

AMERICAN PHYSIOLOGICAL SOCIETY PROCEEDINGS

FALL MEETING, SEPTEMBER 5-8, 1961

Indiana University Bloomington, Indiana

ABSTRACTS OF PAPERS

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

INTRACARDIAC AND INTRAVASCULAR BLOOD TEMPERATURES IN HUMANS.
S. Afonso*, G. G. Rowe, C. A. Castillo* and C. W. Crumpton. Cardio-vascular Res. Lab., U. of Wis. Medical School, Madison, Wisconsin.

Intracardiac and intravascular blood temperatures were measured in a group of 17 afebrile patients undergoing cardiac catheterization. 5 patients had ventricular septal defects, 6 had atrial septal defects and 6 were hemodynamically normal. Measurements were made using thermistors mounted at the tip of cardiac catheters, in the following sites: internal jugular vein, superior vena cava, inferior vena cava (below and above the opening of the renal veins), renal and hepatic veins and in the right atrium, pulmonary artery, pulmonary artery wedge position, and left atrium and pulmonary veins (in atrial septal defect and patent foramen ovale). Data obtained confirm observations, by other investigators, of a consistent gradient of increasing temperature in the IVC as it approaches the heart. Furthermore, temperature recordings in different sites of IVC, SVC and right atrium show variations phasic with respiration. Pulmonary artery, pulmonary artery wedge, left atrium and pulmonary vein blood temperatures were found to be very nearly the same.

THE ROLE OF NITROGEN IN THE PROBLEM OF OXYGEN TOXICITY

S. C. Allen. Dept. of Physiol., Chicago College of Osteopathy,
Chicago, Illinois

The author recently reported on the toxic effects of 100% O₂, at one atmosphere, on the development of chick embryos. More recent experiments indicate that O₂ may not be the sole gaseous factor responsible for the observed effects. Fertile hen eggs incubated in an atmosphere of 20% O₂, with helium replacing the nitrogen, show the same retardation of development. The addition of nitrogen to the extent of 10% of the partial pressure is not sufficient to support adequate development of the embryo.

FACTORS DETERMINING BOLUS CONSISTENCY OF PEANUTS MASTICATED TO

SWALLOW THRESHOLD by J.P. Allgood (intr. by S.C. Harris)

Northwestern University Dental School, Chicago, Ill.

An index of the consistency of a bolus of peanuts at swallow threshold was obtained on 53 subjects. Hypotheses considered were that "reduction" of peanuts would be determined by number of chews per unit bolus wt.; available tooth surface for chewing; and swallow threshold. The index was obtained by having each subject, on 2 separate occasions, chew a bolus of self-determined wt. to a self-determined swallow threshold; this bolus was then divided into six fractions by passing through a nest of sieves of 10, 20, 40, 80, 160 mesh per inch, and residue on filter paper. Fractions were dried and weighed. Weight of each fraction, expressed as % of total recovered wt., was multiplied by the reciprocal of the log mean particle size for that fraction, and the 6 products were summed, this sum constituting the index. Analysis of variance showed no significant difference between replications, either for indices or for the ratio of masticatory strokes per gram bolus wt. The index was correlated with the ratio of masticatory strokes per gram bolus wt. ($r = 0.63$, $p < .001$), with the index considered as the dependent variable. Regression analysis indicates that less than half of the variation among subject indices is attributable to the number of masticatory strokes per unit wt. to which the bolus is subjected.

A BIOCHEMICAL CORRELATE OF GALVANOTAXIS IN SLIME MOLD PLASMODIA. John D. Anderson*, Babette T. Stewart* and Peter A. Stewart. Physiol. Depts., U. of Illinois, Urbana, Ill. and Emory Univ., Atlanta, Ga.

Plasmodia of the slime mold, Physarum polycephalum, which have been oriented by direct current in the agar substrate (3.0 to 5.0 microamps per mm²) migrate towards the cathode at normal speed. The posterior reticulated regions contain 30% less potassium per gram wet weight than the anterior continuous regions. The anterior regions have the same potassium concentration as that of controls, approximately 32.0 microequivalents per gram wet weight. Differences in potassium concentration between anterior and posterior regions of control plasmodia, not oriented by electric current, are less than 5%. Sodium, in contrast to potassium, is generally less concentrated in the anterior than in the posterior regions of electrically oriented plasmodia, but sodium concentrations are extremely variable. Protein concentrations are uniform throughout both oriented and control plasmodia. 25% of the total potassium, but none of the sodium, is found in acidified alcohol precipitates from plasmodial homogenates. Potassium, but not sodium appears to be closely associated with the processes which differentiate anterior from posterior in an electrically oriented plasmodium.

PEPSIN OUTPUT AT VARIOUS STEADY STATES OF HISTAMINE STIMULATION

Hubert E. Appert*, John C. Scott and Markian T. Onuferko*

Dept. of Physiol. Hahnemann Medical College Philadelphia, Pa.

Nine experiments were performed on five Heidenhain pouch dogs. The experiments lasted from six to eight hours. An attempt was made to establish three steady states of response in gastric secretion by means of histamine infusions. In each experiment three different rates of histamine infusion were employed. There was a positive correlation between acid output and rate of histamine infusion in all experiments. After histamine infusion the pepsin output increased above the basal rate in all experiments. Maximal pepsin outputs ranged from 1 to 3 mg per 15 minute interval. A positive correlation between volume output and pepsin output occurred in seven out of nine experiments. Data obtained on the same animals on different days gave the impression that the slopes of the regression lines varied as greatly within animals as among animals. Pepsin concentration appeared to be independent of volume output or of the rate of histamine infusion in eight out of nine experiments. In one experiment, however, pepsin concentration increased significantly with an increase in volume output. From the data obtained to date, it is concluded that the increased pepsin output occurring after histamine infusion may involve both a "washing-out" effect and an actual stimulating mechanism. The relative importance of each of these mechanisms appears to vary within animals as well as among animals. (Supported in part by PHS Grant #A-3669)

ARE SEROTONIN, NOREPINEPHRINE AND ACETYLCHOLINE MOLECULES DIPOLAR IONS AT PHYSIOLOGICAL pH? M.H. Aprison, T.L. Folkert* and J.W. Wiggs*. Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, Indiana.

In a recent theory for the mechanism of action of serotonin (5-HT), Aprison suggested that 5-HT was not a neurohormone but a possible modulator of the acetylcholine (ACh)-cholinesterase (ChE) system (Fed. Proc. 19, 275, 1960; Biol. Psychiatry, Vol. 4, 1961, Grune and Stratton). This action was possible by direct competition of 5-HT molecules with ACh molecules both at the ChE surface and the ACh-receptor protein. Depending on the level of 5-HT present an explanation of its biphasic action is possible. Preliminary titration data with 5-HT support this concept since the pK of the OH group at position 5 is approximately 4.9, while the pK of the NH₂ group is 9.6. Additional preliminary studies with norepinephrine (NE) show that the pK of the OH group in position 3 is approximately 6.0. Recently Burn (Adrenergic Mechanisms, Ciba Foundation, 1960) reported that ACh releases NE peripherally. Data cited by Burn suggest that NE, once released, can modulate the action of ACh at the ACh-receptor protein site. The same phenomenon may occur centrally. All these facts provide a basis for an explanation of the function of 5-HT and NE as modulators of ACh action in their respective nervous system divisions. Supported by grant MY 3225 from the National Institute of Mental Health, Public Health Service.

OBSERVATIONS OF LIVING VASCULATURE IN COMPACT BONE. Kenneth A. Arendt, J. Hughes* and J. Schull*. Department of Physiology, College of Medical Evangelists, Loma Linda, California.

Radiographic techniques have not completely elucidated the nature of blood vascular elements ramifying the compactum of long bone. On the basis of histological observations, some investigators have suggested that the cortex of tubular bone is vascularized almost entirely by capillaries of uniform size and distribution and that the flow of blood is essentially from the medullary arterial system outward to the diaphyseal surface. In this study, living vessels of the rabbit tibiofibula were observed with reflected visible light. Removal of the periosteum revealed a profuse superficial vascularization of the cortex. The elements were arranged parallel to the long axis of the bone with numerous intersegmental anastomoses. Stasis was broadcast and there was no appreciable evidence of bleeding from damaged vessels. A 5 mm. diameter area of compactum was ground down to a depth approximately 2/3 way to the medulla. The surface was then cleared with mineral oil. At this level vascular distribution was considerably less dense and brisk blood flow was observed in many segments. Vascular damage was attended by a welling-up of blood into the oil layer. Typical diverging arteriolar nets and venous drainage units were identified and photographed. Arterioles constricted markedly in response to topical applications of nor-epinephrine (1:100x10³). Administration of amyl nitrite produced an augmentation of blood flow in some instances. It is apparent that the vasculature of compact bone consists of more than a simple capillary ramification. It may also be inferred that some of the cortical blood supply is derived from the periosteum. (Supported by Grant A-1762, National Advisory Council on Arthritis and Metabolic Diseases, N.I.H.).

PRESSORECEPTORS VERSUS CHEMORECEPTORS AS SOURCE OF FEEDBACK FOR ARTERIAL PRESSURE VASOMOTOR WAVES IN DOGS. G. G. Armstrong, Jr.* and L. S. Irby* (intr. by J. W. Crowell). Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

Investigations in this laboratory about ten years ago indicated that the carotid and aortic pressoreceptors could supply the necessary feedback to cause vasomotor waves of the Mayer type. This postulation was refuted by Heymans and Neil (Reflexogenic Areas of the Cardiovascular System. Boston, Little, Brown and Company, 1958. p. 181). They contended that the chemoreceptors were the elements responsible for the feedback. In the present studies, we have observed these waves in dogs even after the chemoreceptors were destroyed with N/2 acetic acid. The effectiveness of chemoreceptor destruction was verified by the absence of a respiratory response to cyanide or lobeline. Furthermore, we were able to produce damped vasomotor waves and found these waves to be relatively unaltered by destruction of the chemoreceptors. In the dog the presence of intact chemoreceptors was definitely not necessary for the occurrence of vasomotor waves. Since this laboratory's previous investigations demonstrated the disappearance of vasomotor waves following denervation of the carotid sinuses and division of the vagus nerves (thus removing the possibility of feedback from both pressoreceptors and chemoreceptors), it would certainly appear that the pressoreceptors did supply sufficient feedback to the vasomotor system for production of vasomotor waves. (Supported in part by a grant from N.I.H. and in part by a grant from the Mississippi Heart Association.)

SUPPRESSION OF THE OCULO-CARDIAC REFLEX BY MEANS OF RESPIRATORY MOVEMENTS. E. Aserinsky and D. DeBias, Dept. Physiol., Jefferson Medical College, Philadelphia, Pa.

Pressure upon the eyes has been known to induce bradycardia. Since depression of respiration is a noted side effect of ocular compression, the speculation is entertained that the cardiac slowing is actually a resultant of the apnea. Seven nembutalized dogs were hyperventilated for 7 to 10 min. to arrest spontaneous breathing. Digital pressure exerted upon the eyes during the ventilating procedure caused slight changes, if any, of the heart rate. Immediately upon stoppage of the respirator, the heart rate fell radically, or was completely arrested. Either upon resumption of spontaneous breathing or of forced ventilation the heart rate rose despite the maintained pressure on the eyes. The O₂ saturation of the blood in the ear, monitored with an oximeter, indicated that the resumption of the normal cardiac rhythm was not due to any oxygen changes in the blood. This was further confirmed by inflating the lungs with pure nitrogen; the heart rate rose with each burst of nitrogen. In instances in which a hypoxic state was induced, a slow ventricular ectopic rhythm developed. However, with each expansion of the lungs a sinus rhythm reappeared approximately 0.8 seconds after the beginning of each burst of nitrogen. When the artificial respirator was maintained at a rate of 12 strokes/min., pressure on the eyes sustained for half a minute caused no significant bradycardia to appear. It seemed that distension of the lungs was the factor involved in suppressing the vagal effects of ocular compression. The sinus rhythm appeared during spontaneous inspiration when the recorded intrathoracic pressure was low. Also, the rhythm appeared during forced ventilation when the intrathoracic pressure was high. Common to the spontaneous inspiration and the forced ventilation was the distension of the lungs.

EFFECT OF HEART DENERVATION AND THORACOABDOMINAL SYMPATHECTOMY ON SOME CARDIOVASCULAR FUNCTIONS AT REST AND EXERCISE. E. Ashkar* and W. F. Hamilton. Med. Coll. of Ga., Depts. of Physiology & Pharmacology, Augusta, Georgia.

Mean pressure and pulse contour recordings were made simultaneously with blood sampling for Fick determinations in unanesthetized dogs. A comparison of resting values and different rates of exercise on a treadmill was made with the following results: 1. The oxygen consumption and the arteriovenous difference increased with exercise only up to a certain limit. 2. The cardiac output and stroke volume increased with mild exercise but no further increases occurred with heavy exercise. 3. The peripheral resistance and the mean pressure were clearly decreased and fairly well related to the increase in the speed of the treadmill. 4. The expected heart rate increase of 5-15 beats per minute, as observed by others, was confirmed. In sympathectomized animals with denervated hearts, the normal increase in oxygen consumption and cardiac output with exercise is restricted. (Supported by the Cardiovascular Training Grant HTS-5044, National Heart Institute).

SODIUM AND FLUID ABSORPTION BY DIFFERENT REGIONS OF RAT INTESTINE IN VITRO. K. A. Aulsebrook (intr. by J. K. Sherman). Department of Physiology, Univ. Ark. School of Med., Little Rock, Ark.

A method similar to the procedure of Wilson (J. Physiol. 123:116, 1954) has been used to study absorption of Na and fluid by segments of rat intestine. Segments of small intestine 12-15 cm. in length or 7-8 cm. segments of colon everted and partly filled with a Ringer-bicarbonate buffer having glucose were placed in crystalizing dishes containing buffer and incubated in a Dubnof for 1-3 hours. The concentration of Na in the fluid moving into the serosal (inside) compartment increased from jejunum to colon, being about the same as that in the buffer in middle ileum. When glucose in the buffer was replaced by mannitol, the concentration of Na in the fluid moving across jejunum and upper ileum increased to about that in the buffer, while that in lower ileum remained unchanged. Without glucose, the amount of Na and fluid absorbed decreased by about half in small intestine and fell to nearly zero in the colon. The inhibitory effects of Ca concentrations above and below 1 mM. on Na and fluid absorption by ileum reported by Dumont et al in vivo (J. Gen. Physiol. 43:1119, 1960) were observed in this preparation. It is concluded that the concentration of Na in the solution absorbed from buffer with glucose under these conditions is relatively low in the upper small intestine and high in the lowest ileum and colon, but is increased in upper small intestine when glucose is not present, and that Na and fluid absorption by ileum are greatest at a Ca concentration of 1 mM. Supported by NIH Grant A-1905.

A PHYSIOLOGICAL BASIS FOR PARKINSONIAN TREMOR. G.Austin & C.Tsai*.
Division of Neurosurgery, University of Oregon Medical School,
Portland, Oregon.

The typical history of patients with Parkinsonian tremor states that the tremor amplitude is increased with emotion and depressed by fatigue or sleep. The worse the tremor, the greater the increase with emotional stimulation. This suggested the following 2 differential equations to describe the tremor at rest:

$$(1) \quad \frac{dY}{dt} = K Y (M-Y); \quad K = (F/I - 1)$$

$$(2) \quad \frac{dY}{d(F/I)} = K Y (M-Y)$$

F/I = ratio of facilitation to inhibition

M = maximum tremor amplitude

Y = tremor amplitude

These equations were tested by using increments of adrenalin to simulate emotion and increments of hand-squeezes or amytal to simulate fatigue. Tremor amplitude was recorded by E.M.G. in the arm. The curves for adrenalin all confirmed the theoretical effect of emotion; the curves for fatigue were confirmatory in 60% of cases. It is therefor postulated that Parkinsonian tremor represents an abnormal response of brainstem facilitatory mechanisms to emotional stimulation. This implies that the multiple lesions of the disease inactivate inhibitory regions of brainstem and cortex with respect to their downstream effects on cranial nerve and spinal cord nuclei.

ALKYLATING AGENTS AND ALLERGIC ENCEPHALOMYELITIS.
R.W. Austin* and J.D. Thomson. Dept. of Physiology, College of
Medicine, State University of Iowa, Iowa City, Ia.

Neutrophilic granulocytes and lymphocytes appear to participate in the production of autoallergic diseases, including experimental allergic encephalomyelitis, neutrophils being essential for antigen ingestion and lymphocytes for antibody production. Leukeran depresses lymphocyte production more than granulocyte production, and Myleran depresses both granulocyte and lymphocyte levels. Adult male guineapigs were inoculated with homologous brain plus Freund's complete adjuvant; at the same time, one injection of Leukeran (1.0 mgr/100 gr body weight) in oil was given subcutaneously to one series, and one dose of Myleran (same concentration) was given orally to another series. Leucocyte counts (total and differential) were taken twice weekly and animals were observed for signs of the disease. Myleran both delayed the onset of and protected against EAE while Leukeran did not delay, but did offer some protection against the disease. There was evidence that these responses were influenced by initial leucocyte levels and by upper respiratory infections. (This investigation was supported wholly by Grant No. 243 from the National Multiple Sclerosis Society.)

CHANGES IN BLOOD FLOW FROM REST TO MAXIMUM EXERCISE. Bruno Balke, Gunnar Sevelius*, and Everett E. Phillips*. Civil Aeromedical Research Institute, Oklahoma City, Oklahoma.

The radioisotope surface counting technique for measuring cardiac output and partial blood flow to various organs is particularly adaptable to exercise conditions. It was used during rest and treadmill work, in combination with the cardio-respiratory measurements of pulse rate, blood pressure and oxygen consumption, for studying functional changes during adaptation to increasing metabolic demands. During the initial phase of rather light work the increment in arterio-venous oxygen difference appeared more substantial than the increase in cardiac output. The latter, in this phase of work, gained from accelerated heart rate rather than from augmentation of stroke volume. At higher energy expenditures, however, the art.-ven. O_2 difference levelled off while cardiac output then increased linearly with oxygen requirements. Estimations of stroke volume indicated that regularly exercising subjects doubled their resting stroke volume, "normal" individuals increased it by about 33 per cent, but "inactive" ambulatory hospital patients showed no elevation from the resting level. Relative changes of the pulse-pressure x frequency product (suggested by Liljestrand-Zauser as indication of changes in cardiac output) proved far less correlated with the relative changes of cardiac output during work than the relative changes in the product of only systolic pressure and pulse rate. Coronary blood flow appeared to be approximately 7.5 per cent of the cardiac output in the work intensity ranges tested.

A MATHEMATICAL DESCRIPTION OF THE DISPERSION OF INDICATOR IN BLOOD TRAVERSING AN ARTERY. James B. Bassingthwaighe, Homer R. Warner and Earl H. Wood. Mayo Foundation, Rochester, Minnesota, and Latter-Day Saints Hospital, Salt Lake City, Utah.

The time-course of indicator concentration at any downstream point following a sudden injection upstream may be described by a combination of two processes: the first is a random distribution of transit times around some average value (t_1), and the second is a single mixing chamber with mixing volume (\bar{V}) and flow (F). This is expressed as:

$$dc/dt = \frac{K e^{-\frac{1}{2} \left(\frac{t-t_1}{\theta} \right)^2}}{\bar{V}/F} e^{-c} ,$$

in which θ is the standard deviation and K is a constant representing the peak concentration predicted by the normal density function alone. This hypothesis has been tested by comparing the time-course of dye concentration predicted by a solution of this equation with the time-course of dye concentration recorded in the blood of the femoral artery and dorsalis pedis artery in normal men following injections into the iliac artery, thoracic aorta, and right atrium during rest, exercise, and infusion of vasoactive substances. The optimal set of parameters was found by repeated solution of the equation, using an analog computer, until an optimal match between the theoretical and the recorded curves was obtained. Once the optimal values for the parameters have been determined to describe the time-course of indicator concentration at the femoral artery and dorsalis pedis artery following a sudden single injection into the thoracic aorta, these equations will accurately predict the time-course of indicator concentration at these sites following two sudden injections made within 2 to 4 seconds of each other.

GANGLION BLOCKING DRUG ON MOUSE PLASMA GLUCOSE LEVEL. Lyle V. Beck and Su Chien Chen. Univ. of Pittsburgh School of Medicine, Pittsburgh, Pa.

Each mouse tail blood sample was collected using a microhematocrit tube. Using ultramicrochemical procedures, plasma glucose was estimated by the specific Glucostat method, blood non-protein sulfhydryl by the nitroprusside method. In some but not all fasted "hyperglycemic obese" mice (Jackson Lab.), glutathione (GSH) IP, 0.0025 mols/kg, induced significant elevation of plasma glucose above the fasting level. To study the possibility that GSH induced elevation of plasma glucose might be due to GSH stimulation of epinephrine secretion by the adrenal medulla, effects on mouse plasma glucose of the ganglion blocking drug chlorisondamine dimethochloride (ECOLID), IP, 5 or 10 mg/kg, were also tested. This drug, whether used alone or in combination with GSH, invariably induced an appreciable to marked decrease in plasma glucose level, whether "obese hyperglycemic", litter mate control, or CFW male mice were employed, and whether the mice had or had not previously been fasted. This finding suggests that in the mouse adrenal medullary activity plays an important role in determining plasma glucose level. Experiments with other drugs and procedures are in progress. The interesting observation was also made that elevation in blood non-protein sulfhydryl level induced by GSH administration subsided very slowly in the "obese hyperglycemic" mice. This research was supported by NIH Grant A-3957.

A METHOD OF TESTING OLFACTORY THRESHOLDS IN DOGS. R. F. Becker, J. E. Markee* and J. E. King*. Duke University Medical Center, Durham, N. C.

Test odors in decreasing concentration were presented to trained dogs at 5 odor stations arranged in an 8 foot circle around a central rotary fan which cleared the area of odor between trials. Four samples of odor solvent served as comparison media for the test sample in each trial. In the final testing, odor material was diluted in ethanol, and one drop at any concentration was allowed to evaporate from a 3" x 1", clean, glass slide. One drop of absolute alcohol similarly evaporated served as the comparison media. Test odor remained as a barely discernible film on the test slides. As a check against the possibility of adsorbed alcohol in the test sample, two odor substances of comparable vapor pressure were paired, using one as the rewarded sample in one experiment and the other as the rewarded sample in the next experiment. Test samples appeared randomly 5 times at each station in any 25 trial block. Dogs pretrained to work off leash for a small meat reward, sat beside the station which they felt contained the test odor trace. When successful detection just differed significantly from 20%, or chance performance level, threshold was reached. In terms of molecules available for sniffing, this was 1.09×10^{15} and 1.61×10^{15} for two substances of very low vapor pressure, a value 10,000 fold lower than for humans working the same problem. For more potent odors such as clove or anise, human thresholds were only 10 to 100 fold higher than dog thresholds.

CHANGES IN MALIC DEHYDROGENASE ACTIVITY OF EXCISED RAT TISSUES AFTER THYROIDECTOMY. Samuel G. Benson* and Howard M. Klitgaard. Department of Physiology, Marquette University School of Medicine, Milwaukee 3, Wisconsin.

The oxygen consumption of the whole animal and of most tissues decreases after thyroidectomy. In vitro studies by Barker have shown that with the addition of thyroxine, malic dehydrogenase activity is decreased. This study was an attempt to determine the in vivo relationship of malic dehydrogenase (MDH) capacity to the metabolic alterations resulting from thyroxine lack after thyroidectomy. At intervals from one through twenty-eight days after thyroidectomy, the MDH activity was measured using the manometric technique described by Potter. Liver enzyme activity based on $\mu\text{l O}_2/\text{mg. tissue N}_2/\text{hr.}$ showed a statistically significant increase (<1%) from the second through the twenty-eighth day with a maximum (125%) at day twenty. Malic dehydrogenase activity of the brain varied until it peaked (135%) on day three and remained significant thereafter. Psoas MDH enzyme showed variable results during the first few days, tending to plateau at an elevated level with a maximum value (111%) on day twenty. Kidney MDH exhibited no statistically significant change after thyroidectomy. The capacity of the enzyme was correlated with the previously determined oxygen consumption of the tissues excised from thyroidectomized animals. Correlation coefficients were: Liver ($r = -0.70$), Brain ($r = -0.47$), Psoas ($r = -0.47$) and Kidney ($r = 0.09$). The above results show augmentation of malic dehydrogenase capacity in all tissues except kidney. This supports the findings of Wolff and Ball that thyroxine in vitro decreases the above enzyme, and that the inhibitory action of thyroxine is a competitive one with DPN for malic dehydrogenase. (Supported by PHS Grant A-957.)

NON-SELECTIVITY IN THE REGENERATION OF NEUROMUSCULAR CONNECTIONS IN THE RAT. Jerald J. Bernstein* and Lloyd Guth. Lab. Neuroanat. Sci., N.I.N.D.B., N.I.H., Bethesda, Md.

The following experiments were performed in an attempt to determine whether the fibers of the sciatic or tibial nerves that normally innervate the soleus and plantaris muscles regenerate selectively to these muscles after injury to the respective nerves. In addition to 9 unoperated control rats, 37 operated animals were studied four months after one of the following procedures: sciatic nerve transection and resuture in adults (9), sciatic nerve crush in adults (8), tibial nerve transection and resuture in adults (5), tibial nerve crush in adults (5), sciatic nerve transection in neonatal rats (5), sciatic nerve crush in neonatal rats (5). Recordings were made of the isometric tensions (T) developed by the soleus and plantaris muscles during supramaximal tetanic stimulation of lumbar roots L4 and L5 singly and simultaneously (L4+5). In normal rats L4 supplies a proportionately greater functional innervation to the plantaris than to the soleus, the ratio TL_4/TL_5 being significantly higher in the plantaris than in the soleus. In none of the six operated groups could any such difference in the ratio of the two muscles be demonstrated. Consequently there is no evidence of selectivity in the regeneration of the plantaris and soleus nerve fiber constituents of the sciatic or tibial nerves. Both the plantaris and soleus muscles of each operated group showed greater tension overlap than the corresponding muscles of the unoperated control group. Tension overlap was computed as follows $\frac{\text{TL}_4 + \text{TL}_5 - \text{TL}_{4+5}}{\text{TL}_{4+5}}$. Gold chloride impregnations of motor endplates indicate that the increased overlap results in part from increased numbers of dually innervated (presumably bisegmentally innervated) muscle fibers.

THYROXINE-INDUCED SWELLING OF LIVER MITOCHONDRIA FOLLOWING COLD EXPOSURE. Joseph B. Boatman, Marvin J. Rabinovitz* and Marie M. Boucek*, Wm. H. Singer Memorial Research Laboratory, Allegheny Gen. Hosp., Pgh., Pa.

Previous studies showed tissue slices from cold-exposed animals exhibited progressive changes in hydration (Boatman, et. al., Am. J. Physiol. 199:256, 1960). This study reports liver mitochondrial swelling under similar conditions in a standard sucrose media, with and without added thyroxine. Mitochondrial suspensions were prepared in the cold by standard methods from livers of rats and hamsters after 0, 1, 2, 5, 10, 15 and 20 days of cold exposure between 3-5°C. Swelling was measured by change in absorbance at 520 mμ in a Beckman DK-1 recording spectrophotometer. 25 μ volumes of mitochondrial mix prepared from 2.5 gm of wet liver, was added to 2.0 ml of 0.3 M. sucrose and absorbance recorded for the following 10 minutes in 1 cm. quartz cells with distilled water reference at 36° - 38°C. All runs were made in duplicate with and without added 0.20 μmole l-thyroxine per 2.0 ml sucrose and dry weight of all mitochondrial preparations were determined. Rat mitochondria swelled at a rate approximately twice that of from hamsters on an equal weight basis, and the total rat mitochondrial yield per gram of liver increased with continued cold from 1 to 20 days. Hamster equivalent yields increased initially to 5 days and then declined to or below control values through the 20 days of cold exposure. Added thyroxine increased mitochondrial swelling of both species by an approximately constant quantity. The results suggest that hamster mitochondria, more resistant to osmotic swelling and equally responsive to thyroxine as rat mitochondria, are less susceptible to disruption of oxidative processes by hydration changes occurring with cold exposure. (Supported by U.H.P.H.S. - A-3543.)

BLOOD FLOW THROUGH THE HIND LIMBS OF ANESTHETIZED DOGS DURING VARIOUS ENVIRONMENTAL STRESSES. D. J. Boon (intr. by J. P. Marbarger). Aeromedical Lab., Univ. of Illinois, Chicago, Ill.

Mongrel dogs (11.1 - 20.0 Kg.) were divided into three groups (Grp. I - 30 min. control with ambient pO₂ 150; Grp. II - 15 min. pO₂ 150 followed by 15 min. pO₂ 75; Grp. III - 15 min. pO₂ 75 followed by 15 min. pO₂ 150) in order to assess circulatory adjustments during exposure to combinations of temperature (1 or 23° C.), barometric pressure (393 or 744 mm. Hg) and hypoxia (pO₂ 75). Oxygen partial pressures of 75 and 150 mm. Hg were simulated with decompression chamber and gas mixtures. Femoral arterial flow decreased progressively in Grp. I exposed to cold and/or altitude. Hypoxia in Grps. II and III always produced elevations in femoral arterial flow, femoral systolic and diastolic pressures, heart rate and respiratory rate. Maximum increases in flow occurred in Grp. II dogs at 23° C. during reduced barometric pressure; minimum alterations, in Grp. III animals at 1° C. with reduced pressure. Femoral arterial pressures increased approximately 12% during hypoxia and were independent of the other environmental conditions. Venous pressure variably increased with hypoxia. These data therefore indicate that the combined stress of altitude and cold more rapidly causes a decrease in basal blood flow and more effectively decreases the response of the hind limbs to hypoxia than does altitude or cold alone.

SKELETAL MUSCLE FUNCTION DURING ACUTE POTASSIUM DEPLETION. S. Y. Botelho, S. B. Beckett* and G. D. Webster, Jr.* Depts. of Physiology and Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia 4, Pennsylvania.

Under nembutal anesthesia, peritoneal dialysis (with potassium-free solution for from 1 to 4.9 hrs.) removed 0.90 to 3.16 mEq K^+ from 9 cats. Knowing the plasma K^+ and assuming an extracellular fluid volume of 288 ml/kgm, the extracellular K^+ loss was determined and found to be insufficient to account for the K^+ in the dialysis fluid. Determinations of urine K^+ were not done. Skeletal muscle function was studied before and during dialysis by recording the action potential and isometric tension developed by the *in situ* triceps surae muscle upon stimulation of the sciatic nerve. Comparison with similar data obtained from 6 undialysed control cats indicated the following alterations of function in the K^+ depleted cats: 1. The area and duration of the integrated action potential were increased. 2. Post-tetanic potentiation of single twitch tension was decreased. 3. The ratio of tetanus:single twitch tension was decreased without a change in single twitch tension. 4. The intact muscle was less stiff. 5. There was no evidence of change in nerve conduction or neuromuscular transmission. When these changes in skeletal muscle function occurred, there were no significant changes in ECG, EEG or mean arterial blood pressure. (Supported in part by a grant from the U.S.P.H.S. National Institute of Neurological Diseases and Blindness, B-128).

THE FAST INITIAL RATE OF MYOSIN ATPASE ACTIVITY. W. J. Bowen, L. C. Stewart* and H. L. Martin*. National Institutes of Health, Bethesda, Md.

When glycerol-treated rabbit psoas muscle (g-t) fiber-bundles (150-200 μ wide) are made to do ATP-induced work by lifting loads, they do about 40% of the work of which they are capable in the first second and 70% in the first three seconds. This burst of energy utilization occurs during the fast initial phase of the splitting of ATP by myosin as described by Weber & Hasselbach and elaborated upon by Kitagawa & Tonomura. In fact, the latter state that the initial burst may be necessary for muscle contraction (J. Research Inst. for Catalysis, Hokkaido Univ.).

We tested the possibility that the extra phosphate produced during the fast phase is an artifact caused by the action of TCA on PA which was used to stop the reaction. It was found that the fast initial phase occurred when the reaction between myosin B (made with Weber-Edsall solution) and ATP was stopped by applying $CuSO_4$. With myosin B as the ATPase, ADP, determined enzymatically, was produced at the same fast initial rate that phosphate was; however, in our experience the magnitude of the fast phase varied from none to considerable in different preparations of myosin B. Using fiber bundles as ATPase by holding them nearly isometric in 0.05 ml of 10 mM ATP and $MgCl_2$ (pH 7.0) for 3, 10 and 30 seconds, the fast initial phase occurred in each of the g-t preparations tested. Also, using APPP32 as substrate the ratio of counts per minute to μM phosphate released indicated, as Tonomura & Kitagawa maintain, that all the phosphate comes from the ATP and none from the fibers. This leaves the fast initial phase as an enzymatic attribute of myosin ATPase.

THE EFFECTS OF SARIN ON THE CHOLINESTERASE SYSTEM OF RABBIT BRAIN AND CEREBROSPINAL FLUID. M. B. BOWERS, JR., AND G. KETNER (INTR. BY J. H. WILLS). USA CHEM RES & DEV LABS, ARMY CHEMICAL CENTER, Md.

IN CONJUNCTION WITH STUDIES ON THE CENTRAL EFFECTS OF ORGANOPHOSPHATE CHOLINESTERASE INHIBITORS, CERTAIN CHANGES IN CEREBROSPINAL FLUID AND BRAIN WERE INVESTIGATED AFTER SUBCUTANEOUS ADMINISTRATION OF VARYING DOSES OF SARIN. CONTROL LEVELS OF CHOLINESTERASE ACTIVITY IN CSF WERE DETERMINED IN THREE ANIMAL SPECIES (RABBIT, DOG, GOAT) USING SUBSTRATES WHICH DISTINGUISH BETWEEN SPECIFIC AND NON-SPECIFIC CHOLINESTERASE. SPECIFIC CHE ACTIVITY WAS FOUND IN THE CSF OF ALL THREE SPECIES. USING THE ISOLATED CLAM HEART, ACETYLCHOLINE WAS NOT DETECTABLE IN CSF FROM UNTREATED ANIMALS (THRESHOLD ABOUT 10^{-9} GM/ML CSF). IN POISONED ANIMALS, ACETYLCHOLINE ACTIVITY IN CSF ROSE MARKEDLY (TO LEVELS OF $2-8 \times 10^{-8}$ GM/ML CSF) AFTER CSF CHOLINESTERASE ACTIVITY FELL TO ABOUT 15% OF CONTROL VALUES. THE PRESENCE OF ACETYLCHOLINE IN CSF COULD FIRST BE DETECTED AFTER ADMINISTRATION OF 1 LD₅₀ OF CHE INHIBITOR. INHIBITION OF CHE AND ACCUMULATION OF ACETYLCHOLINE ALSO OCCURRED IN BRAIN, BEING SLIGHTLY GREATER ON A PERCENTAGE BASIS THAN THE CORRESPONDING CSF CHANGES FOR A GIVEN DOSE OF INHIBITOR.

PATHOPHYSIOLOGY OF THE URETER: III - PARTIAL LIGATION OF THE URETER OF THE DOG. Saul Boyarsky and Jose Martinez (intr. by - Alfred Gilman). Albert Einstein College of Medicine, New York.

Large dogs underwent partial ligation of the upper ureter over #3 French catheter or #25 wire for 2-70 days. The effect increased with the duration of the ligation; uniform strictures were not produced by this technique. Immediately after ligation, the effect on the ureter was: 1) cessation of urine flow at the orifice, even during diuresis; 2) cessation of peristaltic contractions below the ligature; 3) interruption of peristaltic transmission at the point of ligation; 4) dilatation of the ureter above the ligature; 5) response to histamine was present. The late effect was: 1) marked diminution of efflux and peristalsis; 2) response to histamine retained. At autopsy only one dog showed complete obstruction. Two interpretations might explain the completeness of the peristaltic block - 1) conduction defect in ureteral muscle; 2) overdistension with muscle decompensation above a mechanical block. The late effect on the kidney was to produce a hydro-nephrosis; 1) intravenous urograms showed dilatation and diminished excretion; 2) minimal urine flow at the orifice; 3) intrapelvic pressure was elevated above normal; 4) renal artery pulsation was transmitted by the pelvic contents; 5) during diuresis, the intrapelvic pressure rose further even though the pelvis was completely distended; 6) on production of ureteral spasm by histamine, the intrapelvic pressure rose in some dogs and fell in others. (Supported by a grant from U. S. P. H. S.)

THE EFFECT OF RESTRAINT STRESS ON GASTRIC SECRETION IN THE CHRONIC GASTRIC FISTULA RAT. David A. Brodie, Richard W. Marshall, and O. M. Moreno (intr. by C. A. Winter). Merck Institute for Therapeutic Research, West Point, Pennsylvania.

A recent report has shown that restraint stress markedly decreased gastric secretion in the pylorus-ligated rat and concluded that gastric acidity was not involved in the production of restraint ulcers. In order to investigate further the role of gastric acidity in restraint stress, stainless steel cannulae were implanted in the rumen portion of the stomach of male Holtzman rats, and gastric contents were collected in 4-hour periods over 24 hours in free moving and restrained rats. The volume of gastric secretion in the unrestrained chronic fistula rats was 5.3 ml. in the initial collection period and approximately 3 ml./4 hours in the subsequent 5 collections. When these rats were restrained, the volume of gastric secretion was reduced in the initial period to 3.9 ml. and in subsequent periods to about 2.0 ml./4 hours. Free acid secretion in the unrestrained fistula rat was 36 mEq./L. initially, and the acid level gradually increased to 52 mEq./L. at the end of the 24-hour collection. When the fistula rats were restrained, the initial free acid values increased to 70 mEq./L. and remained at approximately this level for the duration of the test. Total acid values paralleled the free acid changes. This study suggests that increased gastric acidity may be a factor in restraint-induced ulcers in rats.

ANALOG COMPUTER SIMULATION OF THE REGULATION OF BODY TEMPERATURE.

A. C. Brown (intr. by A. M. Scher). Dept. of Physiology & Biophysics, Univ. of Washington, Seattle, Wash.

An electronic analog computer has been constructed to solve simultaneously the equations of thermal balance of a model simulating a human. The analog was divided into three segments. The first evaluates environmental thermal demands and resulting heat fluxes from the body. The equation governing temperature distribution within the body— $C(\partial T/\partial t) = \text{div}(K \text{ grad } T) + H_m + C_b Q(T_a - T_v)$, where C and C_b = heat capacities of tissue and blood respectively, T = tissue temperature, K = thermal conductivity, H_m = metabolic heat generated per unit volume, Q = blood flow, and $(T_a - T_v)$ = temperature difference between the blood entering and leaving a given volume element—is solved by the second segment by dividing the analog of the body into a finite number of parts thus approximating the partial differential equation by a difference equation. The third segment incorporates the feedback control of metabolism, vasomotor state, and sweat rate. By a suitable choice of parameters such an analog can be made to agree with experimental results for steady states and, if the feedback from internal and surface temperatures is modified by the transfer function $(a_1 s + 1)(b_1 s + 1)(a_2 s + 1)(b_2 s + 1)$, the analog reasonably predicts transient changes. Both a_1 and a_2 are in the order of minutes, b_1 and b_2 are in the order of hours, and $a_1 > a_2$, $b_1 > b_2$. The analog shows little instability or oscillation over a rather wide range of feedback parameters, indicating an inherently stable temperature regulation system. (Sponsored by Wright Air Development Division, ARDC, USAF).

PLASMA IRON TURNOVER (PIT) AND SERUM IRON DURING AND AFTER CYANIDE ADMINISTRATION IN DOGS. E. Brown, P. J. Sanazaro* and N. Pearl, Cardiovascular Research Institute and Dept. of Medicine, Univ. of California, San Francisco.

Sodium cyanide (5.8-22.2 mM/Kg) was infused for 6 hr into upper abdominal aorta of 5 dogs prepared with morphine and promazine. Marked respiratory and circulatory changes and reduction of urine osmolality occurred only at the higher doses of cyanide. O_2 was administered; arterial pO_2 was 134 to 370 mm Hg. Serum $[Fe]$ and disappearance rate of injected Fe^{59} from plasma were determined at various intervals. PIT (mg/24 hr/Kg), calculated from these data and expressed as % of control PIT for each dog, was depressed during the infusion (29-56%) but usually recovered within 48 hr. In 3 animals studied for longer periods, PIT rose further before day 4, reached 174%-212% by day 10 to day 14 and returned to control level in 3-4 weeks. Similar elevations of PIT occurred in 2 of 3 dogs subjected to 20-24 hr of isovolemic anemia (hematocrit 24-29%). Curves showing time-course of serum $[Fe]$ and PIT were roughly parallel in most experiments. Plasma collected 6-48 hr from beginning of experiment in the anemic and cyanide-treated animals showing high PIT had only slight, if any, erythropoiesis-stimulating property when assayed in fasted rats.

THE EFFECT OF CARBON DIOXIDE INHALATION ON SWEATING AS MEASURED BY RESISTANCE HYGROMETRY. R. W. Bullard, Department of Physiology, Indiana University School of Medicine, Indianapolis.

Sweating is commonly observed during the inhalation of carbon dioxide, yet few studies exist on the nature of this response. Human arm and hand sweating rates were measured by blowing 25 to 50 liters/min. of dry air over the chamber enclosed limb and continuously recording the relative humidity of the effluent air with rapid response, narrow range, electrical resistance hygrometer elements. In an ambient temperature of 38°C. inhalation of 6% carbon dioxide in air produced a transient two to four fold increase in the integrated minute sweating rate in all subjects studied. Characteristically the sweating rates peaked at 4 to 6 minutes after the start of the carbon dioxide inhalation, then levelled off at higher than control values after 8 to 10 minutes. Following the inhalation period the sweating rates declined rapidly and remained lower than control values for 6 to 12 minutes. The sweating increase was still seen after the hand was effectively removed from the system by covering with a rubber glove. However, the response with 6% carbon dioxide was greatly diminished or completely absent at an ambient temperature of 26°C. The response is not the emotional stress sweating associated with the palmar surfaces, but appears to be thermal sweating. The characteristics of the sweating rate curve on carbon dioxide inhalation and the marked decline following inhalation suggest the speculation that carbon dioxide may act by readjusting thermal regulatory set points at a slightly lower level. Supported by Contract # DA-49-007-MD-947 from the Research and Development Division, Office of the Surgeon General, U. S. Army.

24-HOUR RHYTHM OF POTASSIUM EXCRETION AS INDICATOR OF PEAK EFFICIENCY TIME. H.A. Cahn* and G.E. Folk, Jr. (intr. by G.W. Searle). Department of Physiology, State University of Iowa School of Medicine, Iowa City, Iowa.

Hourly photometric measurements in microequivalents/minute were made of urinary potassium excretion rate in eleven male human subjects. The measurements were made while the subjects were in an air-conditioned environmental chamber over a time span of 32 hours. The raw data graphs and Fourier series best-fit curves illustrate a sequence of "high-setting" points and a "low-setting" sequence approximately 12 hours later. This was considered presumptive evidence of a physiological day-night setting commonly referred to as a 24-hour rhythm. By comparing the subject's impression of his usual time of maximum efficiency (morning, afternoon or evening) with the time of the "high-setting" sequence, it was found that they coincided in ten out of eleven subjects. It was concluded that potassium high-setting time (as the mean time of the "high-setting" sequence) is as satisfactory an indicator of peak efficiency time as Kleitman's (Physiol. Rev. 29: 1, 1949) use of the temperature high-setting time. (Supported by Iowa Mental Health Research Fund.)

THE TEMPORAL OCCURRENCE OF THE OXYGEN DEBT DURING EXERCISE.

P. Caldini*, D.N. Gupta*, T.E. Cuddy* and R.M. Cherniack. Departments of Surgery and Medicine, University of Manitoba.

Although it is known that an oxygen debt develops during exercise, the time taken to develop this debt has not been quantitated. Oxygen consumption was measured with the open-circuit technique on normal human subjects at rest, during three levels of exercise on a treadmill for increasing periods of time, and during recovery. The oxygen debt appeared to develop in two stages. In the first minute of exercise, at various work loads, the greatest part of the oxygen debt was already contracted. If the duration of exercise was lengthened there was a further much slower rise in the oxygen debt. Both the initial stage and the slope of the second stage increased with the severity of the exercise. This suggests that the oxygen deficit contracted during exercise is an expression of: a) depletion of the oxygen stores of the body in the early period of exercise before local and general readjustments of the cardiovascular and respiratory systems take place, and b) accumulation of anaerobic metabolism during the "steady state".

EFFECT OF TRANSIENT CHANGES OF PERFUSING BLOOD PHOSPHATE ON RENAL EXCRETION OF ACID. Gaspar Carrasquer*, Larry A. Raymond*, Carole A. Caras*, and William A. Brodsky. Department of Experimental Medicine, University of Louisville, Louisville, Kentucky.

Transient net secretion of phosphate has been demonstrated reproducibly after injection of H_2PO_4^- into the renal artery of acidotic dogs with underlying plasma phosphate of 3-6 mM/L (Carrasquer and Brodsky A.J.P. 199:1239, 1960). This suggests that tubular secretion of H_2PO_4^- ions could be a mechanism of urinary acidification during phosphate loading. Even when net secretion of phosphate is not demonstrated (alkalosis, HPO_4^- instantaneous injection, steady state conditions of neutral phosphate loading), paradoxical aciduria observed suggests the presence of H_2PO_4^- secretion into the tubule. Transient paradoxical aciduria was observed after close arterial injection of Na_2HPO_4 (500 μM) under both acidotic and alkalotic conditions. Injection of equimolar amounts of K_2HPO_4 into the same dogs under the same conditions did not induce paradoxical aciduria. Doubling the dose of injected Na_2HPO_4 (1200 μM) also eliminated paradoxical aciduria. Paradoxical aciduria after Na_2HPO_4 injection may be due to tubular secretion of H_2PO_4^- . Obliteration of paradoxical aciduria after injection of higher amounts of Na_2HPO_4 may be due to "flooding" of the tubule with HPO_4^- ions in amounts sufficient to buffer the pH effects of any acid secreted. The potassium effect described could be due to "flooding", or to competition of K^+ and H^+ for a common carrier.

FIXATION OF EXPERIENCE IN THE RAT SPINAL CORD. T. J. Chamberlain*, P. Halick* and R. W. Gerard. Mental Health Research Institute, Ann Arbor, Michigan.

Gerard and others (see "Fixation of Experience." Symposium on Brain Mechanisms and Learning, Montevideo, ed. A. Delafresnaye, Blackwell Scientific Pub., 1961, England) have suggested that a certain time interval is required for a learning experience to become "fixed." A model for further investigation of this hypothesis is provided by DiGiorgio (Arch di Fisiol. 27:515, 1929) who demonstrated that a postural asymmetry in the limbs of dogs, rabbits and guinea pigs, produced by a unilateral brain lesion, would persist after the spinal cord was transected. We have confirmed and extended her findings. For the determination of fixation time in the rat spinal cord, cerebellar lesions were made which yielded hind-limb postural asymmetry. At varying time intervals following the development of these asymmetries, the spinal cords were transected. In 7 animals, when the cords were sectioned after a short interval (less than 40 minutes), the postural asymmetries did not persist. In 18 animals, when the cords were sectioned after long intervals (more than 45-50 minutes), the asymmetries persisted. These asymmetries were tonically maintained, resisting passive displacement. In the "long interval" animals, the fixated asymmetries were often not measureable during spinal shock, but would become manifest as the reflexes returned. In 5 cases, where the original asymmetry was transient and irregular, no persistence was seen, even after long intervals. A fixation time of 45 minutes is required to produce enduring material changes in the neural systems of the spinal cord. Electrophysiological and biochemical studies are currently in progress to follow the cord changes which occur during fixation.

THE CHEMICAL COMPOSITION OF BRAIN TISSUES AND ITS CHANGES DUE TO X-IRRADIATION AND DISTURBANCES IN FLUID BALANCE. Shu Chien*, C. P. Pallavicini* and M. I. Gregersen. Dept. of Physiology, Columbia University, New York City.

Dogs were acutely sacrificed with Nembutal or by hemorrhage and various brain tissues (grey matter, white matter, caudate nucleus, etc.) were quickly removed. With the use of the method of Gregersen and Pallavicini (Fed. Proc. 14: 63, 1955), it was found that the average water content (and S. E. m) was 79.90% (0.13) for the grey and 67.86 (0.29) for the white; lipid: grey 4.75 (0.13), white 16.99 (0.36); protein: grey 12.27 (0.23), white 10.88 (0.13). The electrolyte concentrations (meq/L H₂O) were-- Na: grey 78.6 (1.31), white 78.5 (1.14); K: grey 125.2 (1.35), white 124.6 (0.96); Cl: grey 52.4 (0.67), white 55.9 (1.27), and Mg: grey 11.4 (0.46), white 15.1 (0.90). After salt depletion (peritoneal dialysis), the Na and Cl of the grey and the white decreased, whereas the water increased slightly. Opposite effects were found after i. v. 30% NaCl. In water intoxication, the water of the grey, white and caudate increased significantly, whereas the electrolytes decreased. After sucrose diuresis, the water of the white and the caudate decreased, whereas the electrolytes increased. Three days after 1000 r total-body x-irradiation, the water increased in grey and white as did Na, whereas K decreased. Four to 10 days after 2000-4000 r head irradiation, only Na increased. Twenty hours after 15000 r head irradiation, the water decreased in the white, and Na and Cl increased in the caudate. The results suggest that the water and electrolyte changes in brain after total-body irradiation are probably secondary.

ELECTRODERMAL REACTION OF CHRONIC THALAMIC CATS. R. W. M. Chun*, R. Emmers* and G. H. Wang. Laboratory of Neurophysiology, University of Wisconsin, Madison, Wis.

At the last Autumn Meeting, Ladpli and Wang (Physiologist, 1960, 3:99; J. Neurophysiol., 1960, 23:448) reported the presence of synchronized spontaneous potential waves in the four paws of unanesthetized normal and chronic striatal cats and their absence in the paws of cats with lesions of the CNS caudal to the interbrain. They ventured the hypothesis that the center for synchronizing the spontaneous potential waves of the four paws lies in the interbrain. They also emphasized the necessity of making observations on the spontaneous potential waves in the four paws of chronic thalamic cats--i.e., cats with the cerebral cortex and striatum removed bilaterally. Now we have done such experiments and found that unanesthetized chronic and thalamic cats do not have spontaneous potential waves synchronized in the four paws. This fact rejects the hypothesis mentioned above, and, together with observations of Wang and Akert on chronic striatal and thalamic cats described elsewhere, indicates that the striatum is an important center for coordinating and regulating the activities of somatic and autonomic motoneurons in the spinal cord. (Supported by Grant B-1460 from NINDB)

ENDOGENOUS CARBON MONOXIDE FORMATION IN MAN. R.F. Coburn*, R. Kamener*, W.S. Blakemore, and R.E. Forster, Dept. of Physiology, Grad. School of Med., and Dept. of Surgery, Med. School, Univ. of Pa., Phila., Pa.

Previous work has suggested, but not conclusively proved that carbon monoxide (CO) is produced endogenously in man. In order to investigate this problem we utilized two different types of experiments. (1) We measured blood carboxyhemoglobin (COHb) during 100% O₂ breathing for 4 to 8 hours in three subjects. The blood COHb did not decrease exponentially toward zero concentration, but leveled off at values of 0.11 to 0.14% COHb. (2) We measured blood COHb in four subjects aged 22 to 30 while they rebreathed in a closed circuit for four hours. The blood COHb rose at a rate equivalent to a CO production rate (\dot{V}_{CO}) of 0.00696 \pm S.E. 0.0003 ml/min. COHb was measured by liberating the CO with K₂F₈(CN)₆ and measuring the resulting CO in a gas volume of 250 ml with an infrared CO meter. The S.D. of this method with a 2 ml blood sample is 0.007 ml/100 ml CO in the range studied. These data indicate that CO is produced in man. If CO originates from the alpha methene bridge C atom of the heme which is cleaved during Hb degradation according to the Lemberg schema, as suggested by Sjostrand, a theoretical mean \dot{V}_{CO} can be calculated assuming an average red cell survival time of 120 days. This calculated value, 0.0069 ml/minute is not significantly different from our measured \dot{V}_{CO} . Blood COHb did not decrease significantly after 24 hours of antibiotic suppression of intestinal flora in three non smoker patients. This suggests that the normal CO production is not caused by bacteria in the lower gastrointestinal tract. We have derived an equation relating the steady state blood COHb and \dot{V}_{CO} , the diffusing capacity, alveolar ventilation and alveolar PO₂.

PHARMACOLOGICAL ANALYSIS OF EVOKED GENERALIZED NEOCORTICAL DISCHARGES. B. Cohen*, G. Marini*, and D.P. Purpura. Dept. of Neurological Surgery, Columbia University, New York.

Surface and subsurface (focal) synaptic components of long-latency neocortical responses evoked in barbiturized cats by hippocampal and peripheral stimulation have been analyzed with strychnine and ω -amino aliphatic acids. Variabilities in wave form and latency of hippocampal evoked generalized discharges (HGD's) and 'secondary discharges' (SD's) to sciatic nerve stimulation at deep levels of barbiturate narcosis are eliminated by systemic strychnine. Topical strychnine inverts the polarity and markedly enhances late components of HGD's and SD's in sensorimotor cortex and may completely invert surface and focal responses in suprasylvian gyrus. Spontaneous paroxysmal discharges are identical to evoked SD's and HGD's after strychnine. Elimination of surface evoked activity and depression of focal responses is observed after topical ϵ -amino caproic acid (C₆). Topical GABA exerts relatively little effect on both varieties of responses. Addition of GABA to sites previously treated with strychnine or C₆ restores components of responses eliminated or inverted by the latter compounds. This restoration proceeds through stages during which surface and focal responses are differently affected. Interpretation of the observed effects in terms of the possible synaptic organizations involved in the overt and drug-altered SD's and HGD's indicates that the polarity reversals result from axodendritic epsp's developing after strychnine-blockade of ipsp's. It is inferred that ipsp's are major components of the surface positivity in the overt response.

THE RELATIONSHIP BETWEEN IN VIVO RENAL EXCRETION AND METABOLISM OF α -KETOGlutARATE (α -KG) AND THE PAH TRANSPORT PATHWAY IN THE DOG. Julius J. Cohen and Evelyn Wittmann*. Univ. of Rochester, Rochester, New York

Exogenous α -KG may serve as a model for studying the relationship between renal utilization and transport of metabolites: its utilization in vivo may account for the entire renal O_2 consumption; also, α -KG undergoes net tubular reabsorption in clearance studies with characteristics of an active transport mechanism. Reports from other laboratories indicate that α -KG blocks both PAH uptake by rabbit kidney slices as well as Tm-PAH in dogs. We have studied renal utilization and excretion of α -KG during administration of substances known to affect PAH transport. Renal clearance and stop-flow techniques were used to characterize α -KG excretion; right renal A-V differences for diodrast and α -KG were used to determine renal blood flow and metabolism of α -KG. Stop-flow analysis experiments show α -KG reabsorption (disappearance) occurs in the proximal tubule. Examples of the relationship of α -KG reabsorption to the PAH transport pathway are seen by the effects of A, probenecid; B, 2,4-dinitrophenol; and C, acetate: A & B enhance net reabsorption of α -KG. C, on the other hand, decreases net α -KG reabsorption; in some instances net secretion of α -KG is observed with acetate. The effects of A & B are limited to transport of α -KG alone; C however, reduces both reabsorption and utilization of α -KG. Thus, the utilization of α -KG is not completely separate from its effects on the PAH transport mechanism.

PHYSICAL AND REFLEX FACTORS IN FLUID ASPIRATION. H.J.H. Colebatch and D.F.J. Halmagyi (intr. by J.H. Comroe, Jr.). Dept. of Med., Univ. of Sydney, Sydney, Australia.

The introduction of small quantities of fresh water into the trachea of lightly anesthetized, intubated, spontaneously breathing sheep produced a gross fall in lung compliance (C_L) accompanied by a reduction in arterial oxygen saturation (1). The mechanism of this reaction was investigated. Studies with 100% oxygen showed that the C_L fall represented airway closure, the blood flow through non-ventilated areas being responsible for the fall in arterial oxygen saturation. As a per cent of the control value, the C_L fall after 1 ml/kg fresh water in 12 intact sheep was 71 ± 9.4 . A non-foaming fluid with a surface tension of 27 dynes/cm had the same effect as fresh water. Prior vagotomy significantly reduced the C_L fall (47 ± 11.6), ($P < .01$). After 0.2 mg/kg atropine the C_L fall (29 ± 9.8) was significantly less than after vagotomy ($P < .02$). In vagotomized animals the reaction to water was markedly intensified with prostigmine. Intravenous infusion of isoproterenol reduced the C_L fall after water, but greater protection was obtained after aerosol administration. Inflation of the lung after sea water caused a further fall in C_L (1). Atropine prevented this reaction and facilitated reinflation of the lung. Further improvement was obtained after aerosol isoproterenol. The findings indicate that the reaction to water is a reflex response of the parasympathetic nervous system with both central and peripheral components, and provide the basis for improved treatment of fluid aspiration.

1. Colebatch, H.J.H. and Halmagyi, D.F.J. J. Appl. Physiol., 1961, in press.

CONTINUOUS I.V. INFUSION OF VERY SOLUBLE INERT GAS (ETHERS) SOLUTIONS TO MEASURE BLOOD FLOW. Thomas L. Connolly*, Alfred W. Brody, James J. Navin*, James J. Shehan*, James R. Wagner*, and Michael J. Weaver*. The Creighton University School of Medicine, Omaha, Nebraska, aided by grant from Nebraska Heart Association.

During I.V. infusion of a sufficiently soluble gas, equilibrium may occur in the lungs before recirculation. Rapid physical methods of analysis permit measurement of equilibrium tension in expired air. For inert gases, Henry's Law permits calculation of the dilution rate of the injectate using only a single calibration point. This dilution rate is the blood flow. The method has been validated in experiments on models and on cats. "Slug" injection also produces curves which may be read for flow rate. Advantages of this method are the lack of need for an arterial sample or for cardiac catheterization, ease in calibration, and rapidity and ease of calculation.

EFFECT OF MICROWAVE INDUCED HYPERTHERMIA ON THE CARDIAC OUTPUT OF THE RAT. Theodore Cooper, Teresa Pinakatt* and Alfred W. Richardson, Dept. of Surgery and Dept. of Physiology, St. Louis University School of Medicine, St. Louis, Missouri

Previous studies of circulatory adaptation in rats subjected to microwave hyperthermia indicated consistent increases in heart rate and arterial blood pressure but did not detail changes in cardiac output. The thermodilution method for the measurement of cardiac output has been adapted to the rat for serial measurements over a wide range of body temperature. Studies on 28 albino rats, anesthetized with pentobarbital sodium and exposed to 2450 megacycle cw microwaves, have shown that the cardiac output increased 26% at a rectal temperature of 40°C., 65% at 40.5°C., then regressed to a 47% increase at 41°C. Further increases in rectal temperature were accompanied by decreases in cardiac output until final respiratory and cardiac failure ensued. Termination of irradiations at rectal temperatures of 41°C. or below resulted in recovery of the animal. During microwave exposure as the rectal temperature rose from 37.4°C. to 40.5°C. there were increases in heart rate, arterial blood pressure and pulse pressure, and cardiac stroke volume. At higher rectal temperatures arterial pulse pressure and cardiac stroke volume were the first to decline, followed by heart rate, arterial blood pressure, and cardiac output. In summary, these observations indicate that maximum cardiac output during microwave induced hyperthermia in the rat is reached at a rectal temperature of 40.5°C. and that greater thermal stress leads to progressive circulatory failure.

*Supported by contract NR 102-362, Office of Naval Research

A THERMAL EQUIVALENT OF SUNSHINE FOR CLOTHED MEN AT WORK IN A HUMID ENVIRONMENT. F.N. Craig and E.G. Cummings*. U.S. Army Chemical R&D Labs., Army Chemical Center, Maryland

Two men clad in long underwear and a utility uniform, wearing a protective mask and helmet liner and carrying a 20 pound pack walked on a treadmill outdoors at an average air temperature of 85°F and water vapor pressure of 20 mm Hg and indoors at 85°, 100° and 115°F at the same vapor pressure. The cloud cover averaged 26 percent and solar intensity averaged 580 Cal/sq m/hr. The best index of physiological strain was the slope of increase in mean body temperature with time. From the regression of the index on indoor air temperature, the temperature required to produce the same index as observed outdoors in the sun was found to be 10°F higher than the outdoor air temperature.

SHORT-CIRCUIT CURRENT ACROSS MAMMALIAN RETINA.

Donald R. Crapper* and Werner K. Noell. Dept. of Physiology, Univ. of Buffalo, Buffalo, N. Y.

A lucite chamber secured within the eye bulb after removal of the anterior portion of the eye electrically isolated the retina from anterior current shunt between inside of the eye and extra-ocular tissue. The system was kept under 10 - 20 mm Hg pressure, thus maintaining the normal contour of retina and sclera. Current was measured by a negative feed-back circuit (Menninger et al, Rev. Scient. Instr., 31: 519, 1960) which clamped the transretinal current path at ground or other selected potentials. Current values were obtained for all light induced responses which produce electroretinographic potentials. Highest short-circuit current, up to 200 μ A, resulted from intravenous injection of sodium azide which is known to increase the D.C. potential across the eye instantaneously and reversibly (Am. J. Physiol. 170: 217, 1952). The azide induced current was linearly related in magnitude to transocular clamping potential over a wide range; it reversed in direction at inside plus 75 mV. This reversal voltage did not vary significantly in relation to azide concentration or response magnitude at ground potential. These and other observations suggest that azide affects the "internal resistance" of an active ion transport system across a retinal barrier, probably associated with the pigment epithelium. Light induced potentials which were unaffected by azide displayed an entirely different relationship between clamping voltage and current generated.

Supported by USPH Grant B-2710.

SERUM GLUTAMIC-OXALACETIC TRANSAMINASE CHANGES FOLLOWING EXERCISE IN TRAINED AND UNTRAINED MEN. Jerry B. Critz and Arthur W. Merrick. Dept. of Physiology and Pharmacology, Univ. of Missouri, Columbia.

Normal levels of SGOT were determined in untrained men, and freshmen and varsity athletes before and immediately after exposure to the Harvard Step Test. The serum enzyme was analyzed also in the same varsity athletes immediately after a time trial in their track event. SGOT was depleted significantly in untrained men following exercise. No depletion was observed in either group of trained athletes following exercise. After a time trial, however, varsity athletes exhibited a significant decrease in SGOT. This decrease may be related to adrenocortical activity. Increased adrenal cortex activity has been reported in athletes before crew time trials (Hill, et al., Arch. Int. Med. 97: 269, 1956). Adrenal cortex activity increases if psychological stress is present (Mason, et al., Science. 133:1596, 1961) and in a highly competitive, individual sport, such as track, emotional stress is not an improbability. Cortical secretions do not increase, however, in response to physical exertion if there is no psychological implication (Connell, et al., Acta Endocr. 27:179, 1958). Cortisone has been shown to cause a mobilization of GOT to skeletal muscle, heart and liver. Cortisone also increased the work performance of rat muscle (Ingle, et al., Endocrinology. 51:487, 1952). The explosiveness with which energy is expended in a track event may make it necessary to utilize this mechanism to restore metabolic equilibrium subsequent to a maximum competitive effort. SGOT changes in untrained men may be interpreted as an attempt to make more fuel (oxalacetic acid) available to the citric acid cycle to meet the unusual demand placed on the individual. The athlete may not need this mechanism to accomplish a routine exercise when psychological stress is not involved.

EFFECT OF OXYGEN ON PERFUSED LUNGS OF DOGS. G.J. Cropp and K.S. Gullixson (intr. by R.H. Kellogg). Cardiovascular Research Inst., Univ. of Calif. Med. Center, San Francisco.

During initial studies on 16 dogs (pentobarbital anesthesia) we perfused pulmonary and systemic circulations separately. By ventilating the vascularly isolated lungs with different gas mixtures, we altered pulmonary blood gas tensions without affecting systemic blood gases. When we changed the inspired gas from nitrogen or air to oxygen, or from 5% CO₂-air to 5% CO₂-O₂, pulmonary vascular resistance and pulmonary arterial pressure rose, but left atrial and airway pressures changed little. Changing from nitrogen to air breathing had no effect. To determine the mechanism of this phenomenon we cut both vagi and destroyed the stellate and T₁ to T₃ ganglia in 1 dog and also perfused lungs in situ without body perfusion in 6; responses to inspired oxygen persisted. Addition of atropine, dibenzylene, hexamethonium and procaine to the perfusate of an isolated lung in situ did not abolish the responses. In 1 dog with separate perfusion of pulmonary and systemic circulations, isopropylarterenol aerosol abolished the responses. The increase in P.V.R. and P.A.P. during ventilation with oxygen in vascularly isolated lungs usually became greater during an experiment. It was less evident in 3 other dogs in which pulmonary venous blood flowed through the systemic circulation before re-entering the pulmonary artery. This suggests the possibility that chemical substances may accumulate in or be lost from the perfused lungs whenever the pulmonary perfusate does not circulate through the body. This chemical change is a necessary condition for the increased vascular resistance during oxygen breathing. (Supported in part by U.S.P.H.S. Grant H-4029.)

INFLUENCE OF RIGHT VENTRICULAR PRESSURE UPON FLOW IN RIGHT AND LEFT CORONARY ARTERIES. C. E. Cross (intr. by P. F. Salisbury). St. Joseph Hospital, Burbank, California

In open-chest dogs the right ventricle was bypassed and all venous blood returned to the pulmonary artery (calibrated pump - oxygenator). Arterial pH and pO_2 were constant. The left main coronary artery was cannulated and perfused with arterialized blood from a separate reservoir. The right ventricle ejected into an overflow reservoir with adjustable elevation, thus permitting intentional variation of right ventricular pressures and measurement of total coronary venous flow. Left coronary artery inflow was measured by a calibrated pump which kept the level of the perfusion reservoir constant. Pressures were measured in both ventricles, the perfusion system and the ascending aorta. The difference of total coronary venous outflow and left coronary artery inflow represented right coronary artery flow. In both the right and the left coronary arteries, flow was a straight line function of mean coronary driving pressure (Cross et al., Circ. Res. 9:589, 1961), which was derived for the right coronary from the right ventricular and aortic pressures. When the pressure in the right ventricle exceeded a certain threshold level, usually 50/10 mm Hg, regression lines relating right and left coronary flows to right and left mean coronary driving pressures became sharply elevated. Distention of the right ventricle beyond the threshold pressure thus resulted in relaxation of vasomotor tonus in both right and left coronary trees.

BREATH HOLDING AT THE BEGINNING OF EXERCISE. E.G. Cummings (intr. by F.N. Craig). U.S. Army Chemical R&D Labs, Army Chemical Center, Md.

The stimulus to breathe during voluntary breath holding at rest, steady state exercise, and post exercise rest has been described. In the present experiment, men stood astride a moving treadmill belt and at a verbal signal held their breath, jumped on the treadmill belt, and walked or ran at a series of speeds up to 9 mph until the breaking point was reached. Breath holding time decreased sharply with increasing exercise rates, but began to level off at approximately 30 seconds duration between 6 and 9 mph. Breaking point alveolar pO_2 decreased and pCO_2 increased with increasing treadmill speeds. When these two factors were applied in the Otis, Fenn and Rahn ventilation equation to describe ventilation at the breaking point, the V.R. increased and it was observed that the men withstood a stronger stimulus to breathe as the work rate increased, even though the breath holding time remained fairly constant at higher work levels. Apparently at the beginning of work the stimulus to breathe is the combination of a relatively weak neurogenic stimulus and also an accumulating chemical stimulus. It is postulated that the constancy of beginning breath hold times at high work rates may reflect a transport time for the chemical stimulus to reach the receptor area from working muscles via the circulation. Others have shown a leveling in cardiac output at increasing work in the present oxygen consumption range of 2.5 to 3 liters/ O_2 /min which may account in part for the observations.

THE EFFECT OF Na IONS ON THE REACTIVITY OF THE DENERVATED RABBIT EAR. S. A. D'Agostino* and W. F. Hamilton. Med. Coll. of Ga., Depts. of Physiology & Pharmacology, Augusta, Georgia.

The denervated rabbit ear has been perfused with two different perfusates, one containing normal Locke solution with 4% PVP and a second one in which all the NaCl was replaced with isosmotic quantities of dextrose. Both perfusates had the same cryoscopic point, Ph and temperature, the only difference being that in the second perfusate the only Na ions available were those coming from the NaHCO_3 . The viscosity relative to water, determined in the Ostwald viscosimeter, were 2.57 and 2.73 respectively. The perfusion was carried out at a constant pressure by pressurizing the perfusates with O_2 at 100 mm Hg. The flow was recorded constantly with a drop counter flowmeter. The perfusion with the Na free solution increased the resistance about threefold. Epinephrine seemed to be more effective with the sodium free solution. However, when the perfusion with sodium free perfusate was continued for 1 hour the effect of epinephrine was greatly diminished or abolished. Changing the perfusion back to the fluid containing normal sodium caused the preparation to become reactive again. The inference that these changes in reactivity are related to the sodium gradient from inside to outside the cell is suggested. (Supported by the Cardiovascular Training Grant HTS-5044, National Heart Institute and a fellowship from the Argentine National Research Council).

SMALL VESSEL RHEOLOGY. L.S. D'Agrosa,* Department of Physiology, St. Louis Univ. School of Med., St. Louis, Mo.

The method is based on objective photometry of individual small blood vessels (0.130-0.286 mm in diameter). The variation in light transmitted through flowing blood in a microscopically isolated blood vessel is recorded by a photocell and conventional bridge system. The microscopic opacity pulses of the individual vessel varied in amplitude with blood flow as observed visually during the actions of epinephrine and during spontaneous or mechanically induced changes in blood flow. In pulsatile perfusion experiments on individual vessels (0.864-1.270 mm in diameter), the correlation of flow and opacity pulses was approximately linear.

(Supported by USPHS grant H-3489 and USPHS predoctoral Fellowship GF-12,818)

DIGITAL COMPUTER FOR MEASURING CARDIAC OUTPUT. G.K. Danielson*, A. Summers*, D. Norman* & W.S. Blakemore. Harrison Department of Surgical Research, Schools of Medicine, Univ. of Pennsylvania, Phila. 4, Pa.

A portable computer based on a digital computation of the input signal has been developed to compute cardiac output using indicator dilution technics. The final answer is obtained 30 seconds after completion of the first circulation of the indicator and the cardiac output may be read directly from a meter as l./min. The unit has been used with a tricarbo-cyanine dye and arterial blood sampling using a densitometer, and with radioisotopes combined with a scintillation crystal for external precordial counting. The computer is composed of two units: the first unit computes the area under the curve up to a selected point on the downslope of the curve, at which point the second unit is switched in and the exponential portion of the curve is computed ($y=Ae^{-kt}$). The point on the downslope of the curve is selected by visual observation, and the second stage of the computer allows a two second time lapse between this point and a second point on the curve which are then used for computation of the exponential, thus removing difficulty posed by the recirculation curve. Precalibration of the computer to provide for quantitative information is done by using blood mixed with known concentrations of indicator. All operations are centrally controlled by two operations dials, and the computer is independent of the controls on the directwriter recorder, which produces a simultaneous permanent record. Studies using a peristaltic action pump show reproducibility of repeated determinations with a S.D. of $\pm 5\%$ of the mean. Using 10 dogs which have the pulmonary artery blood flow measured by an electromagnetic square wave flowmeter values, tricarbo-cyanine dye values are obtained with a S.D. of $\pm 8\%$ of the mean flowmeter values (200 cc/min to 1500 cc/min).

ELECTROLYTES OF FROG GASTRIC MUCOSA. Horace W. Davenport and Fernando Alzamora* Department of Physiology, The University of Michigan.

When frog gastric mucosae are soaked in Na_0 120 and K_0 9 mEq/L inulin space ranges from 300-400 gm/kg wet wt, increasing slightly with time. Arabinose, mannitol and sucrose spaces are 450-550 gm/kg wet wt. In fresh tissue total electrolytes are Na 51, K 52 and Cl 41 mEq/kg wet wt. Intracellular electrolytes of fresh tissue calculated on basis of inulin space at 0.5 hr soaking (334 gm/kg wet wt) and plasma concentrations are Na_i 31, K_i 106 and Cl_i 31 mEq/kg H_2O . Calculated on basis of inulin space of sartorius at 0.5 hr soaking (102 gm/kg wet wt) the values are Na_i 57, K_i 73 and Cl_i 47 mEq/kg H_2O . Total electrolytes of mucosae soaked 1 hr in Na_0 118, K_0 9 and Cl_0 105 mEq/L with 0.1 mM histamine are Na 70, K 58 and Cl 46 mEq/kg wet wt, and inulin space is 360 gm/kg wet wt. With longer soaking total Na remains constant, K rises and Cl falls, giving Cl_i absurd negative values when calculated on basis of inulin space. Intracellular values for mucosae soaked 1 hr in solutions with Na_0 120 and 0.1 mM histamine but with K_0 ranging from 0 to 126 mEq/L are Na_i constant and both K_i and Cl_i increasing in direct linear proportion to K_0 . In similar 1 hr soakings with $\text{Na}_0 + \text{K}_0$ constant at 135 mEq/L, $\text{Na}_i + \text{K}_i$ is constant as Na_i rises and K_i falls. Results suggest at least three spaces: 1) A true extracellular space the same volume as in sartorius (ca 140 gm/kg wet wt); 2) An intracellular space accessible to inulin and containing high Na_i and Cl_i and low K_i but from which Cl_i can be extruded; 3) An intracellular space containing high K_i and low Na_i and Cl_i . All boundaries are permeable to K and Cl and behave to varying K_0 as does sartorius. Calculations of intracellular electrolytes on this basis gives plausible values. Supported by Grant RG-4831(C4) from NIH.

THE RENIN-ANGIOTENSIN SYSTEM IN THE CONTROL OF ALDOSTERONE SECRETION.
James O. Davis, Carlos R. Ayers,* and Charles C.J. Carpenter.*
 National Heart Institute, Bethesda, Md.

Evidence has been presented for secretion of an aldosterone stimulating hormone by the kidney following acute blood loss (J. Clin. Invest. 40:684,1961), during chronic thoracic caval constriction and secondary hyperaldosteronism (Fed. Proc. 20:178,1961), and during chronic Na depletion (Endocrine Society Abstracts, 1961). In the present study, the renin content of kidneys was found to be 6-fold greater in 8 dogs with caval constriction than in 7 normal dogs (1.49 units/gm. for caval dogs compared with .22 units/gm. for normals; $P < .01$). Renin was extracted and assayed by a modification of the method of Haas and Goldblatt (Am. J. Physiol. 197:1103,1959). The arterial pressure response to a single intravenous injection of synthetic angiotensin II at 4 dose levels (0.5, 1.0, 2.0, and 4.0 ug.) was 50% less in dogs with caval constriction and in Na depleted dogs than in normal animals. Acute aortic constriction above the renal arteries in 15 hypophysectomized dogs increased aldosterone secretion from an average control value of .008 to .020 ug./min. ($P < .01$); corticosterone secretion was also frequently increased. Measurements of renal blood flow in 6 of the 15 dogs showed a marked reduction in every instance. The response in steroid secretion to aortic constriction was almost identical to that observed previously (J. Clin. Invest. 40:684,1961) following acute hemorrhage in hypophysectomized dogs. The present data are consistent with the view that either a decrease in arterial pressure and blood flow through the kidney or some functional change secondary to these alterations leads to release of renin which increases the plasma level of angiotensin II and that angiotensin II augments aldosterone secretion.

ROLE OF K IN THE PRODUCTION OF CYCLOPROPANE EPINEPHRINE VENTRICULAR TACHYCARDIA. L. D. Davis*, P. R. Helmer* and Q. R. Murphy. Dept. of Physiology, Univ. of Wisconsin, Madison, Wis.

Following portal caval shunt in 31 dogs anesthetized with cyclopropane epinephrine injection failed to produce a significant rise in plasma K in all 31. Twenty-six were protected from cyclopropane epinephrine ventricular tachycardia, 2 continued to show ventricular tachycardia and 3 had ventricular fibrillation. Of the 26 protected 16 had ventricular tachycardia when epinephrine was injected with KCl. The dose of KCl injected was one that mimicked closely the normal curve of K rise when a control dose of epinephrine is injected into an intact animal. In 10 experiments the injection of KCl and epinephrine did not result in ventricular tachycardia. It is concluded that in some dogs the effect of epinephrine in releasing K from the liver is a contributing factor to the production of cyclopropane epinephrine ventricular tachycardia.

VARIATION IN GASTRIC ACID RESPONSE TO INSULIN-HYPOGLYCEMIA IN BEAGLES. R. A. Davis* and F. P. Brooks, Depts. Neurosurgery and Physiology, Univ. of Pennsylvania School of Medicine, Philadelphia, Pa.

The gastric acid output of 7 pure-bred beagles weighing 9-11 Kg., with chronic gastric fistulae (Thomas) following 1.5u/Kg commercial insulin intravenously was determined in 50 experiments. During 150 min. after insulin, the mean total acid output varied from 1.1-7.4 mEq with standard errors of 0.2-3.1 mEq. The 30 min. collection period with greatest output gave mean concentrations of total acid 50-108 mEq/L and volumes of 9-25 ml. Std. errors varied from 4-14 mEq/L and 3-7 ml respectively. In 42 experiments the period of maximum acid response followed directly after the lowest venous blood sugar. Mean values of lowest blood sugars in individual dogs varied from 21-48 mg/100 ml by the glucose oxidase method. In 8 experiments two definite phases of acid response were seen, 7 in 2 of the 7 dogs. The same dogs gave acid responses lasting up to 5 hours in contrast to the usual 3 hours. These late responses were not correlated with the level of the venous blood sugar. Blood reducing substances were determined continuously in 4 dogs by means of an autoanalyzer. (Technicon Instruments Corp., Chauncey, N.Y.) Two min. after insulin injection, an elevation of reducing substances occurred. 16 minutes after insulin, the level began to fall, with a maximum rate of 6 mg/100 ml of blood/min. The nadir was reached at 35 min. after insulin. Thereafter a gradual return to control levels occurred reaching pre-insulin values 4 1/2 hours after injection. (Supported by Grant No. A-3596 C2, National Institutes of Health.)

EFFECT OF CHLORIDE AND THIOCYANATE ON FROG'S GASTRIC MUCOSA BATHED IN CHLORIDE-FREE SOLUTIONS. T. L. Davis*, C. Chandler*, and W. S. Rehm. Univ. of Louisville School of Med., Louisville, Ky.

Gastric mucosae were mounted between chambers with sulfate Ringer's on the nutrient side and a sulfate solution on the secretory side (sulfate replacing Cl ion and sucrose making up osmotic deficit). The PD, resistance and H⁺ ion secretory rate were measured, the latter with a pH stat method. In resting mucosae the average PD was -0.8 mv with a range of from -13 to +7 mv (minus sign means nutrient-negative), and the average resistance 860 ohm cm². Histamine addition to nutrient resulted in a decrease in PD to an average level of -24 mv (range -14 to -33 mv), an average decrease in resistance of 160 ohm cm², and an average secretory rate of 0.8 ueq cm⁻²hr⁻¹. During secretion addition of SCN to secretory side (final concentration 8 to 14 meq/l) resulted in a decrease in secretory rate to zero, an increase in PD to an average value of +2 mv (range -6 to +11 mv), and an average decrease in resistance of 215 ohm cm². Comparable experiments with the addition of a similar amount of Cl ion to the secretory side resulted in no significant change in secretory rate, a decrease in PD of a few mv, and an average decrease in resistance of 150 ohm cm². Replacement of the sulfate secretory solution with a 0.08 M NaCl solution resulted in no significant change in secretory rate, a decrease in average PD of from -21 mv to -29 mv, and an average decrease in resistance of 220 ohm cm². The above indicates that SCN and Cl ions penetrate the secretory surface in such a way as to decrease the resistance. The findings are not compatible with a simple pore theory, since the nutrient side should become more negative than it does. They support the concept that an electrogenic anion pump is present on the secretory surface. (Supported by NIH and NSF grants.)

HEART RATE IN MAN AS RELATED TO AGE, EXERCISE AND ENVIRONMENTAL TEMPERATURE. D. B. Dill and F. Consolazio.* Anat.-Physiol. Dept., Indiana Univ., Bloomington, Ind.

In 1942 Dill reported the relation between metabolic rate, environmental temperature and the heart rate of two subjects, the authors of this communication. The two families of curves shown in that paper had been prepared by L. J. Henderson from experiments carried out in 1931 and 1932. The exercise was continuous for 10 min. on the bicycle ergometer. The heart rate was recorded on the cardi tachometer, using the rate in the 10th minute of work for comparison. At the higher temperatures a humidity of $50 \pm 5\%$ was maintained. New observations have been made on the two subjects after the passage of nearly 30 years; our ages now are 50 and 70. On Dill the heart rates are virtually the same as 30 years ago both in easy work, oxygen used 0.6 l./min., and in moderate work, 1.5 l./min. except at 50°C where the rates are about 20 beats per minute greater. In Consolazio at all work levels the heart rates are the same from 0° to 20°C, and about 10 beats lower at 30° and 40°C. At 50°C his heart rates are 10 beats higher in easy to moderate work and the same in hard work. Some of these changes are related to the lowered capacity for work. In this form of exercise, Dill's capacity for oxygen consumption has declined from 2.75 to 2.1 l./min.; in Consolazio the drop is from 3.1 to 2.65 l./min.

HEART RATE AND CARDIAC OUTPUT IN EXERCISING DOGS AFTER PARTIAL AND COMPLETE CARDIAC DENERVATION. David E. Donald and John T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Complete cardiac denervation was attempted in seven dogs by the method of Gilbert and Cooper (1). Preoperative and postoperative measurements of heart rate and cardiac output (dye-dilution technic) were made in five animals during a standard set of exercises 2 minutes in duration and of graded severity. Postoperative studies were made in two animals. Cardiac vagotomy was complete in all animals, as verified by stimulation of the vagus nerves and by atropinization. Stimulation of the cardiac sympathetic nerves at the completion of each study resulted in cardiac acceleration in two animals. Following complete cardiac denervation the heart rate became stabilized at 100 to 110 beats per minute with absence of sinus arrhythmia; there was no immediate acceleration in heart rate when the animals were startled or suddenly excited. The animals performed the standard exercises as competently as before operation, although the cardiac output at any level of exercise tended to be lower than the corresponding preoperative determination. With the most severe exercise (13 km. per hour, 15-degree slope) the heart rate increased slowly to a plateau value of 140 to 160 beats per minute and slowly declined after exercise was stopped. This pattern was characteristic of all levels of exercise. Before operation, increased heart rate usually made the major contribution to increased output; after denervation, changes in stroke volume played a greater part, but the maximal stroke volume did not usually exceed the preoperative value. (Supported by U.S.P.H.S. Grant H-6143.)

(1) Circulation Research 9, 275, 1961.

VASCULAR RESPONSE FOLLOWING INDUCED PERIODONTITIS IN DOGS. Homer L. Dorman* and Jack G. Bishop. Baylor Univ. College of Dentistry, Dallas, Texas.

Unilateral periodontitis was induced in the lower quadrant of dogs by removal of approximately one mm. of bone from the alveolar crest of the mandible. Three to six weeks following surgical induction, bilateral blood pressure measurements were made during perfusion of blood into the cannulated mandibular vessels. A decrease in peripheral resistance and in back pressure was observed in animals operated four weeks prior to perfusion, and further decrease occurred in animals perfused five and six weeks after induction. These observations may be satisfactorily explained by assuming formation of new artery to vein shunts or increased utility and development of existing shunts.

SEASONAL VARIATIONS IN THE CALORIC INTAKE OF DOGS LIVING IN AN ARCTIC ENVIRONMENT. John L. Durrer* and John P. Hannon. Arctic Aeromedical Laboratory, Fort Wainwright, Alaska.

Previous work (Scholander, et al, Biol. Bull. 99:237, 1950) has indicated that the zone of thermoneutrality for the larger Arctic species, including dogs, extended from $+30^{\circ}$ to -40°C . Since the summer and winter temperatures in most Arctic areas are almost always within the above range, we might predict no seasonal variation in metabolic rate. To test this prediction, Alaskan Husky dogs were exposed continuously to an outdoor Arctic environment for one year using daily caloric intake and body weight as measures of seasonal variation in metabolic energy expenditure. For comparative purposes, these two variables were also studied in the poorly insulated beagle dog. The well insulated Husky dogs responded with a 63% increase in food consumption during the winter exposure period over summer control levels. The beagle dogs exposed similarly, but to less severe temperature, responded with a 75% increase over warm indoor control levels. Body weight variations were similar in both groups of animals. Whereas a significant negative correlation existed between the monthly food consumption and the ambient temperature, there was no consistent relationship between daily food intake and ambient temperature. The results indicate that the energy expenditure of the well insulated Husky dog is considerably increased during the winter months thereby suggesting a higher critical temperature for these animals than had previously been reported.

A Rebreathing Method for the Rapid Determination of the Ventilatory Response to Carbon Dioxide. R. E. Dutton* C. Yoshimoto* F. Fuleihan,* H. H. Hurt* and R. L. Riley.

A rebreathing method has been devised for the rapid determination of the ventilatory response to CO_2 . Ventilation and CO_2 concentration are monitored continuously during a rebreathing period of up to six minutes. A modified McKesson Vitalor, which is used as the rebreathing bag, contains 3 to 4 liters of oxygen at the start. During the early part of the rebreathing period the CO_2 in the lung-bag system equalizes and the A-V difference in CO_2 tension narrows. During the latter part of the rebreathing period, the CO_2 tension of the lung, bag, pulmonary artery and pulmonary vein all rise together and are nearly the same, as indicated by the small variations at the mouth. Calculations show that the Pco_2 at the mouth is less than 2 mm Hg. below pulmonary arterial Pco_2 . It is thus possible to plot ventilation against the Pco_2 of both arteries and veins with considerable accuracy. The ventilatory response to CO_2 as determined by this continuous method corresponds closely to spot determinations of ventilation and mixed venous Pco_2 as estimated by a modification of the method of Campbell and Howell. Daily variations occur in the CO_2 response curve of normals at rest. Exercise in normals for periods of less than fifteen minutes is not accompanied by a change in the CO_2 response curve. Exercise for longer periods shifts the CO_2 response curve to the left, resulting in a greater ventilatory response to a given CO_2 stimulus without changing the slope of the curve. The response slowly returns to normal during the recovery period. Patients with metabolic acidosis also shift their CO_2 response curve to the left. These data suggest that ventilation reflects buffer base and the intracellular hydrogen ion concentration of the receptor cells.

Departments of Environmental Medicine and Medicine, The Johns Hopkins University, Baltimore, Maryland

HABITUATION TO RECURRENT ICE-WATER IMMERSION OF THE FINGER. C. J. Eagan*. Arctic Aeromedical Laboratory, Fort Wainwright, Alaska.

It was shown previously (Eagan, *Physiologist*, 3(3):51, 1960) that ice-water immersion of the finger for 2% of the elapsed time, over 17 days, caused a marked habituation in pain sensation in the absence of any adaptation in the vascular reaction. In the present study, one middle finger of each of 6 USAF airmen (3 Negro and 3 white) was immersed in stirred ice water for 10 minutes, 6 times per day, for 125 consecutive days. For each of the 750 immersions, each subject recorded the maximum pain experienced using a 5-unit scale. At the end of this regimen, the responses of the test finger, during 10 min of ice-water immersion, were compared with those of its contralateral control under identical test conditions for the fingers and with the subject in a basal state. The protocol was: 126th day -- simultaneous comparison; 127th day -- control and test fingers in sequence; 128th day -- test and control fingers in sequence. The results of the previous study were confirmed. It was found also, for Negro and white subjects alike, that both the test and control fingers tended to show a vascular reaction similar to that of Alaskan Eskimos and Indians. Mercury gauge plethysmography and thermometry showed, in general, a less intense and more transient vasoconstriction compared with other indoor subjects. Two types of habituation are indicated: a diminution in pain sensation specific to the recurrently cooled extremity and a change in the psychological "set" of the subject relative to the experimental procedure.

CORPUS CALLOSUM AND ANTERIOR COMMISSURE CONNECTIONS IN THE CAT. F. F. Ebner* and R. E. Myers. Johns Hopkins University School of Medicine, Baltimore, Maryland.

The cortical distribution of the interconnecting fibers of the forebrain commissures were studied using the Nauta-Gygax silver impregnation technique. After total commissurotomy the striate cortex or visual area I was remarkably free of degenerating fibers while peristriate or visual area II demonstrated them in dense profusion. The somatic sensory arm area appeared degeneration free while the leg and face areas revealed heavy degeneration. The somatic motor area of the anterior sigmoid gyrus also contained dense degeneration. The auditory areas I and II both showed diffuse and relatively heavy degeneration while auditory area III which is approximately coextensive with somatic area II was degeneration free. Cingulate cortex was only very sparsely infiltrated with commissural fibers while the ventral portions of the ectosylvian complex remained entirely free of such fibers. These results will be discussed in relation to similar findings in the racoon. (Aided by Air Force Office of Scientific Research grant #61-38.)

FRACTIONATION OF PANCREATIN FOR GROWTH PROMOTING SUBSTANCES IN THE PANCREATIC DUCT-LIGATED RAT. L. E. Edwards, A. C. Brehme*, and D. A. Knight*. Medical College of Virginia, Richmond, Virginia.

Since pancreatin did relieve the pancreatic deficiency in duct-ligated rats, the first approach to isolating the active principle was made by fractionating pancreatin. Pancreatin was treated with various concentrations of $(\text{NH}_4)_2\text{SO}_4$. Four fractions were obtained; precipitates from .25, .5, .75 and 1.0 saturations of added $(\text{NH}_4)_2\text{SO}_4$ were collected for the test fractions. Each fraction was tested on many animals at a one-third per cent level in the diet. The .5 saturation fraction gave excellent growth in the assay animals. This is the range where the proteolytic enzymes precipitate out of solution. Since most of the pancreatic enzymes precipitate out at this saturation we tested several of the enzymes individually. Crude commercial enzyme preparations were first tested at a one-third per cent level in the diet. Crude trypsin and lipase gave us good growth by our assay method and amylase gave us very poor growth. Crystalline trypsin was assayed at several concentration levels in the diet. The level of good growth was obtained with a diet containing 1/3000 parts trypsin in the diet, which represents about .33 mgs. of trypsin in each gram of diet. We could not obtain a pure or crystalline preparation of lipase. Growth produced by pancreatin in the duct-ligated rat is related to the presence of pure trypsin. The part played by lipase can not be answered until a crystalline preparation has been tested.

Supported in part by NIH A-1390.

Influence of season and exposure to cold on thyroxine secretion rates in two subspecies of *Peromyscus maniculatus* and the Swiss mouse. B. E. Eleftheriou* & M. X. Zarrow, Department of Biological Sciences, Purdue University, Lafayette, Ind.

Thyroxine secretion rates (TSR) were determined as $\mu\text{g.}$ of L-thyroxine per 100 g. body weight and found to vary with the season although the animals were kept under constant conditions of light and temperature. TSR increased from a low of 0.5 for both *Peromyscus maniculatus bairdii* and *P. m. gracilis* during the summer to a high of 2.5 in December through March for *P. m. bairdii* and October through December for *P. m. gracilis*. The TSR was also determined after exposure to low ambient temperatures in both of the two subspecies of deermice and the Swiss mice during the summer. No change in TSR was noted at 12°C but at 7.2°C both *bairdii* and the Swiss mouse showed an increased TSR of 3.5 and 3.25, respectively, and *gracilis* a TSR of 2.76. At 2.2°C , *bairdii* showed an increased TSR of 3.76 and the Swiss mouse a TSR of 3.5 at 1 day of exposure which increased to 5.2 after 6 days. No significant change in TSR was seen in *gracilis*. No thyroid stimulation was seen in any of the 3 animals at -3.3°C . It is of interest to note that 80% of both subspecies of deermice survived after 20 days at -3.3°C whereas none of the Swiss mice survived.

(Aided by a grant from the Purdue Research Fdn. PRF-2105).

MEASUREMENT OF PULMONARY CAPILLARY TEMPERATURE.

L. E. Farhi, A. W. T. Edwards*, and T. Velasquez*. Dept. of Physiology, The Univ. of Buffalo, Buffalo, N. Y.

This method is based on temperature-dependent changes of solubility of two inert gases. Pulmonary capillary temperature affects the solubility of any inert gas in blood and therefore governs its concentration at a given partial pressure. Whereas concentration can be determined in the arterial blood, it is not possible to measure precisely the partial pressure, since this pressure is different in individual alveoli and capillaries and in the arterial blood. This difficulty has been overcome using a mixture of two inert gases, helium and argon. During steady state conditions the ratio of partial pressures of He to A present in the inspired gas prevails in all alveoli and all capillaries regardless of the absolute pressures in each compartment. For a given inspired gas mixture the He/A content ratio depends on the He/A solubility ratio, hence on the temperature of pulmonary capillaries. This He/A solubility ratio in human blood varies by 0.0145 per degree centigrade. In practice, the subject inspires an O_2 -He-A mixture for 25 minutes, at the end of which an arterial sample is withdrawn and analyzed for He and A on a gas chromatograph. Another aliquot of the subject's blood is tonometered with the inspired mixture at a known temperature and analyzed in the same fashion. From these two sets of data pulmonary capillary temperature can be calculated. In 9 experiments on 5 normal subjects this temperature ranged from 37.7° to 38.1° , with a mean of 37.5° .

RESPONSE OF ANEURAL SMOOTH MUSCLE TO EPINEPHRINE AND TO NOREPINEPHRINE. John Ferguson. Dept. of Physiology and Pharmacology, Creighton Univ. School of Medicine, Omaha, Nebraska.

A study was made of the response in motility of non-innervated smooth muscle (chick amnion) to the levo isomers of epinephrine and norepinephrine, and their relationship to ergotamine tartrate and dibenamine hydrochloride. The crystalline compound was used in each instance. Strips were prepared and each was suspended in oxygenated Sollmann-Rademakers' solution. Records were made before and after the application of the drug. When freshly prepared solutions of epinephrine or norepinephrine were added to the bath in which a muscle was contracting spontaneously, the results varied with the concentration of the drug. Large to moderate doses depressed, while very dilute concentrations very often enhanced activity. Computed as base, epinephrine in 2×10^{-8} or higher, and norepinephrine in 3×10^{-8} approximately or higher, lessened activity; while either drug in 1.25×10^{-9} feebly increased motility frequently. Unless the bath solution was renewed, a preceding dose of either drug often modified the response to a subsequent dose. But with renewal of solution, successive doses of the same concentration were similar in result. Ergotamine tartrate in concentration of 4×10^{-7} enhanced rhythmicity, but it in no way inhibited the ensuing depression brought on by epinephrine or norepinephrine. However, it antagonized partially the excitant effects of both compounds. Also, after dibenamine hydrochloride the results obtained appeared to be quantitatively similar to those with ergotamine, but dibenamine blocked more fully the excitant effect. (Aided by Nebraska Heart Association.)

A CALCULATION OF THE P_{CO_2} OF THE CENTRAL CO_2 CHEMORECEPTORS BEFORE AND AFTER DIAMOX ADMINISTRATION. T.N. Finley*, E.P. Guy* and J.W. Severinghaus. Cardiovascular Research Inst. and Dept. of Anesthesia, Univ. of Calif. Med. Center, San Francisco.

We assume that the central CO_2 chemoreceptors (CR) respond to their environmental P_{CO_2} . This P_{CO_2} is determined by (1) $PaCO_2$, (2) local CO_2 production and (3) blood flow to the CR. The curve relating CR P_{CO_2} to ventilation will lie to the right of the curve relating $PaCO_2$ to ventilation. As an approximation to the CR P_{CO_2} we measured cerebral cortical P_{CO_2} directly in 12 chloralosed dogs breathing O_2 with various CO_2 concentrations and found that the cortical $P_{CO_2}-\dot{V}_E$ curve lay parallel to and 16 mm Hg to the right of the $PaCO_2-\dot{V}_E$ curve. If the cortical $P_{CO_2}-\dot{V}_E$ curve represented the actual curve of the CR, it should be unaffected by inhibition of carbonic anhydrase by Diamox. Diamox, however, displaced the cortical $P_{CO_2}-\dot{V}_E$ curve 12 mm Hg to the right without altering its slope. This suggests that the CR P_{CO_2} did not rise so much as the cortical P_{CO_2} after Diamox, presumably because of its greater blood flow to metabolism ratio. Another possibility might be that Diamox changed the threshold of the CR to P_{CO_2} . We have attempted to demonstrate an effect on the CR threshold by injecting large doses of Diamox in mock spinal fluid intrathecally. In 7 chloralosed dogs breathing pure O_2 , Diamox given this way had no effect on either the ventilation or its response to inhaled CO_2 . The $PaCO_2-\dot{V}_E$ curve after Diamox was shifted to the left 5 mm Hg, suggesting that the CR P_{CO_2} was slightly higher than $PaCO_2$. We have calculated from these shifts that the actual CR P_{CO_2} is 3 mm Hg higher than $PaCO_2$ before Diamox and 15 mm Hg higher after Diamox. (Supported in part by U.S.P.H.S. Grant H-3961.)

RENAL O_2 CONSUMPTION AND SODIUM REABSORPTION DURING URETERAL OCCLUSION. James S. Fleming* and Donald W. Rennie. Dept. of Physiology, The Univ. of Buffalo, Buffalo, N. Y.

We have observed that upon initiation of urinary stop-flow in anesthetized dogs breathing O_2 the renal venous pO_2 rises on the average 86 mm Hg, although directly measured blood flow is not affected. Renal O_2 consumption during stop flow is reduced 0.04 mmoles O_2 /min/100 g (15% below control values). The mechanism has been explored in dogs with partial ureteral occlusion that permitted the collection of urine, for under these conditions also renal venous pO_2 is increased above normal and renal O_2 consumption is decreased. Tubular anoxia was ruled out since Tm Diodrast was not changed by elevated ureteral pressure; also altering tubular glucose load did not affect O_2 consumption. The reduced Na load that occurs during elevated ureteral pressure was therefore implicated. The relationship between reduced Na load reabsorption and renal O_2 consumption averaged 26 mEq Na per mmole O_2 ; $SE \pm 3$. Other investigators have recently shown a ratio of 24-32 mEq Na reabsorbed per mmole O_2 consumed. Assuming that this relationship holds during stop-flow, it follows that the observed decrease in O_2 consumption can be accounted for by only a 10% reduction in active tubular Na reabsorption.

OBSERVATIONS ON THE 24-HOUR (CIRCADIAN) RHYTHM OF HEART RATE IN HUMAN SUBJECTS. G.E. Folk, Jr., H.A. Cahn*, and P.E. Huston*. Departments of Physiology and Psychiatry, State University of Iowa, School of Medicine, Iowa City, Iowa.

During a study of the phase relations of four physiological rhythms, evidence accumulated that the rhythm of resting heart rate is not entirely environmentally determined as stated by some authors. Hourly measurements on 14 human subjects included body temperatures, heart rates, urine volumes, and urine electrolytes, with subjects prone for 30 minutes before each reading. A reproducible sequence of five hourly "high" resting heart rates usually did not overlap with five hourly non-sleeping "low" heart rates approximately 12 hours later. The terms high-setting and low-setting are proposed for these periods. These settings persist: (1) after exercise (Quart. J. Exp. Physiol. (1959) 44), (2) during 24-hours of inactivity, (3) when hourly liquid meals are taken, (4) when placebo meals are consumed, and (5) when out of phase with peaks of resting body temperature and kidney function. (Supported by Iowa Mental Health Research Fund.)

Respiratory and Circulatory Responses of Hyperthermic Chickens and Rats.
H. Frankel, K. Hollands* and H. Weiss. Dept. of Physiol. & Biochem. and
Dept. of Poultry Sci., Rutgers Univ., New Brunswick, N.J.

Heart rate, blood pressure, respiratory rate, tidal volume and rectal temperature were measured simultaneously in male Leghorn chickens exposed to an environmental temperature of 41°C . Respiratory and circulatory responses were found to be correlated with rectal temperature apparently irrespective of the time taken to reach the temperature. Initial rectal temperature averaged 41.0°C (S.E. 0.05). Average respiratory rate reached a maximum value of 158 breaths/minute (S.E. 10.2) at a rectal temperature of 44.1°C (S.E. 0.23). Tidal volume response paralleled respiratory rate response. Blood pressure was approximately constant until a rectal temperature of 45°C was reached. Above this temperature blood pressure decreased even though heart rate did not reach a maximum value (489 beats/minute, S.E. 9.6) until a rectal temperature of 45.6°C (S.E. 0.08). Female chickens gave essentially the same responses as male chickens. Preliminary experiments with rats indicate a similar sequence of respiratory and circulatory changes occur with increased body temperature. Thus the respiratory system shows the earliest signs of the detrimental effect of hyperthermia. It is suggested that decreased respiratory response with increased body temperature is the first indication of brain malfunction.

VASOMOTION DEMONSTRATED BY AN INJECTION CASTING METHOD. Wallace G. Frasher*, Sidney S. Sobin and Herta M. Tremer.* College of Medical Evangelists, Los Angeles, California.

Controlled retrograde infusion of a specially prepared non-wettable polymer (Physiologist 3:146, Aug. 1960) has been used to demonstrate differential vasomotion in paired structures under physiologic conditions. The unique characteristics of the material permit filling of the microcirculatory bed with normal pressures and without significant alteration of the vessel wall. Effects of differential warming and cooling of rabbit ears have been studied. Election of defined geographic areas in each of the paired structures permits quantification of the difference in numbers of active channels, and identification of the magnitude of vessels involved in the disparate patterns.

PREPYRIFORM ELECTRICAL STIMULATION IN CATS. W. J. Freeman, Department of Physiology, University of California, Berkeley.

Two or more pairs of electrodes were implanted in the prepyriform cortex of 12 adult cats. The effects on behavior of iterative electric stimulation were analyzed in terms of concomitantly evoked electrical changes in the cortex. Four kinds of effects were found. (a) At stimulus intensities 6 - 10 x threshold for single shock evoked potential, an orienting reflex was obtained in cats naive to the stimulus or not recently exposed. (b) At 8 - 12 x threshold there was behavioral arrest often followed by flight, or, if stimulation was prolonged, by a petit mal-like seizure. (c) After appropriate conditioning, bar-press responses were obtained at or slightly above threshold intensity for the electrical response. (d) At stimulus intensities 1.3 - 5 x threshold in cats naive or habituated to the stimulus, modulation of behavior was obtained.

This modulation was detected by training the cats to work in an ergometer and comparing the rate of work done during alternated pairs of stimulated and nonstimulated runs. The effect was proportional to the Q value of the stimulus (1). (Q is an index of and is proportional to the duration of a single shock evoked potential. It is measured by repetitively stimulating the cortex at different frequencies and plotting the r.m.s. amplitude of trains of evoked potential against stimulus rate. Q is high in cats attentive to the stimulus and low in cats habituated to it.) In naive, attentive, or fatigued cats with high Q values, rate of work was augmented by up to 5%. In habituated cats with low Q values it was decreased by a similar amount. These findings show the value of measuring the electrical response of a stimulated structure in assessing the behavioral responses to stimulation of that structure.

(1) Freeman, W. J. J. Appl. Physiol., 1961, in press.

REGULATION OF SODIUM CHLORIDE INTAKE BY RATS. M. J. Fregly, J. M. Harper, Jr.* and J. Berger**. Dept. Physiol., Univ. Florida, Med. School, Gainesville, Florida.

Laboratory animals seldom have an opportunity to demonstrate whether they can regulate their NaCl intake. We attempted to provide such an opportunity for rats. Three experiments were performed; the first used 15 male Holtzman rats while the last two used 10. All rats were given choice between water and a solution of NaCl to drink. In Exp. 1 the concentration of NaCl solution was .15 M., Exp. 2, .20 M., and Exp. 3, .25 M. Food was NaCl-loaded in each experiment in the following sequence: 0, 2, 4 and 6% added to a sodium-deficient diet. Rats were given each diet for 4 days. Food and fluid intake and rat weight were measured daily. In all three experiments water intake increased in direct proportion to the amount of NaCl ingested. However, intake of NaCl solution remained constant in spite of increases in NaCl content of the diet. In all experiments intake of sodium in fluid varied from 1.2 to 1.4 mEq/100 gm. B. W./day. This is approximately the level of sodium required for normal growth and reproduction in young rats. We conclude that water intake is closely regulated to the NaCl content of the diet. Intake of NaCl appears to be regulated by a separate mechanism but only as NaCl in solution.

Observations on coronary sinus drainage and measurement of left coronary artery flow by indicator dilution technic in the dog. Friesinger, G.C., Schaefer, J. and Gaertner, R.A. intr. by R.S. Ross, The Johns Hopkins Hospital, Baltimore, Maryland.

The indicator dilution principle has been employed to study coronary blood flow and the venous drainage into the coronary sinus (CS). In open chest dogs, a Gregg cannula was fixed in the ostium of the left coronary artery (LCA) and its flow measured with a rotameter. The right coronary artery (RCA) was isolated and perfused from the femoral artery. Blood was withdrawn from two sites in the CS simultaneously through equally sensitive densitometers following injection of "Cardiogreen" dye into the various sites in the coronary arterial tree. When dye is injected into the posterior circumflex branch of the LCA, the indicator dilution curve from the downstream or ostial site in the CS is larger than that from the upstream or venous site. When the anterior descending branch is injected the upstream curve is the larger. Under certain conditions identical curves can be obtained when injection is made in the LCA proximal to the bifurcation. RCA injection was followed by CS appearance only when large amounts of dye were used. These data indicate that the major venous drainage pathways of the anterior descending artery enter the CS upstream from the veins draining the distribution of the posterior circumflex. This fact coupled with the identity of the curves from the two sites following LCA injection has been taken as evidence that complete mixing of blood and indicator can be achieved in the LCA proximal to the bifurcation. This differential sampling method has been employed in an attempt to develop an indicator dilution method for measuring LCA flow.

ELECTROPHYSIOLOGICAL ANALYSIS OF GUSTATORY, TONGUE TEMPERATURE, AND TACTILE REPRESENTATION IN THALAMUS OF ALBINO RAT. G. P. Frommer* and C. Pfaffmann, Brown Univ., Providence, R. I.

Responses to gustatory, tongue temperature, and tactile stimuli were recorded with nichrome wire electrodes (50-125 μ) from primary thalamic relay of albino rats under pentobarbital sodium anesthesia. Responses were quantified with an electronic integrator circuit. Median integrator responses to five representative taste stimuli were ordered as follows: .1 M NaCl > .005 M HCl > 1.0 M Sucrose = .1 M KCl > .01 M QHCl. The gustatory thalamic response is qualitatively and quantitatively similar to responses at more peripheral loci. The gustatory relay lies in a .5 x .2 x .3 mm area in the medial extension of ipsilateral ventral nucleus in agreement with prior lesion and degeneration studies. Tongue temperature activity was maximal at "resting" temperature (about 25°C). Warming or cooling from this baseline depressed the discharge. This response could be attributed to the activity of "cold units" like those in cat's lingual nerve. The temperature responsive area is located in the contralateral ventral nucleus, lateral to the gustatory relay and extends anteriorly to it. Strong tongue tactile responses were found together with a portion of the temperature response but also independently. A precise topographical representation of the body was observed more laterally, fairly well limited to the contralateral ventral nucleus. (Supported by NSF Predoctoral Fellowship and NSF Grant G-2541. First author's present address: Natl. Insts. of Health, Bethesda, Md.)

Failure of Angiotensin to Deplete Adrenal Ascorbic Acid. Donald S. Gann* and E. S. Redgate, Western Reserve University Medical School, Cleveland, Ohio.

It has been shown recently that angiotensin II stimulates secretion of hydrocortisone, corticosterone and aldosterone in the hypophysectomized nephrectomized dog. Since ACTH has similar effects, the present study was undertaken to see if angiotensin induces adrenal ascorbic acid depletion in hypophysectomized rats, a standard assay for ACTH. Both aspartyl (Bumpus, Cleveland) and asparaginyl (CIBA) angiotensin II were assayed. Neither form of angiotensin induced significant ascorbic acid depletion with doses ranging from 0.1 to 40 μ g per rat. This is in marked contrast to the effect seen with ACTH. The angiotensin preparations used were assayed for pressor response in dogs and rats and corticosteroid response in dogs, and were effective in all cases. Maximum doses of angiotensin (10 μ g) and ACTH (1 unit) produced comparable rates of corticosteroid secretion in nephrectomized dogs. The results suggest that angiotensin and ACTH may act at different sites to stimulate corticosteroid biosynthesis. The adrenal ascorbic acid depletion test affords a useful means of distinguishing the two substances in crude mixtures such as plasma. (Supported by Cleveland Area Heart Society Grant 1603 and National Institutes of Health Grant B-3238.)

MATERNAL INFLUENCES ON THE FETAL CARDIOVASCULAR SYSTEM. William F. Geber* (intr. by A. W. Richardson) State University of South Dakota Medical School, Vermillion, South Dakota.

Continuous recordings of the fetal carotid artery blood flow, blood pressure, heart rate, renal, brain, uterine and cotyledon blood flow, maternal carotid artery blood pressure, and heart rate were made during and following varied types of maternal stimulations and chemical injections in three anatomically different types of placental-uterine-fetal arrangements as exemplified by the sheep, dog, and rabbit. Included in this series was pinching of the ear, eyeball pressure, asphyxia, pure tones, stroking of the viscera, vagal stimulation, and intravenous injection of epinephrine, nor-epinephrine, isopropyl arternol, acetyl choline, serotonin, lysergic acid, and sodium pentobarbital. In all three animal species the fetal physiological responses were, in general, the same for any particular type of maternal stimulus or chemical injection. The fetal renal and brain vasculature were the most sensitive to any particular maternal influence with fetal blood pressure next, and fetal cardiac rate the least sensitive. Fetal renal and brain vasculature responded in the same qualitative manner to all maternal influences whereas fetal blood pressure and cardiac rate were markedly variable in their responses. All fetal responses were distinguished by their long duration, especially the renal and brain vascular responses.

ALDOSTERONE SECRETION IN MAGNESIUM DEFICIENT RATS. H. Earl Ginn and Robert Cade (Intr. by E. Lovell Becker). Dept. of Medicine, The New York Hospital - Cornell Medical Center, New York.

Studies of steroid and electrolyte excretion, and histology of the adrenal glands were made in Holtzman rats on a magnesium deficient diet which contained less than 1 mg. of magnesium per 100 grams of diet. Control animals were pair fed 60 mg. of magnesium per 100 grams of diet. After one month, the mean plasma magnesium concentration in 14 deficient animals was 0.71 mEq/L and 1.99 mEq/L in 14 control animals ($P=.001$). In experimental animals, aldosterone secretion via adrenal venous blood was 0.067 $\mu\text{gm}/\text{min}$. The pair fed control animals secreted 0.038 $\mu\text{gm}/\text{min}$ ($P=.005$). Corticosterone secretion was 1.66 $\mu\text{gm}/\text{min}$ in the deficient rats and 1.72 $\mu\text{gm}/\text{min}$ in the control rats. The urinary excretion of sodium in the magnesium deficient animals was 1.43 mEq/24 hrs with 2.07 mEq/24 hrs in the controls ($P=.001$). Renal potassium excretion, on the other hand, was 0.433 mEq/24 hrs in the experimental and 0.307 mEq/24 hrs in the control rats ($P=.001$). Muscle potassium concentrations were lower and sodium higher in the magnesium deficient rats. Histological examination of the adrenals revealed large lipid filled vacuoles in the zona fasciculata. These studies would indicate a significant increase in aldosterone secretion and its consequences, in animals on a diet deficient in magnesium.

RESPIRATORY CHANGES DURING TILTING AND THEIR CONTRIBUTION TO THE HEART RATE EFFECT. Frank Girling, John Fletcher* and Joseph Rubin*. Environmental Group, Physiology Wing, Defence Research Medical Laboratories, Toronto, Canada.

Thirty men aged 17-24 breathed 100% oxygen from a closed circuit spirometer while lying at rest on a tilt table. Respiratory frequency, tidal volume and change in expiratory reserve volume were recorded at 5 pre-determined angles each maintained for 5 periods of 1/2 minute. In a separate non-tilting series heart rates and end-expiratory % CO_2 were measured in the sitting position with the same subjects maintaining different levels of ventilation. Pooled results showed that as the subjects moved from the head-up position to the head-down position the tidal air decreased, the respiratory rate increased slightly and the expiratory reserve volume decreased by 700 ml. Minute volumes, which ranged from 6 to 22 litres in different subjects, did not change appreciably with tilting. With ventilation at 5, 10 and 20 litres per minute (tidal volume 800 cc), sitting subjects did not demonstrate any marked changes in heart rate (72, 75 and 78 beats per minute) although the end-expiratory % CO_2 decreased continuously (5.3, 4.8 and 4.5%). It is concluded that the respiratory changes observed during tilting do not account for the large change of 38 beat/min. in heart rate previously demonstrated by the authors.

IMMEDIATE EFFECTS OF ACETYLCHOLINE ON THE CORONARY VESSELS IN DOGS. F. Göksel*, H. Feinberg, L.N. Katz and D. Rabin*. Cardio. Dept., Med. Res. Inst., Michael Reese Hosp. and Med. Center, Chicago, Ill.

The coronary flow response to acetylcholine (Achol) has been studied in several species with inconsistent results. The present report studied Achol, with and without atropine, in the open chested anaesthetized dog prepared to measure total coronary flow (CF) and myocardial oxygen consumption (O_2C). The preparation can be operated at constant cardiac input and intermittently paced to avoid rhythm changes or standstill subsequent to Achol. Achol in single injection into the paced heart decreased the mean aortic pressure and the cumulative area under the left ventricular pressure curve (pressure area effort index). The rate of ventricular pressure development (dp/dt) also decreased -- evidence of the negative inotropic effect. But this was not accompanied by a decrease in O_2C unless Achol was continuously infused. Thus, O_2C was high relative to the cardiac effort. CF increased in relation to the cardiac effort or O_2C , and there was a simultaneous decrease in oxygen extraction (O_2E). Atropine abolished the effect of Achol on CF and cardiac effort. It is concluded that: 1) Achol acts to increase O_2C relative to effort, since O_2C was not decreased as was effort; 2) Achol specifically acts to increase CF and decrease O_2E relative to the effort or O_2C .

PHYSIOLOGICAL AND BIOCHEMICAL EFFECTS OF RUMEN INSUFFLATION IN CALVES. A. L. Good and C. M. Stowe. College of Veterinary Medicine, Univ. of Minn.

Each year bloating in cattle causes extensive loss to the livestock industry. It was felt that a more thorough understanding of the physiological changes induced by rumen insufflation might lead to better methods of controlling the disturbance under field conditions. The following parameters were studied: cardiac output; arterial and venous blood oxygen; venous carbon dioxide; oxygen consumption; blood pH; and arterial lactate and pyruvate. A polyethylene catheter was placed in the right heart and arterial blood was obtained from the aorta or carotid artery. The animals were anesthetized with pentobarbital sodium and the intraruminal pressure increased to 20-45 mm.Hg. In general, it was found that the cardiac output tended to decrease during bloat as did the arterial and venous oxygen concentrations. Oxygen consumption decreased and blood pH fell markedly. The lactate-pyruvate ratio increased markedly during the period of insufflation as did the calculated oxygen debt. If the animal were given oxygen during the experiment, the lactate and pyruvate concentrations and oxygen debt did not show this marked increase. These experiments suggest that during bloat there is a rather severe cellular hypoxia and an acidosis, the latter being due to the accumulation of lactic acid and retention of carbon dioxide. Apparently the increased pressure within the rumen mechanically interferes with normal respiratory movements.

HEMODYNAMIC CHANGES IN CORONARY AND MESENTERIC ARTERIAL BEDS FOLLOWING SYMPATHETIC NERVE STIMULATION. L. Granata,* A. Huvos* and D. E. Gregg
Walter Reed Army Institute of Research, Washington 12, D. C

The effects of electrical stimulation of sympathetic nerves on coronary and mesenteric arterial beds have been studied in chronic unanesthetized dogs. Blood flow was measured by means of electromagnetic flow meters implanted on the main left coronary artery or one of its major branches in one group of dogs, and on the superior mesenteric artery in another group. In some animals, an additional flow meter was placed around the ascending aorta. Unipolar or bipolar platinum electrodes were placed around the left stellate ganglion or the anterior limb of the left ansa subclavia in the coronary group, and around the splanchnic nerve in the mesenteric group. All studies were performed several days after the animal had recovered from the operating procedure. Cardiac sympathetic stimulation produced an increase in both diastolic and systolic coronary flows, the diastolic changes being more pronounced. In some dogs this was preceded by a short period of reduced flow. Increased flow was accompanied by a rise in blood pressure and cardiac output, whereas a decrease of these parameters was observed during the occasional initial reduction of flow. A decrease in mesenteric flow associated with arterial hypertension was produced by stimulation of the splanchnic nerve. Flow was reduced and, in some instances, completely stopped during diastole, whereas systolic flow was only moderately affected.

EFFECT OF ESTROGEN UPON SECRETION AND UTILIZATION OF THYROID HORMONE IN THE RAT. Clark E. Grosvenor. Univ. of Tennessee, Memphis, Tenn.

Daily injections of 0.75 or 2.0 ug/100g 1-thyroxine were given to castrate female rats starting 24 hours after I^{131} injection and continuing for 10 days. The rats were fed Purina lab chow. Tapazole was added to the drinking water to prevent recycling of iodine. Estradiol benzoate (1.5 ug/100g) injected concurrently with 0.75 ug/100g level of thyroxine the last 5 days evoked marked acceleration in thyroidal I^{131} release resulting in a $T_{\frac{1}{2}}$ of 4.8 days compared with a $T_{\frac{1}{2}}$ of 14.5 days obtained during the first 5 days with thyroxine alone. The same dose of estradiol did not have this effect in rats whose rate of thyroidal I^{131} release was more completely blocked ($T_{\frac{1}{2}}$ of 58 days) by 2.0 ug/100g dose of thyroxine. These results suggest that the stimulatory effect of estradiol upon thyroid hormone secretion is not a direct effect upon the rat thyroid. In another experiment the daily administration of 1.5 ug/100g estradiol to castrate female rats for 4 weeks significantly increased 48 hour urinary and fecal excretion of I^{131} 1-thyroxine without significantly altering serum PBI or thyroid weight. Though daily body weight gain was reduced (but not halted) by estradiol, the animals were livelier and healthier in appearance than were their controls. These data suggest that estradiol in the dose employed increases secretion of thyroxine by the thyroid gland (probably by effecting an increase in secretion of pituitary TSH) while also increasing its rate of utilization by the organism. Supported by Senior Research Fellowship SF-365 and Grant A-3637 from the Public Health Service

METABOLISM OF THE TRANSPLANTED HEART. S. Gudbjarnason *, C. Chiba *, A. Chrysohou *, and R.J. Bing, Wayne State University College of Medicine, Detroit, Michigan.

Homografts of dog hearts were prepared according to the method of Mann. Carbohydrate metabolism and myocardial extraction of malic dehydrogenase and aldolase were studied by analyses of samples of arterial and coronary vein blood of the graft. Extraction of glucose was greater than could be accounted for by aerobic metabolism of the transplant, indicating glycolysis. As glucose was utilized anaerobically (oxygen extraction ratio greater than 100 percent), the RQ increased and exceeded unity. Conversion of carbohydrates into fats in the transplanted heart was suggested by negative myocardial ketone balances and by increased pyruvate extraction occurring with a rise in the respiratory quotient. The respiratory chain in heart muscle appeared to be intact since the difference in oxidation-reduction potential between arterial and coronary sinus blood remained negative. However, there was interference with the citric acid cycle as suggested by negative ketone balances and negative pyruvate balance. It appears likely that the increased cell permeability underlying this metabolic defect results in leakage of substrates, coenzymes and enzymes from the cell. Activity of malic acid dehydrogenase in serum was relatively greater than that of aldolase. Shortly after transplantation, injection of cofactor, as for instance, thiamine, increased both the extraction of pyruvate and the respiratory quotient of the heart. When homograft rejection proceeded at an accelerated pace, the metabolic changes were more severe and occurred at a more rapid rate. The results demonstrate that homograft rejection is accompanied by increased cell permeability affecting primarily enzymes connected with the tricarboxylic cycle.

SELECTIVITY IN THE REESTABLISHMENT OF SYNAPSES IN THE SUPERIOR CERVICAL SYMPATHETIC GANGLION OF THE CAT. Lloyd Guth and Jerald J. Bernstein*. Lab. Neuroanatomical Sciences, N.I.N.D.B., N.I.H., Bethesda, Md.

Two experiments were performed to determine whether regenerating preganglionic sympathetic fibers establish synapses randomly with any postganglionic cell or selectively with specific cells. Experiment I. In normal cats the cervical sympathetic trunk (CST) is composed of nerve fibers from thoracic sympathetic rami T1-7. Of these, T1 contributes largely pupillodilator fibers and T4 contributes largely vasoconstrictor fibers (i.e., stimulation of T1 produces pupillary dilation without decrease in ear temperature and T4 produces a decrease in ear temperature without pupillary dilation. Following transection and regeneration of the CST these relationships are reestablished, indicating that the sympathetic preganglionics from T1 have established synapses preferentially with pupillary postganglionic cells and that the preganglionics from T4 preferentially with vasomotor postganglionic cells. Experiment II. In normal cats pupillary dilation is elicited by stimulation of T1-3 but not T4-7. However stimulation of T4-7 does produce pupillary dilation one month after crushing T1-3 (i.e., before the crushed fibers have regenerated). This effect results from the formation of terminal collateral connections between the residual nonpupillary (T4-7) preganglionic nerve fibers and pupillary postganglionic cells. Six months postoperatively pupillary dilation is elicited by stimulation of T1-3 but not T4-7. Apparently, after T1-3 fibers have regenerated, the nonpupillary collaterals (T4-7) become inactive and the regenerated fibers again establish functional connections with the pupillary postganglionic cells. From these two experiments we conclude that there is a strong specific affinity between regenerating sympathetic preganglionic fibers and their appropriate postganglionic nerve cells.

NEGATIVE TISSUE PRESSURE IN THE NON-EDEMATOUS STATE--POSITIVE PRESSURE IN EDEMA. Arthur C. Guyton, Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

A year ago we reported that perforated capsules implanted in the tissues develop a negative intracapsular pressure, and we submitted reasons for believing that this negative intracapsular pressure is equal to the tissue pressure surrounding the capsule. In the present studies, tissues were made edematous in three different ways: (1) by impeding the venous return from a leg, (2) by injecting fluid into the tissues, and (3) by intravenous infusion of large quantities of fluid. The control, non-edematous tissue pressure measured by the capsule method varied from -4 to -7 mm Hg in comparison with +2 to -1 mm Hg when measured by the usual needle method. In the non-edematous state the pressures measured by these two methods were never in equilibrium, but, when the tissues were made edematous, both methods recorded positive pressures; above approximately 2 mm Hg the two methods recorded identically the same pressures. In the non-edematous state, the measurements by the needle method were very erratic depending upon the placement of the needle, movement of the needle, and time that the needle had remained in place. All these factors have made us believe that the needle method for measuring tissue pressure is completely inaccurate in the non-edematous state and that the true normal tissue pressure is negative rather than positive.

TEMPORAL ASYNCHRONY OF RECOVERY OF EXCITABILITY IN VENTRICLE. J. Han* and G.K. Moe. Masonic Medical Research Laboratory, Utica, New York.

The time course of recovery of excitability at numerous surface points at varying distances along six radial axes from an epicardial point of stimulation was tested in exposed dog ventricles. Temporal dispersion of the recovery process was estimated as the range of $R_1 - S_2$ intervals at the various points when S_2 was twice the diastolic threshold. At points equidistant from the stimulated site the range was about 11 msec. after a basic driven beat, increasing to 24 msec. after early premature beats. The degree of inhomogeneity was not significantly altered by vagal stimulation but was slightly increased by sympathetic stimulation and by increased ventricular pressure; it was markedly increased by hypothermia and by ouabain intoxication. Non-toxic doses of ouabain decreased the degree of dispersion.

EVIDENCE OF A LOCAL ARTERIO-VEINUS REFLEX DEMONSTRATED IN THE DOG INTESTINE. K. M. Hanson* and P. C. Johnson. Indiana University Medical Center, Indianapolis, Indiana.

Experiments utilizing the isolated dog ileum preparation have indicated that there is an active local arterio-venous reflex mechanism which operates to increase venous resistance (R_v) as the arterial pressure (P_A) is decreased. Evidence is given which identifies this phenomenon as a local axon reflex, serving to keep capillary pressure (P_c) relatively constant in the face of decreasing P_A and flow (F). The gut segment is perfused from the femoral artery while the venous effluent passes through a Venturi flow meter and back into the jugular vein of the animal. It is enclosed in a plastic box and suspended from a variable inductance balance permitting a continuous record of its weight. P_A and venous pressure (P_v) are adjusted by clamps on the inflow and outflow tubing such that the preparation may be held in an isogravimetric state. When P_A is decreased a total of 80 mm Hg. in a stepwise fashion, R_v is increased two or three-fold. A direct measurement at zero flow is taken by holding the weight constant by means of raising or lowering a venous reservoir. According to the relationship, $P_c = F \cdot R_v + P_v$, the P_v under these conditions is equal to P_c . Using this value R_v may then be calculated for any point on the curve. The reflex mechanism is reduced or abolished by intraarterial infusion of Regitine, Pontocaine or Dibenzylamine as well as by chronic denervation after waiting ten or more postoperative days. Hexamethonium had no significant effect indicating that a ganglion cell is perhaps not involved.

VASCULAR SMOOTH MUSCLE CONTRACTION IN HIGH POTASSIUM SOLUTIONS. Verle E. Headings* and Paul A. Rondell. Dept. of Physiology, Univ. of Michigan, Ann Arbor, Michigan.

It has been shown by Evans et al (CIBA Symposium, Adrenergic Mechanisms, 1960) and by Furchgott et al (ibid.) that contractile activity of many smooth muscles, other than vascular, can be influenced by catecholamines during depolarization in isotonic potassium-Ringer solutions. The current study indicates that in vascular smooth muscle incubated in 117 mM KCl or 156 mM K_2SO_4 solutions, pressor amines are capable of "bridging" the membrane and more directly influencing the contractile elements. Intra- and extracellular electrolyte composition was estimated from ECF measurements and tissue electrolyte analysis values corrected for bound Na (Am. J. Physiol. 199: 783, 1960) and its exchange for K in high K solutions. Calculated K-diffusion potentials were low (-6.7 to -10.4 mV in 117 mM KCl). Although epinephrine-induced contraction was weak when superimposed on K contracture initial relaxation toward baseline tone with nitroglycerine or acetylcholine permitted considerably greater contraction in response to this same stimulation. (Supported by a grant from the Michigan Heart Association.)

MATURATION OF TEMPERATURE REGULATION IN RAPIDLY AND SLOWLY GROWING INFANT RATS. F. W. Heggeness, University Rochester School of Medicine and Dentistry, Rochester, New York

Maturation of temperature regulation during cold exposure was studied in infant rats whose rates of weight gain were varied within wide limits. Two and three fold differences in body weight, fat and protein content in pre-weanling animals of the same age were achieved depending upon the relative availability of the maternal milk supply. Rectal temperatures of large, intermediate sized, and small animals were followed during one hour air exposures at an environmental temperature of $2^{\circ}\text{--}4^{\circ}\text{C}$. Observations were made on 5, 10, 15 and 20 day old animals. At all ages studied, rectal temperatures decreased less rapidly during cold exposure in large as compared to small animals. Rectal temperatures of 5, 10 and small 15 day old animals weighing between 12 to 14 gm decreased similarly during exposure to the temperature of $2^{\circ}\text{--}4^{\circ}\text{C}$. In animals 5 and 10 days of age, rectal temperatures after 30 and 60 minutes in the cold were proportional to the log of the body weight. In rats older than 10 days, body temperature during cold exposure were both age as well as weight dependent. At 20 days, only animals weighing 40 gms or more were able to maintain a rectal temperature of 35°C after 30 minutes of cold exposure. Rectal temperatures of smaller 20 day old animals were significantly above that of comparable weight 10 day old animals. Ten day old animals differed only slightly from equivalent weight 5 day old animals in their response to cold. In older animals age was also a significant factor.

RELIEF OF CONDUCTION BLOCK IN PERIPHERAL NERVE BY ULTRASOUND. E. Henneman, Harvard Medical School, Boston, Mass.

Irradiation of peripheral nerves with focused ultrasound (1.0-2.7 megacycles per second) of sufficient intensity causes blocking of conduction. By suitable control of the dosage parameters a temporary or permanent block can be produced. After conduction has been abolished without subsequent recovery, conduction can sometimes be restored temporarily by further irradiation. This restoration occurs during the period of irradiation and for a few seconds thereafter. The effect has been observed in frog sciatic and cat saphenous nerves, more dramatically in the former. It resembles the facilitatory effect of irradiation near the stimulating cathode upon response to sub-maximal shocks.

RELATION OF BIRTH ASPHYXIA TO CEREBRAL HEMORRHAGES.

Emerson Hibbard* and William F. Windle, Lab. Perinatal Physiol., NINDB, NIH, PHS, USDHEW, Bethesda and San Juan.

The common view that birth asphyxia is an important cause of cerebral hemorrhage is unsupported by experiments in rhesus monkeys asphyxiated and resuscitated at birth. Brains of 32 monkeys asphyxiated for 5 to 16 minutes after separation of the placenta at cesarean section, and later resuscitated, showed neither extra- nor intramedullary hemorrhages after fixation by perfusion. The series included 4 prematures (140-147 days gestation; term being 168 days). One 3-day old full-term monkey, killed in status epilepticus, had fresh red corpuscles extravascularly in the cerebral cortex. Subarachnoid and intramedullary hemorrhages were found in the brain of another monkey that had undergone a prolonged traumatic breech delivery during which it had died. It is possible that cerebral hemorrhage in the newborn is an agonal phenomenon taking place at death in weakened thin-walled vessels with the shift of blood from arterial to venous sides. The monkeys that lived and were killed by perfusion-fixation while in good health failed to exhibit cerebral hemorrhages.

A CONTRAST OF SORPTION IN THE DUODENUM AND ILEUM. William Hindle* and Charles F. Code. Mayo Clin. and Mayo Found., Rochester, Minnesota.

Previous work has indicated that the mucosa of the duodenum serves to equilibrate its contents quickly with the blood, while the mucosa of the ileum is fixed to serve absorption. To test this hypothesis, solutions of isosmotic and twice isosmotic mannitol were placed simultaneously in segments of duodenum and ileum in 11 anesthetized dogs. The volume, total osmolality, and sodium and mannitol concentrations of the contents were determined at intervals of 30 minutes for periods of 4 hours. The changes that occurred in both solutions in the duodenum were strikingly different from those in the ileum. When the isosmotic solution was placed in the duodenum, the volume did not change during the 4-hour period, whereas this solution was completely absorbed by the ileum. The osmolality of the solutions did not change at either site. Mannitol disappeared from the contents of both segments at nearly equal rates. Sodium entered the contents of the duodenum to take the place of the insorbed mannitol, while in the ileum the enterosorption of sodium was slight. Similar but more striking differences occurred when the twice isosmotic solution of mannitol was used. The volume of the contents of the duodenum quickly doubled, whereas that in the ileum changed little until late in the test, when it was reduced. The osmolality of the solution in the two regions was quickly reduced. This was accomplished in the duodenum by the enterosorption of water and sodium and in the ileum by the insorption of mannitol. Thus, in the ileum the action of the mucosa seemed directed solely toward absorption of the contents, while in the duodenum there was, in addition, a movement of large quantities of water and sodium out of the contents, as if to equilibrate them with blood. (Supported by Grant A-2827 from the Public Health Service.)

THE ABSENCE OF AUTOREGULATION IN THE ISOLATED PERFUSED DOG FORELEG AND INTESTINE. L. B. Hinshaw, Department of Physiology, University of Minnesota, Minneapolis, Minnesota.

Autoregulation, i.e. an increase in vascular resistance with a rise in arterial pressure, has been reported by numerous investigators in the kidney. The present series of experiments were carried out on the dog foreleg and intestine in order to determine pressure-flow-resistance characteristics of vascular beds other than the kidney. Legs and intestines were perfused at a controlled arterial pressure by means of a pump-lung apparatus previously reported (Am. J. Physiol. 196: 489, 1959; 197: 309, 1959). Intestines were transferred to the perfusion apparatus without interruption of blood flow. Small vein pressures and changes in organ weights were continuously recorded in all limb and intestine experiments. Edema formation was carefully avoided and organs were isogravimetric during control periods. Results show the absence of autoregulation in all experiments. Total resistance (art. press. - orifice vein press./flow) fell rapidly at first, and then declined gradually as the arterial pressure was increased from 40 to 200 mm. Hg. Total resistance usually fell very gradually above 150 mm. Hg and in several instances remained nearly constant at high arterial pressures. In two edematous leg experiments, small vein pressures rose rapidly and the venous segment resistance increased as a function of a rise in perfusion pressure, while the pre-venous segment resistance (art. press. - small vein press./flow) progressively fell. These findings lend further support to the role of extravascular pressure in the regulation of renal blood flow (Proc. Soc. Exp. Biol. & Med. 103: 373, 1960). No evidence for the presence of a "myogenic reflex" was obtained in any experiment. (Supported by USPHS Grant no. H5023).

VASOCONSTRICTION IN RESTING AND ACTIVE SKELETAL MUSCLE DURING CAROTID PRESSOR REFLEX. Leo Hirvonen* and R. R. Sonnenschein. Department of Physiology, UCLA Medical Center, Los Angeles, California.

In cats under chloralose-urethane anesthesia, arterial flow to the entire musculature of the skinned leg (6 expts.) or the gastrocnemius-soleus group alone (9 expts.) was continuously measured 1) while muscles were at rest or 2) during 2/sec. supramaximal stimulation of the tibial nerve with isometric recording of gastrocnemius force. During the first phase of bilateral carotid occlusion, the perfusion pressure in the experimental leg was maintained constant by clamping the arterial inflow; in the second phase, perfusion pressure was allowed to rise freely. An increase of 0-26% in resistance occurred in both resting and active muscle with no consistent differences in the two states, except for 3 occasions in resting muscle when resistance increased by 40, 70 and 160%. With some exceptions, flow increased with increased pressure and muscle force changed in direct relation with flow. Conclusions: vasoconstrictor responses in carotid pressor reflex are usually approximately equal in resting and active muscle; they are considerably less than can be induced by sympathetic chain stimulation (Hirvonen and Sonnenschein, Fed. Proc. 20:104, 1961); the rise of pressure is generally proportionately greater than that of resistance, resulting in increased flow and functional capacity of the muscle. (Supported by USPHS grant H-5157).

THE ACTIVE TRANSPORT OF HALIDE ANIONS BY THE DOGFISH GASTRIC MUCOSA.
C. Adrian M. Hogben and Robert W. Hobson, II*, Mount Desert Island Biological Laboratory, Salisbury Cove, Maine and The George Washington University Medical School, Washington, D. C.

The monovalent anions Cl^- , Br^- and I^- are actively transported across the isolated gastric mucosa of Squalus acanthias from serosa to mucosa between identical solutions, and in the absence of a significant transepithelial potential difference (see Science 129:1224, 1959). At 15° C. the following values were obtained in 8 paired experiments for Cl^- and Br^- using double labelling and 9 for Cl^- and I^- :

	<u>Cl^- Flux $\mu\text{Eq/hr/100 mg}$</u>	<u>Rate constant ratio</u>
Cl^- (128 mEq/l)		$\text{Cl}^- : \text{Br}^-$
Serosa to mucosa	1.76 ± 0.18 (S.E.)	1.08 ± 0.05
Mucosa to serosa	1.02 ± 0.05	0.88 ± 0.02
Cl^- (228 mEq/l)		$\text{Cl}^- : \text{I}^-$
Serosa to mucosa	4.68 ± 0.44	1.83 ± 0.24
Mucosa to serosa	1.78 ± 0.21	1.20 ± 0.07

The relative rates of transfer are very similar to those previously reported for Rana catesbiana, though there is less discrimination between Cl^- and I^- . In contrast to the bullfrog where the magnitude of the Cl^- mucosa to serosa flux indicates 'exchange diffusion', the Cl^- mucosa to serosa flux of the dogfish was not substantially greater than the D.C. conductance of the mucosa. The unique electrophysiological character of the dogfish stomach will be considered in terms of the uremic habitus of the elasmobranch.

INFLUENCE OF PRIOR COLD EXPOSURE ON PERIPHERAL VASCULAR REACTION ON RABBIT EAR INDUCED BY ABRUPT COLD EXPOSURE.
N. Honda* W. V. Judy*, L. D. Carlson, Dept. of Physiology, Univ. of Kentucky, Lexington, Kentucky.

The influence of prior cold exposure on vasoconstriction induced by abrupt cold exposure has been studied on the rabbit ear. Dutch breed rabbits were individually caged outdoors (4) (Max. temp. 21°C., Min. -7°, Ave. 5.9°C.) and a control group (3) kept 27°C. over a five month period. Three groups of four New Zealand rabbits were exposed to 27°C.; 5°C.; and 5°C. day and 27°C. night temperatures respectively. Rectal, ear and body surface temperature, heat loss from the ear and blood flow in the ear were recorded at 27°C., 23°C. and 5°C. In general at 23° and 27°C. there was no difference between the groups of rabbits. After one hour exposure to 5°C., outdoor and 5°C. groups had a low blood flow to the ear with no decrease in rectal temperature. Other groups, however, had a decrease in rectal temperature and higher ear blood flow. After twelve to eighteen hours exposure to 5°C. rectal temperature returned to original values in the 27°C. animals; blood flow to the ear decreased slightly. Outdoor and 5°C. rabbits ear blood flow increased during this period.

RIGHT ATRIAL AND ESOPHAGEAL PRESSURES DURING FORCED HIGH FREQUENCY RESPIRATION IN DOGS. W. E. Hull and E. C. Long*. Dept. of Physiol. and Pharmacol., Duke Univ. School of Med., Durham, N. C.

Various sites within the chest have been used to measure forces which produce inflation and deflation of the lungs during respiratory movements at normal frequencies. In this study, dogs were force-ventilated at frequencies between 1 and 17 c.p.s. using a whole body respirator. Pressure variations were recorded in the right atrium with a miniature catheter-tip transducer and in the thoracic esophagus with a long, thin air-filled balloon and catheter connected to an external electrical transducer. Sinusoidal forcing pressures of 18-28 cm. H₂O amplitude and at frequencies up to 8 c.p.s. resulted in pressure variations of similar amplitude at the two sites. Above 8 c.p.s., increasing frequency accompanied progressive divergence of recorded pressures. At these higher frequencies, pressure amplitudes in the esophagus were lower than those in the right atrium. Some implications of these results will be discussed.

HEMODYNAMIC STUDIES IN SHOCK. A. Huvos,* L. Granata,* T. Tsunekawa* and D. E. Gregg. Walter Reed Army Institute of Research, Washington 12, D. C.

Flow-pressure relationships in different vascular beds of pre-operated, unanesthetized dogs were studied during the course of hemorrhagic hypotension and hemorrhagic shock. Blood flow was measured by electromagnetic flow meters implanted around the ascending aorta, main left coronary artery or its circumflex branch, mesenteric artery, renal artery, and external iliac artery. Blood pressure was measured by an indwelling aortic catheter. All studies were performed several days following the operative procedures. Graded hemorrhage was produced by bleeding into a reservoir connected to the femoral artery; the shed blood was reinfused through the femoral vein. Flow and pressure measurements were obtained at various blood pressure levels during the initial bleed-down, at the end of which the dog was maintained at a pressure (35 to 45 mm.Hg) and time interval (1½-3 hours) thought to be sufficient to produce irreversible shock. Blood was then reinfused and flow and pressure measurements repeated during the spontaneous hypotension that developed, ending in death. Comparing the pressure-flow curves observed during shock to those of hemorrhagic hypotension revealed no change or a slight increase in total peripheral resistance, and in resistances in the mesenteric, renal and iliac arterial beds. Only the coronary arterial bed showed decreased vascular resistance. It is concluded that the pathogenesis of shock cannot be attributed to "peripheral vascular collapse" at the arteriolar site, and the hemodynamic disturbance is post-arteriolar in location.

INFLUENCE OF CARBON DIOXIDE ON THE PULMONARY CIRCULATION. R. W. Hyde*, W. H. Lawson Jr.*, and R. E. Forster, Dept. of Physiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Penna.

Prior work from this laboratory indicates that inhalation of 7.5% CO₂ in man increases the single breath CO diffusing capacity (D_L) and the pulmonary capillary blood volume (V_C). In order to uncover the mechanism of this response D_L and vascular resistance were measured in isolated perfused cat lungs exposed to varying concentrations of CO₂. Ventilation of 8 lungs with 5-10% CO₂ so that the capillaries and veins were exposed to elevated CO₂ tensions, produced a 93% rise in vascular resistance (P<.001) and a 20% rise in D_L (P<.005). Perfusion of 5 lungs with blood equilibrated with 5-10% CO₂ while breathing room air, so that only the pulmonary arteries were exposed to an increased concentration of CO₂, produced a 69% rise in vascular resistance (P<.005) but no consistent change in D_L (P=0.4). When the direction of blood flow through the lungs was reversed so that blood entered the lungs through the pulmonary veins, ventilation with 7.5% CO₂, which exposed both capillaries and arteries to elevated CO₂ tensions, increased vascular resistance and D_L; perfusion with blood equilibrated with 10% CO₂ while breathing air, which exposed only the veins to high CO₂ tensions, increased vascular resistance but not D_L. These findings indicate: (1), arteries as well as veins will constrict when directly exposed to elevated CO₂ tensions; and (2), if the capillaries and downstream vessels are exposed to elevated CO₂ tensions, D_L is increased. A likely mechanism for this increase in D_L is that constriction downstream from the capillaries produces a rise in transmural pressure which causes an increase in V_C. Among alternative explanations for the changes in D_L is the possibility that CO₂ increases the speed of the reaction between CO and Hemoglobin.

THE EFFECT OF SEVERE COLD STRESS ON THE N-BALANCE OF MEN UNDER DIFFERENT DIETARY CONDITIONS. B. Issekutz, Jr., K. Rodahl, and N. Birkhead*. Division of Research, Lankenau Hospital, Philadelphia 51, Pa.

Four groups of healthy young men consumed for 10-day periods at an ambient temperature of 22°C: 3000 Calories 70 g protein (Diet I); 3000 Calories 4 g protein (Diet II); 1500 Calories 70 g protein (Diet III) and 1500 Calories 4 g protein (Diet IV) respectively. Diets II and IV caused a marked, and III a moderate loss of body N. Switching to diet I during the follow-up period caused in every case a marked positive balance. The metabolic response to these four diets was investigated in nine nude subjects living for three to nine days at an ambient temperature of 8°C. This environment induced almost constant shivering and a resting metabolic rate about twice the BMR. A negative N-balance was observed on diet I and the N-loss characteristic for diets II, III, and IV was markedly increased. Switching to diet I and room temperature of 22°C during the follow-up period during which time the BMR was normal, the negative N-balance persisted for 4-6 days, in spite of an 18-fold increase of the protein intake (in the case of diets II and IV). It is suggested that an increased activity of the thyroid and/or the adrenal cortex may be responsible for this after-effect of cold exposure.

STUDIES ON "GASTRIN". A.C.Ivy, H. Kato, R. Wojciech,
Dept. Clinical Science, Univ. of Illinois, Chicago.

It has been reported by others and by us that a "gastrin" preparation devoid of "free histamine" may be made by appropriate methods. We have found that four different "gastrins" may be separated by isoelectric precipitation. Two and possibly three polypeptide carriers and two mucopolysaccharide carriers of gastrin have been separated by paper chromatography. On aqueous phenol extraction it was found that the "gastrin" activity remains in the phenol polypeptide layer while the mucopolysaccharides pass into the aqueous layer. We doubt that the "gastrin" we are studying is a releaser of a gastrin.

EFFECTS OF NEMBUTAL AND URETHANE ANESTHESIA ON THE BODY
TEMPERATURE OF RATS OF VARIOUS BODY SIZE.

Richard L. Jackson and Richard L. Landry*. Loyola
University and Louisiana State University School of
Medicine.

It has been a general experience to find a decline in body temperature in mammals under the influence of anesthesia. Essex(1952) reported that the body temperature under the influence of adrenalin and nembutal varies according to body size. Krog(1959) found that at an environmental temperature between 20-25°C smaller dogs tended to cool off while larger dogs tended to warm up under nembutal. Using rats, our data shows that the body temperature drops more in young rats than in old using nembutal and an environmental temperature of 20-25°C. This relationship is reversed using urethane. In this case the drop in body temperature was greater in the older animals. Sodium amytal brings about a relatively uniform drop in body temperature irregardless of body size. The ambient temperature varied from 20-25°C. The dosage for each anesthesia is as follows: urethane .375 grams/300 grams body weight; nembutal .20cc/300 grams(lcc= 60 mgm. pentobarbital sodium); amytal sodium .15 cc/300 grams (lcc=100 mgm ambobarbital sodium). The time to reach maximum depression level varies between 4 to 7 hours.

MEMBRANE IONIC CURRENT FLOW DURING THE ACTION POTENTIAL OF STRIATED MUSCLE. Howard Jenerick. Emory University, Atlanta.

Propagating action potentials recorded by impaling microelectrodes from single fibers of the frog sartorius were displayed on an oscilloscope in phase plane coordinates (membrane voltage V , on horizontal axis; first time derivative dV/dt , on the vertical axis). Photographs of the action potential pattern were enlarged, traced, and fitted by several mathematical functions. The action potential as recorded was thus reduced to a set of differential equations ($dV/dt = f(V)$) which were integrated to give analytic functions describing the time course of the action potential ($V = f(t)$). These functions in turn were mathematically differentiated singly and doubly, and substituted into the cable equation along with several required constants. This last equation was solved numerically for the membrane ionic current associated with the action potential. Appropriate plotting of these data gave voltage-current relationships in the active muscle membrane which resemble results obtained by others from the voltage-clamped squid giant axon. Our calculations indicate peak ionic currents of about 4 mA/cm and an active membrane resistance in the order of 10 ohm-cm² (compared with a resting resistance of 2500 ohm-cm²). Experimental changes in external fluid concentrations (Na and Ca withdrawal or K addition) reduce the current magnitude. In addition, Na shifts the plots in a manner consistent with the altered sodium potential, while Ca and K primarily affect the membrane conductance but not the "sodium potential". (Aided by grants from the National Institutes of Health (B-861 and B-3272) and the McCandless Fund of Emory University.)

COMPARISONS BETWEEN SOMATIC SENSORY THALAMUS AND CEREBRAL CORTEX OF RACCOON. J. I. Johnson, Jr.* and W. I. Welker. Laboratory of Neurophysiology, Univ. of Wisconsin School of Medicine, Madison, Wis.

The purpose of the present study was to compare the pattern of organization of somatic sensory thalamus and cerebral cortex. The somatic sensory area of the raccoon ventrobasal thalamus was mapped using electrophysiological recording and retrograde degeneration techniques. The pattern of organization and relative areal enlargement so obtained were compared with those described for the cerebral cortex in a previous study (Welker & Seidenstein, 1959). Physiologically, the somatic sensory thalamus was mapped in four animals using evoked single unit activity. The general pattern of organization of the thalamic representation is similar to that found in cats and monkeys (Mountcastle & Henneman, 1952; Rose & Mountcastle, 1952). However, in the raccoon the thalamic hand representation is relatively larger, constituting about half the thalamic somatic sensory volume. These proportions are similar to those found at the cerebral cortex. The SI hand region of the cerebral cortex of the raccoon is contoured by sulci, dimples, and spurs, which demarcate physiological subdivisions. Thus separate gyri are formed which represent the projections of individual digits and the palm. These anatomical landmarks were used as guides in the chronic ablation of individual digit and palm pad areas of the cortical hand region in a series of seven animals. Subsequent reconstruction of degenerated areas within the thalamus of each of these animals confirmed the results obtained by the physiological method regarding size and pattern of organization of the thalamic hand representation.

EFFECT OF ARTERIAL PRESSURE ON ARTERIAL AND VENOUS RESISTANCE.

P. C. Johnson and K. M. Hanson* (Intro. by J. J. Friedman). Department of Physiology, Indiana University School of Medicine, Indianapolis.

Studies of intestinal blood flow have shown that vascular resistance decreases when arterial pressure is reduced. However, no data have been obtained on the site of the resistance change. To determine arterial and venous resistance separately the isogravimetric technique of Pappenheimer (Am. J. Physiol. 152:471, 1948) was employed on a completely isolated loop of intestine. Arterial pressure was reduced in a stepwise fashion, adjusting venous pressure concurrently to keep the intestinal weight constant. Measurements of plasma protein in the venous effluent show that weight change is indicative of capillary filtration. Arterial inflow was ultimately clamped off with venous pressure again adjusted to obtain the isogravimetric state. At this time venous and capillary pressure should be equal. This pressure can be taken as the isogravimetric capillary pressure. The pressure drop from large artery to capillary to large vein can be estimated and arterial and venous resistance calculated. In all experiments reduction of arterial pressure led to an increase in venous resistance which was an active rather than a passive phenomenon. By contrast, in most experiments arterial resistance decreased with arterial pressure reduction. This arterial vasodilation is localized between the small arteries (0.5 mm. o.d.) and the capillaries. It is significant that both responses tend to make capillary pressure independent of arterial pressure. Supported by a grant from the American Heart Association.

THE NATURE OF THE NEGATIVE ENDOCOCHLEAR POTENTIAL. B.M. Johnstone and V. Honrubia (intr. by J.O. Hutchens). University of Chicago, Ill.

The normally positive endocochlear potential (EP) becomes negative during anoxia. If the anoxia is continued, the negative EP decreases to zero over a period of from 1 to 4 hours. The change in conductance of the endolymph in the scala media was followed during this period using the single micropipette method of Strickholm. This technique uses the fact that the resistance of a micropipette is a function of the conductance of the fluid bathing the tip as well as that which fills it. The decline in negative EP was paralleled by a decrease in the conductance of the endolymph. When the negative EP finally reached zero, the conductance of the endolymph had fallen to a value close to that of the perilymph. The results are consistent with the hypothesis that the conductance changes reported reflect a change in the composition of the endolymph (high K^+ and hence high conductance) towards that of the (high Na^+ , low conductance) perilymph; and that the negative EP is generated by an ionic concentration gradient, probably K^+ , its decline during prolonged anoxia being due to the equalization, by diffusion, of the ionic differences between endolymph and perilymph within the cochlea.

RESPONSE OF BUFO MARINUS, B. VALLICEPS, AND B. WOODHOUSEI
TO ANTIDIURETIC HORMONE

Jeanne M. Jordan* and Marvin L. Riedesel
Biology Department, University of New Mexico

Three species of toads, Bufo marinus, B. valliceps, and B. woodhousei were investigated as assay animals for the antidiuretic hormone, Pitressin. B. marinus was more sensitive to the hormone than B. valliceps or B. woodhousei at the 1; 10; 100; 1,000; and 10,000 microunit dosages. There was a significant response of B. marinus to one microunit and B. valliceps and B. woodhousei to 10 microunits of Pitressin. Bufo valliceps absorbed the hormone more readily from the lymph sac and excreted it faster than B. marinus or B. woodhousei. The differential responses of the three species correlated with variance in skin thickness and response to soaking in chlorine-free water. The target organ for the hormone appeared to be the skin since decreased urine production was similar in all three species. The response of the animal to soaking in water indicated B. marinus had a better osmotic regulating mechanism.

Supported in part by N. S. F. grant no. G-14495.

THE RESPONSE OF THE HUMAN ESOPHAGUS TO ATROPINE. P. A. Kantrowitz, C. I. Siegel and G. A. Bair (Intr. by C. tum-Suden). USA Chem Res & Dev Labs, Army Chemical Center, Md. and Dep't of Med, Johns Hopkins Univ Sch of Med, Balto., Md.

Anticholinergic agents are known to exert different effects on smooth and striated muscle. Since the human esophagus contains both types of muscle, esophageal motor studies were performed to determine whether or not the two portions of esophagus differ in their response to atropine. Simultaneous intraluminal pressures were recorded, employing open-tipped catheters. Six normal human subjects were studied, before and after the intramuscular administration of 0.65 mg and 2.0 mg doses of atropine sulfate. In all subjects peak control peristaltic pressures were maximal in the middle third of the esophagus; following the administration of atropine there was a marked and dose-dependent reduction in peristaltic pressures throughout this area. The lowest peristaltic pressures were consistently observed five to six centimeters below the crico-pharyngeus. Orad from this point the amplitude of the peristaltic waves rose progressively. Atropine did not affect the peristaltic pressures in this segment of the esophagus. In the lower three centimeters of the esophagus marked variability in peristaltic amplitude was observed and no consistent atropine effect was noted. These studies demonstrate that atropine has no effect on peristalsis in the upper--purely striated muscle--portion of the esophagus while it decreases peristaltic amplitude in a dose-dependent fashion in the lower--smooth muscle--portion.

THE EFFECT OF CO_2 ON RESPIRATION IN CROSS-CIRCULATED DOGS. Frederick F. Kao, Remedios Suntay* and George McCoy*. Dept. of Physiology, State Univ. of New York, Downstate Medical Center, Brooklyn, N.Y.

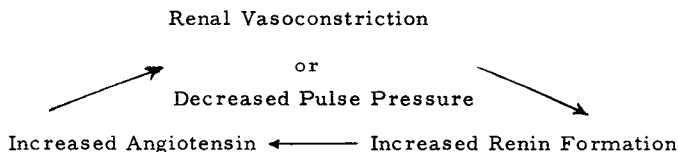
The quantitative effect of CO_2 on respiration was tested in nine pairs of cross-circulated dogs. The cross-circulation technique employed was the same as in our earlier reports (Kao, Am. J. Physiol. 184:145, 1956) except the carotid arteries of the donor dog were anastomosed to the vertebral arteries of the recipient. In this arrangement, the heads of both dogs were perfused by blood from their vertebral arteries and the carotid components which may influence respiration were inactivated. Complete vascular separation of the recipient's head from its own body was done by massive ligations of the vessels and muscles in the neck, and subsequently verified by means of lipoidal and latex injections. The donor dog was made to inhale CO_2 (3,5,7,% with 20% O_2 and balance N_2) for 30 min. Ventilatory responses, arterial Pco_2 , H^+ of the donor, and that of the recipient's body were determined before and during the steady state of CO_2 inhalation. The ventilatory responses of both dogs were found to be similar in time course and in sensitivity of the respiratory centers. Arterial Pco_2 of the recipient's body dropped precipitously while its head was being perfused with hypercapnic blood.

Supported in part by a grant from NIH H-4032 C7.

EFFECT OF ANGIOTENSIN ON THE JUXTA-GLOMERULAR CELLS

Yale J. Katz, Paul Patek*, Sol Bernick*, Departments of Medicine and Anatomy, University of Southern California School of Medicine, Los Angeles

Two micro-grams of pure angiotensin, as the octapeptide, were injected sub-cutaneously in mature rats three times a day over periods of from one to twelve days. As early as the second day there was an increase in prominence of the renal juxta-glomerular (JG) cells and their granules. Similar changes in the JG cells have been shown by others to be associated with increased renin formation or storage. The present observations give support to the following suggestion made by one of us (1), based on studies of the effect of angiotensin on the renal pulse wave:



It is conceivable that this chain of events as a feed-back mechanism could in time lead to irreversible renal vascular changes, particularly in the preglomerular vessels.

(1) Katz, Y. J., Lancet, 1:1006, 1961

Studies supported by American Heart Association, Los Angeles County Heart Association, and Grant H-4867, U. S. P. H. S.

ENERGY METABOLISM OF THE RENAL MEDULLA. E. L. Kean, P. H. Adams, R. W. Winters and R. E. Davies (intr. by John R. Brobeck). Depts. of Biochemistry and Physiology, Univ. of Pennsylvania, Philadelphia, Pa.

Studies have been made of the rates of oxygen consumption and of anaerobic glycolysis of tissue slices from the inner medulla and from the cortex of the dog kidney, slices of the inner medulla were found to have a much lower Q_{O_2} (-2.26 ± 0.084) than those of the cortex (-14.1 ± 0.72). Increasing the osmolality of the medium by addition of sodium chloride caused a progressive decrease in Q_{O_2} to a proportionate degree in both types of slices. Mitochondria from the inner medulla were inhibited to a greater degree by increased osmolality of the medium than were those from the cortex. Study of the respiratory pigments showed that mitochondria of inner medulla were qualitatively similar to cortical mitochondria, but that the absolute amounts of $cyt\ b_5$ pigment were significantly less in medullary mitochondria. The Q_{O_2} of inner medullary slices was found to be quite high (5.1 ± 0.35) compared to that of cortical slices (1.4 ± 0.06). Increasing osmolality of the medium by sodium chloride caused no significant change in the Q_{O_2} in the medullary slices until a level of 1100 to 1300 mOsm. was reached; cortical slices by contrast were progressively inhibited by increasing osmolality. These differences could not be demonstrated in cell-free homogenates of the two tissues. The above results point to some unusual biochemical properties of inner medulla. They further suggest that this tissue *in vivo* may utilize anaerobic rather than aerobic pathways for energy metabolism, a suggestion in accord with recent evidence concerning the nature of the blood flow to this region. (Supported by U.S.P.H.S. Grant No. RG-7106 and Smith Kline and French Laboratories.)

LEFT VENTRICULAR VOLUME AND PRESSURE IN DOGS, HORSES, CATTLE AND SWINE. H. Kines*, J. P. Holt, E. A. Rhode* and S. A. Peoples* Heart Laboratory, Univ. of Louisville and Univ. of California School of Veterinary Medicine.

In anesthetized closed-chest dogs, horses, cattle and swine subjected to plethora and hemorrhage left ventricular end-diastolic pressure (EDP) and end-systolic pressure (ESP) were measured, and end-diastolic volume (EDV), end-systolic volume (ESV), and stroke volume determined by means of an electric conductivity method described earlier by one of us (J.P.H.). In animals in the control state, ranging in size from 15.5 to 836 Kg., there was an approximately linear relationship between EDV and ESV, ($ESV = 0.57 \text{ EDV}$), and between EDV and stroke volume, ($S = 0.43 \text{ EDV}$); and a curvilinear relationship between cardiac output (CO) and EDV, ($CO = 106 \text{ EDV}^{0.77}$), and between heart rate (R) and EDV, ($R = \text{EDV}^{-0.23}$). In all animals studied a several fold increase in EDV, from the minimum value consistent with life, was associated with little or no change in the EDP; while a small increase in ESV, from the minimum value consistent with life, was associated with a steep rise in ESP to a certain level, while further increase in ESV was associated with little or no increase in ESP. (Supported by USPHS Grants #1534 and #2075; the Ky., Louisville and American Heart Associations.)

ABILITY OF DOGS TO DETECT HUMAN ODOR TRACE. J. E. King*, R. F. Becker and J. E. Markee*. Duke University Medical Center, Durham, N. C.

Using the method of Becker, Markee and King (see abstract) we investigated how long a slight human odor trace might last and still be capable of detection under various conditions of weathering. Light fingerprints were impressed upon clean, 3" x 1", glass slides prepared two lots at a time, one for indoor storage, the other for outdoor weathering. Four unhandled, unmarked slides were set out with each odor slide. Indoor storage trays were kept in a cabinet on separators; outdoor trays were placed in a 3' x 4' flat box on the laboratory roof exposed to blown dirt, sunlight and rain. Indoor and outdoor samples along with their unmarked comparison slides were presented to dogs at the end of 6, 12, 24, 48, 72 and 96 hours, and after 1, 2 and 3 weeks in our 5 station testing circle. In a test block of 50 trials the marked sample appeared 10 times randomly in each of the odor stations. Equally aged indoor and outdoor samples were used on alternate trials. Four to seven 50 trial tests were run at each time interval. Dogs detected 3 week indoor samples reliably, less so at 6 weeks and not at all by the end of 8 weeks. Equally aged outdoor samples were never so readily detected as indoor samples, and the reliability of detection was not significant at the end of two weeks. None of the parameters of weathering that were measured correlated significantly with the deterioration of the outdoor trace.

EFFECT OF SEROTONIN ON REGIONAL METABOLISM. H. Kleckner, G. Galansino, and W. C. Shoemaker. Michael Reese Hosp. and Med. Center, Chicago, Ill.

The effects of serotonin (as 5 hydroxytryptamine creatinine phosphate) were measured in unanesthetized dogs whose hepatic vessels had previously been catheterized. Blood samples were withdrawn from the arterial, portal and hepatic venous catheters at 10 second intervals. Hepatic plasma flow was measured by a modified bromsulphalein method (J. Appl. Physiol. 15; 473, 1960); plasma concentrations of glucose, sodium and potassium were measured.

Hepatic plasma flow decreased to approximately half the control values 1 to 2 minutes after femoral injection of 0.2 to .5 mgm/Kg. A minimum value was reached between 1 and 1 1/2 minutes after serotonin injection. An increase in portal venous potassium, often over 2 meq/L, occurred 1 to 2 minutes after injection. This was followed by an increase in hepatic venous potassium concentration. Minimal increases in arterial, and femoral venous potassium concentrations were observed.

Multiplication of concentration differences by flow values showed a marked output of potassium from the nonhepatic splanchnic area, followed by an hepatic potassium output. There was a fall in arterial, portal and hepatic venous glucose levels and an uptake of glucose by the nonhepatic splanchnic area or gut.

IONIC CONTENT OF GLIAL CELLS. Alan Koch, James B. Ranck, Jr. and Bertha L. Newman. Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle, Wash.

Electron microscopy indicates that less than 10% of the volume of brain tissue is interstitial. The high Cl^- content of brain tissue therefore suggests existence of a population of cells containing much Cl^- . If these cells are glia, the Cl^- content of samples of brain tissue composed solely of glia should be higher than that of samples of normal brain. A glial preparation was developed from the lateral geniculate body in cats. Neuronal degeneration was induced by bilateral enucleation and unilateral ablation of the visual cortex. Nissl stains of the lateral geniculate body ipsilateral to the cortical ablation showed that the changes were complete at 4 months. The neuronal elements had disappeared almost completely and there was only slight mesenchymal reaction. Both lateral geniculate bodies were dissected out of the fresh brain and were analyzed for their contents of Na^+ , K^+ , Cl^- and H_2O . Such analyses were also conducted on lateral geniculate bodies from normal cats. In normal animals the values were: Na^+ , $64.4 \pm 1.7 \mu\text{eq/g}$ wet tissue; K^+ , $90.2 \pm 0.9 \mu\text{eq/g}$; Cl^- , $46.5 \pm 1.8 \mu\text{eq/g}$; and H_2O , $79.7 \pm 0.2\%$. With transneuronal degeneration (in the lateral geniculate contralateral to the cortical ablation), the values were: Na^+ , $78.2 \pm 4.6 \mu\text{eq/g}$; K^+ , $89.0 \pm 1.6 \mu\text{eq/g}$; Cl^- , $43.1 \pm 1.5 \mu\text{eq/g}$; and H_2O , $78.4 \pm 0.9\%$. With retrograde degeneration, the values were: Na^+ , $113 \mu\text{eq/g}$; K^+ , $88.3 \pm 5.0 \mu\text{eq/g}$; Cl^- , $60.7 \pm 2.4 \mu\text{eq/g}$; and H_2O , $76.8 \pm 0.9\%$. These observations indicate that the $[\text{Cl}^-]$ in glia is high. The $[\text{Na}^+]$ also appears high, but the $[\text{K}^+]$ appears to be about the same as that in neurons. Such findings are compatible with the view that glia are low-voltage cells and that some of the cation in them is not present in ionic form. [Aided by grants (B5082 and H4469) from the National Institutes of Health, USPHS.]

EFFECT OF ENVIRONMENTAL TEMPERATURE ON BODY FAT COMPOSITION OF THE HAMSTER. A. Kodama* and N. Pace. Department of Physiology, University of California, Berkeley, California.

Previous investigators have shown that the body fat of various mammals is modified during exposure to low environmental temperatures. Lower melting points and higher iodine numbers have been found in fat taken from cold-exposed animals when compared with that obtained from control animals. As a first step in the examination of the mechanism whereby the increased fluidity is achieved, the proportions of the fatty acids in perirenal and subcutaneous fat of hamsters exposed to 35° , 27° and 6°C for 1 to 12 weeks were compared by gas chromatographic analysis. Melting points of the fat were determined concurrently. Differences in melting point or fatty acid composition of perirenal and subcutaneous fat were not apparent between control (27°C) and warm-exposed (35°C) hamsters. Fat obtained from cold-exposed (6°C) hamsters showed a lower melting point accompanied by a lower mole fraction of palmitic acid and a higher mole fraction of oleic acid throughout the experimental period. After 2 weeks of cold exposure, the melting points of fat from both sites were found to be lower by 2°C when compared with that taken from control animals. The mole fraction of palmitic acid was reduced by .037 (15.9% change, $P < .001$) and the mole fraction of oleic acid was increased by .056 (16.6% change, $P < .001$). There was no detectable difference in the mole fraction of stearic acid between control and cold-exposed animals. Approximately four weeks of exposure to cold were required before the changes in fat composition became stabilized. The "softening" of body fat on cold exposure is probably the result of events of greater complexity than the direct desaturation of saturated fatty acids to their unsaturated homologues. (Supported under ONR Contract Nonr-222(38).)

EFFECTS OF CHLORPROMAZINE ON PHYSICAL AND CHEMICAL TEMPERATURE REGULATION. J. Kollias*, R.W. Bullard, F.W. Hughes*. Depts. Physiology and Pharmacology, Indiana University School of Medicine, Indianapolis.

The alterations produced by chlorpromazine on the physical and chemical mechanisms of temperature regulation have been studied at various ambient temperatures. At 23.5°C. chlorpromazine (25 mg./Kg.) treated rats had a colonic cooling rate almost twice that of animals breathing 10% O₂ even though the groups had similar O₂ consumption depressions. This finding and the observations that treated rats had higher tail temperatures and high tail blood flows, as shown plethysmographically, indicate a loss of peripheral vasoconstriction in a cool environment. Piloerection was also decreased in the treated animals. At an ambient temperature of 35°C. the treated rats warmed at a much greater rate than did controls. However, O₂ consumptions for both groups were similar. Chlorpromazine decreased survival time in the heat but did not alter the lethal colonic temperature. The greater heating rate at 35°C. with chlorpromazine is due paradoxically to a decrease in peripheral blood flow. Salivation in the heat was also decreased in treated animals. Chlorpromazine appeared to inhibit all temperature regulatory mechanisms that were studied. Supported in part by Contract #DA-h9-007-MD-947 from the Research and Development Division, Office of the Surgeon General, U. S. Army.

IS CHOLESTEROL AN OBLIGATORY PRECURSOR OF ADRENAL STEROIDS IN THE DOG?

Alvin A. Krum, Manfred D. Morris* and Leslie L. Bennett. Dep't of Physiology, Univ. of California Medical Center, San Francisco, and U.S. Naval Hospital, Oakland, California.

A synthetic diet containing 4C¹⁴ cholesterol of known specific activity (S.A.) was fed for a period of approximately 5 weeks to two mongrel dogs. The S.A. of the plasma cholesterol plateaued in one dog, but equilibrium was not achieved in the other. The right adrenal vein was cannulated and, after a sufficient amount of blood had been collected, ACTH was given and more blood obtained. Cortisol and S_R were separated by paper chromatography and derivatives made before the S.A. was determined. In the dog in which the S.A. of the plasma cholesterol had plateaued, the S.A. of cholesterol from plasma and adrenal gland was indistinguishable from the S.A. of the steroid hormones, both before and after ACTH. This indicates that cholesterol was an obligatory precursor. In the dog in which equilibrium was not reached, the S.A. of the cortisol and S_R was somewhat lower than the S.A. of the adrenal cholesterol. However, the data indicates that at least 80% of the adrenal hormones were derived from cholesterol. The discrepancy in the data between the 2 animals may be accounted for by the fact that equilibrium was reached in only one of them.

(Supported by Grant A-1369 from the Natl. Insts. of Health)

EFFECTS OF BLOOD FLOW AND LEFT ATRIAL PRESSURE ON RESISTANCE IN THE PULMONARY VEINS. K. Kuramoto * and S. Rodbard, University of Buffalo Chronic Disease Research Institute, Buffalo, N. Y.

The pulmonary wedge pressure is commonly considered to approximate pulmonary capillary venous and left atrial pressures. A catheter with an outside diameter of 0.6 to 0.9 mm. was placed as far as possible into a pulmonary venule. In 11 thoracotomized dogs insufflated with maximal air pressure of 6 mm. Hg, mean pulmonary arterial, venular, and left atrial pressures averaged 19, 9, and 4 mm. Hg respectively. Flow through each lung was modified by clamping either the left or right main pulmonary artery. Venular pressure exceeded left atrial pressure by 25 to 50% of the gradient from artery to atrium, depending on the volume of blood flow. When pulmonary venous pressure was low, its elevation in 8 isolated uninflated lung lobes decreased the pulmonary venous resistance; arterial and capillary resistance also fell but to a lesser extent. Since pulmonary venular pressure varies with blood flow and with the pulmonary arterial and left atrial pressures, these mechanical factors must be evaluated before implicating pulmonary venomotion as the basis of changes in vascular resistance.

EXTRA-THYROIDAL EFFECTS OF PROPYLTHIOURACIL ON THYROID HORMONES.

S. Lang and B. N. Premachandra*. Jewish Hospital, St. Louis, Mo.

There is increasing evidence that propylthiouracil (PTU) has an extra-thyroidal action. The present experiment is concerned with an observed difference in the peripheral effect of PTU on thyroxine (T₄) as compared with triiodothyronine (T₃). Rats pretreated with PTU and subsequently injected intravenously with I^{131} -T₃ lose more isotope in their bile than control animals during a four hour observation period. The serum precipitable iodine falls faster in the control animals than in the PTU treated rats. Since these changes do not occur during the four hour observation period when I^{131} -T₄ is used, there is a possibility that serum carriage of T₃ is altered by PTU. It is also possible that either cellular metabolism or cellular entry of thyroid hormones is affected by PTU and the apparent lack of effect on T₄ is related to the firmer binding of this moiety by its plasma binding proteins. The four hour observation period might thus not be long enough to see the changes which are characteristic of PTU on T₃. (Supported by USPH Grants #A-2342 and #A-5107)

Secretion of calcium and phosphate by the dog parotid gland. L. L. Langley, O. R. Grimes, Jr.*, and D. F. Cockrell, Jr.* Univ. of Ala. Med. Centr., Birmingham, Alabama.

In dog parotid saliva, calcium is 2-3 times more concentrated than it is in the plasma. Phosphate in the saliva is less than one-fifth that of the plasma. Increasing the plasma phosphate level by a factor of 7 increases the saliva phosphate only twice. Salivary calcium varies almost proportionately with plasma calcium. After parotid secretion begins, the concentrations of both calcium and phosphate progressively decrease until a steady state is reached. Calcium and phosphate concentrations increase slightly in the saliva as the secretion rate decreases. At very slow rates there is a more marked increase. During the stop-flow procedure both calcium and phosphate concentrations increase, but to a strikingly different degree and at different sites in the gland. The increase in phosphate is almost exclusively the organic fraction. It is concluded that water and electrolytes are transferred from plasma to saliva by processes that are not coupled, and that proceed at varying and independent rates. The site of these transfers is distal, probably at the level of the ducts. (Supported by USPH-D-329-C4).

EFFECT OF NOREPINEPHRINE INFUSION ON RENAL BLOOD FLOW. Jimmy B. Langston. Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

Previous studies from this laboratory have indicated that norepinephrine has a direct and an indirect effect on the kidney. The direct effect results in an immediate decrease in urinary output while the indirect effect, mediated by changes in arterial pressure, causes first an increase in urine flow which is followed by a decrease in urine flow. Experiments have now been completed which indicate that changes in urinary output are the result of concomitant changes in renal blood flow. The renal blood flow was measured directly while increasing or decreasing the rate of norepinephrine infusion in two groups of animals. In one group the renal perfusion pressure was maintained constant and in the second group this pressure was allowed to vary with the infusion of the drug. In both cases the animals were rendered areflex by complete spinal anesthesia. It was found that when the perfusion pressure was not allowed to vary each increase in drug infusion resulted in a decrease in renal blood flow. When the perfusion pressure was allowed to increase with each increase in drug infusion, the renal blood flow and urinary output first increased but reached a peak when approximately 0.0006 mg/kg/min of norepinephrine was given. With further increase in drug infusion, the renal blood flow decreased and complete anuria resulted. (Aided by grant from the National Heart Institute. U.S.P.H.S.)

EFFECTS OF GAS DENSITY ON CARBON DIOXIDE ELIMINATION.

Edward H. Lanphier and Richard A. Morin*. Dept. of Physiology, The Univ. of Buffalo School of Medicine, Buffalo, N. Y.

Retention of carbon dioxide has repeatedly been suggested as a partial or complete explanation for "inert gas narcosis," exemplified by CNS depression experienced by divers breathing air at greater depths. Respiratory and alveolar gas studies have indicated that the role of carbon dioxide retained because of decreased pulmonary ventilation must generally be small. However, the possibility of impaired carbon dioxide elimination related to increased alveolar gas density per se has not been ruled out. In anesthetized dogs treated with succinylcholine and ventilated with a constant volume pump, arterial P_{CO_2} was measured continuously with a Severinghaus P_{CO_2} electrode and Beckman physiological gas analyzer. Respiratory gas density was changed 5- to 30-fold by alternation between air and He-O₂ mixtures at normal pressure and at 6 atm. abs. Differences in P_{aCO_2} associated with such alterations in density were indistinguishable from normal trends and fluctuations. In dogs with constant ventilation, large alterations in respiratory gas density do not produce detectable changes in carbon dioxide elimination.

Supported by ONR Contract Nonr 969(03).

EVIDENCE FOR A TUBULAR SECRETORY MECHANISM FOR CREATININE IN THE GUINEA PIG. Richard J. Laurence* and Ewald E. Salkurt, Dept. Physiology, Indiana University School of Medicine, Indianapolis, Indiana.

Data were obtained using the clearance technique in the guinea pig which indicated the presence of a tubular creatinine secretory mechanism. All animals were males, ranging in weight from ca 600 gram to 900 gram and were anesthetized with pentobarbital administered I.P. Inulin, PAH and creatine in Ringer's solution were given I.V. at a rate of .06 or .08 cc/min. Plasma creatine concentrations of 12 to 260 mgs % were obtained by varying the concentration of creatinine in the infusion. Clearance periods of 30 min duration were begun one hour after the start of infusion. Blood samples of 2 cc were withdrawn from a carotid catheter midway through each period. Urine was collected by direct catheterization of the bladder in one experiment, in the rest by catheterization of the ureters. Clearance ratios of creatinine/inulin in 27 clearance periods completed to date varied from 2.22 at lower plasma levels (at ca 10 mg/%) to 1.02 at a plasma concentration of 176 mg/%. Thus, the mechanism of creatinine handling in the guinea pig is similar to some other mammals (primates, rat), but differs from the dog, seal, and rabbit which handle it solely by glomerular filtration.

OXYGEN AND MYOCARDIAL CONTRACTILITY, IN VITRO. Eugene A. Lentini and Richard I. Park. Dept. of Physiology, Univ. of Oregon Medical School, Portland 1, Oregon.

The inotropic response of myocardial tissue exposed to various partial pressures of oxygen has not been quantitatively investigated. The present study was designed to examine the magnitude of isometric developed tension from rats' trabeculae carneae aerated with known percentages and tensions of oxygen. The myocardial preparations were stimulated to contract at a frequency of 1/sec and bathed with 45 ml of King's glucose solution at a flow rate of 8 ml/min. Contractile responses were recorded over a three hour period. Two percent CO₂ was incorporated in the various oxygenating gas mixtures. The balance composition of the experimental gas mixtures consisted of N₂. It was found that the mean developed tension increased progressively as the partial pressure of oxygen was increased from 50 mm to 700 mmHg (95% O₂). Preparations aerated with O₂ tensions of 760 mmHg exhibited a large variation in response and the mean developed tension was not statistically different during the first two hours from the mean developed tension of those muscles aerated with 95% O₂ + 2% CO₂. Muscles oxygenated with their respective O₂ tensions, excluding those aerated with an O₂ tension of 760 mmHg, revealed a contractile response which was characterized by a minimal variation in the isometric developed tension. In conclusion, the data indicate 95% O₂ + 2% CO₂ + 3% N₂ as a suitable gas mixture for the aeration of rat trabecula carneae as determined by the magnitude and constancy of contractile response, the full recovery of developed tension after an initial transient depression and the minimal variation in the development of isometric tension between myocardial preparations. (Supported by grants from the NIH (H-4562) and the Oregon Heart Association)

THE ROLE OF THE PANCREAS IN THE PRODUCTION OF CLEARING FACTOR.

Harry H. LeVeau, Prudence Giordano* and Samuel Zinberg*. VA Hospital and State Univ. of N.Y., Brooklyn, N.Y.

Present literature suggests that clearing factor is delivered into circulation from the vascular wall. Others consider it identical to lipoprotein lipase. The hind extremity of the dog was perfused with heparin containing blood. Clearing factor was not demonstrable in the venous return. Similar infusion of isolated omental fat failed to produce circulating clearing factor. Insignificant lipolytic activity was encountered from organ extracts in the normal dog even after addition of suitable quantities of heparin and plasma. The pancreas was the only exception but this was ascribed to pancreatic lipase. Clearing factor could not be distinguished from pancreatic lipase by differential inhibition contrary to published data. Since only pancreas alone exhibited such high lipase activity, serum clearing factor was determined in dogs following pancreatectomy. Total pancreatectomy produces a precipitous fall in the circulating post heparin induced clearing factor which tends to return after two or more weeks. Serum amylase activity was tested in 20 normal subjects before and after heparin injection. Heparin induced a significant rise in circulating serum amylase and clearing factor. Isolation of the pancreas and injection of heparin into the pancreatic artery caused a significant rise in lipolytic activity of pancreatic venous blood. The data suggests that the pancreas as a lipase producing organ contributes significantly to circulating clearing factor. No clear distinction should be made between pancreatic lipase and clearing factor. Other organs which produces lipase contribute less significantly to circulating clearing factor. The situation is not unlike that of circulating phosphatase. Supported by N.I.H. Grant No. A-1652.

INCREASED RATE OF GROWTH OF EXPERIMENTAL HOSTS ASSOCIATED WITH FOREIGN AUTONOMOUS CELLS. D. R. Lincicome and J. Shepperson*, Dept. of Zool. Howard Univ., Washington, D.C.

Trypanosoma lewisi and T. duttoni live as foreign autonomous cells in the blood stream of the rat and mouse respectively. The relationships of these cells with their sheltering hosts especially those involving metabolic exchanges have not been studied extensively or at all, and serve therefore as the basis for this report. Rats weighing 56-180 g and mice 9-11 g were inoculated IP with fresh saline suspensions of cells from donor animals (two levels used). Body weight rate gains were calculated for 30 days. Five replicate experiments employing the lewisi cell in rats and 3 using the duttoni cell in mice were completed. Trypanosome populations in tail bloods of hosts were measured by hemacytometer. Irrespective of starting weights used, all rats having trypanosomes grew faster than control uninfected animals. In one experiment mature animals (180 g) receiving the larger inoculum of cells grew at a slightly lower rate (1-5%). Maximal orders of difference in growth of experimental over control hosts were: 1) 4% for 180 g rats; 2) 12% for those of 111 g; 3) 5% for 84 g; 4) 16% for 77 g; and 5) 33% for 56 g. Comparable results were obtained with the duttoni cell in mice. Among possible mechanisms to explain these findings are: 1) infected animals ate more food; 2) host cell reproductive or metabolic rates were enhanced; 3) inadequate water balance; 4) enhanced activity of the pituitary gland and/or the thyroid; and 5) immune response producing enlarged livers and spleens.

BILIARY EXCRETION OF CERTAIN ORGANIC ACIDS. David Ling* and K. C. Huang, University of Louisville, School of Medicine, Louisville, Ky.

The study is primarily concerned with the hepatic excretion of certain organic acids with the expectation of determining whether there is a similarity between the hepatic and renal tubular transport mechanisms. The organic acid was injected into the hepatic artery first and into the portal vein half an hour after the first experiment. Creatinine was injected simultaneously as a substance which is excreted in the bile mainly by a passive diffusion process. It was found that the biliary excretion of PAH was slower than that of creatinine in the first 4 minutes after the intra-arterial injection. However, the excretion increased gradually and reached a maximal plateau 10 minutes later. At that time the excretion ratio between PAH and creatinine was 3 to 4. The experiment with acetyl-Telapaque showed that the excretion ratio between this compound and creatinine was 20. It suggests that both PAH and acetyl-Telapaque were secreted by the hepatic cells. The experiment with intraportal injection has shown that the biliary excretion of PAH or Telapaque was smaller than that following an intra-hepatic arterial injection. This may mean that the biliary excretion of these compounds is located in parenchymal cells which obtain the major blood supply from the hepatic artery. (Supported by a Grant-in-Aid from the Society of Sigma Xi and A.M.A. Research Council).

RELEASE OF SEROTONIN AND CATECHOLAMINES INTO THE BLOOD OF THE PANCREATO-DUODENAL VEIN. R. Litta-Modignani*, G. Galansino* and P. P. Foà. Dept. of Physiology and Pharmacology, The Chicago Med. School, Chicago 12, Ill.

Previous work in this and other laboratories (Sirek et al, Am. J. Physiol. 188, 17, 1957; Galansino et al, *ibid.* 198, 1059, 1960) suggests that the area drained by the pancreato-duodenal vein may produce at least two types of hyperglycemic materials: one type which is released by growth hormone (STH) and which, like serotonin and the catecholamines, is blocked by DHE and another type, which may be released by deserpidine and which, like glucagon, is unaffected by DHE. Deserpidine (1 mg/Kg) injected into the pancreato-duodenal artery of anesthetized dogs causes an increase in the concentration of serotonin, epinephrine and nor-epinephrine in the blood of the pancreato-duodenal vein 30 minutes after the injection. This rise happens too late to explain the hyperglycemia, which starts after 5 minutes and reaches its maximum after 20 minutes. Furthermore this phenomenon is not limited to the pancreato-duodenal area, because a similar rise of serotonin and catecholamines occurs in the blood of the femoral vein. Injections of STH (3.5 mg/Kg) into the femoral vein cause no rise in the serotonin content of pancreatic blood, but increase its catecholamine content. By exclusion the pancreatic hyperglycemic material released by deserpidine may be glucagon and that released by STH may be a catecholamine and/or the phosphorylase-activating factor(s) described by Makman et al (Federation Proc. 20, 189, 1961). Blood serotonin and catecholamines were determined using an Aminco-Bowman spectrophotofluorometer. This work was aided by NIH Grants A-522 and 2A-5102.

CARDIAC OUTPUT AND BLOOD VOLUME. Larissa Lukin and Eric Ogden. The Ohio State Univ., Department of Physiology, Columbus, Ohio.

Assuming that the relation between blood volume and cardiac output is directly proportional, a deviation of the volume from normal in either direction would produce a corresponding change in cardiac output. But it could also be expected that autoregulation would maintain a constant cardiac output despite changes in volume and thus homeostasis would be preserved. Experimental data show that the immediate result of hemorrhage is a fall in cardiac output, and namely, the greater the reduction in volume the greater is the reduction in output. In moderate plethora, on the other hand, cardiac output does not change significantly; homeostasis is maintained. Beyond this plateau, that is in excessive or sudden hypervolemia, cardiac output falls again. Thus, in the normal state the balance between volume and output is fixed at an extreme end of the plateau. Is this position of any significance? Would not a position in the center, from which not only hyper- but also hypovolemia could be counteracted, be more advantageous? Additional data suggest that it would not. The fall in cardiac output after hemorrhage is, to a large extent, a reversible change because restoration of blood volume restores the cardiac output and, according to available evidence, the recovery is complete. But marked plethora may damage the cardiac muscle and cause circulatory failure. Removal of excess blood aggravates the failure; a permanent damage to the myocardium is done. Thus, the position of the normal balance at the extreme left of the plateau keeps the circulatory system near the reversible change but far away from irreversible damage. We wish to acknowledge the contributions of Dr. Leo A. Sapirstein.

REDUCED FOOD INTAKE AS A CAUSE FOR SLOWER GROWTH AT HIGH GRAVITY. Lorenz O. Lutherer*, Charles C. Wunder, and William J. Moressi*. State Univ. of Iowa, Iowa City, Ia.

High gravity, simulated by continual centrifugation, can result in slower growth of mice and other organisms. For white mice a transient reduction in food intake also occurs. Pair-feeding of control mice can cause growth responses similar to those for mice centrifuged at 3 and at 5 G's. Centrifugation has a selective effect upon the growth of various structures. Lowered caloric intake is known to reduce some neoplastic growth. For these and other reasons a selective effect upon tumors would be anticipated. Tumors resulting from foot-pad injections of Sarcoma-180 cells can grow at fields as intense as 7 G's. Preliminary results indicate that tumor growth can be decreased during the centrifuge-induced period of lowered caloric intake and the effect is greater than would be expected solely from the altered intake.

THE RELATIONSHIP OF SPINAL FLUID AND ARTERIAL CARBON DIOXIDE TENSION AND PH. Harold A. Lyons and Chin-Tang Huang (intr. by Ludwig W. Eichna). State University of New York, Brooklyn, New York. This work was supported by Grant B 1594 (C2) USPHS.

Eighteen subjects, nine with normal pulmonary function, six emphysematous patients without hypercarbia, and three emphysematous patients with hypercarbia, had simultaneous spinal fluid and arterial blood determinations of pH and $p\text{CO}_2$ during normal room air breathing and during the end of a 10 minute breathing period of high concentration of carbon dioxide. Unlike previous studies made on dogs, results of this study consistently showed $p_{\text{sf}}\text{CO}_2$ greater than $p_{\text{a}}\text{CO}_2$. The pH of the spinal fluid was always lower. This occurred in both normals and those subjects with hypercarbia, although the latter had spinal fluid values nearer the arterial blood findings. After breathing 6 per cent carbon dioxide appreciable change of spinal fluid values in any of the patients was not noted, even though arterial $p\text{CO}_2$ and pH appropriately deviated and ventilation responded normally. These results indicate that CO_2 stimulation of the respiratory center is unrelated to any changes of pH and $p\text{CO}_2$ in the spinal fluid.

EFFECT OF CEPHALIC PERFUSION ON DEVELOPMENT OF HEMORRHAGIC SHOCK.

D.M. MacCanon, J.E. Abbott,* and D.D. Eitzman.* Dept. of Physiol. and Pharmacol. State Univ. of So. Dak., Sch. of Med. Sci. and Div. Exper. Cardiol. of The Chicago Med. Sch., Chicago, Ill.

Current thought regarding the genesis of hemorrhagic shock concentrates on circulating dilator materials and peripheral ischemia as causative factors. However, some laboratories still persist in the older theory of vasomotor center "fatigue" and "exhaustion" despite evidence of reflex vasomotor responses until the onset of vascular collapse. In order to clarify these views the effects of head perfusion on the hemodynamic consequences of hemorrhagic hypotension (aortic mean pressure of 30 mm. Hg) were studied in 10 experiments. Although, hemodynamic responses to hypotension were not significantly altered by the procedure, the 'shock time' was lengthened from 61 ± 16 min. (control experiments) to 318 ± 160 min. ($P < 0.001$). These results suggest that preservation of 'normal' vasomotor activity was highly successful in combatting hemorrhagic shock. (Supported by the U.S. Army Medical Research and Development Command, Department of the Army under Contract No. DA-49-007-MD-1008 and Grant No. DA-MEDDH-61-17.)

EFFECT OF VARYING CEREBRAL ARTERIAL PRESSURE ON

CEREBRAL VENOUS FLOW. Paul P. Machowicz*, Gabriel Sabo*, George Lin*, Carlos E. Rapela and Harold D. Green. Bowman Gray School of Med., Winston-Salem, N. C.

In dogs, anesthetized with sodium pentobarbital, the cerebral venous outflow was measured by cannulating the confluence of the sagittal sinus with the lateral sinuses, the latter being occluded in order to avoid communications between intra and extracranial circulation. Cerebral arterial pressure was measured by way of catheters, inserted into both vertebral arteries at the point where they enter the transverse canal; the catheters were passed as far as possible towards the base of the cranium. The cerebral arterial pressure was varied by controlled constriction of both common carotid arteries. Lowering the cerebral blood pressure to values above 30 mm. Hg did not produce a proportional decrease in cerebral venous outflow; a greater reduction in pressure produced an abrupt decline in flow. Following release of the carotid constriction the cerebral venous outflow increased and remained above the control values (120 to 150 percent of control) for two to four minutes. These changes in flow can be interpreted as due either to an autoregulatory mechanism or to changes in spinal fluid pressure. Aided by a grant from LIMRF.

A TECHNIQUE TO MEASURE THE CAPACITANCE OF THE VEINS IN THE ARM. Ian F. S. Mackay and Roger L. Walker* Department of Physiology, University College of the West Indies, Jamaica, West Indies.

With the arm in the upward and vertical position the gravitationally drained veins can be refilled by applying a venous occluding pressure to a cuff placed near the axilla. If at the same time a record is made from a hand plethysmograph, an interval will elapse between the application of the cuff pressure and the commencement of the increase in the hand volume. This interval is called the venous filling time; that is, the time taken to refill the veins in the segment of the limb between the pressure cuff and the wrist junction of the hand plethysmograph. From a determination of the arm-hand blood flow it is possible to measure the volume of blood that flows into the limb during the venous filling time. This volume is taken as a measurement of the capacitance of the venous system in the arm. The residual volume in the veins following gravitational drainage was shown to be small.

REGULATION OF SODIUM, CHLORIDE, AND WATER ABSORPTION BY THE INTESTINE.

David Mailman* and R.C. Ingraham, Univ. of Ill. College of Medicine, Dept. of Physiology, Chicago, Illinois.

The absorptive capacity for sodium, water, and chloride under physiologic conditions was determined in an isolated segment of dog ileum into which a known volume of NaCl-MgSO₄ had been placed. The volume of the various body fluid compartments was altered by standard methods in order to determine whether such procedures altered the absorptive capacity of the gut in a manner similar to the renal tubules. Intravenous infusion of isotonic saline, hypertonic saline, and head-down tilting caused a decrease in the amount of Na and water absorbed as well as a decrease in the ability of the gut to reduce the concentration of Na in the lumen. The concentration of NaCl in the fluid absorbed was increased except in the case of hypertonic saline infusion. The absorption of Cl roughly paralleled Na but was, in general, absorbed to a greater extent. Isoncotic dextran had little effect on absorption. Hemorrhage had a variable effect, yielding results which suggested either accelerated absorption or decreased absorption relating to hypoxic damage to the gut. Head-up tilting caused greater impoverishment of Na by the intestine. These results demonstrate a regulation for absorption of Na, Cl, and water by the intestine and a mechanism similar to renal regulation is implicated.

COMBINED FLOWMETER-DYE DILUTION STUDY OF THE ACUTE EFFECTS OF CHANGES IN HEART RATE BY VAGAL STIMULATION ON THE DEGREE OF EXPERIMENTAL AORTIC REGURGITATION. Donald A. Malooly,* David F. Donald, Hiram W. Marshall* and Earl H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The upstream sampling dye-dilution technic for quantitating aortic regurgitation was used with the Spencer electromagnetic flowmeter probe on the ascending aorta of open-chest dogs to study the acute effects of vagal stimulation on the degree of aortic regurgitation, which was determined by the flowmeter ratio of regurgitant volume (RV) to total stroke volume (TSV) and the correlated ratio of the early appearing portions of the left ventricular (LV_A) and femoral arterial (FA_A) dye curves after injection of indocyanine green into the aortic root. Validation of flowmeter measurements of stroke volume was obtained by a double-calibration technic using dye curves in vivo and bidirectional perfusion of the isolated aorta at the end of each experiment. At heart rates of 140 to 200/min. the degree of acutely produced aortic regurgitation ranged from 25 to 80 per cent of left ventricular output with regurgitant flows of 0.3 to 3.8 L./min. Stimulation of the peripheral cut end of the right vagus nerve with a Grass stimulator caused an increase in the RV/TSV ratio by 14 to 70 per cent at heart rates of 48 to 71/min. Dye curve ratios LV_A/FA_A also increased. RV values calculated by using the orifice formula with transvalvular pressures correlated closely with the simultaneously recorded flowmeter values. This agreement indicates that the changes in RV/TSV with heart rate can be explained by straightforward hydrodynamic considerations.

MEASUREMENT OF THE PAIN THRESHOLD OF THE HARD PALATE. R. A. Margarida*, J. D. Hardy and H. T. Hammel, Department of Physiology, University of Pennsylvania, Philadelphia, Pa., and the Aviation Medical Acceleration Laboratory, Johnsville, Pa.

Using thin-walled aluminum thermodes individually fitted to the roof of the mouth, the pain threshold of the hard palate was measured in four subjects. By rapidly circulating hot water and water at 37°C alternately, the temperature of the thermode could be raised and lowered between a neutral and a test level. The temperature within the thermode was measured in every observation by a fine wire thermocouple in the circulating water. The temperature between the thermode and the hard palate was also measured over the entire range of temperatures studied and a correction for the gradient across the thermode wall was determined and applied to the water temperature. Stimuli between 40°C and 49°C were administered according to a fixed plan which divided the temperature continuum into 0.5° intervals. Each subject was exposed to 288 stimuli in six experimental periods and following each stimulus noted his sensations in a written record that was analyzed at the end of the experiment. The pain thresholds, as determined by 50% pain report, were 46.1°, 46.4°, 46.9° and 47.0°C. The range of stimuli reported as painful were from 44.5° for the first reports of pain to 47.7°C which always evoked pain. A preliminary study was made of the phenomenon of drinking hot beverages, and evidence indicates the sipping of air with the liquid limits the rise of the tissue temperature.

EFFECTS OF EPINEPHRINE ON CARDIOVASCULAR RESPONSE TO LEG EXERCISE IN MAN. Robert J. Marshall and John T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Ten studies of cardiac output were made on five experienced subjects while supine. Cardiac output while at rest (A) was 5.2 to 6.8 (mean 6.2) L. per minute; it increased during intravenous infusion of epinephrine bitartrate at 15 μ g. per minute (B) by 2.0 to 7.2 (mean 3.7) L. For each subject, supine leg exercise was undertaken (C) to produce a similar increase (2.1 to 7.0, mean 4.7 L.). When an infusion of epinephrine was given during identical exercise (D), cardiac output increased by 6.2 to 12.2 (mean 8.2) L. This was almost the sum of the increases produced by the two previous maneuvers. Oxygen saturation of femoral venous blood was 70% (A), 86% (B), 30% (C) and 50% (D). Thus, both at rest and during infusion of epinephrine. Therefore, either the increased flow due to epinephrine traverses vessels that do not supply the metabolic needs of active muscles, or, if it traverses nutritive vessels, the cardiac output is not precisely adjusted by the amount of oxygen available to the active muscles.

EMPTYING OF CERTAIN LUNG REGIONS BY VOLUNTARY CONTROL OF THE EXPIRATORY FLOW RATE. C. J. Martin*, A. C. Young and William Pace*. Firland Sanatorium and Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine, Seattle, Wash.

Following a breath of oxygen, man normally has a rising nitrogen concentration on the alveolar plateau of the next expiration. In normal subjects and patients with emphysema the nitrogen and carbon dioxide concentrations following a breath of oxygen were monitored. Voluntary exaggeration of the normal expiratory flow curve with high initial peak flows (ca. 70 l/minute) and a rapid decline will flatten or, in some instances, slightly invert the alveolar nitrogen plateau. Reversal of this flow pattern with increase of flow throughout the expiration results in an accentuation of the rise in nitrogen concentration so that the rise in a normal man mimics more closely the pattern with emphysema. During an expiration in which flow rates are rapidly varied between 3 and 80 l/minute, higher flow rates result in rising and lower flow rates in falling nitrogen concentrations. Poorly ventilated regions of lung empty preferentially during high flow rates and well-ventilated pulmonary areas empty during low flow rates. The latter regions also have a different mean ventilation-perfusion ratio, so that there are changes in the carbon dioxide curve during expiration.

MECHANISMS UNDERLYING THE HYPOTENSIVE EFFECT OF POSITIVE PRESSURE BREATHING IN DOGS. R. L. Maulsby* and H. E. Hoff. Baylor Univ. College of Med., Houston, Texas.

Cyclical volume changes of the right ventricle were qualitatively measured by means of a variable resistance strain gauge sutured to the right ventricular wall. Artificially created decreases in venous return as well as cardiac tamponade to a degree sufficient to produce hypotension were found to decrease the volume of the right ventricle. Increased right ventricular outflow resistance, however, produced a marked increase in the right ventricular volume. With hypotensive levels of continuous positive pressure breathing, the right ventricular volume was found to increase in the animal with a wide open chest; the volume decreased with the chest closed. It is concluded, that in the open-chest condition, the hypotensive mechanism of positive pressure breathing is an increase in pulmonary vascular resistance; while in the closed-chest condition, decreased venous return and/or cardiac tamponade are predominantly responsible for the hypotension.

THE EFFECT OF OVARIAN HORMONES ON PLASMA LUTEINIZING HORMONE (LH) ACTIVITY IN THE OVARIECTOMIZED RAT. S. M. McCann. Dept. of Physiology, Univ. of Pennsylvania School of Medicine, Philadelphia, Pa.

Using the ovarian ascorbic acid assay for LH, no LH could be detected in plasma from normal donor females, but detectable quantities were found in plasma of ovariectomized donors. This activity was decreased by single subcutaneous (sc) injections of estradiol benzoate (Eb). This effect was demonstrable within a day of injection of large doses and was maximal three days after injection, at which time the minimal effective dose to produce a decrease in LH activity was of the order of 0.1 μ g. A slight decrease in LH activity was demonstrable within one hour of a massive intravenous dose of estradiol. Decreased LH activity was found in the absence of proestrous or estrous vaginal smears but was always found if the smear was in proestrous or estrous stage. A large dose (25 mg) of progesterone (P) sc produced a slight depression of LH activity in ovariectomized rat plasma on assay 2-3 days later; a marked depression of activity resulted only if a second injection of 25 mg. of P was given 2 days after the first with estimation of the activity on the third day. Five mg. of P a day for 3 days had no significant effect. Large doses of Eb or Eb plus P failed to block the action of a hypothalamic extract with LH-releasing activity which suggests that the inhibitory effects of these steroids on LH secretion are mediated at some point proximal to the pituitary, presumably the hypothalamus. (Supported by U.S.P.H.S. Grant No. A1236(C4) and Air Force Grant No. AF49(638)-685.)

THE IMMEDIATE EFFECTS OF CATECHOL AMINES ON PLASMA FIBRINOGEN IN CONSCIOUS AND ANESTHETIZED DOGS. Jess M. McKenzie, William B. Stavinoha* and Larry J. O'Brien. Civil Aeromedical Research Institute, Oklahoma City, Oklahoma.

Previous findings that injection of catechol amine preparations caused an immediate rise in levels of circulating fibrinogen in the dog indicated the presence of a labile pool(s) of fibrinogen. In the present study the immediate hyperfibrinogenemic effects of l-epinephrine, norepinephrine, and isopropyl norepinephrine were evaluated in dogs that had been anesthetized with either sodium pentobarbital or pentothal-chloralose as well as in dogs that had received no anesthetic. The experimental animals were drawn from two populations; one group was obtained directly from the pound; the other group was housed for 27 to 57 days in veterinary hospital quarters. Plasma fibrinogen was estimated according to a semi-micro technique using triplicate assays on each sample. Control blood samples were drawn from the femoral artery (anesthetized dogs) and from the antecubital vein (conscious dogs). Samples were obtained periodically up to 60 minutes after injection of the catechol amine. No change in plasma fibrinogen was detected after the administration of l-epinephrine, norepinephrine, or isopropyl norepinephrine. It is concluded that exogenous catechol amines are not involved in the immediate increase in plasma fibrinogen as has been previously reported.

An Evaluation of Specific Activity of Digitonin-Precipitable Sterols Obtained from Rat Liver. J.M. Merrill, Bonnie Keith*, and Janet Lemley-Stone*. VA Hospital and Vanderbilt University, Nashville, Tenn.

In short term experiments using C^{14} acetate for study of cholesterol biosynthesis, "high counting companions" are known to interfere with accurate determination of specific activity of cholesterol. The dibromide purification method (Arch. Biochem, 40:334, 1952) which gives a fixed specific activity is laborious and unsuitable for small amounts of tissue. In an attempt to find a simple extraction method which would give specific activity figures similar to the dibromide method, four different extraction procedures were used. Rats were injected intraperitoneally with acetate- $l-C^{14}$ and killed 30 minutes later. Radioactive and chemical measurements were made on digitonin precipitates of liver. Extraction with alcohol and ether yielded a fraction having the highest specific activity while the lowest specific activity was obtained from livers treated with sodium ethoxide and subsequent extraction with petroleum ether. Extraction with methylal-methanol or with chloroform-methanol gave similar results which were intermediate between the former two methods. Of the methods used, the sodium ethoxide procedure gave a specific activity closest to that of the dibromide purification. These results emphasize the variability of specific activity of digitonin-precipitable sterols obtained by different extraction methods.

THE RELATIONSHIP OF A RESPIRATORY REFLEX TO THE ACETYLCHOLINE CONTENT OF THE PONS AND MEDULLA. Bernard Metz. Department of Physiology, Medical College of South Carolina, Charleston, S.C.

The question of whether cholinergic neurons are involved in the transmission of respiratory activity in the central nervous system remains uncertain. Experiments indicate a significant correlation between respiratory function (as measured by the reflex response to electrical stimulation of Hering's nerve) and the acetylcholine (ACh) concentrations in the pons and medulla, after the intravenous injection of a hemicholinium, HC-3 (α, α' dimethylethanolamino 4, 4' biacetophenone), a drug which inhibits the synthesis of ACh. With a decreasing respiratory reflex response there is a concomitant progressive and gradual decrease of the ACh in the brain areas. Although controversy still exists as to the site of action of HC-3 (i.e. central or peripheral), these studies corroborate previous experiments (Metz, B. Neurology 11 : 37, 1961) that acetylcholine concentrations and acetylcholinesterase activity levels were correlated with the potentiation or inhibition of the reflex under investigation. Therefore, these experiments lend additional support to the hypothesis of the presence of a cholinergic factor in central respiratory control. (Supported by a grant from the National Institutes of Health, B-954).

THE PHYSIOLOGIC SIGNIFICANCE OF SUPERFICIAL MEDULLARY RESPIRATORY CHEMOSENSITIVITY. R.A. Mitchell*, H.H. Loeschke*, W.H. Massion* and J.W. Severinghaus. Cardiovascular Research Inst., Univ. of Calif. Med. Center, San Francisco.

Previous perfusions of the 4th ventricle (Leusen, Loeschke, Mitchell) with mock C.S.F. (cerebral spinal fluid) of high P_{CO_2} or low pH stimulated respiration; nicotine applied locally to the 4th ventricle depressed ventilation. Our recent studies suggest that the perfusion fluid is actually acting downstream and that the pH- and P_{CO_2} -sensitive areas are near the entrance of the 8th and 9th cranial nerves rather than in the floor of the 4th ventricle or area postrema. Perfusion of the 4th ventricle with tracer dyes has no effect unless the lateral surfaces of the medulla are stained; perfusion of the lateral surfaces of the medulla stimulates respiration even though the 4th ventricle and area postrema are not stained. Nicotine and acetylcholine applied locally to the lateral surfaces of the medulla cause immediate hyperpnea; procaine and cold C.S.F. depress ventilation. The physiologic significance of these areas was tested by perfusing them with mock C.S.F. of varying pH and P_{CO_2} and noting the stimulating or depressing effect on respiration. The slope of the respiratory response curve to increasing C.S.F. P_{CO_2} was 30% of the inhaled CO_2 response curve. (Supported in part by U.S.P.H.S. Research Grant 5881.)

Local Effects of Anions and the Hydrogen Ion upon Vascular Resistance in the Dog Forelimb. J.I. Molnar* and F.J. Haddy. VA Research Hospital and Northwestern University Medical School, Chicago, Ill.

We have previously reported [Physiologist 3:122, 1960; Fed. Proc. 20:99, 1961] that the effect of slight increase in limb blood concentration of K^+ , Mg^{++} , or Acetate is active limb arteriolar dilation whereas that of Ca^{++} is active constriction. Na^+ , Cl^- , SO_4^{--} , or HPO_4^- seem to have little effect. The actions of other anions and the hydrogen ion have been studied in 30 dogs. Brachial arterial blood flow was held constant at 100 ml./min. and pressures [P] were measured in the brachial artery [ba], small artery [sa], small vein [sv], and cephalic vein [cv]. In 9 experiments, isosmotic solutions of NaCl, $NaHCO_3$, Na Lactate, $NaNO_3$, Na Pyruvate, Na Citrate, HNO_3 , Na Acetate and $NaNO_2$ were infused into the brachial artery at 6.4 ml./min. [1.0 mEq./min. except for Na Citrate]. Pba-Pcv changes from control 1 min. after onset of infusion were 0, +1, -1, +1, -19, -23, -25, -53 and -56 mm. Hg, respectively. Isosmotic solutions of Hydrochloric, Lactic, Pyruvic, Acetic and Citric acid, infused at 1.6, 1.8, 1.8, 2.0 and 0.6 m Eq./min., respectively, decreased this gradient by 21, 33, 41, 39, and 30 mm. Hg, respectively. All of the changes resulted mainly from decrease in Psa-Psv. Limb blood pH decreased ~0.4 units during infusion of the acids but was unaffected by the Na salts. This study shows that the local effect of slight excess of blood Pyruvate, Acetate, Nitrite, Citrate, or Hydrogen ion is active arteriolar dilation and that the activities of Acetate and Nitrite exceed that of Pyruvate.

MEASUREMENT OF CIRCULATING BLOOD VOLUME AND OF BLOOD MOBILIZATION IN THE ISOLATED PERFUSED LUNG. James C. Moore and John N. Diana*. Univ. of Louisville School of Med., Louisville, Ky.

A modified indicator-dilution procedure has been utilized for the measurement of circulating blood volume in the isolated, perfused lung. The method involves the washing out and collection of a tag which has been allowed to distribute itself uniformly throughout the lung circulation. The entire procedure is performed periodically while the lung is being perfused and does not disturb total outflow, outflow pressure or any other measured parameter. While recirculation is being prevented, T-1824 is introduced at the inflow by continuous infusion until a constant outflow concentration (plateau) is attained. The infusion is then discontinued and the entire outflow collected until the indicator concentration of the outflowing blood is at or near the pre-infusion level. The quantity of indicator obtained, divided by the concentration at which it existed in the lung (plateau), provides a measure of circulating lung blood volume. This method is accurate to $\pm 3\%$ in model systems. Results of previous experiments using less satisfactory techniques (Fed. Proc. 18: 107, 1959) indicated that a portion of blood in the pulmonary circuit was stagnant during low blood flows, but was mobilized into the active circulation at higher flows. The existence of such a phenomenon has been verified by the current studies. A comparison of changes in circulating lung blood volume, as measured by the above method, with changes in lung weight has been carried out under experimentally produced variations in lung blood flow. The discrepancy between these two measures of lung blood volume change provides a quantitative indication of blood mobilization or demobilization. (Supported by U.S.P.H.S. Grant No. H-3260.)

EFFECT OF UTERINE DISTENTION ON THE ESTROUS CYCLE OF THE GUINEA PIG.¹
 W. W. Moore, Dept. of Physiology, Indiana University Medical Center,
 Indianapolis, Indiana.

Thirty adult female guinea pigs were utilized in a study of the effects of uterine distention on the length of the estrous cycle. A glass bead (1.5 mm diam.) was sutured into the lumen of a uterine horn on the 3rd day or on the 8th day of the estrous cycle after 2-4 normal estrous cycles had been completed. Unoperated control animals had a cycle length of 16.3 ± 0.18 days. A group of 6 animals were sham-operated and their cycle length was 16.6 ± 0.16 (mean \pm standard error of the mean) days. The 9 animals in which the uterine distention was started on day 3 had cycles of 11.7 ± 0.43 days, but in 6 animals denervation of the uterine segment containing the bead caused the cycles to return to normal, 16.7 ± 0.38 days. Uterine distention of 15 animals started on day 8 of the cycle induced an increase in cycle length to 22.4 ± 0.42 days. Denervation of the distended segment in 9 animals was accompanied by normal cycles, 16.6 ± 0.33 days. The results confirm earlier observations on the ewe and suggest that mechanical stimulation of nerve endings in the uterine wall by an implanting embryo causes an increase in the secretion of luteotrophin and/or a decrease in FSH and LH from the adenohypophysis which leads to a prolongation of corpus luteum function.
¹Supported by PHS Grant B1296 from Institute of Neurological Diseases and Blindness.

RESPONSE OF HEPATIC VEIN SPHINCTERS TO INTRAPARENCHYMAL INJECTION OF RADIOPAQUE IODINATED COMPOUNDS INTO THE LIVER OF ANESTHETIZED DOGS.
A.H. Moreno, L.M. Rousselot, A.R. Burchell, R.F. Bono, and J.H. Burke. (intr. by J.G. Chusid). St. Vincent's Hosp. N.Y.C. and N.Y. Univ. School of Med.

Low pressure, hepatic, intraparenchymal injection of 10 ml. of sodium diatrizoate and related compounds in anesthetized dogs did not result in radiological demonstration of the outflow tracts of the liver similar to that previously observed when proportionally smaller doses were used in rats and guinea pigs. The intraparenchymal (not intravascular) injection of these compounds into the liver of mongrel dogs appeared to trigger contraction of hepatic vein sphincters and resulted in massive dilatation of segments of hepatic veins proximal to contracted sphincters. Injection of epinephrine prior to the iodinated compound seemed to prevent contraction of the sphincters and resulted in radiological demonstration of the hepatic vein system and vena cava. Equal doses of exogenous epinephrine failed to release contraction once the sphincter mechanism had been set in operation. In some animals artificially induced stress appeared to prevent contraction of the sphincters. Local tissue reaction from the intraparenchymal injection rather than irritation of the intima of the vessel by the iodinated compound seems to have been responsible for the contraction of the sphincters since direct intravascular injection into the hepatic veins themselves failed to produce this response. The unusual ability of the hepatic veins to dilate massively seems to provide visual evidence for the blood reservoir function of the canine liver. Prevention of sphincter contraction by exogenous and possibly endogenous epinephrine may relate this function to homeostatic mechanisms not completely understood at this time.

THE EFFECTS OF TASTE-ABOLISHING THALAMIC LESIONS ON THE EXAGGERATED RE-ACTIVITY OF STATIC PHASE HYPOTHALAMIC OBESE RATS TO DIETARY SENSORY QUALITIES. P. J. Morgane. Univ. of Tennessee Medical Sch., Memphis, Tenn.

Heightened reactivity of static phase obese rats to dietary stimuli has been reported by Teitelbaum (J. Comp.Physiol.Psychol., 48/156,1955) and confirmed in this laboratory. Ventromedially lesioned hypothalamic rats (VM) in the static phase of obesity sustain elevated body weights in an entirely euphagic state but show exaggerated responses to certain stimulus aspects (e.g., taste and texture) of their diets. The present experiments were designed to test the hypothesis that these behavioral alterations are due to modified taste perception. Bilateral fulgurations were performed in the medial halves of the ventro-posterior parts of the ventral thalamic nuclei sufficient to significantly raise rejection thresholds of normal rats to quinine adulterated diets. The competency and reproducibility of this lesioning technique was tested in switched 2-bottle choice situations with adulterated liquid diets and in feeding tests in which adulterated powdered foods were randomly switched with unadulterated diets. Four animal groups were utilized: a normal group, a dorsomedial thalamic-lesioned group, VM lesioned rats in the dynamic phase of obesity, and VM lesioned rats in the static phase of obesity. Only static phase VM lesioned animals showed the "gourmet" syndrome manifested by Epicurean food habits. Following superimposed taste-abolishing thalamic lesions, each group with the exception of the static phase animals fed equally well on unadulterated and adulterated liquid and solid diets. Dynamic phase rats continued to show hyperphagia and obesity progression. Static phase obese rats continued as "gourmets" by refusing quinine adulterated foods but eating significantly more of proffered delicacies such as dextrose. "Supersensitivity" of static phase obese rats to dietary sensory qualities does not, therefore, seem based on altered primary taste perceptivity. (Support:Grants B-2797, USPHS).

ELECTRICAL ACTIVITY RECORDED BY MEANS OF CHRONICALLY IMPLANTED ELECTRODES IN THE OLFACTORY BULB OF THE RABBIT. David G. Moulton. (intr. by L. M. Beidler). Div.of Physiol., Florida State University, Tallahassee, Florida.

Since electrophysiological investigations of spike activity in the olfactory bulb have been largely confined to acute preparations, a study was made of olfactory responses in intact unanaesthetised rabbits. Up to 50 stainless steel electrodes were implanted in the olfactory bulbs and peripheral olfactory structures, while connectors were housed in a lucite container permanently attached to the skull. The rabbits were tested in a sound-attenuated chamber having a one-way glass screen. Filtered air or odor from an olfactometer was delivered to a face mask or permanently implanted catheter. Although the phase and frequency of waves recorded simultaneously from different parts of the bulb varied, frequencies in the range of 55-75 cps were prominent following the introduction of odor. More interesting is the spike activity. Fluctuations in amplitude of spike discharges from the bulb of the undisturbed animal appeared to be related in part to the degree of attentiveness of the rabbit and responses to a given odor were not always consistent. Frequently, however, a brief initial volley was followed by several seconds of reduced activity, terminated by an increase in activity. Responses recorded simultaneously by means of electrodes in peripheral structures showed enhanced activity with no evidence of inhibitory effects. This suggests that in the olfactory bulb of the intact, unanaesthetised rabbit spike activity in response to odor can be modulated by inhibitory mechanisms. (Supported by USPHS grant B1083(C5)).

SLOW WAVE AND UNIT ACTIVITY EVOKED BY SOUNDS FROM COCHLEAR NUCLEUS OF UNANESTHETIZED CAT. George Moushegian,* Allen Rupert,* and Robert Galambos. Walter Reed Army Institute of Research, Washington, D.C.

Electrical activity recorded with tungsten microelectrodes advanced through cerebellum and brain stem to cochlear nucleus of unanesthetized cat shows 'slow wave' and single unit responses to various sounds. A click stimulus produces characteristic slow wave responses at the tip of an electrode lying near to or within the cochlear nucleus, and the actual anatomical locus of the tip can be reliably predicted from close examination of the latency and wave shape of these responses. Response areas for single units like those previously described in anesthetized preparations occur in both dorsal and ventral cochlear nuclei. Furthermore, in both nuclei, tones suppress spontaneously active units, and units driven by one tone can be suppressed by a second tone sounded simultaneously. If significant differences exist in cochlear nucleus activity recordable from anesthetized and unanesthetized preparations, these have thus far eluded the analysis.

EFFECTS OF INTRA-ARTERIAL CONTRAST MEDIUM ON KIDNEY FUNCTION. Thomas F. Mullady,* Khalil G. Wakim, James C. Hunt* and Owings W. Kincaid.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

After control values for kidney function tests were established in trained dogs the bladder trigone was exteriorized aseptically and the renal clearances of para-aminohippuric acid (PAH) and creatinine, and the volume, specific gravity, osmolality and sodium content in the urine of each kidney individually were determined before and at specified intervals for several weeks after 10 ml. of 50 per cent hypaque were injected directly into the left renal artery. Immediately following the arterial administration of hypaque a radiogram was taken of the kidney. At the end of the study both kidneys were removed for histologic examination. Exteriorization of the bladder trigone induced no significant change in kidney function tests. The kidney receiving the hypaque showed reduction in the clearances of PAH and creatinine and in urine volume but an increased concentration of urinary sodium. However, the total sodium excreted by the injected kidney was less and the specific gravity and osmolality were greater than those of the contralateral noninjected kidney.

LOCALIZATION OF SOMATIC SENSORY FUNCTIONS IN CORPUS CALLOSUM. R. E. Myers, W. H. Niemann* and F. F. Ebner*. Johns Hopkins University School of Medicine, Baltimore, Maryland.

Transfer of training between the hands has been studied in normal and brain operated monkeys and chimpanzees. A high degree of cross-education occurs normally in animals of both species. Section of the forebrain commissures, however, prevents intermanual transfer of training. Partial commissure section may or may not interfere with transfer of training depending on the portions allowed to remain intact. Preservation of that portion interconnecting predominantly the precentral cortical regions supports near complete transfer of latch box solving while it will maintain only very incomplete tactual discrimination transfer. Preservation of that portion of the commissure interconnecting predominantly the parietal regions sustains high level tactual discrimination learning transfer while it brings about only a partial transfer of latch box training. Tactual or tactuokinesthetic learning functions were not sustained by the anterior body, genu, rostrum, anterior commissure, or splenium either separately or in combination. (Aided by U.S. Public Health Service grant #B-2627.)

LOCALIZATION OF THERMALLY-SENSITIVE NEURONS IN THE ANTERIOR HYPOTHALAMUS OF URETHANIZED CATS. T. Nakayama and J. S. Eisenman (intr. by H. T. Hammel). Department of Physiology, University of Pennsylvania, Philadelphia, Pa.

During investigation of the responses of single neurones in the anterior hypothalamus to local heating and cooling, selected areas containing heat sensitive neurons were marked for histological localization. The Prussian Blue marking technique of Hess and of Marshall was used. A current of 10-30 microamps was passed through the steel recording microelectrode, causing the electrolytic deposition of iron from the tip. The cats were sacrificed by perfusion with saline-acacia solution, followed by formalin-acacia. During this perfusion 10-20 cc of saturated potassium ferrocyanide was injected through the perfusion cannula. Frozen sections 100 micra thick were made, stained with neutral red, and permanently mounted for study. The correct position of the recording tip was determined by comparing the sections with the stereotaxic atlases of Jasper and Ajmone-Marsan and of Bleier. Coordinates given are those of Jasper and Ajmone-Marsan. Neurons responding to heating were found in the anterior hypothalamic and preoptic areas from Fr. 14.5 to Fr. 17.0. The dorso-ventral range was from H. -1.0, in the horizontal plane of the anterior commissure, to H. -4.0, very close to the lower border of the preoptic area. 50% of the marking spots were within 0.5 mm. of the midline, although heat sensitive units were found as far lateral as 2.5 mm. Many of the rostro-medial neurons were located in the nucleus of the diagonal band of Broca. Exploration in the posterior hypothalamus revealed no thermally sensitive neurons.

NATURE OF THE NEGATIVE AFTER-POTENTIAL INCREASED BY THE INSECTICIDE ALLETHRIN IN COCKROACH GIANT AXONS. Toshio Narahashi (intr. by Julian M. Tobias). Lab. of Appl. Entomology, Univ. of Tokyo, Tokyo, Japan.

The insecticide allethrin is a synthesized derivative of pyrethrins. It was found that this insecticide caused the negative after-potential (NAP) to increase when low concentrations ($1-3 \times 10^{-7}$) were used, but in higher concentrations ($>10^{-6}$) it brought about immediate conduction block. In the allethrin-treated axons, the time constant of decay of the NAP was much longer than the membrane time constant. Upon repetitive stimuli, there appeared a remarkable addition of the NAP's. These observations imply that the NAP increased by allethrin is produced by an accumulation of some depolarizing substance inside or outside of the axon membrane, and that the substance is removed slowly. However, the possibility of potassium being the depolarizing substance has been excluded by the fact that the membrane potential during the increased NAP does not behave in response to stimulation as it does in K-rich solutions. Allethrin caused little or no change in the voltage-current relation, suggesting that the K conductance rise normally accelerating the falling phase of the spike was not affected. The augmented and prolonged NAP, or the delayed repolarizing phase seen after the spike, could be produced after a large and prolonged depolarization in the axons rendered inexcitable by the removal of Na from the external medium. It seems, therefore, that the NAP is not related to the entry of Na across the membrane, and that the depolarizing substance in question is accumulated not only by a spike potential but also by a large and sustained depolarization. Further, temperature had a remarkable effect on the NAP increased by allethrin, a rise of temperature causing it to increase in height and to shorten in duration. This naturally leads to the supposition that certain metabolic processes are essential for the elimination of the depolarizing substance.

Nonradioactive Sodium Space: Importance and Interpretation

William A. Neely, M. D. and M. D. Turner, Ph. D.

Interpretation of various sodium spaces has not been clear in the past. There is renewed interest concerning the role of sodium deficits in the etiology of shock in certain types of surgical patients. Prompt and accurate correction of such deficits can prove lifesaving. Most current schemes for correction are based upon estimated ECF volume, but the present study casts doubt upon their validity. Sodium chloride (2 mg./Kg. body weight) was injected (IV) into 23 dogs whose urinary output was continuously returned intravenously. Measurements of non-radioactive sodium space (amount injected ÷ change in serum sodium concentration), radioactive sodium (Na^{24}) space before and after the sodium chloride infusion, and D_2O space were made on each animal. All spaces were corrected to a standard 12-Kg. animal. The mean nonradioactive sodium space was found to be 8.16 ± 1.49 liters whereas the D_2O space was 7.69 ± 0.51 liters. The difference between the two spaces was not significant. Thus these findings again indicate that cells do behave as accurate osmometers and that most fluid shifts can be explained by assuming water transfer without net sodium transfer across the cell membrane.

Departments of Surgery and Biochemistry, University of Mississippi Medical Center, Jackson, Mississippi.

This research is supported in part by Army Grant No. DA 49-007-MD-627 and Grant No. RG 7181 of the National Institutes of Health.

HUMAN RESPIRATORY COMPENSATION IN METABOLIC ALKALOSIS. Louis R. Nelson, Albert Munson, Michael P. Naeve, Marvin Harrah, and Bryan Bomberg (intr. by John L. Chapin). Physiology Dept., Univ. of Colo. School of Medicine, and National Jewish Hospital, Denver, Colorado.

Various experimenters at sea level have published data indicating that respiratory compensation does not occur in either acute or chronic alkalosis. This experiment was undertaken to ascertain if this data holds for people living in Denver, which is 5,280 feet above sea level. In the experiment endtidal P_{CO_2} , total venous CO_2 , and venous pH were measured on 6 normal adult subjects in a resting state, and also 1½ and 3 hours after ingestion of 24 to 34 grams of sodium bicarbonate. Venous pH was measured on a Cambridge research model pH meter with anaerobic glass electrode water-jacketed at 37.5°C. Whole blood buffer base (WBBB) was calculated for each sample using the Hastings-Singer nomogram. Whole blood buffer base was assumed to remain constant from venous to arterial side. Regression analysis was carried out on pooled data. Results showed a rise of 0.6 mm Hg P_{CO_2} per mEq./liter WBBB. Arterial pH rose 66% of that rise which would be expected if no compensation had occurred. Since the probability that slope was actually zero was less than 0.01, it can be said with reasonable certainty that respiratory compensation does occur for people living in Denver when WBBB is elevated by ingesting sodium bicarbonate. These results suggest that the altered physiology of residents at high altitude may predispose to a greater respiratory compensation to acute metabolic alkalosis than is evidenced at sea level. These alterations might include lower total CO_2 , increased hypoxic drive to respiration and an increased threshold and sensitivity to P_{CO_2} .

TISSUE UPTAKE OF INJECTED VITAMIN K_1 IN RATS. T.E. Nelson, Jr. and Marines Perez (intr. by R. W. Whitehead). Department of Pharmacology, School of Medicine, San Juan 22, Puerto Rico.

Vitamin K_1 injected intravenously accumulates primarily in liver and spleen in rats according to Dam et al., Acta pharmacol. et toxicol. 10, 1954, and Taylor et al., Can. J. Biochem. Physiol. 35, 1957. Dam and associates suggest that the reticulo-endothelial system (R.E.S.) may be involved in this process. We have confirmed their observations. Uptake of vitamin K_1 (Hephyton, courteously supplied by Mr. Monserrat, Merck, Sharp and Dohme) by rat liver and spleen occurs within 3 hours of injection. The concentration of vitamin K_1 in liver is about twice that in spleen. Concentration in other tissues assayed were negligible. Block of the R.E.S., attempted by pre-treating animals with thorotrast, causes some reduction of uptake by liver. However, uptake by spleen increases by a factor of 2 to 5. The rate of disappearance of K_1 from blood is decreased to one tenth in thorotrast-treated animals. Exposure to carbon tetrachloride vapor appears to stimulate rather than depress both liver and spleen uptake of vitamin K_1 . It may be concluded that although the R.E.S. may be involved in the removal of vitamin K_1 from the blood, it is doubtful that it plays a primary role in its selective accumulation by tissues.
(Supported by Grant H3552 USPHS-NIH).

ONE-TRIAL CARDIAC CONDITIONING IN DOGS. Joseph E.O. Newton, Fred Royer,* James Whitman,* and W. Horsley Gantt. VA Hosp., Perry Point, Md.; and Johns Hopkins Univ., Baltimore.

Acceleration of heart rate to a conditional stimulus, a well-known phenomenon, is considered a learned emotional response. There has been a question as to whether one-trial conditioning exists, various claims having been made that each species has some response which can be the basis for conditioning in one trial. However, demonstrations of this are rare and perhaps unconvincing. This study was designed to test whether the heart rate acceleration accompanying one electric shock could become a conditional response. In 3 dogs trained to sit quietly on a stand in an isolated room, with many previous applications of a soft tone, one particular time the tone was followed by a shock of 25-100 volts to the foreleg. Thereafter the tone was repeated many times without the shock. EKG and respiration were recorded. RESULTS: Dogs showed no average heart rate increase to the tone before conditioning. There was 10-20 beats/min average acceleration in 10-30 trials subsequent to reinforcement. No specific motor CR's developed in as many as 30 trials. CONCLUSIONS: One-trial conditioning to such emotional stimuli as electric shock is manifested in dogs by tachycardia despite absence of specific motor components. This is further evidence for the concept of schizokinesis and for the value of cardiac measures of emotionality in dogs.

STOP-FLOW LOCALIZATION OF THE RENAL SITE OF ACTION OF PARATHYROID HORMONE. T. Frederick Nicholson. Univ. of Toronto, Toronto, Canada.

The finding that U/Pp(phosphate): U/Pcr(eatinine) ratios were greater in proximal stop-flow samples obtained twenty minutes after parathyroid extract injection than in analogous samples from the same kidney immediately before P.T.E. injection has been taken as evidence that parathyroid hormone inhibits proximal tubular reabsorption of phosphate (Samy et al., Endocrinology, 67:266, 1960). As it seemed possible that the first stop-flow might affect tubular function during the second stop-flow, the U/Pp: U/Pcr ratios in samples obtained from pairs of stop-flow periods done twenty to forty minutes apart, with no intervening injection of parathyroid extract, were determined. The U/Pp: U/Pcr ratios in the proximal samples from the second stop-flow were definitely higher than those in similar samples in the first stop-flow. Further the U/Pp: U/Pcr ratios in proximal stop-flow samples obtained twenty to forty minutes after the injection of P.T.E. in animals on which no previous stop-flow experiment had been done, were as low as those obtained when no P.T.E. was given. Phosphate practically disappeared from some of these samples. It appears that the preliminary stop-flow can itself inhibit phosphate reabsorption in subsequent stop-flows and that P.T.H. does not inhibit proximal reabsorption of phosphate.

(Supported in part by a grant from the National Research Council of Canada).

Effect of Epinephrine and Norepinephrine on Gastric Secretion and Blood Flow. D. M. Nicoloff*, E. T. Peter*, A. S. Leonard*, H. Sosin*, and O. H. Wangersteen (intr. by N. S. R. Maluf). Dept. of Surgery, Univ. of Minn. Medical School, Minneapolis 14, Minnesota.

The etiology of stress ulcers remains obscure. During stress epinephrine is released from the adrenal and norepinephrine from peripheral nerve endings. The effect of these substances on gastric secretion has been examined by various investigators with controversial results. Dogs with Heidenhain pouches were fed a standard meal and secretions collected for 3 hours. During this time they received 0.25, 0.5, 1.0, and 1.5 $\mu\text{gm}/\text{kilo}/\text{min.}$ of epinephrine or norepinephrine I. V. In another group of dogs the effect of these drugs on gastric blood flow was determined by (1) electromagnetic flowmeter (large vessel flow) and (2) injection of india ink particles into the celiac artery (capillary flow) when 0.5 or 1.0 $\mu\text{gm}/\text{kilo}/\text{min.}$ of epinephrine and norepinephrine were administered I. V. With administration of epinephrine and norepinephrine secretions from the Heidenhain pouch decreased in volume and free acid. Epinephrine had an inconsistent effect on flow in the large vessels; norepinephrine consistently gave a decrease. Mucosal flow reflected by the injection of india ink particles was consistently decreased but to a lesser extent with norepinephrine.

THE EFFECT OF FORWARD (+G_x) ACCELERATION ON ARTERIAL OXYGEN SATURATION. A. Clark Nolan*, Hiram W. Marshall*, Lucille Cronin* and Earl H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Arterial oxygen saturation was monitored by ear oximetry and in blood withdrawn continuously from the radial artery during 3 minutes at 2, 3½, 5 and sometimes 6 G in six subjects. Observations were made during the breathing of: air, 99.6% oxygen, air with a positive pressure of 40 mm. Hg, and air during hyperventilation. Thoracic roentgenograms were made before and 30 to 50 seconds after the 5 G accelerations. Pressures were recorded in the aorta, radial artery, right atrium, esophagus and rectum (intra-abdominal). During the breathing of air there was a progressive decrease in arterial oxygen saturation with increasing levels of G, beginning approximately 30 seconds after the onset of exposure, which at 5 G attained at stable level averaging 87.3% about 80 seconds later. When acceleration ceased, a return toward control value occurred over approximately 70 seconds; however, at 5 G this return often was incomplete, being up to 3% saturation lower than control. When 99.6% oxygen was breathed, this decrease was prevented, or its onset was delayed, and the magnitude of desaturation was much less, 95.5% being the lowest figure obtained at 5 G. A progressive increase in right atrial pressure occurred with increasing G, reaching a mean of 32 mm. Hg (3 times control) at 5 G. Esophageal pressure similarly increased, but to a lesser mean of 19 mm. Hg (control 0 mm. Hg) at 5 G. It is postulated that the oxygen desaturation is due to blood flow past atelectatic alveoli in dependent portions of the lungs, atelectasis resulting from increased segmental blood volume and pressure due to hydrostatic effects, plus an apparent increase in intrathoracic pressure. Atelectasis in the lower lung fields was demonstrable roentgenographically after exposures to 5 G.

EFFECT OF SODIUM CYANIDE ON CARDIAC OUTPUT. Bengt Öberg^{*}, Travis Q. Richardson^{*}, and Arthur C. Guyton. Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

In order to evaluate the effects of histotoxic anoxia on cardiac output, a series of experiments were performed on dogs receiving infusions of sodium cyanide. Cardiac output, mean arterial blood pressure, and right atrial pressure were recorded continuously. Some dogs were rendered areflexic by spinal anesthesia and by cutting the vagus nerves; others were left with intact cardiovascular reflexes. The results obtained were quite similar in the two groups. With increasing infusion rates of cyanide, the cardiac output increased to an average maximum of 150% above the resting value. Simultaneously the arterial blood pressure decreased, which implied a pronounced decrease of the peripheral resistance. If the cyanide infusion was maintained or increased when the maximum values for cardiac output were reached, the cardiac output fell and the right atrial pressure rose, implying a developing heart failure. The mechanism by which cyanide causes an increased cardiac output is most likely a peripheral one in which cyanide induced tissue anoxia causes peripheral vasodilatation which in turn favors venous return to the heart.

DISTENSIBILITY CHANGES OF THE ISOLATED LEFT VENTRICLE AS MEASURED BY PRESSURE VOLUME CURVES. Larry J. O'Brien, Civil Aeromedical Research Institute, Oklahoma City, Oklahoma.

Pressure-volume measurements were made on the isolated left ventricle of cats and rabbits. Hearts were excised and a large, multi-holed, wedge-shaped cannula was placed in the left ventricle via the aorta. The mitral orifice was occluded by a ligature placed tightly around the left atrium as near the mitral valve as possible. The heart was then suspended in a saline bath at room temperature. In some experiments, graded volumes were injected into the left ventricle from a microburette; in others, a pump was used for infusion and withdrawal. The hydrostatic level of the saline bath was maintained constant throughout the experiment. Pressure-volume measurements were made within 10 to 20 minutes after isolation of the heart and periodically during the next several hours. When fluid was withdrawn from the ventricle, a subatmospheric pressure was produced which tended to return slowly toward atmospheric pressure even though no fluid was allowed to re-enter the ventricle. Upon subsequent addition of fluid, the pressure became positive. The hearts became progressively less distensible as the experiments progressed; hysteresis curves became steeper and were displaced to the left. This was partially reversed when the ventricle was forcibly stretched with a volume similar to that infused at the beginning of the experiment. The decrease in distensibility is presumably due to shortening of muscle fibers since there was a decrease in ventricular volume at any given pressure. The dissipation of the subatmospheric pressure in the empty heart may be interpreted to be the result of stress relaxation.

AXOPLASMIC FLOW IN SPINAL CORD VENTRAL ROOTS. S. Ochs and D. Dalrymple*. Department of Physiology, Indiana University School of Medicine, Indianapolis.

Injections of small volumes of P^{32} into the L7 and S1 spinal cord segments were made 3 days before taking ventral roots for sampling of their content of P^{32} . A slotted shield was placed under a Geiger counter and small parts of the roots sampled at 3 mm increments along their lengths. An outflow of P^{32} was indicated by the uniform decrease of P^{32} with increased distances from the cord. When small volumes of 2 to 10% sodium cyanide (CN) were injected into the lumbar region, cell bodies in the region injected, including motoneurons, were destroyed. CN was injected on one side and Ringer's on the other. A decrease in outflow of P^{32} on the CN injected side was found. A decreased outflow of P^{32} was also found after pressure ischemias of the cord produced one week before P^{32} injection. After such ischemias (30 to 45 minutes) most of the motoneurons are destroyed. A corresponding decrease of P^{32} outflow was found. These results supported the idea that P^{32} is taken up by the motoneuron before it moves outward inside the ventral root fibers. The effect of CN on the cell bodies in the cord appeared to be all-or-none as indicated by the unchanged rate of efflux in axons of those cells outside the region reached by CN injection. With longer periods of pressure asphyxiation a decrease in the rate of output was found. Cats injected with Dial were maintained at low body temperatures (av. 29°C.). In these animals a decreased rate of efflux of P^{32} was found. The evidence of this and previous work indicates that outflow occurs inside the ventral root axons. The mechanism of efflux is as yet not understood. Supported by NSF GL3192.

CONCENTRATION GRADIENT IN RENAL TISSUE AFTER INFUSION OF 4% UREA. R. M. O'Dell and J. Cuellar*. Div. of Urology, Dept. of Surgery, Tulane University Medical School, New Orleans, La.

It has been shown that urea in concentrations of 200-700 mM has a bacteriostatic effect in culture on the bacteria associated with pyelonephritis. It has also been found that a loss of concentrating ability accompanies this disease. In association with these findings, we wished to determine the possible concentration of urea that could be established in a kidney by infusion. After 24 hours of dehydration, dogs were anesthetized and catheters placed in each ureter. One kidney was removed after collection of the urine sample and the tissue analyzed for urea concentration gradient. In this manner each animal served as its own control. The dog was then infused with 4% urea in 5% dextrose and water at approximately 10 drops /min for a period of two hours. The remaining kidney was removed and the tissue analyzed for urea. The dehydrated kidney had the expected gradient from cortex to papilla with urine concentrations of urea fairly close to those of the papilla. In the kidney after urea infusion, the gradient was lower than the control kidney, but still above the minimum bacteriostatic level of 200 mM. Infusion of 5% dextrose and water alone resulted in the abolishment of a urea gradient.

THE RELATIONSHIP OF CELLULAR HYDRATION TO OXYGEN UPTAKE IN RABBIT ERYTHROCYTES. Edwin G. Olmstead (intr. by H.E. Ederstrom).

Physiology Dept., Univ. of No. Dakota, Grand Forks, N.D.

Previous studies have suggested that oxygen uptake in nucleated and non-nucleated mammalian cells may be affected by changes in cellular hydration. In the present study oxygenated rabbit erythrocytes were suspended in buffered NaCl pH 7.4, 300 mos. with 100 mgm % glucose and 10^{-5} methylene blue at 37°C. and oxygen uptake was measured by the Warburg technique. Intracellular water content was varied by increasing or decreasing the osmolarity of the extracellular solution. The rate of oxygen uptake was not significantly altered by cellular over-hydration but was significantly decreased by cellular dehydration. This decrease was temperature dependent being most marked at 42°C. and least marked at 32°C. within the temperature ranges studied. Total oxygen uptake was greatest with cellular overhydration at 32°C. and least with cellular dehydration at 42°C. It was concluded that although the concentrations of intracellular reactants and substrate are increased in cellular dehydration, an increased reaction rate as monitored by oxygen uptake does not occur as would be expected in an ordered chemical reaction but that, paradoxically, a decreased reaction rate follows. (Supported by a Grant from the North Dakota Heart Association)

EFFECT OF INTRAVENOUS ESTROGEN PREMARIN ® ON PULMONARY DIFFUSION CAPACITY. Louis J. Pecora, Louis R. Putnam* and Gerald L. Baum*. Veterans Administration Hospital, Cincinnati, Ohio.

Evidence indicates that Premarin ® increases the consistency of the ground substance surrounding the walls of the capillaries to a firmer gel state and also increases the length of the acid mucopolysaccharide molecules of the ground substance. These reactions suggest that the diffusion capacity might be reduced because of the thickened consistency of the capillary wall. The single breath CO diffusion method was used to study 9 male and 3 female normal subjects 20-30 years of age. Nine were given 40 mg., two 20 mg. and one 60 mg. of Premarin ® I. V.. A basal DLCO was made 24 hours before the test, one on the day of the test before injection and one 15 min., 2 hours, 24 hours and 48 hours after the injection. The mean values for 9 subjects who showed a decrease in DLCO were:

M & F Subjects	DLCO Pre-inject.	15 Min.	45 Min.	2 Hrs.	24 Hrs.
9	42.7	40.5	37.7	38.3	38.7

Three male subjects given 20, 40 and 60 mg. respectively showed no change from the basal level. The results obtained thus far indicate that Premarin ® I. V. might decrease the pulmonary diffusion capacity.

The Effect of Pitressin on Portal Hemodynamics. E. T. Peter,
D. M. Nicoloff, A. S. Leonard, and N. H. Stone (intr. by O. H. Wan-
gensteen). Dept. of Surgery, Univ. of Minn. Med. School, Minnea-
polis 14, Minnesota.

Since the first use of pituitrin for the control of bleeding esopha-
geal varices by Kehne, Hughes, and Gompertz in 1956, there has
been considerable interest in the effect of pituitrin on portal hemody-
namics. The portal hypotensive effect of pituitrin has previously been
reported by Bainbridge & Trevor, Clark, McMichaels, and others.
It is the purpose of this study to further elucidate the flow, pressure
and resistance changes in the portal system during pitressin adminis-
tration. Blood flow was measured in the portal vein, hepatic artery,
mesenteric artery, and epiploic arteries of dogs by means of a non-
cannulating gated sine wave electromagnetic flowmeter. Aortic and
portal pressures were also monitored. After obtaining control flows
and pressures, pitressin was administered intravenously at the rate
of .01 pressor units/kg/min. Following the administration of pitres-
sin, there was a 67.8% reduction of flow in the mesenteric artery.
Flow in the portal vein was reduced 47.8% while flow in the hepatic
artery remained essentially unchanged. Portal pressure was reduced
on an average of 49%. It is concluded that the flow and pressure re-
duction in the portal vein is the result of increased capillary and ar-
teriolar vascular resistance and decreased flow in the splanchnic bed.

INTESTINAL BLOOD VOLUME MEASUREMENTS IN INTACT UNANESTHETIZED DOGS.
G. Pinardi*, R. J. Adolph* and R. F. Rushmer. Dept. of Physiology &
Biophysics, Univ. of Washington School of Medicine, Seattle, Wash.

Measurements of the blood volume changes of the splanchnic bed are
important to an understanding of its reservoir function. Since such
measurements in intact unanesthetized animals have not previously been
reported, the present study was undertaken to elucidate the normal res-
ervoir function of the splanchnic vessels. A segment of the small in-
testine, including its blood supply, was enclosed in a plastic plethys-
mograph, without interruption of the continuity of the blood vessels
or the intestinal lumen. A loop of bowel was folded into the plastic
box so that both ends of the loop and its blood supply entered through
a single orifice. After about one week functional sealing of the or-
ifice occurred without evidence of intestinal obstruction or interfer-
ence with the blood supply. Volume changes within the plethysmograph
were measured using a float recorder registered by a photo-electric
cell. Epinephrine (1 $\mu\text{g/kg}$) injected intravenously caused a reduction
in the recorded volume. Acetylcholine (15 $\mu\text{g/kg}$) given intravenously
caused a variable increase in the volume. (Aided by the Cardiovascular
Training Grant (H755117) from the National Heart Institute.)

OBESITY IN THE ABSENCE OF ABSOLUTE HYPERPHAGIA IN HYPOTHALAMIC MONKEYS. A PRELIMINARY STUDY. L. J. Poirier, A. M. Mouren-Mathieu and C. L. Richer (intr. by E. Pagé). Département d'Histologie, Université de Montréal

Various data concerning body weight, locomotor activity, water and food intakes, body temperature, blood pressure and metabolic and hormonal determinations were recorded during periods of controlled and ad libitum feeding in a series of eleven monkeys including three sham-operated animals before and after the placement of lesions in the hypothalamus. Three of these animals developed obesity on a restricted diet which did not produce any significant change of weight in the controls. Only one of these obese monkeys showed an increased appetite when fed ad libitum. The same three animals showed a lowered body temperature and two of them a markedly decreased locomotor activity, one of which also had a marked fasting glycosuria and increased nitrogen excretion. One non-obese monkey became markedly hyperactive and developed a voracious appetite without any significant weight increase. Three other obese monkeys obtained in previous experiments and not as extensively studied showed also a lowered body temperature associated in one of them with marked glycosuria and increased nitrogen excretion. A decreased locomotor activity and a depressed calorogenic production possibly associated with neuroendocrine disturbances appear to be more important factors than absolute hyperphagia in the appearance of obesity following hypothalamic lesions which exclude the ventromedial hypothalamic nuclei in the monkey. (Aided by grants from National Health Grants and the Medical Research Council of Canada).

AIRWAY RESISTANCE IN NEWBORN. G. Polgar (intr. by H. Montgomery) Dept. of Physiology, Grad. School of Med., Univ. of Pa., Phila., Pa.

Adapting the plethysmographic method of DuBois et al. the resistance of the airways to the flow of air and the lung gas volume were measured in 15 newborn infants. Their average age was 3 days (range: 1/2-17) and their average weight was 3250 g (range: 1980-4450). Four of them were premature, without respiratory or other complications. The mean airway resistance of all subjects was 18.1 cm H₂O/L/sec (SE: + 6.26). The mean lung volume at which the resistance was measured was 0.195 L (SE: + 0.066); the mean lung volume at end-expiration was 0.157 L (SE: + 0.057). The latter value gives an approximate ratio of 0.050 L lung volume/kg body weight, which is higher than reported by others for infants. There was linear correlation between the lung volume and the reciprocal of airway resistance, i.e. conductance. The regression of mean conductance on mean volume for 15 individuals was; conductance in L/sec/cm H₂O = 0.01 + 0.275 x volume in L. The same relationship for all 112 measurements was; conductance = 0.0102 + 0.291 x volume. According to Briscoe and DuBois in healthy subjects from 4 to 87 years of age, with lung volume from 0.93 to 5.78 L, the relationship approximated; conductance = 0.2 x volume in L. About one half of all present values of conductance were greater than their upper limit of normal conductance as related to lung volume. This suggests that the ratio, effective cross section area of the resistant airways/total lung volume, is larger in newborn than in older children or adults. Individual variations of regression may be related to variable distensibility of the airways.

FOREARM METABOLISM IN OBESITY AND ITS RESPONSE TO INSULIN.
D. Rabinowitz* and K. L. Zierler. Dept. Med., Johns
Hopkins Univ. and Hosp., Baltimore, Md.

The question of whether or not there is a metabolic defect fundamental to obesity was investigated by assessing metabolism of forearm muscle and adipose tissue in six young men and women, 20% overweight but otherwise healthy. Measurements of arterial and deep venous concentrations and of forearm blood flow suggest that, in the basal state, obese subjects have hyperinsulinism evidenced by increased potassium and glucose uptake by muscle and, equivocally, by decreased FFA release from adipose tissue. Despite evidence of endogenous hyperinsulinism in obesity, the response of the obese forearm to intra-arterial insulin (constant infusion of 10^{-4} units/kg·min for 26 minutes) was less than normal, suggesting that a standard dose of exogenous insulin was diluted by a large endogenous pool in obese subjects. Hyperinsulinism in obese subjects probably represents one of the adjustments to overeating and facilitates storage of fat and carbohydrate. For example, although muscle takes up more glucose than normal, it produces less lactate and consumes oxygen at a normal rate. R.Q. of forearm muscle in obesity is 0.7, as in normal muscle, compatible with oxidation of lipid, so that there is no quantitative defect in lipid oxidation at rest.

(Supported by ONR, MDAA INC. and NIAMD (A-750))

DEPRESSION OF DISCRIMINATION AS BASIS OF PAIN RELIEF FOLLOWING LEUKOTOMY. M. Rafiullah* & G. Austin. Division of Neurosurgery, University of Oregon Medical School, Portland, Oregon.

Multiple discrimination tests were done pre and postoperatively on patients undergoing chemical leukotomy or cordotomy for relief of intractable pain. Control studies were done on 4 patients having right temporal lobectomy for psychomotor seizures. Discrimination tests included tactile (von Frey hairs), pain (algometer), electric pulse duration (at constant 2MA current), and time discrimination (interval between two clicks). Following cordotomy only pain discrimination was depressed. Following right temporal lobectomy there was no consistent evidence of discrimination change. After chemical lobotomy, all discrimination curves were significantly depressed.

These tests suggest that a major factor in relief of intractable pain after frontal leukotomy is depression of sensory discrimination. The fact that time discrimination is also depressed may further alter conditioned patterns of pain.

ESTIMATION OF ARTERIAL AND VENOUS P_{CO_2} FROM FRACTIONAL ANALYSIS OF SINGLE BREATH. H. Rahn, T. S. Kim* and L. E. Farhi.

Dept. of Physiology, The Univ. of Buffalo, Buffalo, N. Y.

This method is based upon the O_2 and CO_2 analysis of several gas samples collected successively during a single expiration of 7 - 10 seconds. During this period the CO_2 rises and the exchange ratio (R) falls rapidly.

Theory: (1) A decrease in blood CO_2 content, with no change in O_2 content ($R = \infty$) lowers the P_{CO_2} . An increase in O_2 content, with no change in CO_2 content ($R = 0$) increases the P_{CO_2} . When R is equal to 0.32, P_{CO_2} remains constant. (2) During expiration the alveolar P_{CO_2} increases, reducing the CO_2 output while the O_2 uptake remains unaffected. Thus R is directly related to CO_2 exchange, which in turn is governed by the venous-alveolar CO_2 tension difference. As long as the mixed venous P_{CO_2} remains unaltered, there must be a linear relationship between alveolar P_{CO_2} and R, provided the arterial O_2 content remains essentially constant.

Application: In each of the gas samples, P_{O_2} , P_{CO_2} and instantaneous R are determined. When R is plotted versus P_{CO_2} , a straight line is obtained as predicted. The true mixed venous P_{CO_2} can be read at an R value of 0.32, the arterial-alveolar P_{CO_2} at the appropriate R, and the "oxygenated venous blood" P_{CO_2} at an R of 0. Cardiac output determined by this method at rest and moderate exercise agree with those obtained by blood analysis methods.

EEG Changes during "Working Attentive Behavior" in Intact Cats and in Cats with Bilateral Caudate Lesions. L. Rakic*, E. J. Wyers* and N.A. Buchwald. Brain Research Institute, UCLA, U. Southern Calif., and U.S.V.A. Hospital, Long Beach.

Electrophysiological and behavioral studies were made in intact cats and in cats previously subjected to bilateral lesions in the heads of the caudate nuclei. For the first 2 or 3 weeks, p.o., the "caudate" cats showed an inability to learn the bar pressing task which normal cats accomplish in 2-3 days (c.f. Knott et al., 1960). Following this early period lever pressing ability was attained at a high rate. In both intact and "caudate" cats the resting EEG showed 10-13 c/s rhythms in the motor and occipital cortices with slower rhythms subcortically. In early training in intact cats, the motor cortex EEG desynchronized while a characteristic α -like rhythm appeared in the occipital cortex during attention or bar pressing for food. In the same training period the EEG of the entire cortex of "caudate" cats began to show the α -rhythm during attention and bar pressing, but this activity alternated with similar rhythms from the ventral anterior nucleus and from other subcortical structures. The intact cats were trained in a conditioned approach situation with secondary auditory reinforcement. They showed a sequence of rhythms in motor and visual cortex which will be compared with results of similar training in "caudate" cats.

RELATION of MEAN SKIN TEMPERATURE TO REGIONAL RECRUITMENT OF SWEATING. Randall, W.C. and R.O. Rawson, Department of Physiology, Stritch School of Medicine and the Graduate School of Loyola University, Chicago.

When a subject is exposed to a steadily rising ambient temperature (T_a), the onset of sweating in different skin regions occurs at widely varying local skin temperatures (T_s). It is clear therefore, that local T_s is not the determinant of the initial appearance of local sweating. Mean skin temperature (MTs) has frequently been related to the threshold for generalized body sweating, but Benzinger has pointed out that such a relationship may be more fortuitous than real (Fed.Proc. 19:Suppl. 5, 1960). Our conclusions concerning the functions of the cutaneous thermoreceptors are at variance with those of Benzinger, but it should be remembered that his experiments were carried out in stable environments while in ours, T_s was continuously changing. It is conceivable that thermoreceptors, like other receptors, may adapt under constant stimulation and thus leave hypothalamic temperature as the principle variable in the control of sweating.

Sweating begins on the lower extremity at considerably lower values for MTs than on the upper trunk, head, and arms. This pattern of recruitment generally remained consistent when only one half the body was exposed to a high T_a , even though the remaining half was maintained in a neutral or cool environment. In a few subjects who were rapidly heated the interval between the initial appearance of sweating on the lower extremity and that on the upper trunk and head was greatly reduced. The onset of sweating on the lower extremity, regardless of local T_s , and in the presence of rising, falling, or unchanging oral and tympanic membrane temperatures suggests an important relationship between the sequence of recruitment and MTs. The latter, in turn, implies an associated relationship with the level of afferent facilitation within CNS.

THE "GESELL PHENOMENON" AND BLOOD BRAIN BARRIER FUNCTION. S.I.Rapoport* and W.H.Marshall. Natl. Insts. of Health, Bethesda, Maryland

The phenomenon of the acid response of the CSF to i.v. injection of NaHCO_3 , in contrast to the alkaline response of the blood, was reported first by Gesell and Hertzman (Am. J. Physiol., 78: 610 (26)) in 1926. These authors used MnO_2 electrodes, placed in the fourth ventricle of the dog, to record pH continuously. It was suggested that restriction of HCO_3^- passage by the "cerebral membranes", but adequate CO_2 diffusion, explained this phenomenon. "Impaired impermeability" from a variety of causes resulted in an alkaline response of the CSF to i.v. NaHCO_3 .

Subsequent work by other authors, in which the Nims type of glass electrode was placed on the surface of the cat cerebral cortex, failed to confirm the "Gesell Phenomenon".

For our set of experiments, a capillary pH electrode of the Nims type was juxtaposed to the AgCl pore electrode (the reference electrode). Both were placed upon the undamaged pial surface of the cortex of ten nembutalized, curarized, artificially respired cats. The resistances of the pH electrodes were about 1000 megohms. A high impedance dynamic capacitor electrometer recorded voltage changes. Blood pH was monitored in some experiments.

Upon i.v. injection of .9N NaHCO_3 (1-3cc), the blood became alkaline and the cortex became acid within 8 seconds. This confirms the "Gesell Phenomenon" and points to its use as an indicator of blood brain barrier breakdown.

SOME DETERMINANTS OF CORONARY FLOW IN INTACT DOGS. C. R. Rayford,* A. Huvos,* E. M. Khouri* and D. E. Gregg Walter Reed Army Institute of Research, Washington 12, D. C.

The respective roles of central arterial blood pressure and peripheral coronary resistance in determining coronary blood flow under certain physiological conditions were studied in pre-operated, unanesthetized dogs. Phasic coronary flow was measured by electromagnetic flow meters implanted around the main left coronary artery or its circumflex branch. Phasic blood pressure was measured either through a chronically indwelling aortic catheter or a Gauer manometer inserted under local anesthesia at the time of the study. All studies were performed between 1 and 14 days following the implanting operation with dogs lying on a training board. 1. Tilting the dog in the head-down position resulted in an elevation of both systolic and diastolic blood pressures, accompanied by a slight increase in coronary flow. 2. Excitement, provoked by auditory and visual stimuli, produced blood pressure elevations equal to or less than those resulting from tilting but coronary flow increased markedly both during systole and diastole, with or without an acceleration of the heart rate. 3. Intravenous injection of 3 to 6 micrograms of epinephrine produced no change in blood pressure or heart rate, whereas coronary flow increased markedly. 4. Temporary occlusion (for about 10 seconds) of the coronary flow was followed by a very marked increase of both systolic and diastolic flow in the absence of significant changes in blood pressure or heart rate. It is concluded that, in the last three situations, peripheral mechanisms are more important in controlling coronary blood flow than is the arterial blood pressure.

ISOLATED BRAIN AND ACTH RELEASE IN CATS. E.S. Redgate, S. Yoshida* and M. de la Lastra*. Western Reserve Univ. Medical School, Cleveland, Ohio

The concept that rapid release of ACTH is under control of neural structures located in the hypothalamus has been tested by several investigators in experiments involving lesions and stimulations in preparations with intact central nervous systems. One of the problems involved in the interpretation of the results of these experiments is that direct effects of the lesion or stimulation be distinguished from indirect effects. To overcome this difficulty experiments have been carried out in cats 90 minutes after C₁ cord section, carotid sinus denervation and high cervical vago-sympathetic nerve section. Adenohypophyseal ACTH release has been estimated by collecting jugular vein blood samples from which ACTH is extracted by resin chromatography and assayed in hypophysectomized rats by the adrenal ascorbic acid depletion method. This method of ACTH assay in a standardized preparation (the hypophysectomized rat) avoided the problem of alteration in sensitivity of the adrenal of the assay animal during the course of an experiment involving extensive surgery. Blood pressure was recorded and maintained constant during the experimental procedures by injecting defibrinated donor cat blood. EEG activity and cortical evoked potentials were monitored. Our results indicate: 1) that ACTH output in the partially isolated brain in absence of inhibitory input from baroreceptors is not maximal; 2) stimulation through an electrode near the central tegmental tract in the midbrain reticular formation elicits an elevation of jugular vein blood ACTH levels; 3) stimulation under the same conditions in the pes pedunculus does not elicit elevation in jugular vein blood ACTH. (Supported by NIH Grant B-3238 and U.S.A.F. Contract 49 (638) 443.)

EFFECT OF POSITION AND THORACOTOMY ON DISTRIBUTION OF AIR AND BLOOD TO EACH LUNG DURING INTERMITTENT POSITIVE PRESSURE BREATHING. Kai Rehder,^{*} Richard A. Theye^{*} and Ward S. Fowler. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The distribution of tidal air and blood flow to each lung and the CO_2 elimination from each lung during intermittent positive pressure breathing were studied in 10 anesthetized and paralyzed dogs. Ventilation via a divided tracheal airway (Wright-Lategola) at a constant rate and constant volume ($\pm 5\%$) with 65% oxygen in nitrogen was provided by a Bird ventilator. \dot{V}_{O_2} , \dot{V}_{CO_2} , blood flow (nonshunted) and tidal

volume of each lung and P_{aCO_2} were measured. In the supine position

the mean percentages of the total tidal volume and blood flow distributed to the right lung were 57 and 58% respectively. These values were 51 and 61% respectively in the right lateral decubitus and were 37 and 55% respectively after left thoracotomy in this position. In the left lateral decubitus these values were 67 and 55% and after right thoracotomy, 82 and 70%. The mean percentage of the total CO_2 elimination from the right lung was 59% in the supine position, 52% in the right lateral position and 41% after thoracotomy in this position. In the left lateral decubitus this value was 68%, and 88% after thoracotomy in this position. In the supine position, the ventilation-perfusion ratios of both lungs were approximately equal. In the lateral decubitus position with and without thoracotomy the relative ventilation and ventilation-perfusion ratio of the upper (nondependent) lung increased. The increased carbon dioxide elimination of the upper lung compensated for the decreased carbon dioxide elimination of the dependent lung. (Supported by Research Grants # H-3588 and H-4881, U.S.P.H.S.)

ENZYMATIC FORMATION OF MONIODOTYROSINE BY LACTATING MAMMARY TISSUE.

E. P. Reineke, Department of Physiology and Pharmacology, Michigan State University, East Lansing, Michigan.

Lactating mammary tissue was incubated with I^{131} in either M 199 tissue culture medium or Ringer-phosphate-buffer at pH 7.4 and digested overnight with pancreatin at pH 8.0. Iodinated compounds were separated by paper chromatography (Collidine 125 ml: H_2O 44 ml), radioautographed, and the radioactive spots counted separately. Fifty-two % of the I^{131} was found combined in moniodotyrosine (MIT), 37% as iodide and 11% in diffuse form. Storage of mammary tissue at 7°C . for 6 days prior to iodination, as expected from earlier results (Am. J. Physiol. 199:829, 1960), caused a 3-fold increase in I^{131} accumulation, but the proportion of MIT formed was similar to that in fresh tissue. MIT formation was blocked by boiling, by thiouracil (0.04 mg/ml), and greatly reduced by KSCN (0.1 mg/ml). Tissue homogenates were separated into a water-soluble fraction and a mitochondrial fraction by centrifugation. Significant amounts of MIT were formed from tyrosine incubated aerobically with I^{131} in phosphate buffer alone. The soluble fraction from lactating mammary gland and parotid gland, but not from liver, readily catalyzed formation of additional free MIT from added tyrosine in the presence of Cu^{++} when incubated in phosphate buffer at pH 7.4 under aerobic conditions. MIT formation was enhanced slightly by Mn^{++} and was greatest with $\text{Cu}^{++} + \text{Mn}^{++}$. The mitochondrial fraction from lactating mammary tissue formed MIT without addition of a catalyst when incubated with I^{131} in Krebs-Ringer-phosphate buffer. All except a trace of the MIT in this system was in combined form until released by hydrolysis with pancreatin. The enzymatic nature of both the soluble and mitochondrial fractions is shown by their heat lability.

RIGHT ATRIAL PRESSURE AFTER CARDIAC FIBRILLATION AS AN INDICATOR OF MEAN CIRCULATORY PRESSURE. Travis Q. Richardson*, Bengt Öberg*, and Arthur C. Guyton (intr. by W. Lane Williams). Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

A simplified method for estimating the mean circulatory pressure has been developed in which this pressure is calculated from right atrial pressure measurements made after fibrillation of the heart. The mean circulatory pressure was determined in 10 mongrel dogs by fibrillating the heart and then pumping blood from the femoral artery into the femoral vein until the arterial and venous pressures equilibrated. Also in each of these animals the right atrial pressure was measured exactly 5 seconds following fibrillation of the heart (this time before pumping blood from the arteries to the veins). A definite correlation was found between this pressure and the mean circulatory pressure. The mean circulatory pressure was raised and lowered by rapidly infusing blood into the dog and rapidly removing blood. The measured mean circulatory pressures ranged from 4 mm Hg to 34 mm Hg, and the right atrial pressure measured 5 seconds after fibrillation ranged from 0 mm Hg to 30 mm Hg. Under the test conditions the mean circulatory pressure was $4 \text{ mm Hg} \pm 0.9 \text{ mm Hg}$ (standard deviation) higher than the corresponding right atrial pressure. Therefore, it is concluded that the mean circulatory pressure can be determined reasonably accurately by (1) fibrillating the heart, (2) measuring the right atrial pressure 5 seconds following fibrillation, and (3) adding 4 mm Hg to the pressure measured in the right atrium.

INTEGRATION OF DEGLUTITION AFTER VARIOUS TRANSECTIONS OF MEDULLA OBLONGATA. W. H. Richmond*, A. T. Storey* and R. W. Doty; Dept. of Physiology, University of Michigan, Ann Arbor, Michigan.

In decerebrate cats or dogs electromyograms from 6 or more muscle pairs were analyzed for symmetrical bilateral activity in swallowing evoked by stimulation of each superior laryngeal nerve (SLN). Transverse hemisections or longitudinal midline cuts were then made through the exposed fourth ventricle. Occasionally after midsagittal sections from aqueduct to C₁ unilateral swallowing could be obtained with preservation of temporal pattern of action in those muscles that continued to participate. With less drastic cuts it could be seen in the cat that action of the inferior constrictor was contralateral to SLN stimulation while other action was either ipsi- or bilateral. Full-depth midline sections in the region of the obex which preserved bilateral swallowing resulted in a cessation of respiration. Usually midline sections increased or decreased duration of swallowing activity in individual muscles and produced prominent changes in background activity; there was also a general disruption and diminished vigor of swallowing as length of the cut was extended. However, small midline regions, apparently at any level from C₁ to rostral medulla, can support bilateral coordination after all other cross connections have been cut. The pontine region does not appear to be critical, except, of course, for passage of fibers to trigeminal nuclei. Symmetry can be achieved by alternative pathways, either in upper cord, central or rostral medulla. Much of the evidence suggests that the swallowing "center" may be composed of multiple, widely distributed subunits. (Supported by USPHS Grants B-1068 and 2B-5252).

EFFECTS OF AMBIENT PRESSURE ON THE RATE OF COLLAPSE OF THE RAT'S LUNG. W. G. Robertson* and L. E. Farhi. Dept. of Physiology, The Univ. of Buffalo, Buffalo, N. Y.

The present study was undertaken to investigate the effect of ambient pressure on the rate of lung collapse (atelectasis) resulting from tracheal occlusion while breathing O_2 . Anesthetized rats were tracheotomized, cannulated, and placed in a specially constructed body plethysmograph. After 5 minutes of oxygen breathing the cannula was occluded at the end of a normal expiration. Changes in body volume were interpreted as changes in lung volume. Thirty-three experiments were conducted at ambient pressures varying from 190 to 1500 mm Hg. In each animal the rate of lung collapse (dv/dt) remained constant and was found to be inversely related to ambient pressure. This rate can be predicted accurately when alveolar CO_2 and water vapor are taken into account. At sea level dv/dt was 0.20 ml/sec/kgm. Time required for producing complete atelectasis was 26.6 sec at a pressure of 760 (sea level), 3.4 sec at a pressure of 190 mm Hg (equivalent to an altitude of 33,000 ft), and 63 sec at 1500 mm Hg (2 atmospheres).

PRESSURE/VOLUME RELATIONS IN ISOLATED ATELECTATIC RAT AND GUINEA PIG LUNGS AFTER IN VIVO AEROSOLATION WITH BRONCHODILATORS AND BRONCHOCONSTRICTORS AND AFTER DUST INHALATION. E. Robillard, Y. Alarie* and H. Stone*. Department of Physiology, University of Montreal.

Bronchoconstricting aerosols of carbachol, acetylcholine, serotonin and histamine and bronchodilating aerosols of isoproterenol, ephedrine, cyclopentamine, phenylephrine, diphenhydramine and cyproheptadine were breathed for various periods of time by rats and guinea pigs. The lungs were atelectatized and isolated and their static pressures were related to the volume of air injected into them according to the technique of Radford. The bronchoconstricting and bronchodilating effects were studied and related to the action of aluminum dust inhalation. Inhalation of aluminum fine particles was followed by dilation in the rat and by constriction in the guinea pig. Serotonin content increased in the guinea pig lung after aluminum dust inhalation. Supported by a grant from the Department of Health and Welfare, Ottawa, and from the "Ministère de la Santé, Québec".

EFFECTS OF DIETARY PROTEIN ON PHYSICAL PERFORMANCE CAPACITY IN MEN EXPOSED TO SEVERE COLD STRESS.

K. Rodahl, S. M. Horvath, N. Birkhead* and B. Issekutz, Jr.

Division of Research, Lankenau Hospital, Philadelphia 51, Pa.

The effect of 4 different diets (I: 3000 Calorie 70 g protein; II: 3000 Calorie 4 g protein; III: 1500 Calorie 70 g protein; IV: 1500 Calorie 4 g protein) on physical performance capacity (treadmill running at 7.5 mph and 8.6% grade) was studied in normal young men at ambient temperatures of 22°C and 8°C. At 22°C there was no difference between the diets with respect to performance capacity. At 8°C no significant deterioration in physical performance capacity was observed in nude subjects living on Diet I for 9 days, but a marked deterioration occurred after 4-5 days on Diet IV. A significant deterioration also occurred on Diet II as well as on Diet III. It is thus evident that a marked reduction in calories or in protein causes deterioration in physical performance capacity in men exposed to severe cold stress. In the cold, resting metabolism increased two-fold, resting pulse rate increased by about 20 beats per minute, and the pulse rate at submaximal work load was similarly increased. There was a significant increase in the urinary excretion of catecholamines in the cold.

COMPARISON OF THE UTEROTONIC EFFECT OF OXYTOCIN AND ITS ANALOGUES WITH THEIR EFFECT ON THE RENAL EXCRETION OF SODIUM, POTASSIUM AND WATER. R. Rosas*, L. Barnafi*, T. Pereda* and H. Crocatto*. (intr. by S. W. Hoobler). Physiology Laboratory, School of Medicine, Catholic University, Santiago, Chile.

The effect of oxytocin and two analogues, Val³-Oxytocin and Phe²-Tyr³-Oxytocin, on the contraction of rat uterus isolated in Tyrode solution, was compared with their effect on the renal excretion of Na, K and water. The subcutaneous threshold dose of oxytocin for Na excretion was 0.25 mU/100 g; for K and water excretion, 0.5 mU/100g. These doses were subthreshold for uterotonic activity. When oxytocin was treated with thioglycollate or chymotrypsin a loss of 95% of the uterotonic effect was seen, with the simultaneous disappearance of its effect on renal excretion of sodium and water. Kaliuretic action remained, but at a lower level than with untreated oxytocin. As a natriuretic Val³-Oxytocin was approximately 25% less active than an equivalent uterotonic dose of oxytocin, while Phe²-Tyr³-Oxytocin was approximately 80% less active. This suggests a lack of parallelism between the action of these substances on the isolated uterus and their action on the renal excretion of Na. (Supported by the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command, under contract N^o AF 49 (638)-504.).

INFLUENCE OF INSULIN ON IODINE CONCENTRATION BY STOMACH. Lionel W. Rosen* and M. H. F. Friedman. Department of Physiology, Jefferson Medical College, Philadelphia, Pa.

The stomach may extract from the plasma and secrete iodine in concentrations 30-70 times above plasma iodine levels. Procedures which effectively depress iodine concentrating functions by the stomach are known, but little attention appears to have been paid to procedures which may enhance this mechanism. Acute experiments were performed on dogs under light pentobarbital anesthesia. The animals were provided with either total stomach pouches or pouches of the antrum, corpus, and cardia. Both the gastric mucosa: plasma and the gastric juice: plasma ratios of I^{131} concentrations were found to range between 150:1 and 450:1 following administration of insulin. This represented a 2 to 15 fold increase in the iodine concentrating power of the stomach. The high gastric iodine concentrations following insulin administration were not related to blood sugar levels and were not inhibited by bilateral vagotomy or concomittant infusion of glucose solutions. It was also found that following insulin administration thiocyanate was not an effective agent in abolishing the gastric iodine concentrating mechanism. Insulin was without effect on the iodine concentration by gastric tissue in vitro.

PULMONARY VASCULAR RESISTANCE AND THE DIFFUSING CAPACITY OF ISOLATED CAT LUNGS. Edith Rosenberg. Department of Physiology, University of Montreal, Montreal, Canada.

It has been shown in isolated cat lungs that, using the diffusing capacity of the lungs as an index of the size of the pulmonary capillary bed, an increase in intravascular pressure produced by increasing blood flow from 50 to 230 ml/min. increases the size of this bed (J. Appl. Physiol. 15: 883, 1960). Since normal blood flows in the cat are probably not as low as 50 ml/min. it is necessary to extend this study to higher blood flows before concluding that this mechanism is important in vivo. The blood flow that can be passed through isolated cat lungs is limited by their relatively high vascular resistance. At flows above 200 ml/min. the intravascular pressure rises rapidly and edema formation and loss of blood into the perivascular tissues occurs. Attempts to improve the condition of the preparation by adding CO₂ to the inspired gas failed. However, some improvement was obtained by changing the perfusion circuit and the system of cannulating. The diffusing capacity for CO at constant lung volume was measured at blood flows up to 500 ml/min. while left atrial pressure was kept constant at approximately zero. In every experiment pulmonary vascular resistance decreased as diffusing capacity increased. Diffusing capacities were measured by the single breath method for CO using a 0.3% CO, 2% SF₆ mixture and analyzing both gases on a Perkin-Elmer gas chromatograph. The gases were separated by passing the mixture over a silica gel column followed by a molecular sieve column as suggested by Robert L. Johnson. (Supported by grant MA 890 from the National Research Council of Canada).

DETERMINATIONS OF FRC BY BODY PLETHYSMOGRAPH AND GAS DILUTION METHODS IN PATIENTS WITH EMPHYSEMA. Joseph C. Ross, John D. Teays, Thomas J. Lord, and David E. Copher. (Intr. by John B. Hickam). Dept. of Medicine, Indiana University School of Medicine, Indianapolis, Indiana.

The body plethysmographic technique gives an accurate determination of FRC in patients with emphysema since it measures all gas, whether in free communication or not. Tierney et al showed that lung volumes determined by nitrogen washout (7 minute) were much lower than the plethysmographic values in patients with emphysema. The present study was carried out to determine the reliability of the open-circuit helium technique in estimating the FRC in patients with emphysema. FRC was measured by body plethysmograph (FRC_p), 7 minute nitrogen washout (FRC_n) and open-circuit helium washout (FRC_{he}) in 4 normal subjects and in 9 patients with emphysema. In the 4 normals, mean values for FRC were: FRC_p-2.98 L., FRC_{he}-2.94 L., and FRC_n-3.09 L. In the 9 patients with emphysema, mean FRC values were: FRC_p-6.33 L., FRC_{he}-5.51 L., and FRC_n-4.93 L. FRC by open-circuit helium washout was higher than nitrogen washout FRC in 8 patients and the same in 1. When the nitrogen washout was carried on to total "washout" of nitrogen, mean FRC in 9 patients was 5.47 L. by this technique. In 2 patients, large cysts were demonstrated by X-ray. When these 2 patients were omitted, mean values for FRC in 7 patients were: FRC_p-5.86 L., FRC_{he}-5.68 L., and FRC_n-5.12 L. These studies again demonstrate that the body plethysmograph provides the most accurate determination of gas volumes in the emphysematous lung. FRC determined by open-circuit helium washout is a much more valid measurement than the 7 minute nitrogen washout FRC in estimating gas volumes in patients with emphysema. In patients with emphysema who do not have large cysts demonstrable by X-ray, the open-circuit helium FRC is closely comparable to the plethysmographic FRC.

PRESSOR RESPONSE IN DOGS ELICITED BY LIMB STRETCHING. L.W. Roth, Dept. of Pharmacology, Riker Laboratories, Inc., Northridge, California.

Mean arterial pressure of 39 pentobarbital-anesthetized dogs, supine or in side position, with no limb restraint, was found to be 106 ± 3.6 (s.e.) mm.Hg. Strong extension of fore and hind limbs caused a rise in blood pressure which was sustained as long as the stretch was continued. This rise amounted to a mean of 47 ± 4.5 (s.e.)%, with a range from 9% to 140%. A variety of agents and procedures were tested in an attempt to modify or abolish the pressor response. Those not having significant effect included:-anoxia, vagotomy, 100% oxygen, atropine, adrenergic blocking drugs, acute injection of TEA or hexamethonium, succinylcholine, d-tubocurarine. Variable to complete block was obtained by:-continuous infusion of TEA, chronic administration of guanethidine, spinal transection at C-1. This response is of considerable importance when animals must be secured to the board for tilting experiments, and the possibility of variable blood pressure levels in comparative experiments could lead to inaccurate interpretations or erroneous conclusions. The possible mechanism of action will be discussed.

INDEPENDENT INFLUENCES OF PULSE PRESSURE AND MEAN PRESSURE ON VASCULAR CAPACITY AND BLOOD FLOW. Allen A. Rovick, Department of Physiology, Stritch School of Medicine and the Graduate School of Loyola University, Chicago, Illinois.

Blood flow (F) and vascular capacity (VC) were measured gravimetrically, under steady state conditions in the isolated perfused dog's tongue. Alterations of capacity and flow generally corresponded in direction to induced step changes in mean pressure. P/F and P/VC curves exhibit hysteresis similar to that described by others and is possibly due to stress-relaxation. PP/F and PP/VC curves are also hysteretic but the shape of the curves does not permit an interpretation of stress-relaxation. Qualitative and quantitative non-conformity of flow and capacity changes induced by pulse pressure alterations are reflected in contour differences of the simultaneously determined PP/F and PP/VC curves. It often appears that pulse pressure changes can independently influence capacitance and resistance vessels. Both the mean pressure level and the prior exposure of the tissue to alterations in mean pressure appear to affect the vascular response to pulse pressure changes. Differences in the magnitude and direction of response to pulse pressure from those previously reported by others may be explained on the basis of the dependence of PP/F and PP/VC values on P/F and P/VC curve contours.

UNIT RESPONSES EVOKED BY SOUNDS FROM EIGHTH NERVE OF UNANESTHETIZED CAT. Allen Rupert,* George Moushegian,* and Robert Galambos. Walter Reed Army Institute of Research, Washington, D.C.

Single units in the eighth nerve of normal unanesthetized cats were isolated with tungsten microelectrodes and their electrical response to sound stimulation examined for up to an hour or longer. The units studied are presumed to be primary auditory nerve fibers. The majority displayed spontaneous activity in the absence of known sound stimuli and all could be driven by tones, clicks or noise. Some could, in addition, be suppressed by weak intensities of adequate stimuli. Many exhibited response areas similar to those of cochlear nucleus units, but some did not. In response to a continuous pure tone a given unit discharged sometimes at random and sometimes in synchrony with the stimulus frequency; the shift from one to the other of these modes of response could not be brought under experimental control. Postmortem histological sections established the electrode location in every case as being in the eighth nerve at the time of recording. An electrode in this location records a slow wave response to click stimulation that closely resembles the neural activity recordable by a large electrode at the round window membrane of the cochlea, a physiological fact of considerable value in locating the electrode position during an experiment.

BRAIN SUBCELLULAR PARTICLE DENSITY CHANGES WITH MATURATION.
Frederick E. Samson, Jr., William M. Balfour* and
T. C. Fuller*. Dept. of Physiology, Univ. of Kansas,
Lawrence.

Brain mitochondria are known to increase in number per gram of tissue during neonatal maturation in the rat. The question arises: Do the subcellular particles also change in their physical properties during neonatal maturation? Brains from rats 1, 10, and 21 days old were homogenized in 0.25M sucrose--0.001M EDTA and the homogenate centrifuged at 100,000 g. for 90 minutes in a sucrose gradient. Various density layers were examined with phase-contrast microscopy. Particles identified as mitochondria with phase microscopy were distributed over a wide density range. In the 21-day rat the population curve peak was at a density of 1.15, with 85% of the particles (30×10^{10} per gm.) within the limits of 1.11-1.18. In the 1-day rat, the density distribution curve was lower with the peak at 1.13 and 85% of the particles (12×10^{10} per gm.) were within the limits of 1.11-1.17. It appears that the subcellular particles of brain undergo measurable changes during maturation and with more information it may be possible to relate these changes to the physiology of the brain. (Aided by Nat'l Inst. of Health, Grant B-1151)

ABSENCE OF PROPRIOCEPTIVE DRIVE IN DIAPHRAGMATIC FUNCTION
G. Sant'Amrogio, Michael F. Wilson, and D. T. Frazier
(intr. by L. Boyarsky). Dept. of Physiology, Univ. of
Kentucky, Lexington, Kentucky.

Previous workers have described muscle spindle organs in the diaphragm, and afferent activity from the cut distal end of the phrenic nerve with spontaneous respiration and artificial stretching of the diaphragm. In the present experiments electromyograms of the diaphragm were recorded, in anesthetized or decerebrate cats, as a measurement of spontaneous respiratory activity with and without afferent connections, in control experiments and under the influence of negative pressure breathing (NPB) and abdominal compression (AC). Silver wire electrodes, insulated with polyethylene tubing except for their terminal 2 cm, were inserted into the dome of the diaphragm by an abdominal approach. NPB was produced by connecting the tracheal cannula to a 20 liter chamber in which the internal pressure was controlled. AC was achieved either manually or with a sphygmomanometer cuff. With the vagi intact, both NPB and AC produce continuous activity in the diaphragmatic electromyogram. When the vagi are cut, frequency of respiration decreases and the duration and amplitude of the electromyographic activity increases. This pattern is unchanged by NPB, while AC still causes a continuous activity. The above described patterns as well as the basal respiratory activity are not appreciably or consistently altered by surgical removal of all somatic afferent connections. (Aided by a NATO Grant)

DETERMINATION OF BLOOD FLOW TO THE HUMAN BRAIN
WITH RADIOPOTASSIUM AND IODOANTIPYRINE. Leo A. Sapiirstein, Dept. of Physiology, Ohio State Univ., Columbus.

The indicator fractionation technique has been applied to the measurement of cephalic blood flow using iodo¹³¹antipyrine as the indicator, and measuring the cephalic content of label with a large well counter. The results show that the head has about the same extraction ratio for iodoantipyrine as the body during the first minute. In this time therefore, fractional uptake of indicator by the head corresponds to the cephalic fraction of the cardiac output. When K⁴² is used the head count shows a plateau after a spike. Animal experiments suggest that the spike is associated with the rapid passage through the brain of K⁴², for which there is no cerebral reservoir, and that the plateau is associated with the uptake of K⁴² by non-cerebral tissues. The existence of the plateau suggests that the extraction ratio of non-cerebral tissues for K⁴² is the same as that of the rest of the body and that the fractional uptake of K⁴² by the head corresponds to the fraction of the cardiac output received by non-cerebral cephalic tissues. By subtracting the values obtained with K⁴² from those obtained with iodoantipyrine a value for the cerebral fraction of the cardiac output has been obtained in 40 human subjects. See also Sapiirstein, Fed. Proc. 17, 141, 1958. The value is in good agreement with that obtained by other methods. The sources of error of the method, and its application in altered physiological circumstances will be discussed. Supported by W.P.A.F.B., U.S.A.F.

MULTIPLE DILUTION CURVES OF CARDIOGREEN IN NORMAL DOGS. Clorinda Scarpa-Smith* and Philip Dow. Department of Physiology, Medical College of Georgia, Augusta.

The extension of our studies on indicator mixing and the natural and artificial factors which determine the shape of the dilution curve has required a re-evaluation of old principles and new materials. In ten dogs, 145 cardiogreen injections were made and 383 dilution curves were obtained in pairs and threes from the aortic arch (all cases), the right ventricle (43), pulmonary artery (102) and a femoral artery (93). Injections were made high or low in a jugular vein or in the inferior vena cava. Two Waters X-100A and one Gilford 103IR densitometer were used in various combinations with long and short catheters. Samples were drawn by Harvard constant-speed syringe-pullers with only a PVP solution entering the syringes, and the samples were returned to the animals immediately. Areas of the curves from a single injection showed random differences. These were usually small, but occasionally quite large, especially after jugular injections. A few instances of persistent bias may have been due to problems of baseline adjustment, calibration, sampling flow, stream sampling, or extrapolation. Mean transit times were reasonable, but the calculated N-N volumes and volume differences for some individual injections were hard to accept. If simultaneous multiple dilution curves are to be compared, the type of densitometer is not necessarily pertinent. Sampling techniques are certainly important. (Supported by grants from the USPHS and the Life Insurance Medical Research Fund).

ANOMALOUS OSMOSIS IN THE ISOLATED TURTLE BLADDER. Theodore P. Schilb*, Marshall Primack*, Allan Goretsky*, and William A. Brodsky. Dept. of Experimental Medicine, University of Louisville, Louisville, Kentucky.

Isolated bladders of *Pseudemys scripta*, immersed in oxygenated turtle Ringers solution were filled with solutions that were isotonic, hypotonic, and hypertonic to interstitial solution. Bladders lost weight (0.1-0.3 gm/hr) even against osmotic gradients. When the osmotic activity of the mucosal fluid was as much as 100 mOSM/L greater than that of serosal fluid, bladders lost up to 0.07 gm/hr. In such cases, the NaCl concentration of mucosal fluid was significantly lowered in a 5 hour period. Data can be interpreted in terms of a salt pump, acting to lower the NaCl concentration by 50 mM/L at the mucosal interface. Data are compatible with the three compartment system of Curren, whereby water moves from the first to the third compartment against osmotic gradients. Addition of mecholyl chloride (10^{-4} M) to the interstitial bath induced acceleration of net movements of water in all instances, including those where water was moving against osmotic gradients.

CINEROENTGENOGRAPHIC STUDY OF VENTILATORY MOTION OF THORACIC STRUCTURES OF THE CAT. C. DuWayne Schmidt* and Ward S. Fowler. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

There is need for information about the extent and temporal sequence of ventilation of various regions of the lungs. Cineroentgenography has been used to record simultaneously the motion of ribs, diaphragm and tracheobronchial tree that occurs in one plane during the respiratory cycle of anesthetized cats in several postures. With supine position and postero-anterior projection, amplitude of longitudinal and transverse motion was essentially symmetric bilaterally, and longitudinal displacement exceeded transverse. Longitudinal displacement and percentage change of diameter of peripheral (lower lobe) bronchi exceeded those of the lower trachea. In lateral decubitus positions, position and motion became asymmetric bilaterally. Motions of ribs and hemidiaphragms were synchronous in supine position, but occasionally asynchronous in lateral positions. After introduction of bronchial contrast medium, asynchronous motion of ribs, hemidiaphragms and bronchi was often observed. (Supported in part by Research Grant H-3588, USPHS.)

ELECTROLYTE AND WATER NET SHIFTS IN RAT SALIVARY GLAND SLICES. L. H. Schneyer and C. A. Schneyer. Univ. Alabama Med. Ctr., Birmingham, Ala.

Net movements of water and electrolytes have been investigated in slices of rat submaxillary gland in an attempt to delineate transport mechanisms of possible significance in normal secretion. Gland slices gain weight in oxygenated Krebs-Ringer-phosphate (KRP) medium due to excess of net water influx over net efflux of solids. Tissue potassium content is decreased, while that of sodium and chloride increases. Slices in KRP gassed with N_2 , similarly, gain weight and water and lose solids. Gain of Cl in N_2 also is of comparable extent but net shifts of Na and K, while in the same direction, exceed in extent those observed in oxygenated medium. Readmission of O_2 after anaerobic incubation results in inconstant net efflux of water but consistent further loss of solids. K is consistently reaccumulated and Na leaves the tissue. Tissue chloride is not reduced, possibly due to loss of organic anions. Net Na efflux is against a chemical concentration gradient and, on the basis of other work (Lundberg: Physiol. Rev. 38:21, 1958), probably also against an electrical potential gradient and hence appears to be attributable to active transport. (USPHS Grant D-931.)

X-IRRADIATION EFFECTS ON BRAIN WAVE CORRELATES OF CONDITIONED BEHAVIOR. R.L. Schoenbrun*, M. Mass*, T.J. Haley* and W.R. Adey. University of California School of Medicine, Los Angeles 24, California.

We have studied the effects of whole head and regional brain irradiation on the EEG correlates of conditioned approach behavior. 7 adult male cats were chronically implanted with bipolar stainless steel electrodes placed in temporal lobe structures, including the amygdala, hippocampus and entorhinal cortex. All behavioral procedures were carried out in a light-proof, sound attenuated, electrically shielded room using a T-maze box with one end partitioned into right and left sides, each with a light, lever and milk dispenser. 2 cats in an avoidance situation were trained to make a lever press to avoid air blast to the ears, using visual cues. 5 cats were trained in a discriminative positive reinforcement approach paradigm with a light cue and milk reward. After reaching stability the avoidance cats were given whole head irradiation of 100 and 400r per week, respectively. The approach cats were divided into a group receiving 400r whole head and a group receiving 400r focally to the hippocampus. This selective regional irradiation was accomplished in unanesthetized cats by rigid stereotaxic head fixation allowing use of a collimated X-ray beam 4mm. in diameter delivered at 23r per min. from a 250KV machine. EEG abnormalities were clearly present long before behavioral changes were detected. Notable in this respect was a 3-fold increase in hippocampal spiking following irradiation which did not interfere with behavior. At total dose levels of 200r widespread synchronization of temporal lobe structures was manifest by sustained bursts of 4-5 cycle per sec. activity. At total doses above 400r there was a decline in dominant frequencies of both resting and approach records. In addition transient changes not seen in pre-irradiation records were observed, i.e. short bursts of 20 cycle per sec. appearing in hippocampal and entorhinal leads.

ACTION OF 3,4,5-TRIMETHOXY PHENYL-BETA-AMINOPROPANE ON DIRECTLY AND INDIRECTLY STIMULATED SKELETAL MUSCLE. Robert T. Schopp and Raymond R. Walsh. Department of Physiology, University of Colorado School of Medicine, Denver, Colorado.

The influence of 3,4,5-trimethoxyphenyl- β -aminopropane (TMA) on the response of dog tibialis anticus muscle has been investigated. TMA is an hallucinogenic agent structurally related to mescaline. The muscle was alternately activated directly and indirectly (via peroneal nerve) and the action of close intra-arterial injection of TMA (4, 8, 12 or 16 mg/kg) determined. The muscle was stimulated supramaximally at a frequency of about 1/sec. and the muscle tendon was attached to a torsion band and stylus which recorded the contraction on a kymograph drum. The initial response of indirectly stimulated muscle following the administration of TMA showed a decrease of contraction occurring within a few seconds succeeded by an increase in contraction to or toward the preinjection level. The degree of initial fall and amount of rapid transient recovery varied with the quantity of agent injected. After the initial response (30-60 sec.) the magnitude of contraction gradually diminished leveling off at a lower amplitude dependent upon the amount of drug given. At higher dosages the muscle was at times unable to respond to indirect stimulation. The muscle, when stimulated directly, showed a similar but less intense initial response to TMA followed by a moderate depression of contraction with larger doses and a very mild depression with smaller doses. Thus the degree of depression of contraction observed with TMA in the indirectly stimulated tibialis anticus muscle is due in part to a direct action on the muscle. Eserine opposes the diminution of muscle contraction seen with direct or indirect stimulation. The eserinated muscle when stimulated indirectly, however, manifests a relatively greater improvement of contraction than when stimulated directly.

EFFECT OF ANTIOXIDANTS ON VITAMIN E-DEFICIENT GUINEA PIG MUSCLE MYOGLOBIN. B.A. Schottelius, D.D. Schottelius*, R.D. Buckley*, Dept. of Physiol., State Univ. of Iowa, Iowa City, Ia.

The purpose of this study was to determine whether supplementation with antioxidants would maintain the myoglobin levels of vitamin E-deficient animals as does supplementation with vitamin E. Five groups of 33 day old guinea pigs were maintained on the following dietary regimens: normal; vit. E-deficient, (E-); vit. E-supplemented, (E+), 45 mg/week; methylene blue supplemented, (MB), 120 mg/week and N,N'-diphenyl-p-phenylene diamine, (DPPD), 30 mg/week, for 15, 21 and 30 days. Myoglobin and non-collagen-nitrogen values were determined for gastrocnemius and masseter muscles. At 15 days the myoglobin concentration in both muscles from E- animals was significantly higher than either E+ or DPPD animals. In addition, the concentration of myoglobin in the E- masseter muscles was significantly greater than in masseters of MB supplemented. At 15 days the myoglobin concentrations of the three supplemented groups are similar. At 21 days myoglobin concentration in E- animals was decreased when compared to 15 day animals, whereas in supplemented groups it was increased. At 30 days this trend continued. Another group maintained on an E- diet for 15 days was divided into 4 categories: (1) E-, (2) E+, (3) MB, (4) DPPD, and supplemented until day 21. Supplemented animal myoglobin concentrations were similar and were lower than in E- animals. These results indicate that MB and DPPD are partially effective in replacing vit. E. (Supported by MDAA, Inc.)

OXYGEN CONSUMPTION OF SOLEUS MUSCLES FROM NORMAL AND VITAMIN E-DEFICIENT AND SUPPLEMENTED GUINEA PIGS. D. D. Schottelius*, J. W. C. Bird*, and B. A. Schottelius, Dept. of Physiology, State Univ. of Iowa, Iowa City.

Guinea pigs, 30 days old, were maintained on the following dietary regimens: normal (N), E-supplemented (E+) and E-deficient (E-) for 15, 21 and 30 days. Oxygen consumption, $QO_2(NCN)$, of contralateral muscles, one a resting control and the other stimulated, was determined in a modified Warburg flask ($30^{\circ}C$, $98\%O_2$ - $2\% CO_2$, pH 7.2). The oxygen consumption of stimulated muscles was compared with their respective contralateral resting muscles at three successive 10 min. periods: rest, stimulation (30V. 2 msec. duration, 2 per sec.) and recovery. At 15 days, resting E- muscles had a higher oxygen consumption than N or E+ muscles; this relationship was reversed at 21 and 30 days. Stimulation increased oxygen consumption of all muscles regardless of dietary duration. The increase was greater for N than for E- or E+ muscles. In E- muscles it was greater in the 21 day than in 15 or 30 day studies. During the recovery period the oxygen consumption of N and E+ muscles was greater than for E- muscles from the 21 and 30 day series. (Supported by MDAA, Inc.)

CRITICAL FLICKER FREQUENCY AND PHOTIC FOLLOWING IN THE CAT. Arthur S. Schwartz* and Donald B. Lindsley. UCLA and Long Beach VA Hosp., Cal.

The existence of a direct relationship between the critical flicker frequency and the photic following limit of the cortex has been suggested by several authors. The present study compared these two variables in the same subjects under identical testing conditions. Five cats were operantly conditioned to discriminate between a flickering and a steady light. The flicker rate was then increased until the discrimination was no longer apparent, and the critical flicker frequency was identified between the highest frequency discriminated and the next higher frequency tested — a range of 2 cps. Recordings were made periodically from the lateral geniculate bodies and visual cortex by means of chronically implanted gross electrodes. Electrical recording test trials were made with flicker rates from 15 to 100 cps. The cortex was found able to follow flicker frequencies from 10 to 18 cps higher than the behavioral critical flicker frequency in at least four cats. The lateral geniculate bodies followed from 27 to 58 cps higher than the critical flicker frequency. The amplitude and per cent following time was, in general, inversely related to the frequency of flicker, especially in the case of the cortex. The data confirm the findings of others in that the cortical following limit is lower than the subcortical visual stations. However, the demonstration of cortical ability to follow frequencies higher than the critical flicker frequency suggests that the relationship between these two variables is not a direct one. (Supported in part by Contract No. NONR 233(32) and by Carnegie Corp. of New York.)

CARBON DIOXIDE AND TEMPERATURE REGULATION. L.C.Senay, Jr.*
L. Prokop,* M. Christensen,* A.B. Hertzman, Department of
Physiology, St. Louis Univ. School of Med., St. Louis, Mo.

Respiratory alkalosis occurred in normal resting subjects exposed to 45° C. for three hours whether or not dehydration was prevented by 0.1% NaCl in amount equal to the weight loss. Restoration of alveolar CO₂ to preheat control levels by administration of a mixture of 2.7% CO₂ - 97.3% O₂ (values corrected to the chamber temperature of 45° C.) did not appreciably influence skin temperatures, cutaneous blood flows (skin pulses), regional sweating, and arterial blood pressures, but it did augment heart rate and the I-J wave of the ballistocardiogram. Respiration was also markedly augmented thus confirming other work that heat increases the sensitivity of the respiratory controls to CO₂. However, the sensitivity of the thermo-regulatory controls apparently is not affected by CO₂.

(Supported by USAF Contract and USPHS).

PLASMA VOLUME RESPONSE TO GRADED HEMORRHAGE. Kenneth D. Serkes*,
Morton D. Pareira,* and Stanley Lang. Jewish Hospital and Washington
University School of Medicine, St. Louis, Mo.

Previous investigations have measured sequential changes produced in the components of the circulating blood volume after a single large hemorrhage. The present study was undertaken to determine whether the magnitude of plasma volume restoration after hemorrhage in rats is quantitatively related to the magnitude of the hemorrhage. Male albino rats were bled amounts of whole blood approximately equal to various predetermined percentages of body weight. At 4 hours after hemorrhage red cell and plasma volume were directly measured by simultaneous radioactive isotope dilution techniques. At 4 hours plasma volume was restored to control values regardless of the magnitude of the hemorrhage. A decrease in effective capillary pressure was thought to best explain the observed events.

REGULATION OF VASOPRESSIN RELEASE BY RECEPTORS WITHIN THE VASCULAR SYSTEM. Leonard Share and Matthew N. Levy. Western Reserve Univ. and St. Vincent Charity Hosp., Cleveland, Ohio.

The development in this department of a specific chemical procedure for the extraction, purification and concentration of vasopressin in small volumes of blood has made it possible to investigate in a definitive fashion the role of vasopressin in the regulation of extracellular fluid volume. This method has been employed to demonstrate that a reduction in extracellular fluid volume by peritoneal lavage in dogs results in an increased release of vasopressin. The present study is concerned with the location of the receptors for this response. The selective expansion of vascular volume during the early stages of lavage by the infusion of isotonic dextran solution prevented any further increase in vasopressin release. These data plus reports that hemorrhage is a potent stimulus for vasopressin secretion suggested that the receptors in question lie within the vascular system. The results of further attempts to localize these receptors follow. Occlusion of both common carotid arteries, vagi intact, was without effect on vasopressin release. Bilateral cervical vagotomy increased the concentration of vasopressin in jugular vein blood from a control of 12 μ U/ml blood to 23 μ U/ml. Subsequent occlusion of both common carotid arteries in the vagotomized dogs resulted in a further increase in the blood titer of vasopressin to 74 μ U/ml. It is concluded that receptors regulating vasopressin release are located within the vascular system. The afferent nerve fibers for one group of these receptors are carried within the vagi. Another group of receptors lie within the distribution of the carotid arteries. (Supported by grants from the U.S. Public Health Service and the Cleveland Area Heart Society.)

ELECTRICAL ACTIVITY IN MESENTERIC NERVES AFTER PERFUSION OF THE GUT LUMEN. K.N. Sharma* and E.S. Nasset. Dept. of Physiol., Univ. School of Med., Rochester, N. Y.

The electrical activity, picked up from the peripheral cut end of mesenteric nerves to selected intestinal loops of the anesthetized cats, was fed into an RC coupled amplifier system and recorded oscilloscopically. In another set of experiments, chronically prepared dogs with Thiry-Vella loops and with electrodes implanted in mesenteric nerves were used. The loop was perfused with different isomolar solutions at constant temperature and pressure. Spontaneous and evoked activity in mesenteric nerves varied from strand to strand selected and even in the same strand at different intervals. After glucose perfusion of the lumen there was an increase of 20-100% in frequency of firing of smaller fibers and of 100-400% in larger fiber groups. The latency of response varied from 20-30 seconds to 4-5 minutes. Increase in activity observed after perfusion of single amino acids were more conspicuous in smaller fibers. Perfusion with Amigen (amino acid mixture, dextrose and salts) presented mixed patterns. No appreciable changes could be observed with 0.9% NaCl, Tyrode solution and 0.025 N NaOH. The possibility of some chemoreceptor mechanism in the small intestine is suggested. Probably the majority of afferent impulses from these receptors travel in the splanchnic nerves.

COMPENSATORY HYPERTROPHY OF THE THYROID, ADRENAL AND GONAD IN RATS. C.J. Shellabarger, and R.C. Mason*. Zoology Department and Medical School, University of Michigan, Ann Arbor; Medical Department, Brookhaven National Laboratory, Upton, N.Y.; and Physiology Dept., Seton Hall College of Medicine, Jersey City.

Compensatory hypertrophy has been a classical technique for the study of the interactions between the pituitary and its target organs. In the present experiments, one half of the thyroid gland, or one adrenal gland, or one gonad was removed singly or in all possible combinations from young rats. After a period of either 14 days (males) or 21 days (females) the rats were killed and the weights of the intact or operated organs were obtained and subjected to factorial analysis. In singly operated animals the remaining portion of the thyroid gland, or the single adrenal gland, or the single ovary, each underwent compensatory hypertrophy. When the operations were combined, again each of these organs underwent compensatory hypertrophy. All hypertrophy interactions in multiple-operated animals were additive and there were no synergistic effects of one organ on hypertrophy of another. These results are interpreted to mean that the pituitary is competent to secrete sufficiently increased amounts of TSH, ACTH, and gonadotropins simultaneously in order that simultaneous multiple compensatory hypertrophy of the thyroid, adrenal and gonad may occur.

(Supported in part by the U.S. Atomic Energy Commission)

PRESUMPTIVE EVIDENCE FOR A SUPRASPINAL LOOP RELAYING INTER-LIMB REFLEXES. M. Shimamura (intr. by R. B. Livingston). Natl. Insts. of Health, Bethesda, Md.

In decerebrate cats segmental reflex evocation yields the usual early mono- and poly-synaptic responses at the same segmental level plus a response that is delayed for about 6 msec. at the cervical level and about 10 to 20 msec. at the lumbosacral level. This interval of delay is between the end of the polysynaptic response and the beginning of the delayed response, and is characterized by no activity in the motor root. If subtetanic doses of strychnine are given, the intervals are shortened to 5 msec. at the cervical level and 8 to 9 msec. at the lumbosacral level. Interlimb reflexes ascending between hind- and fore-limbs are visible in strychninized animals after a delay of about 10 msec. Spinal transection at C1 eliminates the delayed segmental reflex and the ascending interlimb reflex. Recordings have been made of ascending impulses in the dorsolateral quadrant of the spinal cord, in the bulbar reticular formation, and descending responses evoked by bulbar stimulation, which correspond satisfactorily with time requirements for a spinal-bulbar-spinal recurrent discharge which might account for both the delayed segmental reflex and the ascending interlimb reflex. Time relations between long interlimb and segmental ipsilateral and crossed reflexes support the notion that a supraspinal conduction pathway may be involved in the integration of a variety of interlimb reflexes.

EFFECT OF INSULIN ON HEPATIC CARBOHYDRATE AND FAT METABOLISM IN NORMAL, ADRENALECTOMIZED AND DEPANCREATIZED DOGS. W.C. Shoemaker, P.J. Carruthers, I.C. Powers, L.J. Wedel, and D.H. Elwyn. Michael Reese Hosp. and Med. Center, Chicago, Ill.

The rate of hepatic uptake or output of plasma glucose, nonesterified fatty acids, total fatty acids, cholesterol, cholesterol esters and phospholipids were measured in a series of unanesthetized dogs whose hepatic vessels were previously catheterized. Four series of animals were used: normal, depancreatized, adrenalectomized, and adrenalectomized-depancreatized. Hepatic blood flow was measured by a modified bromsulphalein method. Blood was sampled from arterial, portal and hepatic venous catheters by constant withdrawal at 10 minute intervals before and after insulin administration. HGF-free insulin (Lilly) was administered by single injection, and by constant infusion into the portal vein at the rate of 0.0016 to .0033 units/Kg/min.

No measurable decrease in the rate of hepatic glucose output was observed in normal, adrenalectomized or depancreatized dogs given insulin by either single injection or by constant infusion. The hepatic uptake of nonesterified fatty acids increased from .05 meq/min in the control period to .15 meq/min after insulin in normal dogs ($P=.001$). Diabetic dogs in a poor nutritional state showed a control hepatic uptake of .19 meq/min, and an uptake of .28 meq/min after insulin. Diabetic dogs in a good nutritional state showed a control hepatic fatty acid output of .17 meq/min; there was a decrease to a mean hepatic uptake of .02 meq/min after insulin infusion. An increase in the mean hepatic uptake of free cholesterol and an increase in the output of esterified cholesterol and total fatty acid were also observed after insulin administration.

DIFFERENTIATION OF HEPARIN-RELEASED LIPOLYTIC ACTIVITIES OF PLASMA. B. Shore, V.G. Shore and N. Rosenstock (intr. by G. M. Schoepfle). Dept. of Physiology, Washington Univ. of Medicine, St. Louis, Mo.

Activities for the hydrolysis of unemulsified mono- and diglycerides, but not triglycerides or ethyl esters, of C_{16} and C_{18} fatty acids were released into plasma by intravenous heparin injection. These activities, unlike lipoprotein lipase activity, were not inhibited by the non-ionic detergent, Triton X-100, or by 1 M NaCl and were not activated by serum high density lipoproteins. By differential adsorption on and elution from calcium phosphate gel, lipoprotein lipase and the activities for the hydrolysis of the unemulsified glycerides were separated. In the presence of 0.15 M NaCl, the latter activities are more tightly bound to the gel than lipoprotein lipase. All activities were inhibited by preincubation of the enzyme preparations with diethyl-p-nitrophenyl phosphate, atoxyl, pentachlorophenol or thyroxin before addition of substrate. The inhibition by thyroxin was not changed by dialysis or addition of Mg^{++} or Ca^{++} to the enzyme preparation before addition of thyroxin. Diiodotyrosine and eserine did not inhibit. These observations suggest that more than one enzyme may be involved in a stepwise degradation to glycerol and fatty acids of triglycerides transported in chylomicra or S_f 20-400 lipoproteins. (Supported by USPHS grants H-3629 and RG-4566.)

SUBMAXIMAL EXCITATION OF NON-CONDUCTING STRIATED MUSCLE.

F. J. M. Sichel and Gretchen Hebb Bean*, Dept. of Physiol. and Biophysics, Univ. of Vermont Coll. of Med., Burlington.

In an earlier report we showed that for threshold direct current excitation the optimal angle between the direction of the muscle fibers and the direction of the stimulating current is the same for conducting and for non-conducting muscle. The purpose of the present experiments was to determine the most favorable angle for submaximal excitation. Frog and toad sartorius muscles were used. Muscles were made non-conducting by K^+ -enriched Ringer's solution (12-14 mM K^+ /liter) or by use of choline chloride Ringer's solution or of procaine hydrochloride. All these agents yielded stable preparations which responded to appropriate stimulation for long periods and regained conduction on return to normal Ringer's solution. Duration of rectangular shocks was 8-50 msec. Isometric tension developed was recorded. Independently of the agent used to suppress conduction, it was found that at low field strengths (slightly above threshold) the tension response was greater for longitudinal than for transverse currents. With greater strengths of stimulation, responses to transverse and to longitudinal current pulses became equal. At still higher field strengths, response to transverse currents exceeded response to equal longitudinal currents. In some cases very strong currents had a depressing effect on the production of tension but the efficiency of transverse current still exceeded that of longitudinal current. It may be concluded that the larger currents have an effect on a structure which is differently oriented than the target of the smaller currents. (Supported by a research grant, H-336, from the Natl. Heart Inst., PHS).

EVOKED AND SPONTANEOUS POTENTIALS IN THE PITUITARY GLAND.
E. B. Sigg and T. D. Shopiro*, Geigy Research Laboratories, Ardsley, New York

While control of the neurohypophysis by supraoptic and paraventricular nuclei is an established fact, structures influencing the adenohypophysis are not well known. Reports in the literature indicate that the anterior pituitary is linked with the limbic system. The purpose of the study is to elaborate further on this relationship by electrophysiological methods. In cats, anesthetized with pentobarbital and/or immobilized with d-tubocurarine, fine bipolar electrodes were implanted into the hypophysis by the trans-sphenoidal approach. Stimulation of various brain areas was executed through stereotactically introduced concentric electrodes. Compound action potentials in the pituitary gland and in the infundibular part of the hypothalamus were recorded most readily in response to stimulation of the hippocampus and fornix and, occasionally, the amygdala. The pituitary gland itself, however, was not electrically excitable, as evidenced by the absence of evoked potentials in the hypothalamus and rhinencephalon. Repetitive stimulation of the amygdala or hippocampus produced recruiting responses and spike-like after discharges. High frequency stimulation of the mesencephalic reticular formation sometimes caused 2-3 cps high voltage slow waves in the hypophyseal leads. Spontaneous activity exhibited various patterns from spike-like to low voltage-fast activity potentials. From the data it is inferred that rhinencephalic structures are linked to the hypophysis by neural pathways.

LIVER AND THE CALORIGENIC ACTION OF ADRENALINE AND NORADRENALINE.
A. T. Skarin*, M. L. Lockwood*, and F. R. Griffith, Jr., Dep't. of
 Physiology, Univ. of Buffalo School of Medicine, Buffalo, N. Y.

The intravenous infusion of adrenaline and noradrenaline into eviscerated cats results in artifact effects which by decreasing the functional residual capacity interfere with a recording of true oxygen consumption by conventional closed-circuit spirometry. With the use of a thermostated compensating body chamber, which frees the oxygen consumption record from any dependence on lung volume, infusion of adrenaline and noradrenaline at rates of $4\mu\text{g/kg/min.}$ for 5 minutes results in an increase in oxygen consumption during infusion to an average 121% and 123% of control, respectively, with return to control in the 15 minute period following infusion. A similar response is obtained in normal cats during adrenaline infusion, but only in this group is a secondary or delayed rise to an average 110% of control noted in the 15 minute period following infusion. It is suggested that the calorigenic action of adrenaline might be separated into an immediate effect occurring during intravenous infusion which is independent of the presence of the liver, and a delayed or secondary effect occurring after infusion, requiring the presence of the liver.

(Supported by USPHS grant RG4242).

ADAPTATION OF BIRDS TO CHRONIC ACCELERATION^{1/}. A. H. Smith and
C. F. Kelly* University of California, Davis.

Chronic acceleration, produced by long-term centrifugation, is physiologically equivalent to a change in gravity. As such it represents a completely new environmental stress, the earth's gravity having remained constant, and the ability of animals to adapt and the nature of the adaptation is of interest. A special strain of chickens has been selected for survival after seven weeks exposure to forces up to three to four G. The fifth selected generation (S₅) shows a marked resistance to chronic acceleration:

exposure to 2.5 G
 lethal to 50%

Acceleration selected line	60 days
Unselected (control) birds	11 days

By comparing the intensity of various physiological phenomena under a variety of accelerative forces, it is possible to resolve normal processes into two components: one which is "mass-determined" and the other, "weight determined." Implicit in this analysis is a prediction of the physiological effects of sub-gravity exposure.

^{1/} Supported by a grant from the Office of Naval Research.

AN "IRON HEART" MODEL FOR STUDY OF CARDIAC IMPULSE TRANSMISSION (16 mm silent film). Edward E. Smith and A. C. Guyton. Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

A passivated iron sphere suspended in nitric acid, like the iron wire described by Lillie, shows remarkable similarities to excitable tissue. When the surface of such a sphere is electrically or chemically stimulated a single wave of activity passes over the sphere and annihilates itself on the opposite side. When, however, the excitability of the sphere is unusually high or when it is rapidly and successively stimulated, a self-propagating activity is set up. This is seen to consist of irregular waves which by repetitive splittings and recombinations continue to wander over the sphere indefinitely. Electrical records taken during this activity strikingly resemble the EKG of the fibrillating heart. For this and other reasons it is felt that the study of the passivated iron sphere may advance our understanding of the mechanism of cardiac fibrillation. The accompanying film illustrates some of the types of behavior seen in the "iron heart" and describes the studies that have been undertaken to characterize its properties.

THE RELATIONSHIP BETWEEN SULFHYDRYL LEVELS AND MITOTIC ACTIVITY IN REGENERATING LIVER. H. Millard Smith (intr. by J. E. Whitney). Univ. of Arkansas School of Med., Little Rock, Ark.

To determine if sulfhydryl levels and cathepsin activity in a mature growing tissue, such as regenerating rat liver oscillate with respect to mitosis in the fashion similar to sea urchin eggs and lily anthers, or yeast was the object of the study. Twelve, 24, 36, 48, 96 hours after partial hepatectomy protein sulfhydryl (PSH) and non-protein sulfhydryl (NPSH) levels in liver homogenate were determined by amperometric titration, and cathepsin activity by the hemoglobin method of Anson. The NPSH level showed no change until 24 hours, when it rapidly increased with a maximum at 36 hours, followed by a decline. The PSH level fell continuously. Cathepsin activity decreased from normal at 24 hours, and then increased slowly. Mitosis peaked at 36 hours. NPSH levels follow mitotic activity in regenerating liver in contradistinction to sea urchin eggs and lily anthers where the level is inversely related to mitosis. Cathepsin activity does not seem to be related in time to mitosis. A reciprocal relationship between NPSH and freely reacting protein sulfhydryl moieties (PSH) does not seem to exist. This work was supported by a grant from the American Cancer Society.

THERMOGENIC ACTIVITY OF THE HIBERNATING GLAND IN THE COLD-ACCLIMATED RAT. Robert E. Smith. UCLA Med. Center, Los Angeles 24, California.

The interscapular, brown adipose "hibernating gland" of the Long-Evans male rat was found to have increased in mass during 40 days of continued exposure to 6°C by a factor of 2.4 over equal weight controls kept at 26°C. Individual caging and a 12 hour light cycle were employed with Simonsen White Diet and water ad libitum. The freshly excised tissues were prepared for in vitro respiration measurements as slices, homogenates in sucrose (0.25 M), and a twice washed mitochondrial fraction. The respective values of $QO_2(N)$ from cold-acclimated rats were significantly elevated over controls in both slice and homogenates by factors respectively of 1.61 and 1.53. On the wet weight basis slices (in glucose-phosphate medium) were elevated to 2.2 times the respiration of controls. Mitochondrial respiration and to a lesser extent that of homogenate were highly sensitive to total N content of the system. $QO_2(N)$ of mitochondria, though very high, was not significantly greater in cold than in controls. Both were accelerated to the values of around 700 (at 37°C) by addition of 6 mg/ml bovine serum albumin to the flasks containing ca 0.3 mg mitochondrial N. It is concluded that the interscapular brown adipose of the rat at 40 days of cold-acclimation may contribute of the order of $2.2 \times 2.4 \approx 5$ times the heat production of this gland in the rat at normal ambient temperature. Supported by Grant C-4271 (C2) from Nat. Cancer Inst., USPHS.

MICROVASCULAR BED OF THE PULMONARY ARTERY WALL. Sidney S. Sobin, Wallace G. Frasher* and Herta M. Tremer*. College of Medical Evangelists, Los Angeles, California.

The microvascular bed of the blood vessel wall has neither been well recognized nor well described. The rich vasa vasorum of the pulmonary artery demonstrated by the silicone elastomer injection method (Physiologist 3:146, Aug. 1960) have a characteristic capillary bed. Small arteries and arterioles course obliquely from the adventitia deep into the media and give rise to preferential channels and vertically oriented precapillaries and true capillaries. Venous drainage via collecting venules and small veins similarly is obliquely outward. This recognizable microvasculature is similar to the prototype described by Zweifach in 1937.

TRANSCAPILLARY BLOOD GAS REACTION KINETICS MEASURED IN LIVING ANIMALS. Jorge Soni*, Khalil A. Feisal* and Arthur B. DuBois, Dept. of Physiology, Graduate School of Medicine, University of Pennsylvania, Phila., Pa.

A sensitive manometric method has been used to study the reaction rates of the liberation and absorption of gases in living animals. This procedure was performed on 5 dogs, anesthetized, curarized, ventilated with a respiration pump and placed in a body plethysmograph. A catheter was placed at the root of the pulmonary artery. Capacitance manometers were used to monitor pulmonary artery pressure and the pressure within the plethysmograph. During a pause in respiration 0.5 ml of 1.2 M lactic acid was flushed in rapidly through the catheter causing a liberation of gas. In a similar fashion 0.5 ml of 1 M tris(hydroxymethyl)aminomethane was flushed in causing the absorption of gas. To be able to differentiate between the reaction time and the circulation time, an inert gas, ether, dissolved in alcohol or an oil emulsion was flushed in. The sudden increase in the plethysmograph pressure indicated the arrival and transfer of ether into the lungs in 0.9 sec. An injection of ether preceded each injection of acid or THAM. The injection of lactic acid while the dog was ventilated on air gave off 3.0 ml of carbon dioxide and oxygen with a half time 0.4 sec. longer than that of ether. When the injection of acid was given while ventilating with oxygen to eliminate the Bohr effect, 2.2 ml of gas were given off with a half time 0.2 sec longer than ether. THAM caused an absorption of 3.1 ml of gas with a half time 1.0 sec longer than ether. Carbonic anhydrase given immediately before THAM speeded up the reaction to 0.16 sec. Acetazolamide was given to observe the effect of the inhibition of carbonic anhydrase. The reactions in which the enzyme is active were slowed up.

UPTAKE OF FREE FATTY ACIDS BY THE LIVER IN NORMAL AND DIABETIC DOGS. John J. Spitzer and William T. McElroy, Jr. Dept. of Physiology, Hahnemann Medical College and Hospital, Philadelphia, Pa.

Hepatic uptake of free fatty acids (FFA) was compared in normal and in diabetic dogs in vivo. Thirteen normal and twelve diabetic animals were employed in the study. The arterial and the portal FFA concentrations in diabetic dogs were significantly higher than in normal ones. Uptake of FFA by the diabetic liver was significantly higher than the normal liver. Estimated hepatic plasma flow and per cent of utilization of FFA (i.e. portal-hepatic conc. /portal conc. X 100) were not different in the two groups. Within the diabetic group, the uptake of FFA was in direct relation to the portal FFA concentration. A similar relationship has been demonstrated previously with regard to the normal liver. Insulin decreased the release of FFA by adipose tissue in vivo, and also decreased the hepatic uptake of FFA in diabetic as well as in normal dogs. Actively working skeletal muscles (direct electrical stimulation) showed an uptake of FFA in both diabetic and normal animals. The administration of epinephrine, norepinephrine or insulin had similar effects on FFA uptake by the liver in diabetic and in normal dogs. The rise in FFA after epinephrine or norepinephrine was not as great or consistent in the diabetic animals as in the normal ones. (Supported by the National Heart Institute.)

EFFECTS OF PROLONGED AUDITORY STIMULATION ON ELECTRICAL ACTIVITY IN THE CENTRAL NERVOUS SYSTEM. A. Starr* and R.B. Livingston. National Institutes of Health, Bethesda, Md.

Our goal is to observe functional changes in the central nervous system which are substantially longer lasting than milliseconds and seconds. One evidence that such changes may occur is the commonplace experience of perceptual persistence in man following prolonged auditory, vestibular, somesthetic and visual stimulation. Our experimental approach is to attempt to identify changes in the general level of electrical activity which may be induced along sensory pathways by exposing animals to prolonged stimulation. Cats with chronically implanted electrodes in several locations (including round window, cochlear nucleus, superior olive, inferior colliculus, mesencephalic reticular formation, medial geniculate body and temporal cortex) have been exposed to white noise at 95 db - SPL - for time intervals up to 24 hours. This stimulation induces identifiable changes in each of the recording sites. Changes are most pronounced at the round window and cochlear nucleus and least evident at the medial geniculate and temporal cortex. Exposure to continuing stimulation is associated with gradual shifts in recorded activity which are likewise not uniform throughout the auditory pathway. At the cessation of sound stimulation, there is a diminution in activity in certain central auditory stations which may persist for many minutes before recovery to prestimulatory levels. This long persisting change is not observed when the cats are anesthetized.

IS THERE EVER A MEASURABLE ALVEOLAR-ARTERIAL O_2 GRADIENT DUE TO DIFFUSION? N.C. Staub* (Intr. by K. Wasserman). Cardiovascular Research Inst., Univ. of Calif. Med. Center, San Francisco.

To perform the Bohr integration procedure, the A-a PO_2 diffusion gradient must be known. The method for determining the gradient experimentally is that of Lilienthal et al. Recently, Asmussen and Nielsen (Acta Physiol. Scand. 50:153, 1960) studied healthy men at rest and at work while breathing air and while breathing low oxygen and explained the entire A-a PO_2 gradient on the basis of unevenness of ventilation-perfusion ratios. Unpublished data of Finley et al. report the same thing in patients having "alveolar-capillary block." Using new data on the oxygen diffusivity of human red cells at varying O_2 Hb saturations, θO_2 (Staub et al., J. Appl. Physiol., in press), DMO_2 (taken as $1.23 \times DMCO$) and V_c (determined by $DLCO$ measurements), and measurements of cardiac output, \dot{V}_O_2 and SAO_2 , we have calculated the course of pulmonary capillary red cell PO_2 rise in a forward type of Bohr integration, using capillary erythrocyte transit time as the limiting factor rather than end-capillary PO_2 gradient. Calculations based on one normal subject during rest, strenuous exercise, and breathing 12% O_2 at rest show no measurable (> 1 mm Hg) PO_2 gradient. Calculations based on a patient with a fixed capillary volume of 20 ml also showed no gradient at rest, although the SAO_2 was 89%. The ratios V_c/DM and $V_c/\text{stroke volume}$ are useful for analyzing the effects on the diffusion gradient of pulsations in the pulmonary capillary flow, reduced capillary bed or high cardiac output, and pulmonary membrane defects. In normal subjects under many conditions and in patients with severe pulmonary disease, the A-a PO_2 diffusion gradient is < 1 mm Hg and has little effect on lowering arterial saturation. These findings suggest that the lungs have a large safety factor for diffusion. (Supported in part by Calif. TB and Health Assn. and U.S.P.H.S. Grant H-4029).

Effects of Carbon Dioxide on Isolated Nerve-Muscle Junction.

Wm. W. Steinberger. Univ. of Michigan, Ann Arbor, Michigan.

End-plate potentials (epp) were recorded by means of glass micro-pipette electrodes inserted at the neuro-myal junction of a frog sartorius nerve-muscle preparation maintained in a moist chamber. The preparation was curarized to prevent mechanical contraction. Stimuli were applied to the nerve through platinum wire electrodes. Moistened oxygen was passed through the chamber except during application of the carbon dioxide mixture. Application of an 8-10% carbon dioxide (balance oxygen) mixture produced one of three effects: (1) a complete loss of the epp; (2) a decrease in the epp accompanied by increased conduction time and an increase in time from onset of the epp to 1/2 decay; or (3) an increase in the epp accompanied again by an increase in conduction time and an increase in onset to 1/2 decay time. The abrupt loss of the epp is probably due to a change in excitability in the nerve by the carbon dioxide because increasing the stimulus strength would sometimes reverse it. Increased conduction time (stimulus artefact to epp response) also is probably related to effects of carbon dioxide on the nerve fiber. A decrease in the epp indicates reduced acetylcholine production that could be a result of the carbon dioxide blocking some of the fine terminal arborizations of the nerve fiber. An increase in the epp accompanied by a longer 1/2 decay time indicates a reduced cholinesterase activity permitting a greater effect from the acetylcholine produced. It would appear then that carbon dioxide may act at the neuro-myal junction to block acetylcholine production and/or as an anticholinesterase to enhance the end-plate response.

(Supported by funds from the Rackham School of Graduate Studies.)

CEREBRAL BLOOD FLOW BY EXTERNAL ISOTOPE COUNTING. S. H. Steiner, K. Hsu, L. Oliner and R. H. Behnke (intr. by S. Bondurant). Dept. of Med., VA Hospital and Ind. Univ. School of Med., Indianapolis, Indiana.

Measurement of human cerebral blood flow has been essentially limited to the nitrous oxide method, or radio-krypton modifications. Sapiirstein has used 4-Iodo¹³¹ antipyrine (4IAP) and Rubidium⁸⁶ Chloride (RbCl) to measure cerebral flow. This study describes a method whereby these tracers are used to measure human cerebral blood flow. 4IAP crosses the blood brain barrier with ease, but RbCl has an exceedingly small exchangeable pool. 4IAP, after a rapid intravenous injection, is distributed to a sufficiently large body and brain pool that the cephalic washout rate (brain, head, and neck) is slow enough to permit semi-logarithmic extrapolation to maximum concentration at zero time. RbCl has been demonstrated to distribute to a sufficiently large body pool in one circulation so that after a rapid intravenous injection the organ content remains stable for a considerable period of time and is, therefore, proportional to the distribution of the functional perfusion of the organ. Since the brain pool for Rb is small the non-cerebral cephalic content can be determined with this tracer. The difference between the 4IAP uptake and that of Rb, corrected for the cerebral Rb pool and recirculated Rb, is that fraction of the cardiac output distributed to the brain. Cardiac output was measured by the indicator dilution technique using cardiogreen. In 16 subjects the cardiac index was $3.13 \pm .53$ L./m²/min., and cerebral blood flow was 751 ± 179 ml./min. which agrees favorably with the Kety method.

LIMBIC AND THALAMIC RELATIONSHIPS OF THE BASAL FOREBRAIN RECRUITMENT AREA. M. B. Sterman and C. D. Clemente. Univ. of Calif. at Los Angeles and Veterans Administration Hospital, Sepulveda, California.

Recently Sterman and Clemente (Fed. Proc. 1961) described an area in the basal forebrain which upon low frequency (5-7/sec.) and low voltage (2-3 volts) stimulation induced an immediate and sustained cortical recruitment in adult cats. Anatomical mapping of the recruitment zone disclosed a relatively specific locus in the lateral preoptic area including the nucleus of the diagonal band of Broca. The effective stimulation points became more diffuse caudally except for a secondary focus within the medial and basal amygdaloid nuclei. In a series of chronic preparations stimulation of the basal forebrain recruitment area rendered adult cats behaviorally asleep within one minute from the commencement of stimulation. More recent experiments involve an extension of this study in an attempt to determine the physiological interactions of the basal forebrain recruitment area with other parts of the brain. A series of acute experiments were performed on the brains of adult cats in which electrodes were placed stereotaxically into this recruitment zone. Evoked activity was recorded in other subcortical areas by several exploring electrodes during active cortical recruitment. A systematic study of responding thalamic, rhinencephalic and brainstem structures revealed that cortical recruitment was accompanied by high amplitude recruitment-like activity in distinctly circumscribed loci of the ventromedial thalamus and subthalamus. Furthermore, direct "following" responses were observed in the fornix, the hippocampus, the subthalamus and the posterior hypothalamus. It is our feeling that the central mechanisms regulating sleep involve the reduction of afferent input into the reticular activating system and the onset of an active forebrain inhibition influencing thalamic and limbic structures.

CARDIOVASCULAR RESPONSE TO ADRENALIN FOLLOWING ACUTE METOPIRONO (SU4885) TREATMENT. H. L. Stone (intr. by F. R. Steggerda). Department of Physiology, University of Illinois, Urbana, Illinois.

The effect of Metopirone[®] (Ciba), an adrenal cortical inhibitor, on the responsiveness of the cardiovascular system to I.V. and I.A. doses of Adrenalin[®] (Parke Davis) was determined by measuring the left ventricular contractile force, aortic and femoral arterial blood pressures, and femoral arterial blood flow in closed-chest, anesthetized normal and adrenalectomized dogs. In the normal animals there was no significant change in the magnitude of the vascular response to I.V. Adrenalin after treatment with Metopirone. Metopirone treatment in adrenalectomized animals does not appear to alter the response to Adrenalin. Elevation of steroid level in a normal animal by giving an infusion of comp. F (5.2 $\mu\text{g}/\text{min.}$) and comp. B (1.0 $\mu\text{g}/\text{min.}$) appeared to increase the vascular response to Adrenalin at lower dose levels, but no changes were seen at the higher dose levels. Elevation of the steroid level in a normal animal produced a significant decrease in cardiac response at all dose levels of Adrenalin, but with Metopirone treatment a decrease in cardiac response was only seen at higher dose levels of Adrenalin. Therefore, Metopirone appears to act only on the adrenal cortex and lowers the circulating levels of adrenal steroids without altering the vascular response to Adrenalin.

NEURALLY INDUCED CONTRACTION OF NERVE TRUNKS IN APLYSIA. Felix Strumwasser (intr. by D. McK. Rioch). Walter Reed Army Institute of Research, Washington, D. C.

When a presynaptic nerve to the parieto-visceral ganglion of Aplysia californica is excited (electrically, mechanically, through peripheral receptors), the two long visceral nerve cords, connecting this ganglion with the remaining rostrally-located central ganglia, contract longitudinally. Such contractions of the visceral nerve cords can still be elicited when the parieto-visceral ganglion alone with its attached nerves is dissected from the animal and studied in a chamber. The effectors lie, at least in part, within the nerve trunks, for direct electrical stimulation of the isolated visceral nerve cords will also cause contraction. Since Aplysia alters its body form remarkably while locomoting and on noxious stimulation of the body surface, coordinated changes in nerve trunk length would presumably be adaptive by minimizing mechanical stresses due to sudden changes in body form. Perhaps such changes also occur in other organisms with rapid changes in body form but have been previously overlooked. The finding raises several fundamental questions as to the nature of the effector and the mechanism of its activation. The contraction is too large to be explained by the known volume changes in nerve with activity which is several orders of magnitude smaller. Histology of the nerve trunks does not reveal so far any obvious muscle fibers; elastic fibers are present but they are predominantly oriented in the cross-sectional plane. Conceivably, the satellite cells surrounding the nerve fibers could contract but then the orderly activation of such elements in association with the nerve impulse raises certain formidable questions.

THERMAL ELECTRODE BASED ON "PELTIER EFFECT." D. G. Stuart, L. H. Ott and F. C. Cheshire (intr. by E. Eldred). Univ. of Calif. School of Med., Los Angeles 24, Electronics Dept., Hughes Aircraft Co., Culver City and Veterans Administration Hospital, Long Beach, California.

When a direct current is passed between two dissimilar metals, there is a transfer of energy in the form of heat between the metals' junction and the surroundings ('Peltier effect'). Depending on the direction of current flow, heat is either absorbed or liberated by the junction, the reverse effect occurring at the opposite poles of the metals. We have used this principle to construct and test an electrode for cooling and warming small brain regions. A silver wire is connected to such a junction (between bismuth telluride, n-type and bismuth telluride, p-type) and inserted into the brain. Small brain regions can be warmed or cooled plus or minus 2°C. from normal temperature or heated excessively within 3-10 minutes, depending on junction temperature (a function of I) and the extent of thermal insulation along the silver wire. To evoke greater cooling, the junction metals have to be independently cooled, otherwise the increase in temperature at the opposite poles of the metals overwhelms the cooling effect at the junction. In this paper the construction, advantages and disadvantages of this type of electrode for localized cooling and warming of small brain regions in anesthetized and unanesthetized animals will be discussed and appropriate physiological measurements illustrated.

TEMPERATURE REGULATION IN MICE REANIMATED FROM DEEP HYPOTHERMIA.

F.N. Sudak and W.B. Essman* Albert Einstein Coll. Medicine, New York.

The ability of mice reanimated from deep hypothermia to regulate body temperature after brief cold exposure was assessed. Four groups of mice were initially exposed to cold air ($2.0^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$) for one hour. Hypercapnic anoxia was produced in 3 groups by enclosing the animals in sealed containers. The fourth group was kept in open metal cages. Following this procedure one hypercapnic, anoxic group and the caged control group were warmed until colonic temperatures reached normal range. The other groups were taken through a second stage of cooling until colonic temperatures were below 5°C . One group was immediately reanimated using intermittent positive pressure and radiant heat. The remaining group was reanimated, using this procedure, after it had been below 5°C . for 20 min. At successive intervals after reanimation, animals were exposed to cold air for 30 min. Ability to regulate body temperature was assessed by change in colonic temperature with cold exposure. Cage and jar control groups were able to maintain or increase temperature. The acutely hypothermic group was not able to regulate until 3 wks. after reanimation. The group kept below 5°C . for 20 min. showed impaired thermoregulatory ability for as long as 6 wks. following reanimation. Degree of temperature loss with cold exposure was a function of time since reanimation. Preliminary data on mice made hypercapnic in a high O_2 atmosphere and subsequently rendered hypothermic (20 min. below 5°C .) indicates a similar impairment in temperature regulation. The data suggest that deep hypothermia produces a transient change in the mechanisms responsible for temperature regulation, and anoxia probably does not account for thermoregulatory impairment. (Supported in part by Grants H-3836 and 2M-6418, USPHS)

COMPARATIVE ABSORPTION OF SQUALENE AND SQUALANE. R. Suzuki, P.V. Laakso, and A.C. Ivy, Dept. Clinical Science, Univ. of Illinois, and Chemical Laboratory, Bauer and Black Co., Chicago.

In a previous paper, it was reported that an average of 43.7% of the fed squalene is absorbed from the intestine in intact rats. It was suspected that the double bonds in the squalene molecule might in some way be related to its absorability. To obtain more information on this point, the absorability of squalane, the totally hydrogenated squalene, was studied in intact rats under conditions comparable to those of the previous experiment using the balance method. An average of 96.8% of 57.2 mg of squalane fed daily was recovered in the feces as a hydrocarbon fraction. The data will be discussed from the standpoint of the absorption of sterols in general.

VARIATIONS IN THE ELECTRIC RESISTANCE OF THE SKIN IN RELATION TO SWEATING. K. Takagi, T. Ogawa, E. Terada and M. Kobayashi (intr. by F. R. Steggerda). Department of Physiology, School of Medicine, Nagoya University, Nagoya, Japan.

Variations in the electric resistance of the skin (ESR) in relation to sweating were investigated on various parts of the body during each season of the year. The ohm-resistance between two silver plate electrodes was determined by using a vacuum tube volt-meter. A peculiar phenomenon was observed when measurements were made in a hot environment using conductive paste containing concentrated NaCl or KCl. The ESR on all skin areas other than the palm of the hand decreased with depression of sweating; however, when the conductive paste contained dilute saline, the ESR increased on all areas of the skin including the palm of the hand when depressions of sweating occurred. Under these conditions, the ESR decreases with enhancement of sweating. These observations can be repeated using non-polarized AgCl-NaCl electrodes. Furthermore, the resistance of a single sweat pore and non-glandular parts of the skin surface were recorded. Detailed relationships between variations in ESR and the rate of sweating were also investigated by means of continuous, simultaneous recordings of ESR and sweating rates.

IN VITRO STUDIES ON HUMAN UTERINE MUSCLE. Martin F. Tansy*, Atef W. Moawad*, and M. H. F. Friedman. Departments of Physiology and Obstetrics, Jefferson Medical College, Philadelphia, Pa.

Motor activities of muscle strips from the excised uterus of 10 pregnant and 17 non-pregnant women were studied. In the non-pregnant uterus only muscle segments taken from the anterior wall and fundus showed spontaneous activities but no area could be regarded as a motor "pacemaker." In the pregnant uterus spontaneous activity was uniformly absent from all regions. Pituitrin and epinephrine were equally effective stimulants of both pregnant and non-pregnant uterine muscle; the anterior wall muscle exhibited greater amplitude of contractions and higher tonus changes than did other regions. Acetylcholine, serotonin and barium chloride were effective stimulants of only the non-pregnant uterus. Pretreatment of the non-pregnant uterine muscle *in vitro* with relatively large doses of progesterone or estrogen made the muscle refractory to acetylcholine but the effects of pituitrin and epinephrine were not influenced.

THE ROLE OF THE VAGUS IN ANTRAL INHIBITION OF GASTRIC SECRETION

James C. Thompson and Harvey J. Lerner (intr. by Jonathan E. Rhoads)
Surgical Research Laboratory, Pennsylvania Hospital and University of
Pennsylvania School of Medicine, Philadelphia.

Previous studies from this laboratory (Journal of Surgical Research, July 1961) have demonstrated the release of a humoral agent, from the isolated, innervated gastric antrum irrigated with acid, that inhibits gastric acid production. The present work evaluates the importance of vagal antral innervation to this inhibitory mechanism. Two groups of studies were performed, in both of which serial cross-transfusions were carried out between pairs (A & B) of alert, non-anesthetized dogs. In group I, one of the pair (A) was prepared with an isolated innervated antrum, a Heidenhain pouch and an indwelling portal vein catheter; the other dog (B) had a Heidenhain pouch and a femoral vein cannula. Dogs in group II were identical except that the antrum of dog A was denervated. Gastric secretion was stimulated by feeding dog B 400 g. Pard. In test experiments, the antrum of dog A was irrigated with N/10 HCl; control studies were identical except that the antrum was irrigated with saline (pH 7.0) or not irrigated.

RESULTS: In group I, cross-transfusion with animals with acidified innervated antra resulted in an 80% inhibition of 4-hour Heidenhain pouch acid output (control=2.61 mEq., test=0.52 mEq.; average of 5 paired test-control studies). In group II, similar cross-transfusions with animals with acidified denervated antra resulted in a 78% inhibition (control=1.86 mEq., test=0.41 mEq.; average of 4 paired test-control studies). **CONCLUSION:** Vagal innervation of the antrum is not required for the production of an inhibitory hormone by the acidified antrum.

CHANGES IN INTESTINAL NET WATER MOVEMENT AND PHENOLSULFONPHTHALEIN ABSORPTION PRODUCED BY ETHYLENEDIAMINETETRAACETIC ACID.

C. S. Tidball and K. K. Peterson (intr. by C. A. M. Hogben).

Physiology Dept., The George Washington University, Washington, D. C.

Spontaneous net water movement in a 30 cm exteriorized canine loop preparation under pentobarbital anesthesia varied from -10 ml/hr (absorption) to +15 ml/hr (secretion) when the lumen of jejunal segments was perfused with a balanced physiologic saline at a rate of 1.8 ml/min. Subcutaneous injection of atropine, starting at 0.1 mg/kg with a doubling of the dose for each subsequent hour, shifted the net water movement toward absorption and values as high as -20 ml/hr were obtained. Incorporation of 10 mM/l moniodoacetic acid in the perfused solution shifted the net water movement toward secretion and values as high as +25 ml/hr were observed. Phenolsulfonphthalein (phenol red) was absorbed to a small extent (clearance of less than 2 ml/hr) during intestinal secretion. With increasing levels of net water movement from lumen to blood, phenol red absorption rose (clearance up to 4 ml/hr). With the addition of 25 mM/l ethylenediaminetetraacetic acid (EDTA) to the perfused solution, the water movement in 10 experiments was changed from a mean of -4.6 ml/hr to a mean of +15.1 ml/hr. The difference in osmolarity between the two solutions was too small to account for this change. The absorption of phenol red was uniformly increased in the 10 experiments with EDTA (clearance up to 10 ml/hr). The mean clearance value for these experiments was 4.5 ml/hr. The mean clearance value of 9 experiments without EDTA but with water movements in the same range was 0.9 ml/hr. Thus the ability of a chelating agent to enhance the intestinal absorption of a strong acid of moderate molecular weight is demonstrated.

FACTORS IN TENSION-AREA RELATIONSHIPS OF PULMONARY SURFACE FILMS.
D. F. Tierney and R. P. Johnson (intr. by J. A. Clements). Army
Chemical Center, Maryland.

We prepared pulmonary surface films by mincing dog lung in saline (saline extracts) and by spreading lyophilized pulmonary edema foam on distilled water. We collected the foam by a modification of Bondurant's method, (J. Clin. Invest. 39: 973, 1960) using saline perfusion of the pulmonary artery. Preparations from normal lungs usually gave minimal surface tension below 10 dynes/cm when the film-covered surface was compressed to 1/5th of the original area. Some films required compression to less than 1/5th of the original area before tensions below 20 dynes/cm developed. If the subphase was acid (pH 3-4) the films developed low tensions with less compression. Addition of petroleum ether extracts of dried tissue or of the edema foam or oleic acid, prevented the development of surface tension below 20 dynes/cm. We confirmed the observation of Finley et al (The Physiologist 3: 56, 1960) that whole lung extracts failed to exhibit very low tensions (below 20 dynes/cm) if the pulmonary artery had been occluded. We found minimal surface tension of 4-14 dynes/cm however, when the lyophilized foam from the same lungs was used. Failure to demonstrate very low surface tension by the saline extract method does not permit the conclusion that highly surface active material is absent from the lung. Substances are present in the lung which can prevent the development of very low surface tensions.

THE RELATIONSHIP BETWEEN CHEST EXPANSION AND FRACTIONAL LUNG VOLUMES.
E. Y. Ting and P. E. Garrell (intr. by M. H. Williams, Jr.). Albert
Einstein College of Medicine, New York.

Chest circumference was measured with a pneumograph at a level just below the nipple line in 10 normal non-obese male subjects. Measurements were made while the subject breathed in and out of a spirometer permitting recording of the circumference at five different lung volumes including the residual volume, functional residual capacity and total lung capacity.

In the sitting position the chest expansion was found to be linearly related to the inspired volume throughout the full range from residual volume to total lung capacity when this volume was expressed as a percent of the vital capacity of the individual. The slope of this relationship was similar among the 10 subjects (13.5% of vital capacity per cm chest expansion, $SE \pm 0.75$). This relationship was unaffected by positive pressure breathing (+5 to +20 cm) or by performance of the Valsalva and Muller maneuvers.

In the standing position this relationship became curvilinear. Although the total expansion exhibited between the residual volume and total lung capacity was not significantly different from that measured while sitting, chest movement was significantly less during inspiration of the first 80% of the vital capacity and significantly greater during inspiration of the final 20% of the vital capacity.

In the supine position the total chest expansion was again not significantly different from that exhibited in the sitting position for the full range of the vital capacity. However, a shallow S-shaped curve related the expansion to the inspired volume.

THE EFFECT OF MUSCULAR ACTIVITY ON THE HEART RATE OF THE RAT.

C. M. Tipton (intr. by F. R. Steggerda). Department of Physiology, University of Illinois, Urbana, Illinois.

The fact that sustained muscular activity results in a resting bradycardia in humans is well documented. The present study was undertaken to investigate the cardiac response of rats under similar conditions. Heart rate data were collected from animals with subdermal electrodes. Exercise was simulated with a motor driven revolving treadmill at speeds varying from 0.33 miles per hour to 1.72 miles per hour. Distances varied from 0.33 miles per day to 2.00 miles per day. Only results from animals who completed a ten week training period were compared to non-exercising controls.

Data obtained showed that the hooded rat has a greater capacity for muscular activity than the albino. With the hooded rat there is a tendency to show a greater reduction in resting heart rate when compared to non-exercising animals. Resting data from the exercising and non-exercising albino showed little group differences. Vagal sectioned animals resting heart rate data also failed to reveal major differences between the exercising and non-exercising animals. Heart hypertrophy was evident in both species but was not present in exercising animals with a sectioned right vagus nerve. Plasma sodium and potassium levels showed little differences between the various groups.

END PRESSURE VERSUS SIDE PRESSURE IN THE PULMONARY ARTERY. Robert A. Tolman*, Hampden C. Lawson and James C. Moore. Univ. of Louisville School of Med., Louisville, Ky.

Simultaneous end and side pressures were recorded by means of double lumen catheters or double lumen metal sounds placed in the pulmonary arteries of anesthetized, open-chest dogs. The difference between these two pressures was measured at peak systolic and at diastolic levels, and the pressure difference which would occur at mean pulmonary artery pressure was calculated. Since the catheters faced downstream, the end pressure was lower than the side pressure by an amount which was related to the velocity of flow or kinetic energy of the blood passing through the pulmonary artery. Measurements of such differences at peak systolic pressures during the resting state varied between 2 and 8 mm Hg. The magnitude of the values was influenced somewhat by the position of the catheter in the vessel. Pressure differences at peak systolic and mean pressures rose markedly following epinephrine injection or stenosis of the pulmonary artery. From the results obtained, it would appear that pressures recorded from the pulmonary artery, by passing an open-end catheter into it, are subject to errors which increase as pulmonary arterial flow increases. (Supported by U.S.P.H.S. Grant H-5619.)

SOME EFFECTS ON THE LUNGS OF BLOOD FROM A PUMP OXYGENATOR. W.H. Tolley, T.N. Finley and R. Gardner (intr. by I. Edelman). Cardiovascular Research Inst. and Dept. of Pediatrics, Univ. of Calif. Med. Center, San Francisco.

We reported previously that congestive atelectasis following cardiopulmonary bypass resembles that noted in the respiratory distress syndrome of the newborn. In both, when we compressed a lung extract on a modified Wilhelmy balance, the surface tension (ST) did not decrease to less than 18 dynes/cm (normal 1-8 dynes), and the normal hysteresis loop of ST plotted vs. surface area (SA) was reduced. We bled donor dogs, pumped their blood through an Abbott Pulmo-pak oxygenator with a Kay Anderson pump for 1-12 hours and then transfused the blood into normal dogs. Four dogs transfused with blood oxygenated for 4 hours or longer died within 12 hours with respiratory distress. Their lungs were atelectatic, and there was intra-alveolar hemorrhage. The minimal ST of compressed extracts of these lungs was 18-22 dynes/cm. ST of lung extracts from 2 dogs receiving blood oxygenated less than 4 hours was 12 and 14 dynes/cm. We mixed extracts of 6 normal lungs with 5 ml of normal whole blood or 5 ml of the blood described above. In every instance, the minimal ST of the compressed material was 15-22 dynes/cm when pumped blood was added and 2-6 dynes/cm when normal blood was added. (Supported in part by U.S.P.H.S. Grant H-4247.)

EFFECT OF ANTIDIURETIC HORMONE UPON WATER ABSORPTION IN THE ASCENDING COLON OF THE DOG. Eugene J. Towbin and Carl B. Ferrell. (intr. by J. K. Sherman). V.A. Hosp., Little Rock, and Depts. of Med. and Physiol., Univ. of Ark. School of Medicine.

A growing body of evidence indicates that antidiuretic hormone has a role in the control of water movement at non-renal sites. We undertook a study of the ascending colon, a known site for water absorption. The brain anterior to the pons was removed from 15 anesthetized dogs. Three to four hours following surgery a water diuresis was induced and the ascending colon was intubated just beyond the ilio-cecal valve and some 10 cm. distally, thereby making an isolated loop thru which warmed isotonic saline containing tritiated water flowed at a rate of 7.5 cc per minute. A mesenteric vein draining this loop was catheterized and radioactivity of this venous plasma was measured by liquid scintillation counting. Intraluminal pressure of the gut-loop was recorded during 8 of the experiments. Antidiuretic hormone levels in the systemic plasma was measured by toad bioassay and shown to be low during the initial phase of the experiment and elevated by the infusion of 500 mU of Pitressin over a 10 minute period. In 7 experiments definite increase in absorption, 25 to 100% increase in venous radioactivity, immediately followed the Pitressin infusion. In 3 experiments increase in absorption was delayed 10 minutes following Pitressin. Three experiments showed changes of questionable significance and 2 showed no change. Blood flow thru the loop was temporarily reduced by the Pitressin infusion but neither this factor nor minor changes in motility seem to account for the total change in water absorption.

SPONTANEOUS SLOW WAVE RHYTHMICITY IN THE VENTRAL TEGMENTAL AREA UNDER BARBITURATES. Bruce Tremblay and Jerome Sutin (intr. by A. Brodish)
Department of Anatomy, Yale University School of Medicine.

Rhythmic 6-8 per second high voltage activity has been observed in 15 cats in a restricted region of the mesencephalon under barbiturate anesthesia. This region is situated ventral to the red nucleus and encompasses the interpeduncular nucleus and ventral tegmental area of Tsai. This phenomenon is not seen in conscious animals, in normal sleep, or under non-barbiturate sedation, and bears no apparent relationship to cortical spindling. Stimulation of the rostro-medial portion of the globus pallidus at 1-2 per second blocks or disrupts the rhythmic activity. Evoked responses in the same tegmental area are seen following stimulation of the thalamic ventralis anterior nucleus and the immediately subadjacent dorsal hypothalamus. The evoked response, along with the rhythmicity, turns over in polarity at a point lateral to the dorsal margin of the interpeduncular nucleus. Repetitive stimulation of ventralis anterior at 3-8 per second drives the tegmental rhythm at the stimulus frequency. This driven activity is distinct from the evoked response. The evoked potential is superimposed upon the 6-8 per second spontaneous rhythm whereas the driven activity replaces it. Ablation of the cortical projection area of ventralis anterior does not alter the evoked potential or the spontaneous activity in the mesencephalon. These observations suggest a functional interrelationship between the globus pallidus, ventralis anterior, and the ventral tegmental area of the mesencephalon.

THE HEPATIC INACTIVATION OF ENDOGENOUS ANTIDIURETIC HORMONE. Shunichi Usami and Shu Chien (intr. by Magnus I. Gregersen). Department of Physiology, Columbia University, New York City.

In dogs under Nembutal anesthesia (33 mg/kg), the left hepatic vein was catheterized with the aid of fluoroscopy. The hepatic blood flow was estimated from the clearance and extraction of bromsulfalein. Ten to 30% of the total blood volume was removed from a femoral artery in order to elevate the circulating antidiuretic hormone and to alter the hepatic blood flow. One-half to 1 hour after the hemorrhage, blood samples were taken simultaneously from the hepatic vein and a femoral artery, and the plasma was used for the assay of antidiuretic activity in rats (Dicker, J. Physiol., 122: 149, 1953). The ADH concentration of the hepatic venous sample was consistently lower than that in the arterial sample. The hepatic extraction ratio $\{ (A-V)/A \}$ of the endogenous ADH averaged 0.30 and tended to become lower when the hepatic blood flow was reduced significantly. Over a range of hepatic blood flow from 50 to 300 ml/min/10 kg, there was a positive correlation between the hepatic ADH clearance (ml plasma/min) and the hepatic blood flow. The posthemorrhage decrease of the hepatic ADH clearance was greater than that of the plasma volume, and the ratio (hepatic ADH clearance/plasma volume) was reduced after bleeding. Our findings indicate that: (1) ADH is inactivated in the hepatic circulation, (2) the rate of hepatic inactivation of ADH is directly related to the hepatic blood flow, and (3) the posthemorrhage elevation of the circulating ADH concentration is due at least in part to a decreased hepatic inactivation of this hormone. (Supported by Grant H-6139 from the National Heart Institute, National Institutes of Health).

STUDIES ON THE RENAL EXCRETION OF CHOLINE IN THE DOG. Arthur J. Vander. Dept. of Physiology, School of Medicine, The University of Michigan, Ann Arbor, Michigan.

Experiments on dogs, utilizing clearance and stop-flow technics, demonstrated that choline is reabsorbed and secreted by the proximal tubule, both processes being active. These processes seem to occur simultaneously, net reabsorption predominating at normal plasma concentrations, net secretion often becoming manifest when plasma choline was elevated. Secretion could be inhibited by either cyanine dye #863 or a hemicholinium. Transport rates were extremely variable in different animals, and constant in a single animal only for several hours. The distal nephron was found to be impermeable to choline. The degree of proximal permeability could not be quantitated. Passive transport did not appear to be significantly involved in choline excretion.

THE EFFECT OF AUTONOMIC NERVE STIMULATION ON THE ELECTRICAL AND MECHANICAL ACTIVITY OF THE INTESTINAL SMOOTH MUSCLE. G. L. VanHarn (intr. by C. L. Prosser). Department of Physiology, University of Illinois, Urbana, Illinois.

The electrical activity and mechanical activity of segments of cat small intestine are modulated in response to autonomic nerve stimulation. The intestine responds to repetitive (5-10/sec.) vagus stimulation with a depolarization and an increase in spike and mechanical activity. The response to repetitive stimulation (1-10/sec.) of the sympathetic trunk or splanchnic nerve is either an excitation or an inhibition. When the intestine is active and spike potentials are present, sympathetic nerve stimulation inhibits the spike potentials, mechanical activity and produces a hyperpolarization. When the intestine is atonic and no spikes are present, sympathetic nerve stimulation causes a depolarization and initiates spike and mechanical activity. Increasing the intraluminal pressure brings an atonic intestine into activity, after which sympathetic nerve stimulation will produce an inhibition. After treatment of the cat with reserpine (2 mg/kg.) for two successive days, sympathetic nerve stimulation gave only an excitatory response. It is difficult to observe blockage of the excitatory response to sympathetic nerve stimulation by atropine and scopolamine. These cholinergic blocking drugs will inhibit intestinal motility at lower concentrations than is required to block the response to nerve stimulation. At rather high concentrations, Dibenzyliline and Ismelin, adrenergic blocking drugs, will block the inhibitor response to nerve stimulation. The dual response of the intestine to sympathetic nerve stimulation appears to be due to two transmitters. The dominant response seems to be determined by the level of excitability of the intestinal smooth muscle.

THE EFFECT OF SULFADIAZINE FEEDING IN BUB MICE.

Huberta E. van Heyningen (intr. by J. Walter Wilson)

Department of Biology, Brown University, Providence, R. I.

A 0.5% sulfadiazine containing diet was fed to BUB mice for 0, 3, 6, 9, 12, and 15 days. At each of these intervals the I^{131} uptake and retention were determined, as well as the chromatographic distribution of the radiiodinated compounds in the thyroid; routine H & E slides were also prepared. The initial effect of sulfadiazine consists of a decreased I^{131} uptake, an increased I^{131} output rate and an increased histological activity of the thyroid; the MIT/DIT ratio is elevated and no thyroid hormone can be detected. During the second week of sulfadiazine feeding there seems to be a new steady state, in which the I^{131} uptake, the I^{131} output rate and the histological activity are higher than normal; the MIT/DIT ratio is still elevated and a subnormal percentage of thyroid hormone is present. These findings suggest a new equilibrium in the pituitary-thyroid axis. From the radiochromatographic distribution in the sulfadiazine treated thyroid it is concluded that sulfadiazine affects the synthesis of thyroid hormone by inhibiting the iodination reaction from MIT to DIT to a stronger extent than the iodination of tyrosine to MIT, as well as by inhibiting the coupling reaction to form thyroid hormone.

Supported by Grants CRT-5007 and C-510 from the National Cancer Institute, U.S.P.H.S.

HYPERTROPHY OF VARIOUS PORTIONS OF THE HEART BY HYPOXIA. Edward J. Van Liere, Barbara Bangh* and David W. Northrup. Dept. of Physiology, W. Va. Univ. Med. Center, Morgantown, W. Va.

Twenty-four female and 24 male albino rats were exposed to hypoxia (303 mm. Hg barometric pressure) for eight hours daily for 24 days. At the end of this period both control and experimental animals were weighed and killed. The hearts were removed and weighed uniformly and then separated into four sections: atria, left ventricle, right ventricle, and interventricular septum. Ratios of these weights to the individual body weights were determined, averages calculated and the t-test performed. The percentage increases in females and males were respectively as follows: total heart weight, 23 and 36; left ventricle, 27 and 33; right ventricle, 54 and 54; atria, 23 and 36; and septum, 0 and 24. All of these differences were statistically significant. It is of interest that there was a pronounced hypertrophy of the right ventricle; this would be expected since it is known that hypoxia produces a pulmonary hypertension.

POTASSIUM EFFECTS DURING OUABAIN TOXICITY. Mario Vassalle*, Kalman Greenspan* and Brian Hoffman. Dept. of Physiology, SUNY, Downstate Medical Center, Brooklyn, N. Y.

Potassium is used to treat arrhythmias caused by toxic concentrations of digitalis. Since different cardiac tissues show selective K sensitivity, its site of action is uncertain. In anesthetized dogs intoxicated by Ouabain, graded vagal stimulation was used to study automaticity of ventricular specialized tissues before and after infusion of KCl. The first change due to KCl was abolition of multifocal ventricular extrasystoles and fast ventricular rhythm caused by Ouabain. Subsequently, ventricular rate during vagal stimulation decreased progressively until there was no escape. Late during KCl infusion P waves disappeared from the ECG although atrial activity might still be recorded through a cavity lead. At this stage the QRS complex was a large, broad diphasic wave; however, vagal stimulation still caused arrest. When all recorded spontaneous activity had disappeared, direct stimulation of the ventricles elicited electrical and mechanical responses. It appears that an early effect of K is depression of automaticity of ventricular Purkinje fibers and that this is one of the mechanisms of the therapeutic action of K in digitalis toxicity. The large ventricular complexes seen late during K infusion result from disturbed conduction of impulses originating in a supraventricular pacemaker and are not due to an idioventricular rhythm since they disappear on vagal stimulation. Potassium induced cardiac arrest results from suppression of pacemaker activity or failure of conduction in specialized tissues and not from depolarization of ventricular muscle; this is shown by the response to direct ventricular stimulation. These studies confirm the in vitro demonstration of selective K^+ sensitivity of cardiac tissues. (Supported in part by a grant from the Am. Heart Assoc. #AH59G48 and a U.S.P.H. grant #HT55282(C1)).

THE HEPATO-SPLANCHNIC FACTOR IN ENDOTOXIN SHOCK. J. A. Vick*, K. C. Burnes*, M. M. Jordan*, L. F. Wittmers* and L. B. Hinshaw, Dept. of Physiology, University of Minnesota, Minneapolis, Minnesota.

Previous work has suggested that the gastro-intestinal tract plays a major role in the development of irreversible endotoxin shock in the dog. Our data parallel the reports that intact dogs given endotoxin show hypotension, hemoconcentration, hemolysis, acidosis and have a mean survival time of 10 hours. The present study is concerned with the role of the liver and intestine in endotoxin shock. Two groups of dogs were eviscerated in a one stage operation, one with the hepatic artery ligated, the other with the hepatic artery patent. The totally eviscerated dogs receiving endotoxin had a shorter survival time than sham controls and intact animals. Eviscerated dogs with the hepatic artery intact survived a significantly longer time than totally eviscerated animals. The results of these studies suggest that the liver has a protective role in endotoxin shock. It would also appear that the intestine is not essential for the development of endotoxin shock since totally eviscerated dogs die more quickly than intact animals. These findings are consistent with the view that the intestines are not responsible for the development of the irreversible phase of shock due to endotoxin, which agrees with our data obtained from parallel studies on the cat, rabbit and monkey. Current investigations in this laboratory have suggested other possible explanations for the development of the irreversible phase of endotoxin shock. (Supported by a grant from the Minnesota Heart Association).

HOW DOES ACTH REDUCE PROTEINURIA IN NEPHROSIS? Khalil G. Wakim, Bernard F. McKenzie,* Warren F. McCuckin,* Arnold L. Brown, Jr. and Archie H. Baggenstoss.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

On finding that ACTH administered to nephrotic, pediatric patients ameliorated their clinical condition and reduced their proteinuria and consequent hypoproteinemia, we became interested in determining the mechanism of action of ACTH in nephrosis. Experimental nephrosis was produced in dogs and rats by the administration of rabbit anti-kidney serum. ACTH was administered intramuscularly before, during and after intravenous injection of nephrotoxic serum (NTS). Chemical and electrophoretic studies were made on blood and urine to determine proteins, lipoproteins, glycoproteins, and total lipids before, during, and for long periods after administering NTS and ACTH. Similarly light and electron microscopic studies were made on kidney specimens before and at intervals after NTS and ACTH administration. The following salient findings were obtained: Proteinuria and hypoproteinemia became evident within hours after NTS administration and were most marked about the sixth or seventh day. β -glycoproteins gradually disappeared from the blood and appeared in the urine. β -lipoproteins increased in the blood. ACTH administration reduced the proteinuria and the hypoproteinemia, prevented reduction of β -glycoproteins and elevation of β -lipoproteins in the serum, and improved the clinical picture. Electron microscopic studies revealed that ACTH reduced and slowed down the glomerular damage induced by NTS, which included disruption of the endothelial lining, separation of this lining from the basement membrane, irregular thickening of and deficiencies in the basement membrane, and fusion of the podocytes. (Supported by NIH Grant A-2045.)

BIGEMINAL RHYTHM AND APPARENT ELECTRICAL ALTERNATION IN THE DOG HEART. Sheppard M. Walker. Univ. of Louisville School of Med., Louisville, Ky.

Some effects of central stimulation of the sympathetic nervous system on the electrocardiogram have been observed. The stimulation was obtained by intracisternal injection of M/6 potassium phosphate solution at pH 7.6. Injection of 0.06 to 0.09 cc of this solution per kg produces acceleration of heart rate and apparent electrical alternation. The alternation may involve the T wave alone or it may involve the R wave and the T wave. While alternation is still present scattered ventricular ectopic beats appear. The scattered ectopic beats invariably have an odd number of regular beats between them. Subsequently, the ectopic beats alternate with normal beats as typical bigeminal rhythm. The ectopic beat is coupled with the preceding normal beat. It is concluded that the apparent electrical alternation, which precedes the bigeminal rhythm, is in reality due to ventricular fusion of coupled ectopic beats with normally conducted beats. (Aided by Grant H-697(C11) from the National Heart Institute and by a grant from the American Heart Association.)

REGULATION OF CARDIAC OUTPUT DURING EXERCISE. Homer R. Warner.

Dept. of Physiology, Latter-day Saints Hospital and University of Utah, Salt Lake City, Utah.

The cause-and-effect relationship among the variables in the circulation has been investigated by observing quantitatively the time-course of each of these variables as the system was changed from one state to another. Pressure and flow in the ascending aorta, pressure in the right atrium, and electrocardiogram were recorded on magnetic tape from indwelling transducers in a dog running on a treadmill, the speed of which was varied stepwise and sinusoidally. These variables were then reproduced from the tape and fed to an analog computer where beat-by-beat values for cardiac output, heart rate, stroke volume, mean arterial pressure, peripheral resistance, and mean right atrial pressure were calculated and plotted as a function of time. Resistance calculated as the ratio of mean arterial pressure to cardiac output falls to one-half of its resting value within five seconds after a step increase in treadmill speed while cardiac output and heart rate rise to a new plateau in twenty seconds. Mean arterial pressure falls transiently and then rises back to or above its control level as cardiac output reaches its new plateau. From these observations it is postulated that the increased cardiac output that accompanies exercise is mediated, at least in part, by pressoreceptors, which are activated by a fall in arterial pressure due to local vasodilation in muscle.

PROPAGATION OF THE ACTION POTENTIAL IN THE NEURON OF THE CRAYFISH STRETCH RECEPTOR ORGAN. Yoshiaki Washizu* and Carlo A. Terzuolo. Department of Physiology, University of Minnesota, Minneapolis, Minn.

It has been found that in the neuron of the stretch receptor organ of crayfish the potential change recorded extracellularly from the cell soma during impulse activity is not the second derivative of the action potential recorded simultaneously from inside of the cell body. Therefore the presence of a large negative phase in the extracellular potential does not prove that the soma membrane produces an action potential. Further investigation of the problem, using several approaches, has led to the following conclusions: 1) The intracellularly recorded spike is mostly due to activity of the portion of the soma membrane close to the axon, the dendrite being the major source for this current. 2) The external zero isopotential surface moves during the intracellularly recorded action potential. This results from electrotonic spread rather than from propagation of impulse. It is not possible to exclude, however, that some portion of the soma membrane, possibly close to the origin of dendrite, might fire. 3) The region of membrane sensitive to stretch and responsible for the generator potential is never invaded by the action potential.

EFFECTS OF EXERCISE ON THE BLOOD GAS RELATIONSHIP OF THE DOG.

Ronald L. Wathen*, Howard H. Rostorfer, and Jerry Newton*. Dept. of Anatomy-Physiology, Indiana University, Bloomington, Ind.

Arterial and mixed venous blood samples were obtained from normal dogs during rest and in response to several grades of work on a motor driven treadmill. The blood samples were drawn through an in-lying needle in the left exteriorized carotid artery and a polyethylene catheter in the right ventricle. All samples were drawn during the 'steady-state' and were analyzed directly for O_2 and CO_2 contents, O_2 capacity, pO_2 , pCO_2 , and pH. The pO_2 , pCO_2 , and pH were corrected to body temperature. On the average, the data show that the arterial CO_2 content and pCO_2 can be expected to fall as much as 26.3 and 27.4 per cents, respectively, from rest to strenuous work. Concomitantly, arterial pH increased an average of 0.05 pH units, confirming that the dog incurs a respiratory alkalosis during exercise. Arterial O_2 content, pO_2 , and O_2 saturation remained the same or increased slightly from rest to hardest work. Venous blood, on the other hand, exhibited a relative constancy in CO_2 content, pCO_2 , and pH, while venous O_2 content, pO_2 , and O_2 saturation decreased progressively with increased work rate. Body temperature did not show a linear relationship to work rate, but increased only generally with increased exercise. Since venous pCO_2 , CO_2 content, and pH at all levels of work remained near resting values, it would appear the hyperpnea of exercise in the dog, regardless of its cause, results in a regulation of the CO_2 relationship in either active tissues or venous blood. In spite of the fact that the respiratory centers are in the alkalemic environment of the arterial blood during exercise, the increase in the A-V CO_2 difference is brought about by lowering the CO_2 of the arterial blood. (Supported by NSF grant 41-234-56.)

SYNAPTIC ORGANISATION OF MOTOR CORTEX. Donald E. Watson* and Vahe E. Amassian. Albert Einstein College of Medicine, New York, N.Y.

Single pyramidal axon activity was recorded at the level of C1 - C2 in locally anesthetized or barbiturate anesthetized cats, using tungsten microelectrodes. Such activity was identified by demonstrating typical direct activation latencies (0.9-1.5 msec) following a 0.15 msec stimulus to a discrete focus on contralateral cortex. When the cortical stimulus was reduced just below the threshold for consistent direct activation, the latency of the unit "jumped" between direct and indirect values. The jumping interval ranged from 1.2 - 1.6 msec in different pyramidal units, suggesting that a disynaptic linkage is interposed between direct and indirect activation. Repetitive discharge following stronger cortical stimuli has a first interspike interval equal to the jumping interval, indicating that the period of the jump is not due to a threshold effect such as a long response time at a single cortical synapse. Thus the corticospinal neuron receives impulses from a neuron which is not readily excited by surface electrical stimulation. The compact Golgi type II cell is most likely the responsible element and is synaptically excited by a cortical neuron which is readily excited by surface stimulation. The latter neuron is presumably elongated, but has little or no descending projection within white matter because under barbiturate anesthesia, a multiunit pyramidal 'D' wave, but insignificant I waves are elicited by stimulation deep below the cortex. The organisational unit consists of corticospinal neuron-Golgi type II neuron - elongated, nonprojecting cortical neuron and it is much more resistant to barbiturate anesthesia than the coupling between specific afferent input and pyramidal discharge. (Aided by a grant from the United Cerebral Palsy Research and Educational Foundation).

RESPONSES IN DEPOLARIZED VASCULAR SMOOTH MUSCLE AND FREEZE-THAW RELAXATION OF ARTERIES. William H. Waugh, Dept. of Med., Univ. of Kentucky Coll. of Med., Lexington, Ky.

Segments of canine small arteries were perfused with "physiologic" and with K-rich (100-148 mM/L.) buffered electrolyte solutions. Intense vasoconstriction resulted with K-rich perfusion and responses to epinephrine and electrical current were not abolished despite apparently complete smooth muscle depolarization (confirming Evans et al., 1958, for non-vascular smooth muscle preparations). Freeze-thaw produced arterial relaxation and prevented both the K-induced contracture and the constrictor responses to epinephrine and electrical current. ATP added to 20 mM/L. and extra Ca ions in the perfusate failed to produce contraction of the freeze-thaw vascular preparation. It is concluded that the excitation-coupling-contractile response of vascular smooth muscle, which is abolished by freezing and rapid thawing, is probably largely initiated not by a membrane potential change but by an ionic permeability change or some other means.

(Supported by grants H-6092 and H-6347 C1 from the National Heart Institute, P.H.S.)

THE EFFECT OF SURFACTANTS UPON THE RUBIDIUM EFFLUX FROM FROG SCIATIC NERVES. George D. Webb* and Raymond R. Walsh. Physiology Department, University of Colorado School of Medicine, Denver, Colorado.

Employing isotopic tracer techniques, desaturation curves were determined for frog sciatic nerves that had been incubated in buffered frog Ringer's containing a trace of Rb^{86} . The efflux of Rb^{86} , like that of potassium, is rather slow; it is, however, accelerated slightly in the presence of the nonionic surfactant, Tween 20. The efflux is increased appreciably by the cationic surfactant, cetylpyridinium, and the anionic surfactant, lauryl sulfate. A very marked increase in Rb^{86} efflux is effected by Aerosol OT and cetyltrimethylammonium, anionic and cationic surfactants respectively.

Experimental Group	$t_{1/2}$ (50% desaturation, in minutes)
Normal control	ca. 540
Tween 20	430
Lauryl sulfate	87
Cetylpyridinium	88
Aerosol OT	49
Cetyltrimethylammonium	46

There is a rather good correlation between the action of the various surfactants in blocking axonal conduction and their effect upon Rb^{86} efflux. The results from our experiments are consistent with the hypothesis that surfactants, like cetyltrimethylammonium, exert disruptive or dispersive actions upon various permeability barriers in a whole nerve trunk, such as the frog sciatic nerve (Am. J. Physiol. 197:547, 1959). (Supported by USPHS Grant B-2772.)

CARBOHYDRATE ENZYME LEVELS IN KIDNEY. George Weber (intr. by Sidney Ochs). Indiana Univ. School of Med., Indianapolis, Ind.

The object of this study was to investigate the presence and activities of enzyme systems involved in glycolysis, gluconeogenesis and glycogenesis in the kidney. Rat kidney cortex homogenates were prepared in isotonic KCl and the supernatant fluid was obtained by centrifuging the homogenates at 100,000 g for 30 minutes at 0°C. Glucose-6-phosphatase was measured in the homogenate; the other enzymes were measured in the supernatant fluid. There were 275 million cells in one gram kidney cortex. Glucose-6-phosphatase, fructose-1,6-diphosphatase and phosphohexoseisomerase were in the same activity range as found in the liver. However, only very low activity was found for the phosphoglucomutase reaction which was less than 10% of hepatic values. The presence of powerful specific phosphatases is in line with the gluconeogenic ability of the kidney. The weak phosphoglucomutase activity may explain, partly at least, the lack of kidney glycogen deposition after cortisone administration which leads to extensive glycogen storage in the liver. Various key carbohydrate enzyme systems were studied in rat kidney cortex and it appears that the activity of these enzymes can be correlated with the overall carbohydrate metabolism of this tissue. (Supported by United States Public Health Service (CY-5034).

INDIVIDUAL CHROMATOGRAPHIC PATTERNS OF HUMAN GASTRIC JUICE. Jack D. Welsh*, Lois Russell* and Stewart Wolf. Dept. of Medicine, Univ. of Oklahoma and the Oklahoma Medical Research Foundation, Okla. City, Oklahoma.

The method of chromatographing the large molecular components of gastric juice on an Amberlite resin column (Richmond et al, 1957) has been modified and adapted to individual specimens. A more rapid and more complete separation of protein and hexose containing peaks has been achieved. As with the older method, pepsin, gastricsin and blood group substance A have been concentrated in separate single fractions. In addition, blood group substance B was found to be concentrated in the same fraction as substance A. The size of the two proteolytic peaks, II and III, reflected approximately the proteolytic activity of the two enzymes, pepsin and gastricsin. Moreover, the size of the 6 protein-containing and 3 hexose-containing peaks of the eluate correlated in a striking way with the concentration of hydrochloric acid in the original specimen. There was a positive correlation between the acid and the area of individual peak II (pepsin) and peak III (gastricsin). However, there was an inverse correlation with the protein peak IV. There was also a negative correlation between the original acid and the total hexose eluted and the hexose in peak I, although there was a positive correlation of the acid with the hexose in peak V. The patterns were easily compared. Those obtained from the same subject under uniform circumstances were nearly identical.

INSULIN-LIKE ACTIVITY IN VARIOUS TISSUES OF DEPANCREATIZED DIABETIC DOGS. J. E. Whitney and O. E. Cutler*. Department of Physiology, School of Medicine, University of Arkansas, Little Rock, Ark.

We have recently demonstrated insulin-like activity (ILA) in a variety of malignant tissues and in a few instances in non malignant tissues from human patients. This work has been followed by an examination of the ILA content of tissues from normal and depancreatized dogs. All animals were lightly anesthetized with Nembutal and killed by exsanguination. The tissues were rapidly removed and quickly frozen. Five gm. portions of tissue were extracted by the method of Pettinga (Biochem. Preps. vol 6, p. 28, 1958) and tested for ILA by the ability of the fraction to stimulate glucose uptake of both hemidiaphragms and epididymal fat pads from fasted rats. Extracts of both normal and diabetic brain, heart, kidney and lung have consistently stimulated the glucose uptake of both fat pads and hemidiaphragms. Stimulation of glucose uptake has been obtained occassionally with extracts of liver, muscle, spleen and skin. The material responsible for the ILA has not, as yet, been identified. Supported by NIH Grant A-1535.

THE EFFECT OF SEVERAL 5-HYDROXYINDOLE DERIVATIVES ON RED BLOOD CELL CHOLINESTERASE. J. W. Wiggs* and M. H. Aprison
Inst. Psychiatric Res. Indiana Univ. Med. Center, Indianapolis, Ind.

Recent studies (Fed. Proc. 19, 275, 1960) have shown that serotonin (5-HT) inhibits brain and red blood cell cholinesterase (ChE). Since 5-HT is actively metabolized, a study of the effect of 5-hydroxytryptophan (5-HTP) and 5-hydroxyindole acetic acid (5-HIAA) seemed in order. The variation in inhibitory effect of 5-HTP, 5-HT, and 5-HIAA indicated that the charge distribution on these indoles was the determinant of their action upon ChE. To elucidate the effect of the charged groups on the indole molecule, the following derivatives, together with 5-HT, 5-HTP, and 5-HIAA were tested against ChE at pH 7.35, 37°C, and with ACh at $1.5 \times 10^{-3}M$ (listed according to decreasing inhibitory effect): 5-HT, bufotenin, 5-HIAA, 5-methoxytryptamine, N-acetyl-5-methoxy-tryptamine and 5-HTP. Kinetic studies reveal that the inhibition noted was of the "mixed" type similar to that described by Krupka and Laidler (J. Am. Chem. Soc. 83, 1445, 1961). The compounds exhibiting the strongest inhibitory properties possessed charge distributions most similar to ACh. Studies with 5-HTP indicate that in the presence of ACh, but without enzyme, the pH of the reaction mixture drops. In our assay this is indicative of hydrolysis of ACh. The theoretical significance of these findings will be discussed. Supported by grant MY 3225 from the National Institute of Mental Health and grant PX-254-3, Public Health Service.

PULMONARY HYPERTENSION OCCURRING IN NORMAL CATTLE TAKEN TO HIGH ALTITUDE. D.H. Will, R.F. Grover, J.T. Reeves and S.G. Blount, Jr. (intr. by F.X. Gassner). Colo. State Univ., Fort Collins and Colo. Univ. School of Med., Denver, Colo.

Nine weeks residence at an altitude of 12,700 feet produced significant pulmonary hypertension in 10 previously normal steers born at 3,500 feet. Control values (at 5,200 feet) for pulmonary arterial (PA) pressure averaged 29 ± 3 mm. Hg. Residence at 12,700 feet promptly elevated the mean PA pressure in all animals; in 2 to 5 days, the average pressure was 41 mm. Hg. Thereafter, further increases in pressure were variable. Four animals showed an average final mean pressure of 53 mm. Hg, while three others had a final mean pressure of 79 mm. Hg. The remaining three animals had final mean pressures exceeding 100 mm. Hg. One animal in this group developed congestive right heart failure in the ninth week with a mean right atrial pressure of 26 mm. Hg. All other steers had normal venous pressures. At postmortem, all animals showed right ventricular hypertrophy proportional to the degree of hypertension. Severe hypertension was observed in the absence of elevated wedge pressures. Because oxygen uptake and A-V oxygen difference decreased, no overall change in cardiac output occurred at high altitude. Associated but not commensurate with the level of hypertension was an arterial oxygen desaturation. Changes in blood pH, $p\text{CO}_2$, $p\text{O}_2$, O_2 saturation and tidal volume suggested that alveolar ventilation increased during the first week at altitude but was not sustained. A shift of the Hb- O_2 dissociation curve to the left was noted to occur at high altitude which could not be related to changes in blood pH. The hemoglobin and hematocrit values decreased initially at altitude then increased to only slightly above control values. A marked increase in blood clotting time from 9 to 19 min. was observed in all animals at 12,700 feet.

A NEW METHOD FOR THE CONTINUOUS RECORDING OF LEFT VENTRICULAR DIMENSIONS. Michael F. Wilson (intr. by L. D. Carlson) Dept. of Physiology, Univ. of Kentucky, Lexington, Kentucky.

The mutual-inductance principle has been used for continuously recording across a transverse diameter of the left ventricle in chronic unanesthetized dogs. Coils weighing less than one half gram each, with an external diameter of 7 mm and a thickness of 5 mm, have been constructed, and used as the sensing device by attaching them to opposite sides of the left ventricular chamber. The wave form of this measurement across a transverse diameter of the left ventricle resembles published cardiometer records of combined ventricular volume curves. The left ventricular dimensions are essentially in agreement with those obtained by sonocardiometry. For example the mean diameter and stroke change in diameter are greatest when the animal is reclining and become smaller on standing. With exercise on a treadmill at 3 m.p.h. on a 5 per cent grade, the stroke change in diameter is usually larger than when the animal is standing quietly and approximately equal to the reclining stroke change in diameter. This greater stroke change in diameter response to exercise usually occurs at the expense of the systolic diameter but the response may occur by an increased diastolic diameter. With the animal exercising at 6 m.p.h. the maximum excursion often exceeds the reclining stroke change in diameter. When the dog is resting quietly, changes in left ventricular diameter have been observed which correlate best with an apparent alerting response.

SOME ELECTRICAL PROPERTIES OF ODONTOBLAST CELLS. H. F. Winter* and Homer L. Dorman* (introduced by J. G. Bishop). Baylor Univ. College of Dentistry, Dallas, Texas.

A study of the electrical properties of the odontoblast cells was undertaken to determine the role of the odontoblasts in the transmission of pain from the dentinal structure. An osmic acid marker technique was used to visually observe the intracellular micropuncture site. Resting potentials were in the range of 20-50 millivolts negative with respect to the extracellular fluid with an average electrically inexcitable to both depolarizing and hyperpolarizing current shocks. The results indicate that the odontoblast cell is not directly concerned with the transmission of pain impulses through the dentine to the pulp cavity.

THE EFFECT OF TEMPERATURE ON REACTIVE HYPEREMIA IN SKELETAL MUSCLE. Lloyd R. Yonce. Univ. of North Carolina School of Medicine, Chapel Hill, N. C.

The gracilis muscles of eight dogs were isolated (acutely denervated) in a temperature controlled oil bath. Arterial blood pressure and venous blood flow were the parameters measured to indicate the circulatory resistance. Reactive hyperemia was produced by occluding the artery and vein. After a series of 3 occlusions (30, 60, 120 seconds) at 37.5° C, the temperature was lowered progressively to 25° C, 18° C, and 7° C and the series of occlusions repeated at each temperature. At each temperature level the time required for recovery of reactive hyperemia to the control blood flow (cc/min/100 gm) is the same for all periods of occlusion. The control blood flow appears to determine the time required for recovery; slow flow causes long recovery time and fast flow causes short recovery time. The amount of reactive hyperemia decreases with the decreased temperature as would be expected if the reactive hyperemia were a result of the effect of temperature on metabolism. Supported by Grant H3757, NIH, National Heart Institute, and Contract DA-49-007-MD-1002, Department of the Army, Office of the Surgeon General.

EFFECT OF EXERCISE ON THE URINARY NITROGEN, ELECTROLYTE, AND ADRENAL HORMONE EXCRETION IN DOGS. Donald R. Young. Quartermaster Food and Container Institute for the Armed Forces, Chicago, Illinois.

Studies with post-absorptive dogs indicate that during long-sustained work (10-15 hrs.), 50 to 70 percent of the total energy is derived from the oxidation of carbohydrate, and only a minor portion of the energy is obtained from protein. These findings suggest conversion of body fat to carbohydrate. Studies have been undertaken to more fully evaluate protein metabolism. Because of the probable influence of the adrenals on metabolism during work, measurements have been made to assess various parameters of adrenal activity. Urinary non-protein nitrogen, amino acids, Na, K, 17-hydroxycorticosteroids (17-OHCS), and nor-adrenalin (NE) have been examined in seven post-absorptive male beagle dogs. Comparisons have been made of the excretion patterns observed during two periods of rest -- 24 hrs. (700 Cal) and 3 hrs. (68 Cal), and one period of aerobic work -- 3 hrs. (600 Cal). Additionally, the influence of varying amounts of work on the urinary excretion of 17-OHCS and NE was studied. Over a 3 hr. period, the non-protein nitrogen, Na, and NE excretion was 0.5 g, 3.9 meq, and 3.7 micrograms, respectively, and uninfluenced by physical work. The resting urinary excretion of K and 17-OHCS was 1.6 meq and 98 micrograms, respectively; these were increased significantly during work. Of the 18 amino acids studied, only taurine and cystathionine showed significant changes during work. It is concluded that nitrogen metabolism is unrelated to a) the calorie deficit incurred during work, b) the apparent gluconeogenesis occurring during work, and c) increased excretion of adrenal hormones.