pulmonary blood flow could be externally adjusted. After recovery acetyl-strophanthidin (AS), Ouabain and Digoxin was given to the awake unsedated dog with normal pulmonary blood flow. In all instances, heart rates slowed while peak stroke velocity, aortic pressure and systemic vascular resistance increased. Cardiac output did not change following Ouabain, decreased slightly after AS and showed the greatest decrease after Digoxin administration. Significant change in pulmonary vascular resistance (PVR) occurred only with AS, with an increase in pulmonary artery pressure, and a fall in left atrial pressure. Since cardiac output changed relatively less, PVR remained elevated for 20 minutes. With all digitalis drugs, stroke velocity increase and increased SVR persisted after heart rate had returned to normal. With increased pulmonary blood flow, the main difference was marked increase in cardiac output following digitalis administration. Pulmonary artery and left atrial pressures increased but pulmonary vascular pressure gradient remained relatively stable. PVR decreased significantly. The rise in pulmonary vascular pressures when digitalis further augmented cardiac output in the dog with increased pulmonary blood flow may indicate pulmonary vasoconstriction or that the pulmonary vessels were near their maximal distensibility.

CARDIAC OUTPUT AND PERIPHERAL RESISTANCE AT CONTROLLED HEART RATE DURING EPINEPHRINE INFUSION IN THE INTACT DOG. *John W. Lister and *Benjamin J. Scherlag. Department of Pharmacology, College of Physicians and Surgeons, New York.

In 6 dogs weighing 12-22 kg. a cooling coil was chronically implanted over the sinus node and a pacemaker electrode was implanted on the right atrial appendage. The animals were permitted to recover from the operation for variable periods of time (1-3 weeks) prior to hemodynamic studies.

The dogs were anesthesized with morphine sulfate 1.5-2, 5 mg/kg and Na-pentobarbital 10-20 mg/kg. An electrocardiogram, left ventricular and aortic pressure and cardiac output were obtained at various controlled heart rates during control periods and during epinephrine infusions (0.5-2, 0mcgm/kg/min). In two dogs epinephrine was infused one hour after alpha blockade with phenoxybenzamine (3mg/kg). The heart rate was controlled by cooling the sinus node and atrial pacing.

Cardiac output was not significantly altered within a wide range of heart rates. Cardiac output was independent of mean aortic pressure. There was a close linear relationship between cardiac output and peripheral resistance.

The results of these experiments suggest that the peripheral arterial pressure is a poor index of the state of the cardiovascular system, whereas peripheral resistance may be a sensitive indicator of the cardiovascular status.

EFFECT OF pH ON POTASSIUM CONTRACTURES OF FROG MUSCLE
H. Lorkovic*(intr. by C. Edwards) Department of Physiology, University of Minnesota, Minneapolis, Minnesota.

Potassium contractures have been studied in the toe muscle of the frog in Na^+ and Cl^- -free tris-methanesulphonate solutions. The threshold [K] was about 7 mM at pH 9, 15 mM at pH 7 and 50 mM at pH 5 in the presence of 1 mM Ca. If [Ca] was increased to 4 mM the threshold [K] was slightly higher at pH 7 and 9 and lower at pH 5. The resting membrane potential and the depolarization caused by increasing [K] were independent of the pH changes. Recovery of the ability to give a second K contracture after prior exposure to K occurs only if the K level is reduced below the threshold for contracture; the level necessary for recovery changed with pH in the same direction as did the K threshold. No influence of pH changes on submaximal tension development in response to 0.6 mg/ml caffeine was found when acid or alkaline solutions were applied a few minutes before caffeine. An increase of responses by prolonged treatment with both acid and alkali was observed but the muscle was unable to recover fully. Studies with tracer Ca^{45} and Co^{58} suggest that a superficially bound fraction of divalent ions is increased in alkaline and decreased in acid solutions. (Aided by NIH Grant NB-02712).

MINIMAL AMOUNTS OF ICSH REQUIRED, TOGETHER WITH FSH, FOR FOLLICULAR DEVELOPMENT, UTERINE GROWTH, AND OVULATION IN THE HYPOPHYSECTOMIZED RAT. Ardis J. Lostroh, Hormone Research Lab., Univ. of Cal., Berkeley.

Female rats were hypophysectomized at 28 days of age. 7 days later, single daily subcutaneous injections of the ovine hormones were initiated. The ICSH had an activity 2-3 times that of NIH-LH-S1, the FSH an activity 30-35 times that of NIH-FSH-S1. Neither ICSH nor FSH alone stimulated the release of sufficient estrogen to cause uterine development. However, 0.2 μg of ICSH injected together with 3 μg of FSH for a period of 3 days effected maximal increases in the uterine weights, and as little as 0.02 μg in combination with the FSH stimulated small increases. A daily dose of 1 μg of FSH promoted neither follicular development nor stimulated increases in the weights of the ovaries, and was likewise ineffective in stimulating estrogen secretion even though combined with as much as 20 μg of ICSH. Follicles that contained large antra and showed evidence of beginning luteinization were observed when 1 μg of ICSH together with 3 μg of FSH was injected for a period of 3 days, and corpus luteum formation was induced with the same combination injected for 4 days, followed by 3 μg of ICSH on day 5, and 20 μg of ICSH on days 6 and 7; ova enclosed within small "lutein bodies" were not observed. (Supported in part by a grant from the U.S. Public Health Service (AM-6097).

THE CONTINGENT NEGATIVE VARIATION IN SUBHUMAN PRIMATES. Morton D. Low*, Robert P. Borda*, James D. Frost*, and Peter Kellaway. Baylor Univ. College of Medicine, Houston, Texas.

Since the report by W. Grey Walter et al. in Nature, 203:380 (1964) concerning the appearance of a surface negative slow potential in frontal regions of the brain during states of expectancy in man, we have confirmed the original observations and offered evidence that the slow potential is a cerebral electrical correlate of conative states; Low et al., Neurology, 15:280 (1965). To further test this thesis, a set of experiments was done using Rhesus monkeys, recording EEG activity through chronically implanted chlorided silver epidural electrodes. Three basic conditioning paradigms were used: escape conditioning with a warning cue, discrimination task with aversive reinforcement following S^D, and discrimination with appetitive reinforcement. Trials were presented in blocks of twelve and averaged on line with an Enhancetron electronic averager. In each case, during acquisition trials, a surface negative slow potential gradually developed only following the evoked response to S^D and preceding the meaningful stimulus. No shift followed the unreinforced stimulus. During extinction trials, the shift gradually diminished. During discrimination reversal, a negative shift developed following the previously unreinforced stimulus, while the shift following what had been S^D gradually diminished. These results demonstrate the appearance of the contingent negative variation in experimental primates and support the contention that this shift is a result of cerebral electrical activity during conation. (USPHS grant MH 05204-04A1)

PACEMAKER ACTIVITIES IN THE TURTLE HEART. H. H. Lu*, G. Lange, C. McC. Brooks. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Pacemaker activity within the sinus venosus, atrium and ventricle was studied. The origin and propagation of activity was determined by multiple leads. Drives of various rates and durations were imposed and post-drive effects recorded. Multiple pacemaker actions were found within the sinus venosus. One such (usually of the right side) normally drove the heart. Stimulation of a vagus nerve suppressed pacemaker action of the same side more markedly, often merely shifting the site of beat origin. It was also possible to block sinoatrial conduction without complete suppression of sinus pacemaker activity, but sufficient to permit atrial pacemaker action to develop. Rapid drive suppressed pacemaker activity especially in areas adjacent to the stimulating electrodes. Moderate rates of drive gave the greater post-drive depression. Fast driving was frequently followed by acceleration. Prostigmine enhanced post-drive suppression and atropine reduced it. Atrial drive had little effect on sinus pacemaker actions. S-A conduction was depressed following rapid drive of the atrium. The ventricle followed atrial drive at moderate rates but at rapid rates, A-V conduction failed. Post-drive suppression of the atrium and of S-A and A-V conduction permitted idioventricular beats to occur. Ability of the atrium to follow ventricular drive was limited, V-A block developing as drive accelerated. It was not possible, as in the mammal, to block sinus pacemaker activity by driving the ventricle. Both retrograde and orthograde conduction in the turtle heart were more readily depressed by driving various chambers than were intrinsic pacemaker actions. (Supported by the Life Insurance Medical Research Fund. *Fellow, China Medical Board of New York, National Defense Medical Center, Taiwan.)

OXYGENATION OF BLOOD DURING INHALATION OF A LIQUID MEDIUM. L. Lukin. Biomechanics Laboratory, University of California, San Francisco, California.

To investigate further the adequacy of transport of respiratory gases across the pulmonary epithelium during spontaneous liquid pulmonary ventilation, 9 anesthetized or well sedated dogs were submerged in a hyperbaric chamber containing Ringer's solution equilibrated with O_2 at 8 atm. All animals were able to breathe the liquid for at least 8 minutes, and those that survived maintained liquid-breathing for 1 hour. As long as the animals breathed the solution, their arterial O_2 concentration was adequate or above normal; however, CO_2 gradually accumulated in the blood. Five of the dogs died in the chamber as a result of sudden apnea or of dyspnea and bronchiospasm followed by apnea. Histopathological examinations performed on those that died revealed hyperemia and vascular lesions in the lungs but no atelectasis. Vascular lesions were also observed in the central nervous system; those in the medulla may have been responsible for the sudden apnea. Despite the positive finding that the respiratory muscles are able to pump liquid into and out of the lungs and provide adequate ventilation of blood, the survival rate in this study was low and the sequence of events leading to apnea and death remains to be investigated.
(Supported by NASA Contract NASw-674)

ACID-PEPSIN STUDIES IN WHOLE STOMACH AUTOGRAFTS. Gary W. Lyons, William G. Manax and Richard C. Lillehei, Univ. of Minn. Medical School, Minneapolis, Minn.

Seven dogs having gastric autografts have been studied for periods of 39 to 52 months following transplantation. Awake fasted dogs were subjected to subcutaneous triple histamine stimulation (0.5 mg. histamine base) and the gastric secretions were collected for 30 minutes with a gastric tube passed into the stomach. This was repeated three times at 30 minute intervals and samples collected for acid and pepsin determinations. A specific test for pepsin was done on another day by injecting 4 mg. pilocarpine subcutaneously. Following salivation, samples were collected and analyzed for pepsin. Response to hypoglycemia following intravenous injection of 10 units of U-40 Iletin insulin was measured by determining acid production one hour after injection. All dogs have been subjected to prolonged stress (6 months) by daily (30 mg.) histamine in beeswax administration without evidence of peptic ulcer diathesis. Achlorhydria to histamine stimulation occurred in 5 of 7 animals, and only mild response (0.24 and 0.36 mEq./l.) was seen in two animals 41 and 42 months respectively, after autotransplantation. All dogs showed achlorhydria when stimulated by induction of hypoglycemia, indicating complete vagolysis. Pepsin secretion following pilocarpine stimulation has remained depressed (too low to detect) in all dogs. The normal dog responds to pilocarpine injection with pepsin secretion of over 1 mg./ml. expressed as tyrosine units. All dogs have retained normal nutrition following transplantation and the microscopic appearance of stomach mucosa has remained normal.

THE RETROGRADE CATHETER: A TECHNIQUE FOR THE MEASUREMENT OF PRESSURE IN SMALL BRONCHI. P.T. Macklem and J. Mead. Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

In order to measure pressure in small bronchi, a catheter, "belled" at one end and pointed at the other, was inserted pointed end first into the lungs via the trachea, advanced through the bronchial tree and pushed through the parenchyma and pleural surface. It was then pulled until the bell wedged in a bronchus thereby enabling the measurement of lateral bronchial pressure at the site of the bell. By varying the size of the bell, pressures in different sizes of bronchi could be measured. Any artifact introduced by the catheter should increase the pressure difference in the airways between the catheter and the alveoli. However, when a catheter with a bell 3 mm. o.d. was employed in intact and excised dog, cat and monkey lungs, there was virtually no pressure drop in these airways at lung volumes greater than FRC, even at high flow-rates (i.e., their flow-resistance was negligible). As volume decreased below FRC a finite resistance was detectable but the major increase appeared to be in larger airways. Post mortem dissection revealed that the catheter measured pressure in bronchi 1.5 - 2.5 mm. i. d. in the collapsed state. In excised human lungs the same result was obtained with a catheter bell of 2 mm. o.d. (Supported by grant # 6648-2).

EFFECTS OF HAEMORRHAGE ON RENAL BLOOD-FLOW. N.S.R. Maluf and Lyman Rust*, Dept. of Physiol., Univ. of South. Calif. Sch. of Med., Los Angeles, Calif.

Blood was removed from anaesthetised dogs which had just undergone application of electromagnetic flowmeters. Increments of blood-loss were usually 50 cc. Typically, before bleeding, incisions were closed and lungs inflated; endotracheal tube was removed and breathing normal. Operations were done with little blood-loss and usually no fluids were given. Fall in renal vascular resistance until loss of about 21% of estimated blood-volume explained concomitant stability of renal blood-flow and rise in renal fraction of cardiac output to 25% from initial of 17%. Renal, mesenteric and iliac flows varied directly with mean arterial pressure (150 down to 5 mm.Hg.). This direct relation was most striking for iliac flow. In some instances renal flow tended to be constant down to pressures of 100-110 mm. Hg. Raising arterial pressure well above normal (by 65 mm. Hg., or to 255 mm.Hg.), by constriction of both common carotids, did not raise renal arterial flow (autoregulation). When fall in renal arterial pressure was due to constriction of distal thoracic aorta, fall in renal blood-flow per unit decrement of arterial pressure was strikingly less than in hypotension from haemorrhage and, unlike hypotension from haemorrhage, the resistance typically continued to fall. Flow differences between hypotension from haemorrhage and from aortic constriction were also striking for the iliac artery.

HYPOPHYSIAL REGULATION OF THE DURATION OF PSEUDOPREGNANCY IN RATS. P.V. Malven*, W. Hansel and C.H. Sawyer. UCLA School of Medicine, Los Angeles, California and Cornell University, Ithaca, New York.

The mechanisms regulating the duration of corpus luteum function in pseudopregnant rats are incompletely understood. The present experiments revealed the inability of two possible luteotrophins, prolactin and luteinizing hormone (LH), to increase the duration of pseudopregnancy in intact rats to that occurring normally in hysterectomized animals. Daily injections (10 I.U. ovine prolactin/day in saline or a 5% beeswax-sesame oil slow-release medium, or 50 ug ovine LH/day in oil) were begun at various times after cervical stimulation in order to minimize negative results due to antibody formation. The following means (no. rats/mean) represent the interval between the initial and terminal ovulations of pseudopregnancy for nine treatment groups, respectively: intact control, three aqueous prolactin groups (begun days 1, 5, and 9), two oil-suspended prolactin groups (begun days 1 and 9), two oil-suspended LH groups (begun days 1 and 9), and a hysterectomized control — 12.8 (19), 15.5 (8), 13.3 (9), 14.1 (8), 13.0 (8), 12.6 (8), 11.5 (6), 13.0 (8), and 17.2 (18). The fact that neither prolactin nor LH consistently extended the duration of pseudopregnancy to that of hysterectomized rats suggests the presence of an endogenous luteolytic mechanism capable of terminating secretory function. While uterine stimuli may influence the timing of this mechanism, the failure of exogenous prolactin and LH in another experiment to lengthen pseudopregnancies of hysterectomized rats suggests that the luteolytic mechanism can operate in the absence of uterine stimuli. A luteolytic action of LH, i.e., the shortening of pseudopregnancy in hysterectomized rats, was occasionally noted but could not be consistently demonstrated.

RESPONSE OF PRESERVED CANINE HEARTS TO CARDIOSTIMULANTS. William G. Manax,* Gary W. Lyons* and Richard C. Lillehei, Univ. of Minn. Med. Sch., Minneapolis, Minn.

Dogs hearts may be preserved in vitro by hypothermia (HPT)(2°C.) and hybaroxia (OHP)(3, 8 or 15 ATA) for periods up to 72 hours, resuming coordinated activity when homotransplanted to the neck of recipients. The heart is a good model for evaluating preservative effects because this method allows direct visualization of activity upon reestablishment of coronary flow, as well as the effects of cardiotonic agents given intravenously. The expected pharmacologic response to a given stimulant is one indicator of preservation success. Hearts are removed, perfused with cold, heparinized 5% low molecular dextran in buffered balanced salt solution, and stored up to 72 hours by HPT and OHP. Prolonged storage to 72 hours is possible by increasing the atmospheric O_2 pressure (3, 8 and 15 ATA for storage periods of 24, 48 and 72 hours respectively). Following cervical transplantation and restoration of a regular beat, isopropylnorepinephrine, norepinephrine or procaine amide are given i.v. Isopropylnorepinephrine increases ventricular rate, force and muscle tone. Norepinephrine causes a similar response to a lesser degree. Procaine amide induces atrioventricular block in a regularly contracting heart with eventual ventricular fibrillation in over 50%. However, procaine amide in a replaced heart with irregular rhythm usually results in coordinated activity. Drug response is identical in preserved and non-preserved (immediate) transplanted hearts. This study provides further support that hearts stored in this fashion are viable when transplanted.

CONTROL OF INSULIN SECRETION IN SHEEP: THE EFFECT OF VOLATILE FATTY ACIDS AND GLUCOSE. J. G. Manns* and J. M. Boda. Department of Animal Husbandry, University of California, Davis.

Ruminants begin postnatal life as typical monogastrics. However, they rapidly develop functional rumens which supply volatile fatty acids to provide the primary metabolic substrate for adult animals. Since glucose is derived almost exclusively from gluconeogenesis in adults, postprandial fluctuations in blood glucose are minimal. To determine if controls on insulin secretion other than those associated with blood glucose fluctuations operate in this species, experiments were conducted with sheep varying from 2 weeks of age to mature adults. Volatile fatty acids (2.5 mM/kg body weight) and glucose at varying levels were injected intravenously; blood samples were collected at intervals for measurements of glucose, ketone bodies, and serum insulin. Insulin titres were determined by a double-antibody immunochemical technique. Butyrate or a metabolite, but not acetate nor propionate, promoted insulin secretion much in excess of that explainable by the hyperglycemia resulting from this compound. With increasing age, concomitant with decreased glucose tolerance, there appeared to be a reduction of insulin mobilization to stimulation by both glucose and butyrate.

HYPOXIC SUPPRESSION OF THE ANAPHYLACTOID REACTION OF RATS TO DEXTRAN. Louise H. Marshall, National Institutes of Health, Bethesda, Md.

The reaction of untreated S-D rats to intravenous dextran (60 mg/kg) is characterized by edema in alert rats, and by hypotension, hemoconcentration, and hyperglycemia in anesthetized rats (pentobarbital). In rats exposed 16 to 19 hrs to hypoxic decompression (23,000 ft simulated altitude) and given dextran immediately after recompression, these signs did not appear. Sensitivity was regained if challenge was delayed 4 to 5 hrs after recompression. Other non-specific stresses (fasting, heat, cold, hemorrhage followed by reinfusion) did not modify the reaction. Animals resistant to dextran after hypoxia were still sensitive to exogenous histamine or serotonin, as estimated by edema in the hind paws after subcutaneous injection. Also, the reaction to subcutaneous administration of the histamine-liberator, compound 48/80, was unchanged. The data suggest indirectly that hypoxic suppression occurred early in the reaction sequence: dextran→intermediary→histamine and/or serotonin, and support the concept that dextran acts in the rat as an antigenic rather than as a pharmacologic agent.

THYROID I-131 UPTAKE AND ORGAN WEIGHTS AFTER THYMECTOMY AND SHAM OPERATION. Constance R. Martin, Carol Weller*and Philip Costa*, Hunter College, City Univ. of New York and Long Island Univ., Bklyn., New York.

Previously demonstrated influences of thymectomy and sham thymectomy on growth of reproductive structures of male rats may be associated with changes in thyroid function. Male hooded rats were surgically thymectomized (TMX) or sham thymectomized (S) at 6 to 6½ weeks of age. Groups of TMX and S rats were sacrificed 1, 7, 14, 18, 21 and 28 days after surgery, along with unoperated controls (U) of the same age. Body weights and wet organ weights were recorded at autopsy. I-131 was injected subcutaneously 2, 4 or 24 hours before sacrifice, and % uptake was determined on whole isolated thyroid glands. TMX, S and U rats showed no significant differences in I-131 uptake 1, 7 or 14 days after surgery. At 18 days, I-131 uptake was lower in S than in either TMX or U animals. At 21 days, values for S and U animals were approximately equal, while those for TMX rats were significantly higher. Values for S rats appeared higher at 28 than at 21 days. Body weight gains and weights of thyroid and adrenal glands were similar in TMX, S and U animals throughout the study. No differences in weights of accessory reproductive structures were observed in TMX, S and U rats autopsied 1, 7, 14 or 18 days after surgery. At 21 days, however, ventral prostate glands and seminal vesicles of S rats were significantly smaller than those of U or TMX rats.

STUDY OF THE EFFECT OF HYPERTENSIN II, CIBA ON SODIUM TRANSPORT IN ISOLATED FROG SKIN. R.D. McAfee* V.A. Hospital, New Orleans, La. and Wm. Locke, Alton Ochsner Medical Foundation, New Orleans, La.

Hypertensin II, Ciba brand of angiotensin amide, and also acetylcholine (1), stimulates short circuit current (SCC) and net Na+ flux when added in doses of 1 μg/ml to the inside solution bathing isolated short circuited skins of female winter* Rana pipiens. In 37 SCC experiments the mean increase in SCC from Hypertensin II was 56% with the sample standard deviation, s = 33%. In 7 isotope experiments SCC and net Na+ flux were not significantly different (mean = 23 $\mu A/cm^2$, s = 2.8 $\mu A/cm^2$ and mean = 19 $\mu A/cm^2$, s = 3.8 $\mu A/cm^2$ respectively. $P > 0.5$). It has been proposed that the effect of angiotensin on intestinal segments is in large part the result of stimulation of these segments by acetylcholine released by postganglionic nerves (2). To see if Hypertensin II acts on the SCC by releasing acetylcholine, the inside bathing medium was treated with atropine (1 μg/ml), which did not alter SCC, followed by Hypertensin II, which was only slightly less effective than its control (9 experiments, mean stimulus with atropine pretreatment, 9 $\mu A/cm^2$, s = 5 $\mu A/cm^2$ without atropine stimulus = 12 $\mu A/cm^2$, s = 8 $\mu A/cm^2$. $P > 0.5$). The effect of acetylcholine was completely blocked, however. (Acetylcholine following atropine 6 experiments - no stimulation whatever. Acetylcholine without atropine 6 experiments mean stimulation increase in SCC 65% s = 11%). Therefore, in these experiments SCC and net flux is in large part not mediated by release of acetylcholine.

*Summer frogs have not been studied, but spring frogs appear to be less sensitive to Hypertensin II.

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EXCRETION OF RADIOMETABOLITES OF 1,2-H^3-d-ALDOSTERONE BY THE RAT. Connie S. McCaa and L. L. Sulya (intr. by William A. Neely). Department of Biochemistry, Univ. of Miss. Med. Center, Jackson, Miss.

Tritiated aldosterone has been administered to rats and the routes of excretion of the labeled metabolites determined. In addition, information has been obtained as to the nature of the metabolites in bile. Four microcuries of 1,2-H^3-d-aldosterone, specific activity 80 mc/mg, was intravenously injected into six male Holtzman rats. During the first 24 hours after injection, 25% of the administered radioactivity was excreted in urine and 43% was excreted in feces. During the second through the fourth 24 hour periods, 4% was excreted in urine and 25% in feces with a total mean recovery of 97%. In three rats anesthetized with sodium pentobarbital the bile ducts were cannulated and bile collected after injection of the labeled hormone. Within 9 hours, 94% of the injected dose was excreted in the bile while less than 2% was in urine. Ligation of the bile duct in four rats prevented fecal excretion of radiometabolites illustrating that secretion of the steroid by the intestine does not contribute to fecal excretion. Enterohepatic circulation of aldosterone metabolites is indicated since radioactivity was recovered from urine as well as feces when bile samples containing the labeled metabolites were given intragastrically to four rats. Only 1% of the radioactivity in bile was contributed by free aldosterone, 14% was liberated by incubation with glucuronidase, 20% was liberated by boiling for 30 minutes in 6 N HCl, and 60% remained in the aqueous fraction.

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INHIBITION OF LOCAL SWEATING BY REGIONAL COOLING IN MAN. *R.D. McCook and R.D. Wurster**. Department of Physiology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Illinois.

It is well-known that cooling of the skin inhibits sweating. However, neither the local effect nor the temperature at which inhibition occurs has been fully delineated. Nude male subjects were placed in one of twin climate chambers and exposed to an ambient temperature of 62°C. Throughout the experiment, 8 areas of sweating, 6 areas of cutaneous volume pulses (photo-electric plethysmograph) and 12 areas of cutaneous temperatures were continuously recorded. Also recorded were tympanic, oral and computed mean skin temperatures. After complete recruitment of sweating was established, half of the body was quickly moved into the cool chamber with an ambient temperature of 18° to 30°C. At the lower of these temperatures, sweating was completely inhibited on all areas of the body (including those still exposed to heat) although reduced sweating sometimes returned. At the higher of these temperatures, there was little or no inhibition to the regions that remained in the hot chamber, but definite inhibition to the cooled areas. When the temperature of the cool chamber was near 25°C, it was possible to completely inhibit the cooled half of the body with little or no change in sweating on the other half. These relationships were obtained regardless of which half of the body was cooled although some differences in sensitivity were detected between the rostral and caudal portions. Therefore, under the conditions of these experiments, inhibition of sweating seems to be mainly dependent upon local skin temperatures, with some influence from mean skin and deep temperature. Plethysmographic pulses, on the other hand, were influenced by both core and skin temperatures. (Supported by Public Health Service Grant HE 08682.)

THE FORM OF THE ARTERIAL FLOW WAVE. D. A. McDonald*, H. Sugawara*, W.v. Engelhardt*, and E. O. Attinger. Research Institute, Presbyterian Hospital, Philadelphia, Pennsylvania.

Pulsatile flow has been recorded simultaneously at 4 or 5 points along the arterial tree with Medicon electromagnetic flowmeters. The pressure at each site was measured with Statham P23 or SF-4 manometers using needles inserted through either the 'cover' of the probes or the wall close by. Use of probes in series demands precision of fit to avoid the physical distortion of the artery in one place that may alter the pre-existing flow pattern recorded in another. Flexibility of choice of site along the aorta, renal, femoral and carotid arteries usually allows this to be done but it is more difficult on vessels with a short unbranched section such as the superior mesenteric artery. A flow and pressure recording was made in the ascending aorta in each experiment and the frequency spectrum of the systemic input impedance determined. Analog recording on magnetic tape, with frequent immediate on-line checks ('semi-on-line') was used to make a Fourier analysis of all curves with the LINC computer; fluid impedances were also calculated at each site. At the end of each experiment all probes were calibrated in situ with an oscillatory pump over the range of mean arterial pressure recorded in vivo. Impedance patterns presently obtained are consistent with the early data of McDonald, 1960 ('Blood flow in arteries') but are more elaborate in detail. Supported by NIH Grants HE 8606, HE 6836, and FR 00148.

SOLUBLE CANINE BONE MARROW SPECIFIC ANTIGENS. Norman M. McDuffie* and G. Bonar Sutherland Dept. of Physiol. & Pharmacol. University of Saskatchewan Saskatoon, Sask. Canada.

Soluble tissue specific antigens have been demonstrated in canine bone marrow using rabbit antisera. Exhaustive, fractional absorption of the antisera with representative normal canine tissue extract does not remove the tissue specific antigens. Extensive cross reaction studies, with the absorbed and unabsorbed antisera have indicated that these antigens are present in neither homologous nor heterologous serums and tissues. The specific antigens are demonstrable immunoelectrophoretically in the alpha and beta globulin regions. Isolation attempts, to date, have had only limited success.

SODIUM RETENTION AND β ADRENERGIC RECEPTOR BLOCKADE IN DOGS WITH SPONTANEOUS HEART FAILURE. J. McGiff, R. Burns, R. Kizell and J. Etnoyer (intr. by D.K. Detweiler). Depts. of Pharmacology and Medicine, Edward B. Robinette Fdn., and Comp. Cardiovasc. Studies Unit, U. of Penn.

The sympathetic nervous system has been considered to be responsible in part for sodium retention in congestive heart failure. The β-adrenergic receptors were proposed to mediate the antinatriuretic effects of augmented sympathetic activity. The renal hemodynamic and excretory response to exercise was determined in normal dogs and in dogs with spontaneous congestive failure before and after β receptor blockade (Pronethalol 2-3 mg/kg, i.v.). In 3 normal dogs, renal plasma flow (RPF; PAH clearance) either increased or declined slightly during exercise, GFR declined moderately, whereas Na^+ excretion was increased by exercise. Pronethalol did not alter the pattern in normal dogs. The 4 dogs in heart failure were treated as 2 groups depending on the severity of the failure. In 9 experiments in the 2 dogs in moderate failure, a striking reduction in GFR, RPF and Na^+ excretion was produced by exercise: RPF C (control) 235, E (exercise) 138 ml/min, GFR: C 99, E 61 ml/min; Na^+ excretion: C 61, E 24 μEq/min. The 2 dogs in severe failure (control Na^+ excretion, 2.9 and 13 μEq/min) died following injection of pronethalol before their studies were completed. In one of these dogs β receptor blockade was successful on first administration, but death resulted from a second administration. In this dog an alteration of the response to exercise was produced by β receptor blockade: increased RPF, GFR and Na^+ excretion. To further evaluate the role of β receptors in mediating Na retention, 2 dogs in moderate failure were loaded with saline and their Na excretion followed for four hours. Their capacity to excrete a sodium load (500 ml saline) was reduced further or unmodified by β receptor blockade.

SOMNOLENCE, RECOVERY FROM SOMNOLENCE, AND HYPOSOMNIA FOLLOWING POSTERIOR HYPOTHALAMIC LESIONS IN RATS. Dennis J. McGinty (intr. by Philip Teitelbaum). Univ. of Penna., Phila., Penna.

Normal rats exhibit regular cycles in the alternation of sleep and wakefulness and, during sleep, in the alternation of slow wave sleep (synchronized EEG) and activated sleep (desynchronized EEG and disappearance of neck muscle EMG activity). Bilateral posterior hypothalamic lesions were followed by four stages of abnormalities in the patterns of sleeping and waking. 1. Initial motor hyperactivity was observed when lesions were produced under brief ether anesthesia through implanted electrodes. 2. Somnolence then emerged and lasted 1 to 5 days. This state was characterized by continuously synchronized EEG patterns and persistent EMG activity. Thus, during this period there was no activated sleep. Brief behavioral arousal could be elicited but without EEG desynchronization. 3. In the next stage all rats gradually recovered regular cycles of waking, slow wave sleep, and activated sleep. However, the rats were lethargic, so much so that they often appeared somnolent. The recovery of activated sleep paralleled the recovery of wakefulness, although activated sleep sometimes produced the first prolonged incidence of EEG desynchronization. 4. Hyposomnia, consisting of a 20% to 60% reduction in sleep time, followed recovery from somnolence in many animals. Hyposomnia persisted without recovery for months.

These results suggest that both arousing and sleep-inducing mechanisms are disturbed by lesions in the posterior hypothalamus.

DEPRESSION OF HYPOTHALAMIC CONTENT OF LUTEINIZING HORMONE RELEASING FACTOR (LRF) BY ESTROGEN AND TESTOSTERONE. Joseph Meites and Bela E. Piacsek*, Dept. of Physiol., Michigan State University, East Lansing, Michigan.

Sixty mature female and 60 mature male rats were gonadectomized. Thirty females and 30 males received 0.1 ml of oil per day for 21 days, and served as controls. Thirty females received 0.8 µg of estradiol benzoate and 30 males received 1.0 mg of testosterone propionate in 0.1 ml of oil per day for 21 days. At the end of the treatment period, the rats were sacrificed and the hypothalami were collected, homogenized in 0.1 N HCl, boiled, and neutralized before use. Pituitaries from adult, male rats were incubated in medium 199 with two hypothalamic equivalents of neutralized extract per incubated pituitary. The medium was assayed for luteinizing hormone by the ovarian ascorbic acid depletion method of Parlow. The above experiment was repeated with the same number of animals. The results are expressed as relative potencies of NIH-LH-S5 equivalent, with the 95% confidence limits in parentheses. Experiment I: Control females, 0.980 (0.670-1.281), estradiol benzoate-treated females, 0.351 (.101-0.641); control males, 1.393 (0.976-1.989), testosterone propionate treated males, 0.537 (0.242-0.909). Experiment II: Control females, 0.781 (0.521-1.088), estradiol benzoate-treated females, 0.327 (0.129-0.472); control males, 0.106 (.080-0.132), testosterone propionate-treated males, .073 (.058-0.085). These results indicate that in the ovariectomized female and castrate male rat, the hypothalamic content of LRF can be depressed by the respective gonadal steroids. Supported by Grant No. AM-4784-04.

DELAYED REPOLARIZATION OF A-V NODAL CELLS. Carlos Mendez and Gordon K. Moe. Masonic Medical Research Laboratory, Utica, New York.

In the isolated rabbit heart, transmembrane potentials of A-V nodal cells were recorded during the propagation of stimulated premature beats. With selected patterns of stimulation it was possible to obtain conduction block at different levels inside the A-V node. When failure of transmission occurred, the action potentials recorded just proximal to the sites of block were of relatively short duration. During successful propagation, the action potentials obtained from the same cells were considerably longer. The refractory phase of these cells is a function of the duration of their action potentials. The results suggest: 1) the intrinsic duration of the action potential of A-V nodal cells is relatively brief; 2) the prolongation of the action potential duration observed during successful propagation is due to electrotonic back spread of the travelling impulse; and 3) as a result of this phenomenon, the refractory phase of nodal cells is dependent upon the characteristics of transmission.
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HUMAN CARDIOVASCULAR PERFORMANCE DURING HEAT STRESS. Joseph V. Messer, Hugh S. Levin, and Joseph Pines (intr. by William C. Kaufman). Circulation Laboratory (Tufts), Boston City Hospital, Boston, Mass.; St. Joseph's Hospital, Omaha, Nebr.; and Beth Israel Hospital, Boston, Mass.

Eleven normal males each experienced 4 supine exposures, about 3 weeks apart, to 80 F (3 hr), 100 F (3 hr), 130 F (2 hr), and 160 F (1 hr) at 10 mm Hg water vapor pressure. Arterial and central venous catheterization and remotely controlled instrumentation allowed serial measurements of cardiovascular function. The control 80 F exposures produced insignificant functional changes. During exposure to higher temperatures, cardiovascular changes correlated closely with body heat storage (Q_S). At 100 F, moderate increases occurred in Q_S, cardiac output (CO), heart rate (HR), systolic ejection rate (SER), and left ventricular work (LVW), with decreases in arterial (BP) and right atrial (RAP) pressures, central blood volume (CBV), peripheral vascular resistance (PVR), mean circulation time (MCT), and arteriovenous oxygen difference (A-V O_2); however, after 1 hr all variables achieved a stable plateau, suggesting equilibrium between subject and environment. At 130 F and 160 F, no plateau occurred, and multiple regression analyses indicate qualitatively uniform, although quantitatively differing, responses at these temperatures. At 160 F, significantly greater heat storage occurred than at 130 F, and a distinct break occurred in the mode of cardiovascular adjustment at a Q_S of 72 to 77 Cal/m^2. The rate of rise of Q_S, CO, LVW, and HR increased abruptly, stroke volume fell, and after initial reductions, A-V O_2, BP, and tension-time index increased. Thereafter, sweating increased only slightly, and all subjects rapidly approached voluntary tolerance limits. These changes suggest a malignant progressive disequilibrium between subject and environment and identify the level of Q_S at which the onset of such changes may be anticipated.

IN VIVO GEOMETRY OF LARGE AND SMALL ARTERIES. M. M. Meyer* (intr. by M. B. Visscher), Dept. of Physiol. Univ. of Minn., Mpls., Minn.

If arterial walls show negligible change in volume (ΔV) and length (ΔL) with a change in blood pressure (ΔBP), then in vivo geometry might be studied by injecting a vulcanizing, non-wetting, inert material. A segment of the vessel was used to evaluate the assumption of negligible ΔL. A section of vessel was freed and measurements were made of the external diameter (D) at BP levels and after injection, as well as diameter of the cast by using a calibrated ocular micrometer. A low viscosity liquid silicone rubber was injected into the mesenteric arteries of dogs or cats. The ΔL in small arteries averaged +0.3% for a $\overline{\Delta BP}$ of 70 mm Hg and ΔD averaged +18.2% for a $\overline{\Delta BP}$ of 73 mm Hg. The ΔL and ΔD averaged +0.9% and +45.8% from the injection at $\overline{\Delta P}$ of 101 mm Hg. Comparison of dimensions at BP levels and after injection showed a $\overline{\Delta L}$ of -0.5% and a $\overline{\Delta D}$ of +4.1% in the aorta, whereas in the small arteries $\overline{\Delta L}$ was +0.7% and $\overline{\Delta D}$ was +5.4%. Assuming a negligible ΔV and ΔL, mean radius ($\bar{r}$), wall thickness (b), and $\bar{r}/b$ ratio can be calculated at BP levels. Average values for the aorta were: $\bar{r}$ = 1.96 mm, b = 0.21 mm, and $\bar{r}/b$ = 10.3; for the superior mesenteric artery: r = 1.17 mm, b = 0.19 mm, and $\bar{r}/b$ = 7.0. Relating the mean radii of the small arteries to their $\bar{r}/b$ ratio demonstrated a significant positive correlation. Those having a $\bar{r}$ of 0.5 mm had a $\bar{r}/b$ of about 15:1; those with a $\bar{r}$ of 0.1-0.2 mm had a $\bar{r}/b$ of about 3:1. Under certain conditions, the injection method may be useful for obtaining a good approximation of $\bar{r}$ and b of vessels at various in vivo pressures and possibly a better value for the tangential stress-strain relationship. (Supported by NIDR grant DE 01796).

THE RESPONSES OF MIDDLE AGED MEN TO EXERCISE OVER AN EXTENDED PERIOD OF TIME. Ernest D. Michael, Jr.* and Steven M. Horvath. Institute of Environmental Stress, Univ. of Calif., Santa Barbara, Calif.

Nine middle aged (40-60 years) men were studied each year over a 3-5 year period to note changes occurring when no exercise training program was undertaken. Basal measurements of respiratory function, electrocardiograms and metabolism were obtained. The responses to submaximal and maximal bicycle ergometer tests indicated that both submaximal and maximal physiological parameters relating to the heart rate and oxygen uptakes either remained the same or decreased with time depending on the age range or the body type with reference to weight and body fat. The submaximal tests could be used to predict the maximal parameters and work capability once the individual was classified.

HORMONAL AND NON-HORMONAL FACTORS IN AMPHIBIAN WATER AND SALT BALANCE. S. Middler*, C. R. Kleeman, J. R. Brand*. Div. of Med., Cedars-Sinai Medical Center and UCLA School of Med., Los Angeles, California.

Cystectomy in the toad Bufo marinus allows the reflux of urine into the colon, thus causing errors in collection and making it available for reabsorption. Bilateral ureteral catheterization was used as a "functional cystectomy". This procedure resulted in a severe salt wasting by the animal with falls of plasma osmolarity of up to 50% being recorded. In addition ureteral catheterized animals appear unable to form an isotonic urine as can normals. Dehydration of two animals revealed maximum urine osmolarities of 80 mOsm/l (isotonic is about 267). Salt loading sufficient to cause anuria in a catheterized animal and a weight gain of 15% resulted in a urine of 24 mOsm/l, or 1/10 of isotonicity. An analogy is obvious between the amphibian bladder and the mammalian distal and collecting ducts in handling water and salt.

We have found that total and adenohypophysectomy also results in a marked reduction of plasma solutes with decreases of up to 100 mOsm being recorded for such operated animals. This is probably due to a defect in sodium conservation by the kidneys and/or bladder.

Preliminary studies on corticosteroid metabolism have been started. Inferior vena cava blood levels of 77.5 and 79.4 mcg% for corticosterone and 20.8 and 17.4 mcg% for cortisol (Porter-Silber chromagen) have been found in two normal animals. The effects of hypophysectomy are being studied at the present time.

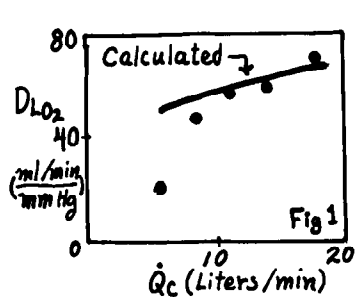
The injection of dehydrated toad serum into a full hydrated animal with bilateral ureteral catheters resulted in a decrease in "relative" free-water clearance (C_{H2O}/Creat.Cl.). This experiment is being reconfirmed, but suggests the presence of a circulating antidiuretic principle in the dehydrated animal.

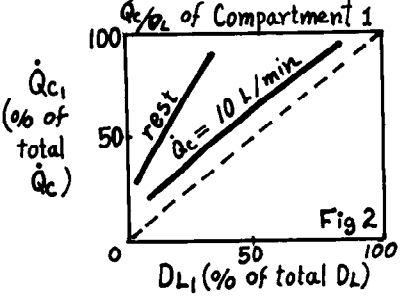
ELECTROCARDIOGRAM-RELATED NEURAL ACTIVITY IN MEDULLA OF CAT. Samuel Middleton,* Clinton N. Woolsey, and Jerzy E. Rose. Laboratory of Neurophysiology, University of Wisconsin, Madison, Wisconsin.

Metal microelectrodes introduced stereotaxically were used to explore the medulla, after removal of the caudal half of the cerebellum, in cats anesthetized with nembutal. To date 58 penetrations have been made in 10 cats. In 22 of these penetrations, neural activity correlated in time with the heart beat, was encountered. The activity was monitored by a loudspeaker and unit activity was displayed on one beam of a dual beam cathode ray oscilloscope, while the electrocardiogram and respiration were exhibited on the other. The loudspeaker provided the more sensitive method of detection. Recordable activity consisted of single units or cluster discharges of small amplitude. The latter began during the ST segment of the electrocardiogram and continued during the rising phase of the T wave. Well isolated single unit discharges of one or more spikes were observed early in the ST segment. The region of the medulla, in which heart-related neural activity uncomplicated by other activities was most often found, seems to be a thin layer immediately beneath the dorsal column nuclei, particularly beneath nucleus gracilis. Audible cardiac-related activity was most frequently encountered by the penetrating electrode immediately after disappearance of tactilely induced responses. On penetrating beyond the "cardiac" layer, units related to respiration or other types of activity were detected. The heart-related activity may involve fibers rather than cell bodies. Recording sites are being identified microscopically. (Supported by NIH grant NB-03641).

EFFECT OF NONUNIFORM PULMONARY BLOOD FLOW ON OXYGEN DIFFUSING CAPACITY. J.M. Miller* and R.L. Johnson, Jr. Dept. Med., U. Tex. Southwestern Med. Sch., Dallas, Texas.

We compared the oxygen diffusing capacity (D_{LO_2}) measured by the Lilienthal-Riley technique with D_{LO_2} calculated from single breath membrane diffusing capacity for CO and pulmonary capillary blood volume (V_C) (Fig 1). The measured D_{LO_2} (•) is appreciably lower than the calculated D_{LO_2} at rest but approaches the calculated value as pulmonary blood flow ($\dot{Q}_C$) increases. The discrepancies cannot be explained by the unevenness of ventilation/perfusion in normal subjects. We have determined the possible combinations of perfusion/diffusing capacity for a two-compartment system which can explain the observed discrepancies (Fig 2). We conclude that the distribution of blood flow with respect to diffusing surface improves as pulmonary blood flow increases.





ANTAGONISM OF EXPERIMENTALLY INDUCED BRONCHOCONSTRICTION BY CRANIALLY-IMPRESSED ELECTRIC CURRENTS. John D. Minor* and William B. Wood, Dept. of Pharmacology, Univ. of Tennessee Medical Units, Memphis, Tenn.

Vigorous bronchoconstriction, induced by intravenous infusions of serotonin, was produced in 15 pentobarbitalized (30 mg/kg), artificially respired, mongrel dogs. Dilation of the constricted bronchioles was then effected by the trans-cranial passage of alternating currents (700 c.p.s.). A roof of the mouth to top of the head electrode placement was employed and current intensities to 60 milliamperes were tested. Higher current intensities usually produce an undesirable and pronounced vagally-mediated bradycardia. Systolic/diastolic arterial pressures and central venous pressure were continuously monitored. Since bronchomotor activity was measured by using the chest of the animal as an onchometer, succinylcholine choride (500 mcg/kg) was administered to eliminate current-induced (and other) contractions of skeletal muscles. Current-induced bronchodilatation was reduced about 30% by bilateral adrenalectomy and 20% by dichloroisoproterenol (10 mg/kg). Tetraethylammonium chloride (10 mg/kg) virtually eliminated it. Bronchodilatation, in these studies, is presumed to be caused primarily by an activation of central sympathetics which innervate bronchiolar smooth muscle. This procedure, or modifications of it, may possess a clinical potential in the alleviation of certain asthmatic states. (Aided by Memphis Heart Association)

THE OXYGEN DEBT IN NORMAL MEN. John G. Mohler*, Oscar J. Balchum, and Bruce W. Armstrong. Department of Medicine, University of Southern California School of Medicine, and The Los Angeles County Hospital, Los Angeles, California.

We have made 30 measurements of oxygen debt (O_2D) at various submaximal workloads in normal men after 6 minutes of steady state exercise on a treadmill. O_2D was defined to equal Σ [$\dot{V}o_2$ (recovery) - $\dot{V}o_2$ (rest)] Δ time. The subjects had a mean age of 29.5 (± 7.5) years, mean weight 171.5 (± 24.9) lbs., mean $\dot{V}o_2$ 1.7 (± .77) L/min., and mean O_2D 2.04 (± 1.20) Liters. At least five samples of exhaled gas were collected throughout at least 15 minutes of recovery from exercise, usually with 1,1,3,5, and 5 minute collection times. Two samples were taken during a rest period prior to the exercise and at least one sample was taken during the last two minutes of exercise. Samples were analyzed with the 0.5 cc Scholander gas analyzer. The correlations obtained were: r O_2D · weight: + 0.32, r O_2D · $\dot{V}o_2$: + 0.84, r O_2D ··· $\dot{V}o_2$ · weight: 0.84. The equation describing the relation between these three variables was: O_2D = 0.014 (± .0057) weight + 1.4 (± .186) $\dot{V}o_2$ - .585. (SEE = .732 L). Two oxygen debt values determined previously at another laboratory in one of us (B.A.) were within one standard error of the estimated value. Oxygen debts of normal subjects measured by Huckabee (J. Clin. Invest. 37:255, 1958) were consistently smaller than our estimates. The mean of the measured O_2D of Huckabee's subjects was 1.85 L; our estimate of this mean O_2D (based on the mean weight and mean $\dot{V}o_2$) was 2.71 L. SUMMARY: This is a preliminary definition of O_2D as a function of weight and $\dot{V}o_2$ in normal men doing steady state treadmill exercise. (This work was supported by funds from the Attending Staff Association of The Los Angeles County General Hospital, and NIH Grants FR-5356-04-5, and 1-F2-HE-19,932-01)

SINGLE UNIT STUDY OF AFTERDISCHARGE IN NEOCORTEX. K. Mori† N. Morlock† and G. Sypert* (Intr. by A.A. Ward,Jr.) U of Wash., Seattle, Wash.

In the past, single unit studies of electrically induced afterdischarge were based on findings obtained from neurons in the vicinity of the stimulating electrodes. These neurons may well have been involved by stimulus current directly. The present study was performed to observe changes in the cellular activity associated with afterdischarges elicited by purely synaptic drives. In cats anesthetized with Evipal afterdischarge activity was recorded in the pericruciate cortex following tetanus of the motor cortex of the opposite hemisphere. EEG was recorded by means of a gross electrode in the vicinity of the microelectrode used to record the single units. Both PT neurons and unidentified neurons were observed extracellularly during period of paroxysmal EEG activity elicited by the tetanus transcallosally. Of those units recorded during afterdischarge three types were observed. Those cells most commonly encountered simply ceased firing for 1 - 2 min. following the tetanus, after which the unit returned to pretetanus firing patterns. A second group of cells responded with a high frequency burst for a short period, usually during the tetanus, following which they ceased firing 1 - 3 min., and then gradually recovered. During the recovery occasional clonic burst activity was observed. Lastly a small number of units appeared not to be involved in the afterdischarge activity, though in an area involved with an afterdischarge. In those cells exhibiting tonic burst activity attenuation of both A and B spike potentials was observed. Attenuation of the extracellularly recorded action potential most likely indicates spike inactivation secondary to depolarization. It is tentatively thought that excessive excitatory synaptic drive is responsible for the depolarization noted. Supported by NIH grants NB04053 and NB00193

EVALUATION OF SEVERAL ACUTE DRUG INDUCED NEUROPHYSIOLOGICAL PREPARATIONS IN THE CHRONIC CAT. K. Mori, R.O. Bauer, C.E. Spooner & W.D.Winters (intr. by N.A. Buchwald). Brain Research Institute & Depts. of Anesthesiology and Pharmacology, Univ. Calif. at Los Angeles.

In the present study several anesthetics and immobilizing drugs used for acute neurophysiological preparations were examined in cats with chronic superficial and deep brain electrodes. Gross behavior, EEG, & averaged Auditory Evoked Responses (AER) were examined during natural wakefulness and sleep, and compared with the various drug induced states. Prior studies demonstrated AER changes in waveform & amplitude during the various natural states. Following ether, halothane, or pentobarbital AER were reduced in amplitude, and during surgical stages only a small short latency wave persisted. Following α-chloralose (65 mg./Kg.) or ɣ-hydroxybutyrate (GHB-400mg./Kg.)-both so called "anesthetic" agents with convulsant properties-AER were essentially unaltered until a spiking pattern appeared in the EEG, then a progressive increase in amplitude ensued. During spiking with electrical silence AER were 4-10X greater than controls in all brain areas monitored. Myoclonic jerks appear during the EEG hypersynchrony or spiking. After GHB grand mal seizures could be provoked during spikes with electrical silence. Following gallamine triethiode (Flaxedil) the EEG and AER were almost identical to that seen during rhombencephalic sleep or the alert distracted state. These preparations represent 3 distinct states i.e., ether, halothane, pentobarbital: CNS depression; α-chloralose & GHB: CNS hyperexcitation (epileptoid); and gallamine: highly alert. Each preparation has a place in neurophysiology providing the investigator is aware of the shortcomings as well as the benefits of each and its relationship to the particular program under investigation. (Supported in part by USPHS 5TI-MH-6415.)

THE RELATION BETWEEN MATERNAL P_{CO_2} AND pH AND FETAL OXYGENATION
E. K. Motoyama*, G. Rivard*, F. M. Acheson*, and C. D. Cook.
Department of Pediatrics and Division of Anesthesiology, Yale School of Medicine, New Haven, Connecticut.

Previous work has indicated that the extrauterine adaptation of the lungs of the lamb may be interfered with by prenatal asphyxia. In this investigation the effect on fetal oxygenation of changes in maternal P_{CO_2} and pH is presented. In an examination of individual determinations it was found that fetal P_{O_2} was significantly ($p<.01$) lower when maternal P_{CO_2} was low (or pH high) than when P_{CO_2} was normal or high (or pH normal or low). When the P_{CO_2} of the ewe was systematically changed, in all cases there was a direct relation between P_{CO_2} in the ewe and P_{O_2} in the umbilical vein and fetal carotid artery. When pH was altered independently of P_{CO_2} by the administration of $NaHCO_3$ it was found that alkalosis was associated with the decrease in fetal P_{O_2}. Since the effect of both respiratory and metabolic alkalosis appeared quantitatively similar (a decrease in umbilical vein P_{O_2} of approximately 5 mm Hg/0.1 pH unit increase), it was concluded that the change in pH rather than the change in P_{CO_2} was the critical factor. In addition, it was shown that maternal alkalosis resulted in a reduction in umbilical arterial blood flow (a decrease of approximately 7%/0.1 pH unit increase) while acidosis produced a similar increase. Thus, because of both decreased oxygenation of the fetal blood in the placenta and decreased umbilical blood flow, significant respiratory or metabolic alkalosis would be expected to result in severe asphyxia of the fetus and this was found to be the case. Analysis of published data indicated that these findings have their counterpart in humans and have important clinical connotations.
(Supported by N.I.H. Grant HD-00989-01).

LOWER BODY NEGATIVE PRESSURE AS A PROVOCATIVE TEST FOR THE CIRCULATORY SYSTEM.
R. Murray*, J. Krog*, L. Carlson and J. Bowers*

Negative pressure (n.p.) (0 to 40 mm. mercury) was applied in ascending and descending 10 mm Hg increments to the lower body. The following measurements were taken: calf and forearm circumference and blood flow; pulse rate; shift in center of gravity; blood pressure; plasma volume; hematocrit; and plasma proteins. Three experimental conditions were used: Group 1. 4 subjects, basal state, n.p. test before and after 500 ml. venisection; Group 2. 5 subjects, six hours sitting prior to test; Group 3 (same six subjects as Group 2) six hours water immersion prior to test. After venisection the increase in heart rate with n.p. was augmented with decreased pulse pressure. During the initial n.p. there was a loss of plasma water and a further loss after venisection followed by presyncopal symptoms. After sitting, there was no plasma water loss with n.p. Following immersion, the heart rate response to n.p. was augmented and there was a marked loss of plasma water although the subjects were asymptomatic. Plasma volume decreased 326 ml. during sitting and 941 ml. during immersion. During the exposure to n.p. blood flow and circumference decreased in the arm, in the calf, circumference increased and blood decreased.

From the Department of Medicine, Indiana University Medical Center and the Department of Physiology and Biophysics, University of Kentucky. This work was carried out at the Aeromedical Research Laboratory, W-P AFB, Ohio under contracts AF 33(616)8378 and AF 33(657)-9331.

RESPONSE OF VEINS DURING ACTIVE HYPEREMIA IN SKELETAL MUSCLE. F. Nagle* J.Scott*, B.Swindall and F.Haddy. Univ.of Okla.Med. Ctr. Okla. City

An examination of the resistance to flow through veins in skeletal muscle during active (AH), reactive (RH) and mechanically induced hyperemia (MH) has been made in the dog. The hindlimb was prepared so that blood entered via the femoral artery and left via the femoral and saphenous veins. These veins were cannulated and the blood led to the inferior vena cava. T tubes in the circuit allowed separate measurement of muscle (Fm) and skin venous outflows. Pressures were measured in the femoral artery (Pa), femoral vein (Pv), medial saphenous vein, small skin vein and small muscle vein (Pvs). Flows and pressures were measured before and after a period of faradic stimulation (3v-4/sec.-2ms.) of the femoral and sciatic nerves with the myoneural junction normal (AH), and blocked (B), and before and after release of partial femoral artery occlusion (RH). Measurements were also made before and after mechanically induced hyperemia (MH) and before and after faradic stimulation with femoral artery flow constant (MS).

		Before					After				
	n	Pa	Pv	Pvs	Fm	Rvm*	Pa	Pv	Pvs	Fm	Rvm
AH	17	95	7	13	93	.071	91	8	28	226	.110**
B	7	93	6	11	115	.045	94	6	10	118	.044
RH	11	103	7	12	109	.063	86	8	17	225	.059
MH	10	68	5	8	41	.081	147	5	13	171	.042**
MS	10	114	5	10	92	.049	53	6	22	125	.142**
MH	10	117	6	11	94	.057	129	5	11	126	.046

* Muscle venous resistance (Rvm) = Pvs - Pv/Fm, ** P<0.05

Thus muscle venous resistance was elevated by active hyperemia and this could not be explained by activation of the sympathetic nerves by the stimulus. These findings suggest that the venous vascular smooth muscle is activated during active hyperemia.

VARIATIONS IN OXYGEN UPTAKE FOLLOWING MODERATE HEMORRHAGE G.G. Nahas, H.S. Small*, L. Triner*, A. St. J. Lee* and D. V. Habif* Depts. of Anesthesiology and Surgery, College of Physicians and Surgeons, Columbia University, New York, N.Y.

A computer spirometer system (A. St. J. L.) was used for the continuous measurement of O_2 uptake ($\dot{V}_{O_2}$) in 15 paralyzed mechanically ventilated beagles. Stimulation of the sympatho-adrenal system was produced by a blood loss of 25 ml/kg. A significant increase in $\dot{V}_{O_2}$ (from 7.1 to 8.2 ml/kg/min.) occurred when arterial pH (pH_a) and $PaCO_2$ were maintained close to normal (7.33 ± 0.07 and 33mmHg ± 3). This was accompanied by an elevation of plasma glucose and free fatty acids (F. F.A.) over control. However, there was no change in $\dot{V}_{O_2}$ in a similar preparation when hypercapnic acidosis (pH_a 7.21, $PaCO_2$ 61 mmHg) was produced by hypoventilation, although blood glucose levels were markedly elevated. It is postulated that the increase in $\dot{V}_{O_2}$ that occurs after moderate hemorrhage could be due to the stimulation of the sympatho-adrenal system and catecholamine release which would, in turn, produce an increased mobilization of glucose and F. F.A., an accelerated turnover of F. F. A. and resynthesis of triglycerides. As shown previously (Fed. Proc., 23:468, 1964), hypercapnic acidosis would inhibit this calorigenic effect of the catecholamines. (Supported by Army Contract DA-49-193MD-2265, and N. I. H. grants GM-09069-03 and RIO-CA-06601-03).

RENAL HEMODYNAMIC PRESSURE-FLOW RELATIONSHIPS AS AFFECTED BY CHANGES IN PLASMA OSMOLAL CONCENTRATION. L. Gabriel Navar*, Arthur C. Guyton, and J. B. Langston. Dept. of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

One theory concerning autoregulation of renal blood flow suggests that there is a feedback at the juxtaglomerular complex from the distal tubular fluid to the pre-glomerular arteriole. These experiments were designed to test the theory and to determine quantitative relationships between plasma osmolal concentration and the ability of the kidney to autoregulate. Dogs were anesthetized with sodium pentothal and prepared so that solutions could be administered and blood samples taken. Arterial pressure was elevated by occlusion of the carotid arteries. Through a flank incision, the left kidney was exposed and an electromagnetic flowmeter probe was placed around the renal artery. Distally, an adjustable clamp was secured, and a 20 gauge needle was inserted for pressure determinations. Pressure flow relationships were obtained by stepwise constriction of the renal artery for the attainment of several renal perfusion pressures. Following this, a blood sample was taken for analysis. Infusions of sodium chloride (5.85%) or mannitol (18.2%) altered the normal autoregulatory pattern to one more closely approaching a passive behavior. This was a gradual effect and could be associated with the increasing plasma osmolality whereas sodium levels rose upon infusion of the hypertonic saline but fell with infusion of the mannitol solution. Increases in plasma osmolality as low as 12% to 27% were capable of eliciting a maximum response. The results appear to be compatible with the theory and seem to indicate that the feedback mechanism is of an osmotic nature. (Supported by PHS Grant H-4736 (C4).)

EFFECTS OF GLUCAGON ON GASTROINTESTINAL MOTILITY AND CIRCULATION. Heinrich Necheles. Michael Reese Hospital and Med. Center, Chicago.

We have reported at these meetings that glucagon depresses gastrointestinal motility and pancreatic secretion in the dog. In further studies we have found that glucagon increased the oxygen content in the portal blood, and Shoemaker et al reported that it increases the rate of blood flow in the portal area. These findings were considered to be important physiologically and clinically, and therefore Dr. H. Jensen* in my laboratory has continued our studies. He found that glucagon not only increased the oxygen content in the portal blood, but also in the blood of gastric and mesenteric veins. Furthermore, venous pressures were increased in the portal vein, and in gastric and mesenteric veins. An explanation that we may offer for these findings is opening of arterio-venous anastomoses in the splanchnic bed which deviate blood flow from the mucosa and thereby increase oxygen content and venous pressure.

*Holder of Bispebjerg Fellowship at Michael Reese Hospital.

EFFECT OF OXYGEN TENSION CHANGE ON THE PERFORMANCE OF THE HEART (HEART-LUNG PREPARATION). Nasser Nejad (intr. by Eric Ogden), NASA Ames Research Center, Moffett Field, California.

Starling heart-lung preparations (mongrel dogs 7.7 - 10Kg)were ventilated with a pump connected to a spirometer filled with gas mixture of O_2, CO_2, and N_2 (02 2.5% - 45%; CO_2 4%; balance N_2). The preparations were maintained by a continuous infusion of glucose (10mg/min.) and insulin (0.008 Units/min.). A portion of systemic flow was shunted through a modular cuvette with multiple electrode assembly for continuous measurement of PO_2, PCO_2, and pH. The systemic flow was recorded with a Wilson rotameter, and a square wave (medicon) electromagnetic flowmeter was used to measure the pulmonary flow. Performance was evaluated by comparison of work curves. Left atrial pressure was plotted against stroke work(pulmonary flow x mean aortic pressure/heart rate). No change in the work curve was observed as the blood oxygen tension was changed in the range of 250 mm Hg to 35 mm Hg. Below 35 mm Hg the performance of some hearts declined while others performed effectively down to 20 mm Hg. Restoration of the oxygen tension immediately resulted in complete or partial recovery. In our system a few pilot experiments show the accumulation of lactate and pyruvate at PO_2 of 16 mm Hg or less where the heart had shown a significant depression in its work performance.

A COMPARISON OF THE NEGATIVE INOTROPIC EFFECTS OF PROCAINE AMIDE, LIDOCAINE, AND QUINIDINE. D. H. Nelson and D. C. Harrison (intr. by R. H. Maffly). Stanford U. School of Med., Palo Alto, California.

Since it is generally known from in vivo studies in man that antiarrhythmic drugs depress myocardial function, these investigations were carried out in order to define the nature of this depression. The depressant effects of various concentrations of procaine amide, lidocaine, and quinidine were compared on isolated 1 mm^2 by 7 mm strips of guinea pig right ventricle in an oxygenated muscle bath at 37°C with a stimulation rate of 60/min. Isometric force and dF/dt were recorded continuously in 36 experiments to determine dose response curve for each drug. At a concentration of 64 μg/cc, procaine amide produced very small changes in isometric force and dF/dt, quinidine decreased force and dF/dt to 67.5% of control, and lidocaine decreased force and dF/dt to 36.1% of control values. In all studies and at all concentrations lidocaine produced greater depressions than either quinidine or procaine amide. Muscle preparations from guinea pig which were treated with reserpine to deplete myocardial catecholamines gave dose response curves which were not significantly different from the normals. Norepinephrine, one μg/cc, produced improvement in the isometric force and dF/dt in all depressed strips of muscle but did not return the lidocaine depressed muscle to resting levels. Paired electrical pacing was successfully carried out in normal and depressed muscle strips with increases in isometric force and dF/dt. These studies suggest that antiarrhythmic drugs directly depress myocardial tension development and that this can be partially restored with catecholamines and paired electrical pacing. It is also clear that lidocaine and quinidine are greater depressants of myocardial function in vitro than procaine amide.

EFFECT OF INTRALUMINAL GAS ON GUT TRANSPORT. R. Nelson. Geo. H. Scott Research Laboratory, Fairview Park Hospital, Cleveland, Ohio.

This study was undertaken to assess the effect of intraluminal gas on gut transport. A 60 cm. segment of duodenum and jejunum was isolated in 18 dogs. Control tests were performed in which a test solution was perfused and recirculated through the intestinal loop. Following this, either N_2, O_2, or CO_2 was bubbled through the segment at a rate of 1 l./min. along with the test solution. In 11 dogs, Tyrode's solution was used. In 7 dogs, Tyrode's and sodium free mannitol solutions were used. In these latter dogs, gas accompanied the Na free solution through the gut loop. The first group of dogs were on total body, extracorporeal perfusion, the second group were not. It was found that bubbling gas through the intestinal lumen increased, by more than two-fold, net glucose absorption and the bidirectional flux rates of sodium. The Na increase was similar in both rates, consequently, no change in net sodium transport was noted. Net potassium and water transport were not affected by the presence of gas. Hypothermia of gut contents (24° C.) reversed the above effects and brought rates to control levels. The hypothermia results with gas were still much greater than those established for luminal hypothermia of gut contents without the presence of gas. When sodium free solutions were perfused through the gut lumen, glucose absorption rate was approximately one-half of that absorbed from Tyrode's solution. In the presence of gas, glucose absorption from sodium free solutions was equal to, or exceeded absorption rates from Tyrode's solution. It was concluded that, under the condition of these tests, interaction exists between intraluminal gas and transport of sodium and glucose. The results also suggested that glucose absorption in the dog may proceed at a normal rate from relatively sodium free solutions if augmented by intraluminal gas.
Supported by N.I.H. Grant #AM 06446-04.

CARDIOVASCULAR RESPONSES TO NOVEL AND CONDITIONAL STIMULI EVALUATED BY SUCCESSIVE BEATS. Joseph E.O. Newton and Jorge Perez-Cruet*. Pavlovian Laboratory, Johns Hopkins Univ. Sch. Med., Baltimore, Md.

We have shown in many experiments that prominent heart rate (HR) and blood pressure (BP) changes occur during classical defensive conditioning of dogs. These changes are usually analyzed as average HR and BP during control periods versus averages during conditional stimulus (CS) and unconditional stimulus (US) periods. A new method has been developed for evaluation of these functions, viz., analysis of successive beats beginning at CS-onset and working backward (control period) and forward (CS-period). Nine awake dogs were chronically studied: 4 of them with HR and peripheral aortic BP; 4 with only HR; one with HR, central and peripheral aortic BP, and stroke volume (electromagnetic flow). Results: A drop in HR occurs 1 to 2 beats after CS-onset (often noted as a dropped beat on individual trials). Two or 3 beats later HR reaches its maximum during the CS-period, thereafter falling slightly, but still above baseline. At US-onset (foreleg shock) HR rises rapidly to a peak greater than CS-maximum. BP follows HR changes fairly closely, diastolic better than systolic. Stroke volume progressively decreases from the 3rd beat after CS-onset, to a minimum on the 6th beat, than increases again during CS. At US-onset stroke volume decreases quickly to near CS-minimum for 2 or 3 beats, thereafter rapidly increasing above the baseline. These results indicate that 1) this method can reveal transients previously unsuspected, 2) a prominent initial bradycardia commonly occurs in conditioning in dogs, possibly a persisting orienting response, 3) latent period of peak tachycardia is quite short (1.5 to 2.5 secs.) and 4) BP follows HR directly whereas stroke volume is inversely related to HR.
(Supported by NIH Grant HE 06945-03 and by NASA Grant NsG 520).

THE CERULOPLASMIN CONCENTRATION OF SYNOVIAL FLUID AND ITS IN VITRO EFFECT ON VISCOSITY OF HYALURONIC ACID SOLUTIONS. William Niedermeier (Intr. by E. B. Carmichael), Div. of Rheumatic Diseases, Dept. of Med., Univ. of Ala. Med. Center, Birmingham, Alabama

Blood serum copper levels were slightly elevated in patients with rheumatoid arthritis, while synovial fluid levels of both total copper and ceruloplasmin copper were markedly elevated. The mean total copper and ceruloplasmin copper concentrations were 50 μg % (SD = 14) and 15 μg % (SD = 5.7); 48 μg % (SD = 17) and 21 μg % (SD = 14.4) 107 μg % (SD = 22) and 81 μg % (SD = 25.3) respectively in synovial fluid from 6 "normal" volunteers, 12 cadavers and 23 patients with rheumatoid arthritis. Non-ceruloplasmin copper was determined by difference to be approximately 27 μg % both in synovial fluid and blood serum of the "normals" and patients with rheumatoid arthritis. Essentially all of the increase in total copper concentration of synovial fluid of patients with rheumatoid arthritis was accounted for by an increase in ceruloplasmin. These findings were confirmed by three different methods of analysis. Total copper was determined by a wet ashing procedure and treatment with oxalyldihydrazide.

In vitro tests using purified hyaluronic acid of high intrinsic viscosity revealed that ceruloplasmin does not degrade hyaluronic acid when incubated with it alone at 30° C in phosphate buffer pH 7.4. Hyaluronic acid was rapidly degraded when incubated under these conditions with 0.08 mM/l ascorbic acid. When 0.0047 mM/l ceruloplasmin was mixed with 50 mg % hyaluronic acid, the degradation of hyaluronic acid induced by 0.08 mM/l ascorbic acid was markedly inhibited. This apparantly does not reflect the ascorbic acid oxidase activity of ceruloplasmin. Similar observations were made when the polysaccharide was treated with dehydroascorbic acid in the presence of and in the absence of ceruloplasmin.

CHANGES IN MALIC DEHYDROGENASE ACTIVITY FOLLOWING THYROIDECTOMY, R. R. Nielson and Marcia Collins.* Miami University, Oxford, Ohio

Changes in malic dehydrogenase activity of rat liver, kidney, cardiac and psoas muscles were followed over a 28 day period following surgical removal of the thyroid gland. Manometric techniques were used for the enzyme assay. The changes in enzyme activity show the progresive development of the hypothyroid condition with respect to this enzyme. The results are compared to a previous study (Am.J.Physiol. 200:55, 1961) in which the changes in oxygen consumption of the various tissues were followed for 28 days after thyrodectomy to show the development of the hypothyroid state with respect to oxygen consumption. The decrease in malic dehydrogenase activity came at a later time and with the exception of kidney were of a lesser degree than the changes in the tissue oxygen consumption. Liver malic dehydrogenase activity showed a significant fall (P= .024) at 28 days after thyroidectomy to 90% of the normal value. By comparison liver tissue slices showed a significant fall in oxygen consumption by 8 days after thyroidectomy, decreasing 80% of normal. Kidney also showed a significant fall (P= .001) at 28 days to 71%. Kidney oxygen consumption fell significantly at 20 days to 82% of normal. Cardiac muscle showed a significant fall (P= .007) by day 16 to 80%, while the oxygen consumption of cardiac muscle shows significant changes by day 4 with a value 78% of normal. Psoas muscle also showed a significant fall (P= .003) by day 16 to 79%. Psoas oxygen consumption had dropped to 62% by 4 days after thyroidectomy. The study shows that the changes in metabolism found in the hypothyroid animal is indicated by oxygen consumption preceed changes in malic dehydrogenase activity, suggesting that malic dehydrogenase is not a critical enzyme in the regulation of metabolism by the thyroid hormone.

ION DISTRIBUTION PATTERNS IN A THREE COMPARTMENT MATERIAL TRANSFER SYSTEM. L. F. Nims, R. Butera,* and U. Schnappauf.* Biology Dept., Brookhaven Natl. Lab., Upton, N. Y. 11973.

A three compartment transfer system containing terminal phases α and β separated from a central compartment by cellophane membranes has been constructed. Phase α of the system is perfused at a constant rate with a solution of urea, lithium and potassium chlorides and maleic acid. The concentrations of the constituents in the three compartments can be made equal at the start of an experiment. If urease is now added to the central compartment, a spontaneous chemical reaction, the enzymatic hydrolysis of urea begins. This reaction provides an internal source of energy which drives the system towards a non-equilibrium stationary state. During the approach to the stationary state the lithium, potassium and chloride ions are transferred through the cellophane membranes against their concentration gradients. In the stationary state the lithium and potassium ions are found at higher and the chloride ion is found at lower concentrations in phase β than in phase α. The system thus exhibits a small degree of ion selectivity and in the stationary state it is found that the ion selectivity ratio $K^{\beta}Li^{\alpha}/K^{\alpha}Li^{\beta}$ is a near linear function of the rate of ammonia production by the system, a result which is in accord with the thermodynamics of irreversible processes and is to be expected from a simple mechanical theory of transfer. This system is offered as a model for those biological material transfer systems in which enzymatically catalyzed chemical reactions occurring in the biological barriers furnish the energy required to bring about the non-equilibrium stationary state ion distribution patterns.--Research carried out at Brookhaven National Laboratory under the auspices of the U. S. Atomic Energy Commission.

BETA-ADRENERGIC BLOCKADE AND HEART RATE IN DOGS. G. S. O'Brien, S. Afonso,* I. A. Will,* and G. G. Rowe, Cardiovascular Research Laboratory, University of Wisconsin, Madison, Wisconsin.

The expected reduction in heart rate associated with Beta-adrenergic blockade following pronethalol is not observed in dogs anesthetized with morphine-sulfate and Dial-urethane. In order to explain this discrepancy, the effect of pronethalol 5 mg/Kg on heart rates and arterial blood pressure was studied in dogs anesthetized with 1) Na-pentobarbital 32 mg/Kg or 2) morphine-sulfate followed by a mixture of Dial-urethane and Na-pentobarbital (MS-DUN). After bilateral vagotomy the effect of pronethalol was determined in the same animals. In dogs anesthetized with Na-pentobarbital with initial heart rates of 155-185 beats/min., pronethalol uniformly reduced the rate. Vagotomy did not prevent the fall in heart rate but accentuated the fall in arterial blood pressure caused by pronethalol. In dogs anesthetized with MS-DUN with initial heart rates of 50-88 beats/min., pronethalol produced an increase of heart rate without a rise of arterial blood pressure persisting at least 30 minutes. In these dogs, after vagotomy, pronethalol caused a fall of heart rate and arterial blood pressure similar to that in dogs anesthetized with Na-pentobarbital, with or without vagotomy. These results suggest that the increase of heart rate produced by pronethalol in dogs anesthetized with MS-DUN is of reflex origin, mediated by a reduction of vagal tone to compensate for the systemic arterial blood pressure fall. Since heart rates did not increase after pronethalol in either group of vagotomized dogs, there is no evidence for direct Beta-adrenergic stimulation on the heart from this dose of pronethalol.

AXOPLASMIC FLOW THROUGH A COOLED PORTION OF VENTRAL ROOT. S. Ochs and H. Sawyer*. Dept. of Physiology, Indiana Univ. Med. Ctr., Indianapolis, Indiana.

The precursor p^{32} phosphate injected into the ventral horn region of L7 or S1 segments of cat spinal cords becomes incorporated into labeled phosphorous compounds in the cell bodies of the motoneurons and is then carried down by axoplasmic flow into the corresponding ventral roots (Ochs, et al. Expt. Neurol. 5:349, 1962). Cooling animals to 30°C for a period of 3 days slowed the rate of efflux. This, however, could be due either to an effect of lowered temperature on incorporation and synthesis or an effect on the mechanism of axoplasmic flow which appears to be a property of the nerve fibers. In order to differentiate between these two possibilities, a means of localized cooling of an 11 mm length of ventral root down to 12°C with the remaining portions of the root kept at 38°C has been devised. The cord segments were injected with p^{32} phosphate on both sides, the uncooled side serving as a control. For the duration of the experiment which varied from 1 to 3 days, the animals were kept anesthetized with injections of pentobarbital. The efflux showed a normal pattern down to the cooled region with a small increase of labeled material just before it, presumably due to damming, and then a decrease in efflux rate in the cooled region. At the present time it does not seem possible to distinguish between a "metabolic" or a "physical" mechanism of movement on the basis of temperature effects on rate of efflux. However, the present experiments have shown that the decreases found in the cooled region are consistent with the mechanism responsible for axoplasmic flow being present in the nerve fibers all along their lengths. (Supported by NSF Grant # G13192.)

FURTHER EVIDENCE OF THE POSTSYNAPTIC NATURE OF THE PRIMATE INTRARETINAL P-WAVE. Thomas E. Ogden, Div. of Neurology and Dept. of Physiology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

Electrical stimulation of the optic tract of the monkey evokes a positive slow potential, the P-wave, in the inner plexiform layer of the contralateral retina (J. Neurophysiol., 1964, 22:682). Because of its graded nature, long latency, susceptibility to barbiturate, and intraretinal location, the P-wave is thought to be a postsynaptic potential. Since retinal ganglion cells are not known to have recurrent collateral fibers, it is suggested that the P-wave results from activation of efferent fibers in the optic tract. If the optic tract is excited with paired shocks a second, smaller amplitude P-wave is evoked with intershock intervals as small as 2 msec. Stimulation with a train of shocks results in fusion of the P-waves after the 3rd or 4th shock at a frequency of 4-500 cps; the electrode then leads off a sustained positivity throughout the duration of the train. At the end of the train the positivity decays with the same time constant as a single P-wave. This sustained positivity, recorded from the inner plexiform layer during a train of optic tract stimuli, is interpreted as representing the fusion of hyperpolarizing I.P.S.P.s. Thus this finding directly supports the above hypothesis. (Supported by USPHS Grant NB-04135)

INFLUENCE OF CERTAIN DICARBOXYLIC ACIDS AND METABOLIC INHIBITORS ON SULFATE RELEASE FROM THE HUMAN RED CELL. Akira Omachi. Univ. of Ill. Coll. of Med., Chicago, Ill.

In a recent investigation, the release of previously incorporated radioactive inorganic sulfate (S^*) was found to be inhibited by 2,4-dinitrophenol (DNP) but not by iodoacetate (Science 145: 1449, 1964). One possible explanation for this result is that DNP inhibits certain metabolic reactions which take place in the region of the red cell membrane and which may be involved in the control of anion permeability. In the present study, S^* release was determined in the presence of some substrates and inhibitors related to mitochondrial metabolism. When 10 mM l-malate, oxalacetate, or succinate was present in the Ringer-Locke's medium, the isotope appearance in 60 minutes was 118, 113, and 93%, respectively, of the amount appearing in the medium in the absence of substrate. When glutamate, α-ketoglutarate, or fumarate was present, the S^* released was not statistically different from the control. Amytal (5 mM) and phenazine methosulfate (1 mg/ml) depressed S^* exit and the latter, in addition, prevented the malate effect. These results appear to provide circumstantial evidence in support of the working view that certain biochemical processes, resembling partial reactions in mitochondrial oxidative phosphorylation, may be associated with the regulation of anion permeability in the red cell membrane.
(Supported by USPHS.)

EFFECT OF SPLENIC CONTRACTION ON THE OPTICAL DENSITY OF CIRCULATING BLOOD. D.F. Opdyke and R. Apostolico*. New Jersey College of Medicine and Dentistry, Jersey City, New Jersey.

Injection of l-epinephrine into dogs shortly before the beginning of the inscription of an indocyanine dye dilution curve resulted in a sustained elevation of the downslope of the dye concentration curve above base-line. Experiments with the spleens exteriorized or removed showed that release of RBC by splenic contraction accounted for the effect. Injection of 8-10 ml splenic blood or an equivalent concentration of arterial RBC produced changes in optical density nearly equivalent to injection of 0.88 mgm of indocyanine dye measured at 800 μ by a Colson densitometer. The optical density tracing made after injection of splenic blood or concentrated arterial RBC intersected the base-line approximately at the point predicted by semi-log extrapolation of the descending limb of the curve. There was little evidence of re-circulation of the injected RBC.

MEASUREMENT OF REGIONAL BLOOD FLOW IN THE DOG AND MAN BY A MODIFIED INDICATOR-DILUTION TECHNIQUE. H.W. Overbeck*, R.M. Daugherty*, and F.J. Haddy. Depts. of Physiol. and Med. University of Okla. Med. Center and V. A. Hospital, Oklahoma City, Oklahoma.

We recently reported the development of a new needle, which improves indicator mixing in constant infusion indicator-dilution measurement of regional blood flow (Clin. Res. 13:95, 1965). This needle has 2 side holes of diameter 0.006" and the tip opening sealed. With infusion rate of 8 ml/min. the needle produces 2 jet streams directed laterally. We concluded that these jet streams do not produce significant hemolysis, because forelimb vascular resistance in the dog did not change during intrabrachial arterial infusion of isotonic NaCl solution through the needle. In the present study, we have investigated the accuracy of the flow measurements obtained with this needle in the dog forelimb. We have also used the needle to measure upper extremity blood flow before and during local infusion of angiotensin in man. In 5 pump perfused dog forelimbs, indicator-dilution flow measurements using this needle correlated within 5% of the actual venous outflow over a wide range of flows (45 to 170 ml/min.). In 14 human upper extremities, mean calculated resting blood flow was 6.3 ml/min/100 ml extremity volume, with range of 3.4 to 9.8. These figures agree well with those reported by others using venous occlusion plethysmography. There were no complications. Intrabrachial arterial infusions of 0.025 to 0.10 μg/min angiotensin produced a fall in calculated flow in all cases. We conclude that this jet needle allows accurate measurement of regional blood flow by constant infusion indicator-dilution techniques.

COMPARATIVE ASPECTS OF O_2 TRANSPORT BY BLOOD. J. T. Parer*, A. S. Hoversland* and J. Metcalfe. Heart Research Laboratory, University of Oregon Medical School, Portland, Oregon.

The resting rate of O_2 consumption per unit of body weight is inversely related to body weight. The extra O_2 is delivered to the tissues of smaller animals in part by a higher cardiac index, and in part by an increase in arteriovenous O_2 difference. Calculations from data in the literature and our own direct measurements (in sheep) yield values for mixed venous O_2 tension ($P\bar{v}O_2$) between 35 and 41 mm Hg in 6 species ranging in size from cattle to rats. Mixed venous O_2 concentration varies more widely, the relative stability of $P\bar{v}O_2$ being due to displacement of the O_2 dissociation curve to the right with decreasing species size. However, blood from each of 2 tigers (ca. 6 mos. age; 30 kg weight) became half-saturated with O_2 at a P_{O_2} of 42.8 mm Hg and blood from a young lion (24 kg weight) reached half-saturation at a P_{O_2} of 42.3 mm Hg. Average blood O_2 capacities were 16 and 18 vols% for the tigers and lion respectively. Despite this unusual combination of low O_2 affinity and high O_2 capacity, a $P\bar{v}O_2$ similar to that in other animals could result from either of two possible alternatives: cardiac output could be decreased to half the value expected on the basis of body weight or the rate of O_2 consumption per unit weight could be twice the predicted value. On the other hand, if cardiac output and O_2 consumption are both within the usual range for animals of this size, the peripheral tissues of these carnivores are perfused with blood containing unusually high tensions of O_2.

EFFECTS OF PREGNANCY ON RENAL HYPERTENSION IN SHEEP. Harold R. Parker and Donald L. Dungworth (intr. by Douglas Stuart) University of California, Davis, California

Sheep respond to partial renal artery constriction with a sustained hypertension in which the mean blood pressures may exceed 200 mm Hg. A group of ewes in which the blood pressure had been measured at frequent intervals during the course of a single lambing cycle was made hypertensive by a modified Goldblatt technique. Blood pressure recordings were continued for a second lambing cycle. Pregnancy affected blood pressure by aggravating hypertension during the first stages of gestation and by producing a fall in the last trimester of both the normotensive and hypertensive periods. Soon after delivery, blood pressure rose to a level comparable to, or greater than, the levels of the second trimester. The rapid return to normal or hypertensive levels after delivery suggested the action of a hypotensive factor of fetal or placental origin. Malignant hypertension was seen in two ewes and was characterized by convulsions, retinal vascular spasms and hemorrhage, and albuminuria, but did not occur during pregnancy. Histological lesions of major importance were confined to the blood vessels and kidneys. Intimal thickening was seen in the small arteries accompanied by a generalized hyperplastic arteriolosclerosis. More severe changes consisted of arteriolar hyalinosis and fibrinoid necrosis. An inconstant, mild glomerulosclerosis characterized the renal lesion. Pregnancy appeared to offer some protection to the vascular bed.

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NEUROMUSCULAR MECHANISMS IN CRUSTACEAN ABDOMINAL EXTENSOR MUSCLES. I. Parnas and H.L. Atwood (intr. by C.A.G. Wiersma). California Institute of Technology, Pasadena.

The axons supplying the medial and lateral heads of the deep abdominal extensor muscles, DEAM and DEAL, (Pilgrim & Wiersma, J. Morphol. 113, 453, 1963) of the crayfish, Procambarus clarki, and rock-lobster, Palinurus interruptus, were stimulated individually or in combination while recording from single muscle fibers. In both species the DEAL is divided into two parallel bundles with different distribution of the innervation. DEAM receives two excitor axons and an inhibitor from the ganglion of the same segment, plus an excitor and inhibitor from the next anterior one. $DEAL_1$, the central bundle, has a similar innervation, whereas the most lateral bundle, $DEAL_2$, receives only one (lobster) or two (crayfish) excitor axons and the inhibitor, common for the three bundles. From the anterior ganglion $DEAL_2$ receives only a branch of the inhibitor. Four excitors enter each segment from its ganglion. Each bundle receives one specific excitor. An additional common excitor innervates all three bundles in the crayfish and DEAM and $DEAL_1$ in the lobster. The excitors evoke large spike potentials in the DEAM and $DEAL_1$ but usually junction potentials which facilitate with repetitive stimulation to give a spike in $DEAL_2$. Correct timing of inhibitory impulses relative to excitatory ones can abolish partially or completely spike potentials and their associated muscular contractions. The junction potentials in $DEAL_2$ are little affected in magnitude but reduced in duration. In these muscles most of the inhibitory effect appears to be on the muscle fiber membrane rather than on the mechanism of release of the excitatory transmitter substance. Supported by N.S.F. grant GB 2785 to Dr. C.A.G. Wiersma.

MOTOR CONTROL BY PULSE RATE SIGNALS

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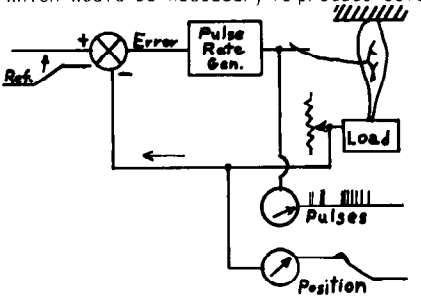
Muscles' responses to pulse rate signals are nonlinear, lagging, load positionings, with marked latch like, hysteresis. Motor unit activity (emg) is also not simply related to resulting movements. Tests were conducted, to find the nature of the pulse rate signal which would be necessary to produce several simple movement patterns.



Motor nerve stimulation was given with rates adjusted according to error between actual load position and the desired load position. The resulting movements and stimulus patterns were recorded. The relationships so developed resembled in many ways, those seen in physiological movements. Stimulus pulse rate change, appreciably leads position change. After a position change was accomplished, the pulse rate decreased markedly while the position was held. Pulse patterns involving pulse pairing was common. It was necessary to introduce an adaptation like action in this, pseudo-myotatic-reflex system, to prevent severe clonus like oscillations. The complex relationships between unit emg and movement is largely due to the complexity of muscle response to pulse rate signals.

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GLUCOSE METABOLISM IN NORMAL AND PANCREATECTOMISED DOGS DURING EXERCISE.

P. Paul,* H. Miller and B. Issekutz, Jr. Lankenau Hosp., Div. of Research, Philadelphia, Pa.

Dogs with indwelling arterial and venous catheters were trained to run on a treadmill for 30-60 minutes. Glucose-C^{14} (U) was infused I.V. at a constant rate for 3-1/2 hours. O_2 uptake, $C^{14}O_2$ output, plasma FFA and hepatic sugar output were measured. In normal dogs exercise increased the rate of hepatic glucose output 1.5-2.5 times. Although this was immediately oxidized, it represented only 6-20% of the total CO_2 output. The plasma FFA usually decreased during exercise. Since there is a straight line correlation between the plasma FFA level and the turnover rate of FFA (Am. J. Physiol. 207, 583, 1964) it can be estimated that in this case only 25-30% of the 6-7 fold elevated O_2 uptake was used for the oxidation of these two plasma constituents. The hepatic glucose output was 2-3 times higher than the controls in the resting diabetic animals, but only about 10% of the glucose output was converted to CO_2, which contributed some 5-12% of the total CO_2 output. Exercise induced a 15-50% increase of the glucose output but only 20-50% of this was immediately oxidized which represented 3-10% of the exhaled CO_2. In resting dogs an inverse correlation was found between the logarithm of plasma FFA level (range 0.19-3.0 μEq/ml) and the logarithm of the percent participation of plasma glucose in the CO_2 output. (Supported by an NIH Grant HE-07687).

EFFECT OF BENDROFLUMETHIAZIDE UPON SODIUM TRANSPORT BY THE ISOLATED TOAD BLADDER. R. G. Pendleton* and L. P. Sullivan, Departments of Pharmacology and Physiology, University of Kansas Medical Center, Kansas City, Kansas.

The effect of bendroflumethiazide (BHFT) on sodium transport in the isolated toad bladder was studied using the short-circuit current (SCC) technique. At a dose level of 1.6×10^{-4}M, BHFT depresses the SCC an average of 32μamp (mean SCC= 160μamp) when placed in the serosal bathing medium for 30 min. The transbladder potential difference (P. D.) falls an average of 2 mv (mean PD= 37 mv) and the resistance rises an average of 41 ohms (mean R= 286 ohms). When the drug is placed in the mucosal bathing solution a small (10%) stimulation of SCC and PD is seen, which reaches a peak within 30 minutes after administration. Placing the drug simultaneously on both sides of the bladder causes an initial rise and/or latent period in the SCC response followed by a rapid decline. BHFT accumulates in the bladder to a level 5 times that in the medium when placed on the serosal side for 30 minutes. No drug enters the mucosal medium. This accumulation is not depressed by prior administration of 5×10^{-4}M KCN. When the drug is placed in the mucosal bathing solution, no drug enters the bladder or serosal fluid. Thus, the bladder contains two thiazide receptors; one, causing a stimulation of the SCC, located at the mucosal surface; and a second, at the serosal surface or inside the cell, causing a depression of the SCC. (Supported by USPHS Grant HE-06974 and NSF Grant GB-655).

SUPERIOR COLLICULUS OSCILLATORY RESPONSE TO ELECTRICAL STIMULATION Sterling G. Pickering* and Walter J. Freeman
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The electrical activity of the superior colliculus following electrical stimulation to the contralateral optic nerve in the anesthetized cat was monopolarly recorded and mapped in space and time. At the point in time on the waveform where the response had its peak amplitude, a map of isopotential surfaces was constructed and superimposed on photographic enlargements of histological slides at different coronal planes through the colliculus. These maps showed that the electric field had the characteristics of a warped dipole layer, one pole (source) lay in the stratum opticum and the other pole (sink) lay above the dorsal surface of the structure. The zero isopotential was in the stratum zonale and was stationary in time. The waveform of the structure was diphasic with initial surface negativity. Bipolar recording electrodes were implanted in chronic animals across the dipole layer so that one electrode tip was located in each pole. Optic nerve electrical stimulation to animals in a lighted background evoked a response similar to that seen in the acute preparations. During similar experiments on blindfolded cats, the waveform had the characteristics of a frequency modulated, exponentially damped sine wave, which took from 150 to 300 milliseconds to decay back to the spontaneous activity level. The first two peaks of the oscillatory waveform were similar to those seen in the lighted background conditions. The frequency of oscillation and decay rate were dependent on degree of arousal. Mild nociceptive stimulation was accompanied by a decrease in decay rate and an increase in frequency. The amplitude of the initial positive peak did not change.
NIH Grant MH 06686 USPHS Fellowship 1-F1-MH 23,510-01

THE RELATION BETWEEN PLASMA CONCENTRATIONS OF GLUTAMINE AND GLYCINE AND UTILIZATION OF THEIR AMIDE AND AMINO NITROGENS AS SOURCES OF URINARY AMMONIA. Lou Ann Pilkington* and Robert F. Pitts. Cornell Univ. Medical College, New York, N.Y.

Glutamine, labeled with N^{15} either in the amide or in the amino position, or N^{15}-labeled glycine, was infused into one renal artery of chronically acidotic dogs. Urine was collected from each kidney. The per cent of urinary ammonia derived from the amide or amino nitrogen of glutamine was measured when plasma concentrations of glutamine were in normal ranges (control periods) and when plasma concentrations of either glutamine, glycine or alanine were increased over a four-fold range. The results show that with increased plasma glutamine, both the amide and the amino nitrogens of glutamine are utilized in increased amounts as precursors of urinary ammonia. Elevation of plasma glycine or alanine result in small increases in utilization of the amino or amide nitrogen of glutamine. This increase is attributed to increased plasma concentration of glutamine. The contribution of N^{15} labeled glycine to urinary ammonia was studied as plasma concentration of glycine was increased. Glycine nitrogen is the source of much of the extra ammonia excreted when plasma glycine is elevated.

EFFECT OF ALPHA ADRENERGIC BLOCKADE ON MYOCARDIAL REACTIVE HYPEREMIA. B. Pitt*, E. M. Khouri* and D. E. Gregg. Dept of Cardiorespiratory Diseases, Walter Reed Army Institute of Research, Washington, D. C.

Elimination of sympathetic coronary artery constrictor tone has been claimed to abolish the reactive hyperemia characteristics of the heart resulting in a state of coronary artery rigidity. It has been postulated that chronic diminution of sympathetic coronary artery constrictor tone with consequent coronary artery rigidity is the mechanism responsible for angina pectoris. In an attempt to determine the influence of sympathetic coronary artery constrictor fibers on myocardial reactive hyperemia, peak coronary blood flow (PkCBF) obtained with an electromagnetic flowmeter, and central aortic pressure were recorded before and after coronary artery occlusion. In 3 open-chest dogs, 10 second coronary artery occlusions prior to administration of adrenergic blocking agents resulted in PkCBF 50-280% greater than control flow. Intracoronary (i.c.) dibenamine 30-40 mg, as well as subsequent i.c. hexamethonium 5-25 mg, i.c. dinitrophenol 5 mg, and i.v. dibenzylene 1-5 mg/kg resulted in PkCBF during reactive hyperemia 45-180% greater than control flow. In 2 closed-chest unanesthetized dogs, PkCBF during reactive hyperemia was 100-750% greater than control flow. Dibenzylene 1.5-15 mg/kg i.v. resulted in PkCBF during reactive hyperemia 50-400% greater than control flow. Propranolol 1-2 mg/kg during the period of alpha blockade failed to significantly alter PkCBF during reactive hyperemia. In no case was reactive hyperemia eliminated by adrenergic blockade. Elevation of aortic pressure after alpha blockade to control levels (by means of aortic constriction in the open-chest dogs and i.v. angiotensin in the unanesthetized dog) restored PkCBF during reactive hyperemia to values closer to those obtained prior to blockade. In summary, pharmacologic elimination of coronary artery constrictor tone failed to abolish the reactive hyperemia characteristics of the heart.

A STUDY OF THE KINETICS OF AMMONIA PRODUCTION AND EXCRETION IN THE ACIDOTIC DOG. Robert F. Pitts and Georges Fulgraff*. Cornell University Medical College, New York, New York.

The Chinard technique of rapid injection into one renal artery of a glomerular marker (creatinine) and a compound whose utilization or excretion is under investigation has been employed in a study of the time courses of production and excretion of ammonia. Urine was collected from the two kidneys separately at 20 sec. intervals and rates of excretion of creatinine and ammonia were corrected for recirculation. Following the injection of $N^{15}H_4Cl$ or amide N^{15} glutamine, the label appeared in the urinary ammonia within a partially corrected time interval of 11 sec. or less, suggesting that, in both instances, the labeled ammonia entered the urine as far along the nephron as the convoluted portion of the distal tubules and cortical collecting ducts. Creatinine appeared in the urine after a delay of 60 to 100 secs. Following injections of amino N^{15} glutamine, appearance of label in urinary ammonia was delayed about 20 sec. relative to that observed following injection of amide N^{15} glutamine. The time course of disappearance of label from the urine suggests that deamidation of glutamine is not rate limiting for ammonia production and excretion, whereas deamination of glutamine may well be. Per cent recovery of label as urinary ammonia in one circulation following injection of N^{15} glutamine is conditioned by rate of uptake of glutamine by tubular cells. Per cent recovery following injection of $N^{15}H_4Cl$, a substance which rapidly enters tubular cells by non-ionic diffusion, is conditioned by rate of secretion of hydrogen ions.

CHANGES IN THE TRANSCALLOSAL RESPONSE WITH AGE IN THE RAT. V. J. Poon (intr. by D. E. Woolley). Dept. of Physiology, University of California, Berkeley, Calif.

The electrophysiological characteristics of the transcallosal response were investigated in adult and developing rats anesthetized with pentobarbital (30 mg/kg). Surface monopolar recording was from the parieto-occipital cortex near the longitudinal fissure; bipolar stimulation was in the contralateral homologous cortex or in the corpus callosum. In the adult the response consisted primarily of a negative wave with a peak latency of 11 msec, wave duration of 20 msec, and 50-100 μV amplitude at two times threshold stimulus intensity. For developmental studies, stimulation was both at a constant stimulus intensity (200 μamp) and duration (0.05 msec) or at twice threshold at chronaxie. Characteristics of the negative wave recorded from the surface were compared at 10, 14, 16, 18, 22, 24, 44 and 68 days. The transcallosal response underwent the following changes with age: amplitude showed the greatest increase between 18 and 22 days; peak latency and chronaxie decreased, especially between 10 and 18 days; and wave duration decreased, primarily between 14 and 18 days. The developmental changes may be correlated with histological studies by other investigators on dendritic growth in the cortex and myelination of parietal-occipital callosal fibers in the rat. (Supported by NIH.)

Splanchnic Circulation and Metabolism During Hemorrhage in Normal Man. H. L. Price, S. Deutsch*, B. E. Marshall*, and G. W. Stephen, Department of Anesthesia, University of Pennsylvania, Phila., Pa.

The effects of hemorrhage (15 per cent of blood volume) were studied in 10 supine normal human volunteers. Splanchnic blood flow was estimated by giving a constant intravenous infusion of indocyanine green and sampling from a femoral artery and hepatic vein. Splanchnic blood volume was estimated from indicator dilution, using I^{131}- tagged albumin. Cardiac output was estimated, using either Evans blue or indocyanine green. Arterial and venous pressures were measured, respectively, from a femoral artery and hepatic vein. The blood was analyzed for oxygen content and tension, as well as for lactate and pyruvate concentrations. Hemorrhage had no consistent effect upon arterial pressure, venous pressure, splanchnic blood flow, splanchnic vascular resistance or splanchnic oxygen consumption. Venous oxygen tension and lactate/pyruvate ratio were also unaffected, as was cardiac output. In contrast, the splanchnic blood volume was depleted by 40 per cent and of the amount of blood removed, more than half came from the splanchnic viscera. The results suggest a reflex increase in splanchnic venomotor tone unaccompanied by arteriolar constriction.

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SIMULTANEOUS RESPONSES OF THE FOUR HEART CHAMBERS TO GRADED l-NOREPINEPHRINE INFUSION. *D.V. Priola*. Department of Physiology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Illinois.

Fifteen mongrel dogs were anesthetized with Sernylan (2 mg/kg-im) and α-chloralose (80-100 mg/kg-iv), the chest opened and the four cardiac chambers cannulated. All data were recorded using an ink-writing oscillograph with a frequency response of 125 cps. Following bilateral cervical vagotomy, freshly-prepared l-norepinephrine was infused via a cannulated femoral vein using a syringe pump. The changes from control values in pulse pressure and dP/dt in each heart chamber were measured at steady state during the infusion. Delivery rates were 0.03, 0.07, 0.16, 0.33, 0.66 and 1.65γ/kg/min. Although considerable variability in responsiveness was observed from animal to animal, the four cardiac chambers were found to be differentially sensitive to norepinephrine in terms of: 1) threshold dose, 2) dose-response curve contour and 3) maximum response. In general, the left ventricle was most sensitive and the left atrium least sensitive. The right ventricle exhibited a lower threshold and a higher maximum response than did the right atrium. The sensitivity of the S-A node, as measured from the heart rate response, was found to be significantly different from that of the right atrium. Changes in dP/dt generally corresponded with changes in pulse pressure within the same cardiac chamber. (Supported by Public Health Service Grant HE 08682.)

PHARMACOLOGICAL EVIDENCE OF A DUAL ARTERIOMOTOR CONTROL OF FOREARM SKIN. Leon D. Prokop* and Alrick B. Hertzman. St. Louis University School of Medicine, St. Louis, Missouri.

Cutaneous vasomotor controls in forearm skin were studied by local blockade and stimulation of adrenergic and cholinergic endings. Following local adrenergic blockade by ergotamine, vasoconstrictor reflexes elicited vasodilatation, methacholine caused a further increase in local cutaneous blood flow, atropine resulted in slight vasodilatation and presented vasodilator responses to vasoconstrictor reflexes. Methacholine following ergotamine and atropine blockade elicited vasodilatation. These pharmacological data support the concept of a dual arteriomotor innervation of forearm skin. Drugs were administered locally by electrophoresis. Vascular responses were recorded by photoelectric plethysmograph. Supported by USPHS Grant HE-04939.

BLOOD FLOW IN THE ORAL MUCOSA AND SALIVARY ACTIVITY IN RESPONSE TO THERMAL STRESS. Juan E. Quejada* and Alrick B. Hertzman. University of the Philippines College of Dentistry, Manila, and Saint Louis University School of Medicine, Saint Louis, Missouri.

Vascular responses in oral mucosa and forearm skin, and parotid secretion and electrolytes were recorded during exposure of semi-nude male subjects to rising ambient temperatures. Vasodilatation in forearm skin was not accompanied by corresponding changes in the oral mucosa. Parotid secretion increased almost twofold from 0.017 ± 0.004 ml/min. to 0.029 ± 0.007 ml/min. ($P < .025$). Salivary Na/K ratio decreased from 6.84 ± 1.74 mEq/L to 1.27 ± 0.15 mEq/L ($P < .025$), due to decrease in Na and increase in K. A photoelectric plethysmograph with fiber optics was designed for application to the oral mucosa. Supported by PHS Grants 1 SO 1 FR-05324-01 and HE-04039.

THE ROLE OF THE PROXIMAL RENAL TUBULE IN THE EXCRETION OF TITRATABLE ACID IN RESPIRATORY ACIDOSIS. A.G. Ramsay (intr. by H.V. Murdaugh). Univ. Ala. Med. Center, Birmingham, Ala.

Previous studies have shown that upon exposure to high pCO_2, the dog initially increases the excretion of titratable acid. Subsequently, titratable acid excretion becomes negligible. This suggests that the phosphate titratable acid mechanism of H^+ excretion may play an important role in the initial defense against acute H^+ loads in hypercapnia. As clearance techniques have shown that acute acid base changes have no effect on renal tubular reabsorption of phosphate, the increased T.A. in acute hypercapnia suggested that more localized changes in reabsorption of phosphate may occur within the tubule. To more definitively delineate this, 2 stop-flow experiments were performed in each of 8 dogs during high and low pCO_2. These showed that induction of high CO_2 tension following hypocapnia produced a significant increase in phosphate concentration in samples from the proximal area. When compared to hypocapnia, this increment in phosphate concentration ranged from 50-200 %. When hypercapnia preceded hypocapnia, there was a 40-60 % decrement in phosphate concentration after lowering pCO_2. Hypercapnia produced a striking increase in the stop-flow T.A. pattern. Calculation of $HPO_4^=$ and $H_2PO_4^-$ delivery into the proximal tubule showed that this was about equimolar during hypercapnia, but during hypocapnia delivery of $HPO_4^=$ was almost sixfold that of $H_2PO_4^-$. The results suggest that $HPO_4^=$ may be actively reabsorbed in the proximal tubule and that $H_2PO_4^-$ reabsorption may be a passive process. Delivery of a greater proportion of total phosphate as the less readily reabsorbed univalent anion into the proximal tubule may enable this area of the nephron to make a significant contribution to the excretion of titratable acid in acute hypercapnia.
(Supported by U.S.P.H.S. grant AM-09036)

REGIONAL ORGAN BLOOD FLOW IN THE IMMATURE PIG. R. P. Rathmacher*, L.L. Anderson* and R. M. Melampy. Iowa State University, Ames, Iowa.

$Rb^{86}Cl$ was used as an indicator for determining regional organ blood flow in 20 young male and female pigs (19 to 55 kg). Following injection of the indicator into the femoral vein the animals were electrocuted at intervals of 30, 60, 120 and 180 sec. Five pigs were killed at each time interval (2 males and 3 females). Using the same indicator, cardiac output was determined simultaneously in 10 of 20 animals. Tissue and blood samples were counted with a gas-flow proportional counter. Values for organ blood flow were obtained by multiplying the unit percent activity of the organ by the estimated cardiac output (based upon body wt). Cardiac output $\pm$ SE for 10 pigs averaged 156 ± 10 ml/min/kg body wt or 5.1 ± 0.5 l/min. There were no significant changes in blood flow with time in semimembranosus muscle, testicle, ovary, spleen, liver, adrenal or heart. Mean blood flow values $\pm$ SE in these organs in ml/min/g of wet tissue were 0.036 ± 0.004, 0.09 ± 0.02, 0.29 ± 0.03, 0.36 ± 0.02, 0.40 ± 0.03, 0.82 ± 0.07, 0.90 ± 0.08, respectively. Estimated blood flow of the lung $\pm$ SE decreased ($P < .001$) from 1.22 ± 0.12 (30 sec) to 0.48 ± 0.02 (180 sec) ml/min/g of wet tissue. Estimated blood flow of the kidney $\pm$ SE increased ($P < .01$) from 1.70 ± 0.31 (30 sec) to 2.72 ± 0.21 (180 sec) ml/min/g of wet tissue. Estimated blood flow of the uterus $\pm$ SE decreased ($P < .05$) from 30 sec (0.83 ± 0.11 ml/min/g) to 60 sec (0.43 ± 0.15). However, there were no differences ($P > .05$) between 60, 120 (0.36 ± 0.05) and 180 sec (0.28 ± 0.05). Results suggest that $Rb^{86}Cl$ can be used to determine regional organ blood flow in these organs with the exception of the lung and uterus. Differences in activity of the uterus as an indication of blood flow changes at certain reproductive stages could be used when pigs are killed between 60 and 180 sec. This method may be used to determine ovarian blood flow at certain reproductive stages in the pig.
(Supported by USPHS NIH Grant HD 01168-06)

PULMONARY VENTILATION DURING EXERCISE AT LEXINGTON, KENTUCKY (1,000 FEET) AND LEADVILLE, COLORADO (10,200 FEET). John T. Reeves, Robert F. Grover, and Jerome E. Cohn. Department of Medicine, School of Medicine, University of Kentucky, Lexington, Kentucky and University of Colorado, Denver, Colorado.

Respiratory measurements were obtained at Lexington and Leadville in 5 champion high school track men at performance levels ranging from the basal state to maximum exercise (treadmill). During maximal effort (V_{O_2}) oxygen consumption (STPD) and (V_E) minute ventilation (STPD)were less at Leadville than Lexington but the (V_E)minute ventilation (BTPS), (V_T) tidal volume (BTPS), respiratory frequency (f), and expired oxygen concentration ($F_{E_{O_2}}$) were similar.

	V_{O_2} L/min	$V_{E_{STPD}}$ L/min	$V_{E_{BTPS}}$ L/min	$V_{T_{BTPS}}$	f	$F_{E_{O_2}}$
Lexington	4.28	108	132	2.7	49	.169
Leadville	3.24	81	144	2.8	52	.168

For the entire range of metabolic activity oxygen uptake had a relation to each variable which was curvilinear and characteristic for the altitude. However the curvilinear relationships became independent of altitude when V_E (BTPS), f, V_T(BTPS), and $F_{E_{O_2}}$ each were related to the ratio $V_{O_2}/_{max}V_{O_2}$ rather than V_{O_2} per se. When the data of Pugh et al (JAP 19:431,1964) from the 1961 Himalayan expedition were examined this way V_E (BTPS), (f), V_T, and $F_{E_{O_2}}$ were, in general, independent of altitude. The complex relationships of ventilation to altitude and to degree of exertion are simplified. The similarities of the data from altitudes ranging from sea level to 24,000 feet suggest that ventilation is regulated in part by some mechanism which senses a given effort in terms of exercise capacity. (Supported by Grants DA-49-193-MD-2551 (U.S. Army), HE 06780-03 (NIH), and HE 08932-01(NIH)

CYANOCOBALAMIN (VITAMIN B_{12}) UPTAKE BY Ochromonas malhamensis. Robert B. Reeves and Fredric S. Fay*, Division of Biological Sciences, Cornell University, Ithaca, New York.

As the nature of the uptake process for vitamin B_{12} (MW 1357) is unknown for any cell, this process has been studied in Ochromonas, a phytoflagellate requiring the vitamin for growth. Uptake of Co-60-cyanocobalamin was measured at 25 C in washed cells suspended in NaCl, 0.1 M; OH-butyrate buffer, pH 4.5, .005 M; NaCN, 7×10^{-3} M; vitamin B_{12}, 30 mug/ml. Uptake occurs in two phases, a rapid initial uptake of .4 ug/ml packed cells complete in 1 min, and a slower phase reaching a steady state of 2-3 ug/ml packed cells in 4 hours. Both phases show saturation kinetics (half-max. conc. for rapid phase <5 mug/ml; slow phase, 8 mug/ml) but only the slower phase is sensitive to metabolic inhibitors. No differences were seen in cells grown under B_{12} sufficient versus deficient conditions. B_{12} uptake is pH dependent falling off rapidly above pH 6.5; at higher pH, calcium ion (half-max. conc. 2×10^{-3} M) will completely restore uptake. Two-fold stimulation of B_{12} uptake at pH 4.5 (but not at pH 6.5) by acetate concentrations exceeding 15 mM was noted. Tracer uptake in the steady state gave a single exponential function; steady state tracer wash-out observations were best fitted to the sum of two exponential functions, suggesting intracellular compartmentation. Direct sub-cellular localization of Co-60-labeled B_{12} on sonicated cells by ultracentrifugation showed 55% in the 30,000 g pellet and 24% in the 195,000 pellet; only 12% was found in the 195,000 g supernatant. These data suggest that B_{12} enters the cytoplasm by carrier mechanism or pinocytosis against little or no concentration gradient and that binding or concentration by intracellular organelles accounts for large observed uptakes.
(Supported in part by NSF grant G19562)

INFLUENCE OF GOITROGENS ON I^{131} TURNOVER IN THYROIDS OF THYROXINE-TREATED RATS. E.P.Reineke. Physiology Dept., Michigan State Univ., East Lansing.

Male rats housed at 78°F were fed low iodine diet, alone or with added I^-. Thyroidal I^{131} turnover was determined by in vivo counting. In groups receiving 1.5, 3.75 and 6.75 γ I^- daily per rat, I^{131} output rate (K_4) decreased progressively with increasing I^- intake. At all I^- levels 10 γ of T_4 injected daily in both control and NaSCN-treated rats reduced output to about 1.0% daily, comparing closely to that in hypophysectomized rats. In rats given thiouracil or methimazole before and during T_4 treatment output persisted at 5-10% daily in different experiments. Treatment with T_4 prior to and during thiouracil administration blocked I^{131} output for 3-4 days and then output was resumed at the same level as when thiouracil was given prior to T_4. Hypophysectomized rats were given 2 injections of AP extract to stimulate thyroidal uptake of I^{131} and daily thyroid counts were taken. Twice-daily injections of 5 mg thiouracil after the 4th count had no effect on output rate. Thyroidal iodine partition and measurements of urinary and fecal radioactivity did not provide conclusive information on the nature of the iodine released during thiouracil administration. However, the overall results are compatible with the view that goitrogens block the re-entry of I^- released by thyroidal iodase into the organic cycle of the thyroid and it leaks into the systemic circulation.

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MECHANISM OF LIVER ARTERIAL VASCULAR RESPONSE TO ENDOTOXIN. Dale A. Reins* and L. B. Hinshaw. Dept. of Physiology, Univ. of Okla. Med. Ctr. and Dept. of Surgery, V.A. Hosp., Oklahoma City, Okla.

Endotoxin shock in dogs is characterized by congestion and pooling of blood in the liver. The intimate mechanism of this phenomenon has not been elucidated, although portal venous pressure elevation has been repeatedly observed. The present experiments were designed to study the arterial and venous vascular responses of the denervated liver to endotoxin, and to determine the underlying mechanisms of the responses. Isolated denervated dog livers were perfused through the portal and hepatic artery with blood from the inferior vena cava and abdominal aorta, respectively, of a donor dog. Pressures were maintained in the physiological range and the liver was isogravimetric during control periods. Two different types of experiments were performed: (a) a lethal injection of endotoxin, calculated from the body weight of the liver donor dog, was injected into the liver inflow; (b) the hepatic venous outflow was partially occluded by mechanical compression. Results showed that hepatic arterial resistance increased significantly in each instance, and similar weight gains occurred. Changes in portal vein pressure were passive in both types of experiments. In additional experiments it was not possible to duplicate the liver vascular response to endotoxin by injection of vasoactive drugs, and the responses were not abolished by injection of phentolamine. Results suggest a myogenic response of the arterial branches of the liver vascular bed as a consequence of both endotoxin injection and mechanical elevation of hepatic venous pressure. (research partially supported by USPHS grant 06313)

CARDIOVASCULAR RESPONSES TO HISTAMINE AND COMPOUND 48/80 IN LOWER VERTEBRATES. Ola Bodvar Reite* (intr. by L. D. Carlson). Department of Physiology and Biophysics, University of Kentucky Medical Center, Lexington, Kentucky.

Previous work in this laboratory indicates that neither histamine nor compound 48/80 have any effect on the blood pressure of cyclostomes, elasmobranches and teleosts. Either substance is able to induce blood pressure changes in birds and mammals. The present investigation was initiated in an attempt to locate the stage in vertebrate phylogenesis where the vascular system became sensitive to histamine. Cardiovascular responses to histamine and compound 48/80 were studied in amphibians and reptiles. Bullfrogs (Rana catesbeiana) and pond terrapins (Pseudemys scripta) were the principal species investigated. The experiments were performed under urethane anesthesia. Animal body temperatures ranged from 10 to 20°C. Arterial blood pressure was recorded continuously during intravascular injections of histamine and compound 48/80.

In the bullfrog histamine had no effect on blood pressure, whereas compound 48/80 produced an increase in blood pressure without affecting the heart. The blood pressure increase caused by compound 48/80 was maximal at the first injection of this substance and gradually disappeared following subsequent injections. In the pond terrapin histamine produced an increase in the force of the heart contractions and also gave rise to peripheral vasoconstriction. Compound 48/80 had no influence on the vascular system of the pond terrapin when given before histamine. However, occasionally an injection of compound 48/80 following administration of histamine would mimic the peripheral vasconstrictor response elicited by histamine itself. (Supported by an International Postdoctoral Res. Fellowship from U.S. P.H.S.).

KIDNEY HEAT PRODUCTION. D. W. Rennie. Dept. of Physiology, State University of New York at Buffalo. Buffalo, N. Y.

A method is described that holds promise for studies of local metabolic rate within intact kidneys. Heat production within dog kidneys was estimated from the initial transient rise of tissue temperature during 5-second arrest of the kidney circulation (see Stow and Schieve, J. Appl. Physiol. 14: 215, 1959, for theory). A thermistor-tipped needle was inserted measured distances into the kidney along a tract perpendicular to the frontal plane, penetrating first the anterior cortex, then the medulla, and finally the posterior cortex. Brief occlusion of renal blood flow caused an increase in thermistor temperature at an initial rate that was highly reproducible with the thermistor in any one location (S.D. between 24 paired occlusions = 0.015 C/min). In 7 normal kidneys this initial rate of rise averaged 0.35 C/min, S.E. 0.04 in posterior cortex; 0.13 ± .02 C/min in outer medulla, and 0.06 ± .02 C/min in inner medulla. Assuming tissue thermal capacity to be 90 cal/C/100 g throughout the kidney, tissue heat production was 31 cal/min/100 g cortex, 12 cal/min/100 g outer medulla, and 5 cal/min/100 g inner medulla. The effects on heat production of altering net sodium reabsorption were tested by mechanically reducing glomerular filtration rate and by infusion of ethacrynic acid. As would be predicted, a highly significant direct proportionality existed between cortex heat production and net sodium reabsorption when the latter was reduced by elevation of ureteral pressure. Heat production of the outer medulla was reduced to zero by ethacrynic acid.

(Supported by a grant from the Life Insurance Medical Research Fund.)

TECHNIQUE FOR MYOTHERMIC MEASUREMENTS. N.V. Ricchiuti* and W.F.H.M. Mommaerts. Cardiovascular Research Laboratory, Univ. of Calif., Los Angeles.

Details for the construction of thermopiles suitable for use with a commercially available amplifier will be described.

Briefly, a continuous constantan wire is wound around a pair of threaded, anodized mandrels. Appropriate sections of the helix thus formed are masked then electrolytically etched and silver plated. The central region between the mandrels is pressed to about 12 μ thickness, the threads of the supporting mandrels assuring equal spacing. The assembly is then insulated with Teflon or Saran film.

With this technique thermopiles with an output of 650 μv per degree C. per mm pile length have been constructed. Typically the signal to noise ratio for the heat production in a twitch is greater than 50 to 1 over a 100 cycle bandwith. Their heat-loss is exponential, about 2.5 percent per second for a muscle pair of 200 mg, which during the course of a measurement is corrected for by an integrating circuit.

Special designs of the thermopile can be made for specific purposes, such as the measurement of heat production in nerve or in papillary muscle.

HEMODYNAMIC ALTERATIONS PRODUCED BY THE CUSHING REFLEX. Travis Q. Richardson. Dept. of Physiology, Univ. Miss. Med. Center, Jackson, Miss.

When cerebrospinal fluid pressure is elevated above the mean arterial pressure, there is an increase in the latter. This effect is now known as the Cushing reflex or the central nervous system ischemic response. Since previous studies from this laboratory have shown that this response produced changes in hemodynamics, these studies were performed to determine what happens to cardiac output, pulmonary arterial pressure, right atrial pressure, and left atrial pressure when cerebrospinal pressure is elevated in dogs anesthetized with chloralose. Thirteen mongrel dogs were used in this study. Catheters were placed into the right atrium, pulmonary artery, left atrium, and aorta for measuring the respective pressures. Pressures were recorded by connecting the catheters to Statham pressure transducers which were connected to a Grass polygraph recorder. In addition to measuring the above listed pressures, cardiac output was monitored with a continuous cardiac output recorder employing the Fick principle. Cerebrospinal fluid pressure was increased to 150 mm Hg, 175 mm Hg, and 200 mm Hg, respectively, and was maintained at a given level for ten minutes. This procedure was followed to allow the circulatory system to reach equilibrium following each increase in cerebrospinal fluid pressure. It was found that elevation of cerebrospinal fluid pressure to 200 mm Hg for ten minutes produced the following: (1) mean arterial pressure increased 55 mm Hg, (2) cardiac output increased 35 ml/kg, (3) mean pulmonary arterial pressure increased 11 mm Hg, (4) right atrial pressure decreased .57 mm Hg, and (5) left atrial pressure decreased .5 mm Hg.

(This study supported by N. I. H. Grants HE-07137 and HE-09512-01.)

PARASYMPATHETIC CONTROL OF GASTRIC BIOELECTRIC POTENTIAL IN RATS. H. Allan Ridley*, Burton E. Vaughan and Joseph T. Cummins* U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.

The gastric bioelectric potential of the rat as measured in vitro was consistently lower in stunned rats than in rats anesthetized with ether or completely decapitated. The depressed potential resulting from stunning was eliminated by vagotomy, by subcutaneous injection of atropine and by instillation of atropine directly into the stomach. The potential across stomach maintained in vitro was sharply reduced by almost 50% when the solution bathing the mucosal surface was made 10^{-2} M in acetylcholine (ACh). The effect of ACh on potential showed concentration dependence over the range from 10^{-5} M to 10^{-2} M. Rinsing the chamber and replacing the solution with fresh Ringer allowed partial recovery of the potential. The fall in potential resulting from ACh_4 addition was irreversibly blocked by the presence of atropine at 10^{-4} M. Tubocurarine up to 10^{-3} M did not change the response of the potential to ACh. Physostigmine at 10^{-4} and 10^{-3} M enhanced the effect of ACh on the potential. The ACh analogues, acetyl-β-methylcholine, acetylthiocholine and carbamylcholine at 10^{-3} M caused a comperable reduction in potential to ACh at 10^{-3} M. Carbamylcholine, which is not appreciably hydrolized by acetylcholinesterase, showed a slightly greater effect on potential than ACh. The results are discussed from the aspect of cholinergic control of bioelectric potential mediated through the vagus innervation. The potential difference across isolated rat stomach has been shown to be independent of HCl secretion (Nature 205: 1329, 1965) and generated by Na^+ transport mechanism (Biochim. Biophys. Acta 94: 280, 1965).

RENAL TUBULAR INFLUENCE OF EPINEPHRINE IN DOGS. C. A. Robb and M. L. Zatzman (intr. by D. K. Meyer). University of Missouri Medical Center, Columbia, Missouri

The effect of a constant infusion of epinephrine, at the rate of 1.2 to 1.5 micrograms/kilogram/minute, on renal function in anesthetized dogs was studied in a two-fold manner: (1) A study was performed to determine how the excretion of different substances varied with time. The time course of action of epinephrine on glomerular filtration rate, effective renal plasma flow and rate of urine flow was also determined. (2) A stop-flow study was performed to determine if the changes noted in the time study were the result of a direct influence of epinephrine on tubular transport systems or merely a reflection of changes in renal hemodynamics. Decreased excretion rates of sodium and chloride were found to correlate well with changes in urine flow and/or effective renal plasma flow. Potassium excretion, on the other hand, correlated well with changes in filtered load. The ratio of glucose tubular maximum to glomerular filtration rate (Tm_G/GRF) increased with time as compared to the controls. Urine flow and glomerular filtration rate demonstrated a short transient decrease during the epinephrine infusion. Effective renal plasma flow, however, remained reduced throughout the period of epinephrine administration. No evidence was obtained in the stop-flow series to suggest that any of the changes noted were due to a direct tubular action of epinephrine. Thus, it was concluded that, with the possible exception of glucose, epinephrine's influence on urine composition is mediated through changes in intra- and extrarenal blood flow. (Supported by NIH grant AM-06316.)

A RAT HEAD PERFUSION TECHNIQUE DEVELOPED FOR THE STUDY OF BRAIN UPTAKE OF MATERIALS. Robert C. Robertson*, Thomas A. Bauer* and Alan M. Thompson. Dept. of Physiology, Univ. of Kansas Med. Ctr., Kansas City, Kansas.

The advantages of the organ perfusion technique for certain types of transport studies have been demonstrated (Thompson et al. Am. J. Physiol. 197: 897, 1959). Particularly the ability to maintain constant or to rapidly vary the inflow concentration of materials is useful. For this purpose a rat head perfusion technique (in situ) has been developed which involves perfusion through the aortic arch of the rat and collection of the fluid returning via the two superior vena cavae at the inferior vena cava. Flow through the heart and forelimbs and azygous return is prevented. The 15% hematocrit perfusion fluid is recirculated through a typical pump-oxygenator system. The technique is such that no period of ischemia or hypoxia is necessary. Light barbiturate anesthesia is maintained. Using criteria of viability such as normal respiratory efforts, pupillary response to light, degree of pupillary constriction, and corneal blink response, it is judged that the brains remain functional for as long as three hours. EEG's and brain histology are essentially normal. T-1824 distribution volume in the brain varied randomly from 0.01 to 0.06 ml fluid/g brain in perfusions of 33 to 78 minutes, suggesting that the blood-brain barrier is not greatly altered from normal. CO_2 uptake curves by the perfused brain are essentially those found in normal intact rats. Preliminary studies in a similar system, but with double circuits to permit rapid switching of the brain from a CO_2 tension of 40 mm Hg to 200 mm and back to 40, suggest a CO_2 "washout" effect, the final tissue CO_2 being lower than that initially. (Supported by PHS grant GM-10429).

THIAMINE IN AGING HOUSE FLIES. M. Rockstein and W. B. Hawkins.* Department of Physiology, University of Miami, School of Medicine, Coral Gables, Florida.

This study was undertaken to determine the age-dependent changes in thiamine by Haugen's (1961) method, whereby thiamine is oxidized to thiochrome and the fluorescence properties of the latter measured. The abdomens showed the greatest and the thoraces the least concentration of thiamine and phosphothiamine. Thiamine content per gram of wet weight of thorax showed a pronounced increase (by 100%) in males, from one hour to a maximum level at 4 days of age, with a rapid decline from the 4th to 8th day and then a more gradual steady fall to old age. In females, a similar doubling of thoracic thiamine occurs from the 1st to 8th days, with a very slow, gradual decline thereafter. These changes in thiamine content parallel closely (chemical) changes in Mg-activated adenosine triphosphate (ATP-ase) and alpha-glycerophosphate dehydrogenase activity, in relation to senescence (loss of) flight ability of the male house fly with advancing age. These data confirm a genetically determined complex pattern of biochemical events responsible for and attendant upon the total process of aging of the motor function of flight.

(Supported by USPHS Grant No. HD 00571 from the National Institute of Child Health and Human Development)

VASCULAR CONDUCTANCE AND INDUCED "HYPEREMIAS" IN THE ISOLATED FIBRILLATING HEART PERFUSED WITH CHENOWETH SOLUTION. Simon Rodbard and Lajos Takacs.* City of Hope Medical Center, Duarte, California.

In the isolated, fibrillating dog heart, cannulas were connected into the (1) left circumflex coronary artery, (2) aorta, (3) right atrio-ventricular cavity, (4) left atrio-ventricular cavity, and (5) extracardial space (bottle filled with Ringer-Locke). Pressures in all cannulas were controlled. Left circumflex coronary artery flow was measured by rotameter. ¶ Coronary conductance varied with arterial pressure, approaching maximal values between 100 and 180 cm. water. The preparation showed limited autoregulation. Conductance decreased progressively with time. Conductance fell as extracardial pressure was raised. Elevation of venous pressure did not affect coronary flow until venous pressure exceeded extracardial pressure; conductance then increased to a maximum. Critical closing pressure increased with time, or with elevations in extracardial pressure; it decreased with elevation in venous pressure. ¶ Magnitude and half-time of reactive hyperemia increased with the duration of arterial occlusion. Peak hyperemia varied with arterial pressure. Hyperemia decayed logarithmically. Peak conductance of the hyperemia was approximately constant at perfusion pressure between 70 and 180 cm. Extracardial compression of the heart or combinations of arterial occlusion and compression were followed by greater hyperemia peaks and half-times than after arterial occlusion alone. ¶ The foregoing data can be interpreted as indicating that many aspects of coronary conductance may be accounted for on the basis of transmural pressure, presumably at the level of the capillary. (Aided by U.S.P.H.S. Grant #HE 08721.)

TISSUE BLOOD FLOW CHANGES IN THE HAMSTER MELANOMA DURING GROWTH. W. Rogers, R. F. Edlich, and J. B. Aust (intr. by Nathan Lifson). Univ. of Minn. Med. School, Minneapolis, Minn.

The blood supply of transplanted tumors has been the subject of many investigations, but quantitation of tumor tissue blood flow has rarely been performed. Previous estimates of blood flow of experimental tumors have been lower than surrounding tissue. Using a modification of Johnson, J. A., et al (Am. J. Physiol. 200:551, 1961) with Iodine I^{131} tagged Antipyrine, tissue blood flow was estimated in a hamster amelanotic melanoma implanted in the thigh. Blood flow determinations demonstrated that tumor blood flow changes with respect to age and size of tumor. During the first 15-18 days after implantation, the mean tumor flow (.682 ± .157 cc/min/gm) is 6-8 times greater than adjacent skin and muscle flow. After 36 to 44 days of growth, a 68% reduction in tumor blood flow (.220 ± .055 cc/min/gm) was noted. Microscopic sections of tumor tissue at different stages of growth demonstrated a correlation of tumor necrosis with diminished blood flow.

NOREPINEPHRINE VASODILATATION IN SKELETAL MUSCLE OF THE CAT. Gordon Ross* and Fred N. White. U.C.L.A., Los Angeles, California.

Non-cannulating electromagnetic flow probes bilaterally placed on the femoral arteries were used to compare the blood flow and vascular resistance changes produced by norepinephrine in the normal and denervated hind limbs of cats. Following the intravenous injection of norepinephrine, vasoconstriction occurred in the denervated skinned limb and vasodilatation in the contralateral innervated limb. This vasodilatation was still obtained after simultaneous bilateral carotid occlusion, vagotomy and occlusion of the celiac and mesenteric arteries. It persisted after atropinisation and histamine blockade with tripelennamine but was abolished by beta adrenergic blockade with propranolol. It is concluded that norepinephrine dilatation in the skeletal muscle of the hind limb is dependent on a neural mechanism and on beta adrenergic receptor stimulation.

FORCE-VELOCITY RELATIONS IN ACUTE HEART FAILURE. J. Ross, Jr., J. W. Covell,* E. H. Sonnenblick, and E. Braunwald, Cardiology Branch, Natl. Heart Inst., Bethesda, Md.

Recently, the effects of isolated variations in afterload on the dynamics of left ventricular contraction in the dog were analyzed; the findings indicated that alterations in myocardial contractile state result in changes both in the maximum velocity (V_{max}) of contractile element shortening (V_{CE}) and maximum wall tension relative to muscle length (P_o), while variations in end-diastolic fiber length produce changes in P_o alone. A simplified preparation has permitted extension of these studies to the analysis of single, isovolumic ventricular beats. In 6 dogs, heart rate and ventricular end-diastolic pressure were held constant, left ventricular dp/dt was recorded, and diastolic ventricular volume was determined directly. V_{CE} and wall tension (WT) were calculated at 10 msec intervals during isovolumic beats induced by sudden balloon occlusion of the ascending aorta; measurement of ventricular ejection rate was therefore not required. The inverse relation between V_{CE} and WT was curvilinear. During norepinephrine infusion, these curves were shifted upward and provided a sensitive indication of increases in the speed and the force of ventricular contraction; this method for determination of the velocity-tension relation during isovolumic beats thus appeared to offer an approach to assessment of contractile state in the intact heart. When acute heart failure was induced by barbiturate infusion, the curves relating V_{CE} to WT were consistently shifted downward, and reductions both in V_{max} and P_o were observed. In view of these findings, it is proposed that barbiturate-induced heart failure is associated with a reduction in the rate of those processes which determine the intrinsic velocity of contractile element shortening.

ACTIVE VASCULAR CAPACITY RESPONSES TO STEP CHANGES IN ARTERIAL PRESSURE.
A.A. Rovick. Department of Physiology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Illinois.

Tissue weight changes that occur subsequent to modification of the amplitude of pulse pressure differ sufficiently from resistance alterations to suggest that active venoconstriction occurs (Rovick and Robertson, *Circulation Res.* 15: 208, 1964). Capacitance responses to step changes in arterial pressure in other vascular beds have been interpreted as passive (Folkow and Öberg, *Acta Physiol. Scand.* 53: 105, 1961 and Johnson, *Am. J. Physiol.* 199: 311, 1960) or as the result of a local reflex (Hanson and Johnson, *J. Appl. Physiol.* 17: 509, 1962). Capacity responses to step-function changes in arterial pressure were, therefore, studied to compare the reactions in the isolated, pump-perfused dog tongue with other vascular beds. Pressure changes produced alterations in blood flow and preparation weight. The latter were determined to primarily reflect changes in venous volume. If the preparation was passive, initial flow and weight changes were maintained as long as the pressure shifts were sustained. If the preparation was active, the initial change was succeeded by secondary reactions that returned flow and/or weight toward or to their former levels. Secondary capacitance responses may be demonstrated to be active since: 1) they occurred when resistance vessels reacted passively; and 2) they were reduced or absent in some cases when resistance vessels exhibited marked reactivity. In both instances, a lack of correlation existed between the pressure-induced alterations in venous transmural pressure and the changes in capacity. (Supported by Public Health Service Grants HE 07246 and HE 08682.)

VENOUS PLASMA $[K^+]$ DURING REACTIVE HYPEREMIA IN SKELETAL MUSCLE.
M. Rudko* and F. Haddy, Univ. of Okla. Med. Ctr., Okla. City, Okla.

Since a slight increase in blood $[K^+]$ produces vasodilation, and the venous $[K^+]$ rises during skeletal muscle activation, it has been suggested that active hyperemia results at least in part from a rise in the tissue fluid $[K^+]$. In this study we have examined the venous $[K^+]$ during reactive hyperemia. The dog hindlimb was prepared so that all blood entered the limb via the femoral artery and left via the femoral vein. The latter vessel was cannulated and the blood led to the contralateral femoral vein. A T-tube in this circuit permitted periodic measurement of venous outflow with a graduate and stopwatch. Venous blood was sampled for the measurement of plasma $[K^+]$ during a control period, during faradic stimulation (6/sec, 3v, .2ms) of the femoral and sciatic nerves (Active Hyperemia), during faradic nerve stimulation plus partial occlusion of the femoral artery (Stim.+Occl.), at 0.5 to 1.0 sec. intervals for 10 to 20 sec. immediately following release of a 4 min. total occlusion of the femoral artery (Reactive Hyperemia) and following a 10 min. period of rest. Venous blood was also sampled for measurement of pH. In 3 experiments femoral artery blood was sampled for measurement of $[K^+]$.

	n	Control	Active Hyperemia	Stim.+ Occl.	Reactive Hyperemia	Control
Flow(ml/min)	9	173	473*	161	404*	180
pH	7	7.38	7.31*	7.26*	7.28*	7.36
K^+(mEq/l)	9	3.46	4.24*	4.69*	3.45	3.42

* = signif. diff. from control ($P = <0.01$)

The $[K^+]$ did not rise above the control value in any of the 20 tubes collected during reactive hyperemia. Arterial plasma $[K^+]$ was essentially the same as venous plasma $[K^+]$ during the control periods and did not change during any maneuver. This study shows that the venous plasma $[K^+]$ does not rise during reactive hyperemia in skeletal muscle.

THE EFFECT OF DIISOPROPYL FLUOROPHOSPHATE ON GASTRIC SECRETION AND ATPase. G. Sachs* and B. I. Hirschowitz. Department of Medicine, Division of Gastroenterology, University of Alabama Medical Center, Birmingham, Alabama.

Diisopropyl fluorophosphate (DFP) has been shown to be a potent inhibitor of gastric secretion in the in vitro frog mucosa. There is at 2 x 10^{-2} M concentration, inhibition of PD, acid secretion and short circuit current. The resistance shows an initial rise followed by a subsequent fall. At lower doses of DFP there is a slight rise in the PD with a slight depression of acid secretion. In sulfate solutions the PD and acid rate fall clearly to 0 as they do in chloride solutions, and a plot of PD versus H^+ rate is a straight line intersecting the PD axis at 0. This inhibition is obtained whether DFP is added to the nutrient or secretory side of the membrane with very similar characteristics. DFP also irreversibly inhibits the microsomal ATPase prepared from the frog gastric mucosa at a concentration of 10^{-2} M. After 30 minutes pre-incubation the inhibition is apparently somewhat reversible, but after 60 minutes pre-incubation the effect is irreversible. When the ATPase is prepared from DFP inhibited gastric mucosae, it shows 50% inhibition when compared to control mucosae. Attempts to overcome the irreversible inhibition by DFP of the intact mucosae with various nucleophilic reagents were unsuccessful.

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RESPONSE OF CAPACITY VESSELS IN HUMAN LIMBS TO HEAD-UP TILTING AND APPLICATION OF SUCTION TO LOWER BODY, Shlomo L. Samueloff,* Norman L. Browse* and John T. Shepherd, Mayo Clinic and Mayo Foundation, Rochester Minnesota.

Ten normal men were studied to examine the response of the capacity vessels in the limbs to tilting 70° head-up and to transferring blood to the legs when horizontal by application of subatmospheric pressure (60 mm Hg) to the body below the iliac crests (Brown, Goei, Greenfield and Plassaris, J. Physiol., 170:21P, 1964). The occluded-limb technique was used for continuous monitoring of reflexly mediated changes in venous tone. Both procedures caused a transient increase in venous pressure in hand, foot, and forearm whose circulation was arrested, in contrast to a sustained decrease in forearm blood flow. On return to the horizontal or release of suction, another transient rise in venous pressure often occurred associated with an increase in forearm blood flow. The transient venous responses, unlike the response of the resistance vessels in the forearm, could not be related to the redistribution of blood caused by these procedures. It seems that reflex changes in tone of the capacity vessels in the limbs are not an essential part of the compensatory vascular responses for maintenance of systemic arterial blood pressure in the upright position, although the transient increase in wall tension in the capacity vessels may aid the resistance vessels in reducing the rate of pooling of blood in dependent parts. (Supported in part by NIH Grant HE-05883.)

A STUDY OF THE RELATIONSHIP BETWEEN VITAMIN E AND CERTAIN SULFHYDRYL ENZYMES. N. Sandler* and J. W. C. Bird. Dept. of Physiology and Biochemistry, Rutgers-the State University, New Brunswick, N. J.

Guinea Pig heart, masseter, and gastrocnemius muscles were separated into myofibrillar and supernatant fractions and their ATPase activities were assayed. The effects of normal (N), vitamin E deficient (E^-), and vitamin E supplemented (E^+) diets on these sulfhydryl (SH) dependent enzyme systems were compared. After 21 days of dietary regimen, $p \leq 0.05$ for the following comparisons: Both E^+ and E^- masseter fibrillar ATPases were larger than N. This was also observed in the gastrocnemius where in addition E^+ ATPase activity was higher than E^-. In the supernatant fraction, E^+ heart ATPase was greater than E^-; E^+ masseter activity was greater than N; E^+ gastrocnemius was greater than E^-. The relaxing activity of the supernatant was higher in the E^+ and E^- masseter preparations than in the N. A comparison of the content of free SH groups among heart, masseter, and gastrocnemius fibrillar and supernatant fractions of E^+ and E^- animals showed no significant difference. However, addition to the assay systems of the SH inhibitor N-ethyl maleimide (NEM) caused a greater decrease in free SH groups in E^- heart supernatant than in E^+. These findings indicate that Vitamin E does not protect cellular SH groups in general. But an early symptom of E deficiency is decreased activity of several SH enzymes and an increased susceptibility of certain SH groups to NEM.

CAFFEINE EFFECTS INDICATING RETICULAR REGULATION OF Ca^{2+} IN CONTRACTION OF NORMAL AND DENERVATED MUSCLE. Alexander Sandow, Allen Isaacson and Hanna Preiser*. Institute for Muscle Disease, New York.

Denervation causes caffeine-insensitive normal rat muscle (extensor digitorum longus) to develop contracture on exposure to 20 mM caffeine (Gutmann and Sandow, Life Sciences, 4:1149, 1965). Correspondingly, we find that the mobility of Ca^{2+} induced by caffeine is greater in the 6-day denervated muscle than in the normal: (a) the increase in efflux of Ca^{45} caused by applying 20 mM caffeine to muscles during their slow phase of Ca-loss, is more rapidly and markedly produced in the denervated muscle, and (b) the 10' uptake of Ca^{45} under caffeine-treatment is greater in the denervated muscle (0.0924 ± 0.0123 μmoles/gm wet muscle weight) than in the normal (0.0477 ± 0.0012 μmoles/gm). These differences are not due to variation in permeability to caffeine since the caffeine space and the efflux kinetics of C^{14}-caffeine are the same for normal and denervated muscles. Since, furthermore, these muscle parameters for the rat have about the same values as for the frog (Bianchi, J. Pharmacol. 138:41, 1962), the caffeine-contracture-insensitivity of normal rat muscle is not due to impermeability to caffeine. Twitches of frog sartorii in 5 mM caffeine show abnormally long relaxation periods. Recalling that Ca^{2+} evidently activates contraction, and that caffeine affects isolated reticulum by inhibiting uptake, and causing release, of Ca (Herz and Weber, Fed. Proc. 24:208, 1965), we infer that the above mechanical effects reflect variations in concentration of free activator Ca^{2+} caused by caffeine-induced changes in sarcoplasmic reticular activity. (Aided by grants from the U.S.P.H.S. (NB-04262-03) and the Muscular Dystrophy Associations of America.)

EFFECT OF ANESTHESIA ON THE DISTRIBUTION OF CEREBRAL BLOOD FLOW IN THE RAT. Leo A. Sapirstein. Department of Radiology, Stanford University.

The present studies were undertaken in an attempt to determine whether the distribution of cerebral blood flow was altered by general anesthesia. Rats with catheters implanted in the femoral vein received Carbon-14 labelled antipyrine in a single injection and were killed 30 seconds after the administration of the label. The brains were sectioned after freezing and radioautographs were prepared. The distribution of blood flow in the unanesthetized rat was compared with that observed in animals receiving pentobarbital sodium ii anesthetic doses (40 mg/kg I.P.) 15 minutes before the measurement. No differences could be observed in the patterns of blood flow distribution between conscious and anesthetized animals. The results fail to support the idea that alterations in consciousness are associated with alterations in cerebral perfusion patterns. (Supported by a Grant-in-Aid from the United States Public Health Service HE-09210-01).

THE USE OF TECHNETIUM-99m IN STUDYING THYROID PHYSIOLOGY-DOUBLE LABEL EXPERIMENTS-^{99m}Tc - ^{125}I - W.J. Schindler, T.S. McHorse* and D.M. Krause*, Baylor University, College of Medicine, Houston, Texas.

In T/S ratio determinations, organic binding of iodide must be blocked by a thiocarbamide goitrogen eg. Tapazole (TAP) prior to radioiodide injections. Pertechnetate (TcO_4^-) and perrhenate (ReO_4^-) are concentrated by the thyroid, probably by a transport mechanism similar to that of I^-, but are not metabolized there (J. Wolff, Physiol.Rev. 44: 45,1964). T/S ratios using $^{99m}TcO_4^-$ were compared with the conventional T/S [I^-] in groups of mice maintained for the previous 3 days at 5°, 24°, or 30° C to simulate hyper, eu, or hypothyroidism.

Group	Substances used to determine T/S	T/S Ratios (mean of 6 mice ± S.E.) 5° C	24° C	30° C
1	$^{99m}TcO_4^-$	120.8 ± 12.6	85.6 ± 9.5	71.1 ± 14.5
2	$^{99m}TcO_4^-$ + $^{125}I^-$	127.9 ± 20.2	87.5 ± 18.0	58.1 ± 10.2
3	TAP + $^{99m}TcO_4^-$	145.8 ± 19.0	70.4 ± 5.0	78.2 ± 11.8
4	TAP + $^{125}I^-$	167.9 ± 36.9	102.8 ± 15.3	67.6 ± 18.0
2	1 hr. Uptake %	3.5 ± 0.7	2.8 ± 0.6	2.2 ± 0.5

The above results demonstrate that TcO_4^- can be used without a goitrogen to determine T/S ratios comparable to those obtained with I^- plus a goitrogen. In both cases the values were inversely related to environmental temperature. Group 2 mice were injected with both radioisotopes 1 hr. before killing and thyroidal and serum ^{125}I and ^{99m}Tc radioactivity were determined by γ-ray spectrometry in a well-type scintillation counter. Thus in this 1 hr. double label experiment, an estimate of both the "thyroidal iodide pump" (T/S $^{99m}TcO_4^-$) and thyroidal iodide uptake and binding (^{125}I) were obtained simultaneously in the same animal. (Supported by USPH Grant AM 8104).

THE EFFECT OF HYDROCORTISONE AND FLUOROHYDROCORTISONE ON FOREARM VASCULAR RESPONSES TO NOREPINEPHRINE. P.G. Schmid*, J.W. Eckstein and F.M. Abboud. Univ. of Iowa College of Med., Iowa City, Iowa.

Vascular responses to constrictor stimuli may be altered in the presence of corticosteroids. The present experiments were designed to study the effect of acutely administered hydrocortisone and chronically administered fluorohydrocortisone on vascular responses to graded doses of norepinephrine. Forearm blood flow (plethysmograph), blood pressure (cuff or intra-arterial catheter) and pulse rate responses to 4-minute intravenous infusions of norepinephrine bitartrate (NE) in doses of 0.075, 0.15 and 0.30 μg of base/kg/min were observed before and 30 minutes after intravenous hydrocortisone, 200 mg, in 6 subjects. Responses to NE were also observed in 8 other subjects before (Session A); after oral fluorohydrocortisone, 1.0 mg initially and 0.2 mg daily for 7 days, (Session B); and 3 weeks after stopping the drug (Session C). Vascular responses to NE before and after intravenous hydrocortisone were similar. After oral fluorohydrocortisone (Session B) blood flow averaged 3.2, 2.8 and 2.5 ml/min/100 ml of forearm respectively, at low, middle and high doses of NE. Corresponding averages were 3.3, 3.2, 3.4 and 3.4, 3.6, 3.6 respectively, in control Sessions A and C. Decreases in blood flow and increases in forearm vascular resistance with NE were greater in Session B after fluorohydrocortisone ($p<0.01$). Pressor and pulse rate responses to NE were similar in the 3 sessions. These results suggest that acute intravenous administration of hydrocortisone does not alter vascular responsiveness to NE. Chronically administered fluorohydrocortisone, however, increases responsiveness of vascular smooth muscle to NE. (Supported by NIH grant HE-02644 and a grant from the American Heart Association.)

PULMONARY MICROCIRCULATORY SPHINCTERS IN MAMMALS. Charles L. Schneider, Ruby M. Engstrom,* and Nydia L. Meyers,* Wayne County General Hospital, Eloise, Michigan 48132, and The University of Michigan, Ann Arbor.

Until now, intravital microcirculatory studies have been interpreted to deny the existence of vasomotor control of the pulmonary blood flow. However, physiologic considerations require such control. Knisely et al did not observe contractions of long segments of arterioles of 50-150 μ diameter; neither they nor earlier workers reported arteriolar sphincters. Experimental, supralethal "fibrination" produces a fibrin cast of the pulmonary arterial tree; segmental constrictions occur at the sites of histologically identified, arterial circular-muscle "choke" valves. Although these demonstrate the existence of arterial sphincters, it is not permissible to interpret physiologic processes from postmortum or agonal changes in fixed tissues. The pulmonary arteries are hidden deep in the lung, but certain branching arterioles rise into view and bifurcate repeatedly, just beneath the visceral pleura, toward the lobar margins. The circulation within these pulmonary and precapillary arterioles was monitored cinemicrographically. Arteriolar segments, distal to experimental micro-embolic occlusions, did empty and collapse passively, as already noted by Knisely et al. In our experiments, arteriolar "throttle" sphincters sometimes actively closed off blood flow, partially or totally, into arteriolar branches. In instances when such a sphincter was all but closed, there resulted a nozzle-like, spouting fountain of erythrocytes through it. Such sphincters were observed to function at the level 1. of bifurcation of pulmonary arterioles, and 2. of branches from precapillary, endarterioles. Supported in part by NIH research grants H-4022 and HE-09397-1.

CHANGES IN ATP LEVEL OF MAMMALIAN SKELETAL MUSCLE DURING CONTRACTION. B. A. Schottelius and D. D. Schottelius, Department of Physiology, Univ. of Iowa, Iowa City, Iowa.

Concentrations of ATP, ADP, AMP, phosphocreatine (PC), free creatine and, in some instances, inorganic phosphate were determined in resting and stimulated anterior tibial muscles of the mouse and soleus muscles of the rat. Paired excised muscles were mounted on a multiple electrode assembly, tested for equivalence in mechanical ability and incubated 15 min. in oxygenated bicarbonate ringer, pH 7.4, at 20 C followed by an additional 15 min. of anaerobic incubation. Anterior tibial muscles were stimulated with 1-10 pulses, soleus muscles with one pulse. Both resting and stimulated muscles were frozen simultaneously by rapid immersion into isopentane at -160 C at selected intervals after the initiation of contraction. No statistically significant breakdown of ATP or PC was observed in isotonically contracting anterior tibial muscles. Even when these muscles were incubated with FDNB (1-fluoro-2, 4-dinitrobenzene) there was only an overall reduction of ATP and PC concentration in both resting and stimulated muscles. In single isotonic twitches of rat soleus muscles, statistically significant decreases in ATP concentration occurred under light (ΔATP 0.20 μM/g), medium (ΔATP 0.26 μM/g) and heavy (ΔATP 0.19 μM/g) loads without detectable change in PC. (Supported by grants from MDAA, Inc. and USPHS grant GM-10205.)

RESPONSE OF DENTINAL RECEPTOR TO THERMAL STIMULATION. Donald Scott, Jr., G.G.Stewart and D. Weber. Univ. of Pennsylvania Medical School, Philadelphia, Pennsylvania.

Single dentinal receptors are located in a dentinal tubule of the cat. Characteristic frequency patterns of impulse firing are seen following either hot or cold stimulation. Correlated changes of membrane potential have been observed which suggest separate loci of excitation on the same receptor for response to hot and cold. Stimulation with heat results in potential changes resembling those observed after depolarization with acetylcholine.

INTERHEMISPHERIC TRANSFER OF BRIGHTNESS DISCRIMINATION IN SPLIT-BRAIN CATS WITH UNILATERAL STRIATE CORTEX ABLATION[1]. J. A. Sechzer (intr. by H. E. Hoff). Dept. of Anatomy, Baylor University College of Medicine, Houston, Texas.

Complete interhemispheric transfer of brightness discrimination occurs in cats after optic chiasm and corpus callosum section. Brightness discrimination is readily learned by cats after bilateral striate cortex ablation. In the present study, cats were trained to make a monocular brightness discrimination after optic chiasm-corpus callosum section and unilateral striate cortex ablation. A special mask was used to cover one eye during training. Each cat learned to select the darker of two panels in order to obtain food. Half the cats were trained with the eye exposed first on the cortically ablated side and the remaining cats were trained with the eye exposed first on the cortically intact side. After learning was complete, the mask was reversed and interhemispheric transfer of the brightness discrimination was tested with the opposite untrained eye. Transfer was complete from the cortically ablated side to the cortically intact side; transfer failed from the cortically intact side to the cortically ablated side. These results indicate that although the striate cortex is not essential for brightness discrimination learning, it is essential for brightness discrimination transfer.

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CLINICAL EVALUATION OF PULSED SHORT WAVES IN PROBLEMS OF THE HEMIPLEGIC SHOULDER. W.A. Selle, Biophysics and Nuclear Medicine, UCLA Medical Center, Los Angeles, California.

The biological effects of high intensity, continuous electromagnetic energy are well known. In recent years pulsed short waves, with pulses up to 600/s and claimed to be "athermal", have been used on a wide spectrum of soft tissue problems with varying results. There is now available through Dynapower Systems Corp., Los Angeles, a pulsed generator of 27.12 megacycles with pulses of energy ranging from 100 to 2600 per second. This equipment produces thermal effects for pulses above 600/s, the heat production being proportional to the frequency of pulses. This new generator, with both "athermal" and "thermal" settings, was evaluated on 85 hemiplegic patients at Long Beach General Hospital having pain, stiffness and limitation of motion of the shoulder. Thirty of these patients were treated with "athermal" pulses (frequencies below 600/s). The remaining 55 were treated with pulses of 2000 to 2600 per second which produced deep heat. The energy was directed in each patient to the scapular, deltoid and pectoral muscles for a period of 15 to 20 minutes. Results indicated that athermal energies are ineffective, while the higher thermal energies are moderately effective in relieving pain and increasing range of motion of the involved shoulder. There is no indication that the results observed are superior to those obtained with lower intensity, continuous short waves of the conventional type.

OXYGEN DISSOCIATION CURVE SLIDE RULE, WITH NEW pH, BASE EXCESS AND TEMPERATURE CORRECTIONS. John W. Severinghaus. Cardiovascular Research Inst. & Anesthesia Dept, Univ. Calif. Med. Sch, San Francisco, Calif.

The quantitative effects of temperature and pH (Bohr effect) upon log Po_2 are virtually independent of oxygen saturation. A slide rule* permits a log Po_2 scale to be aligned to the predicted saturation, when temperature is aligned to pH. Bartels' standard dissociation curve was used (Pflügers Arch. 272:372,1961). Beyond its range (20%-90%), I used the following: 4.3% sat. at 6.5 mmHg Po_2, 37°, pH=7.4 in 53 non-smokers (Astrup, personal comm.); 1.0% sat. at 1.8 mmHg Po_2 (Roughton, personal comm.); 2.3% sat. at 3.8 mmHg Po_2, determining Po_2 and pH after anaerobically mixing aliquots of air-saturated and CO_2-N_2-desaturated bloods; 8 points by this technique between 90 and 100%; 5 published studies in the 90-100% range. The resulting suggested dissociation curve deviates maximally from Dill's (Am. J. Physiol. 132:685,1941) by -4.5% at 14 mmHg and +1.5% at 60 mmHg Po_2. In collaboration with Naeraa, Strange Petersen and Boye, the magnitude of the Bohr effect was shown to be 20% less with base excess (B.E.) variations than with Pco_2 variations, due to a pH-independent effect of CO_2. The combined Bohr effect is: $\Delta \log Po_2 = 0.0015 AB.E. - 0.48 \Delta pH$. Astrup and Engel (unpubl.) showed that the usual correction for the effect of temperature on the dissociation curve was about 20% too small and Munson and I confirmed their results, obtaining a mean at constant pH, between 25 and 38°C of: $\Delta \log Po_2 = 0.024 \Delta T°C$. The slide rule also contains scales for computing 1) Blood Po_2, Pco_2 and pH with anaerobic temperature change. 2) Pco_2 from pH and CO_2 content of plasma or cerebrospinal fluid, or HCO_3^- from pH and Pco_2, from 10°-40°C. 3) B.E. and standard HCO_3^- from pH and Pco_2. 4) True oxygen consumption fraction from mixed expired air analysis. 5) Gas volume correction from ATPS to BTPS or STPD. (USPHS HE-6285 & Res.Career Award 1-K6-HE-19,412)

*Radiometer A/S, Copenhagen, Denmark.

QUANTITATIVE MEASUREMENT OF THE EFFECTS OF PITHING AND ANESTHETICS ON AN ARTERIOLAR NERVE-MUSCLE PREPARATION IN THE FROG (RANA PIPIENS)

George R. Siggins* and Herbert J. Berman, Boston University, Biology Department, Boston, Massachusetts

The retrolingual membrane preparation of Pratt and Reid (Science 72: 431, 1930) was adapted for quantitative study of the responsiveness of arteriolar smooth muscle by stimulation of its innervation. Its blood vessels and associated nerves were observed at 100X. A nerve 3-8 μ in diameter, which appeared to enter the wall of an arteriole in the same microscopic field, was stimulated using a Pt-Ru microelectrode 10 μ in diameter. The duration of the square-wave stimulus was fixed at 0.01 msec.; the preparation observed for constriction after each stimulus; voltage varied systematically until the threshold was found; and amperage calculated from the voltage drop measured on an oscilloscope placed across a 1000 ohm series resistor. The threshold for constriction was taken to be the stimulus that would produce the smallest constriction observable at 100X. Animals either single-pithed or lightly anesthetized with MS-222 (tricaine methane sulphonate) had the lowest thresholds, 0.20-0.50 milliamperes. Their respective arithmetic means (±S.D.) were 0.39 ± 0.09 ma (10 experiments) and 0.38 ± 0.09 (25 experiments). Thresholds exceeded 0.50 ma in animals lightly anesthetized with sodium pentobarbital or urethane with Dial. These two anesthetics often caused stasis and sustained nonresponsive arteriolar dilatation. Tubocurarine chloride evoked intermediate thresholds. Immobilization by single-pithing or MS-222 appeared to provide a relatively reproducible, stable, and responsive preparation. (Supported by grants from NHI and Boston University and a contract from the Dept. of Army.)

ROLE OF CALCIUM IONS AND PHOSPHOLIPIDS IN PLATELET AGGREGATION AND PLUG FORMATION. M.J. Silver, (Intr. by D.B. Doemling) Cardeza Foundation and Department of Pharmacology, Jefferson Medical College, Philadelphia, Pa.

Using a modification of the Chandler wheel method (Lab. Invest. 7, 110, 1958) it was possible to show: 1. Aggregation of platelets in recalcified platelet rich dog plasma occurs in the following stages; a) appearance of barely visible particles, b) occurrence of "snow storm" - a sudden burst of particles rapidly cohering to form large aggregates, c) coalescence of aggregates to form a solid plug, d) addition of a fibrin tail to the plug. 2. These stages occur at an accelerated rate if the platelet rich plasma has been frozen and thawed - suggesting release of available phospholipids from the platelets. 3. These stages also occur at a rapid rate if suspensions of phosphatidylethanolamine or certain interaction products of lecithin and phosphatidylserine are added to platelet poor plasma which is then recalcified. 4. These phospholipids produce all the aggregation stages (but no fibrin tail) when tested in aqueous media (rather than platelet poor plasma) in the presence of calcium ions. 5. ADP (10^{-5}M) appears to accelerate stage a) above and may play a supporting role in physiological aggregation. 6. ADP alone cannot produce large aggregates or plugs. In contrast, the formation of large aggregates and plugs from platelets or exogenous phospholipids will not occur without calcium ions. (Supported by a grant from U.S.P.H.S.).

VISUAL PROJECTION TO THE SUPERIOR COLLICULUS OF RAT. Robert Siminoff*, Horst O. Schwassmann* and Lawrence Kruger. Dept. of Anatomy, and Brain Research Inst., Univ. of California, Los Angeles, Calif.

Multi-unit neural activity was recorded with insulated metal microelectrodes inserted into the superior colliculus of anesthetized rats mounted in a device which permitted 180° access for photic stimulation at a fixed distance with a fiber optics system. A precise retinotopic arrangement of the contralateral visual field across the surface of the mammalian colliculus was found with an arrangement and orientation essentially similar to that of the tectal projection in other vertebrates.

The several varieties of unit discharge influenced by luminous stimuli included: typical "on" and "off" responses related to stimulus position and intensity, units responding slowly to alteration of general illumination level, and highly regular rhythmic discharges triggered by a variety of photic transients. (Supported by USPHS grant B-4578.)

EFFECTS OF ACUTE ACIDOSIS ON RENAL HEMODYNAMICS. D.H. Simmons, T.J. Bersentes*and A. Peery.* UCLA Med. Ctr. and Cedars-Sinai Med. Ctr., L.A.

Renal blood flow (RBF) and systemic blood pressure (SBP) were measured during respiratory and metabolic acidosis in 42 dogs anesthetized with sodium pentobarbital. Changes in renal vascular resistance (RVR) were then calculated. Flow was measured with an electromagnetic flowmeter placed on the left renal artery through a flank incision. Arterial blood pH and pCO_2 were measured anaerobically at deep body temperature. Respiration was controlled with a Harvard respiration pump, adjusting ventilation so that control pH was normal (mean = 7.40). Progressively severe respiratory acidosis was then induced by increasing inspired CO_2 by increments up to 30% then similarly decreasing by increments until control conditions were again reached. Mean pCO_2 rose from 32 to 230 mm Hg, while arterial pH dropped from 7.40 to 6.70. In the first group of experiments (innervated kidneys; 10 dogs) there was a biphasic change in RVR. When pH had decreased a mean of 0.4, RVR decreased 15% below control values. As pH fell further, RVR increased, reaching a maximum of 40% above control values. Since SBP decreased continuously with rising pCO_2 to 15% below control values, changes in RVR were primarily related to changes in RBF. The response was unaffected by total renal denervation, either by stripping the renal pedicle and adipose and connective tissue around kidney (17 dogs) or by cutting the renal artery and reanastomosing with polyethylene tubing (8 dogs). Metabolic acidosis was induced in 8 dogs with innervated kidneys by infusing 0.3 M HCl until arterial pH again decreased 0.7 units. Renal hemodynamic responses were similar to those during respiratory acidosis. These experiments suggest that (1) RVR decreases during moderate acidosis but rises with more severe acidosis; (2) changes in RVR are pH-dependent; and (3) the response is most likely due to local and / or humoral effects. (Supported by USPHS Grant HE08075.)

PERSISTENCE OF ADAPTATION TO CHRONIC ACCELERATION. Arthur H. Smith and Russell R. Burton*. Department of Animal Physiology, University of California, Davis.

Birds adapted to accelerative forces greater than normal gravity (produced by long-term centrifugation) exhibit a variety of physiologic and anatomic changes. Among these are: decreased body mass (growth repression) and increases in feed intake, circulating red cells, plasma proteins, etc. When such animals are returned to normal gravity, the differences between them and their controls disappear (or cease to change) after three or four weeks. Re-exposure of previously adapted birds to chronic acceleration, even after four months at normal gravity is well tolerated -- there being no loss in body mass nor mortality. Consequently, it appears that the persistence of the adaptation to increased accelerative force greatly exceeds the changes in anatomic and physiological parameters which have been investigated.

CHANGE IN MEAN SYSTEMIC PRESSURE INDUCED BY HYPOXIA. Elvin E. Smith and Jack W. Crowell. Dept. of Physiology, Univ. Miss. Med. Center, Jackson, Miss.

Many measurements have been made of the response of the arterial circuit to changes in the oxygen content of inspired air. The responses of the venous circuit is less well known. The present study is an attempt to delineate the contribution of the venous circuit, and in particular that of the venules and small veins, and the response of the total circulation to hypoxia, utilizing the mean systemic pressure as an index of venous activity. Arterial pressure(AP), right atrial pressure(RAP), and mean systemic pressure(MSP) were recorded both prior to and during inhalation of 9% oxygen in nitrogen. The gradient for venous return (GVR) was taken as MSP-RAP. Cardiac output(CO) was recorded by an electromagnetic flow probe implanted several weeks prior to the experiment. After 5 minutes respiration with the hypoxic gas, AP increased 15% above control. CO was elevated 45%. RAP decreased 25%, while MSP increased 26.8%. The changes in RAP and MSP resulted in a net increase in GVR of 27.6%. The rise in AP was not of sufficient magnitude to have resulted in so large a MSP increase. RAP declined, thus ruling out the influence of large veins. Therefore, the major contribution to the increase in MSP was of small vein origin.
(Supported with funds from N. I. H., Grant HE-09160 and Mississippi Heart Assn.)

GASTRIC SECRETORY AND ADRENOCORTICAL RESPONSES DURING SIDMAN AVOIDANCE BEHAVIOR IN INTACT AND AMYGDALECTOMIZED MACACA MULATTA. G.P.Smith, J.J.Boren and W.J.H.Nauta (intr. by F.P.Brooks). Walter Reed Army Institute of Research, Washington, D.C.

Three Macaca mulatta were equipped with chronic gastric fistulae and adapted to primate chairs. Gastric acid and pepsin outputs, and plasma and/or urinary 17OH-CS measurements were made on each animal during 6 hours of training on the Sidman Avoidance Procedure. Training sessions were programmed so that the monkeys had 2 hours of training on each of 3 consecutive days. One naive, intact monkey and one naive, bilaterally amygdalectomized monkey had decreased gastric acid and pepsin outputs and increased plasma 17OH-CS during the avoidance training sessions. The third monkey was studied prior to and following bilateral amygdalectomy. In this monkey, the predominant gastric acid and pepsin response was inhibition, but there was considerable variability. Urinary 17OH-CS were increased during the training sessions prior to amygdalectomy, but they were not increased during the training sessions which followed amygdalectomy. The avoidance behavior of this monkey was much more effective during the training sessions which followed amygdalectomy. We conclude (1) that the amygdaloid nuclei are not essential for the elaboration of these gastric and adrenocortical responses to the avoidance training situation; and (2) that the adrenocortical response to one hour of avoidance training may decrease as the animal acquires effective avoidance behavior.

TIME DEPENDENT RESPONSES OF BROWN FAT IN COLD-EXPOSED RATS. Robert E. Smith and Jane C. Roberts*, Department of Physiology, UCLA Sch. of Med., Los Angeles, California.

Brown fat of the rat upon exposure to cold has been shown to increase in both total mass and unit heat production (Am. J. Physiol. 206:143, 1964), with concurrent changes in the cellular multilocularity appearing transiently during the initial hours in the cold (6°C) (J. Cell. Biol. 23:89, 1964). Reported here are some correlative metabolic changes in brown fat of rats after cold-exposures of from 3 hrs to 60 days. Both interscapular and thoracic brown fat were excised, and homogenized separately in 10 vol. 0.25M sucrose. Mitochrondria (M_w) were obtained from brown fat combined from these sites. Respiration was assayed by direct Warburg method in presence of α-ketoglutarate; with gas phase of O_2 for homogenate and air for M_w. In both systems, qO_2 ($\mu lO_2/mgN/hr$) was depressed 20% or more in the 3 hr rats. In M_w this returned to control values by 6 hrs and in homogenates by 12-24 hrs. Thereafter, qO_2 rose at a slower rate to reach a quasi-steady state by 8 days of cold-exposure. In the mitochondrial system these changes were compensated by adaptive increases in mitochondrial N which minimize the decrease in total caloric output during the period of qO_2 decrease. Supported by NASA research grant NsG-721.

EFFECT OF ENDOTOXIN ON THE KINETICS OF HEMOPOIETIC COLONY-FORMING CELLS OF IRRADIATED MICE. Willie W. Smith, George Brecher*, Sallie Fred* and Roger A. Budd*, National Cancer Institute and Department of Clinical Pathology, National Institutes of Health, Bethesda, Maryland.

Survival of mice given midlethal radiation is largely dependent upon hemopoietic recovery. An injection of bacterial endotoxin the day before irradiation hastens bone marrow recovery and increases survival. Endotoxin given just after irradiation is less effective. The number of units in marrow or spleen which can form colonies (CFU) is estimated from nodules in the spleen of recipient mice given enough radiation to suppress their own ability to form colonies. The number of CFU is immediately reduced by radiation, due to direct killing. Further decrease results apparently from continued maturation while cells are still unable to reproduce. In mice given 400 rads recovery of CFU, at a doubling time of 18 hours, begins in the femur 2 days and in the spleen 3 days after irradiation. In mice pretreated with 25 μ of S. typhosa endotoxin this recovery begins in both femur and spleen one day after irradiation, while CFU continue to drop in the untreated controls. When endotoxin is given after irradiation, CFU in the spleen recover as rapidly as in pretreated mice, but in the marrow recovery is intermediate between pretreated mice and controls. Thus, recovery of CFU in the marrow correlates well with the previously observed recovery of marrow cellularity and survival, while recovery in the spleen does not. Possibly this may be ascribed to the marrow CFU representing pluripotential cells initiating complete marrow recovery, while the spleen CFU contain a higher proportion of stem cells already committed to erythropoietic differentiation.

RENIN SEPARATION BY ION EXCHANGE CHROMATOGRAPHY. S. S. Sobin, L. Freeman* and G. Frankl*. Cardiovascular Research Laboratory, Loma Linda University, School of Medicine, Los Angeles, Calif.

Previous attempts to separate completely renin from other renal proteins in chemically untreated extracts by gradient elution from cationic (CMC) and anionic (DEAE) exchange resins were unsuccessful. Therefore step-wise elution from CMC was carried out with pyrophosphate buffer between 0.014--0.030M, pH 4.5, in 0.004M steps. Each fraction was then chromatographed on DEAE using pyrophosphate buffer, pH 8, 0.002M load and eluted with 0.02M. All ten fractions were then subjected to identical linear gradients on CMC, 0.005--0.040M, pH 4.5, and analyzed for salt, total protein and renin activity. Renin and other protein elution can not always be directly related to prior electrolyte treatment of the CMC resin column, i.e. on gradient elution they appear at molarity levels lower than those at which they were eluted in prior step-wise elution. DEAE treatment increased the separation between renin and non-renin proteins. Renin concentration generally paralleled protein concentration although renin purity did not. These results indicate that in the elution system described renin may exist (1) in different molecular species, (2) in physical aggregates or (3) be bound to non-renin proteins. This peculiar renin behavior may complicate purification procedures.

INTERRELATION BETWEEN REFLEX VASOCONSTRICTION AND EXERCISE DILATATION IN "DIVING". R.R. Sonnenschein and B. Folkow†. Dept. of Physiol., Univ. of Göteborg, Göteborg, Sweden.

During submersion, naturally diving animals commonly manifest intense vasoconstriction with marked reduction in blood flow in skeletal muscles, even while the muscles remain active. In contrast, in man and cat the dilatation of exercise can to a considerable extent overcome neurogenic vasoconstriction. In the present experiments, domestic ducks, which show a moderately pronounced "diving reflex", were studied as representatives of diving animals. In pentobarbital-anesthetized ducks and cats, venous outflow of calf muscles and pressures in the femoral artery and a small artery (0.3-0.6 mm OD) were recorded during exercise (stimulation of motor nerve), vasoconstriction (in the duck, administration of 20% CO_2, often with vagotomy and bleeding; in the cat, stimulation of the sympathetic chain) and combinations of these procedures. Calculations of resistance changes in large artery and small vessel segments revealed that the large arteries of the duck, lying outside the muscle, have a considerably more potent vasoconstrictor innervation than those of the cat. Ascending dilatation, readily demonstrable in the cat, is essentially absent in the duck during reflex vasoconstriction. The ability of diving animals to maintain constriction in muscles during exercise may well reside in this quantitative difference functional innervation. (Supported by PHS Grant HE 05157)

INTRARENAL DISTRIBUTION OF BLOOD FLOW IN DOGS WITH CHRONIC CONGESTIVE HEART FAILURE. H.V.Sparks*, H.H. Kopald*, S. Carriere*, J.E. Chimoskey*, A.C. Barger, Department of Physiology, Harvard Medical School, Boston, Mass.

Although medullary circulation of the kidney is essentially unchanged by tricuspid insufficiency and pulmonary stenosis, cortical blood flow is progressively altered by increasing cardiac incompetence. Using the method of Thorburn et al, distribution of blood flow in the kidney of dogs in chronic congestive heart failure has been measured. After a rapid injection of Kr^{85} into the renal artery the disappearance curve from the kidney can be described as a sum of exponentials, each associated with blood flow through a specific anatomical region of the kidney, e.g. cortex, outer medulla and inner medulla, defined autoradiographically. In a normal dog, cortical blood flow is described by a single exponential with a flow rate of about 500ml/100g/min and the cortex receives about 80% of total renal blood flow. With TI cortical blood flow is no longer described by a single exponential; a decreasing part of the cortex flows at a rate only slightly less than control values, and an increasing volume of the cortex now has a reduced perfusion rate similar to that of the outer medulla (about 200ml/100g/min). The ability to excrete Na^+ is reduced in such an animal. With the addition of PS, and the development of frank failure, with ascites and edema, cortical flow is further reduced, with a larger volume flowing at the rate of outer medulla. (Supported by U.S.P.H.S.)

ABSORPTION OF CALCIUM IN HYPERTHYROIDISM AND HYPOTHYROIDISM. **Herta Spencer, M.D., Isaac Lewin, M.D.*, and Joseph Samachson, Ph.D.* Metabolic Research Unit, Veterans Administration Hospital, Hines, Ill.**

The absorption and excretion of calcium was studied under controlled dietary conditions in patients during different phases of thyroid function. Radioisotope studies, using Ca^{45} and Sr^{85} as tracers, calcium, phosphorus and nitrogen balances, as well as calcium tolerance tests were performed in the hyper-, hypo- and euthyroid states. Marked changes in calcium metabolism were noted in the different phases of thyroid function. During hyperthyroidism, whether spontaneous or induced by desiccated thyroid extract, the intestinal absorption of calcium was markedly lower than in the euthyroid or hypothyroid state. The most striking change was the marked increase in intestinal absorption of calcium in the euthyroid or hypothyroid state following the correction of the hyperthyroidism as was indicated by the very low fecal excretion of calcium, of Ca^{45} and of Sr^{85}, and by a marked increase in the plasma levels of the radioisotopes following the oral administration of Ca^{45} and of Sr^{85}. The endogenous fecal calcium also decreased in the hypothyroid and euthyroid state and the total fecal calcium consisted of endogenous fecal calcium in these states of thyroid function. Hyperthyroid patients with hypercalcemia were also tested with the calcium tolerance test before and after treatment. Correction of the hyperthyroidism resulted in a marked reversal of the abnormal test towards normal and to a great tendency to calcium retention. Supported by U.S. Public Health Service Grant AM-5572.

SPECTRAL ANALYSIS OF MURMURS PRODUCED IN STENOSIS OF LARGE ARTERIES. Merrill P. Spencer and M. E. Fourney.* Virginia Mason Research Center & Dept. of Aeronautics and Astronautics, Univ. of Wash., Seattle, Wash.

Experimental graded coarctation of the dog's thoracic aorta was produced according to a previously described technique using a barium titanate crystal contacting the vessel surface (Am. Heart J. 56:722, 1958). Analysis was made from constant time periods of tape recorded murmurs. Integration of amplitudes from 5 cps band pass filters distributed continuously over the frequency range disclosed murmur frequencies from 200 to 1000 cps. All amplitudes from 200 to 1000 cps increased with progressive stenosis to 2 mm. internal circumference with a major peak around 300 to 350 cps. At 1 mm. internal circumference, the 350 cps peak diminished slightly while the higher frequencies continued to increase. Complete occlusion collapsed the spectrum back to the 50-200 cps control pattern. It is concluded that there is spectral pattern information in murmurs which can be used to predict the degree of arterial stenosis. (Supported by NIH research grant HE-08525.)

ULTRA-LATE PTP OF MONOSYNAPTIC REFLEX RESPONSES IN CAT. W. A. Spencer and R. Wigdor, New York Univ. Med. School, New York, N. Y.

"Early" and "late" components of monosynaptic PTP curves have been delineated by Eccles and Rall (1951). We have analyzed PTP of monosynaptic reflex responses following tetani at 80-500/sec, lasting from several minutes to over an hour, in acute spinal cats lightly anesthetized with pentobarbital. With tetani lasting less than 10 minutes, curves were obtained which are similar to those of previously described "late" PTP. However, with tetani of 15 mins. or longer, a later component, "ultra-late" PTP, became evident. With tetani lasting 1/2-11/2 hours this component often endured an hour or longer. "Late" PTP following a short (6 sec.) tetanus could be superimposed on "ultra-late" PTP. Focal synaptic potentials recorded under deep anesthesia showed "ultra-late" PTP. Focal recordings from motor nuclei also revealed that, following 15 min. tetani, the early part of the "late" PTP component was associated with a reduced presynaptic spike, but the "ultra-late" component was accompanied by a slightly increased presynaptic spike. The latency of the presynaptic spike was increased during the period of potentiation. These data indicate that prolonged tetani can produce increases in synaptic potency measured in hours, but at present we have not been able to demonstrate any permanent increase in synaptic potency, even with tetani of a duration (1/2-11/2 hours) comparable to the minimum periods reported to be required for "fixation of experience" in behavioral experiments. (Supported by USPHS Research Grant NB-05648.)

DISTRIBUTION OF AUDITORY AND VISUAL EVOKED RESPONSES IN THE CENTRAL NERVOUS SYSTEM OF THE UNANESTHETIZED CHICK. C.E. Spooner and W.D. Winters (Intr. by J.E. Hyde) Brain Research Institute and Department of Pharmacology, UCLA Center for the Health Sciences, Los Angeles, California.

The anesthetized bird (pigeon) demonstrates a limited brain distribution of evoked responses to auditory stimuli. A wider distribution may be obtained by utilizing an unanesthetized preparation and averaging techniques. In the present study, the distributions of averaged evoked responses to clicks and flashes were recorded in the superficial striatum and tectum, and brainstem reticular formation of freely moving chicks. Evoked potentials from both modalities displayed: wide distributions, slow wave responses sometimes preceded by a more rapid component, and similar wave forms in the reticular formation but different waveforms in the tectal and striatal areas. Auditory evoked potentials were largest during slow wave sleep, and reduced or absent during behavioral arousal. The auditory responses were reduced or abolished by moderate doses of pentobarbital. The present results suggest: 1) the auditory responses are modulated by elements of the reticular formation; 2) avian visual and auditory modalities are diffusely distributed in common areas, although each appears to be conducted to the forebrain by different pathways.

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CAN SUBSTRATE AVAILABILITY LIMIT MUSCLE METABOLISM? W. N. Stainsby and H. G. Welch*. Dept. of Physiol., College of Med., Univ. of Florida, Gainesville, Florida.

Lactate production and uptake by the gastrocnemius-plantaris and lower leg muscle groups were calculated from measurements of blood flow through the muscle and the arterio-venous blood lactate concentrations. Oxygen uptake was similarly calculated. These measurements were made while the muscle was at rest and during twitch contractions at rates of 0.5 to 10 twitches per second. At rest the muscles usually produced a small amount of lactate. During contractions the muscles took up lactate from the blood at all twitch rates studied. Oxygen uptake increased with twitch rate up to 3 twitches per second but decreased with further increases in twitch rate. Since lactate was taken up, oxygen presumably was not the limiting reactant. There remain the possibilities that something other than oxygen is limiting energy production or that the muscles were unable to use more energy at twitch rates above 3 per second. Maximal oxygen uptake at high twitch frequencies appears to be closely correlated with blood flow, suggesting that some substrate is the rate-limiting reactant. (Supported by NIH Grant GM 06264)

THE EFFECT OF LOW CHOLINESTERASE ACTIVITY UPON THE CONCENTRATION OF ACETYLCHOLINE IN THE BRAIN. William B. Stavinoha*, Leonard C. Ryan*, Joseph A. Rieger, Jr.*, and P. W. Smith. Civil Aeromed. Res. Inst., Oklahoma City, Okla.

In this investigation rats were poisoned daily with 1 mg/kg diethyl ethylthioethyl dithiophosphate. Acetylcholine was analyzed on the gas chromatograph, and cholinesterase activity was measured using a constant pH titration method. Norepinephrine was measured on the spectrophotofluorometer. Although the acetylcholine concentration after poisoning was found to be as high as 4.7 µg/g the concentration declined, even in the presence of the daily administration of the cholinesterase inhibitor, over a period of five to fourteen days to the approximately normal concentration of 3.4 µg/g. At the same time, the cholinesterase activity in brain remained low. Norepinephrine concentration was unchanged. The return of the acetylcholine concentration to normal paralleled roughly the disappearance of the signs of poisoning. These findings indicate that when cholinesterase is chronically inhibited, acetylcholine levels do not remain high but are returned to normal by a regulatory mechanism.

THE EFFECT OF CO_2 ON LENGTH-TENSION RELATIONSHIPS OF PULMONARY ARTERY SMOOTH MUSCLE. N.L. Stephens* and B. Bromberger-Barnea. The Johns Hopkins University, Baltimore, Maryland. (Supported by HTS 5453-USPHS Training Grant).

The effects of CO_2 on the length-tension (LT) relationships of pulmonary artery (PA) smooth muscle were examined in isolated segments of large branches of the PA's of dogs suspended in mammalian Krebs-Ringer solution. Pco_2's from 30-100 mms. Hg., exerted no effect on the resting tension. The LT curve was shifted to the left and its slope was increased along the length axis. Stimulation of the arteries with 35 volts, 60 cycle AC, 15 seconds duration pulses also produced a shift to to the left and increase in slope of the LT curve. During administration of high CO_2 (> 200 mms. Hg) stimulation (35 volts, 60 cycle AC, 15 seconds) produced little further increases in tension. However, by increasing stimulus strength during the high CO_2 state, further increases in tension could be obtained. The increased resting tension seen with high CO_2 appears to be due to a contracture-like response induced by depolarisation of the muscle cell membrane which is reversible.

TROPHIC CONTROL OF THE CREMASTER MUSCLE OF THE RAT. Doris M. Stewart (intr. by A. W. Martin). Dept. of Zool., Univ. of Wash., Seattle, Wash.

Since tenotomy or denervation of a muscle result in atrophies of approximately the same extent both may be caused by disuse. But there may be a trophic substance produced by nerve which is essential for normal maintenance. In addition to denervation and disuse a lack of testosterone can cause atrophy in a few muscles. The cremaster muscles of the rat have been considered testosterone sensitive (Leonard, Proc. Soc. Exp. Biol. and Med. 94: 458, 1957). Since these muscles depend on the testes for tension as well as testosterone an analysis of the effects of denervation, lack of tension, and lack of hormone might give some indication of the relative importance of these factors. By 7 and 14 days after unilateral castration, to remove passive tension, the cremasters were 27% and 38% lighter respectively than the opposite normal muscles. Denervation of the left cremaster resulted in a significant but less pronounced difference in weight between denervated and normal muscles. When both operations were combined the difference in weight of the operated from the control muscles was essentially equal to the sum of the two separate responses. In this muscle, at least, changes due to lack of tension and to denervation cannot be considered to be due to disuse. These results are more satisfactorily explained by a trophic effect of nerve, in addition to tension, than by a reduction in testosterone. When bilateral castrations were performed the weight changes due to lack of tension and innervation were of essentially the same magnitude. Injection of testosterone had no effect on the extent of atrophy in either the innervated or the denervated muscle. In the trophic control of the cremaster innervation and passive tension are more important than the presence of testosterone. (Supported by Grant NB 05294 of the Public Health Service.)

THORACO-ABDOMINAL PRESSURE MEASUREMENTS IN EXPERIMENTAL AND ACQUIRED RESPIRATORY MUSCLE PARALYSIS

Daniel J. Stone, M.D., Harold Weltz, M.D.*, Saul Kaplan, M.D.*
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Simultaneous measurements of respiratory flow curves, intra-thoracic and intra-abdominal pressures were made in the sitting position in normal subjects during quiet respiration and in subjects with experimental and acquired respiratory muscle paralysis. In normal subjects, maximal negative intra-thoracic and maximal positive intra-gastric pressure was achieved at end inspiration. In contrast, subjects with experimental hemi-diaphragm paralysis demonstrated an intra-thoracic pressure change similar to that of normal, but intra-abdominal pressure did not rise during inspiration because of the paradoxical motion of the paralyzed diaphragm. In subjects in whom the diaphragm was the sole-functioning respiratory muscle, the intra-thoracic pressure changes were similar to those of normal subjects, but intra-abdominal pressure rose early in inspiration and fell to baseline by end inspiration. The flow curves also showed significant deviation from the normal in subjects with respiratory muscle dysfunction. In subjects with respiratory muscle dysfunction, maximal flow rates were achieved more slowly than in normals.

IMMUNOLOGIC DETECTION OF FORMALIN TREATED HUMAN MYOGLOBIN IN URINE.

Helen R. Strausser and Edwin L Rothfeld*, Rutgers-The State University, Newark, N.J., and Newark Beth Israel Hospital, Newark, N.J.

Formaldehyde selectively precipitates hemoglobin from solutions containing both hemoglobin and myoglobin. Thus, following extraction of myoglobin from human muscle in 100% saturated ammonium sulfate at pH 8, the small amount of remaining hemoglobin is effectively removed and at the same time the myoglobin is preserved in solution by the addition of formaldehyde. Since heme transfer between the two globins occurs even at neutral pH, it is important in quantitative studies to add the preservative as soon as possible following extraction. Complete hemoglobin precipitation occurs when sufficient formaldehyde is added to bring the solution to pH 4.5. Rabbits immunized with formalin treated myoblobin (F-Mb) produce antibodies which react with Mb and F-Mb. No cross reaction with Hb or F-Hb is obtained, whereas anti-F-Hb cross reacts with Mb and F-Mb. Urines preserved with formaldehyde immediately after extraction were filtered and routinely screened by double diffusion plate and tube techniques for traces of myoglobin. High titered anti-F-Mb gave positive reactions (usually one band of precipitate) against all undiluted urines tested. In instances of recent myocardial infarcts, the urines, if the specific gravity was 1.010 or higher, could be diluted up to 4 times and still give a positive reaction (usually 2 bands). A similar positive reaction was obtained with urines grossly contaminated with bile. Indirect hemagglutination techniques utilizing formalin-preserved red blood cells coated with F-Mb detects urinary F-Mb. Preserved finely ground striated muscle is agglutinated by anti-F-Mb. Urinary F-Mb inhibits this reaction.

THE H-REFLEX IN SPINAL AND NORMAL MAN. Douglas Stuart, Koichi Ishikawa*, Ernest Bors* and Robert W. Porcer. Univ. of California at Davis and Los Angeles and VA Hospital, Long Beach.

Studies on spinal man of direct and reflex EMG responses of the soleus muscle to single shock stimulation of the posterior tibial nerve (M and H waves) revealed the amplitude of the H wave and the H:M ratio to be considerably reduced during periods of heightened spasticity even though the Achilles tendon tap reflex was exaggerated in the same muscle. This seemingly paradoxical finding is in contrast to the reports of others but explainable in terms of reciprocal inhibition induced in soleus motoneurons by hyperactive flexor motoneurons and by evidence that indirectly suggested soleus motoneurons are subjected to an overactive antidromically-driven Renshaw cell system at near-threshhold strength stimulation of the posterior tibial nerve. In spinal man, degeneration, loss of modulation from supraspinal structures and spasticity in differing degree all alter the balance between Renshaw cell, other interneuron, and motoneuron activity to such widely varying extents that spasticity cannot be diagnosed on the basis of H wave amplitude or H:M ratio alone. In contrast, the relation between these parameters and motoneuron excitability is more direct in intact man as evidenced by: 1) a consistent degree of "low frequency depression" of H wave amplitude during repetitive stimuli; 2) a lower stimulus strength necessary to induce the wave during body cooling; and 3) a sharp reduction in amplitude of the wave during the rapid-eye-movement ("paradoxical") phase of sleep.

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MODE OF ACTION OF THE LATERAL LINE ORGAN RECEPTORS IN FISH. E. E. Suckling. State University of New York, Downstate Medical Center, Brooklyn, New York.

The results of a series of electrophysiological studies on the trunk lateral line system in a number of species of marine teleosts will be described. Evidence will be given to show that while in some species the organ seems to be a very definite low frequency auditory receptor in other species this does not appear to be so and that this difference depends on the living habits of the species involved. Observations on the relative importance of pressure changes and on actual water movement as stimulus parameters will be presented. Supported in part by the U.S. Fish and Wildlife Service Bureau of Commercial Fisheries, Honolulu, Hawaii.

THERMOREGULATORY RESPONSE OF THE ANESTHETIZED DOG TO NEUROHUMOR INFUSION. Francis J. Sullivan (intr. by Steven M. Horvath) Dept. Biology, Providence College, Providence, Rhode Island.

In a thermally neutral environment, consequent to pentobarbital anesthesia (Nembutal, 30 mg/kg), rectal temperature declined in 13 dogs, 2.7 ± 0.1°C (± S.D.) in 202 ± 6.7 minutes, whereupon shivering commenced and continued for 163 ± 6.9 minutes, raising the rectal temperature 3.1 ± 0.4°C. During the experimental procedure, various data was collected: temperatures at various places on the animal were continually monitored, respiratory, metabolic and cardiovascular measurements and calculations were performed at designated intervals during the experiment. The response of the anesthetized dog in the two control series was similar: a series in which the animal was prepared but not infused, and a series in which saline was infused into the animal. In the experimental series, serotonin (0.1 μg/kg/min) or l-norepinephrine (1 μg/kg/min) was infused cephalically through the internal carotid artery during the entire experimental procedure. In six serotonin-infused animals, temperature declined 0.2 ± 0.1°C in 172 ± 6.7 minutes, whereupon shivering commenced and continued for 197 ± 6.9 minutes, raising the rectal temperature 1.4 ± 0.3°. In six norepinephrine-infused, rectal temperature declined 1.9 ± 0.1°C in 192 ± 6.7 minutes whereupon shivering commenced and continued for 130 ± 6.9 minutes raising the rectal temperature 3.4 ± 0.3°C.

HUMAN PULMONARY EMBOLI AND SURFACTANT PRODUCTION. Alton I. Sutnick, Louis A. Soloff, and John D. Evans* (dec.) (intr. by Morton J. Oppenheimer). Depts. of Medicine and Physiology, Temple University Medical Center, Philadelphia, Pennsylvania.

Previous studies have indicated that an intact pulmonary circulation is necessary for the production of surfactant by the alveolar epithelial cells. Pulmonary artery occlusion in dogs has resulted in a decrease in surface activity, but similar findings in human lungs have not been described. In order to evaluate this phenomenon in human lungs, 32 lungs the site of pulmonary emboli were studied. Twenty-two were associated with pulmonary infarctions, and the other 10 were acute fatal pulmonary emboli without infarction. Saline extracts were made of all specimens, and surface activity was measured on a modified Langmuir-Wilhemy surface film balance. Minimal surface tensions of 21 normal human lung extracts were below 10 dynes/cm., while 6 (60%) of the 10 uninfarcted lungs with emboli demonstrated similar normal findings. In contrast, only one (4.5%) of the 22 infarcted lungs was normal. These infarcted lungs had a mean minimal surface tension of 18 dynes/cm., while the embolized uninfarcted lungs had a mean minimal surface tension of 9.7 dynes/cm. Slices of lung tissue were also incubated with palmitate-1-C^{14} to determine its conversion to phospholipids. Three infarcted lungs studied were found to be much less active in this conversion than uninfarcted lungs. These findings demonstrate a decrease in surface activity and phospholipid synthesis in human pulmonary infarctions, and support the concept that obstruction of the pulmonary circulation interferes with surfactant production. (Supported in part by Public Health Service Research Grant HE 08595 of the National Heart Institute, and the Heart Association of Southeastern Pennsylvania.

EFFECT OF AORTIC MIXING ON DETERMINATION OF VENTRICULAR VOLUMES BY WASHOUT. H. J. C. Swan, Thomas J. Knopp,* and Paul R. David.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Thermal dilution curves were recorded in the aorta (Ao) or left ventricle (LV) in anesthetized dogs after injection of cold saline (average 2-3 ml) into either Ao or LV (designated Ao-Ao for aortic injection and sampling, LV-LV for LV injection and sampling, LV-Ao for LV injection and Ao sampling). In no instance (approx. 250 dilution curves) did Ao-Ao clear within 2 systoles after injection. It was therefore possible to calculate the proportionate fall in temperature (K) for each of these sites. K_{Ao-Ao} averaged 0.46 (0.15-0.75) and varied directly with heart rate and inversely with stroke volume. It must be concluded that the root of the Ao acts as a mixing chamber and that for beats following C max, K_{LV-Ao} continues to be influenced by mixing of aortic blood with blood just expelled from the ventricle. Since K_{Ao-Ao} is usually relatively large, its influence on K_{LV-Ao} is considerable and precludes calculation of LV volumes by indicator washout, since a major assumption ($C^{A}_{Ao} = C^{A}_{LV}$) is seriously violated. An attempt was made to develop correction factors based on the magnitude of K_{Ao-Ao}. With a 2-sampling-site technic, considerable variability was found in K_{Ao-Ao} with different thermistors. In the same way the value obtained in the outflow tract of the LV (K_{LV-LV}) showed a high degree of variability. It was concluded that the Ao does not act as a conduit but as a mixing chamber retaining a variable quantity of indicator after its cyclical expulsion from the LV. Determination of the rate of clearance of this indicator from the aortic root is a complex function affected by factors in addition to volume relation $SV/_{VED}$. Volumes calculated on the basis of indicator washout will frequently be falsely high. (Supported by NIH Grant HE-09374.)

PULMONARY AND STEROID CHANGES DURING STRESS, Henry E. Swann, Jr., Herman Harvey*, and Myles Maxfield*, Rancho Los Amigos Hospital, Downey, Calif. and Univ. of Southern Calif., Los Angeles, Calif.

Male and female guinea pigs were maintained in a 32 animal stress rig continuously for 60 days. Equal numbers of weight matched controls were maintained without stress. The stress regimen involved (1) individual cubicles, restrictive in size, (2) a 10 second light stimulus, (3) a 0.5 second electrification of the cubicle grid, (4) a 110 second rest period until the next light stimulus. At regular intervals, assessments were made of body weight, heart rate, respiratory rate, total pulmonary resistance, and urinary 17-ketogenic steroid content. The experimental group showed significant reduction of body weight during the study with weight loss still evident at the end of 60 days. Total pulmonary resistance of experimental females had increased significantly by 4 hours and was maximum between 12 and 24 hours, then decreased. A significant increase in urinary 17-ketogenic steroid output was not evidenced until after the 6th day and remained high from then to the end of the study. The rise in steroid output of the experimental animals at this time was coincident with the decreasing resistance values. This suggests that these changes in corticosteroid metabolism induced by our stress regimen may have the effect of counteracting mechanisms which eventuate in an increase in the pulmonary resistance.
Supported by USPHS contract SAph 76476.

FAST AND SLOW PYRAMIDAL TRACT CELLS IN THE CAT. Kunitaro Takahashi. (intr. by S. Hagiwara) Brain Research Institute, U.C.L.A. Calif. and Brain Research Institute, Univ. Tokyo, Tokyo, Japan.

It has been known from physiological observations that the cat pyramidal tract includes two distinct fiber groups of different conduction velocities. Correspondingly, two groups of pyramidal tract cells (P.T. cells) were found on the basis of their antidromic latencies from the pyramid. In the present investigation intracellular techniques were applied to the group with the short antidromic latency as well as that with long latency, and attempts were made to find any relevant differences in spike and membrane properties between the two groups. The results show that the following three factors are correlated positively with the antidromic latency from the pyramid; (1) spike duration, (2) peak time of the after-hyperpolarization of spike, (3) total membrane resistance of the cell. Axonal conduction velocities of the impaled cells were calculated from the difference of the antidromic latencies and the distance between the two stimulating points along the pyramidal tract; pyramid and peduncle, the values being inversely proportional to the antidromic latency from the pyramid. Thus, it was clearly demonstrated that the P.T. cell groups with different axonal conduction velocities display different spikes and cell membranes properties.

INVESTIGATION OF THE MECHANISM UNDERLYING THE ATTENUATION OF RETICULAR RESPONSES TO REPEATED SENSORY STIMULI. T. Takenaka*, H. Encabo*, and J. P. Segundo. Brain Res. Inst. and Anatomy Dept. U.C.L.A.

Reticular neurons respond inconsistently and decreasingly to repeated sensory stimuli (Bell et al, J. Neurophysiol. 1964). We analyzed this phenomenon (using cats and glass microelectrodes) by relating it to several other functional aspects in an effort to understand its causes. A. Extracellular recordings (gallamine). 1. The response probability of each cell to the first stimulus is high, and decays thereafter. Therefore, the multisynaptic character of the chain cannot be the only issue. 2. The sensory properties of individual cells (field size, laterality, position and continuity; effective stimuli) are complex and heterogenous. Only field size was somewhat influential: large (small) fields tended to show (not show) poor following and attenuation; exception to this rule were numerous however. B. Intracellular recordings (gallamine and chloralose). PSP's decay during repetition. No other relevant post-synaptic changes were apparent: neither spike excitability shifts, D C shifts or counterbalancing PSP's. Such mainly negative findings suggest i that the pathway includes certain "weak" links which, though initially reliable, become unreliable for prolonged periods after activity. And ii that "weakness" is determined at remote, perhaps pre-synaptic, level (see Tauc J. Physiologie 1965). Small intracellularly recorded spikes of around 10 mV were frequent. We believe they may reflect recording of distant activity at a normally "non-spiking" region, but cannot reject the possibility of partial damage. (Supported by NIH).

STIMULUS-RESPONSE PROPERTIES OF MECHANORECEPTIVE FIRST ORDER AFFERENTS INNERVATING THE PALMAR SKIN OF THE MONKEY'S HAND. W. Talbot, H. Kornhuber, and V. B. Mountcastle, The Johns Hopkins University School of Medicine, Baltimore.

Single myelinated afferent nerve fibers have been isolated for study by microdissection of the median nerve in the forearm, in macaque monkeys. Stimuli have been ordered, and neural responses collected, measured, and analysed automatically. Of the several classes of palmar skin mechanoreceptive afferents, particular attention was paid to those ending in receptors just in or beneath the epidermal ridges, which are sensitive at low thresholds (displacements of a few microns), and which, after an onset transient determined by displacement rate and depth, discharge at steady rates during at least the first second of stimulation. The neural response is an almost perfectly linear function of displacement, both for the early transient - when displacement rate is rapid - and during the early steady state.

Information transmission reaches a maximum of about 3 bits per stimulus after 100 to 200 msec of the early discharge, and does not increase with longer inspection times. Weber functions constructed on the assumption that the discriminable neural increment from any base level is a set number of impulses resemble those which hold for tactile sensibility in man. Those derived on the assumption that what is just discriminable at any level is a fractional increase do not. (USPHS NB0 1045-10)

THE RESPONSE OF LEFT VENTRICULAR VOLUMES AND THE EJECTED FRACTION TO STROKE VOLUME CHANGES. R.R.Taylor, H.E.Cingolani and R.H.McDonald, Jr. (Intr. by J. P. Gilmore) National Institutes of Health, Bethesda, Md.

Using a canine right-heart bypass preparation the response of stroke volume and fraction of end-diastolic volume ejected to changes in end-diastolic volume was studied. Cardiac inflow was determined by a Potter electroturbinometer, end-systolic and end-diastolic left ventricular volumes were obtained using the thermodilution technique and circumferential fiber shortening during ejection by a mercury-in-rubber gage. Increased cardiac filling at constant aortic pressure and heart rate increased stroke volume with an increase in the fraction of end-diastolic volume ejected and an increase in the fraction of circumferential fiber shortening. For example, in a representative experiment an increase in end-diastolic volume from 34.7 ml to 45.2 ml at a constant mean aortic pressure of 115 mmHg and a heart rate of 120/min increased stroke volume from 9.6 ml to 19.1 ml, the end-systolic volume increasing only 1 ml. The ejected fraction rose from 0.28 to 0.42. Because of the increased end-diastolic volume and radius, calculated peak developed tension increased from 135 to 172 g/cm^2. The small increase in end-systolic volume associated with increasing stroke volume could be offset by simultaneously lowering arterial pressure so as to reduce myocardial tension. The experiments show that the changes in stroke volume associated with changes in end-diastolic volume occur with little change in residual volume. The associated change in ejected fraction is a reflection of the Frank-Starling mechanism and thus cannot be used alone as an index of a change in myocardial contractility.

THE EFFECT OF ISCHEMIC FOREARM EXERCISE ON LACTATE-PYRUVATE RELATIONSHIPS. George B. Theil (intr. by W. E. Connor). University of Iowa College of Medicine, Iowa City, Iowa.

The relationship of lactic and pyruvic acids $(L_n-L_o) - (P_n-P_o) \times L_o/P_o$, has been proposed as an index of anaerobic glycolysis in tissues and peripheral blood. This concept was applied to study the effects of muscle conditioning on the response to a one-minute period of ischemic exercise in the non-dominant arm of four normal subjects. After the ischemic challenge, before a 30-day program of forearm exercise was instituted, the L_n/P_n ratios varied from 12.1 to 138.4 reflecting the marked responses to arterial-venous occlusion. The preconditioning basal venous lactic acid ranged from 1.7 to 6.8 mg.% and the post-conditioning values from 0.3 to 2.9 mg.%. Since basal variations of the same degree are found in venous blood from random subjects, the apparent difference was not significant. The mean pyruvic acid levels (.50 mg. and .75 mg.% before and after conditioning, respectively) were significantly higher ($p < .01$) basally after conditioning as well as at each time interval following tourniquet release in the ischemic performance test. There were no significant differences in the L/P ratios or in the calculated excess lactate before or after muscle training. The failure of excess lactate to decrease with the significant increase in pyruvate suggests an apparent dichotomy between venous lactic and pyruvic acids in these acute experiments.

THE EFFECT OF IMMOBILIZATION ON SKELETAL METABOLISM IN GUINEA PIGS WITH VARYING BONE THICKNESS. Paul A. Thornton. VA Hosp., Lexington, Ky. and Univ. of Ky. Med. School, Lexington, Ky.

It has been shown that metabolism of rat bone tissue from immobilized limbs was markedly altered (P.S.E.B.&M. 114:347, 1963). This study is a continuation of that work with additional observations and considerations. Immobilization of the left rear leg was effected with a plaster of paris cast for a one week period followed by sacrifice of the animal. Observations of the bone tissue (cancellous & compact) for the free and immobilized limb included glucose utilization, lactic acid production and phosphate and calcium movement during in vitro incubation. The citric acid and alkaline phosphatase contents were also determined. Immobilization resulted in an increase of glucose uptake and production of lactic acid. The levels of citric acid and alkaline phosphatase were also elevated by this treatment, particularly the latter. Release of phosphate was much greater in the immobilized bone tissue while calcium movement was lower. In general, it seemed that cancellous bone was more sensitive to the treatment imposed than was compact. Animals with established thin bones did not react differently to immobilization than those with thicker bone structure. However, thin bone tissue compared to thick used greater amounts of glucose and produced more lactic acid. Both phosphate and calcium release were also higher in this tissue. These results raise several interesting questions concerning the basic metabolic activity of bone tissue in individuals with varying degrees of skeletal development. It is concluded that immobilization does alter the metabolic pattern of bone tissue and this may be used as a means of studying cellular activity-demineralization relationships in this tissue. Mutually supported by the VA and by a research grant NSG-675/06-002-006 from NASA.

THE METABOLIC ACTIVITY OF PULMONARY LECITHINS. D. F. Tierney,*† J. A. Clements,‡ H. J. Trahan.* Cardiovascular Res. Inst., Univ. Calif. Med. Ctr., San Francisco, California.

A new method has been developed which separates the diglyceride moities of lecithin according to the number of double bonds, and has been used to determine the quantity of the fully saturated and highly surface-active lecithin present in the lung. Phospholipase C releases the diglycerides which are then separated into four fractions by thin layer chromatography. One fraction contains no unsaturated fatty acids and is 95% palmitate by weight. By this method it has been shown that in rat and rabbit lungs dipalmitoyl lecithin (DPL) is the only strongly surface active lecithin present in significant quantities. Rat lungs contained 4.1±0.9 mg DPL/gm wet weight. Rats were given intravenous injections of palmitate-1-C^{14} complexed to albumin. The half-life of radioactivity was 17 hours for mixed lecithins, 13 hours for saturated lecithin, and 23 hours for monoenoic lecithins. Dienoic and polyenoic lecithins had similar half-lives, but their precise values are not yet determined. From the quantity of DPL in the tissue and its half-life, its rate of turnover was calculated to be 0.30 μmole/gm per hour. This rate will be compared with estimates of DPL turnover in the alveolar lining. (Supported in part by USPHS grant HE-06285.)

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EFFECT ON CARDIAC OUTPUT OF BRACHIOCEPHALIC CONSTRICTION DURING REST AND EXERCISE. W.S.Topham* and H.R.Warner, Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S. Hosp., Salt Lake City, Utah. Supported by a grant from NIH, #HE 03607.

It has been shown that the increase in cardiac output which normally accompanies exercise can be prevented if peripheral resistance is not allowed to fall (Annals of the N.Y.Acad. of Sciences, 115:669, 1964). To test whether baroreceptors play a key role in linking cardiac output to peripheral resistance, experiments were performed in which the aortic arch was stripped of its adventitia to destroy the aortic baroreceptors and a cloth cuff enclosing a balloon was placed around the brachiocephalic artery. Under computer control the balloon was inflated compressing the artery and causing a bilateral decrease in carotid artery pressure. While a 60 percent increase in heart rate resulted, cardiac output remained constant or decreased, independent of whether the constriction was performed with the dog at rest or exercising. Pressure in the aortic arch rose to a level 50 percent above control when the constrictor was applied but increased much slower than the carotid pressure decreased. Resistance also increased by approximately 50 percent. From these results it seems unlikely that baroreceptor activity is as important as the impedance seen by the left ventricle during systole in controlling cardiac output response to exercise.

MYOCARDIAL TEMPERATURE CHANGES DURING CORONARY ARTERIAL OCCLUSION. Louis A. Toth and A. Sidney Harris, Department of Physiology, Louisiana State University School of Medicine, New Orleans, Louisiana.

Left ventricular muscle temperatures were determined in anesthetized dogs with a flexible thermocouple probe before, during and after occlusion of the artery that supplies the region. The circumflex was occluded 19 times in 4 dogs and the anterior descending 54 times in 11 dogs weighing 10 - 15 kgm. The ischemic periods were for 60 - 180 seconds. The probe was inserted to a depth of 2 or 3 mm through a needle after which the needle was withdrawn over the probe. The temperature was read at 10 second intervals on a scale with an accuracy of 0.1^{0} C. The room temperature was 25^{0} - 28^{0} and was constant during an occlusion period. In 36 trials the heart was exposed to the room temperature; 35 of these showed a fall in muscle temperature ranging from 0.15^{0} to 2.10^{0} from the immediate control. In 7 of these the fall was preceded by an increase ranging from 0.05^{0} to 0.2^{0}. In one experiment the temperature did not fall below control level during the occlusion. In 37 trials the chest opening was covered. Of these, 25 occlusions resulted in a fall in temperature ranging from 0.05^{0} to 0.20^{0}. Of the 12 remaining experiments not showing a fall in ischemic muscle temperature in the covered hearts 3 showed no change from the control reading while 9 showed increases ranging from 0.05^{0} to 0.2^{0}.

(Supported in part by Grant No. HE-01109, USPHS.)

EVIDENCE CONTRARY TO THE CONCEPT OF CARDIAC FAILURE IN IRREVERSIBLE HEMORRHAGIC SHOCK. *J. Traxler* and V.V. Glaviano.* Department of Physiology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Illinois.

The concept of cardiac failure in hemorrhagic shock was investigated in 10 open-chest dogs subjected to catheterization of the four chambers of the heart and in 10 closed-chest dogs treated with the cardiac glycoside, Ouabain. In both groups of dogs anesthetized with Nembutal, shock was induced by bleeding the animals to a mean blood pressure of 40 mm Hg; this level of pressure was maintained for 4 hrs and was then followed by reinfusion of the animal's blood. Recordings of right and left intra-atrial pressures and right and left intraventricular pressures of the heart during the oligemic and normovolemic stages of hemorrhagic shock did not give evidence to relate the decline in blood pressure to cardiac failure. However, acute cardiac failure only became evident approximately 30 min before death, during which time a drop in mean arterial pressure to 30 mm Hg was accompanied by a rise in either right or left atrial pressures. The possibility of a cardiac factor in hemorrhagic shock was further explored by measuring the myocardial responses to Ouabain (.035 mg/kg) administered immediately after or just prior to the reinfusion of blood in dogs subjected to 4 hrs of hemorrhagic hypotension. In the Ouabain-treated animals, recordings of cardiac output by the dye dilution method, blood pressure, central venous pressure and electrocardiograms show that after a transitory increase in blood pressure and a decrease in cardiac output, the eventual course of irreversible shock was not altered by the administration of Ouabain. These results imply that heart failure may not play a significant role in the etiology of irreversible hemorrhagic shock. (Supported by ONR Contract 3502(01) and PHS Grant HE 08682.)

MODIFICATION OF THE METABOLIC AND CALORIGENIC EFFECTS OF CATECHOLAMINES BY BUTOXAMINE. L. Triner*, M. Guyonneau* and G.G. Nahas. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, N.Y.

Sixteen pure-bred beagles were anesthetized with pentobarbital (30mg/kg), paralyzed with succinylcholine and mechanically ventilated. O_2 uptake was continuously measured with a closed circuit computer spirometer system. Epinephrine (E) or l-norepinephrine (NE) was infused at the rate of 1.5 μg/kg/min. for 15 min. so that O_2 uptake increased by 29% or 17% respectively. At least 2 hours later, 10 mg/kg butoxamine [erythro(dimethoxyphenyl)butylaminopropanol HCl] was administered I.V., and 15 minutes later the same infusion of E or NE was given. Butoxamine pretreatment decreased O_2 uptake by 87% during E and by 60% during NE infusion. Simultaneously, the butoxamine pretreatment inhibited the increase of free fatty acids (FFA) after either E (by 67%) or NE (by 57%). In addition, it also inhibited by 40% the increase of glucose after the E infusion. A depression of the cardiovascular action of E was also observed indicating that butoxamine has some beta blocking effect. These results indicate further that calorigenic effect of E and NE is dependent upon the mobilization and utilization of FFA and glucose. (This work was supported, in part, by N.I.H. Grants GM-09069-03 and FO5-673-02, and Army Contract DA-49-193MD-2265).

RELATIONSHIP BETWEEN LEFT VENTRICULAR END-DIASTOLIC PRESSURE AND END-DIASTOLIC AREA IN DOGS STUDIED WITHOUT THORACOTOMY. A VIDEOANGIOGRAPHIC STUDY. A. G. Tsakiris*, N. Banchero*, R. E. Sturm*, P. Osypka* and E. H. Wood. Mayo Clinic and Mayo Graduate School of Medicine, Rochester, Minnesota.

A videoangiocardiogram is a continuous recording of a fluoroscopic image of the cardiac silhouette on magnetic tape. Due to the high light sensitivity of the video system used in our laboratory, injections of only 2.5 to 4.5 of contrast medium (69% Renovist) into the left ventricle provide a good outline of the ventricular contour. Thus frequent determinations of the ventricular size in an intact animal are possible with no major interference with ventricular function. The relationship between left ventricular end-diastolic pressure and area in the right anterior oblique position was studied in 6 dogs under morphine-pentobarbital anesthesia while heart rate and atrio-ventricular stimulus interval were maintained constant by driving with coupled pacemakers. A 35-mm. camera, synchronized through an electronic unit with the electrocardiogram recorded on the same videotape, was used to obtain single frame pictures at end-diastole. These pictures were projected, the left ventricular silhouette outlined and measured. Aortic pressure and cardiac output were modified by the step-wise infusion of Angiotensin II and Acetylcholine into the ascending aorta. Mean aortic pressures from 70-180 mm. Hg, cardiac output from 1.1-5.8 L./minute and end-diastolic pressures in the left ventricle from 0-20 cm. H_2O were obtained. Under these conditions, changes in the left ventricular area ranged from approximately +30 to -30% over the control values. An apparently linear correlation was found between the left ventricular end-diastolic pressure and area over the range obtained in these experiments. (Supported by Research Grants NIH HE-03532, AHA CI 10 and AHA CF9.)

TONOTOPIC ORGANIZATION IN AN AUDITORY BRAIN STEM NUCLEUS. Chiyeko Tsuchitani* and James C. Boudreau. U. S. Army Medical Research Laboratory, Ft. Knox, Ky.

The responses of more than 100 units, histologically localized in the S-segment or lateral nucleus of the superior olivary complex, were examined with pure tone stimuli in anesthetized cats. These units were typically without any spontaneous activity and were responsive to ipsilateral stimuli only. Sustained discharge was usually seen when continuous tones were presented. Measurement of response areas in terms of threshold of excitation to tones of different frequency yielded "tuning curves" similar to those reported for the eighth nerve and cochlear nucleus. Units were classified on the basis of the stimulus frequency to which they were most responsive. The location of the units was then determined histologically. Data collected from over 30 animals provides evidence of fairly exact tonotopic organization in the S-segment with the units in the ventral and dorsal tips being selectively responsive to extremely high and extremely low tones respectively. The intermediate frequencies are represented in an orderly and progressive arrangement that follows the curvature of the nucleus. An electrode penetrating through the three limbs of the structure in a ventral to dorsal direction would encounter units most responsive to tones above 20 kc in the ventral limb, units most responsive to tones between 15 and 9 kc in the intermediate limb and finally units unresponsive to tones above 5 kc in the dorsal limb.

EFFECT OF VENTROMEDIAL HYPOTHALAMIC LESIONS ON MOTIVATION AND LEARNING IN THE MOUSE[1]. S. G. Turner and J. A. Sechzer (intr. by W. Schindler). Dept. of Anatomy, Baylor University College of Medicine, Houston, Texas.

Recent studies have suggested that the ventromedial region of the hypothalamus might be concerned with functions other than satiation. To investigate the role of this region in learning and memory, the following study was carried out. Lesions in the ventromedial area of the hypothalamus were produced with goldthioglucose in one group of mice. A second group of mice was untreated and served as controls. Shock avoidance learning was carried out with both groups of animals in an electrified "Y" maze. To avoid shock the mouse had to move from the stem of the "Y" to the correct arm within 5 seconds. Training was continued daily until performance reached 90% for 3 days. Results indicate that the goldthioglucose lesioned group learned significantly faster than the control group. In the lesioned group, the emotional responses to shock such as "freezing", defecation and urination were observed to be markedly less than those of the control group. These results suggest that ventromedial lesions in the hypothalamus alter the emotionality of the animal and thus its motivation in the shock-avoidance situation.

1 Supported by USPHS Grants MH-10792-01 and GRS P-65-8

Medullary Evoked Vasodilatation and Blood Histamine Activity. Richard S. Tuttle, Masonic Medical Research Laboratory, Utica, New York.

An intense and potentially lethal hypotensive response may be evoked by stimulation of a localized area in the midline of the posterior medulla. The response is mediated over ganglionated pathways and potentiated by a decrease in vasoconstrictor tone. Pharmacologically, the active vasodilatation is potentiated by anti-cholinesterases and anti-diamineoxidases, and blocked by atropine and antihistaminics. Activation of cholinergic vasodilator pathways does not result in such an intense cardiovascular response nor do antihistaminics block cholinergic vasodilatation. Consequently, histamine was considered as a possible mediator. C^{14}-Histamine levels were determined by electrophoretic and isotopic techniques in the blood of cats chronically treated with C^{14}-Histidine. C^{14}-Histamine activity was shown to increase 3-4X during a hypotensive response. The medullary evoked hypotensive response was classified as an active cholinergic-histaminergic vasodilatation.

STATIC AND DYNAMIC CHARACTERISTICS OF ACTH ACTION ON THE PERFUSED CANINE ADRENAL. J. Urquhart, C.C. Li*, and W.L. Montgomery*, Departments of Physiology and Electrical Engineering, University of Pittsburgh, Pittsburgh, Pennsylvania.

Modelling of pituitary-adrenocortical control forces attention to the details of the relationship between blood ACTH concentration ([ACTH]) and cortisol secretion rate (F). This was studied in in situ perfused adrenals of acutely hypophysectomized dogs. The static gain of the adrenal cortex is logarithmically nonlinear and is adrenal blood flow (Q) dependent. At normal Q, 1-2 μU ACTH/ml blood elicits F typical of intact dogs, for at such [ACTH] the static gain of the gland is 0.5-1.5 μg F/min/μU ACTH/ml blood. Elevations in [ACTH] decrease adrenal static gain according to the logarithmic nonlinearity, but it appears that the intact control system normally operates in the high gain range of adrenocortical response to ACTH. As Q rises, however, static gain also rises and becomes more nearly linear, until maximal F, which is independent of Q, is attained. The time course of F after a step increase in the rate of ACTH presentation to the gland is a 2-3 min delay followed by a brisk but highly damped rise to a steady or oscillatory final value 5-7 min later. After ACTH is removed, F begins to fall after a 2-3 min delay and reaches a final value 10-15 min later. Aside from the time delay, adrenocortical dynamics are brisk compared with some other elements in the overall control system. Compensation for the adrenal's time delay, and for delays of hormonal transport by blood, is largely achieved by the slow dynamics of cortisol inactivation. Nevertheless, these time delays impose a finite limit, consistent with stability, on the as yet undetermined static gain (and thus the steady state accuracy) of the negative feedback regulation of plasma cortisol concentration. (Supported by grant # AM-07063 from NIH.)

SPECIES DIFFERENCES OF BLOOD VISCOSITY: ROLE OF CELL SIZE AND SUSPENDING MEDIUM. Shunichi Usami*, Shu Chien*, Robert J. Dellenback* and M.I. Gregersen. Columbia University, New York City.

Viscosity was determined on blood obtained from five mammalian species with different mean corpuscular volume (MCV): elephant 112 μ^3, man 87 μ^3, dog 72 μ^3, sheep 37 μ^3 and goat 18 μ^3. Samples of heparinized whole blood and cell suspensions in Ringer solution were prepared from each species with cell percentages varying from 0 to approximately 95%. Viscosity measurements were made in a coaxial cylinder viscometer (Gilinson, Dauwalter and Merrill, Trans. Soc. Rheol. 7:319, 1963) at a temperature of 37°C and shear rates ranging from 0.052 to 52 sec^{-1}. For each species studied the viscosity of whole blood as well as Ringer suspensions increased as cell percentage is raised and also as shear rate is reduced. At a given cell percentage, the viscosity of whole blood showed greater shear rate dependence and had higher values than that of the Ringer suspensions. For a given cell percentage (e.g. 45%) and shear rate (e.g. 0.052 sec^{-1}), a comparison of the viscosities of whole blood in the 5 species showed a direct correlation with MCV. When such comparison is made for the Ringer suspensions in these 5 species, however, only the elephant cell suspension showed a high viscosity and the other 4 species exhibited no significant differences. The data suggest that the species differences in viscosity are only partially related to the variations in MCV and that the nature of the suspending medium also plays an important role.

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THERMOREGULATION IN DESERT HEAT WITH RESPECT TO AGE. W. van Beaumont* (Spon. R. W. Bullard). Indiana University, Bloomington, Indiana.

The thermoregulatory responses of 10 men (age 21-73 yrs) and 31 boys (age 10-17 yrs) were studied during standardized work under desert conditions in Boulder City, Nevada. The standard afternoon walk of 1 hour was performed at a rate of 100 m/min. The daily maximum temperatures at Boulder City ranged from 34 to 43°C during the periods of observation in June and July 1964. The relative humidity was 95% of the time lower than 30%. Under these experimental conditions age proved not to be a limiting factor for the regulation of body temperature in the adults. The recorded rectal temperatures during 56 experiments varied from 38.0-38.9°C (mean: 38.5°C) and the rates of sweating varied from .370-.481 $l/m^2/hr$ (mean: .433 $l/m^2/hr$). Six of the boys attained rectal temperatures of 39.0-39.3°C, accompanied in two cases by signs of syncope. The rectal temperatures of these young males varied from 38.2-39.3°C with a mean value of 38.7°C and the rates of sweating varied from .400-.645 $l/m^2/hr$ (mean: .543 $l/m^2/hr$).

Four of the adults (age 21-73 yrs) walked one afternoon in Death Valley (California) at a temperature of 47.3°C. The times of exposure varied from 51 to 63 minutes. The limitations of thermoregulatory control were approached as indicated by the high rectal temperatures (39.4-39.7°C) and the rates of sweating (.780-.822 $l/m^2/hr$). No age related difference was noticed in the responses of the thermoregulatory systems of these 4 relatively fit men. (Supported by PHS grant CD 00056-01.)

THE EFFECT OF VARYING VENTRICULAR PERFORMANCE BY EXTRASYSTOLE POTENTIATION ON CLOSURE OF THE MITRAL VALVE. R. A. Vandenberg*, J. C. P. Williams*, P. Osypka*, D. E. Donald and E. H. Wood. Mayo Clinic and Mayo Graduate School of Medicine, Rochester, Minnesota.

Cardiac and aortic pressures were recorded without thoracotomy in dogs under anesthesia and intermittent positive pressure respiration, prepared by vagotomy and in some cases by stellate ganglionectomy and acute heart block produced by injection of the A-V node (Fed. Proc. 23: 413, 1964). Four to six milliliters of 69% Renovist were injected into the left ventricle while respiration was temporarily suspended. The resulting angiograms recorded on videotape were analyzed with a video-densitometer (Mayo Clinic Proc. 39:849, 1964) to detect and correlate with the phase of the cardiac cycle reflux of contrast medium into the left atrium. When the ventricles were driven regularly during atrial fibrillation induced by paired atrial stimuli and vagal stimulation, mild systolic reflux across the mitral valve was noted and tended to increase at slow rates and decrease at fast rates (regurgitant index 2-15% at 60 beats/minute; 1-7% at 140-160 beats/minute in 6 dogs). When ventricular contraction was potentiated, systolic pressure and stroke volume increased despite a lower left ventricular end-diastolic pressure and usually a shorter diastolic filling period and regurgitation became negligible at all heart rates. On termination of ventricular potentiation, systolic pressure became abnormally low before returning to control level and during this period regurgitant indexes exceeded control values. It is concluded that ventriculogenic closure of the mitral valve is improved when myocardial contractility is potentiated and impaired when contractility is depressed in the period immediately after cessation of extrasystolic potentiation compared to the control state. (Supported by Research Grants NIH HE-03532, NASA NsG-327, AHA CI 10 and NHF Aust.)

REGRESSION OF CARDIAC HYPERTROPHY FOLLOWING EXPOSURE TO HYPOXIA. Edward J. Van Liere, Barbara B. Krames* and Jeffrey M. Yost.* W. Va. Univ. Med. Center, Morgantown, W. Va.

Cardiac hypertrophy was established in Sprague-Dawley, male, adult rats (wt. from 175-200 gms.) by subjecting them to a simulated altitude of 24,000 feet (7,315 meters) for 8 hours each day (except Sundays) for a period of 4 weeks. At the end of that time the animals were sacrificed and the HW/BW ratios determined. The chambers of the heart were then partitioned and the ventricles weighed separately. The ratios of the ventricles to the body-weight were determined as well as the relation to each other. It was then determined how long cardiac hypertrophy persists following exposure to hypoxia. Rats in groups of from 5-10 were sacrificed at intervals of 5, 10, 15, and 20 days following exposure to hypoxia. It was found that regression of hypertrophy took place in both ventricles, although there was some indication that it was somewhat slower in the right ventricle. Regression in both ventricles was found to be essentially complete in 15-20 days. (Supported by a grant from the West Virginia Heart Association.)

LUNG, THORACIC AND TOTAL RESPIRATORY COMPLIANCES IN NORMAL MEN DURING VOLUNTARY RELAXATION AND NEUROMUSCULAR BLOCKADE. P. van Lith* and J. T. Sharp, V.A.H., Hines, Illinois.

Lung, thoracic and total respiratory compliances were measured supine in 32 cooperative, but not highly trained, normal men in the conscious relaxed state by the method of Heaf and Prime and repeated in the anesthetized paralyzed state. Total respiratory compliance averaged 0.095 $\pm$ 0.004 (S.E.) L/cm H_2O (range: 0.055 to 0.147) in the conscious relaxed state and 0.106 $\pm$ 0.005 (range: 0.057 to 0.186) in the paralyzed state. There was a poor though significant correlation between measurements made in the two states ($r = + 0.34$, $p < .01$). Contrary to the findings of Nims et al. (J. Clin. Invest. 34:744, 1955) the total respiratory system was more compliant in the paralyzed state than in the relaxed state in 22 of the 32 subjects. Total compliances by the two methods agreed within 10% in 8 subjects, within 20% in 16 subjects and within 30% in 24 subjects. Lung compliance averaged 0.198 $\pm$ 0.011, conscious, and 0.206 $\pm$ 0.017, paralyzed, and a poor but significant correlation was observed between relaxed and paralyzed values ($r = + 0.33$, $p < .01$). Thoracic compliance showed the greatest variation and the poorest correlation between conscious and paralyzed observations ($r = + .27$, $p < .05$), means for relaxed and paralyzed observations being 0.317 $\pm$ 0.030 and 0.312 $\pm$ 0.020, respectively. Thoracic and total respiratory compliance measured in the paralyzed state correlated better with vital capacity than relaxed observations. These data suggest that total respiratory and thoracic compliances measured during voluntary relaxation should be interpreted with caution in other than well trained subjects. Total respiratory compliances below 0.050 and thoracic compliances below 0.100 L/cm H_2O should probably be considered abnormal for adult men.

FUNCTIONAL SIMILARITIES BETWEEN AN INTRACYTOPLASMIC MELANIN-CONTAINING ORGANELLE AND MITOCHONDRIA. M.H. Van Woert*and G.C. Cotzias. Brookhaven National Laboratory, Upton, N.Y.

The cytoplasm of the melanocytes located in the liver of the amphibian Amphiuma is packed with large organelles containing melanin granules. In contrast to the hepatocytes, these melanocytes have few mitochondria and no visible ribosomes. Both mitochondria and the melanin-containing organelles were isolated from the Amphiuma liver by gradient centrifugation. Among the known functional properties of mitochondria, metal transport and some enzymatic activities were chosen for intercomparison of these two cytoplasmic inclusions. The melanin-containing organelles concentrated both stable and isotopic manganese in a manner similar to mitochondria. In addition, succinic oxidase and monoamine oxidase activities in the melanin bodies were equivalent to those located in the mitochondria. These studies indicate that some mitochondrial functions are localized in the large melanin-containing organelles of the melanocytes in Amphiuma liver.

USE OF ISOPROTERENOL AND PHENOXYBENZAMINE IN TREATMENT OF ENDOTOXIN SHOCK. James A. Vick (intr. by J. H. Wills). Directorate of Medical Research, USAEACRDL, Edgewood Arsenal, Md., 21010.

Five approaches to the treatment of endotoxin shock in the dog have been evaluated. The effect of endotoxin on physiological functions and survival was noted. Dogs treated with hydrocortisone, isoproterenol, or a combination of the two showed temporary improvement of the physiological functions monitored. Isoproterenol produced a remarkable increase in right ventricular pressure even as systemic blood pressure decreased. In contrast, hydrocortisone resulted in a fall in both right ventricular and systemic blood pressures. There were, however, no significant increases in survival with these forms of therapy. Treatment with phenoxybenzamine corrected systemic acidosis, increased right ventricular output and resulted in a 73 per cent survival. This occurred even as the arterial blood pressure was maintained at seemingly hypotensive levels. The most remarkable results in this study were obtained with a combination of phenoxybenzamine and isoproterenol. The vasodilation and hypotension produced by phenoxybenzamine appear to be attenuated by the cardio-stimulatory effect of isoproterenol. Thus, flow was maintained to vital tissues and systemic blood pressure was supported at more clinically acceptable levels. This form of combined therapy presents a possible solution to the objection to treating an already seriously hypotensive condition with an agent that further reduces blood pressure.

CIRCULATORY AND BLOOD GAS RESPONSES OF EXERCISING DOGS AT HIGH ALTITUDE. James A. Vogel* and John P. Hannon. USA Med Rsch & Nutr Lab., Denver, Colorado

The cardiovascular effects of exercise were studied in four chronically catheterized dogs initially at 5,200 ft. and subsequently every 5 days for a period of 26 days at 11,400 ft. Heart rate (HR), intra-arterial blood pressure (BP) and cardiac output ($\dot{Q}$) by dye dilution were measured at rest and during 45 minutes of treadmill exercise at an approximate $\dot{V}o_2$ of 50 ml/kg/min. Arterial and venous Po_2, Pco_2 and pH, temperature corrected, were measured at rest and at 15 minute intervals during exercise. $\dot{Q}$ was significantly elevated both at rest (28%) and during exercise (49%) on the first day at altitude and generally remained elevated during the entire stay. HR was unchanged while stroke volume increased proportionately to $\dot{Q}$. BP was elevated only during the first week at high altitude both at rest and during exercise. A significant fall in peripheral resistance was evident only on the first day at 11,400 ft. Pao_2 fell from 79 mm Hg at 5,200 ft. to 57 mm Hg after 1 day at 11,400 ft. at rest and from 77 to 59 mm Hg after 45 minutes of exercise. $P\bar{v}o_2$ did not change with altitude at rest from 40 mm Hg but decreased during exercise from 35 to 30 mm Hg. $Paco_2$ and $P\bar{v}co_2$ decreased about 5 mm Hg during the entire period at 11,400 ft. while pH increased approximately .02 - .04 units at rest and exercise on day 1 only. It is concluded that high altitude adaptation in dogs includes definite cardiovascular changes, including an increase in blood flow and perfusion pressure, with minimum changes in pH and Pco_2.

THE EFFECT OF INCREASED BRONCHIAL TONE ON ISOVOLUME PRESSURE FLOW CURVES. J.A. Waddell*, S. Permutt, B. Bromberger-Barnea and R.L. Riley. The Johns Hopkins University, Baltimore, Maryland

Previous work from this laboratory suggests (a) that the horizontal portion of expiratory isovolume pressure-flow curves where flow has reached a maximum ($\dot{V}max$) is dependent on the collapse of airways which then act as Starling resistors; and (b) that in the region of the initial slope of the curves the airways are wide open so that the reciprocal of the slope represents the resistance of the airways when there is no collapse. To investigate the effect of increased bronchial tone, isovolume pressure-flow curves were constructed for anesthetized open-chest dogs before and after giving subcutaneous Mecholyl. Mecholyl caused (1) a reversible fall in $\dot{V}max$; (2) no change in the initial slope of the pressure-flow curves; and (3) usually a decrease in the alveolar minus tracheal pressure at which $\dot{V}max$ was reached (Δ Pmax). These findings can be interpreted as follows:- (1) increased tone causes a fall in $\dot{V}max$ by increasing the tendency for airways to collapse, i.e. raising the transmural pressure at which collapse occurs (Ptm'); (2) if Ptm' increases in all parallel units, Δ Pmax falls, but if some airways have no change in Ptm', Δ Pmax remains unaltered; (3) at low flows where collapse has not occurred increased tone has little effect on resistance. Because smooth muscle tone increases the tendency for airways to collapse, the alterations in pressure-flow characteristics are most apparent at low lung volumes and at high expiratory effort and least apparent at high lung volumes and low expiratory effort.

VASCULAR RESPONSES FOLLOWING RELEASE OF VENOUS OCCLUSION. R.L.Walker*[1] and Ian F.S.Mackay. Dept.of Physiology, The Medical School, San Juan, Puerto Rico and 1.Dept.of Anesthesiology, Jackson Memorial Hospital, Miami, Fla.

Plethysmographic blood flow records following the release of venous occlusion of the forearm showed a biphasic vascular response which was first vasodilator and then vasoconstrictor. Vasodilator Phase; Our results suggested that this was due to two factors: (a) Physical distension increasing the calibre of the blood vessels. (b) The accumulation of 'vasodilator material' due to a reduction in the effective arterio-venous pressure gradient. Vasoconstrictor Phase; From our findings it was considered likely that the major factor responsible for this fall in blood flow below the preocclusion level was a myogenic response to the increase in vascular wall tension. It occurred when this increase in tension was produced by either venous occlusion or by exposure of the forearm to negative pressure. Both the vasodilator and the vasoconstrictor responses became more pronounced when the venous occluding pressure was increased or the period of venous occlusion was prolonged, the vasoconstriction requiring a longer period of venous occlusion for development of a maximal effect than the vasodilatation. The vasoconstrictor effect remained for a constant period of time independent of blood flow through the forearm. The accumulation of perivascular edema or an over-removal of 'vasodilator material' were considered unlikely causes of the vasoconstrictor effect.

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STRUCTURAL MODEL FOR SPREAD OF EXCITATION FROM SARCOLEMMA TO T SYSTEM AND SARCOPLASMIC RETICULUM. S. M. Walker and G. R. Schrodt. Depts. of Physiology and Pathology, University of Louisville School of Medicine, Louisville, Kentucky.

The spread of current from one membrane to another is enhanced by structural continuity between these membranes. It is further enhanced by absence of cytoplasm at points of continuity between these membranes. Electron micrographs show that the sarcolemma invaginates near the A-I junction to form continuities with the membranous walls of the transverse system (T) in rat skeletal muscle fibers. The walls of T are connected with the terminal segments of the sarcoplasmic reticulum (R) by membrane-like structures. The periodicity of the connections between T and R is usually about 150 Å. At the points of connection the distance between the apposed membranes of T and R is about 60 Å. At the interspaces between points of connection the distance between apposed membranes of T and R is about 100 Å. These variations in distance between T and R account for the scalloped appearance of the R membrane facing T. Apparently the interspaces are completely surrounded by membrane-like structures and the apposed membranes of T and R. Hence, the interspaces do not seem to be continuous with the sarcoplasm. If there is no continuity between the interspaces and the sarcoplasm, a physiological "tight junction" exists between T and R. The structural model described here would permit impulse conduction to T and facilitate electrotonic spread of current from T to R. It is suggested that current spread to R plays a role in release of Ca^{++} from R. In turn, Ca^{++} initiates contraction of the myofibrils. Anatomical tight junctions between T and R are not seen in electron micrographs of rat skeletal muscle fibers. Aided by NSF Grant GB-2009 and NIH Grant NB 05444-01.

EFFECTS OF OUABAIN ON CORTICAL CONTENT AND TUBULAR TRANSPORT OF CATIONS. M. Walser and V.E. Nahmod*, Johns Hopkins Univ. Sch. of Med., Baltimore, Md.

Cardiac glycosides promote transcellular ion transport in small doses and inhibit in larger doses. When infused into one renal artery in anesthetized dogs at 5 μg/kg/min for 20 minutes ouabain increases excreted/filtered Na, K, Cs^{137}, Mg, Ca, and Sr^{85} on the infused side but decreases these clearances on the contralateral side. At 10 μg/kg/min, increases are usually seen bilaterally. Changes are most marked for Na and Cs^{137} and least marked for K. Analysis of renal cortex at the end of 20 minutes shows the following statistically significant changes at the smaller dose: on the infused side, Na, +20 mM/kg; K, -28 mM/kg; Ca, +.5 mM/kg; Mg, -1.1 mM/kg. The contralateral kidney, where transport is stimulated, exhibits minor changes in the same direction. At the larger dose, the infused side shows even larger changes: Na, +25 mM/kg; K, -35 mM/kg; Ca, +1.4 mM/kg; Mg -1.3 mM/kg; and significant though smaller changes are seen in the opposite kidney. Even after 5 minutes infusion at 10 μg/kg/min, significant gain of Na (+9 mM/kg) and loss of K (-14 mM/kg) occurs in the infused kidney.

Thus the biphasic effect of this agent on transcellular ion transport is not reflected in cortical composition: Mg and K are partially replaced by Ca and Na, suggesting that cation extrusion from cells is inhibited at all dose levels studied.

COMPARISON OF BEAT-BY-BEAT ESTIMATES OF STROKE VOLUME FROM AORTIC PRESSURE WITH FLOWMETER ESTIMATES. H.R.Warner and W.Rutchquser, Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S.Hosp., Salt Lake City, Utah, and Mayo Foundation, Rochester, Minn. Supported by a grant from the American Heart Assoc.

A modification of the method of Warner, et al (J. Applied Physiol. 5:495, 1953) for beat-by-beat estimation of stroke volume from a recording of central arterial pressure has been developed which permits continuous calculation in real-time of stroke volume, heart rate, mean pressure, cardiac output and resistance directly from the output of the pressure transducer. An analog to digital convertor samples the presure signal at 200 conversions per second into a digital computer. The pattern recognition and calculation is completed within 10 milliseconds after the end of each heart cycle and the 5 derived variables converted back to voltages on 5 analog channels for continuous recording of their time course. Beat-by-beat comparison of such stroke volume estimates against estimates based on integration of the output of an electromagnetic flowmeter around the aorta shows a correlation of .92 to .97 under conditions of rest, exercise and infusion of atropine, norepinephrine and aramine. The method requires calibration against an independent determination of cardiac output once for each subject in order to give absolute values. Generally this is not done, however, since the method is most useful in following relative changes in these variables.

ANALYSIS OF "PACEMAKER" ACTIVITY IN AN IDENTIFIABLE BURST GENERATING NEURON IN APLYSIA. R. Waziri*, W. Frazier* and E. R. Kandel (intr. by W. J. Sullivan). Harvard Med. Sch., Boston, Mass.

One of the identifiable bursting cells in the left upp. quad. (dors. surf.) of the abd. gangl. was examined with two intracellular pipettes. This cell receives input from an inhibitory interneuron (IN-I) which modulates its burst activity. When IN-I is impaled and hyperpolarized, the modulating effect is removed but burst generation continues. Direct hyperpol. of the bursting cell fails to reveal other significant PSPs and direct pulses reset the rhythm suggesting that the pacemaker rhythm is probably endogenous (Strumwasser, 1963). Bursts are followed by a hyperpolarization which decays with time. This decay constitutes the "pacemaker" depolarization (PD); as it brings the membrane voltage to threshold a new burst is triggered. The hyperpolarization has the properties of an after potential; its amplitude and duration are functions of the number of spikes in the burst. Slope conductance during the PD is about two times higher at maximum hyperpolarization than just prior to burst onset. This conductance change is in part voltage dependent and anomalously rectifying, increasing with hyperpolarization and decreasing with depolarization (Tauc and Kandel, 1964; Nelson and Frank, 1965). As in snail neurons (Ochs and Frank, 1965), this anomalously rectifying conductance is altered by changes in $(K^+)_{ext}$. From these findings it appears that the properties of the PD in this neuron may be similar to the PD of Purkinje muscle fibers (Trautwein and Kasselbaum, 1961). It may represent a time and voltage dependent decrease of the high K^+ condutance which was turned on by the post-burst hyperpolarization.

ACTIVITY OF SULFUR AND SELENIUM ISOLOGS OF ACETYLHOMOCHOLINE AND HOMOCHOLINE ON THE ELECTROPLAX. George D. Webb and Henry G. Mautner (intr. by David Nachmansohn). Depts. of Neurol. and Biochem., Coll. Phys. & Surgeons, Columbia University, New York, N.Y. and Dept. of Pharmacol., Yale University School of Medicine, New Haven, Conn.

The action of the chalcogenic isologs of acetylcholine and choline on the monocellular electroplax of Electrophorus electricus have been described (Mautner, Bartels, and Webb, Fed. Proc. 24:611 (1965)). In the present investigation the three carbon analogs of these same compounds exhibited similar actions, although they were often more potent depolarizers than the corresponding two carbon compounds. This is consistent with the speculation that the membrane receptor for depolarization may possess a "hydrophobic bonding site". A significant difference in the two series was the finding that homocholine is far more potent in depolarizing the innervated membrane of the electroplax than is choline, whereas acetylhomocholine (in the presence of eserine) is much less potent than acetylcholine. This further demonstrates the highly specific inactivity of choline as opposed to the higher activity of most other quaternary nitrogen compounds. (Supported by grants from the NSF, USPHS, and the Muscular Dystrophy Associations of America, Inc.)

Calibration and Zero (0) Flow of Electromagnetic Flowmeter Probes on Pulmonary Artery (P.A.) and Aorta (Ao.). K. C. Weber,* J. C. Engle,* G. W. Lyons,* A. J. Madsen,* and I. J. Fox, Department of Physiology, University of Minnesota, Minneapolis, Minnesota.

Flowmeter probes (Electromagnetic Probe Co., Olmsted meter)were chronically implanted on the P.A. in 10 and Ao. in 5 dogs. In 1-2 weeks, under nembutal anesthesia, cardiac output (C. O.) was varied by variable distention of a balloon catheter in the inferior cava and measured both by flowmeter signal and by arterial dilution curves recorded after dye injections into the right ventricular outflow tract (Ao. probes) or into the distal P.A. (P. A.probes). A track-and-hold feedback circuit (Warner, H.R., Unpublished data) held the diastolic part of the flowmeter signal at a preselected 0 point (mean diastolic level of a noise-free, control flow signal). The intercept (a) and its associated standard error (S. E.a) were computed from the regression equations for all 16 P.A. probe series consisting of from 6 to 16 dye-flowmeter comparisons each in which flow was varied an average of 3.1 fold (Range: 1. 3 - 8.6 fold). The mean (a/S.E. a) ratio for all series was not significantly different from 0 (-0.19 ± 0.37). In 10 similar Ao. probe series of 7 to 9 comparisons each in which flow was varied an average of 3.0 fold (Range: 1.7 to 4.2 fold) the corresponding average ratio was significantly less than 0,(-1.05 ± 0.26). Thus, while the mean diastolic level of the flow signal represents 0 flow for P.A. probes, it underestimates 0 for Ao. probes, by 10.0% (Range: 3-26%) at control flow, with the error increasing progressively as C. O. approaches 0 due to the presence of coronary flow. (Supported by USPHS Grant HE 08373).

THE DETERMINANTS OF LEFT VENTRICULAR ISOVOLUMETRIC CONTRACTION TIME Stanley Wegner*, Clarence M. Agress, Eugene H. Lehman, Jr.*, Cedars of Lebanon Hospital Los Angeles, California

The factors controlling the duration of left ventricular isovolumetric contraction classically are considered to be aortic diastolic pressure and rapidity of intraventricular pressure change in dogs. In this study, an examination was made of the relative importance of these parameters as well as heart rate on the duration of isovolumetric contraction by means of linear and quadratic regression analyses. It was found that the isovolumetric contraction interval is virtually independent of both heart rate and the aortic diastolic pressure level but is inversely dependent on the rates of change of intraventricular pressure. It was concluded that measurement of this interval provides a direct index of the rapidity of change of left ventricular tension.

MECHANISM OF CORTICOSTEROID REVERSAL OF FATAL SHOCK AFTER BLOOD LOSS. Max H. Weil, Howard Whigham,* and E. P. Marbach.* Dept. of Medicine, Univ. of Southern California School of Medicine, Los Angeles, California.

Pharmacological amounts of corticosteroid effectively improve survival in experimental hemorrhagic shock in the rat. We have described methods of metabolic and hemodynamic study of paraldehyde sedated Wistar rats during the course of hemorrhagic shock induced by bleeding into a reservoir maintained at 30 mm Hg for 240 minutes. Two hours after reinfusion, mean intra-arterial pressure was increased to 77 mm Hg, but oxygen uptake (60 cc per hour, 40% of normal), pH (7.23 units), bicarbonate (14 mEq/L) and hematocrit (50.9 vol %) were all essentially unchanged. After injection of 8 mg/kg dexamethasone at completion of the bleeding period, oxygen uptake during the next 2 hours was increased to 104 cc per hour, blood pressure to 101, pH to 7.31, bicarbonate to 19, and hematocrit returned to its control value. Blood lactates remained at levels above 4 mM in both control and treated animals. All control animals died within 72 hours, but all corticosteroid treated animals survived. In patients in circulatory shock, dexamethasone increases cardiac output and decreases peripheral resistance (Circulation 31: 523, 1965). The present experiment corroborates that in late shock the increases in oxygen uptake and arterial pressure, and reversal of metabolic acidosis result from increase in effective blood flow brought about by the action of the corticosteroid. Supported by grants from USPHS and The John A. Hartford Foundation, Inc.

Collagen Content and Stiffness of Denervated Mammalian Skeletal Muscle. T. G. Weilepp, Jr. and W. C. Stolov (intr. by J. J. Faber). Department of Physical Medicine and Rehabilitation, University of Washington, Seattle, Washington.

The identity of the predominant passive tension-carrying structures in skeletal muscle is incompletely known. It is unclear whether the non-linearity of major portions of the passive length-tension relationship (L-T diagram) arises from structural inhomogeneity at the cell organelle or the macromolecular level. Since rat tendon collagen has a linear elastic constant ($\Delta T/\Delta L$) it was thought that the near-linear portion of the L-T diagram might be determined by total collagen cross-section. Therefore, $\Delta T/\Delta L$ was measured on an isometric myograph for normal and denervated rat gastronemius muscles in the 300-500 g tension region, the near-linear portion of their L-T diagram. The collagen content of the whole muscle (origin to insertion including tendon) was estimated by determining the hydroxyproline content. The results showed that although denervation atrophy increased the elastic constant, total collagen fell to less than normal quantities. Hence, either collagen was not the predominant tension carrying element in the near-linear region of the passive L-T diagram or alternatively the collagen remaining after denervation atrophy became stiffer due to alterations at a macromolecular level.
Supported by PHS grant AM08818 and in part by OVR grant R&T 3.

A CONSERVATIVE MODEL OF THE SYSTEMIC CIRCULATION. **H. Weinstein, J.S. Ultman, S. Lochaya and A.B. Shaffer. (intr. by L.N. Katz). Dept. of Chemical Engineering, Illinois Institute of Technology and Cardiovascular Inst., Michael Reese Hospital and Medical Center, Chicago, Illinois.**

Measurements of the dispersion of indicator through the systemic circulation of the dog form the basis of this study. Indicator dilution curves were obtained by means of injection of indicator into various locations in the aorta and its branches with sampling in the pulmonary artery, as well as injection into the pulmonary artery with sampling in the aorta. The entire primary response curve to injection in the aorta was predicted by an extrapolation method, utilizing an analog model for dispersion of tracer in flowing fluid, which is more suitable for the conditions under study then is the Stewart-Hamilton technique. This model of the circulation has one path from the right heart to the left and three parallel paths from the aorta back to the right heart. Each path contains, in series, several perfect mixers and a perfect time delay. The model was fitted to the experimental data and the results were consistent with the conservation of indicator. The model parameter values obtained yield mean transit time and, with certain assumptions, the volume of each path.

CIRCULATORY RESPONSES TO NOREPINEPHRINE AFTER PROLONGED TREATMENT WITH CHLOROTHIAZIDE. M.G. Wendling*, J.W. Eckstein and F.M. Abboud. Univ. of Iowa College of Med., Iowa City, Iowa.

Dogs treated for 1 week with chlorothiazide have higher cardiac outputs and heart rates during infusion of norepinephrine than do untreated dogs (J.C.I. 41:1578). It has been suggested that these responses might be altered by longer treatment. Seventeen dogs were caged 5 weeks; 9 received chlorothiazide, 50 mg/kg/day; 8 were untreated. Initially serum Na, K and Cl averaged 151.9, 5.14 and 116.4 mEq/L respectively; corresponding values after 5 weeks of chlorothiazide were 150.2 ($p<0.05$), 4.55 ($p<0.05$) and 114.1 ($p<0.05$) mEq/L. In treated animals average hematocrit increased from 44.2 to 49.3% ($p<0.05$) and average body weight decreased from 15.4 to 14.5 kg ($p<0.05$) in 5 weeks. Na, K, Cl, hematocrit and body weight did not change in untreated dogs. On the 35th day, the dogs were anesthetized with chloralose. Cardiac output, heart rate and mean arterial pressure were measured at the end of 4-min intravenous infusions of graded doses of norepinephrine (0.1, 0.2, 0.4 µg/kg/min). Cardiac output averaged 1.9 L/min during norepinephrine infusions in treated dogs and 1.4 L/min in untreated animals ($p<0.01$). Corresponding average values for heart rate were 96 and 71 beats/min, respectively ($p<0.01$). Mean arterial pressure averaged 134 in untreated and 133 mm Hg in treated dogs during the infusions ($p>0.05$). Norepinephrine infusions repeated after treatment with hexamethonium, 5 mg/kg, were accompanied by hemodynamic responses which were similar in both groups. The results suggest that the altered circulatory responses to norepinephrine induced by chlorothiazide are similar following 1 and 5 weeks of treatment. In these experiments, chlorothiazide appears to reduce the sensitivity of cardioregulatory reflexes. (Supported by PHS grant HE-02644 and a grant from the American Heart Association.)

THE RAT AS A MODEL FOR STUDY OF HEMORRHAGIC SHOCK.
Howard Whigham,* Max H. Weil, E. P. Marbach,* and J. R. Colgan.*
Dept. of Medicine, Univ. of Southern California School of Medicine, Los Angeles, California.

A standardized method for producing hemorrhagic shock in the rat pinpoints hemodynamic and metabolic defects. In male Wistar rats weighing 360 grams, sedated with intraperitoneal injections of paraldehyde or pentobarbital, a femoral artery was cannulated for intermittent pressure measurement and also connected to a reservoir maintained at 30 mm Hg. An average of 9.5 ml were bled into the reservoir. Blood was reinfused after 240 minutes. Since cross transfusions of 10 ml of donor blood in 15 pairs of unselected rats resulted in no detectable illness, samples of arterial blood removed for measurement of pH and bicarbonate by the Astrup microtechnique, the hematocrit by microcapillary method, and blood lactate and pyruvate by techniques described at the spring meeting (Fed. Proc. 24: 341, 1965) were replaced by equivalent amounts of donor blood. Oxygen uptake was measured with a gas tight, oxygen filled glass chamber connected to a miniature recording spirometer with provision for CO_2 absorption and temperature control. Following hemorrhage in a typical group of 5 paraldehyde sedated animals, oxygen uptake was reduced from 155 to 60 cc/hr, pH from 7.36 to 7.19, bicarbonate from 23 to 14 mEq/L, and hematocrit was increased from 40.2 to 50.8 vol %. In the 2-hour period following reinfusion, the mean arterial pressure was elevated to 77 mm, but there were no significant increases in oxygen consumption, pH, bicarbonate, and hematocrit. All animals died 12 to 72 hours later. This technique is uniquely suited for controlled studies on hemorrhagic shock.
Supported by grants from USPHS and The John A. Hartford Foundation.

TRANSPLANTATION OF THE ISOLATED CANINE BRAIN.
R.J.White,M.D.,Ph.D. M.S.Albin,*M.D.,M.Sc.(Anes.),G.Locke,*M.B.,E.Davidson,*M.D. Section of Neurosurgery, Cleveland Metropolitan General Hospital and Western Reserve University Medical School, Cleveland, Ohio.

In these experiments the canine brain is surgically isolated by removing all contigous tissue except portions of skull, and is perfused exclusively by the carotid circulation. This requires the fashioning of vascular loops by preserving the internal carotid and internal maxillary arteries and their anastomotic linkage while simultaneously destroying all other branches of the external carotid systems. Cerebral venous return is provided by a specially designed torcular cannula after the vertebral venous sinuses are occluded with celloidin. The posterior circulation (anterior spinal-vertebral arteries) is closed and neurogenic and osteogenic separation accomplished at C_2. At environmentally produced brain temperatures of 32°C. or lower, the isolated brain is vascularly separated, weighed, immersed in antibiotic solution and transplanted to a skin pouch in the neck of a large recipient dog within 6 minutes. Vascular continuity is effected by interposing the brain graft between the carotid-jugular system of the recipient. The status of the brain graft is continuously monitored via extradural EEG electrodes and a thermoprobe. Cerebral blood flow is measured with an implantable electromagnetic flow meter probe positioned on the recipient's carotid artery. O_2 and glucose consumption, CO_2, lactate and pyruvate production by brain are discontinuously measured utilizing small externalized catheters connected to the cerebral arterial and venous systems. In the anticoagulated state, brain grafts have demonstrated excellent function for as long as 3 days, utilizing electrical and metabolic criteria of viability. Supported by NIH Grants NB 03859-03 and NB 03859-S2 .

POSSIBLE DISTRIBUTIONS OF VENTILATION AND PERFUSION IN THE HUMAN LUNG, AS RELATED TO ARTERIAL NITROGEN TENSIONS. F. Wiener*, C. Hatzfeld*, W.A. Briscoe. IBM ASDD, Yorktown Heights, N.Y. and Columbia University Department of Medicine, Bellevue Hospital, New York City.

Studies on patients with various pulmonary disorders have been analyzed by a conceptual model of the lung made up of three groups of alveoli. Each group has a different ventilation perfusion (V/Q) ratio. In each, diffusion of O_2, CO_2, and N_2 proceeds to equilibrium as expressed by R.H. Shepard's formulation of the dissociation curves. The model must also satisfy equations for mass balance in each compartment and equations defining the parameters of the total system. Measurements include arterial O_2 and CO_2 concentrations, and the composition of inspired and expired gas. Ventilation of the "slow" space is obtained from N_2 washout data and the O_2 a-v difference is assumed. Arterial and venous N_2 tensions are taken to be equal. For a given level of arterial N_2 tension (PaN_2) only one distribution of ventilation and perfusion is compatible with the measured and assumed data. As illustrated in the PN_2-PCO_2 diagram, small variations in PaN_2 are associated with considerable changes in the V/Q ratios of the compartments. The range of PaN_2 for all possible V/Q distributions was found to be narrow. At the lower limit of this range, the model reduces to an essentially homogeneous lung, the slow space behaving nearly as a shunt, and the best ventilated compartment becoming part of the dead space. At the upper limit, V/Q of the slow space becomes identical with that of one of the other two compartments. Any solution in which the three V/Q ratios are different must have PaN_2 between these limits. Furthermore, as additional compartments are introduced, progressing towards a continuous distribution of V/Q ratios, PaN_2 must remain within these same limits.

EFFECTS OF IONS ON TRANSMEMBRANE POTENTIALS OF THYROID CELLS. J.A. Williams (intr. by J.W. Woodbury). Dept. of Physiology and Biophysics, Univ. of Washington, Seattle, Wash.

Effects of K^+, Na^+, Cl^-, and I^- on transmembrane potentials of perfused rabbit thyroid gland cells were measured. The thyroid and larynx were selectively perfused through their own vasculature with Tyrode's Solution modified by the addition of dissolved hemoglobin. Normal resting potential is -43.4 ± 0.3mV (S.E.). In some studies rabbits were pretreated with propylthiouracil for ten days; the resting potential was reduced to -38 ± 0.4mV. An increase in concentration of K^+ in the perfusion fluid depolarized the membrane rapidly and reversibly. When $[K^+]_o$ was $>$ 5mM the membrane potential varied linearly with the log $[K^+]_o$, the slope being 30mV per ten-fold change. Extrapolation of this line to zero voltage predicts that $[K^+]_i$ is 160mM/L. Lowering $[Na^+]_o$ transiently hyperpolarizes the membrane followed by an exponential depolarization (time constant 20 min.) to a new level. When $[Na^+]_o$ was reduced from 147 to 12mM, the transient hyperpolarization was $2.7\pm.6$mV and the maintained depolarization $9.1\pm.7$mV. When Cl^- was replaced by $SO_4^=$ the membrane depolarized slightly. When Cl^- or $SO_4^=$ was replaced by I^- the membrane hyperpolarized. In both cases the membrane potential increased linearly with the log of $[I^-]$ with slopes of 6.5 and 9 mV per ten-fold change respectively. This indicates that at least part of the thyroid cell membrane is highly permeable to I^- as compared with Cl^-. These ion effects do not appear to be consistent with the predictions based on independence of ion movements. (Supported in part by grants NB 01752 and 5T5 GM-22-08 from the National Institutes of Health.)

DETERMINANTS OF ATRIAL CONTRACTILE FORCE IN THE INTACT HEART. John F. Williams, Jr.*, Edmund H. Sonnenblick, and Eugene Braunwald. Cardiology Branch, National Heart Institute, Bethesda, Maryland.

In order to identify the determinants of atrial contractile force, a specially designed strain gauge arch was sutured to the atria of open-chest dogs. Following correction for differences in muscle mass, the resting and active length-tension curves, as well as the maximum forces developed by the atria were found to be similar to those of the ventricles. Maximum active tension ranged from 2.5 to 5.5 g/mm^2 at muscle lengths which exceeded initial lengths by 50% to 60%. Increasing heart rate by atrial stimulation from 150 to 240/min had no significant effect on atrial force, while isoproterenol, calcium, and acetylstrophanthidin all markedly augmented force. Sympathetic stimulation, produced by left stellate stimulation, increased atrial force by 31 $\pm$ 4% (SE) while bilateral carotid occlusion increased atrial force by 21 $\pm$ 3%. Direct vagal stimulation, or carotid arterial hypertension produced by balloon inflation in the thoracic aorta, lowered atrial force. While vagotomy did not alter the augmentation produced by carotid occlusion, it reduced the depression of force resulting from carotid hypertension by an average of 43%. Both atria were depressed more by stimulation of the right vagus nerve than of the left, and the force of the right atrium was reduced approximately twice as much as the left when either vagus nerve was stimulated. This study demonstrates the interrelations between mechanical, nervous and humoral factors in the control of atrial contractile force, and indicates that a purely passive role should not be attributed to these chambers. The ability to alter the force of atrial contraction may represent another mechanism which permits the heart to adapt to conditions requiring a change in cardiac performance.

PROPERTIES OF INTERNEURONS OF THE SPINAL CORD VENTRAL HORN. Wm. D. Willis, Jr. and Jean C. Willis.* Dept. of Anatomy, Univ. of Texas Southwestern Med. Sch., Dallas, Tex.

Interneurons of the ventral horn of the cat spinal cord have been studied by intra- and extracellular recording. The positions of many of the units were identified histologically by a marking technique. At least two categories of interneurons were found, Renshaw cells and "proprioneurons." The Renshaw cells were located in the ventral part of Rexed's lamina VII, while the proprioneurons were often found to be in lamina VIII.

IMMUNOCHEMICAL PROPERTIES OF HISTONES. R.H. Wilson, V. Jurevics*, R. Delaney*, and A. Schram*. V.A. Hospital and Univ. of Tex. Southwestern Medical School, Dallas, Texas.

The question concerning the immunochemical properties of the histones has not been answered. Kunkel reported some positive and some negative CF reactions between histones and the sera of patients with lupus erythematosus (L E). Black reported histone antibodies. On the other hand Blix reported that rabbit histone antisera contained no antibodies against the histones. Six New Zealand white rabbits were immunized with 91 mg of freshly prepared calf thymus histones in CFA 1:1. Eleven rabbits were immunized with 49.7 mg of calf thymus DNAP in CFA 1:1, and six rabbits were immunized against DNA to provide antisera for studies of the antigenic and haptenic properties of the histones, and also cross-reaction controls. Amino acid and immunoelectrophoresis analysis revealed no detectable traces of other proteins in the histone preparation. The molecular weight of the histones was 14,000. Sera from 10 patients with a confirmed diagnosis of L E were also studied for histone reactions. The histone antisera from the rabbits were tested with the CF, Ouchterlony, PCA, precipitin and Arthus procedures. In no instance were antibodies found against the histones with any of the tests utilized. All of the lupus sera in all of the tests revealed negative reactions with the histones. It is concluded that the histones were not antigenic in this experimental design.

RESPIRATORY RESPONSES TO CO_2 ADMINISTRATION AT DIFFERENT VOLUMES OF THE LUNG. Sabbo Woldring* and Guy Owens, Roswell Park Memorial Institute, Buffalo, New York.

In anesthetized cats arterial p CO_2 has been varied to different values between 20 and 55 mm Hg by administration of CO_2 to the inhaled air. The volume of the lungs was changed to values varying from 20 ml below to 100 ml above functional residual volume by reducing or increasing the pressure of the respired air. Respiratory activity was measured from the minute volume of breathing and from the integrated electrical activity of diaphragm and abdominal muscles.

If the respiratory responses to administration of CO_2 and pressure breathing are plotted as a function of p_aCO_2, a family of curves is obtained that show the relationship between respiratory activity and p_aCO_2, with lung volume as independent parameter. The slope of these curves gradually decreases with increasing p_aCO_2. Minute volume and inspiratory activity reach higher values with decreasing volume of the lungs. Expiratory activity is variable. In most experiments expiratory activity appeared to be determined by lung volume changes only; in a minority of cases a dependence on p_aCO_2 was found however.

Electrophysiological correlates of cell division in frog eggs. D. Woodward* (intro. by J. B. Ranck Jr.) Dept. Physiol., U. of Mich., Ann Arbor, Mich.

Transmembrane potential, resistance, and capacity were measured in eggs of Rana pipiens during the first three divisions. The intracellular potential becomes more negative coincident with the growth of the first furrow changing typically from a steady -20 mv. to a maximum of about -50 mv. The potential falls somewhat after 1st division and then reaches a relative maximum negativity at the appearance of each new furrow. These changes occur in a Ringers solution isotonic to frog skeletal muscle and in 10 and 20% Ringers. The absolute value of the peak negative potential increased in 0 mM K, decreased in 20 mM K, and remained unchanged when Cl was substituted by SO_4. A depolarization at division occurred in 120 mM K. Before the first division membrane time constants are between 30 and 200 msec. A fall in resistance sometimes to as little as 10% of the value before first division is always observed during the early stages of the 1st furrow. The total membrane capacity decreased about 15% after two divisions in 10 and 20% Ringers but increased about 50% in full Ringers. Cleavage is inhibited after 3 to 5 divisions in full Ringers but continues normally in 10 and 20% Ringers. A high resistance between daughter cells has not been found.

Supported by U.S.P.H.S. Grants NB04352, 5T1GM353, and GM-18,986

BRAIN POTENTIAL SHIFTS WITH RESPIRATORY ACIDOSIS. Charles D. Woody,* Wade H. Marshall, Laboratory of Neurophysiology, NIMH-NINDB, Bethesda, Md.

Various data concerning "steady potential" shifts in brain arousal, stages of sleep, etc., suggested the advisability of further observations on shifts of these values as a function of CO_2 changes as pointed up by Tschirgi and colleagues. Preliminary experiments done at Institute Marey with Albe-Fessard and colleagues showed that it was possible to observe negative or positive shifts of cat brain to an extracranial electrode. It was also observed that there was little potential gradient as the electrode was pushed through the brain. The experiments have been continued and show that in rabbit the brain characteristically shifts monophasically positive, with an approximately linear function of voltage vs. alveolar CO_2, confirming Tschirgi et al. The cat shift is complex, characteristically negative for 10% CO_2, and shows a negative-positive trend for higher CO_2 values. There are no significant gradients throughout the brain, including readings from inside ventricles or cisterna. Deteriorated preparations and questionable stray reference lead effects tend to produce positive shifts. Nembutal and chlorolose anaesthesia were used; increasing depth of anaesthesia showed no characteristic change except some evidence of a decrease in amplitude of shifts.

AUDITORY CORTEX OF PUMA. Clinton N. Woolsey, Samuel Middleton*, Hugo O. Adrían,* and Wladimiro Lifschitz*. Instituto de Fisiologia, Universidad de Chile, Santiago, Chile, and Laboratory of Neurophysiology, University of Wisconsin, Madison, Wisconsin.

Auditory cortex was studied electrophysiologically in two 4 month old Chilean and two 1-1/2 year old North American pumas. In one, the total auditory area as defined by responses to 50 msec bursts of white noise was determined. In a second, we undertook to define the cortical potential field in response to white noise delivered to the ipsilateral ear after destruction of the contralateral cochlea. In a third, the areas responsive to high and low frequencies (20 kc and 1 kc) were determined, the latter at 3 different intensity levels (5, 20 and 35 db above threshold), to observe the spread of activity with increasing stimulus strength. In addition "cortical audiograms" were taken at 19 cortical sites, mainly in what should be area AI, in the two Chilean pumas. These audiograms were made by introducing pure tones by means of plastic tubing into the external auditory canal and determining for each frequency (0.2 kc to 49 kc) the intensity required to elicit an evoked response at each cortical site studied. With some minor differences the fissuration of the puma brain resembles that of the cat brain. The extent of the auditory response area likewise is similar, as is also frequency localization. The form of the evoked response is somewhat simpler than in the cat, since the initial negativity so common in AI of the cat is largely absent. (Supported by NIH grants NB-03640 and NB-03641).

CHANGES IN BODY MASS AND IN FOOD INTAKE OF LABYRINTHECTOMIZED FEMALE HAMSTERS DURING CHRONIC CENTRIFUGATION AT 4 AND 5 G'S. C. C. Wunder, B. Milojevic*, and L. Eberly*, University of Iowa, Iowa City.

The extent to which the above changes in normal centrifuged animals are attributable to rotational inner-ear stimulation has been unknown. This study, with Meso cricetus auratus first exposed at 97 rpm. when 5 weeks of age, indicates the major effects to be direct gravitational ones. Conditions were similar to those for Am. J. Physiol. 202: 461, 1962. Two weeks before exposure, labyrinthectomies were performed by combined aspiration and streptomyacin application through surgically perferated oval windows. When exposed to survivable centrifugation, growing warm-blooded animals first decrease in body mass and in food intake. Some recovery follows, but growth generally ceases at smaller size and younger age than normal (as reviewed in Int. Rev. Gen. Exp. Zool., 1:384, 1964). In the present study after 4 days exposure, average body mass loss was 12 ± 1 gm, cumulative food intake being 27 ± 3 gm of Purina "chow"; after 8 weeks they grew to 3 ± 4 gm beyond initial size, cumulative food consumption being 440 ± 12 gm. These values differed from those for sham-operated littermates by 0.5 ± 1.2, 6 ± 2, -4.5 ± 5.3 and 65 ± 33 gm respectively (N = 9, 7, 7 and 5). This approach strengthens applicability of centrifuge experiments to gravitational phenomena. Moreoever, it could supply information basic to design of rotating space stations.

SWEATING AND VASCULAR RESPONSES TO HEAT STRESS IN PATIENTS WITH HIGH SPINAL TRANSECTION. *R.D. Wurster*, R.J. Lewin* and W.C. Randall.* Department of Physiology, Stritch School of Medicine and the Graduate School, Loyola University, Chicago and the VA Hospital and UCLA, California.

Five patients with cervical and two with high thoracic spinal transection were exposed to progressively rising ambient temperatures while sweating, cutaneous volume pulses, deep and skin temperatures were recorded. In a similar series of studies reported earlier (*J. Appl. Physiol. 16:* 796, 1961), sweating was induced. However, the transections were located between T_3 and T_8 and the observations have been subject to the criticism that sudomotor pathways may exit from the cord above the transection and descend through the sympathetic trunk to innervate dependent skin areas. In all patients with complete lesions at or above known levels of sympathetic outflows (T_1), both sweating and cutaneous vascular responses to heat stress were observed. The responses developed with exposure to heat and disappeared upon its cessation. Thus, in patients whose lesions completely separated conventional sympathetic outflows from hypothalamic control, it is concluded that the spinal cord is capable of initiating profound vasomotor activity in palmar and plantar areas and in maintenance and release in constrictor tone in forearm, chest and thigh skin during heating. (Supported by Public Health Service Grant HE 08682 to Loyola University and a gift from the Spinal Cord Research Foundation to the VA Hospital, Long Beach.)

AN ANALYSIS OF THE INTRARETINAL ERG OF THE PIGEON. Richard M. Wylie* and Thomas E. Ogden (intr. by Edward R. Perl). Dept. of Physiology and Div. of Neurology, University of Utah College of Medicine, Salt Lake City, Utah.

The ERG can be recorded by penetrating the retina with a microelectrode introduced into the otherwise intact eye. Previous studies with such intraretinal microelectrodes have shown that the different components of the ERG reach maximum amplitudes at different retinal depths. With 3M KCl filled glass microelectrodes we have recorded the a- and b-waves at different depths within the pigeon retina. The amplitude of each of these components was plotted as a function of the distance traversed by the electrode, and the resulting profiles were compared with a cross section of the retina. The points at which the maximum amplitudes of the b-wave were recorded coincide with the inner nuclear layer. The measured depths at which the maximum amplitudes of the a-wave were recorded, though more variable, fall either within the outer nuclear or the receptor layers. Since retinal depth measurements are subject to error, we also conducted electrode marking experiments. Stainless steel and dye filled glass microelectrodes were used to mark the points at which the amplitude maxima of the a- and b-waves were recorded. The localization of the amplitude maxima thus obtained agreed with the findings of the depth studies. Our localizations of the a- and b-waves of the pigeon ERG agree with the studies of Brown and Wiesel and Brown and Tasaki on the cat ERG. Supported by PHS grants NB-5244, NB-05666 and NB-04135.

INTERNEURONS SELECTING INFORMATION FROM A FIXED DIRECTION IN SPACE.
T. Yamaguchi* and C. A. G. Wiersma. Division of Biology, California Institute of Technology, Pasadena.

The optic nerve of the crayfish contains a number of interneurons responding to light intensity changes, or to movements of objects (Wiersma & Yamaguchi, Fed. Proc. 24: 275, 1965). The movement fibers are subdivided into those responding to jittery slow motions or to fast approaching objects in their specific visual fields. Most of these fibers show no influence of body or eye position on the location of their visual fields projected on the eye surface. However, in both classes of movement fibers at least one special fiber is present whose visual field does not turn when the animal is rotated along its length or its horizontal axis. Both these fibers "look" straight upwards when the animal is in the normal plane, and continue doing so for any eye or body position. These fibers must receive additional input from e.g. sustaining fibers and/or interneurons, reacting to proprioceptors such as the statocysts and the basal joints of the legs. They are presumably of great importance for furnishing the clues for the animal's orientation in space. Supported by NIH grant NB 03627-03.

REGULATION OF BLOOD GLUCOSE DURING PROLONGED PHYSICAL WORK.
D. R. Young. Ames Research Center, National Aeronautics and Space Administration, Moffett Field, California.

The level of blood sugar in postabsorptive subjects has been observed to remain constant after 9 hours of aerobic work. During treadmill studies of the responses to prolonged moderate work, the blood sugar declined gradually to a level of 68 mg/100 ml and then remained relatively stable during continuous work for periods up to 24 hours. Blood lactate remained at a level of 12 mg% . The level of serum free fatty acids stabilized at 2.4 meq/liter indicating a high level of lipid mobilization. After 9 hours of work, the response of the blood sugar to adrenalin was minimal. Following the intramuscular administration of adrenalin, 0.10 mg/kg, the blood sugar increased only 22 mg% , thus indicating a reduced level of liver glycogen reserves. Studies undertaken with uniformly labelled glucose-^{14}C, glycerol-^{14}C, and lactate-^{14}C, administered separately as a single injection after 9 hours of work show a rapid turnover of glucose (T 1/2 = 1.2 hr), and indicate that approximately 50% of the glycerol and 30% of the lactate is recycled as glucose. During comparable periods of rest, there was a greater conversion of lactate and glycerol to glucose, although during resting conditions the glucose pool was larger and the turnover rate of glucose was slower (T 1/2 = 2.3 hr). The greater incorporation of lactate and glycerol into glucose in resting subjects is attributable to the relatively low rate of direct oxidation of these substances.

EFFECT OF BODY POSITION ON THE PERCEPTION OF ADDED INSPIRATORY AIRFLOW RESISTANCE. F. W. Zechman, R. L. Wiley* and W. C. Helton*. Department of Physiology & Biophysics, University of Kentucky College of Medicine, Lexington, Kentucky.

Previous investigations (Marshall, R. and J. G. Widdicombe, Quart. J. exp. Physiol. 43: 320-330, 1958) indicate pulmonary vagal afferent activity increases with pulmonary vascular congestion. The purpose of the present study was to determine if the threshold for perception of airflow resistance increases when going from sitting to a supine (5° head down) position, a condition which tends to increase pulmonary blood volume. Five normal human subjects were presented 8 levels of resistance (range, 0.2 to 1.8 $cmH_2O/l./sec.$) in random sequence, 10 or more times, in each position. Airflow resistance was measured in each subject in both positions before each run. Detection scores plotted against values of added resistance indicates a decrease in the threshold for perception in the supine position. When the increased airflow resistance which accompanied the supine position is taken into account this difference is generally resolved. This is apparent when detection scores are plotted against the ratio, added resistance/total resistance, rather than simply against added resistance. These results suggest a "Weber fraction" may apply to the sensory process related to perception of airflow resistance. (Supported by Contract AF 33(657)-9331 and Grant HE 0932-01)

SYMPOSIUM

HYPOTHERMIA

Chairman: Vojin Popovic

HYPOTHERMIA BY COMBINED IMMERSION AND PERFUSION. E. Converse Peirce, II*(intr. by V. Popovic). Emory University School of Medicine, Atlanta, Ga.

The purpose of this study is to evaluate and compare uniformly and differentially cooled large animals. Dogs of 13 to 16 kg are prepared several days earlier by making an interatrial septal defect and implanting multiple organ thermocouples and a portal vein cannula. A closed chest hypothermia perfusion is carried out at a fixed flow of 30, 60, or 90 ml./ kg./ min. for one hour while blood volume, O_2 consumption, hemodynamic, acid-base, calorie exchange, and organ temperature studies are done. A uniform temperature of 5° to 25° C is then achieved by the addition of immersion hypothermia and the elimination of heat exchange from the perfusion. The interatrial defect prevents lung and heart damage from excessive central pressures. Temperature gradients in excess of 25° C are produced by the perfusion alone and this is accompanied by progressive lactic acidosis and cardiovascular failure. Gradients are reduced to less than 5° C by combining immersion and perfusion. The uniformly cooled preparations show stable blood volumes, O_2 consumption, and levels of metabolic acidosis. The cardiovascular system is surprisingly reactive and exhibits significant responses to drugs such as epinephrine, angiotensin, vasopressin, and papaverine at temperatures of 15° C and below.

ARTIFICIAL RESPIRATION VS. HYPOTHERMIA IN THE RESUSCITATION OF ASPHYXIATED NEONATES. James A. Miller, Jr., and Faith S. Miller.* Tulane Univ., New Orleans, La.

Hypothermia prolongs the survival of experimentally asphyxiated neonates and permits 100% spontaneous recoveries from exposures which are lethal for normothermic litermates (guinea pig, pig, rabbit, cat and dog; Miller, 1964; Miller and Miller, 1965). Since positive pressure ventilation is used for asphyxiated human infants, comparisons were made between the efficacy of the two methods. Resuscitations were performed using 100% O_2 and a rodent respirator (Harvard Apparatus Company). Only one-fourth of normothermic kittens in which resuscitation was begun at 1 1/4 times T.L.G. (time to last gasp) recovered without signs of brain damage. After 1 1/2 to 2 times T.L.G. only a few recovered and all showed damage. Experiments on puppies gave similar results. By contrast, hypothermia induced in puppies before asphyxiation is 4X to 10X as effective in producing recoveries without evidence of brain damage. In kittens it is about 2X as effective. When cooling was initiated during asphyxiation (after 1/3, 1/2, or 99% T.L.G.), 92% of the puppies recovered without evidence of brain damage; when initiated after 1/2 T.L.G. in kittens, all recovered. Artificial respiration can be used as an adjunct to hypothermia. When resuscitation was combined with hypothermia, there was further prolongation of time during which normal recoveries occurred.

THE EFFECTS OF ETHER, ETHANOL, PROPANOL, AND BUTANOL ON TOLERANCE TO DEEP HYPOTHERMIA IN DOGS D.C. MacGregor,* J.A. Armour,* B.S. Goldman,* and W.G. Bigelow* (intr. by V. Popovic). Toronto, Canada.

In the course of investigation into the natural hibernation of mammals and its possible application to clinical hypothermia, it was suspected that ether, ethanol, propanol, and butanol protected the hypothermic heart from ventricular fibrillation. After 2 years preliminary study, a well controlled series of 30 dogs were subjected to lethal, ice-water immersion hypothermia and the effects of these protective agents, administered during cooling, were observed. Rate of alcohol infusion was controlled by estimations of blood alcohol levels. Ether anaesthesia significantly decreased the incidence of ventricular fibrillation and produced a remarkable increase in tolerance to low body temperatures. Intravenous ethanol, propanol, and butanol were less effective. It is suggested that the elevation of plasma catecholamines during ether anaesthesia increases the conduction velocity in cardiac muscle. The conduction time/refractory period is thus reduced and "circus movement", thought to be responsible for ventricular fibrillation, is prevented.

DISAPPEARANCE OF EUTHERMIC TUMORS (37°C) IN SHALLOW HYPOTHERMIA. Vojin P. Popovic and Roberto Masironi*. Dept. Physiol., Emory Univ., Atlanta, Ga.

The work reported here is based on previous experiments (V. Popovic and R. Masironi, Life Sci. 4: 533-543, 1965) in which the entire bodies of hamsters were cooled to 4°C for 10 hours while their tumors (Toolan H.Ad. #1U., originally a human adenocarcinoma) were kept at 37°C. As a result the tumors regressed and disappeared completely without resuming growth. In the present experiments a less drastic cooling, only to a body temperature of 25°C (water immersion), was used since less extreme temperatures are better tolerated by non-hibernators. The tumors were of the same type as in the previous experiments. They were implanted in the cheek pouches of adult hamsters. After a growth period varying from 10-50 days the animals were cooled to a body temperature of 25°C, but the tumors were kept at 37°C by an electrical heater with thermostatic control. It was found that it took 24 hours of this differential type cooling for the tumors to start regressing after rewarming and to disappear eventually (12-15 days).

(Supported by USPHS grants from National Cancer Institute and Division of General Medical Sciences).

HYPOTHERMIC PERFUSION OF CANNINE KIDNEYS FOR 48 HOURS FOLLOWED BY RE-IMPLANTATION. A.L. Humphries, Jr.*, R. Russell,* and W.H. Moretz* (intr. by V. Popovic). Medical College of Georgia, Augusta, Georgia.

For four years various perfusates for kidneys have been tested. All perfusates were oxygenated; most were kept at a temperature of 10°C. and pumped at a pressure of about 45 mm Hg. Diluted blood seemed best; with it, 12 of 18 kidneys perfused for 24 hours were successfully reimplanted even with immediate contralateral nephrectomy, and 4 of 7 kidneys perfused 48 hours were successfully reimplanted with contralateral nephrectomy at 2 weeks. Until recently all perfusates had inexorably slowed, even through those kidneys which survived when reimplanted. Diluted plasma flowed at only 1500 ml/24 hours. Then diluted, pre-filtered serum (on retrospect this "serum" was not completely defibrinated) flowed at 4,300 ml/24 hours. Diluted blood (one part blood to one part salt solution) flowed at 17,000 ml the first 24 hours, slowed to 6,000 the second 24 hours and to 3500 the third; of 10 kidneys perfused for 3 days, only one when reimplanted excreted even a little urine. Recently a millipore filter has been used to completely rid serum of all fibrin. This serum as a perfusate flowed without slowing (even though undiluted) for three days (17,500 ml/24 hours); but, unfortunately, did not yield in nine tries a kidney that survived when reimplanted. A pilot study showed that a perfusate of filtered serum plus red cells and salt solution also flowed without slowing. Therefore, we expect that kidneys can be stored successfully for 3 days or longer.

BRAIN METABOLISM AFTER RESPIRATORY AND CARDIAC ARREST IN HYPOTHERMIA. R.K.Andjus, *N.Hozic* and T.Cirkovic*(intr. by V.Popovic). Institute of Physiology, Faculty of Science, Univ. of Belgrade, Yugoslavia.

In studying the protective effects of different levels of hypothermia against anoxia, an attempt was made to correlate survival and revival parameters with brain metabolism, especially where respiratory and cardiac arrest were due to cooling below 10°C. The brains of rats maintained at different body temperatures(37 to 15°) were analyzed for ATP, ADP, AMP, CrP and lactate(LA) at various times after tracheal occlusion. Other rats were cooled to and maintained at 0°. Their brains were analyzed at different intervals after circulatory arrest and during resuscitation. Within the survival period following tracheal occlusion(persistence of respiratory movements), regardless of temperature, CrP was almost exhausted and the rising phase of the invariably biphasic ADP changes was complete. Only after this period did the ADP/AMP ratio fall below 1, except at 30° where this occurred earlier. Following the survival period, several parameters tended to show a non-linear relationship to temperature, indicating an optimal zone around 22°. At that temperature, the terminal LA concentrations, the rates of LA and AMP accumulation and of ATP depletion were higher than at lower and higher levels of hypothermia. In rats kept at 0° the maximum LA and AMP concentrations were reached only after 90-120 minutes. However, changes induced in reaching 0°(30 minutes cooling below 15°) were already comparable to those recorded 5 minutes beyond the survival period following tracheal occlusion at 15°. Some 15 minutes after the heart beat had been re-established by microwave diathermy and by the time spontaneous breathing reappeared, only CrP lagged greatly(40%) behind its normal level.

EFFECT OF HYPOTHYROIDISM ON MAINTENANCE OF BODY TEMPERATURE OF RATS EXPOSED TO COLD AIR. Melvin J. Freqly, Dept., of Physiol., Univ. of Fla., Coll. of Med., Gainesville, Fla.

Hypothyroidism induced by propylthiouracil (PTU) treatment (1.0g/kg food) increases rate of cooling of restrained rats subjected to air at 5°C. Rate of heat production (oxygen consumption) during exposure to cold does not differ from that of euthyroid controls when compared at the same colonic temperatures. However, mean skin temperature of the hypothyroid rats is higher at any colonic temperature during cooling than it is for controls. Measurements were also made of the spontaneous activity levels (tilt cage method) of lightly restrained, hypothyroid and euthyroid rats during exposure to air at 5°C. Activity levels of both groups increased upon initial exposure to cold. Activity level of euthyroid rats continued to increase and became maximal when colonic temperature fell 0.5 to 1.0°C. Mean colonic temperature of these rats fell no lower than 36°C and was maintained at this subnormal level by adjustment of activity during the 4-1/2 hour experiment. Hypothyroid rats also increased their activity to a similar maximal level but only when colonic temperature fell 3 to 4°C. This maximal effort appeared to occur too late to prevent further fall of colonic temperature to 31°C in 3 hours. The decreased tolerance to cold manifested by hypothyroid rats appears to be related to inability to reduce heat loss rather than an inability to increase heat production. A reduction in spontaneous activity also contributes to the reduced tolerance to cold. (Supported by Contract DA-49-193-MD-2549 with The Office Of The Surgeon General).

RENAL FUNCTION IN HYPOTHERMIA. G.S.Kanter. Albany Medical College, Albany, New York.

The effect of hypothermia on renal function may be viewed in terms of the effect of hypothermia on : 1. renal hemodynamics including renal blood flow (RBF), renal plasma flow (RPF), and glomerular filtration (GFR), 2. renal tubular function including electrolyte and organic constituent handling as well as acid-base regulation, 3. renal concentrating capacity. Areas not adequately investigated and therefore not covered in this survey include the effect of hypothermia on: erythropoietic activity of the kidney, renal regulation of adrenal cortical secretion, and renal hypertensive and antihypertensive function. The alteration in renal hemodynamics includes a marked fall in RBF,RpF, and GFR. Concomitant events include progressive fall of mean arterial blood pressure and effective circulating plasma volume, increase in hematocrit and increase in renal resistance. The alteration in renal tubular function includes general depression of all active processes of reabsorption and secretion. Of interest is the fact that the depression varies from major to minor for specific substances. In a homeostatic sense the depression of tubular function is balanced by reduction in GFR. The loss of fluids, electrolytes and other plasma constituents is thus minimized. Both the renal acidification mechanism and the secretion of ammonia are depressed in spite of the ensuing hypothermic acidosis. The alteration in renal concentrating capacity is shown typically by the occurrence of a diuresis. Work in progress has demonstrated a significant decrease in blood antidiuretic hormone titer during hypothermia. (Supported by USPHS Grant HE 09097).

HYPOTHERMIA AT 18°C IN PUPPIES: TOLERANCE TO CAVAL OCCLUSION. Sadao Ikeda, Alan Lesage, Glenn Young, Jr. and Will C. Sealy. Duke Medical Center, Durham, N. C. (Intro. by V. Popovic).

Fifty-nine young puppies were cooled to 16°C after being anesthetized and intubated. They were breathed mechanically, 18 with room air, 18 with 5% CO_2-95%O_2, 23 others, treated with bicarbonate, isuprel and glucose, were breathed with 8% CO_2-92% O_2. When 18°C was reached, bilateral thoracotomy was performed and both cavae occluded for periods varying from 20 to 60 minutes. The puppies were rewarmed by pouring warm saline in the chest and cardiac massage. In Group I, breathed with room air, 7 out of 18 survived and 3 fibrillated. Four out of 12 survived 30 to 40 minutes occlusion. In Group II, breathed with CO_2 mixture and untreated, 14 survived out of 18. Ten out of 12 survived 30 to 40 minutes occlusion. In Group III, treated and breathed CO_2, 11 out of 13 survived 40 minutes occlusion, 3 out of 5, 45 minutes and only 2 out of 5 survived 60 minutes occlusion. Fibrillation occurred in CO_2 respirated and treated only in puppies occluded more than 40 minutes. Mild acidosis was present in puppies respirated with room air and after 40 minutes occlusion. In the groups respirated with CO_2 mixture occurrence of fibrillation and also paresis of hind legs were lower. In conclusion, caval occlusion for 40 minutes in very young individuals at 18° breathing CO_2 mixture is safe and this method could be useful for surgery in infants beyond the age of possible extracorporeal circulation.

CARDIAC EXCITATION AND CONDUCTION UNDER HYPOTHERMIA. E. T. Angelakos and J. C. Torres. Dept. of Physiol., Boston Univ. Sch. of Med., Boston, Mass.

The cardiac arrhythmic effects of hypothermia are of fundamental interest since they represent a valuable model of a "depressive" state associated with arrhythmias. Ventricular excitability as defined by stimuli of varying duration, polarity, and configuration is differentially reduced and both phases of refractoriness (RP) are prolonged. Ventricular conduction velocity diminished to an equal extent in both myocardial and specialized fibers, the extent of slowing (twofold) being less than the increase in RP (threefold). Temporal heterogeneities in ventricular action potential durations, as reflected in the magnitude of the ventricular gradient increased substantially. In contrast, measurements of the recovery of excitability in various regions of the heart revealed inhomogeneities which are not consistently exaggerated by moderate hypothermia. Irregularities in the pattern of ventricular activation as detected with the first time derivative of the ECG indicate the presence of discrete regions of impaired conduction at low temperatures. Such a condition by favoring the occurrence of re-entrant excitation and self-sustaining activity would account for the high susceptibility of the hypothermic heart to arrhythmias and fibrillation. (Supported by USPHS grant HE-04355 and awards K3-15,457 and K3-HE-7063-01.)

CARDIOVASCULAR RESPONSES IN HYPOTHERMIA AND HIBERNATION. Kenneth M. Kent* and Vojin P. Popovic. Dept. Physiol., Emory Univ., Atlanta, Ga.

It is known that rats cooled to and kept at a body temperature of 15°C die after 8-9 hours, whereas equally cool hibernating animals do not die. In order to investigate the physiological basis for this startling difference, the cardiovascular characteristics of hypothermic non-hibernators (rats) and hibernating hibernators (ground squirrels) were studied. The O_2 consumption, heart rate, and arterial blood pressure of hypothermic animals remained practically unchanged during the whole 8-9 hours of survival, whereas their cardiac output decreased. On the other hand, the cardiac output of the hibernating animals became very low when the body temperature decreased and remained constant throughout hibernation which lasted several months. The hematocrit ratio increased continuously in hypothermic non-hibernators, but decreased in hibernating animals from 55 vol % to a low 35 vol % and remained at this low level during the whole period of hibernation. The arterial blood pressure in hibernation was 48-50 mm Hg, which was much lower than in hypothermic animals. It is concluded that hemoconcentration and decreased cardiac output might result in "cardiocirculatory failure" and that this mechanism limits the survival of non-hibernating animals in hypothermia.
(Supported by USPHS grants from Division of General Medical Sciences of National Cancer Institute).

THE THERAPEUTIC EFFECT OF MILD PERFUSION HYPOTHERMIA ON ACUTE CARDIAC DECOMPENSATION. Frank Gollan, Walter P. White*, and Joanne McDermott*, Veterans Administration Hospital and University of Miami School of Medicine, Coral Gables, Florida.

The rapid induction of perfusion hypothermia has not been attempted in left heart failure because of the danger of ventricular fibrillation. The present work shows that this contraindication may not be valid. Acute left ventricular failure was produced in nembutalized greyhounds breathing air by doubling their blood volume and slow poisoning with 80 mg/kg quinidine. Marked lowering of cardiac output, stroke volume and mean aortic pressure, and a rise in left ventricular end-diastolic pressure were the criteria of failure. Then venous blood from the right atrium was shunted through a heat exchanger into a femoral artery. With a flow rate of one half of the normal cardiac output the esophageal temperature was lowered to 28° C. Due to the increased blood volume the veno-arterial shunt did not lower the cardiac output below the failure level. However, the stroke volume of the slowly beating heart doubled and the left ventricular end-diastolic pressure was reduced to normal. This recovery from left heart failure occurred in spite of prolonged systolic duration and elevated mean systolic pressure, time-tension index and minute work. We concluded that the combination of three temperature induced factors: increase of myocardial contractility, lowering of myocardial oxygen consumption and reduction of effectively circulating blood volume, was responsible for the restoration of external work efficiency.

Supported by U. S. Public Health Service Grant #HE 06178-04.

RESPONSE ACQUSITION IN HYPOTHERMIC RATS. Frederick N. Sudak and Walter B. Essman*. Albert Einstein Coll. of Med., Bronx, N.Y. and Queens Coll., Queens, N. Y.

Four experiments were designed to determine the effect of a reduction of body temperature on response acquisition in rats. Hypothermia was induced by treatment with 2,4-dichlorophenoxyacetic acid and cold exposure (2.0°C ± 0.5°C). In a four-trial water escape problem, animals maintained at a body temperature of 31°C (average deep colonic temperature over the four training trials) did not meet the criterion for learning. Since performance in rats was impaired at colonic temperatures below 31°C, the behavioral deficit in this group may have involved impaired performance. Animals maintained at body temperatures of 33°C, 36°C, and 37.5°C during training acquired the response. These results suggest that the degree of hypothermia necessary to produce a learning deficit in rats was much greater than that previously reported for mice under the same conditions of training (Essman and Sudak, J. Appl. Physiol. 17:113,1962).

(Supported in part by Grants M-5140 and MH-08525-02 from the U.S.P.H.S)

OPERANT BEHAVIOR BY TRAINED ANIMALS AT LOW BODY TEMPERATURES. J. A. Panuska (intr. by V. P. Popovic). Dept. of Biology, Georgetown University, Washington, D.C. 20007.

The performance of a simple motor response, like that involved in the pressing of a lever, is a complex action which requires precise physiological and psychological coordination. The ability of an animal to engage in this type of behavior is dependent on many factors and will be disturbed if any one of the necessary faculties is not functioning properly. Investigations on trained rats have indicated a breakdown of heat reinforcement performance at a colonic temperature of 24.6 ± 1.0°C (J. Cryobiol. In press for Vol. 1, No. 5, 1965). Shock escape studies have shown a collapse of performance efficiency at a similar temperature range, with the percentage of successful responses changing from 60% at a body temperature of 25 - 26°C to only 23% at 23 - 24°C. Sometimes, in individual subjects, performance appears to persist even below 23°C. By considering these and other studies on hypothermic performance, one must conclude that acquired instrumental responses may be maintained to a point of hypothermia just a few °C above the level at which the subject succumbs to complete motor failure. Of course, it cannot be concluded that this low temperature range will be critical for all types of operant behavior since more complex responses may depend on activities already excessively depressed by cold, and simpler responses may persist in even deeper hypothermia. (Supported by U. S. Army Medical Research and Development Command under Research Contract No. DA-49-193-MD-2668.)

CRITICAL BODY TEMPERATURE FOR INTRACRANIAL SELF-STIMULATION IN WHITE RATS. Pava Popovic*, A. B. Silver* and Vojin P. Popovic. Dept. Physiol., Emory Univ., Atlanta, Ga.

Bipolar stainless steel electrodes were chronically implanted in the hypothalamic supra mammillary area ("pleasure center") of twenty-six adult white rats. Ten days after implantation, the rats were placed for the first time into a plastic self-stimulating chamber. The rats explored the chamber and accidentally pressed the lever about 1-2 times per minute, delivering with each pressing an electrical stimulus (50-100 microamp. lasting 0.3 sec.) to their brains. The rats learned to use the lever during the first five minutes of exposure and their rate of performance increased to 50-100 pressings per minute. The rate of performance was the same on three additional exposures (one day apart) lasting one hour each. The fifth time the fur of the rat was clipped and the intracranial self-stimulation apparatus together with the animal was placed in a 4°C cold room. After several minutes each rat became hypothermic and its body temperature continued to sink slowly, reaching eventually 20°C. During the whole period of progressive cooling the animals continued to press the lever for intracranial self-stimulation. The rate of lever pressing decreased in proportion to the body temperature. When the body temperature reached 20°C the rats stopped pressing the lever. This is called "critical body temperature" for intracranial self-stimulation. Body temperature of 20°C is the lowest temperature at which a learned behavior has ever been observed. Since 20°C is the body temperature at which rats lose the ability for locomotion and for standing upright, it may be that the critical factor for the cessation of this learned behavior is a failure of neuro-muscular coordination.

(Supported by a USPHS grant from the Division of General Medical Sciences).

SYMPOSIUM

APPROACHES TO THE NEUROCHEMISTRY OF CENTRAL NERVOUS SYSTEM FUNCTION

Chairman: Arthur Yuwiler

DISRUPTION OF MEMORY FIXATION IN GOLDFISH BY PUROMYCIN. Bernard W. Agranoff*, Roger E. Davis* and John J. Brink*. Mental Health Research Institute and Dept. of Biological Chemistry, University of Michigan, Ann Arbor.

Goldfish were trained to swim over a barrier in response to light paired with shock. Retention was measured 3 days later. We have shown that puromycin, an antibiotic which inhibits protein synthesis, blocks memory formation in the goldfish. Intracranial injection of 90 µg of puromycin immediately following the trials on day 1 resulted in a retention deficit measured on day 4 (Agranoff and Klinger, SCIENCE, 146, 952 (1964)). When 170 µg of puromycin were injected immediately following initial training, performance on day 4 was not significantly different from that seen in naive goldfish on day 1. Injection of puromycin 1 hour following initial training was followed by performance on day 4 which was not significantly different from that seen in uninjected controls (Davis, Bright, and Agranoff, J. COMP. PHYSIOL.PSYCHOL., in press).

Replacement of puromycin by puromycin aminonucleoside or L-p-methoxyphenylalanine showed that these moieties were without effect on memory. The effect of intracranial injections of puromycin on the incorporation of H^3-leucine into goldfish brain protein in vivo was studied. There was a rapid onset of inhibition, the extent and duration of which increased with larger doses of puromycin. There was no effect on the incorporation of P_i^{32} into RNA relative to DNA. Our results suggest that protein synthesis is part of the process of memory formation.

FURTHER EVIDENCE FOR A RELATION BETWEEN ENVIRONMENTAL COMPLEXITY, LEARNING ABILITY, AND NUMBER OF GLIAL CELLS. Edward L. Bennett,* Mark R. Rosenzweig, David Krech,* and Marian C. Diamond.* Lab. of Chemical Biodynamics, Psychology Dept., and Anatomy Dept., Univ. of California, Berkeley, Calif.

Four lines of evidence--two chemical, one anatomical, and one behavioral--suggest relations between glial cell number and behavior. The first three lines indicate that a rat raised under conditions of Environmental Complexity and Training (ECT) has a larger number of glial cells in the cortex than does his littermate brother raised in isolation (IC): (1) The ratio of cholinesterase (ChE) to acetylcholinesterase (AChE) has been used as a chemical indicator for the glial/neural ratio; this ratio is 6% greater in the cortex of ECT rats than in IC rats (7 experiments; 79 pairs of littermates). (2) In another experiment with 10 pairs, DNA (used here as an indicator of cell number) was determined in the visual area of the cortex; the ECT animals showed an increase of 7% in DNA. (3) In 2 experiments with a total of 17 ECT-IC pairs, cells have been counted and classified in a standard section from the visual cortex. The number of glial cells average 13% greater in the ECT rats than in their IC littermates; a difference in this direction was found in 12.5 out of 17 littermate pairs. The average glial/neural ratio was 15% greater in the ECT animals and was found to be greater in 14 of 17 pairs. Behavioral results to date on 94 rats from 8 strains indicate that problem solving scores are correlated about .40 with the cortical-subcortical ratio of ChE to AChE. The findings will be interpreted in terms of hypotheses of glial function.

(Supported by grant or contract from NIMH, Surgeon General's Office, NASA, and AEC.).

CENTRAL NERVOUS SYSTEM CHEMICAL TRANSMITTERS AND BEHAVIOR. M. H. Aprison and J. N. Hingtgen* Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, Indiana.

Although numerous attempts have been made to correlate changes in biochemical components in brain with changes in an organism's behavior, very few have dealt with determination of brain transmitter concentrations and objective behavioral measures in the same animal and over the same time course. Some problems in interpreting data from the latter studies involving neurochemical correlates of behavior are:(a) inability to measure separately free or bound components of the total transmitter pool, (b) the frequent occurrence of differential behavioral effects following the injection of a drug into animals working on either the same or different schedules of reinforcement, (c) multiple synaptic connections (axosomatic, axodendritic, and axoaxonal) with the release of one or more transmitters, and (d) depending on a number of factors, a substance released from nerve endings may function either as an excitatory or inhibitory transmitter. Aware of the above limitations, we have completed a number of studies in this area. Data will be presented on total serotonin, dopamine, norepinephrine, and acetylcholine concentrations in brain parts from pigeons and rats working on various approach and avoidance schedules of reinforcement and injected with such compounds as 5-HTP, α-methyl-m-tyrosine, and tetrabenazine. Although limited to measurement of total transmitter concentrations, speculation about free levels permits formulation of a model for explaining the observed correlations.
(Grant MH-03225-06 from NIMH, PHS).

AMINOBUTYRIC ACID IN THE VERTEBRATE NERVOUS SYSTEM: AN APPRAISAL OF RECENT RESULTS. Claude F. Baxter*, Neurochem. Labs., V.A. Hosp., Sepulveda, Calif. and Dept. of Physiol., Univ. California. Sch. of Med.

Recent investigations into the biochemistry of nervous tissue of vertebrates has shown that a) γaminobutyric acid (γABA) appears to exist in kinetically separate pools; b) no relationship exists between total levels of γABA and the potential for its metabolism in any specific area of the Central Nervous System; and c) γABA metabolism in preparation of brain particles appears to be sodium dependent. These results can be the basis for a reinterpretation of the contradictory data obtained by many investigators who have attempted to correlate overall levels of γABA with the physiological effects of pharmacological agents.

Overall γABA levels [1], specific regional changes in γABA concentrations [2], and metabolism of γABA [3], may each have individual physiological significance. Osmotic stress in the toad changes [1], together with the level of a number of related amino acids. [2] is illustrated by the effects of pentobarbital anesthesia where specific changes in cortical tissue concentrations appear to correlate well with electrophysiological phenomena observed by others. In vivo and in vitro studies of [3] lead to the suggestion that local changes in the rate of γABA metabolism may have physiological significance which is not directly related to the postulated neurohumoral function of γABA. (Supported by USPHS Grant NB 3743).

NEUROCHEMICAL CHANGES ASSOCIATED WITH EXPERIMENTAL MENTAL DEFICIENCY. A.Yuwiler*, E.Geller*, G.G.Slater. Neurobiochem. Lab., V.A. Center Los Angeles and UCLA.

Infant rats fed diets supplemented with 5% L-phenylalanine, to simulate aspects of phenylketonuria, have decreased levels of brain serotonin (0.615 μg/brain) as compared to littermate controls (0.814 μg/brain) although other central nervous system constituents, such as norepinephrine, are essentially unaltered. Liver tryptophan hydroxylase activity is reduced from 1.33 to 0.34 μmoles/hr/gm protein by this treatment whereas other enzymes such as brain 5HTP-DOPA decarboxylase, glutamic acid decarboxylase, and cholinesterase, liver tryptophan pyrrolase and brain and liver tryptophan and 5-hydroxytryptophan transaminases are unchanged. Only liver tryptophan hydroxylase is altered from control levels by feeding a 3% phenylalanine supplemented diet. These data suggest that inhibited brain tryptophan hydroxylation, inhibited transport of peripheral 5-hydroxytryptophan through the blood-brain barrier, or diminished serotonin storage are the most likely mechanisms accounting for this decrease in brain serotonin. Behaviorally, animals fed the 5% diet show impaired performance on some, but not all, behavioral tasks.

Attempts to simulate branch-chain ketonuria by dietary supplementation with L-leucine leads to an analogous decrease in brain serotonin together with a fall in brain dopamine and urinary 5-hydroxyindoleacetic acid excretion. Tryptophan hydroxylase is unaffected.

These and other results will be discussed with regard to possible common factors between several mental deficiencies and their divergent mechanisms, as well as the use of experimental mental deficiency as a tool for exploring biochemical aspects of brain function.

SOCIETY OF GENERAL PHYSIOLOGISTS MEETING

The Twentieth Annual Meeting of the Society of General Physiologists will be held at the Marine Biological Laboratory at Woods Hole, Massachusetts, September 1-4, 1965. A symposium, The Specificity of Cell Surfaces, has been organized by Bernard Davis, Herman Kalckar and Leonard Warren. It will run from 9:00 to 12:00 on each of the four mornings of the meeting. The program in detail is as follows:

I. Bacterial Cell Walls. Chairman: Bernard Davis

1. Deeper layers	Hiroshi Nikaido
2. Optional somatic antigens	Phillips Robbins
3. Fimbriae (pili)	Charles C. Brinton

II. Cell Membranes. Chairman: Herman Kalckar

1. Bacterial membranes	Milton Salton
2. Carbohydrates of membranes	Leonard Warren
3. Lipids of membranes	John Law
4. Isolation from mammalian cells	Donald Wallach

III. Membranes (cont.) Chairman: Salvador Luria

1. Blood group substances	Winifred Watkins, (London)
2. Tumor antigens	George Klein, (Stockholm)
3. Effects of viral infection	Harry Rubin

IV. Models and Tools. Chairman: Harry Eagle

1. Aggregation of sponges	Thomas Humphrey
2. Electron microscopy of surface components	Jean-Paul Revel
3. The immunological model for complementarity	David Pressman

There will be several concurrent contributed paper sessions on each of the afternoons of September 1, 2 and 3. A tentative list of topics follows: Ciliate Physiology (organized by George Holz); Developmental Biochemistry (organized by Maurice Sussman); Gamete Physiology (organized by Leonard Nelson); and Physiological Adaptation (organized by John Kanwisher). In addition, contributed papers are expected on control mechanism, photobiology, nerve and muscle physiology, ion transport, physico-chemical biology, and various other areas of physiology. The meeting is open to all interested persons. Non-members of the Society wishing to contribute 20-minute papers or desiring information about housing or other details of the meeting are invited to write to Roger Milkman, Secretary, Department of Zoology, Syracuse University, Syracuse, New York 13210.