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ABSTRACTS OF PAPERS

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

EFFECT OF HYPERTONIC INJECTIONS ON THE DISTRIBUTION OF I-131 IN BRAIN AND MUSCLE. William F. Agnew,* Chester Hyman, and John Shahinian.* Univ. of So. California and Huntington Inst. of Med. Research, Pasadena.

Tissue/plasma I-131 ratios were determined following intravenous injections of a mixture of I-131 and Fe-59 labelled red cells in rats subsequently infused with isotonic and hypertonic solutions. The total I-131 in the tissues was corrected for residual blood by the amount of Fe-59. The tissue/plasma I-131 ratio at thirty minutes for control rats was 2.10 ± 0.45 for cerebrum, 3.5 ± 1.01 for post-tentorial brain, 2.01± 0.41 for cerebrospinal fluid and 14.90 ± 2.72 for skeletal muscle. Infusion of 1.5 gm/kg NaCl as 25% solution increased I-131 space in brain and in muscle by 300% and 35% respectively. Plasma osmolalities (Fiske Osmometer) at sacrifice ranged from 350 to 365 m.osm/L. Cisternal fluid and cerebral extra-cellular space I-131 levels corresponded in both normal and treated animals. The apparent osmotic load necessary to cause the observed changes in the tissue spaces was calculated using Boyle's Law. For muscle, calculated osmotic pressure levels approached the measured plasma values, however for brain tissue the calculated osmotic load was significantly below the actual plasma osmotic pressure. These results indicate the presence of an extravascular compartment in the central nervous system accessible to plasma I-131 which may be osmotically modified. Skeletal muscle behaves more like a perfect osmometer than does brain tissue.

Supported by N.I.H. Grant number 03077-02.

THE EFFECT OF TEMPERATURE ON THE TURTLE ELECTROCARDIOGRAM. T. K. AKERS and M. G. DAMM.* Dept. of Pharm., Stritch School of Medicine, Loyola Univ.,Chicago,Ill.

The configuration of the ECG of turtles at different cardiac temperatures had not been studied. The present experiments were performed on large, 12 inch, aquatic turtles. Special gold plated electrodes were implanted in the carapace near the legs to obtain the standard limb leads. A bead thermistor was implanted near the heart for core temperature recording. Rectal and ambient temperatures were also recorded. A Grass Polygraph was used for all recordings including ECG Leads I and III. Temperatures ranged from four to forty degrees centigrade. The QRS duration increased as the temperature decreased. The QRS amplitude decreased with decreasing temperature. Heart rate was variable but in general much slower at the lower temperatures. The change in core temperature lagged behind the rectal and ambient temperature changes as the animals were warmed. The ECG of the turtle appears to react to changes in temperature in the manner as the ECG of the fish and the frog as reported by other authors.

FURTHER STUDIES ON THE ROLE OF NITROGEN IN THE PROBLEM OF OXYGEN TOXICITY. Shannon C. Allen. Dept. of Physiology, Chicago College of Osteopathy, Chicago, Illinois.

A previous report from this laboratory has indicated that the development of the vascular system of the chick embryo is dependent upon the presence of nitrogen in the gaseous environment. To rule out the possibility that the other "inert" gases used to replace nitrogen in previous experiments were, per,se, toxic further experiments have been carried out at reduced atmospheric pressures. Fertile eggs have been incubated at various reduced atmospheric pressures and with various combinations of O_2 and N_2 for four days. Eggs incubated in 100% O_2 at a pO_2 of approximately 150 mm Hg show the same lack of development of the vascular system as those incubated in 100% O_2 at one atmosphere. The results indicate that the vascular system, in the absence of gaseous nitrogen, fails to develop even though the pO_2 is at normal, non-toxic levels.

HEART RATE DEPENDENCE ON LUNG VOLUME. A. Angelone* and N.A. Coulter, Jr. Biophysics Div., Physiology Dept., Ohio State University, Columbus, Ohio.

An interest in the phenomenon of respiratory sinus arrhythmia has engendered studies of the relationship between heart rate and static lung volume. The empirical plot of this relation may be closely approximated by an exponential curve, a high heart rate being associated with a small lung volume. Correlations with the works of others suggest an intimate relationship between pulmonary vascular resistance and the above observation. Preliminary data were gathered concerning transient heart rate effects.

COMPLIANCE IN ACUTE BRONCHOCONSTRICTION. N. R. Anthonisen (intr. by S. M. Tenney). Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Lung compliance, conductance and functional residual capacity (FRC) were measured in anesthetized spontaneously breathing rabbits; bronchoconstriction was induced by intravenous injections of acetyl β-methyl choline. The temporal pattern of response suggested that the drug acted via the pulmonary circulation rather than the bronchial. During bronchoconstrictive episodes the FRC regularly increased and dynamic compliance decreased in an amount proportional to the decrease in conductance. Indirect evidence suggested that part of the decrease represented a true decrease in static compliance. Static compliance in artificially ventilated paralyzed animals decreased during bronchoconstriction as it also did in spontaneously breathing animals when inspiratory spasm was induced by phrenic stimulation. This decrease in compliance was thought secondary to bronchial closure.
Supported by U.S.P.H.S. Grant H-3302(C4).

RELATIONSHIP BETWEEN CEREBELLUM AND LIVER MONOAMINE OXIDASE ACTIVITY. M. H. Aprison and T. L. Folkerth.* Inst. of Psychiatric Research, Indiana Univ. Med. Center, Indianapolis, Ind.

In the course of determining monoamine oxidase (MAO) activity by the micro-diffusion (NH_3) technique in the telencephalon, diencephalon plus optic lobes, medulla oblongata-pons, cerebellum, and liver from normal adult pigeons (white Carneaux cocks), the standard deviations of the mean of the cerebellum and liver samples were found to be very large compared to that noted for the other parts. Tyramine was used as substrate (10mM) for the enzyme assay. The temperature was 30°C and the pH 7.2. A plot of cerebellum MAO activity against liver MAO activity from each of the birds indicated that a linear relationship existed between these parameters. The coefficient of correlation was found to be 0.89. When the study was repeated with cerebellum and liver from guinea pigs, the same type of relationship was found. Using the curve obtained for pigeons (13 birds), we were able to estimate the brain cerebellum MAO activity within 10% in 5 other birds by assaying liver for MAO activity. In pigeons injected with different amounts of Parnate or Catron, the relationship between these two parts was found to hold, however the slope of the curve was changed. Apparently, liver MAO activity changes more rapidly than cerebellum. This correlation was not found between liver MAO activity and MAO activity of the other brain parts. Supported by research grant MY 3225 for the National Institute of Mental Health, PHS.

LOCATION OF A PHYSIOLOGIC REFERENCE POINT FOR LEFT ATRIAL PRESSURE MEASUREMENTS IN DOGS. G. G. Armstrong* (intr. by J. W. Crowell). Dept. of Physiol., Univ. Med. Center, Jackson, Miss.

The location of a physiologic reference point for venous pressure measurements in dogs has been reported (Guyton, A. C. and F. P. Greganti. Am. J. Physiol. 185:137, 1956). The location of a reference point for left atrial pressure measurements is now reported. Left atrial pressure (measured by transseptal catheterization) was monitored while dogs were rotated about transverse and longitudinal axes. The intersection of these two axes was varied with respect to the dog's body until left atrial pressure became relatively independent of spatial orientation. Topographically the point was 63 per cent of the manubrium to xiphoid distance, 57 per cent of the greatest posterior to anterior diameter of the thorax, and 2 per cent of the transverse diameter of the thorax to the left of the midline. Anatomical cross sectional studies further located the point to the vicinity of the mitral valve. This compares with the location of the right atrial pressure reference point in the vicinity of the tricuspid valve.

EFFECT OF POTASSIUM REPLACEMENT, ACETAZOLAMIDE AND HYDROCHLOROTHIAZIDE ON ELECTROLYTE ABSORPTION BY SMALL INTESTINE IN VITRO. K. A. Aulsebrook (Intr. by J. E. Whitney) Dept. of Physiology, Univ. of Ark. School of Medicine, Little Rock, Ark.

Absorption of sodium, potassium and water by everted segments of rat small intestine has been studied using a method previously described (Endocrinology, 68:1063, June, 1961). A Krebs-Ringer bicarbonate buffer with glucose was used for both serosal (inside) and mucosal (outside) fluids. When potassium in the serosal fluid was replaced by choline, absorption of sodium and water was depressed. This effect was not observed when mucosal fluid potassium was replaced by choline. Addition of acetazolamide or hydrochlorothiazide to the buffer depressed absorption of sodium and potassium. Hydrochlorothiazide also lowered the serosal fluid Na/K, but acetazolamide did not. It is concluded that absorption is partially dependent on carbonic anhydrase, and in the case of sodium, upon the presence of potassium in the serosal fluid. The latter result suggests the presence of a Na-K exchange mechanism at the basal surface of the mucosal cell similar to that observed in frog skin by Ussing (Acta Physiol. Scand. 42:298, 1958). Supported by NIH grant A-5025-02.

BLOOD VOLUME CHANGES IN DOGS EXPOSED TO ALTITUDE. D. W. Badger* and Nello Pace. Dept. of Physiology, University of California, Berkeley, and the White Mountain Research Station, Big Pine, Calif.

Changes in red cell mass, plasma and total blood volumes were compared in intact and splenectomized dogs sojourning at 12,470 feet altitude. Similar measurements were made in splenectomized dogs, whose aortic and carotid chemoreceptors had been ablated (glomectomized) to prevent respiratory response to hypoxia. All groups showed increased red cell mass. The intact and splenectomized dogs reached 145% of sea level values, the latter more slowly. The glomectomized-splenectomized dogs increased to 250%, hematocrit values as high as 66% being observed. Plasma volume decreased within a few days in all groups, the intact dogs fell to 90% of sea level and returned by 60 days, the splenectomized decreased to 70% and recovered by 240 days, while the glomectomized decreased to 50% and had not recovered by 500 days. The erythropoietic response to hypoxia is slow in splenectomized dogs, although the same degree of increase in red cell mass as in intact dogs occurs eventually. On the other hand, the glomectomized-splenectomized dogs showed a far greater erythropoietic response to hypoxia than the other groups. It is apparent that the chemoreceptors are not needed for the erythropoietic response, but that the spleen may play a role in erythropoiesis. Further, in the absence of hypoxic hyperventilation mediated by the glomi, the erythropoietic response is enhanced, with or without the presence of the spleen. Finally, the early decrease in plasma volume may be accounted for, at least in part, by activation of left atrial stretch receptors by hypoxia-induced increased pulmonary venous pressure, with resultant decrease in ADH secretion.
(Supported by ONR)

RESPONSE TO PRESSURE OF MICROARTERIAL VESSELS IN THE LIVE RAT. Silvio Baez and Harold Lamport, Albert Einstein Col. of Med. N.Y. and Yale Univ. School of Med., New Haven, Conn.

In the isolated perfused mesoappendix, the lumen of microarterial vessels frequently remains constant as internal pressure is varied within a range around physiological pressure. Here these studies are extended to the live rat. Arterial or venous pressure in the intact mesoappendix was varied by controlled obstruction. We assumed as an approximation that the pressure gradient along the vascular bed is the same in relative terms whether the bed is isolated or intact with or without change in regional arterial or venous pressure. Thus, we estimate pressure within a microartery measured under the microscope. Elevation of internal pressure by venous obstruction or its reduction by arterial obstruction frequently revealed apparent microarterial rigidity, but within a somewhat lesser pressure range and at a lower level than that observed in the isolated preparation. Hyperreactivity, in which the vessels constrict under pressure rise and dilate under pressure fall, as required to explain autoregulation, occurred much more frequently than in the isolated preparation and at pressures close to physiological and was often associated with apparent rigidity at other pressures. The apparent rigidity of microarteries is not an artifact seen only in isolated perfused vessels; it is a physiological phenomenon, probably similar in mechanism to hyperreactivity in intact animals. (Aided by grants from Nat'l. Insts. of Health and Conn. Heart Assoc.)

INFLUENCE OF THE THYRO-PARATHYROID SYSTEM UPON THE MYOCARDIAL CALCIFICATION DUE TO CORONARY VEIN OBSTRUCTION. Eörs Bajusz, Gaëtan Jasmin and André Mongeau*. Lab. of Exper. Path., Univ. of Montreal, Montreal, Canada.

Experiments in the rat indicate that following ligature of the two main coronary veins at the point where they enter (separately or after uniting into a single sinus) the right auricle, necrotic foci occur in the subepicardial muscle layers and massive calcification begins in the affected areas. This type of myocardial calcification — unlike the onset of necrosis — was greatly enhanced by parathyroidectomy performed three days before the ligature of the coronary veins. On the other hand, the aggravating action of parathyroid deficiency was counteracted by simultaneous thyroidectomy and could not be restored by replacement therapy with thyroxine (50 to 500 μg/100 gm body weight/day). In fact, following coronary vein ligature, there was less myocardial calcification in the thyro-parathyroidectomized than in the intact animals. From these as well as from additional studies to be discussed, it is postulated that parathyroid deficiency enhances myocardial calcification only in the presence of both thyroxine and another, as yet unidentified, thyroid factor. It is likely that these thyroid principles are responsible for promoting the entry of various ions (calcium, phosphorus, carbonate) in an excess into the damaged tissue areas; alterations in serum calcium and inorganic phosphorus levels normally due to parathyroidectomy were not further changed by removal of the thyroids and/or by administration of thyroxine. (Supported by the Medical Research Council of Canada and the Quebec Heart Foundation.)

INTESTINAL ABSORPTION IN TUMOR-BEARING RATS. R. David Baker. Dept. of Physiology, Univ. of Texas Med. Branch, Galveston, Texas.

Posner has reported that rats bearing Walker carcinoma 256 have defective fat absorption (Cancer Research 20:55, 1960). He has suggested that this defect may be a contributory factor in the development of cachexia in tumor-bearing animals. I have attempted to confirm this potentially important observation. The methods were almost identical to those used by Posner. The thoracic duct of each rat was cannulated according to Bollman. The animals were placed in a new type of restraining cage which allows considerable body movement (Baker, R. D., et al. J. Appl. Physiol. In press) and given access to food and 0.9% NaCl. About 20 hours later 0.5 ml of triglyceride containing 0.6 to 11.0 μc of triolein-I^{131} was fed by stomach tube and was immediately followed by 5.0 ml of water. Lymph was collected for 6 hours. The proteins and lipids of lymph samples were coprecipitated with trichloroacetic acid as described by Posner and counted using a well type scintillation detector. Lymph activity was compared to the activity in a duplicate sample of the test meal. Six of the rats were injected subcutaneously with homogenates of Walker 256 about 3 weeks before the experiment. The final average size of the tumors was 19% of the total body weight. Normal rats ranged in weight from 222 to 396 gm.; tumor-bearing rats were all within this range. Contrary to the results of Posner there was no effect of body weight on fat absorption observed in either the normal or tumor-bearing groups. Lymph collected from 6 normal rats in 6 hours contained from 30% to 46% (mean = 39%) of the initial dose; the values from 6 tumor-bearing rats also ranged from 30% to 46% (mean = 40%). Thus, Posner's results could not be confirmed. The reason for this discrepancy is not apparent. (Supported by a grant from the Medical Research Foundation of Texas).

POSSIBILITY OF AN INHERENT ERROR IN AIRWAY RESISTANCE CALCULATION. Roscoe G. Bartlett, Jr., Naval School of Aviation Medicine, Pensacola, Fla.

An inferred assumption in the calculation of airway resistance is that alveolar pressure and mouth airflow measured simultaneously have a cause-effect relationship. If this were indeed true, it would indicate that there was no time interval between the production of an alveolar pressure and the resultant airflow at the mouth. It has been demonstrated previously that such a lag time, or phase shift, does in fact exist. To the extent that it does exist, an error is introduced into airway resistance estimation resulting in an increase in the apparent airway resistance during breath acceleration and a decrease during breath deceleration. It was the purpose of the present study to ascertain the magnitude of the error so introduced. It has been shown that atmosphere density, breathing frequency, and breathing effort all affect the magnitude of the error. The error has been calculated at increasing, constant, and decreasing breath velocities and during inspiration and expiration. Under some conditions the error is equal to the corrected airway resistance.

Brain O_2 in Exposures to O_2 at High Pressures(OHP). John W.Bean and L. Sullivan*; Univ. of Michigan, Ann Arbor. Earlier observation of profuse bubble formation in blood withdrawn to atmospheric pressure from the external jugular vein of anesthetized dogs exposed to OHP(4-6 atms) contrasted with the absence of such bubbling(Lambertsen et el) in cerebral venous blood from unanesthetized men exposed to O_2 at lower pressures (3.0-3.5 atms.) due to cerebral vasoconstriction by O_2, raised the question of whether bubbling might not occur in cerebral venous blood withdrawn in exposures to O_2 at higher pressures. It was found that while there was no bubbling in blood withdrawn to atm pressure from the sup. saggital sinus of dogs exposed to O_2 below 3.5 atms, there was profuse bubble formation with pressures above 4 atms; this diminished somewhat in prolonged exposures and showed a definite A-V difference suggestive of an appreciable vasoconstriction, but O_2 in the blood was well above precompression level. In an esthetized dogs simultaneous recordings from O_2 electrodes showed a steady and well maintained increase in O_2 availability in both circulating sinus blood and brain tissue. Unanesthetized rats showed more individual variation and lower O_2 valuesthan the anesthetized;simultaneous recordings from electrodes previously implanted in hypothalamic and cortical tissueshowed a general increase in O_2 availability in both areas superimposed upon which fluctuations of increasing intensity developed,often without overt signs of impending convulsions, but the most dramatic rise occurred just preceding and during a seizure. These fluctuations differed quite often in the different areas at any one time and are attributed to local vascular changes.Because of their frequent asynchronicity,lack of parallelism and transiency these changes would be largely masked in mixed venous brain bloodwhich therefore may fail as a reliable indicator of critical local changes in the brain that determine the reaction of the animal as a whole to OHP and probablyto a variety of other conditions. Supported by USPHS grant H-1646.

TISSUE PO_2 DURING INDUCED HYPERBILIRUBINEMIA IN THE NEONATAL RHESUS MONKEY. R. E. Behrman and R. Fleishman (Intr. by W. F. Windle). Lab. Perinatal Physiol., NINDB, NIH, San Juan, P.R.

In vitro studies with various tissues have indicated that bilirubin at the cellular level inhibits heme synthesis and uncouples oxydative phosphorylation. Newborn animal tissues were found to be particularly susceptible. The present report concerns in vivo effects of bilirubin.

While hyperbilirubinemia was being induced in newborn and infant rhesus monkeys, we recorded continuously tissue pO_2 (polarographic measurement), heart rate, respiratory rate, and body temperature. Sustained serum concentrations of 30 mg per cent of bilirubin in the newborn delivered by cesarean section, were associated during the first 10 hours of life with a peritoneal pO_2 of 14-20 mm, compared to steady-state levels of 28-35 mm Hg. Similar studies on a 13-day-old monkey showed little change in tissue pO_2.

Intravenous administration acutely of a buffered bilirubin solution to the newborn resulted in a transient slight increase in respiratory rate and a decrease in heart rate, but a steady state was rapidly established at approximately preinjection levels despite a constantly depressed tissue pO_2. Neither administration of the buffered bilirubin solvent alone nor elevation of body temperature affected this response. Raising the body temperature appeared to be adequately compensated for by cardiac and respiratory adjustments.

The animals were in good condition when killed by a perfusion technique. Post-mortem examination revealed yellow staining of peritoneum and other tissues, including parts of the brain of the newborn animal.

ANAEROBIOSIS IN DIVING TURTLES. Daniel A. Belkin (intr. by A. B. Otis). Dept. of Physiology, Univ. of Florida College of Medicine, Gainesville, Florida.

Certain species of turtles can survive submergences of over 100 times the duration tolerated by other amniotes. Mechanisms allowing prolonged submergence in aquatic mammals (oxygen storage, circulatory shunts, toleration of high concentrations of metabolic wastes) are by themselves unable to account for the extended survival of submerged turtles. I have demonstrated that aquatic respiration and anaerobic energy production are involved, and have attempted to assess the importance of the latter by comparing the survival times of normal and iodoacetate-poisoned turtles in an anoxic environment. The species used in these investigations was Sternothaerus minor. Iodoacetic acid (injected intraperitoneally, 15 mg/kg) was used to prevent glycolytic energy production. The oxygen uptake of turtles poisoned with this dose was well within the normal range, and these turtles survived indefinitely if given access to air. The animals were maintained at 22°C in all experiments. Anoxia was endured by normal turtles for an average of 12.2 hours, and by iodoacetate-poisoned turtles for an average of only 0.32 hours. It is concluded that the energy derived from anaerobic metabolic processes such as glycolysis is the factor responsible for the prolonged survival of anoxic turtles.

THE DETERMINATION OF MYOCARDIAL CLEARANCE OF RUBIDIUM-84 AND CORONARY MICROCIRCULATION USING A COINCIDENCE COUNTING TECHNIQUE. Arvin Bennish*, Vernon E. Wendt*, and Richard J. Bing, Wayne State Univ. Col. of Med., Detroit, Mich.

The myocardial clearance and coronary arteriovenous extraction of Rubidium-84 have been studied in the externally perfused dog heart. Controlled and changing flows as well as pacemaker controlled heart rates were independently studied. The arteriovenous extraction ratio has been shown to be primarily dependent on the arterial concentration of Rubidium-84. An exponential fall related to time was consistently reproduced. Change in coronary flow had no effect on the exponential decline of arteriovenous extraction ratios. Myocardial clearance of Rubidium-84 is directly dependent on myocardial blood flow. The relationship between coronary microcirculation and the myocardial accumulation of this positron emitting isotope justifies a method of myocardial blood flow determination. External coincidence scanning and continuous arterial blood sampling were employed. The coincidence counting method offers the following advantages: precisely defined three-dimensional scanning geometry, the almost complete independence of source to crystal distance on count rates, and highly efficient collimation. This method has been used in patients and the results shown to be entirely consistent with in vitro studies. A functional test of myocardial blood flow in man using external body coincidence counting is presently under study.

SERUM MALIC DEHYDROGENASE CHANGES IN VARIOUS THYROID STATES.
Samuel G. Benson*, Howard M. Klitgaard and Alan S. Lieberthal*.
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Since malic dehydrogenase (MDH) activity in selected excised rat tissue has been shown to be increased after thyroidectomy (Benson and Klitgaard, 1961), an investigation of the relationship of serum MDH in various thyroid states was done. MDH capacities were measured using modifications of Bing's technique which included the addition of gelatin to protect against proteolytic enzymes and internal controls to detect any DPNH oxidase activity. Serum MDH levels were determined in normal subjects and patients with hypothyroidism and Graves' disease, and found to be 25-40 units, 82-225 units and 55-75 units, respectively. Similar studies were performed on four groups of rats in an attempt to duplicate the conditions found in human subjects. These results showed an MDH activity in the thyroidectomized rat of 2100 units, 2050 units in the low iodine rat and 2000 units in the normal, while the hyperthyroid group showed only 1900 units. MDH capacity in human subjects and rats were comparable in similar metabolic states with the exception of Graves' disease and thyroxine-injected rats, where the TSH levels were different. This study suggests that the determination of serum MDH may aid in a better understanding of thyroid function and in the diagnosis of thyroid disease.
(Supported by PHS Grants A-957 and A-1706.)

TRANSIENT SUPPRESSION OF COLOR VISUAL RESPONSES AFTER FOREBRAIN ABLATION IN FISH.
Jerald J. Bernstein*, Lab. Neuroanat. Sci., N.I.N.D.B., N.I.H., Bethesda, Md.

The following experiments were performed in an attempt to determine the role of the telencephalon in the color vision of goldfish. Cardiac deceleration, a conditioned autonomic response, was used as the criterion for learning. Electric shock was the unconditioned stimulus. One eye of the normal fish was occluded and they were trained to discriminate between a red and a green stimulus of equal brightness. To demonstrate interocular transfer and hue generalization the naive or transfer eye was then tested on red and green stimuli that were darker or lighter than the training stimuli. Normal fish and fish with the forebrain contralateral to the trained eye ablated demonstrated interocular transfer and generalization of the hue discrimination. Ten minutes after ablation of the forebrain homolateral to the trained eye or after bilateral forebrain ablation (subsequent to training) operated fish demonstrated a loss in ability to make the interocular transfer to generalizations of hue. However, interocular transfer and hue generalization returned in animals tested 4 hours subsequent to training. Animals trained and tested 6 weeks after bilateral forebrain ablation also demonstrated interocular transfer to generalizations of hue. It is concluded that forebrain ablation transiently suppresses the color visual responses of forebrain ablated fish.

The trans-membrane reaction and the so called action potential. R.H.Beutner, Medical Research Lab. Greentown,Pa. & College of Osteop. Medicine & Surgery, Des Moines, Iowa.

Ion movements which are claimed to be the cause of the "action potential" are actually the result of the stimulation. Electrolytic ions move only when driven in an electric field. We assume that the active membrane produces two mutually opposing single potential differences, one on each side at the contact surface, as in a galvanic cell. On the basis of these assumptions the up- and the down-stroke can be explained by the following consecutive processes: 1) an enzyme-activating ion is driven into the substance of the membrane by the stimulating current;-- 2) within a fraction of a milli-second it is then driven across the very thin membrane by the stimulating current;-- 3) after reaching the opposite membrane-contact-surface, it produces a variation in the opposite direction, leading to the down-stroke of the spike.---- A reversible phospholipid splitting may be the reaction, which causes the action potential (as it is now called). Thus, our theory is that the electrogenic choline is set free, first on one, and then on the opposite membrane-contact-surface. -- Any agent which accelerates phospholipid splitting should be expected to accelerate the down-stroke of the spike, since the trans-membrane reaction can reach the opposing membrane-contact-surface sooner.
(Supported by a research grant of the Natl. Heart Inst.)

THE EFFECT OF MODERATE ALTITUDE ON EXERCISE. Charles E. Billings, Prescott K. Johnson*, George N. Hoover & Donald K. Mathews*. The Ohio State University, Columbus, Ohio.

It is known that ability to sustain muscular exercise is sharply reduced at an altitude of 15,000 feet in unacclimatized subjects. Previous work has also shown no apparent decrement in exercise tolerance at much lower altitudes (3,000'). This report describes controlled studies in an altitude chamber at 720, 620 and 520 mm. Hg barometric pressures (1,500, 5,500 & 10,200 feet pressure altitudes). Eleven male athletes performed mild work (4X resting oxygen uptake) twice at each altitude under identical conditions. The experiment was carried out under double blind precautions. Expired air samples were collected; ventilation, oxygen uptake and carbon dioxide output were determined. It was found that the excess oxygen cost of this mild work was not significantly increased at either 620 or 520 mm. Hg compared with 720 mm. Hg. Minute ventilation during exercise, however, increased incrementally and significantly as barometric pressure was reduced. Increases in respiratory frequency at altitude may explain why no significant difference was observed in respiratory exchange ratios with increasing altitude. This study and others in the literature suggest that a "time-dose" relationship exists for aerobic muscular work performed breathing ambient air at pressure altitudes as low as 5,500 feet. (This study was performed under the auspices of the Mershon Center for Education in National Security.)

MUSCULAR DEVELOPMENT IN WHITE MICE GROWING FOR 8 WEEKS AT HIGH GRAVITY. John W.C. Bird* and Charles C. Wunder. Rutgers-The State Univ., New Brunswick, N.J. and State Univ. of Iowa, Iowa City, Iowa.

Although 4G as simulated by continual centrifugation causes a slower growth for the heart, diaphragm, and gastronemius muscles, some growth of these organs is possible. Body growth actually suffers a more marked retardation; however, relative growth of these experimental organs exceeds control rates. Results are for both sexes of NLW mice whose exposure was initiated at the age of 5 weeks. The fractional water content was almost constant throughout, being only 2.0±0.6% lower in the experimental muscles. Analysis for non-collogen-nitrogen (NCN) was employed as an index of contractile and sarcoplasmic proteins. The fraction of NCN was 18±4% below the control level in the diaphragm tissue. For the heart, the fraction was 26±12% below normal after 2 weeks of centrifugation. However, after 1,4, and 8 weeks, the fractions in both the heart and gastronemius muscles were not measurably different. Although muscular growth would be possible in a gravitational field exceeding the terrestrial intensity, some alteration in the type of musculature would be expected.

ESTIMATION OF THE WATER CONTENT OF TISSUES FROM ADRENALECTOMIZED RATS BY THERMAL CONDUCTIVITY. James H. Birnie. Department of Biology, Morehouse College, Atlanta, Georgia.

The findings of Grayson (J. Physiol., 118:54, 1952.) regarding the relation of water content to the thermal conductivity of tissues have been confirmed and extended. Determinations indicate that the water content is a major factor in limiting thermal conductivity in protein-water systems (gelatin, albumin and hemoglobin) and in tissues from recently killed animals. From estimations of thermal conductivity made with heated thermocouple recorders implanted in various tissues it was possible to obtain calculations of the water content which compare favorably with determinations made by the dry weight method. This procedure provides a rapid determination of tissue water content within reasonable limits of experimental error. The total water content of tissues from intact and adrenalectomized rats has been determined by the use of heated thermocouples and the findings compared with dry weight determinations. There was found to be no statistically significant difference in the total water content of rats which had been determined by the use of heated thermocouples and the findings compared with dry weight determinations. There was found to be no statistically significant difference in the total water content of rats which had been adrenalectomized for seven days as compared with sham operated controls. These findings suggest that the previously observed water and electrolyte alterations in extracellular fluids (Gaunt and Birnie, 1951) is a manifestation of internal fluid shifts rather than a total body dehydration. (Supported by NIH Research Grant A-199-C2.)

CONTRACTIONS OF VASCULAR SMOOTH MUSCLE INDUCED BY ISOSMOTIC REPLACEMENT OF SODIUM CHLORIDE WITH SUCROSE. Herman A. Blair* and William H. Waugh, Dept. of Med., Univ. of Kentucky Coll. of Med., Lexington, Ky.

Working with spontaneously inactive and active visceral smooth muscle, Kao and Gluck concluded (A.J.P. 200: 658, 1961) that external chloride is necessary for the reversal of tonic contractions of mammalian smooth muscle, produced by Cl-deficient media, and that tonic contractions generally result when the external Cl is replaced iso-osmotically with some other anion or with sucrose. This hypothesis was tested and invalidated for vascular smooth muscle, spontaneously inactive. Isosmotic replacement of the Cl and Na of the electrolyte medium was performed with sucrose and with sodium nitrate, bromide, iodide, acetate, n-butyrate, isethionate, acetylglycinate, thiosulfate, sulfate, or ferrocyanide. These various isotonic solutions, which contained also Ca, Mg, K, and glucose buffered by "Tris" (5mM)-HAc at pH 7.4, were perfused through dog intestinal arterial segments. Contractions did not result in any of the Na-rich solutions in which other Na salt was substituted for the NaCl. Tonic contractions did result with use of sucrose-rich, totally Na- and Cl-deficient perfusate. However, they were reversed by use of perfusates containing the above non-chloride sodium salts. The vascular smooth muscle contractions induced by sucrose-rich solution were similarly relaxed by isosmotic use of choline chloride in place of the sodium salts. Since much lower concs. of acetylcholine chloride did not relax these contractions, neither sodium nor chloride appears to play a specific role in promoting relaxation of vascular muscle contraction. It was further found that such contractions induced by sucrose-rich perfusate were externally Ca rather than Mg or K dependent. (Supported by grants HB-06092 and HB-06347 of the National Heart Institute, P.H.S.)

INTESTINAL ACTIVE TRANSPORT UNDER ANAEROBIC CONDITIONS IN NEWLY-HATCHED CHICKS. P. H. Bogner, I.A. Haines,* and P. L. McLain, Jr.* Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

Active transport capacity of small intestinal tissue from 18-day-incubated embryos, 0-, 2- and 8-day-old chicks was estimated with galactose. The in vitro method of study was essentially as outlined by Crane and Mandelstam (Biochim. et biophys. acta 45: 460, 1960) in which the intestine is cut serially into small rings with pieces being taken in rotation for individual flasks in order to approximate random sampling. Embryonic intestine did not concentrate galactose intracellularly under either aerobic or anaerobic conditions. In contrast, tissue from 0- and 2-day-old chicks accumulated this sugar against an apparent concentration gradient in both an oxygen and nitrogen atmosphere. Tissue from 8-day-old chicks was also capable of anaerobic active transport if a 48-hour fast preceded the experiment; anaerobic transport by intestine from chicks fasted 24 hours was not observed. These data suggest that the active transport mechanism for hexoses becomes functional at about the time of hatching and can be driven by energy derived from anaerobic glycolysis for at least a week thereafter.

CARDIOGREEN CONCENTRATIONS IN LEFT VENTRICLE AND AORTA. Clorinda S.-S. Bohler* and Philip Dow. Department of Physiology, Medical College of Georgia, Augusta.

We have been reporting data which forced us to believe that the blood ejected by any systole is not necessarily a homogeneous sample of the whole left ventricular contents at that moment. We have continued our efforts to identify factors which may tend to favor or minimize this discrepancy: e.g., site of injection, mode of sampling, condition of the animal. Apparatus and materials were as previously reported. In six dogs (morphine-chloralose or morphine-pentobarbital anesthesia) a total of 133 injections of Cardio-Green into the left atrium by transseptal puncture gave pairs of dilution curves by simultaneous catheter sampling from left ventricle and ascending aorta. Comparison of areas of corresponding pairs of curves showed more consistent similarity than in the earlier series which involved sampling by needle puncture of the ventricular tip after auricular injection. In the current series, the degree of correspondence between pairs sometimes seemed to be better when the chest had not been opened, but the plotted distributions do not look significantly different. Whenever the aortic appearance time was shorter than the ventricular, the curve areas did not agree, but so far this combination has not been correlated with any of the variables tested. As a possible measure of the homogeneity of the aortic stream, simultaneous carotid and femoral curves were compared in one dog after left atrial injection and in another dog after right atrial injection. This brief series showed no definite trend. Mean transit times of corresponding pairs of curves were also compared without remarkable findings, except for a surprising consistency of the ratio 0.3 for aorta/femoral after the left atrial injections. (Supported by grants from the USPHS and the Life Insurance Medical Research Fund.)

EFFECT OF ANTICIPATION UPON THE HEART RATE AND EEG IN HUMAN SUBJECTS AT REST. Tatiana S. Boks* and Chester E. Leese. Dept. of Physiology, The George Washington University, Washington, D.C.

Most experiments on the nervous control of the cardiovascular system have been carried out under physical or emotional stress. This phase of our study sought to decrease all stresses to a minimum in order to reduce hormonal participation, while correlating cardiac latency and EEG response to anticipation. The aims were to determine (a) the cardiac latency to a signal for answering a simple question (b) cardiac latency to a signal to stop the answer and come to rest but while the answer is still in progress (c) the effect upon the EEG during (a) and (b), and (d) to relate the cardiac and EEG responses with each other. The heart rate increased in all subjects to the signal to answer and decreased to the signal to prepare to stop. These changes usually occurred during the first beat after the signal. The group averaged an increase of seven beats per minute during the first three seconds while anticipating to answer, and decreased an average of six beats per minute while anticipating to prepare to stop answering. The EEG pattern flattened after the signal to anticipate a question and increased in amplitude after the signal to prepare for stopping the answer. These responses occurred simultaneously with the cardiac rate changes. The time relationships suggest that response to the anticipation for action and rest are purely nervous.
(Supported by grant No. H-4861, NIH)

Effect of Oxygen Intoxication on the Surface Characteristics of Lung Extracts. Stuart Bondurant and Cherry Smith*. I. U. Med. Center, Indianapolis, Ind.

The cause of the pulmonary damage associated with oxygen intoxication is uncertain. Klaus et al have shown that the phospholipid fraction of pulmonary surfactant is unstable in air and O_2 but stable in N_2. To evaluate the effect of 100% O_2 in vivo on the surface characteristics of lung extracts, 7 rats were killed by exposure to 8 atmospheres 100% O_2 (20-45 minutes), extracts prepared in an O_2 atmosphere by saline perfusion of the pulmonary vasculature, and 10 mgm samples measured on the modified Wilhelmy Balance. Control animals were compressed to 8 atmospheres of 12% O_2. Maximum and minimum (80% compression of surface area) surface tensions were: Control 46±5 dynes/cm and 11±4 and O_2 53±3 and 18±4 $p<.01$. The index of film compressibility (S) was control 1.21±.21 and O_2 0.96±.14 $p<.025$. Twenty rats were killed by O_2 at 800-900 mm Hg (1-2 days) with control animals exposed to air at the same pressure. Surface tensions of extracts were: Control 55±3 and 17±5 and O_2 53±2 and 14±6. S was control 1.04±.16 and O_2 1.23±0.26. While the differences in the animals compressed to 8 atmospheres are statistically significant, all of the values above are within the range of variation found in different groups of normal animals. The techniques of this study demonstrate no effect of O_2 intoxication on the pulmonary surfactant. (These studies were made possible through the use of the compression chambers of the Dept. of Physiology, University of Buffalo School of Medicine).

Spectral Analysis of Electrical Activity of the Prepyriform Cortex
James C. Boudreau (intr. by W. J. Freeman)
University of California, Berkeley

Mature cats were chronically implanted in the prepyriform cortex with multiple bipolar electrodes. The animals were then trained to perform a simple orienting response to the onset of a light signifying imminent delivery of milk. With the use of an IBM 7044 computer program autocorrelations and power spectra were computed from digitized records of EEG activity during the behavior sequence. Three-second records of activity were analyzed during anticipation and lapping. Frequency estimates were made at 2 cycle intervals from zero to 80 cps. Although great interanimal variability was exhibited in the power spectra, each animal had a characteristic profile which remained fairly stable for several months. The power spectra from most cats showed a large peak at about 40 cps. Some animals had bimodal spectral profiles with a second peak around 50 cps. Approximate submultiples of the modal frequency band were also present in some of the records. Simultaneous records from two different prepyriform sites were virtually identical. Marked changes occurred in the modal (40 cps) peak during lapping. The amplitude decreased from the anticipatory period record and an upward shift in frequency occurred.

RADIOGRAPHIC VISUALIZATION OF STOP-FLOW ANALYSIS.
S. Boyarsky, J. Martinez, N. Kaplan and M. Elkin (intr. by H. Lauson). Albert Einstein College of Medicine, New York, N. Y.

Acute ureteral obstruction for 5-8 minutes at moderate urine flows (1-2 cc/min/ureter) in dogs observed cinefluorographically using i. v. hypaque, glucose & water caused 1) dilatation of ureter, pelvis, and calyces, 2) cessation of peristalsis, 3) transmitted vascular pulsation. Release was followed by slight loss of intensity of the pyelogram (i.e. drainage); peristalsis did not return for 2-4 min.; calyceal caliber recovered promptly but ureteropelvic dilatation persisted. Studying this in more detail with the rapid cassette changer at higher urine flows (2-6 cc/ureter/min. with infusions of 9-12 cc/min.), the starting point of ureteral and pelvic dilatation was greater and the changes due to obstruction were correspondingly less. Calyceal dilatation followed obstruction and regressed within the first minute after release. Nephrographic intensification of the renal shadow developed over 5 min. of obstruction but did not clear completely in 20 minutes after release. The size of the renal shadow remained constant. At the highest flows (8-12 cc/min/ureter) nephrographic intensity and ureteropelvic dilatation were marked; there was little room for increase after obstruction. Significant accumulation of hypaque occurs in the renal parenchyma during osmotic diuresis and obstruction. Some evidence suggests that the obstructive nephrogram is tubular, but this explanation is not consistent with the accepted mechanism of excretion of hypaque. Its site could be interstitial or luminal. (Supported in part by USPHS Grants No. RG 5986, A 3495 & James Picker Foundation.)

ON THE ACUTE CALORIGENIC EFFECTS OF TRIIODO- AND TETRAIODOTHYROACETIC ACID. Pietro O. Bramante and Aurora V. Bramante*, Dept. of Physiology, St. Louis University School of Medicine, St. Louis, Missouri.

Opinions are divided upon the immediate influence on calorigenesis of the acetic derivatives of triiodothyronine(TRIAC) and thyroxine(TETRAC): the early reports of the acute effects of these compounds on the metabolic rate of the experimental animal have been subsequently denied but not conclusively disproved. In a series of 30 experiments, oxygen consumption ($\dot{V}_{O_2}$) and spontaneous muscular activity of albino rats were continuously recorded with apparatus (JAP, 14:1065, 1959) and quantitated with method (JAP, 16:982, 1961) which greatly reduce the variation, dispersion and error inherent in this type of determination (S.E. = ± 4 %). The changes of basal $\dot{V}_{O_2}$ were followed after introduction of different doses of TRIAC, TETRAC and other agents (116 trials) in normal (N) and thyroidectomized (Tx) rats, either anesthetized with urethane (A) or awake (Ā). The results were interpreted as "positive" if a $\dot{V}_{O_2}$ change of 10 per cent or more could be detected within two hours. The results obtained with the acetic derivatives (injected 42 times by various routes) were negative in the N (NĀ and NA) and TxĀ rats but were positive in about one-third of the trials with the TxA animals. On the basis of the previously demonstrated frequent dissociation between $\dot{V}_{O_2}$ and spontaneous muscular activity of thyroidectomized and anesthetized rats (Fed. Proc. 19:174, 1960), these experiments could provide an explanation for the inconsistent results obtained by others. However, the findings support the contention that the acetic derivatives of T_3 and T_4 do not exert any demonstrable acute calorigenic effect in the rat.

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CORONARY BLOOD FLOW - AN IMPORTANT DETERMINANT OF MYOCARDIAL OXYGEN CONSUMPTION. Eugene Braunwald, Richard L. Kahler,* Leslie L.Kelminson,* Laurence Kedes,* and Charles A. Chidsey.* National Heart Institute, Bethesda, Maryland.

The effect of varying coronary blood flow (CBF) and myocardial O_2 delivery on myocardial O_2 consumption ($M\dot{V}O_2$) was studied in 22 experiments. In 14 of the experiments an isolated dog heart was perfused, while in the others the heart of a dog whose systemic circulation was maintained on cardio-pulmonary bypass was studied. The ventricles were kept empty, developed no pressure and performed no external work, while their temperature was held constant. In 15 experiments, the heart was paced electrically at a constant rate and in 7 experiments the ventricles fibrillated. CBF and myocardial O_2 delivery were controlled by pumping blood into the coronary arteries. Total coronary venous return was collected from the right side of the heart and $M\dot{V}O_2$ was calculated during a steady state by the Fick principle. Myocardial anoxia was avoided by maintaining the coronary venous O_2 content above 4 vol.% and myocardial O_2 extraction below 75%. A comparison of $M\dot{V}O_2$ at two levels of CBF (and O_2 delivery) was made in 42 instances, and in 32 of them $M\dot{V}O_2$ increased substantially as CBF was elevated, and vice versa. The ten exceptions all occurred when O_2 delivery greatly exceeded $M\dot{V}O_2$ with O_2 extraction ratios below 35%. Determinations of excess lactate indicated that the energy derived from anaerobic metabolism at low levels of CBF could not account for the lower values of $M\dot{V}O_2$ which occurred under these circumstances. These observations show that when myocardial O_2 extraction is in a physiologic range, $M\dot{V}O_2$ is intimately dependent on CBF and suggest that this dependence should be considered in the interpretation of other experiments on the determinants of $M\dot{V}O_2$.

NET SODIUM CHLORIDE FLUX WHERE DIFFUSIONAL AND OSMOTIC FLUXES ARE OPPOSED. E.H. Bresler, L. Cazenavette* and C. Williams*. Veterans Administration Hospital, New Orleans, La.

In 1957 Mauro (Science, Vol. 126 p. 252) showed that osmotic fluxes of water are largely non-diffusional and, with the collodion membranes studied, much greater than predicted diffusional fluxes. Under such circumstances it might be predicted that a NaCl flux generated by a small osmotic gradient might be larger than one generated by a large diffusional gradient. We therefore placed dilute solutions of NaCl in contact with more concentrated ones across collodion membranes. Polyvinylpyrrolidinone (PVP) was added in about a 2 millimolar concentration to the more concentrated salt solution. Under these conditions it has been found that NaCl will exhibit net movement against a 40 to 50 milliosmolar concentration gradient. The concentration of the macromolecule is not far removed from that of protein in plasma surrounding the renal tubular and intestinal membrane barriers. In systems such as these, where osmotic fluxes may be present, it would appear that the net flux of NaCl against its concentration gradient cannot in itself constitute proof of active cellular transport.

POTASSIUM MOVEMENT AND INTRACELLULAR (H^+). E.B. Brown, Jr., B. Goott, and R. Lade. Depts. of Physiology, Kansas Univ. and Univ. of Minnesota.

Given the factors that operate to maintain a particular K^+ gradient across cell membranes, the problem presented when K^+ moves either into or out of intracellular fluid as a result of acid-base disturbances is that of finding a mechanism to explain this movement. If, as Fenn has said, "...if there is some mechanism which tends to keep the ratio $(K^+)_i/(K^+)_o$ (inside to outside) equal to $(H^+)_i/(H^+)_o$ even though true equality is never attained." (Am. J. Physiol. 185:567) evaluation of the change in the ratio $(H^+)_i/(H^+)_o$ should indicate the direction of change of $(K^+)_i/(K^+)_o$ and predict the direction of movement of K^+ when acid-base disturbances are produced. This hypothesis was tested by determining intracellular (H^+) in muscle (DMO technique) before and during various acid-base disturbances in the dog. In both respiratory acidosis and metabolic acidosis the ratio $(H^+)_i/(H^+)_o$ fell and in both conditions extracellular (K^+) rose as would be predicted. Conversely, in respiratory or metabolic alkalosis the ratio $(H^+)_i/(H^+)_o$ increased and extracellular (K^+) fell. It appears that, in general, the change in ratio of H^+ across muscle cell membranes predicts the direction of movement of K^+ in this tissue.

Effects of circulatory curtailment in steroid production in the cat adrenal - K.A. Brownell, S.L. Lee†, R. Beck†, P.K. Besch†, and F.A. Hartman. Ohio State University, Columbus, Ohio.

A study has been made of the altered in vitro metabolism of C_{14} progesterone by adrenal tissue from animals in which the venous outflow from the gland had been curtailed. Incubation was carried out in Kreb's Ringer-bicarbonate medium containing necessary co-factors, substrates and enzymes. Steroids were resolved by papergrams. With increasing time after venous occlusion there was a decreased production of steroids more polar than Ruchstein's S. with a concomitant increase in compounds less polar than S. Further resolution and identification are under way. Quantitation in μ moles/gm/hr converted will be reported. Apparently partial occlusion of venous outflow impedes hydroxylation in corticoid syntheses.

Supported by a grant from the American Heart Association.

THE MEASUREMENT OF LEFT VENTRICULAR POWER AND WALL TENSION IN MAN. Ivan L. Bunnell*, Colin Grant* and David G. Greene. University of Buffalo Medical School and the Buffalo General Hospital.

From large-film biplane angiograms left ventricular volumes have been calculated throughout the cardiac cycle in unanesthetized patients, allowing volume-time curves to be constructed. These have been manually differentiated to produce flow-time curves. Multiplying each point on these curves by the corresponding left ventricular pressure (measured simultaneously or sequentially) has given instantaneous estimates of the left ventricular power and allowed construction of the time distribution curve of this function. The time-integral (area under the curve) measures total stroke work, providing an alternative display of similar information to that shown on previously described left ventricular pressure-volume figures. Net power output is zero during periods of isovolumic contraction and relaxation, but may be considerable when mitral insufficiency abolishes the former, and may become negative (indicating energy absorption) when aortic insufficiency abolishes the latter. Energy is also absorbed during diastole, and the algebraic sum of areas above the zero line (positive: power output) and areas below the line (negative: energy received) estimates the net left ventricular work per beat. An approximation of average wall tension may be calculated (using a spherical model for left ventricular shape) from the Laplace equation. Left ventricular wall tension increases with cardiac dilatation, up to 80% above normal, while stroke work remains nearly constant, so that the ratio of stroke work to tension decreases and efficiency falls correspondingly.

STUDIES ON THE SOURCE OF SPONTANEOUSLY FORMED UREA IN HOMOGENATES OF FROG KIDNEY. N. J. Carlisky*, W. A. Brodsky, K. C. Huang and E. Munsey*. Dept. of Med., Univ. of Louisville School of Med., Louisville, Kentucky.

Production of urea by homogenates of frog or of dog kidney is apparently an exergonic process, being unaffected by DNP, N_2, or cyanide. Lysine, a reputedly competitive inhibitor of arginase activity, actually increased the rate of urea production by 65% when added (to a concentration of 20 μM/gm.) in frog kidney homogenate. Data on concomitant changes of endogenous arginine, urea and free NH_3 were obtained in one homogenate. For the first 30 minutes of incubation (no exogenous substrate), both urea and arginine increased in concentration. During the next period of incubation (30 to 150 minutes), urea concentration increased by 5.5 micromoles per gram while arginine concentration decreased by the same amount. Exogenous arginine, added to a concentration of 80 μM/gm., induced an almost equimolar increase in urea production after endogenous production had ceased. However, the initial (30 minutes) decrease of exogenous arginine content (80 μM/gm. of undiluted homogenate) was 11 times greater than the concomitant increase in urea content. Then, between 30 and 90 minutes after arginine addition, the amount of urea appearing in homogenates was 3-4 times greater than the amount of arginine disappearing in the same time period. This suggests that renal arginine could be an important source of renal urea, and that arginine disappearance leads to formation of an unknown intermediate complex which breaks down into urea and unknown products. The source of the arginine could be from citrulline or argino-succinate; or from hydrolytic breakdown of tissue proteins. Supported By Grant No. A-461, N. I. H.

DESIGN AND PERFORMANCE OF A HUMAN CALORIMETER. Loren D. Carlson and Nishio Honda* (with mechanical design by H. L. Burns). Dept. of Physiol., Univ. of Ky., Lexington, Ky.

A calorimeter has been designed and tested for measurements on the human in the standing or sitting position or on a bicycle ergometer. The dimensions are: height, 1.83 M, width, 0.76 M and depth, 0.91 M. Direct heat loss through the walls is minimal and measured by heat flow discs. Heat gain in the system is measured by a double set of thermocouples measuring inlet and outlet air temperature. Humidity change and air flow are monitored. Inlet air temperature is controlled between 5 and 50° C. and humidity may be reduced by a precool coil. Air flow from floor to ceiling in the calorimeter may be changed from 4 to 12 feet per minute with a rate of 30 to 90 cubic feet per minute. Air flow may be automatically regulated to maintain an inlet outlet air temperature difference from 1 to 5° C. within certain limits, depending on heat input. Calibration shows agreement within ± 5% of theoretical. The response time of the calorimeter to a change in calorimeter conditions is 2 minutes for 80% response and 10 minutes for 95% response. Indirect calorimetry is accomplished with a pneumotachograph and integrating flowmeter. Gas samples are continuously drawn and analyzed. Skin and internal temperatures are monitored and blood flow to extremities can be measured by plethysmographic techniques. - Supported by NIH Grant RG-8429.

EFFECT OF INSTANTANEOUS CLOSE-ARTERIAL INJECTIONS OF SODIUM AND POTASSIUM SALTS OF FERROCYANIDE AND FERRICYANIDE ON ACIDITY OF URINE IN DOGS. Gaspar Carrasquer and Anita Louise Baldwin (intr. by James C. Moore). Dept. of Med., Univ. of Louisville School of Med., Louisville, Kentucky.

Paradoxical aciduria has been found following intra-renal arterial injection of 500μM of Na_2HPO_4 (Carrasquer, et al.-The Physiologist 4:17, 1961); and in later experiments, following injection of 250μM of K_2HPO_4. Injection of larger amounts of divalent phosphates eliminated transient aciduria. If such aciduria were due to effects of non-permeating anions, it would require existence of both Na^+- H^+ and K^+- H^+ exchange systems. To test further effects of non-permeating anions, $Na_4Fe(CN)_6$, $Na_3Fe(CN)_6$, $K_4Fe(CN)_6$ and $K_3Fe(CN)_6$ were injected close-arterially in amounts of 500μM, under conditions of phosphate acidosis (plasma phosphate = 4-6 mM/l). Urine pH (measured by glass electrode) was reduced by 0.1 unit after Na and K ferricyanide; and by only 0.03 unit after Na and K ferrocyanide. Such maximal and transient changes occurred concomitantly with the peak of excretion of injected material. Addition of ferrocyanide and of ferricyanide to pure solutions containing phosphate in concentrations similar to those in urine induced decrements of pH in the beaker similar to those induced by addition of the salts to urine via the renal artery. Therefore, injection of neutral non-permeating anions produced no change in urinary pH other than that expected from physical chemical laws pertinent to solutions of mixed electrolytes. On the other hand, injection of basic phosphates induces changes of urinary pH opposite to those obtained in pure solution. These data suggest that transient elevation of plasma phosphate had a special role in acidifying urine, possibly by stimulation of $H_2PO_4^-$ secretion. (Supported by N.I.H. #A-4618 - A.H.A. #60 Af 25)

A SIMPLE MICROICTERIC TEST FOR ESTIMATING THE DEGREE OF JAUNDICE. Raymond L. Casella* and Sam J. Piliero. New York Medical College, New York 29, N.Y.

A method has been developed which simplifies the search for early jaundice in newborn infants and adults. Microicteric standards were prepared according to the method of Kolmer, placed in microhematocrit tubes and arranged in serial order as a microicterometer scale. Microicteric (M.I.) and serum bilirubin determinations of blood samples obtained from the same patient revealed that the M.I. and the serum bilirubin values tend to parallel each other. This agreement was found also in patients studied serially during the stages of absence of jaundice, and decreasing or fading jaundice. A comparison of the microicteric scales proposed for adult and infants reveals that in infants, a higher level of total bilirubin is necessary before skin jaundice becomes apparent. The value of the microicterometer lies in its availability, speed, micro blood sample requirement, and ease of determination. Apart from its primary use in the detection of the presence of early jaundice and for studies requiring determinations conducted in an acute manner, the microicterometer can serve as an aid in the selection of cases where a serum bilirubin test should be performed. This screening procedure should be of practical value at blood banking centers. (Supported in part by N.I.H. Grant H-3374(C4).)

DECREASES IN RBC CHARGE AND IN OPTICAL DENSITY (O.D.) OF BLOOD PRODUCED BY POLYBRENE. Aldo Castaneda, Eugene F. Bernstein, Fred G. Emmings and I.J. Fox (intr. by V. Lorber). Dept. of Physiol., Univ. of Minn., Minneapolis.

Hexadimethrine bromide (Polybrene), a polybasic macromolecular polymer, produces RBC aggregation. RBC charge was measured by microelectrophoresis in vitro in Ringer's-RBC suspensions following addition of Polybrene in concentrations up to 0.75 mg/ml. RBC charge decreased consistently and progressively from a mean control value of -0.8×10^{-8} Coulombs to a mean value of $+0.5 \times 10^{-8}$ Coulombs at the highest Polybrene concentration. Similar Polybrene concentrations in plasma-RBC suspensions reduced RBC charge from a mean control value of -1.3×10^{-8} to a mean value of -0.6×10^{-8} Coulombs. RBC aggregation is believed to be related to the decrease in RBC charge with Polybrene. Blood was sampled in dogs through densitometers (800mμ) as for dye-dilution curves from the distal pulmonary artery and femoral artery following injection of Polybrene (5 mg/kg) into the right ventricle. The resulting decreased O.D. of blood produced negative peak deflections of -8.8 and -19.2 cm. at these sites respectively compared to positive peak deflections of +18.2 and +16.0 cm. following injection of 2.5 mg. indocyanine green. Adding Polybrene (1%), low molecular weight Polybrene (1%) and distilled water in vitro in 1:20 dilutions decreased the O.D. of blood at 800mμ by 0.240, 0.145, and 0.03 while indocyanine green (0.625 mg/l) and 20% NaCl increased the O.D. by 0.585 and 0.245 respectively. Densitometry is a sensitive technic for detecting RBC aggregation.

MORPHOLOGICALLY SIMULATED SHUNT CURVES. C. A. Castillo,* J. C. Kyle,* W. E. Gilson,* & G. G. Rowe. Cardiovascular Research Laboratory, Univ. of Wisc. Med. School, Madison, Wisconsin.

Indicator dilution curves morphologically simulating those produced by intracardiac shunts were reproduced by simultaneous injection of indocyanine green into the left and right sides of the heart with continuous recording from a peripheral artery. The morphology as to left to right or right to left shunt and the size of the shunt were determined by the relative amounts of dye injected on each side. The process was reversed to indicate shunts in each direction at the level of each chamber. In these intact animals simulated right to left shunts of the order of 2.5% were clearly detected, and as the magnitude of the simulated shunt increased, the curve was predictably distorted. Left to right shunts simulated by injecting less than 10% of the dye on the right side, were hard to recognize by the morphological change of the curve, but larger concentrations produced definite changes. The procedure shows that even under ideal circumstances where dilution of the dye by the shunted blood does not occur, small left to right shunts are not detected, and emphasizes the need for more refined techniques such as double sampling with curves inscribed both from within the heart and from a peripheral artery.

ALTERED ELECTRICAL ACTIVITY OF HUMAN HIPPOCAMPUS AND AMYGDALA INDUCED BY LSD-25. Loring F. Chapman, Richard D. Walter*, W.Ross Adey, Paul H. Crandall*, Robert W. Rand*, Mary A.B.Brazier, Charles H. Markham*. Univ. California Med. Center,Los Angeles.

LSD-25 (25-50 micrograms) was administered by mouth to 5 patients in whom bipolar electrodes had been stereotactically implanted bilaterally in the amygdala and in several regions of the hippocampus 2 weeks previously during evaluation for surgical treatment of psychomotor epilepsy. With this amount of the agent only minimal subjective and behavioral changes were apparent and no significant alteration in the scalp EEG could be discerned. However, high amplitude slow waves and frequent bursts of paroxysmal spike discharges were observed in the recordings from the depth sites beginning 25-30 minutes after ingestion and persisting for several hours thereafter. These alterations were maximal when environmental stimulation was at a low level and they could be greatly reduced by conversing with the patient or requiring him to perform simple tasks (serial subtraction).

OCULOMOTOR EFFECTS OF AMPULLARY NERVE STIMULATION. B.Cohen & J.Suzuki (Intr. by M.B.Bender) Neuro.Dept., Mt.Sinai Hosp. N.Y. Single pulse stimulation of vestibular nerve branches to semi-circular canals does not produce significant extra-ocular potentials or eye movements. If an ampullary nerve is stimulated by closely spaced pulses or pulse trains, activity develops in eye muscles synaptically linked to that semi-circular canal, and characteristic rapid eye movements are produced. Pulse trains can drive eye movements up to 100/sec. and eye muscles up to 300/sec. Using double pulses, maximal facilitation was demonstrated 2-3.5 msec after the first pulse lasting for 15-20 msec. At stimulation rates above 30-50/sec. longer lasting facilitation was produced. Facilitation in these pathways also occurs if the animal is alerted. Single pulses repeated at frequencies above 60/sec. caused specific deviation according to the canal stimulated. In monkeys and some cats the deviation was interrupted by nystagmus opposite to the eye deviation. When stimulation was halted, the direction of the nystagmus reversed and resembled after-nystagmus. Small doses of Nembutal blocked eye movements during stimulation at low repetition rates. More rapid stimulation gave eye deviations as before but without nystagmus or after-nystagmus. Vestibular nerve potentials from ampullary nerve stimulation were unaffected by Nembutal. Thus, when facilitated strong synaptic security develops in the vestibulo-oculomotor pathways effectively coupling semi-circular canals and eye muscles. This facilitation is decreased by Nembutal which also blocks central processes causing nystagmus and after-nystagmus. USPHS Grant B-294

PHYSIOLOGICAL AND BEHAVIORAL RESPONSES OF ALBINO RATS TO CONFINEMENT AND EXERCISE. Bennett J. Cohen and Louis J. Serrano*, Department of Physiology, University of Michigan, Ann Arbor.

These experiments were undertaken to assay possible effects of confinement and exercise on growth and learning in rats. Eighteen Sprague Dawley origin male rats, one from each of six litters in each of three experimental groups, were raised in small individual cages ($4\frac{1}{2}$" x 8") from 21-61 days of age. Each rat in Group I had free access to an exercise wheel; each rat in Group II was forced to exercise daily in a wheel; Group III was confined without opportunity for exercise. All animals were handled daily; food and water was provided ad libitum. Confined rats weighed more and ate more than exercising rats during this 40 day period. The possibility is suggested that temperature differences among the groups affected the regulation of food intake. The rats were then adapted to a once daily feeding schedule, and were exposed to 3 problems in a Hebb-Williams maze. Freely exercising rats solved the problems more quickly and with fewer errors than either the confined or forced exercise groups. These results illustrate the importance of the housing environment for rats used in such studies. The rats were killed at 84 days of age. The mean thymus weights for Groups I, II, and III were 187 mg., 241 mg., and 321 mg., respectively, a significant difference between I and III. However adrenal and testes weights did not differ significantly among the groups. (Aided by Training Grant 2G-460. Division of General Medical Sciences, N.I.H.).

EFFECTS OF ALKALOSIS ON RENAL EXCRETION AND UTILIZATION OF α-KETOGLUTARATE (α-KG) IN THE DOG. Julius J. Cohen and Evelyn Wittmann*. Univ. of Rochester, Rochester, N. Y.

Using renal clearance, metabolic (A-V differences for α-KG and Diodrast), and stop-flow techniques, we have observed that both acute metabolic and respiratory alkalosis markedly decrease net renal reabsorption ($-\dot{T}_{\alpha\text{-KG}}$) and utilization ($\dot{Q}_{\alpha\text{-KG}}$) of infused α-KG. Net secretion ($+\dot{T}_{\alpha\text{-KG}}$) is observed frequently with respiratory alkalosis. During normal acid-base balance, probenecid, which inhibits para-aminohippurate (PAH) transport, decreases $\dot{Q}_{\alpha\text{-KG}}$ markedly with little effect on $-T_{\alpha\text{-KG}}$; during alkalosis probenecid decreases $Q_{\alpha\text{-KG}}$ further, again with little effect on net α-KG transport. Proximal reabsorptive patterns for α-KG in stop-flow experiments are unchanged by probenecid; this further supports the specificity of probenecid's effect on $\dot{Q}_{\alpha\text{-KG}}$ alone. No net movement of α-KG occurs from the nephron lumen beyond the proximal segment under all conditions studied. These observations are interpreted to indicate that: 1) Extracellular fluid pH and not intracellular fluid pH is a major determinant of α-KG transtubular transport and metabolism in the dog kidney. 2) The mechanism by which α-KG is transported to a site of dissimilation within the tubular cell is shared by the PAH transfer mechanism, while 3) Transtubular transport of α-KG is apparently independent of the PAH pathway. 4) $\dot{Q}_{\alpha\text{-KG}}$ occurs primarily from the anti luminal surfaces of the tubular cells. (Supported by USPHS Grant A-3602)

THE RATE OF THE REACTION OF CO_2 WITH DILUTE HUMAN RED BLOOD CELL SUSPENSIONS. H.P. Constantine*, Margot R. Craw*, J.A. Morello* and R.E. Forster, Dept. of Physiology, Grad. Sch. Med. and Department Anesthesiology, Schools of Med., University of Pa., Philadelphia, Pa.

We constructed a Pco_2 electrode using a glass electrode with a 3 mm diameter flat sensitive tip covered with a 0.00125 cm thick teflon membrane and placed it in the observation tube of a Hartridge-Roughton rapid reaction apparatus at varying distances from the mixing chamber. With an electrolyte solution of 0.1 M KCl, 0.001 M $NaHCO_3$ and 1 mgm/ml of carbonic anhydrase in the electrolyte solution, 95% response times of 15 seconds were obtained. The error in indicated Pco_2 in flowing liquid was less than 3%. The apparatus was tested by determining the reaction rate constant of the dehydration of H_2CO_3 (k_V) by mixing an acetate buffer containing 115 mM acetate at a pH of 4.34 and a Pco_2 of 35 mm Hg with a 30 mM bicarbonate solution with a Pco_2 of 70 mm Hg. An average value of 65 sec^{-1} was obtained for (k_V) at 37°C. Fresh human blood was diluted 1 in 10 in an isotonic solution containing 30 mM $NaHCO_3$, 116.5 mM NaCL and 3.5 mM KCl, and equilibrated at a Pco_2 of 45 mm Hg. A second volume of the same isotonic solution was equilibrated at a Pco_2 of 70 mm Hg. The two were then mixed in the Hartridge-Roughton apparatus and the time course of the reaction followed. The Pco_2 of the mixture fell a total of 5 mm Hg with a half time of 0.1 seconds. The process was only approximately exponential; there appeared to be an initial rapid drop in Pco_2 lasting about 0.030 seconds.

BILATERAL COMMON CAROTID OCCLUSION IN THE UNANESTHETIZED DOG. Adrian Corcondilas,* D. E. Donald, and J. T. Shepherd. Mayo Clin. and Mayo Found., Rochester, Minn.

Heymans and Neil (Reflexogenic Areas of the Cardiovascular System. London, Churchill, 1958) stated that the role of the sino-aortic reflexes is predominantly one of adjusting the circulatory capacity, principally by changes in venoconstrictor tone. Daly and Luck (J. Physiol. 143:343, 1958) supported this contention and pointed out that the resulting changes in systemic blood volume must be accompanied by reciprocal changes in the volume of blood in the thorax. In the present experiments, thoracic blood volume (Stewart-Hamilton method), cardiac output (indicator-dilution technic), heart rate, and systemic arterial and right atrial pressures were measured before and during bilateral common carotid artery occlusion in four unanesthetized dogs. Thirty-three paired observations were made, the second one in each pair being done 1 minute after onset of the occlusion. The following values were obtained:

Thoracic blood volume (ml./kg.)=16 before 16 after occlusion
Cardiac output (ml./min./kg.)=138 before 142 after occlusion
Heart rate (beats/min.)=94 before 98 after occlusion
Mean femoral pressure (mm. Hg)=115 before 150 after occlusion
Mean right atrial pressure (mm. Hg)=0 before 0 after occlusion

Thus, the constant consequence of bilateral common carotid occlusion is constriction of systemic resistance vessels. The cardiac output is frequently unchanged; cardiac contractility is increased. The failure of right atrial pressure and thoracic blood volume to increase suggest that there is no overall reduction in systemic vascular capacity.

PROJECTION OF RETINA ON CORTEX OF SQUIRREL MONKEY. Alan Cowey (intr. by R. W. Doty). Center for Brain Research, University of Rochester, Rochester, N. Y.

In mid-pontine, Nembutal, or chloralose preparations a highly localized surface-positive response of variable amplitude occurs at striate cortex not sooner than 35 msec. after a $1/2^{0}$ - 8 foot lambert - 20 msec. flash. The area of visual field from which it can be elicited at an electrode is about 1^{0} in diameter at the fovea and increases to $3\text{-}5^{0}$ peripherally. This projection is very precise. A later surface-negative wave either follows the early wave immediately or appears alone. It can be evoked from a larger area of the field, e.g. 6^{0} centrally, 12^{0} peripherally. The area of striate cortex to which the hemi-fovea (1^{0} radius) distributes the early wave is about 6 mm across. This is identical with that reported for catarrhine monkeys having up to 5 times the brain weight. However, only 3^{0} of field project to that portion of area striate exposed on the operculum. Flashes at or near the fovea also elicit surface-positive potentials in lateral pre-striate with a latency about 10 msec. later than the early striate wave. This projection is also topographic. When the lateral striate area is stimulated electrically a surface-positive wave, latency 2 msec., appears in a restricted region of adjacent pre-striate. Both photically and electrically elicited pre-striate potentials are abolished by removing a strip of cortex between striate and pre-striate or by ablating the striate cortex. (Supported by a Rockefeller Foundation Fellowship and by USPHS Grant B3606)

CARDIOVASCULAR RESPONSES TO BREATHHOLDING IN AIR AND DURING DIVING IN MAN. Albert B. Craig, Jr., Dept. of Physiology, University of Rochester School of Medicine & Dentistry, Rochester, N. Y.

Diving bradycardia in man is a simple measurable strain of a compound cardiovascular response to multiple stresses. Breathholding after maximal inspiration, the usual preparation for a dive, is a constant feature of all apneic dives. The increased intrathoracic pressure is the relaxation pressure at this lung volume, and is transmitted directly to the carotid sinus causing a reflex slowing of the heart. The hypothesis of the present investigation is that after this initial response the heart rate is dependent upon the venous return, which determines the amount of blood available to the heart to pump and to create the pressure which the carotid sinus senses. If the subject is lying supine in air and maintains full inspiration with the glottis open, there is little change in heart rate during the apnea. If, instead, the subject exerts various positive intrathoracic pressures during standard breathholds, the degree of tachycardia is directly proportional to the pressure. When the subject is tilted to the feet down position after maximal inspiration and closure of the glottis, there is a tachycardia. This is contrasted to the bradycardia which results if the subject is tilted head down after the beginning of the breathhold. In the level position the slight tachycardia can be changed to a bradycardia by passively raising the extremities halfway during the breathhold. These and other experiments in water are presented to emphasize the role of the venous return.

CORONARY VASOMOTOR TONUS AND MODERATE HYPOTHERMIA. Cecil E. Cross (intr.by P.F.Salisbury). St. Joseph Hosp., Burbank Calif.

Coronary flow was measured in isovolumic, donor-perfused hearts and also in open-chest dog preparations. Arterial oxygen tension, pH and temperature were recorded. Coronary vasomotor tonus was measured as described before (Circ. Res.9:589,1961): from the slopes of the regression lines of coronary flow and mean coronary driving pressure (aortic pressure minus left ventricular pressure). The coronary vessels became dilated when blood was cooled after its arterialization, so that oxygen tension was decreased during periods of hypothermia. However, when the temperature of blood was decreased before its arterialization, so that pO_2 in cool and warm blood was of comparable magnitude, coronary vasomotor tonus was not influenced by changes of blood temperature. When maximal coronary vasodilation had occurred after intentional reproduction of "left ventricular failure" (LVEDP above 15 mm Hg) hypothermia or corresponding decrements of arterial pO_2 did not result in further coronary vasodilation. Conclusion: Moderate hypothermia influences coronary vasomotor tonus not directly, but through simultaneous changes of arterial oxygen tension.

THE SMALL EFFECT OF CORONARY RECIRCULATION ON THE SHAPE OF THE TAIL OF THE FIRST-PASS INDICATOR DILUTION CURVE.+ B.L. Crowder II*, W.C. Greer*, and C.W. Sheppard. Dept. of Physiology, Univ. of Tenn., Memphis, Tenn.

In a series of 24 modified Starling canine heart-lung preparations the possible effect of coronary recirculation on the single-pass, dye dilution curve was determined. T-1824 dyed plasma was injected into the inferior vena cava and samples were collected from the arterial outflow cannula and from the coronary sinus. Arterial pressure recordings indicated the stability of the preparation. In this series the coronary sinus flow rate was from 1.9 to 9.0% of the total cardiac output and varied with mean diastolic aortic pressure. About 1.4 to 11.6% of the indicator injected was recovered from the coronary sinus. For the arterial curves the experimental points in 2/3 of the cases were significantly above the curve obtained by exponential extrapolation based on a linear regression performed on the first few experimental points beyond the curve maximum. The excess area was used for evaluation of the tail contribution. Arterial curves obtained after coronary sinus cannulation show a scarcely significant decrease in the tail, and a significant area remains. While coronary recirculation accounts for a small part of the tail it does not account for most of it. It is postulated that at least part of the tail may be due to long circulatory pathways in the heart and lungs. The exponential downslope yielded a reasonable representation of the tail but could be in error at times by several percent.

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SLOWING OF THE HEART AT THE BEGINNING OF EXERCISE. E. G. Cummings* and F. N. Craig. U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland.

In a room at 18°C the heart began to beat faster at the beginning of exercise on a treadmill. In the first minute the increase above the previous standing rate amounted to 20 or 30 beats per minute for walking at 3 miles per hour and 90 or 100 beats per minute for running at 9 miles per hour. When the standing rate before exercise was elevated by increasing the room temperature to 38°C or by injecting atropine, or both, the immediate response to exercise was a retardation of the increase, a continuation of the standing rate, or a temporary depression of the rate below the standing rate by as much as 40 beats per minute. It was concluded that the elevation of the standing rate and the initial changes in response to exercise, were accomplished by increases or decreases in vagal activity. There was a secondary increase, 20 to 30 seconds after the onset of exercise, which was attributed to stimulation of the accelerator fibers.

IMMUNOLOGICAL CAPACITY OF LYMPHO-RETICULAR CELLS FROM THYMECTOMIZED MICE. A. P. Dalmasso* and C. Martinez. Dept. of Physiol., Univ. of Minn. Med. School, Minneapolis, Minn.

The capacity of lympho-reticular cells from thymectomized mice to elicit graft vs. reactions was studied. Mice of the C3H or A strain were thymectomized or sham-operated either at 1-24 hours after birth or at 6, 14, 25 or 35 days of age. At approximately 2 months of age the immunological capacity of their spleen and lymph node cells was studied using Simonsen's graft vs. host assay of histocompatibility, which essentially consists of measuring the spleen enlargement induced in suitable recipients as a result of transplantation of adult lympho-reticular cells. The reaction of A strain cells was assayed in (A x C57B1) F1 recipients and that of C3H in (C3H x DBA/2) F1 hybrids. The results show that in mice, thymectomy performed at 1, 6 or 14 days of age renders their spleen and lymph node cells incapable of producing graft vs. host reactions in F1 hybrids, whereas cells from sham-operated animals regularly elicited that reaction. These results are interpreted as evidence that the cells themselves of the lympho-reticular system of thymectomized mice are immunological defective.

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THE EFFECT OF ATROPINE SULFATE ON PULMONARY DIFFUSING CAPACITY (D_L). Walter J. Daly and Joseph C. Ross (intr. by John B. Hickam). Indiana University School of Medicine, Indianapolis, Indiana.

The intravenous administration of atropine sulfate (2 mgm) results in tachycardia, increase in cardiac output, and evidence of changes in venomotor activity in supine normal subjects. It has been shown that inflation of an anti-gravity pressure suit (G suit) over the lower part of the body produces substantial increases in central venous and pulmonary vascular pressures and increases pulmonary diffusing capacity, either by opening up new capillaries or dilating already open capillaries. These increases in pressures occurring with G suit inflation are absent or greatly reduced after atropine administration. To further investigate possible changes in the pulmonary circulation and blood distribution after atropine administration, D_L (breath holding CO technique) was determined before and 10 minutes after 2.0 mgm atropine sulfate was given intravenously in 5 supine subjects. Mean control D_L was 30.3 ± 5.9 ml/min/mm Hg and mean D_L after atropine was 23.7 ± 7.0 ml/min/mm Hg. ($p=0.025$). This significant decrease in D_L could be due to either an actual decrease in the size of the pulmonary capillary bed or to decrease in the volume of effectively ventilated capillaries as a result of altered ventilation-perfusion relationships. This suggests that atropine may have a direct effect on either pulmonary vasculature or on distribution of ventilation.

EVALUATION OF GASTROINTESTINAL MOTILITY BY OXYGEN TRANSIT. Ivan E. Danhof. The University of Texas Southwestern Medical School, Dallas, Texas.

Gastrointestinal transit motility was evaluated in normal individuals in the fasting state and 2 hours post-prandially after having been maintained for 3 days on each of several diets varying in fiber content. Motility was estimated by slow (7 to 10 minutes) intra-gastric administration of 700, 1000, or 1500 cc of oxygen, collection by displacement of saturated sodium chloride solution of voluntarily passed flatus samples which were timed (zero time taken when one-half of gas volume administered) and analyzed for CO_2, O_2, N_2, H_2, CH_3, and H_2S using a gas chromatograph with a helium carrier. The sample containing an arbitrarily selected 18 % or more of oxygen was taken as the end point for the Oxygen Transit Time (OTT). OTT's (1000 cc volume) for fasting subjects and those on low, moderate, and high fiber content diets were 33.0 $\pm$ 4.1; 46.2 $\pm$ 5.3; 50.9 $\pm$ 3.0; 71.8 $\pm$ 4.8 minutes, respectively. In fasting students under the stress of an upcoming examination, the average OTT decreased from 35 to 18 minutes. Following the administration of therapeutically effective doses of atropine and Probanthine the OTT's were significantly prolonged. Motility was also evaluated in a small group of patients with various gastrointestinal motility disorders. It was found that of the volumes used the studies utilizing the 1000 cc of oxygen as the transit gas proved to be most reproducible and showed the smallest standard deviation. Variations in the gaseous composition of early flatus samples flushed by the transit gas may be used to appraise the type of digestive process predominating in the intestine. Although these results are preliminary it is hoped that the OTT may prove to be of value in the rapid and facile appraisal of gastrointestinal motility overall.

THE STUDY OF NUCLEAR AND CYTOPLASMIC INHERITANCE BY TRANSFER OF NUCLEI IN AMOEBAE. J. F. Danielli (intr. by H. Rahn). Dept. of Medicinal Chemistry, The Univ. of Buffalo Sch. of Pharmacy, Buffalo, N. Y.

Studies of inheritance have been made in amoebae by transplanting nuclei from one amoeba to another by micromanipulation. It has been found that certain characters are controlled exclusively by the cytoplasm. Some evidence has now been obtained that the cytoplasmic characters can be transferred from one cell to another by transfer of cytoplasm. It thus seems possible that an analysis of the problem involved in discovering the physical basis of cytoplasmic inheritance may now be commenced.

SODIUM AND ACID SECRETION OF FROG GASTRIC MUCOSA IN VITRO. Horace W. Davenport. Department of Physiology, The University of Michigan.

The purpose of this work was to see whether intracellular sodium participates in gastric acid secretion. In frog mucosa total tissue Na is high, and if RISA space is true extracellular volume, Na_i is about 35 mEq/kg H_2O. Other common extracellular space markers (inulin, mannitol) have higher volumes of distribution, and if they are not intracellular true Na_i may be much lower. When mucosas are washed 15 min in buffer containing 10 mM TRIS-Cl pH 7.4, 1 mM $CaCl_2$, 0.9 mM $MgSO_4$, 9 mM KCl and 100 mM choline-Cl total tissue Na is 4 mEq/kg. In subsequent 1 hr incubation in same solution acid secretion is 213 ± 13 µEq/mg dry wt/hr compared with 270 ± 40 for mucosas in identical solution except that 100 mM NaCl replaces choline-Cl. At end of incubation total tissue Na is 2.1 ± 0.2 and K is 53 ± 2 mEq/kg for mucosas in choline-Cl solution, whereas Na is 56 ± 1 and K is 61 ± 3 for mucosas in NaCl solution. Water content of mucosas in choline-Cl solution is apparently slightly lower than that of mucosas in NaCl solution. Results support the conclusion that acid secretion does not involve Na for H exchange. Although the question of distribution of sodium in the mucosa is not definitively answered, the results suggest that the ion is readily exchangable and not an essential component of whatever intracellular apparatus is responsible for acid secretion. Supported by Grant RG-4831(C5) from NIH.

AN IMPROVED ANTHRONE METHOD FOR INULIN AND THE SEPARATION OF INULIN FROM GLUCOSE BY GEL FILTRATION. Warren D. Davidson and Marvin A. Sackner (intr. by T.G. Schnabel, Jr.) Phila. Gen. Hosp. and Univ. of Pa. Med. School, Philadelphia, Pa.

Present methods for the determination of inulin in urine and plasma require the removal of glucose and other interfering chromogens. This is accomplished by the tedious procedure of fermentation with yeast or by digestion with NaOH. In this study, the anthrone method for inulin (Young and Raisz:P.S.E.B.M. 80:771, 1952) was modified, by decreasing the concentration of anthrone to 0.08% and the temperature of reaction to 38°C, to minimize color development by glucose. Thus, inulin could be determined without pre-treatment to remove glucose. Using this method, inulin clearances were measured on 12 normoglycemic patients (C_{in} 7 ml to 180 ml/min) and compared to a standard diphenylamine method (Walser, Davidson, and Orloff: J. Clin. Invest. 34: 1520, 1955). The mean ratio of clearances by the anthrone method to the diphenylamine method was 0.996, S.D. 0.026. In diabetic patients or during glucose T_M determinations, high levels of glucose gave large and variable plasma and urine blanks. Sephadex^R G-25, a dextran gel, appeared ideally suited for the removal of glucose because it separates molecules of mol. wt. $>$ 4000 (inulin) from molecules of mol. wt. $<$ 1000 (glucose). Urine and plasma samples which contained up to 1200 mg % glucose were added to a sephadex column and washed through with saline. Passage through the column averaged 20 minutes and the effluent fraction, which contained inulin free of glucose, was analyzed by the anthrone method. Recoveries were virtually quantitative. Retained glucose was removed from the columns by further saline washings to permit reuse of the columns. The improved anthrone method coupled with gel filtration to remove the interference of glucose was superior to existing methods because of simplicity, speed and reliability.

AN EVALUATION OF SMALL VESSEL RESPONSES OBTAINED BY CATHETERIZATION TECHNIQUES. D. L. Davis. Med. Col. Ga., Augusta, Georgia.

Previous studies of segmental responses of the vasculature of the dog paw indicated that the catheterization technique employed may have partially damaged the innervation of blood vessels distal to the point of catheterization. Two experimental findings tended to substantiate this. 1) At maximal rates of sympathetic stimulation the larger arteries, proximal to the level of catheterization, were more effective in stopping flow than were the arteries distal to the level of catheterization. 2) At low rates of stimulation flow in the small vessel segment was increased even though the pressure in the digital artery was increased by arteriolar constriction in neighboring channels. To determine if the earlier technique partially destroyed the innervation, the experiments were repeated and the catheterization technique was modified to reduce the possible nerve damage at the small vessel segment. In the present study a small plastic catheter was introduced into an artery at the metatarsal level and threaded peripherally until the tip was lodged in a digital artery. The inflow to this catheter was from a digital artery of the opposite, unstimulated hind paw. Flow through the catheter was recorded by a liquid-filled drop counter. Small vein pressures were recorded from the side arm of a small plastic catheter loop inserted into either a metatarsal or digital vein. Data obtained by the latter technique showed that the small vessel segment was unable to stop flow completely in response to maximal rates of sympathetic stimulation. This may be due to continued damage of the vascular innervation, or to the fact that the small vessel segment constriction was unable to stop flow completely without simultaneous constriction of larger arteries. (Supported by a grant from the USPHS).

THE ROLE OF VAGAL AFFERENTS IN REGULATION OF THE ABDOMINAL COMPRESSION REACTION. L. D. Davis*, A. S. Hoye* and Q. R. Murphy. Department of Physiology, University of Wisconsin, Madison, Wisconsin.

The abdominal compression reaction (ACR) consists of a steady state contraction of abdominal muscles rhythmically interrupted by breathing which is presumed to promote venous return. Previous study has shown that obstructing blood flow in the ascending aorta causes a decrease in intensity of the ACR. To determine the role of the vagus nerves in this response aortic occlusions were performed before and after bilateral cervical vagotomy. Before vagotomy a decrease in the ACR occurred immediately following occlusion in nine of 10 dogs. After vagotomy a decrease in intensity never was observed. An increase occurred in eight dogs while no change was observed in two dogs. These results suggest that the vagus nerve contains afferent fibers which are inhibitory to the ACR. In an attempt to excite these fibers 18 experiments in three dogs were performed in which electrical stimulation was applied to the central end of the cut vagus nerve. A decrease in the ACR occurred in all experiments. From these results it is demonstrated that afferent fibers in the vagus nerve conduct impulses which are inhibitory to the ACR.

EFFECT OF POTASSIUM ON THE POTENTIAL, SHORT-CIRCUIT CURRENT, RESISTANCE AND HYDROGEN ION SECRETORY RATE OF FROG'S GASTRIC MUCOSAE BATHED IN CHLORIDE-FREE SOLUTIONS. T.L. Davis*, J.R. Rutledge*, and W.S. Rehm
Univ. of Louisville School of Med., Louisville, Ky.

Secreting gastric mucosae (histamine) were mounted between chambers with sulfate solutions on both sides. Both sides were gassed with 95% O_2-5% CO_2. Nutrient solutions contained 25 mM HCO_3^- and in secretory solutions SO_4^{--} was the only anion. All solutions contained 1 mM Ca^{++} and 0.8 mM Mg^{++}. With 4 mM K^+ on both sides the nutrient is negative (ave. = -11 mv) and the H^+ ion secretory rate, expressed as current, is slightly greater than the I_{sc}, (short-circuit current). With 4 mM K^+ initially on both sides, changing nutrient to 80 mM K^+ (K^+ replacing Na^+) results in an increased negativity of PD (ave. = -31 mv), a transient decrease in resistance, no significant change in H^+ ion rate and the $I_{sc}>H^+$ ion current. With 4 mM K^+ initially on both sides, changing the secretory fluid to 80 mM K^+ results in nutrient becoming positive (ave. = +14 mv), a decrease in the average resistance from 670 to 530 ohm cm^2 and an increase in the ave. H^+ ion secretory rate from 0.53 to 1.13 $\mu eq\ hr^{-1}\ cm^{-2}$. Changing K^+ from 80 mM on secretory and 4 mM on nutrient to 80 mM K^+ on both sides results in a decrease in H^+ion rate and a change in PD from plus to minus (ave.= -10 mv). Findings are interpreted to mean that in the absence of Cl^- both surfaces are more permeable to K^+ than to Na^+ (b) K^+ can enter either side in direction of K^+ concentration gradient (on basis of I_{sc}) (c) high K^+ per se does not increase H^+ rate (d) increase in H^+ ion rate with high secretory K^+ due to establishment of electric field across secretory surface in direction to increase H^+ion rate (the H^+ ion rate can be increased fourfold by clamping nutrient at increasingly positive levels). Findings support our theory of an electrogenic H^+ion pump. (NSF-NIH support).

THE EEG OF RHESUS MONKEY FETUSES IN UTERO FROM CHRONICALLY IMPLANTED ELECTRODES. Ofelia Esquivel de Gallardo (intr. by W. F. Windle).
Lab. Perinatal Physiol., NINDB, NIH, San Juan, P.R.

Surgery was performed on pregnant monkeys (M.mulatta) of known conception date in two stages. First, an especially designed pedestal holder for electrode cable was anchored into the pelvis and the cable led subcutaneously to the abdomen. Laparotomy was then performed and five insulated steel wires were led into the uterus and through the fetal membranes; the noninsulated tips of four were hooked into the fetal scalp over anterior and posterior central regions. The fifth was attached to the ear for reference. Records were obtained between 117 and 147 days of gestation. They were compared with the EEG of a 129-day premature monkey.

The spontaneous fetal EEG had frequencies increasing with age from 0.5 to 1.5 cycle/sec, with rapid frequencies superimposed and a generalized microamplitude. There was no difference between anterior and posterior regions in amplitude. Independence of the hemispheres was observed. Electrical brain activity of the fetus in utero was similar to that at birth of the premature of equivalent gestational age. In this instance, the advent of birth failed to elicit a significant change in the EEG. The fetal EEG will be compared with that of the full-term newborn monkey (Robert de Ramírez de Arellano, Exptl. Neurol. 3: 209-224, 1961).

CHARACTERISTICS OF MITOCHONDRIA FROM ESSENTIAL FATTY ACID DEFICIENT RATS. Frederick D. DeMartinis (intr. by H. R. Hafkesbring). Woman's Medical College of Pa., Phila., Pa.

Swelling of liver mitochondria from essential fatty acid deficient rats has been compared to that of control liver mitochondria as well as thyroxine-treated control mitochondria. When isolated by the usual method employing 0.25 M sucrose, essential fatty acid deficient mitochondria (D-M) did not always swell faster than control mitochondria (C-M). Using 0.3 M sucrose as preparative medium, however, D-M have consistently swelled faster than C-M. Swelling of D-M can be prevented, as can C-M, by inclusion in the swelling medium of any of a number of agents: Mg^{++}, Mn^{++}, EDTA, DNP, pyrophosphate and ATP. Swelling of D-M can be increased by addition of Ca^{++} or PO_4 to the swelling medium. Bovine serum albumin (BSA) will prevent swelling of C-M and thyroxine-treated mitochondria (T_4-M) but is not effective with D-M. Preliminary work indicates that reversal of swelling can be brought about with each type of mitochondria by addition of ATP only and by ATP + Mg + BSA, but not with ADP only. However, D-M and T_4-M may be contracted in response to addition of ADP + Mg + BSA while C-M may not. These results confirm other reports that essential fatty acid deficiency results in enhanced swelling of liver mitochondria. The inability of serum albumin to prevent swelling of D-M indicates that U factor is apparently not a major influence on swelling in this case.

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RAPID DETERMINATION OF IMPEDANCE LOCUS OF ION TRANSPORTING TISSUES. W. H. Dennis, John R. Hoard*, and Manuel Schwartz*. Dept. of Physiology and BioTransport Unit, University of Louisville; Louisville, Kentucky.

Tissues capable of active transport of ions demonstrate striking changes in their impedance locus characteristics with changes in ionic transport rate. Previous attempts to study these changes have relied on bridge techniques for the changes at a single frequency, or have used individual determinations at various frequencies with interpolation in time to some arbitrary fixed time. In the case of ion transport by epithelial tissues, the changes in the impedance locus occur over a period of minutes. Because of the moderate rate of change it has been possible to utilize fourier integral techniques and analyze the response to a current step to obtain the complete impedance locus from a single step. The integration has been performed graphically, by means of an IBM 1620 digital computer and by means of a specialized fourier integral computer. The results by these various techniques show the superiority of the specialized computer. Impedance locus determinations have been obtained rapidly and efficiently for tissues undergoing changes in ionic transporting state and during anoxia.

TEMPORAL FACTORS IN CHROMATIC EXCITABILITY. S.P.Diamond. Mt. Sinai Hosp., New York, N.Y.

Monocular chromatic interaction effects were investigated by varying the time interval between 2 brief light flashes with non-overlapping spectra. Psychophysical measurements were made in conjunction with a study of cerebral potentials evoked by the paired stimuli. The observed effects can be divided into 5 time ranges: (1) the time interval over which the appearance of the pair is indistinguishable from the appearance of a physical mixture of the stimuli; (2) the range of stimulus separation during which the perceived hue differs from that of the physical mixture and depends on the order of presentation; (3) the transition interval between the perception of a single event and the recognition of the temporal order of two separately perceived chromatic events; (4) that interval over which the principal interaction effect is upon the saturation of the perceived color; (5) stimulus separations of sufficient length so that each stimulus in the pair appears indistinguishable from that stimulus presented alone. For the particular stimulus values employed, judgements of a hue change were made with flash intervals of less than 5 msec. This shift in hue was invariably in a direction towards the color of the second flash, and the magnitude of the shift was found, over a considerable range, to be an increasing function of time. The trading relation between the relative light intensities and temporal separation of the stimuli was also investigated.

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SURVIVAL AND GROWTH OF JUVENILE TURTLES EXPOSED TO CONTINUOUS CENTRIFUGATION. Christopher H. Dodge* and Charles C. Wunder. State University of Iowa, Iowa City, Iowa.

With hatchling Red-Eared Turtles (Pseudemys scripta elegans), growth could be either enhanced or retarded depending upon field intensity. During 9 weeks of centrifugation at 5 G, turtles grew 112±26% more than their controls. At still higher fields, growth decreased as the field increased. However, at fields as intense as 28 G, a few turtles displayed measurable growth. Times for 50% mortality were 3,7 and 31 days at 28,24 and 21 G respectively. At 6,10 and 13 G there was no significant mortality. The superior ability of turtles to survive high gravity can be attributed to their aquatic environment and the shell, which acts as a natural "anti-G suit."

ABILITY TO EXERCISE AFTER COMPLETE CARDIAC DENERVATION. D. E. DONALD and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

A linear relationship was shown between cardiac output (indicator-dilution technique) and oxygen consumption (collection and analysis of expired air via permanent tracheostomy) in 6 normal dogs exercising up to an oxygen consumption of 70 ml. per kg. per min. In 2 dogs denervated by the method of Gilbert and Cooper the animals seemingly ran as well as before despite a marked change in the response of the heart rate. However, neither animal reached the pre-operative maximal oxygen consumption. In one dog the cardiac output was found to be 20 to 30 per cent lower in the higher levels of oxygen consumption but could be returned to or above the control value by Epinephrine or by Dextran infusion. In the other animal the relation of cardiac output to oxygen consumption was unaltered. Transfusion of 200 ml. blood increased oxygen consumption from 50 to 71% of control maximum. Cardiac output increased to the control value. Normally an increase in hematocrit accompanied the increase in oxygen consumption. After denervation this relationship was more pronounced, the increase in hematocrit at maximum work often providing a volume of oxygen equivalent to the resting consumption of the animal. On beginning exercise the normal dog showed a reduction in stroke volume for 15 to 20 beats, then a return to slightly above control values. After denervation, stroke volume increased slowly to a maximum at 1½ minutes of exercise, the increase in stroke volume running parallel with the slow progressive increase in heart rate.

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SODIUM SPACE DETERMINATIONS IN RENOPRIVAL AND GOLDBLATT HYPERTENSIVE ANIMALS. B. H. Douglas,* J. B. Langston, V. S. Bishop,* and A. C. Guyton (intr. by J. D. Hardy). Dept. Physiol., Univ. Med. Center, Jackson, Miss.

Previous studies in this laboratory have shown that dogs with 70% to 75% of their renal tissue removed will become hypertensive when a 0.9% NaCl solution is substituted for their drinking water. The present study compares the hypertension resulting in four dogs from this effect with that occurring in four Goldblatt dogs. Baselines for mean arterial pressure and sodium space (Na^{24}) were established in both the renoprival normotensive dogs (before making them hypertensive) and in normal dogs in which Goldblatt clamps were to be placed. The renoprival dogs were then given a 0.9% NaCl solution in place of drinking water, and Goldblatt clamps were placed in the normal dogs. The arterial pressures in both types of preparations rose to hypertensive levels within one week (from 117 mm Hg to 150 mm Hg in the renoprival and from 123 mm Hg to 185 mm Hg in the Goldblatt animals). Sodium spaces were measured each week thereafter in all these animals. A transient increase in the sodium space occurred the first week in both types of hypertensive animals, the Goldblatt animals rising 25% and the renoprival dogs rising 16%. Thus, the Goldblatt animals showed both a greater increase in mean arterial pressure and in sodium space. After the second week, the sodium space had returned to normal levels in all dogs and remained there during the succeeding weeks even though the arterial pressure remained elevated. These data indicate that the same mechanism might be responsible for the increase in arterial pressure in both groups of dogs since the two groups gave similar results when successive sodium space determinations were made.

SYSTOLIC PRESSURE PULSES IN THE LEFT VENTRICLE AND ASCENDING AORTA. T. E. Driscol* and R. W. Eckstein. Western Reserve University School of Medicine, Cleveland, Ohio.

A detailed study of the time relationships between the left ventricular pressure pulse and its generated aortic wave was made to clarify the importance of the location of a source cannula in the aorta for phasic coronary flow studies. Rigid cannulae with closed ends and side openings were connected to Statham pressure transducers. One cannula was inserted via the cardiac apex into the outflow tract of the left ventricle just below the aortic valve. The second was passed via the left carotid into the ascending aorta to within a few mm of the valve. Left ventricular pressure (LVP), aortic pressure (AP), and the electronic difference pressure (DP) were recorded simultaneously. In experiments on closed chest, awake or anesthetized, (pentobarbital) animals the aortic pulse has the following features: AP rises 2-15 millisec before LVP reaches AP, and has risen 3-15 mm Hg at the time LVP equals AP. LVP exceeds (or is equal to) AP throughout ventricular ejection (the interval between zero DP and .02 sec prior to the aortic incisura). Retraction of the aortic cannula as little as 1 cm eliminates the early rise in AP, increases the magnitude of the early systolic pressure gradient and shortens its duration to an average of 45% of ventricular ejection. Measurements in open chest dogs revealed small differences in the time and pressure relationships described. Considerable attention must be focused on the site of the aortic pressure sensing instrument whenever exact timing of the aortic pulse is required.

THE EFFECT OF INTERMITTANT CORONARY OCCLUSION ON THE ONSET OF VENTRICULAR FIBRILLATION IN DOGS. S. N. Dutta* and Walter M. Booker. Col of Med. Dept. of Pharmacol., Howard Univ., Washington 1, D. C.

Stephenson, et. al. (Am. J. Cardiol. 5, 77, 1960) reported that acute ligation of anterior descending branch of left coronary artery (LAD) causes fatal ventricular fibrillation in a majority of dogs within a few minutes. The present investigation was designed to study the effects of transient repeated occlusion of LAD and left circumflex arteries, prior to ligation of LAD alone on the development of fatal arrhythmia. In mongrel dogs (10-18kg) whose femoral blood pressure and electrocardiogram (lead II) were continuously recorded, LAD and circumflex arteries were exposed and silk ligatures were placed underneath the arteries by a modified method of Vansant, (Surgery, 49, 307, 1961). Intermittant occlusion of circulation was achieved by lifting the ligatures. The LAD and circumflex arteries were alternately occluded for 20-30 seconds at intervals of 3-5 minutes for two hours before ligation of LAD. Acute ligation of LAD produced ventricular fibrillation and marked hypotension in 100% dogs within 0.5 to 5 minutes. In contrast the ligation of LAD following its intermittant occlusion delayed the onset of fatal arrhythmia by 25 minutes to 4 hours. The dog died only when the circumflex artery was ligated after this period. During intermittant occlusion and after ligation the heart rate invariably increased and there was a slight fall in blood pressure. The EKG, however, did not change markedly from the controls in the majority of dogs. In a few dogs only some characteristic changes in the S-T segment and T wave were seen. These changes however, did not influence the delaying effect of intermittant occlusion.

FACTORS AFFECTING TOLERANCE TO COOLING OF THE FINGERS
C. J. Eagan (intr. by J. P. Hannon). Arctic Aeromedical Laboratory, Fort Wainwright, Alaska.

The responses to finger cooling in 0.0° C water for 10 minutes and in air at -20 to -25° C (with moderate air movement) for 30 minutes, or until fingers cooled to -5° C, were compared in three groups of subjects. The groups consisted of: six control subjects who were on the laboratory staff; four Eskimos who normally lived in northern Alaska but who had lived in a temperate climate on an ordinary mixed diet for nine months previous to the tests; six mountaineers who had undergone rigours of daily cold exposure of the extremities for 45 days in the course of an ascent of Mt. McKinley. All subjects slept overnight at the laboratory and were tested in the basal state. Basal metabolic rate, early morning body temperature, and physical fitness (treadmill test) were measured for each subject. Subjects with higher BMRs tended to maintain higher average finger temperatures during both water and air cooling. Physical fitness scores were in the order: mountaineers> Eskimos>> controls. There was no correlation between level of physical fitness and resistance to finger cooling. The most marked differences between the groups were in the air cooling tests. The fingers of all the control subjects cooled to -5° C before the end of the test (average 22 minutes). All of the Eskimos withstood 30 minutes of cooling. Three of the mountaineers who had not suffered cold injury lasted 30 minutes with their fingers at lower (average 15° C), and hence more economical, temperatures than those of the Eskimos (average 22° C).

EFFECT OF PLASMA K^+ CONCENTRATION ON RENAL Na^+ REABSORPTION. J. Donald Easton* and Alan Koch. Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine, Seattle.

Mongrel dogs were anesthetized, the right renal artery was exposed, and urine was collected separately from the two kidneys. Hypertonic NaCl solution was infused into the right renal artery to keep the Na^+ concentration in the blood perfusing the right kidney nearly constant at 210 meq/liter. A systemic infusion of creatine, for measurement of filtration rate, and of PAH, for measurement of renal plasma flow, was started. The concentrations of K^+ in both systemic blood and right renal arterial blood were altered in a parallel fashion, and the effect on Na^+ reabsorption in the two kidneys was observed. Thus, the effects of changes in $[K^+]_p$ on Na^+ reabsorption when $[Na^+]_p$ was normal (left kidney) could be compared to the effects of similar changes in $[K^+]_p$ when $[Na^+]_p$ was high (right kidney). With a normal $[Na^+]_p$ the percentage of Na^+ reabsorbed decreased in a roughly linear fashion as $[K^+]_p$ increased. With a high $[Na^+]_p$ the percentage of Na^+ reabsorbed either stayed constant or increased slightly as $[K^+]_p$ increased. These relations between Na^+ reabsorption and $[K^+]_p$ were the same regardless of whether $[K^+]_p$ was initially low and was elevated during the experiment, or was initially high and allowed to fall. The changes in cation excretion were accompanied by similar changes in Cl^- excretion. The findings are compatible with a model of renal Na^+ and Cl^- transport which includes a coupled Na^+-for-K^+ pump and a second term describing the diuretic effect of K^+. (Aided by grant H4469 from the National Heart Institute, National Institutes of Health, Department of Health, Education and Welfare.)

FLUID LOSS SHOCK IN NEWBORN DOGS. H. E. Ederstrom. Dept. of Physiol. and Pharm., Univ. of N. Dak. School of Med., Grand Forks, N. Dak.

Shock was induced by intraperitoneal injection of 33% glucose solution in a volume of 3% of body weight. In adult animals this procedure resulted in 100% fatality in 5 hours. Fluid loss into the peritoneal cavity averaged 67 ml/kg of body weight. Hematocrit increased about 50%, indicating that loss of blood volume was considerable. Dogs under 6 days of age had only 10% fatality under the same experimental conditions. The hematocrit increased 20%, indicating less fluid was lost from the blood than in adults. The total fluid loss was 48 ml/kg. With increasing age the resistance to fluid loss shock decreased, and at 30-60 days the response approximated that of the adult. Measurement of total body water by drying indicated that the newborn had 80% water, while in adults 60% has been reported. The comparatively high resistance of the newborn dog to this type of shock may be associated with its high body fluid content, and the consequent better retention of the blood fluid volume.

THE EFFECTS OF RESERPINE ON FATTY ACID MOBILIZATION. John H. Edmonson* and H. M. Goodman. Pratt Clinic-New England Center Hospital and Tufts Univ. Sch. of Med., Boston, Mass.

The recent finding that rat adipose tissue contains significant amounts of norepinephrine suggested the possibility that the free fatty acid (FFA) mobilization which is stimulated by a variety of hormonal agents might be mediated by endogenous catecholamines. The additional finding that treatment of rats with reserpine depletes adipose tissue of norepinephrine provided a means for testing this hypothesis experimentally. In the present study reserpine (5 mg/kg) diminished but did not prevent the FFA mobilization which occurs in response to fasting in rats. FFA mobilization induced by ovine growth hormone (1 mg/rat, i.p.) was not reduced by pretreatment with reserpine. Similarly, adipose tissue from reserpine-treated rats produced as much FFA *in vitro* in response to the addition of corticotropin (0.1 μg/ml) as did the normal. It may be concluded that FFA mobilization induced by either growth hormone or corticotropin is not dependent upon tissue catecholamines. Since the dose of reserpine used in these experiments also produced a mild but persistent hyperglycemia, it cannot be definitely established whether the reduced response to fasting in reserpine-treated animals was due to the depletion of catecholamines from adipose tissue or the hyperglycemia.

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RELATIONSHIP OF INTRAPLEURAL PRESSURES AT MULTIPLE THORACIC SITES TO PERICARDIAL, ESOPHAGEAL, AND ATRIAL PRESSURES IN DOGS WITHOUT THORACOTOMY. Alphonse C. Edmundowicz*, David E. Donald and Earl H. Wood, Mayo Found. and Mayo Clin., Rochester, Minn.

Pleural pressures in dogs were recorded simultaneously from sites in the right and left dorsal and right ventral midcaudad-cephalad regions of the thorax with the use of P23D Statham gauges connected to fluid-filled birds-eye-tip radiopaque Teflon catheters (diameter 1.3 mm.) introduced via no. 17 needles inserted through the chest wall to a depth where intrapleural pressures were obtained. With an airtight seal in the needle, the catheter could then be manipulated with fluoroscopic control in the potential intrapleural space to the desired position in the thorax. The pericardium was punctured intramediastinally near the origin of the great vessels by means of an identical catheter containing a 22-gauge hypodermic needle stylet introduced via a 13-gauge olive-tip needle inserted suprasternally and with fluoroscopic control advanced along the ventral surface of the trachea to the site of puncture. Pressures were recorded in horizontal left and right decubitus and supine positions with the animals under morphine-pentobarbital anesthesia. Pleural pressure gradients of about 0.5 cm. H_2O per cm. of vertical distance were observed. Pericardial and esophageal pressures were closely similar to pleural pressures recorded in the same horizontal planes. Introduction of 0.1 to 10 ml. of Ringer's solution into the pleural catheters caused no or only moderate (0.5-1.0 cm. H_2O), usually transient increases in pleural pressure at the site of introduction, with no change at other sites. Similar volumes of air had similar effects, while 50 ml. caused sustained increases of 1 to 2 cm. H_2O at the site of introduction only.

A SIMPLE TECHNIQUE FOR GREATLY INCREASING THE SENSITIVITY AND RESOLUTION OF VISIBLE SPECTROPHOTOMETERS. W. B. Elliott* and G. F. Doebbler, [Intr. by Hermann Rahn] Univ. of Buffalo School of Med. and the Linde Company, Buffalo, N. Y.

Estabrook has reviewed the advantages of liquid nitrogen temperature spectra [Hematin Enzymes, 1961]. Two techniques have been developed that permit the making of absorption spectra in a cuvette held in a flat sided Dewar flask containing liquid nitrogen. The Dewar fits into the standard cuvette compartment of the Cary Model 11 spectrophotometer. Solutions may be rapidly frozen in cuvettes with removable aluminum sides with coatings to increase the heat transfer, the side plates removed and the plate of ice in the cuvette transferred to the Dewar for examination. Another method is to force the solution through a small gauge hypodermic needle into a rapidly moving film of liquid nitrogen to form droplets. The droplets are homogenized in a pre-cooled Potter-Elvehjem homogenizer and the powder transferred to the cuvette with careful tamping. Both methods give excellent resolution. The first method gives from 4 to 5-fold intensification of spectra and the second method gives twenty-fold intensification. The technique can be employed with several of the manual and recording spectrophotometers in common use and is useful wherever increased sensitivity or resolution is needed to identify components in mixtures of pigments.

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THE WORK OF MAINTAINING FLOTATION IN SEA WATER. R. W. Elsner, P. F. Scholander and E. Hemmingsen. Scripps Institution of Oceanography, University of California, La Jolla, California, and The Lerner Marine Laboratory, Bimini, Bahama Islands.

Non-athletic swimmers of widely varying skill were tested for their ability to stay afloat in tropical sea water (temperature 25 to 27°C.). They were subjected to additional work loads by providing them with lead weights carried on a belt at the waist. Determinations of oxygen consumption, heart rate and rectal temperature were made while the subjects were treading water under a floating open circuit respiratory hood. Air was pumped through the hood, collected in a plastic spirometer and sampled for gas analysis. The lactic acid level in peripheral blood was determined before and after maximum work experiments. An approximately linear relationship existed between both oxygen consumption and heart rate and the load supported in the water. Despite the nearly-neutral buoyancy of the human body, the energy cost of maintaining flotation was found to be three or four times the resting metabolic rate. Added weights markedly increased the oxygen consumption, and the maximum load for most subjects was less than five kilograms of lead. Treading water with arms alone was found to be more efficient than when using legs alone. In spite of the relatively warm water and increased heat production, all subjects experienced a lowering of rectal temperature (average 0.5°C.) during a 30 minute swim. (Supported in part by National Science Foundation grant G7476.)

RELATIONSHIP OF GLUCOSE METABOLISM TO CARDIAC ARREST AT LOW TEMPERATURES. Beth Erasmus* and Benjamin G. Covino. Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

A study of the possible relationship between glucose metabolism and cardiac arrest at low temperatures was carried out in the intact isolated rabbit heart. The ascending aorta was cannulated and the coronary vasculature perfused in a retrograde fashion by means of the Anderson coronary perfusion apparatus. Glucose uptake, oxygen consumption, lactic acid production, and cardiac glycogen were measured in two groups at the following heart temperatures: 37, 30, 25, 20, 15C. In the control group the hearts were perfused with Krebs-Henseleit solution containing 1.2 mg/ml of glucose. A second group of hearts were perfused with Krebs-Henseleit solution containing 10 mg/ml of glucose. The hearts perfused with a high concentration of glucose showed a significant increase in glucose uptake and oxygen consumption at all temperatures as compared with the control group. No difference in lactic acid production was noted between the two groups. In the control hearts the glycogen content was not altered by the cooling procedure. However, in the experimental group a significant increase in cardiac glycogen was observed at low temperature. In addition, the average temperature at which cardiac arrest occurred was significantly reduced from 12.5C in the control hearts to 9.5C in those hearts perfused with high glucose. The data suggest that a reduction in glucose uptake by the hypothermic heart may determine, in part, the temperature at which cardiac arrest occurs. (Supported by U.S. Air Force Contract AF 41(657)302.)

ON THE GUSTATORY NEURAL MESSAGE. R. P. Erickson (intr. by K. Schmidt-Nielsen). Department of Psychology, Duke University, Durham, N. C.

The pattern of activity among single gustatory neurons has been examined as a possible basis for the sensory message. Recordings of the electrical activity of single chorda tympani fibers were obtained in phenobarbital anesthetized rats. The across-fiber pattern analyzed was that formed by the relative number of impulses in the first second of activity in each fiber. For example, in individual units, 0.3M KCl produced response rates proportional to those produced by 0.1M NH_4Cl; units having high response rates to one of these solutions had high response rates to the other, and units having low response rates to one had low rates to the other. In contrast, 0.1M NaCl produced response rates unrelated to the KCl - NH_4Cl rates. In other words, the patterns resulting from the application to the tongue of 0.3M KCl and 0.1M NH_4Cl were similar, but both were different from the 0.1M NaCl pattern. If such patterns are the basis of gustatory quality sensitivity (C. Pfaffmann, J. Neurophysiol., 1955, 18, 429-440), the difficulty of discrimination between taste solutions should be directly related to the similarity of the patterns produced by these stimuli. (NSF Grant G 18124)

ABSENCE OF PSEUDOPREGNANCY IN RATS AFTER OVULATION-INDUCING STIMULATION OF THE PREOPTIC BRAIN. John W. Everett. Duke Univ. School of Med., Durham, N. C.

In the proestrous rat with spontaneous ovulatory release of LH blocked out by pentobarbital, ovulation may readily be induced by an irritative focus electrolytically formed in the medial preoptic area through a stainless steel electrode (Proc. Soc. Exp. Biol. & Med. 108: 604, 1961). Stimulation during late diestrus in the 5-day cyclic rat induces ovulation one day early. Study of long-term effects of such stimulation during either proestrus or late diestrus discloses that most animals continue to have short cycles. Only 5 of 31 (16%) displayed a pseudopregnancy-like period of diestrus following the stimulus, a low frequency like that of "spontaneous" pseudopregnancy in our colony. The group of 31 includes 10 rats stimulated during proestrus and 21 during late diestrus. Electric current delivered was well above threshold for ovulation: 9 proestrous and 10 diestrous rats received 10-15 μA D. C. for 60 sec., while 1 proestrous and 11 diestrous rats received 100 μA for 30 sec. When anesthesia was avoided by use of an indwelling electrode (3 rats), pseudopregnancies were similarly lacking. These observations for the first time differentiate by techniques of brain stimulation a neural process controlling ovulation distinct from that which establishes pseudopregnancy. Whether the distinction has an anatomical basis or a temporal basis related to stage of the cycle when stimulation is applied remains to be determined.

TISSUE N_2 WASHOUT IN THE WHOLE ANIMAL AND IN INDIVIDUAL ORGANS. L. E. Farhi, T. Homma*, D. Berger*, and D. Busby*. Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

Direct determination of dissolved N_2 in blood makes it possible to study the N_2 washout from individual organs as well as from the whole body. (1) Analysis of mixed venous blood following N_2 washout from the lungs shows that in the anesthetized dog 80 to 90% of the total N_2 is stored in a "slow" compartment perfused by 10 to 15% of the cardiac output and having a time constant of 150' to 250'. Most of the remaining N_2 (7 - 15% of total) is in areas receiving 20 to 30% of the total blood flow, the time constant being 10 to 15'. Thus more than 50% of the cardiac output perfuses areas in which less than 5% of the total N_2 is stored. (2) The washout curve of individual organs is obtained by sampling venous blood returning from organs or regions and allows one to determine the elements that contribute to each of the compartments. It is also possible to calculate blood flow to an organ by measuring the time constant of the N_2 washout curve. (Supported in part by U.S. Air Force Contract AF 33(616)6823)

HYPOTHALAMIC SUBSTANCES IN ADENOHYPOPHYSEAL FUNCTION. L. C. Faulkner* and Wm. Hansel. Cornell University, Ithaca, N. Y.

Rats bearing renal autografts of anterior pituitary gland provide an *in vivo* system for studying the effects of various hypothalamic substances on the isolated pituitary. Cyclic female rats were hypophysectomized during metestrus, and the adenohypophysis was autografted beneath the kidney capsule. Treatments were started 20 to 45 days following surgery; all treatments were administered intraperitoneally. At autopsy performed approximately 100 days after surgery the ovaries, uteri and adrenals were removed, weighed and preserved for histological studies. Thyroids, vaginae and autografts were also sectioned. Sellae turcicae were serially sectioned to determine completeness of hypophysectomy. Twice daily injections of six to eight units of oxytocin for an average of 69 days, six to eight units of vasopressin for an average of 73 days, three to four units of oxytocin plus three to four units of vasopressin for an average of 72 days, or homogenates of one-half bovine hypothalamus were similarly effective in causing regression of corpora lutea. Corpora lutea were maintained in untreated controls bearing autografts. Corpora lutea of hypophysectomized rats without autografts were intermediate between treated and untreated rats with autografts. Some evidence was obtained to indicate that the treatments were effective in inhibiting the corpus luteum only when an autograft was present. The results suggest that the treatments stimulated the release of a specific luteal inhibitor from the autograft, although the possibility of a direct effect on the ovaries cannot be excluded.

Carried out during the tenure of a Postdoctoral Fellowship from the Institute of Arthritis and Metabolic Diseases, U. S. P. H. S.

THE METABOLISM OF SATURATED AND UNSATURATED FATTY ACIDS BY RABBIT LUNG AND LIVER SLICES. James M. Felts. Cardiovascular Research Inst., Univ. of Calif. Sch. of Med., San Francisco.

The fate of saturated and unsaturated free fatty acids incubated with lung and liver tissue from rabbits has been compared. Slices (500 mg) were incubated for 1 hour in bicarbonate buffer with either palmitate-1-C^{14} (PA) or with linoleate-1-C^{14} (LA) complexed to serum albumin. Oxidation of these fatty acids to $C^{14}O_2$ and conversion to triglyceride fatty acids (TGFA) and phospholipid fatty acids (PLFA) were measured. Lung slices used considerably more saturated fatty acid than did liver slices. The oxidation of PA and LA by lung slices was identical; however, 2-4 times as much $C^{14}O_2$ was recovered from lung as from liver. Recovery of PA and LA in liver TGFA was 2-3 times greater than in lung. Lung incorporated PA into PLFA 5 times and LA 2 times more rapidly than did liver. Thus, lung uses long chain fatty acids for both oxidation and phospholipid synthesis to a much greater extent than liver. It is possible that lung tissue actively synthesizes phospholipids from plasma free fatty acids and does not derive them directly from the circulation. A physiologic relation may exist between this rapid synthesis of PLFA and the unique surface-active material which lines the lungs. The work of Klaus, Clements and Havel (1961) and E. S. Brown (1962) has established that the surface-active agent contained in crude lung extracts or in lung washings is a phospholipid. The identity of the synthesized phospholipids and the phospholipids of lung extracts remains to be established. (Supported by USPHS Grant H-6285.)

EFFECT OF ELEVATED INTRACRANIAL PRESSURE ON CARDIAC OUTPUT AND OTHER CIRCULATORY FACTORS. J. D. Fermoso,* G. O. Pugh,* T. Q. Richardson,* and A. C. Guyton. (intr. by M. D. Turner). Dept. of Physiology, Univ. Med. Center, Jackson, Miss.

The effect of increasing the intracranial pressure on cardiac output, heart rate, arteriovenous oxygen difference, rate of oxygen consumption, right atrial pressure, and mean arterial pressure was determined on 13 mongrel dogs. Cardiac output, arteriovenous oxygen difference, and rate of oxygen consumption were recorded using a continuous cardiac output recorder. Right atrial pressure, mean arterial pressure, and heart rate were recorded with Statham strain gauges which were connected to a polygraph recorder. When the mean arterial pressure was elevated to a mean level of 200 mm Hg by elevating the intracranial pressure, there was an increase of 64 per cent in cardiac output, a decrease in arteriovenous oxygen difference from 7.6 volumes per cent to 6.08 volumes per cent, an increase in oxygen consumption from 96 cc per minute to 120 cc per minute, and an increase in right atrial pressure from the control of -0.53 mm Hg up to 0.17 mm Hg. There was no significant change in the total peripheral resistance.

ACTOMYOSIN-LIKE PROTEIN OF ARTERIAL WALL. R. S. Filo*, J. C. Ruegg*, and D. F. Bohr (intr. by P. A. Rondell). Dept. of Physiol., Univ. of Mich., Ann Arbor.

An actomyosin-like protein was extracted from arterial wall by Weber-Edsall solution and its ATPase activity under various conditions was compared to that of skeletal muscle actomyosin (Bohr, D. F., R. Filo, and K. Guthe. Physiol. Rev. in press). It has now been found that at low ionic strength a similar protein can also be extracted along with the sarcoplasmic fraction. Fresh carotid tissue was ground in sand, and extracted with 3 vol. of 0.05 M KCl and 0.02 M histidine buffer (pH 7.0) for three hours at 2° C. Particles were removed by centrifugation for 30 minutes at 15,000 x g. Precipitation and separation of the actomyosin-like protein from the sarcoplasm was achieved: 1) by dialysis for 12 hours at 2° C against .05 M KCl; 2) by merely standing for 12 hours at 2° C or for one hour at 25° C (precipitate quantitatively similar to that in #1); or 3) by addition of trace concentrations of Ca^{++} (less than 1 mM, gives immediate and more complete precipitation). The precipitate is redissolved in 0.6 mM KCl containing 1 mM ATP. Like actomyosin it possesses ATPase activity and upon the addition of ATP a significant drop in viscosity occurs (ATP sensitivity = 150%), which is fully reversed after hydrolysis of the ATP. It is suggested that the easily extractable actomyosin-like protein is related to tonoactomyosin (Laszt, L. and G. Hamoir. Biochim. Biophys. Acta 50: 430, 1961) and that its initial high solubility at low ionic strength is due to traces of ATP and/or a "solubilizing factor" which (like relaxing factor) can be inhibited by Ca^{++}. (Supported by a grant from the Life Insurance Medical Research Fund.)

QUANTITATION OF CAROTID CHEMORECEPTOR DRIVE BY TRANSIENT PERFUSION OF COMMON CAROTID ARTERIES WITH BLOOD OF KNOWN P_{O_2}, P_{CO_2}, AND pH. Robert S. Fitzgerald*, Joan Tracz Zajtchuk*, and John F. Perkins, Jr. Department of Physiology, University of Chicago.

Dejours et al have demonstrated a resting ventilatory drive for O_2 and CO_2, the latter process involving the carotid bodies, according to Bouverot, Flandrois and Grandpierre (Compt. Rend. Acad. Sci. 252, 790, 1961). Attempting to quantitate in anesthetized dogs the role of the carotid chemoreceptors during eupnea, we have devised a technique for infusing into the common carotid arteries blood of known P_{O_2}, P_{CO_2} and pH. Into each carotid is tied a 3-way stopcock, the arterial pressure rostral to each being monitored, as are airflow, V_T and f. After a control period, the stopcocks are turned to arrest flow from below and 10-20 ml blood are infused from each of two water-jacketed syringes, pulsatile pressures being provided to maintain systolic and diastolic pressures close to control values, thereby minimizing pressoreceptor effects. Infusion of blood briefly equilibrated with O_2 (P_{CO_2} < 10mm) transiently reduced $\dot{V}_E$ to 38% of control $\dot{V}_E$; infusion of venous blood sometimes tripled $\dot{V}_E$; infusion of animal's arterial blood produced no consistent change in $\dot{V}_E$. These preliminary data support Dejours' concept of a peripheral chemoreceptor drive at rest. (Supported by USPHS Grant No. H-5516, C1.)

DIFFUSION OF CO THROUGH THIN LAYERS OF HEMOGLOBIN SOLUTION. Robert E. Forster and Masaji Mochizuki*. Dept. of Physiology, Graduate School of Medicine, Univ. of Penna., Phila., Penna.

We have measured the rate of CO transfer through a 0.015 cm thick layer of hemoglobin solution supported between two stirred gas chambers by a 'millipore' filter at 37°C. in the presence of O_2 concentrations of 0% (in helium), 7%, 21% and approximately 100%, all at 1 atmosphere total pressure. CO concentration was from 0.1% to 2.5% in one chamber and 0 in the other at the start. Approximately 1.5% neon was included in the gas mixture containing CO and its transfer measured for comparison. All gases were analyzed in a gas chromatograph. The hemoglobin solution consisted of freshly drawn human red cells lysed by freezing and thawing and suspended in bicarbonate buffer (pH 7.4) to make an average concentration of 10.8 g/100 ml. The transfer of CO was increased as much as 15 fold over that expected for diffusion alone. This 'facilitation' was greater, the higher the O_2 concentration. At the same time, the [COHb] difference across the film, calculated from the O_2 and CO tensions in the two gas chambers and assuming chemical equilibrium at the film surfaces, decreases as the O_2 tension rises. We believe these results can be explained on the assumption that CO is diffusing through the film both as dissolved CO and as COHb, but that transport of the latter is partly limited by the rates of the reactions of CO with hemoglobin. Raising O_2 tension serves to increase the net velocity of dissociation of COHb at the surface exposed to minimal CO tension.

Size and Turnover of Potassium Compartment Involved in Potassium Secretion in Rabbit Kidney. E.C. Foulkes, May Institute, Cincinnati Jewish Hospital and Dept. of Physiol. Univ. of Cincinnati College of Medicine, Cincinnati, O. (intr. by I.L. Schwartz)

It is believed that filtered K is completely reabsorbed in the proximal tubule, and that K secretion is a function primarily of the distal nephrons. The present experiments were designed to determine what fraction of renal parenchyma is directly involved in K secretion. Rabbits anesthetized with nembutal were administered a constant intravenous infusion of 10% mannitol. Serial urine fractions were collected from the pelvis with a ureteral catheter. A constant infusion of 2 ml/min of KCl was given through a catheter threaded into the thoracic aorta. Arterial blood was obtained from an iliac vessel. After equilibration, K^{42} and C^{14} -labeled inulin were added to the arterial infusion. Inulin served as a measure of the delay between start of K^{42} infusion and appearance of freshly formed urine. Thereupon, specific activity of K was determined in successive samples of plasma and urine. At the end of the experiment the kidney was removed, weighed, and its K content estimated. Analysis of the S-shaped curve relating the urine specific activity to time permitted calculation of the size of the K compartment through which K passes during secretion from plasma into urine. In kidneys weighing 8-10 gm, the K equivalent to only 0.60 gm of cortex (range 0.43-0.81) was found in 11 experiments to participate in K secretion. No correlation obtains in normal animals between this pool size and a three-fold variation in the rate of K excretion (E_k, μEq/kidney/min). The turnover rate (T) of the secretory pool varies with E_k according to the equation $T\ (\%/min) = 4.8 + 2.3\ E_k$ ($P < 0.01$).

EFFECTS OF OUABAIN ON ACUTE ANEMIC HEART FAILURE. N. O. Fowler and J. C. Holmes*. Dept. Med., Univ. of Cincinnati, Cincinnati, Ohio.

Seven heart-lung preparations were made from mongrel dogs. Cardiac rate and ventricular force measurements were made by a strain gauge arch sutured to the right ventricle. Anemia was produced by exchange transfusion of 1000 ml dextran, decreasing hematocrits from an average of 44 vol.% to 7 vol.%. All preparations showed an increase in cardiac output averaging 24% above the control levels of 390 to 508 ml/min. Ventricular force increased (av. 38%); right and left atrial pressures decreased 25% and 24% respectively in 6 of 7 animals studied. Heart failure was produced by additional exchange transfusions of dextran until left atrial pressure rose at least 5 mm. Hg above control levels with final hematocrit level averaging 3.2 vol.%. Ouabain (250-500 ugm), given through the venous inflow cannula, raised cardiac output in all preparations an average of 20% above the control levels of 400 to 526 ml/min. Cardiac rate increased an average 40% in three preparations following ouabain, while no change in rate was observed in four animals. Ventricular force increased in each animal (av. 89%) above control levels. After ouabain, left atrial pressure decreased 30% to 72% (av. 58%) below that during anemic heart failure. Similar changes occurred in right atrial pressure. These results indicate that ouabain has positive inotropic and chronotropic effects on the heart in which failure has been induced by acute anemia.

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HEMODYNAMIC ALTERATIONS FOLLOWING POLYBRENE INJECTIONS. I. J. Fox*, A. Castaneda*, W. O. Griffen*, K. C. Weber*, and M. B. Visscher. Dept. of Physiol., Univ. of Minn., Minneapolis.

Polybrene, a polybasic polymer, produces red blood cell aggregation which might be expected to cause capillary microembolization. Right ventricular (R.V.) injections (5mg/kg) into 6 intact, anesthetized dogs increased pulmonary artery (P.A.) pressure (systolic: 40%, diastolic: 190%, above control) and simultaneously decreased both femoral artery (F.A.) (systolic and diastolic: 20% below control) and left atrial (L.A.) pressures. These pressure changes were accentuated in R.V. injections in 4 open-chest dogs which permitted continuous pulmonary flow (P.F.) measurement (electromagnetic flowmeter). L.A. injections (10 mg/kg) in 4 open-chest dogs produced an initial F. A. pressure increase (systolic: 20%, diastolic: 40%, above control) and seconds later, a P.A. pressure increase (systolic: 20%, diastolic: 5%, above control) followed by a persistent F.A. pressure fall (systolic and diastolic: 60% below control, 10 minutes later.) Following R.V. injection, P.F., after a 35% fall below control at the height of the P.A. pressure rise, almost returned to control in 2 minutes. Following L.A. injection, contrariwise, P.F. rose slightly initially and progressively fell to 45% below control at 2 minutes. Total pulmonary resistance, after a 400% increase at 5 seconds, returned to normal at 60 seconds following R.V. injection. Total systemic resistance, after an initial 20% increase or an initial 15% decrease following L.A. and R.V. injections respectively, fell to 50% of control 60 seconds following either injection.

Estimation of the Output of a Sensory Cortex
W. J. Freeman, University of California, Berkeley

Previous measurements of evoked potentials and spontaneous EEG of the prepyriform cortex have shown that these waveforms can be described as damped sinusoidal oscillations in transcortical potential. When cats with implanted electrodes were trained to press a bar to obtain milk in response to an electrical stimulus to the cortex used as a conditional signal, the amount of damping decreased, without change in the phase angle of onset of the oscillatory evoked potential. The onset of work to obtain or consume food was accompanied by an increase in damping, with a commensurate increase in phase angle of onset. The amount of damping was inversely proportional to the concomitant rate of work to obtain food. It was concluded that cortical output was 1 : 1 proportional to the product of spontaneous amplitude and the amount of damping, and possibly also to the cotangent of the phase angle of onset.

ESTIMATION OF NUTRITIONAL AND NON-NUTRITIONAL BLOOD FLOW AND PLASMA VOLUME IN THE DOG HIND LIMB. J. J. Friedman, Dept. Physiology. Ind. University School of Medicine, Indianapolis, Indiana .

Total tissue blood flow and volume is primarily determined by the relationship of arterial and venous resistance and vascular capacitance whereas nutritional blood flow and plasma volume depend on pre and post capillary r esistance alone. Therefore an independent evaluation of simultaneous flow and volume in total tissue and nutritional channels should provide an indication of the relative tone of arterioles, precapillary sphincters, small muscular venules, and larger veins. Nutritional and non-nutritional flow and volume are estimated by means of a dual indicator dilution technique. The indicators are injected simultaneously intravenously and assayed continuously in the venous effluent. Total tissue flow is set by a constant flow pump. Tissue plasma volume is estimated with radioiodalbumin in accordance with the Stewart-Hamilton formulation: flow times mean transit time of indicator. Non-nutritional blood flow and plasma volume are estimated from the per cent of injected radio rhubidium (Rb 86) recovered and the rhubidium transit characteristics. It is assumed that rhubidium is completely extracted from the nutritional circuit, consequently any rhubidium recovered on the venous side of the tissue must represent that which passed through non-nutritional channels. The rhubidium assumption is being examined by comparison with A-VO_2 differences under circumstances of different flow rates and different states of vascular tone. Nutritional blood flow is calculated from total flow and per cent rhubidium recovery and nutritional plasma volume as the difference between total tissue and non-nutritional plasma volumes. Preliminary data indicate independent behavior of the various vascular elements of the peripheral circulation. (Supported by PHS 4684C2).

THE SITE OF CARNITINE ACTION ON LONG-CHAIN FATTY ACID OXIDATION: A POSSIBLE NEW PATHWAY FOR ACYL CoA FORMATION IN HEART MUSCLE.

Irving B. Fritz and Kenneth T. N. Yue.* Dept. Physiology, University of Michigan, Ann Arbor, Michigan.

We have previously established that carnitine stimulates the oxidation of long-chain fatty acids by a variety of tissue preparations, and that the general site of action is at a stage prior to acyl CoA formation (Physiol. Revs., 41: 52, 1961). The possibility that the catalysis is mediated via the formation of acyl carnitine derivatives is currently being tested. Palmityl-O-carnitine has been synthesized in low yields from palmitoyl chloride and dl-carnitine HCl, and has been found to be a water-soluble compound, M.P. 142-143°C, whose chromatographic behavior permits ready separation from carnitine and palmitate. This compound has been shown to react with CoA in the presence of a transferase in heart muscle to form palmityl CoA. In addition, we have been able to isolate from rat heart mitochondria incubated with tritiated carnitine, palmitate and ATP an intermediate which moves in three separate chromatographic systems in a manner identical to that of palmityl -O-carnitine. This labeled compound has also been tentatively identified in extracts of liver from a dog injected with tritiated carnitine. On the basis of these findings, we postulate the following pathway:

$$\text{CARNITINE} + \text{PALMITATE} + \text{ATP} \xrightarrow[(Mg^{++})]{(\text{Enzyme})} \text{PALMITYL CARNITINE}$$

$$\text{PALMITYL CARNITINE} + \text{CoA} \xrightarrow{(\text{Transferase})} \text{PALMITYL CoA} + \text{CARNITINE}$$

PRESSURE-FLOW RELATIONSHIP IN THE PERFUSED DOG SPLEEN.

Edward D. Frohlich and Jay Y. Gillenwater (intr. by A. D. Keller). US Army Medical Research Laboratory, Fort Knox, Kentucky.

The relationship of pressure to flow was determined in the perfused isolated and non-isolated preparations of the dog spleen. In both preparations this was done by interposing a pre-calibrated blood pump between the right femoral and splenic arteries and progressively increasing arterial inflow from 20 to 100 ml/min in 10 ml increments. The isolated preparation, however, also required the interposition of polyethylene tubing between the femoral and splenic veins and transection of the splenic artery and the periarterial nerve fibers, after insertion of the perfusion cannula. In both preparations calculated vascular resistance progressively decreased as perfusion pressure gradient increased over a wide range (63 to 310 mm Hg). Vascular pressures and resistances were consistently lower at each perfusion rate in the isolated (denervated) preparation. The data suggest that the fall in vascular resistance is primarily brought about by a passive opening of closed channels and a further distention of open vessels unrelated to neurogenic factors. There is no evidence that the perfused splenic vascular bed maintains an intrinsic mechanism which responds to alterations in perfusion pressure induced by changes in blood flow.

THYROID CONCENTRATION OF S^{35} DERIVED FROM RADIOACTIVE THIOCYANATE. Cullie F. Funderburk* and L. Van Middlesworth, Dept. of Physiol., Univ. of Tenn., Memphis, Tenn.

Rats were fed a low iodine diet or Purina Mink Chow to which was added radiosulfur-labeled KSCN (0.037μc/0.53μg/10 gm. diet). After thirty days of feeding the radioactive diets, tissues of the animals were digested in Pirie's Reagent and the radioactivity was measured in a liquid scintillation counter. Results are expressed as tissue/plasma ratios of S^{35} (counts per minute per 100 mg. tissue/counts per minute per 0.1 cc. plasma). Six Long Evans rats fed a non-goitrogenic low iodine diet had S^{35} thyroid/plasma (T/P) ratios averaging 28.5 (range 17.6-43.5). Two similar rats fed Purina Mink Chow had S^{35} T/P ratios of 18.2 and 35.8. Four albino rats fed a goitrogenic low iodine diet developed thyroids twice normal size and their S^{35} T/P ratios averaged 72.3 (range 49.0-102). Paper chromatograms of homogenized thyroid indicated that the major portion of the S^{35} traveled as sulfate. Other tissues of the four rats with goiter had the following average S^{35} tissue/plasma ratios: muscle, 0.5; liver, 1.0; pancreas, 1.5; skin, 4.2; and hair, 12.2. Six Long Evans rats fed unlabeled low iodine diets were sacrificed 6 hours after subcutaneous injection of 2.1 μg. of S^{35} potassium thiocyanate. The S^{35} T/P ratios averaged 5.0 (range 2.3-10.6). Four similar animals 6 hours after subcutaneous injection of S^{35} sulfate had an average S^{35} T/P ratio of 0.5 (range 0.34-0.58). A thyroid concentration gradient of S^{35} has been found to originate from plasma $S^{35}CN$ and accumulate as thyroid $S^{35}O_4$. The magnitude of this gradient may be directly related to thyroid activity.

Physical Components Of Reactive Hyperemia. William F. Geber and James M. Schwinghamer*. Dept. of Physiology and Pharmacology, SUSD Medical School, Vermillion, So. Dakota.

This study was undertaken in order to evaluate the relative contribution of the physical characteristics of a particular vascular bed to the phenomenon of occlusive or reactive hyperemia. Blood flow and pressure in the femoral artery were continuously measured by the use of a transistorized electromagnetic flowmeter and Statham strain gauge. By the use of vasoconstrictors, vasodilators, hyper and hypovolemia, venous occlusion, very short intervals of flow and occlusion, etc. it was established that the degree of tension or stretch on the vascular walls determines whether or not a period of increased blood flow will follow an arterial occlusion.

IN VITRO EFFECTS OF ANTI-HEMOPHILIC GLOBULIN (AHG) FROM BOVINE AND HUMAN SOURCES ON HUMAN AND BOVINE PLASMAS. P.H. Geisler*, M.F. Eichman* AND L.M. Tocantins. Cardeza Foundation, Jefferson Medical College, Philadelphia, Pennsylvania.

Greater clot promoting activity has been claimed for AHG preparations from bovine plasma than those from normal human plasma. This has been attributed to an actual higher amount of the globulin in bovine plasma. A comparison was made of the effects of bovine and human anti-hemophilic globulins, collected and prepared in the same manner, on the rate of clotting of not only normal and hemophilic human plasmas, but on bovine plasma as well. AHG was prepared from citrated plasma by dilution, acidification, and solution of the washed precipitate in normal saline. While bovine AHG is more effective than human AHG in accelerating the clotting of normal and hemophilic human plasmas, human AHG has a greater effect on bovine plasma than bovine AHG. Moderate dilution of the plasma substrate enhances the clot accelerating action of the homologous AHG. The response of a plasma substrate to AHG preparations is influenced by the presence in plasma of species - specific antagonists which reduce the clot-promoting activity of the homologous AHG, but are less effective against preparations from heterologous sources.

THE EFFECT OF CHEMICAL STRUCTURE OF FATTY ACIDS ON IN VITRO ESTERIFICATION BY THE SMALL INTESTINE. A.M. Gelb* and J.I. Kessler* (intr. by D.A. Dreiling). Mount Sinai Hospital, New York, N.Y.

The effect of chain length and degree of unsaturation of fatty acids (FA) on in vitro esterification by the small intestine was studied. Slices of proximal small intestine of hamsters were incubated in a medium to which C^{14} labelled FA had been added. Lipids were extracted with Dole's solution, and non esterified lipids were removed with alkaline ethanol. Differences in the per cent esterification per 100 mg of tissue between FA were recorded. For saturated FA maximum esterification occurred with a 14 carbon chain. Per cent esterification progressively decreased as chain length either increased or decreased from this length. FA below 10 carbons in length were minimally esterified. As degree of unsaturation of the FA increased, per cent esterification decreased. These differences in esterification of the various FA are in the same direction and may explain in vivo differences in extent of absorption and partition between blood and lymph previously noted by others.

TITLE: ELECTROCARDIOGRAPHIC CHANGES OF HYPERCARBIC EXPOSURE

BY: H. W. Gillen, M. D., Department of Neurology, E. J. Meyer Memorial Hospital and University of Buffalo School of Medicine, Buffalo, New York. (Partially supported by the Office of Naval Research Nonr 969(04) and Sandoz Pharmaceuticals, Incorporated.)

During experiments conducted while studying hypercarbic convulsive phenomena, the electrocardiogram was monitored from unanesthetized, unrestrained albino rats through chronically implanted electrodes. The rats were exposed singly to gas mixtures of carbon dioxide and oxygen, with the CO_2 above 30%. The test exposures lasted from ten to thirty minutes after the exposure. Some animals were exposed only once, but specific tests were done to evaluate the effect of multiple exposures in the same animal. The first exposure to the hypercarbic gas mixture produced immediate bradycardia lasting 2 to 4 minutes with occasional premature auricular contractions, or rarely ventricular extrasystoles. Nodal blocks of varying durations and intensities were common. The heart rate and rhythm then regularized at a slower rate than the controls. Cessation of the hypercarbic exposure produced tachycardia with occasional extrasystoles of random origin initially, followed by a relative but regular bradycardia. Repeated exposures of the same rat at intervals of 24 hours or more initiated fewer induction changes in rate or rhythm, but frequently yielded severe rhythm and rate alterations, multiple extrasystoles, and auricular-ventricular dissociations. These later observations are compatible with the observations of Brown after longer exposures to 40% carbon dioxide, and may be partially of central origin.

THE MICROCIRCULATION OF THE SPLEEN STUDIED BY MEANS OF DYES INJECTED IN THE LIVING ANIMAL. S. J. Godart* and W. F. Hamilton. Depts. Physiol. & Pharmacol., Medical College of Georgia, Augusta.

One of the functions of the spleen is to concentrate and store red cells and in some species to release them to the circulation under various conditions. This implies a selective storage of cells, but the destiny of the plasma is still unknown. We thought it interesting to test the hypothesis that the drainage of the fluid was carried out by lymphatic vessels, whose presence in the deep tissues of the spleen has been denied by many authors. We used Prof. Knisely's transillumination method and injected various dyes, following at the microscope their traversal of the living spleen tissue and its hilus. a) Injected locally into the spleen, Patent Blue fills the veins immediately. Very quickly a clear blue cloud appears all over the field showing the diffusion of dye (without cells) through the interstitial space. After a while, the dye is collected in star-shaped regions possibly lymphatic capillaries and obviously independent of the venous sinuses. As the hilus is observed during such a local injection, the dye appears first in the veins, and later but lasting longer in the lymphatic vessels leading to the nodes. India ink injected locally remains in the veins and is not collected in the spaces filled by the blue dye, nor does it appear in the hilus outside the veins. b) To prevent the trauma of local injection, dye was given intravenously. This method enables us to follow the arrival of the dye by the arteries and their branches, the filling of the interstitial space and the collecting in those star-shaped regions which could be the beginning of the lymphatic capillaries. Beside this work, some injections of methylmethacrylate in the splenic artery of dogs showed the continuity of the blood vessels. (This work was done during tenure of a traineeship supported by USPHS grant HTS-5044 and American Heart Association.)

STUDIES ON THE ISOLATION AND COMPOSITION OF ENTEROCRININ

Dale P.J.Goldsmith* and E.S.Nasset. Dept. of Physiology, School of Medicine and Dentistry, University of Rochester, Rochester, New York.

The isolation and chemical composition of a partially purified sample of enterocrinin is described. Fraction activity was determined in dogs with Thiry-Vella fistulas. Increase in volume of secretion after injection of fraction was compared with increase in volume of secretion after injection of a standard sample of enterocrinin. Hog mucosa was extracted with alcoholic HCl and the extract stirred with MeOH. The MeOH soluble was treated twice with flavianic acid. The second precipitate, after removal of flavianic acid, was re-extracted with MeOH. The MeOH soluble was dialyzed in 0.01N HOAc through acetylated cellophane. The non-dialyzable portion was passed through a column of Sephadex. One active fraction obtained from this column consisted largely of a peptide containing most of the common amino acids. This fraction was placed on paper and eluted with 77% EtOH-2% HOAc. The small amount of material recovered enhanced secretion in test animals at dosages of 100 μg. This material contained a peptide with an amino acid composition similar to that of the parent peptide, except for the absence of basic amino acids. The amino acid composition of this final fraction somewhat resembled the amino acid composition of purified secretin (Jorpes and Mutt, Acta Chem. Scand. 15:1790,1961) except for the presence of large amounts of proline and the absence of as much leucine. (N.S.F. Grant G-13174).

OXYGEN UTILIZATION DURING DEEP HYPOTHERMIA BY VENO-ARTERIAL COOLING.

Frank Gollan, Joanne McDermott* and Judith Winkler*. VA Hospital and Univ. of Miami School of Medicine, Coral Gables, Fla.

If closed chest dogs are cooled to cardiac arrest, by partial cardiopulmonary bypass with a pump-oxygenator and heat exchanger, their arterial oxygen tension (corrected for esophageal temperature) is above 200 mm Hg, their arterial pH is above 7.5 and their pCO_2 is about 15mm Hg. Since, these conditions do not permit dissociation of oxygen at 15°C, the oxygenator was eliminated from the extracorporeal circuit and venous blood (at a flow rate of about 100 cc/kg/min) was cooled and pumped into a femoral artery. Venous blood at this low temperature had an oxygen tension of about 30 mm Hg, a pH of about 7.2 and a pCO2 between 30 and 50 mm Hg, and therefore, presented the animal with the conditions most conducive for the dissociation of oxygen at 15°C. Whereas, dogs perfused with arterialized blood consumed only about 0.3 ml O_2/kg/min (more than 50% in the form of dissolved oxygen), those perfused with venous blood consumed as much as 2.0 ml O_2/kg/min (less than 10% in the form of dissolved oxygen). Under both conditions the animals survived the procedure, since ventricular fibrillation was prevented by pretreatment with quinidine.

EVALUATION OF HYPOTENSIVE CARDIAC DAMAGE WHEN THE HYPOTENSION IS CONFINED TO AORTIC BRANCHES BELOW THE SUBCLAVIAN. O. Gomez* and W. F. Hamilton. Depts. Physiol. & Pharmacol., Medical College of Georgia, Augusta.

In a previous report we showed that the heart was damaged by exposure to 90 minutes of hypotension. The damage was assessed by plotting the rise in venous pressure against the rate of work performed by the heart in response to a standard left atrial infusion of donor blood. The control test showed a small rise in venous pressure, an increase in cardiac output greater than the rate of infusion, and a high work rate. Immediately after the 90 minutes of hypotension the test was repeated and the response was normal. The animal was maintained at normotensive levels and the test was repeated. After the lapse of 120 minutes the heart showed damage in that the standard infusion caused an immoderate rise in venous pressure and a very small increase in rate of cardiac work. Since the above was reported an adjustable clamp was applied to the descending aorta and equilibrium reservoirs were set up so that the heart, head and forelegs could be maintained normotensive while the rest of the animal was made hypotensive. After 90 minutes of such hypotension the whole animal was made normotensive and the tests repeated at intervals. The heart showed no damage at 120 or in some cases 180 minutes, at which time the animals of the first series were damaged. When the damage occurred later, it was very similar in both series. (This work was done during tenure of a traineeship supported by USPHS grant HTS-5044 and American Heart Association).

A COMPARISON OF XENON, ETHER, AND NEMBUTAL ANESTHESIA IN THE RAT. Sheldon F. Gottlieb and Robert V. Jagodzinski*. Research Laboratory, Linde Company, Division of Union Carbide Corporation, Tonawanda, New York.

Cullen and Gross (Science 113, 580, 1951) have shown that an 80% Xe-20% O_2 mixture which is anesthetic to man is not anesthetic to the rat. It was of interest to determine what partial pressure of this chemically inert gas would anesthetize a rat. EKG and cortical EEG electrodes were chronically implanted in adult Sprague-Dawley rats. Respiration was measured by a body plethysmograph. The experiments were performed in a pressure chamber. The chamber was flushed with oxygen; the xenon was superimposed on 1 atm of oxygen thereby preventing hypoxia.

A pXe of 1115±150 mm Hg was required to anesthetize the rat. There was no marked second stage anesthesia, nor were there any abnormal EKG or respiratory patterns. The cortical EEG showed high voltage slow activity during anesthesia. The EEG under xenon was somewhat different than that obtained under ether and markedly different from that obtained under nembutal anesthesia.

THE PRESSURE CONTRIBUTION OF THE LEFT ATRIUM IN MAN, ASSESSED FROM THE PRESSURE-VOLUME LOOP. Colin Grant*, Ivan L. Bunnell* and David G. Greene. University of Buffalo Medical School and Buffalo General Hospital, Buffalo, New York.

Construction of the left atrial pressure-volume figure in ten human subjects, using large-film angiograms for the volume measurements, has allowed the net left atrial work output per beat (LAW) to be estimated. This may be calculated as the product of atrial stroke volume (ASV) and a pressure, the difference between mean atrial pressure during emptying (MAEP) and mean atrial pressure during filling (MAFP)

$$LAW = ASV \times (MAEP - MAFP)$$

where the mean pressures are volume-averages drawn from the pressure-volume figure, and not time-averages. This pressure difference represents the effect of the atrium on the blood it receives and ejects. The chamber simultaneously acts as a pipe conveying blood straight through the open mitral valve, so that ventricular stroke volume is greater than atrial; and the pressure effect on the ventricle is correspondingly less.

This atrial pressure effect (MAEP - MAFP) differs from the recently studied quantity Left Ventricular End Diastolic Pressure minus Mean Left Atrial Pressure (LVEDP - MLAP) in that it measures energy transfers to assess the atrial contribution. It has been found to vary from +6 to -2 mm.Hg in different pathological states.

SURFACE NEGATIVE AUDITORY RESPONSES IN AI EVOKED BY ELECTRICAL STIMULATION OF Ep. Nathan B. Gross and Wladimir S. Lifschitz (intr. by Clinton N. Woolsey). Laboratory of Neurophysiology, The University of Wisconsin, Madison, Wis.

Surface negative responses in the middle ectosylvian gyrus (AI) of the cat under pentobarbital sodium anesthesia, were evoked by electrical stimulation of three loci in the posterior ectosylvian gyrus (Ep). The excitability properties of these interconnections were studied by means of paired electrical stimuli. A refractory period of approximately 10 msec. was found and it was followed by a facilitatory period lasting from 10 to 200 msec. Local application of strychnine to the loci in the posterior ectosylvian gyrus elicited "spontaneous" strychnine spikes which were also recorded in the middle ectosylvian gyrus. Similar results were obtained with penicillin. Microelectrode recordings from various depths of the cortex showed that the surface negative response developed within 400-600 microns of the surface of the cortex. Unit activity evoked by the electrical stimulation could be recorded in the middle ectosylvian gyrus.

INHIBITION OF GASTRIC SECRETION BY EXTRACTS CONTAINING GASTRIN. Morton I. Grossman and Iain E. Gillespie*. Veterans Adm. Center, Los Angeles.

The maximum rate of acid secretion that can be attained by continuous intravenous injection of graded doses of hog gastrin extracts into dogs with Heidenhain pouches is lower than the maximum response to histamine. Supramaximal doses of gastrin produce lower rates of secretion than maximally effective doses. In the present study, it was found that single rapid intravenous injections of hog gastrin extract in doses greater than 6 grams (dose expressed as wet weight of mucosa from which extract was derived) markedly inhibited acid secretion occurring in response to continuous intravenous injection of (a) low doses of the same gastrin extract and (b) histamine, even when this was given in maximally effective doses. Inhibition began within 15 minutes, reached a maximum of 80 to 90% within 30 minutes, and was still present to a lesser degree 2 hours after the single dose of gastrin. There were no side effects such as nausea and vomiting, fall in arterial blood pressure, or rise in rectal temperature. Because highly purified preparations of gastrin display this inhibitory action, it seems probable that gastrin itself is capable of inhibiting as well as stimulating secretion of acid, in this respect resembling the action of choline esters on gastric secretion.

THE CIRCULATING FIBRINOLYTIC POTENTIAL IN HUMAN SUBJECTS. M. Mason Guest and Ted P. Bond*. University of Texas Medical Center, Galveston, Texas.

In this study the fibrinolytic potential of several hundred individuals in various physiologic and pathologic states has been measured with two questions in mind: 1) what is the physiologic significance of the fibrinolytic enzyme system? and 2) are extremes in fibrinolytic potential prognostic of either hemorrhagic or thrombotic states? The fibrinolytic potential assay is performed by measuring the rate of proteolysis of fibrin which is obtained from blood processed at 0° C. and with its pH lowered to 6.4 by phosphate buffer. The level of fibrinolytic activity is expressed as the half life of the fibrin clot under the conditions of the test. The half life of the fibrin from the majority of normal human subjects at rest varies between 60 and 80 minutes. The fibrinolytic potential is roughly doubled in these same subjects immediately following moderate to severe exercise. Obese individuals have a significantly longer fibrin half life. Patients with muscular dystrophy tend to have a decreased fibrin half life. Hemorrhage occurs as a result of fibrinolytic activity only when the fibrin half life is extremely short. No clear cut relationship between thrombosis and low levels of activity are evident. From these studies it appears that variations in the level of fibrinolytic activity among individuals and in the same individual during different states of activity are great and that if fibrinolysis is important in circulatory equilibria another system or systems must counterbalance the wide variations in potential activity which occur. (Supported by USPHS Grant H-3717).

METHYLCELLULOSE HYPERTENSION AND POLYVINYL ALCOHOL HYPERTENSION: CONTRAST AND COMPARISON. C. E. Hall and O. Hall*. The Carter Physiology Laboratory, University of Texas Medical Branch, Galveston, Texas.

Female rats each received daily subcutaneous 1 ml injections of either 1% methylcellulose or 5% polyvinyl alcohol (PVA). They and controls were placed on a diet of Purina Laboratory Chow and given either 1% NaCl solution or distilled water to drink. Methylcellulose caused hypertension only in animals given NaCl solution, affecting 60% of them, although it did not cause increased NaCl intake. PVA caused severe hypertension and marked polydipsia in all treated animals regardless of the fluid consumed. However hypertension was somewhat more severe on high NaCl intake, and polydipsia was earlier in onset. Methylcellulose had no effect upon the weight of any organs when distilled water was consumed, but caused slight cardiac and marked kidney enlargement when NaCl was given. Polyvinyl alcohol, on the other hand caused adrenal, cardiac, splenic and renal enlargement in all animals. Sodium chloride enhanced renal and cardiac, but not adrenal or splenic enlargement, and animals so treated also showed thymic atrophy and were the only ones to develop widespread extrarenal vascular lesions. PVA also caused anemia, most severe in animals on salt. It is concluded that under the circumstances of this study methylcellulose hypertension was dependent upon a high NaCl diet, whereas that induced by PVA was not, although the latter was enhanced when excess NaCl was ingested. Furthermore subcutaneously administered PVA heavily infiltrates the spleen and methylcellulose does not, although both accumulate within renal glomeruli. (Supported by Grants H-4327 and H-2703 from the U.S.P.H.S.)

EFFECT OF VAPOR PRESSURE ON PHYSIOLOGIC STRAIN AND BODY HEAT STORAGE IN HYPERTHERMIA. John F. Hall, Jr., Biomedical Laboratory, 6570th Aerospace Medical Research Laboratories, Wright-Patterson AF Base, Ohio.

Physiologic strain in terms of body heat storage, and other physiologic responses were measured and compared in two series of heat stress experiments performed on human subjects exposed to different ambient vapor pressures. One group of 75 experiments conducted on 5 healthy non-acclimatized male subjects exposed 5 times each to 38°, 54°, and 71°C at 10 mm Hg vapor pressure was compared with a series of 81 experiments performed on 10 similar subjects exposed 1-6 times each to 38°, 41°, and 54°C at 20 mm Hg vapor pressure. Subjects were sitting and wore 1.0 clo insulation. Body heat storage was calculated from initial and terminal weighted mean skin and rectal temperatures. The data show the relation between body heat storage and (a) the modified Craig index of physiologic strain; (b) overall sweat rate; (c) evaporative rate; (d) sweat-evaporative ratio; (e) mean skin temperature; and (f) change of heart rate at the respective vapor pressure levels. The curvilinear relation between overall evaporation (clothed body weight loss) and body heat storage at both vapor pressure levels is shown. The data are applicable to sitting subjects similarly clothed who are exposed to heat stresses within the dry bulb temperature range 38-71°C and 0-20 mm Hg vapor pressure limits. The possible predictive use of the evaporative response and the evaporative-sweat ratio as indices of physiologic strain (in terms of body heat storage) is suggested.

POLYVINYL ALCOHOL: RELATIONSHIP OF MOLECULAR SIZE TO HYPERTENSIVE AND OTHER EFFECTS. O. Hall* and C. E. Hall. The Carter Physiology Laboratory, University of Texas Medical Branch, Galveston, Texas.

Young female rats received daily subcutaneous 1 ml injections of 5% polyvinyl alcohol (PVA). Three polymers having molecular weights of 37,000, 133,000 and 185,000 respectively were used. The animals drank 1% NaCl solution and ate Purina Laboratory Chow. The experiment was continued for 29 days when the animals were killed with ether. Polydipsia and hypertension were severe and effected all animals given the medium molecular weight material, but polydipsia did not develop and hypertension was infrequent and mild with either the lesser or greater molecular weight macromolecules. The medium weight material also caused widespread cardiovascular lesions; enlargement of the liver, heart, kidneys and adrenals, and thymic atrophy. The kidneys, liver, spleen and heart were heavily infiltrated by the polysaccharide. None of these changes were caused by the small molecular weight material; but with the high molecular weight PVA there was some enlargement of liver, kidneys, spleen and heart, and these organs were also heavily infiltrated by the substance. Glomerular infiltration appeared to be substantially equivalent with the medium and large molecular weight polymers, although hypertension was frequent and severe only when the former was used. Similarly the incidence and severity of hypertension were comparable in animals treated with the smallest or the largest molecular weight materials, although the latter caused glomerular lesions while the former did not. It is therefore concluded that hypertension is not dependent solely upon renal ischemia caused by infiltration of PVA into glomerular endothelial and epithelial cells, as earlier studies had suggested. (Supported by Grants RG-4833 and H-4327 of the U.S.P.H.S.)

EFFECTS OF ILLUMINATION UPON THE TRANSRETINAL OXYGEN DIFFUSION GRADIENT. Isao Hanawa (intr. by W. K. Noell). Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

In order to measure changes in the transretinal diffusion of oxygen, the isolated retina and chorioid of Bufo marinus covered the surface of a Clark electrode while the free surface of the retina was exposed to wet 100% oxygen at ambient pressure. Changes in response to light of various intensities and durations were recorded at temperatures between 5 and 20°C, simultaneously with the measurement of the ERG evoked by intermittent brief flashes. At 20°C illumination of the dark-adapted retina decreased reversibly the transretinal oxygen difference to a steady level in proportion to the log of light intensity. The activation energy for this decrease in the O_2 gradient, computed for measurement made at 10, 15 and 20°C, was approximately 15,000 cal/mol; the Q_{10} within this temperature range was 2.5 and equal to the Q_{10} of the latent period of the ERG. These data suggest that the change in O_2 gradient is the manifestation of a decrease in retinal O_2 consumption. At 5°C the ERG and the light-induced change in O_2 gradient were abolished; recovery of these phenomena at 20° after 30 minutes exposure to 5°C was surprisingly slow and always incomplete. An increase in O_2 gradient in response to illumination consistently preceded the decrease at 10°C and occasionally also at 20°C, indicating that the effect of light on O_2 consumption is biphasic under optimal metabolic conditions. (Supported by U.S. Public Health Grant B-2710.)

RELATIONSHIP BETWEEN VASCULAR RESISTANCE AND ARTERIAL PRESSURE IN AUTOPERFUSED DOG HIND LIMB. Kenneth M. Hanson* and P. C. Johnson. Dept. of Physiology and Heart Research Center, Indiana University School of Medicine, Indianapolis, Indiana.

Arterial and venous vascular resistance was studied in 30 isolated dog hind limbs. The preparations were autoperfused from the contralateral femoral artery through a short piece of polyethylene tubing. By application of the isogravimetric technique of Pappenheimer and Soto-Rivera the capillary pressure was determined and the arterial and venous resistances were separately calculated. As arterial pressure in the limbs was progressively reduced from approximately 100 mm Hg down to 20 mm Hg the arterial resistance decreased in 25 of the 30 experiments. The reduction in resistance was particularly evident at arterial pressures below 50 mm Hg. The venous resistance remained relatively constant as the arterial pressure was reduced; a significant rise was seen in only 3 experiments. Arterial and venous blood oxygen and carbon dioxide contents were determined at various levels of blood flow in 10 of the experiments. In general, as the blood flow was decreased, venous oxygen content decreased and carbon dioxide content increased, while oxygen consumption fell. It is concluded that autoregulation of blood flow in the hind limb may, in part, be due to tissue hypoxia. It cannot be explained by the tissue pressure hypothesis. This work was supported by grants from the American Heart Association and the National Institutes of Health (H5200, C3).

EFFECTS OF RESPIRATORY MANEUVERS AND OF EXERCISE ON CARDIAC DIMENSIONS IN INTACT UNANESTHETIZED MAN. Donald C. Harrison,* Allan Goldblatt* and Eugene Braunwald. National Heart Institute, Bethesda, Maryland.

The effects of respiration and of muscular exercise on heart size and on ventricular dynamics have been of interest to physiologists for many years, but have been difficult to elucidate in intact unanesthetized man. A method was developed for the precise measurement of ventricular dimensions throughout the cardiac cycle in closed-chest, unanesthetized human subjects. Three silver clips were sutured to the surface of either or both ventricles of 25 patients undergoing cardiac surgery, and following recovery, cineradiograms were obtained at 30 frames/second. The distances between the clips on each individual frame were measured and related to the simultaneously recorded electrocardiogram and intraventricular pressure. During systole ventricular dimensions decreased by an average of 18.5% of the end-diastolic dimensions. In all 6 patients studied during normal inspiration, an increase in right ventricular end-diastolic dimensions averaging 4.3% occurred, with no detectable or consistent changes in left ventricular dimensions. During deep inspiration, right ventricular end-diastolic dimensions increased by an average of 12.5% of the end-diastolic dimensions existing during expiration, while with deep prolonged inspiration left ventricular dimensions increased slightly (1.5% to 4.4%). Reciprocal changes in the size of the two ventricles were not observed during slow respiration, the changes in the dimensions of the left ventricle following those of the right ventricle by 2 or 3 cardiac cycles. In 6 patients, pedaling a bicycle ergometer in the supine position for 5 minutes consistently decreased both end-diastolic and end-systolic dimensions of both ventricles by an average of 5.4% and 5.0% of control values. In conclusion, this new technic has permitted precise measurement of the effects of a variety of basic interventions on ventricular dimensions in intact man.

Ca^{45}AND Cl^{36} DISTRIBUTION IN AORTA AND VENA CAVA
D.W. Harshaw, H. Ziskind, and P.N. Sawyer, (intr. by H. Lyons) Vasc. Surg. Section, Downstate Med. Center, Brooklyn, New York.

Previous studies by this group have been completed measuring movement of inorganic ions across canine and rabbit aortic and vena caval wall in vitro. The ion movement is different both in rate and direction across aorta, compared to vena cava. In an attempt to measure turnover rates of ions by blood vessel wall as a source of the measured differential flux, the escape rates of Ca^{++} and Cl^{-} were measured by means of radioactive tracers. The experiments used rabbit aorta and vena cava. Ca^{++} ion appears to be bound more tightly to the surface and within the tissues than Cl^{-}. Distribution and kinetics of movement of Ca^{++} is different for aorta, vena cava and a control tissue, tendon, while that for Cl^{-} is quite similar for all three tissues. These differences appear to be due to surface charge on fibers and cells making up the tissues. The probable significance of these findings will be discussed.

PROGRESSIVE MUSCLE ELECTROLYTE CHANGES IN NORMAL AND DYSTROPHIC MICE.
C. F. Hazlewood*[1] and J. M. Ginski. Clin. Physiol. Lab. Univ. of Tenn. Col. of Med., Memphis, Tennessee.

Abnormalities in electrolyte concentration in dystrophic muscle have been suggested, in the past, to be due to differences in growth rate from normal. The present study was undertaken to analyze, in dystrophic and non-dystrophic mice (strain 129), the changes in muscle electrolytes (Na, K, and Cl) that occur between the 21st and 131st day of life. The following changes were found in normal muscle: (1) muscle water (grams H_2O/kg fat-free wet tissue) decreased and (2) Na concentration per unit of fat-free muscle weight decreased. Dystrophic muscle revealed the following facts: (1) muscle water decreased, (2) Na and Cl concentration increased and (3) K concentration decreased. Relative to normal muscle, dystrophic muscle expresses at comparable ages (1) a higher water content after 49 days of age, (2) higher concentrations of Na and Cl from 21 days on and (3) a lower concentration of K from day 21. Ancillary studies show that dystrophic muscle has an expanded extracellular space, and a lower resting membrane potential when compared to normal mouse muscle. An elevated plasma K concentration was also found in the dystrophic animals. The differences between normal and dystrophic muscle becomes greater with age, suggesting that superimposed upon the aging process are changes due to the dystrophic process.

[1]Work done as U.S.P.H.S. predoctoral fellow.

RAT MYOCARDIAL PROPERTIES IN EXPERIMENTAL RENAL HYPERTENSION
J.P.Henry* and W.V. Whitehorn, USVA Hospital, Hines, Ill., and Dept. of Physiology, College of Medicine, University of Illinois, Chicago. (Introduced by J. T. Sharp)

As a continuation of a prior study and as part of a more general investigation of the physiological properties of cardiac muscle in various types of hypertrophy, male albino rats were made hypertensive by the application of latex bags to their kidneys. Body weight, heart weight, actomyosin content and ATP sensitivity were determined on eight experimental animals and eleven sham operated controls. Active and passive length-tension curves were determined in vitro on left ventricular columnae carnae in bicarbonate buffered Ringer's solution. In the hypertensive group of animals the heart weight and the heart weight-body weight ratio were significantly increased. No alteration of water fraction of the tissue was observed. No differences in the nitrogen content, actomyosin percentage, ATP sensitivity, or optimum tension production per milligram of wet weight of myocardial sample were seen. These results suggest that the cardiac hypertrophy associated with experimental renal hypertension is not accompanied by significant changes in either the contractility of isolated cardiac tissues or its composition.

SYNCHRONOUS MOVEMENTS OF SUPERNUMERARY GRAFTED EYES IN RANA SYLVATICA.
Emerson Hibbard (intr. by W. F. Windle). Lab. Perinatal Physiol., NINDB, NIH, Bethesda, Maryland.

I have noted previously that in some specimens of Rana Pipiens tadpoles into which supernumerary eyes have been grafted, these eyes move in synchrony with the normal eyes.

A motion picture film of such synchronous movements in a R. sylvatica tadpole demonstrates that the grafted eye is accepted by the host as "self" not only in an immunological sense but also in a neurological one. The stimulus initiating the movement is apparently not a visual one, nor is it a reflex action due to tactile stimuli, but appears to originate centrally. It occurs at fairly regular periodic intervals while the animal is at rest.

Neuronal relationships between host and graft in this and other specimens are described.

The optic nerve from the implanted eye of this tadpole entered a portion of grafted diencephalon which was extensively fused with the left half of the diencephalon of the host. Structurally the implanted eye appeared to be perfectly formed but no optokinetic responses could be elicited from the tadpole following section of the optic nerves of the normal eyes.

INCREASED ANGIOTENSIN-LIKE ACTIVITY IN THORACIC DUCT LYMPH OF DOGS WITH EXPERIMENTAL SECONDARY HYPERALDOSTERONISM. J. T. Higgins, Jr.*, J. O. Davis, and J. Urquhart*. National Heart Institute, Bethesda, Md.

There is evidence that the renin-angiotensin system provides a potent stimulus for hypersecretion of aldosterone in dogs with thoracic caval constriction (J. Clin. Invest. 41:478, 1962). In the present study, evidence of renin hypersecretion into body fluids was sought by assay of angiotensin-like activity in thoracic duct lymph prepared by the method of Helmer (Circulation 25:169, 1962). Samples were assayed by the blood pressure response to intravenous injection into vagotomized, pentolinium-treated rats, and the response was compared to a dose-response curve obtained in each rat with a 20 mug/ml. synthetic angiotensin II solution injected frequently during assay. Pressor activity is expressed as mug. of angiotensin II. Thoracic duct lymph from 8 normal dogs contained an average of 21 mug/ml. of activity whereas pressor activity in lymph from 7 dogs with caval constriction was 42 mug/ml. ($P < .05$). Lymph flow was 4.29 ml/min. in the dogs with caval constriction and only 0.64 ml/min. in the normal dogs ($P < .01$); activity expressed in mug/min. showed an average value of 172 mug/min. for dogs with caval constriction and 15 mug/min. for normals ($P < .02$). Following nephrectomy in 4 dogs with caval constriction and in 4 of 8 normal dogs angiotensin-like activity in lymph was decreased markedly or disappeared. Those normal animals showing no fall had pre-nephrectomy values at the lower limit of the assay method. These results suggest that increased amounts of renin are released from the kidney into lymph of dogs with thoracic caval constriction.

THE EFFECT OF ACETYLCHOLINE ON ISOTONIC TWITCHES OF THE LOCUST LEG. R. B. Hill (intr. by R. E. Gosselin). Department of Physiology, Dartmouth Medical School, Hanover, N. H.

The peripheral role of ACh in insects is still obscure although more is now known of its effects on synapses in the insect CNS. In previous work it was found that ACh application did not alter the tension of isometric twitches of the extensor tibialis of Schistocerca gregaria. "Fast" twitches of the extensor tibialis, due to repetitive stimulation of the crural nerve trunk, have been recorded isotonically while ACh solution was superfused. 10^{-7} to 10^{-2} M ACh caused a gradual increase in the amplitude of isotonic twitches of the extensor tibialis. Fully isometric twitches are not affected by the same concentrations of ACh, which may explain some previous negative results of the application of acetylcholine to insect nerve-muscle preparations. It may be of interest that acetylcholine has an effect opposite to that of 5HT which can inhibit twitches of the extensor tibialis.

RHYTHMICAL OSCILLATORY ACTIVITY IN VISUAL RESPONSES FROM THE UNANESTHETIZED MONKEY. John R. Hughes and John A. Mazurowski,* Meyer Mem. Hosp., Buffalo Univ. Med. School, Buffalo, N. Y.

The present study deals with fast oscillatory rhythms, lasting for as long as 300 msec, evoked by single flashes (15 μsec in duration) and noted mainly in the unanesthetized, alert monkey. The early portion of the evoked response is negative in polarity and shows superimposed wavelets occurring every 5-7 msec; multiples of this spacing are noted from the later wavelets, which appear every 10-14 msec and finally every 20-30 msec. Different electrode placements throughout both the mesial and lateral cortical surfaces show different latencies for the onset of the evoked response, but the later wavelets tend to appear at the same latency throughout the entire visual cortex. Responses with short latencies to the initial negativity show the largest number of wavelets; responses with longer latencies to the initial negativity show fewer wavelets. An increase in the intensity of the light flash decreases the onset-latency of the response and increases the number of wavelets, but the later wavelets tend to appear with a constant latency, regardless of intensity of stimulation. The induction of deep pentathol or nembutal anesthesia converts a polyphasic response with a short onset-latency (18-22 msec) with 7-9 distinct wavelets into a response with a long onset-latency (55 msec) with only one negative wave. Lighter anesthesia progressively shortens the onset-latency and increases the number of wavelets. Later recovery stages are defined only by the addition of more wavelets without change in latency of either of the onset of response or of the existing wavelets. It seems, at least, possible that some coded neurophysiological information may be contained in the presence or absence of these wavelets. (Supported by grant B-1564 from NINDB, NIH.)

THE EFFECT OF ANGIOTENSIN AND NOREPINEPHRINE ON CARDIAC ACTIVITY AT LOW BODY TEMPERATURE. D.A. Hurley* and J. Hunter. Defence Research Medical Laboratories, Toronto, Canada.

It has been shown previously that the maintenance of cardiac activity in deep hypothermia is dependent upon the continuance of circulation through the kidneys and upon an adequate oxygen supply to the animal. The kidney contribution to this maintenance of cardiac activity and blood pressure has been studied further. The kidneys of the animals were exteriorized so that these organs could be either warmed or cooled. The trachea was cannulated so that artificial ventilation with 95% O_2 and 5% CO_2 could be given when colonic temperature reached 25°C. The animals were cooled by being packed in ice. Blood pressure, heart rate and colonic temperature were recorded. Animals which received ventilation and whose kidneys were warmed during the cooling process maintained a mean systemic blood pressure of over 100 mm. Hg. to a colonic temperature of 12°C. All other procedures resulted in a much lower blood pressure at that temperature. The infusion of angiotensin into the jugular vein of animals with cooled kidneys receiving ventilation, however, resulted in a maintenance of the blood pressure as seen in the group with warmed kidneys plus ventilation. The effect of norepinephrine in the same experimental procedure was to elevate blood pressure only at higher colonic temperatures. It is concluded that a functioning kidney is necessary for the maintenance of blood pressure during hypothermia.

RATE OF DISAPPEARANCE OF A STABLE CO_2 ISOTOPE ($C^{13}O_2$) FROM THE ALVEOLAR GAS DURING BREATHHOLDING. R. W. Hyde* and R. E. Forster, II, Dept. of Physiology, Grad. Sch. of Med., Univ. of Pa., Phila., Pa.

We have measured the rate of disappearance of labelled CO_2 ($C^{13}O_2$) in reference to neon from alveolar gas during breathholding from 2.9 to 14 seconds. Subjects first rebreathed rapidly from a 2 liter bag containing 10% CO_2 for 10 seconds in order to equilibrate alveolar and mixed venous CO_2 tensions, thereby maintaining alveolar CO_2 tensions relatively constant at about 50 mm Hg during subsequent breathholding. Next a gas mixture containing 0.6% $C^{13}O_2$, 6% $C^{12}O_2$, 0.5% Neon, 0.5% acetylene (C_2H_2), 20% O_2, and 72% N_2 was inspired maximally. After breathholding an alveolar sample was collected, the concentration of total CO_2 and other gases were measured on a gas chromatograph, and the ratio of $C^{13}O_2$ to total CO_2 on a mass spectrometer. $C^{13}O_2$ had an initial rapid disappearance (58% of the isotope lost from the alveoli in 2.9 seconds), followed by a moderately rapid logarithmic decline ($\frac{1}{2}$ of the remaining $C^{13}O_2$ disappearing every 9 sec). These data can be explained by the assumption that alveolar CO_2 equilibrates with pulmonary capillary blood (V_c) and parenchymal tissues (V_t) in less than 1.5 seconds and thereby produces the initial rapid fall of $C^{13}O_2$. Thereafter the blood carries away the $C^{13}O_2$ in the alveolar gas as well as the $C^{13}O_2$ stored in the pulmonary tissues (V_t). From measurements of V_t determined by the C_2H_2 decline, of V_c by the CO method, and of the initial loss of $C^{13}O_2$, we calculated the CO_2 content of V_t. At a P_{CO_2} of 50 mm Hg one ml of V_t contained 0.5 ml CO_2 STPD. Pulmonary capillary blood flow calculated from the rates of disappearance of C_2H_2 and $C^{13}O_2$ showed good agreement (C_2H_2: 6.5 L/min., $C^{13}O_2$: 6.2 L/min.). The apparent rapid interchange of $C^{13}O_2$ with the bicarbonate in V_t supports the evidence of others that the enzyme carbonic anhydrase is present in lung tissue.

RELEASE OF A "GASTRIN" FROM PYLORIC MUCOSA ON APPLICATION OF AMINOGUANIDINE. **A.C.Ivy, R.Wojciech*, K.W.Liepins*, and E.K.Ivy*. University of Illinois Medical School, Chicago.**

Two dogs with a pouch of the entire stomach received 12 mg/kg of 0.4% aminoguanidine (AG) in normal saline solution subcutaneously, or applied to the pouch, or introduced into the intestine. HCl output during 11 hr. post administration was 30.7 and 57.6 mg, respectively, when the AG solution was given subcutaneously; when applied to the pouch for 1 hr., 118 and 144 mg; when introduced into the intestine 461 and 469 mg. Procainization of the entire stomach pouch prevented response to application of AG to the pouch. Heidenhain pouch dogs did not respond to AG solution applied to their pouch for 1 or 2 hr. The only interpretation possible at present is that AG released a "gastrin" from the pyloric mucosa.

ELECTRICAL RESPONSE OF THE OLFACTORY BULB IN THE TURTLE. Y. Iwase (intr. by G.H. Bishop) Dept. of Zoology, Washington Univ., St. Louis, Mo.

Olfactory nerves were stimulated, and activity patterns in the bulb were analyzed extracellularly with u-pipets. The main components recorded at the surface were 2 successive negative potentials, initial spike and slow potential. The spike was prominent in the anterior region, and the slow potential in the mid-posterior.

In the depth recording the initial spike had a largest amplitude at the upper layer, and the slow potential gradually decreased in amplitude as the electrode advanced, and finally reversed in polarity in the deeper layer. A deep spike of about 4 msec duration was recorded at various depths (0.3-0.8mm) depending on the recording region. This spike was recorded either following the initial spike or superimposed on the sharp initial phase of the positive potential which was a mirror image of the slow potential recorded at the cortical surface. In double shock experiments the initial spike recovered first, but the deep spike had a long recovery of 2 sec or more which coincided with that of the slow potential. GABA applied topically abolished the slow potential and also the deep spike, while the initial spike remained unaffected. Following the deep spike a unit discharge (4-7mV) was recorded, probably indicating excitation of the mitral cell soma. Spontaneous unit discharges were often interrupted during the excursion of bulb potential. The data indicate that the impulse conducted orthodromically in olfactory nerves (initial spike) evokes eventually excitation in the mitral cell soma. The deep spike suggests that excitation of the secondary elements results from the depolarization of terminal or some region of the apical dendrite. (supported by NIH Grant B-1602(C_4) to Rita Levi-Montalcini)

EFFECT OF HISTAMINE, NOREPINEPHRINE AND ACETYLCHOLINE ON GASTRIC VASCULAR RESISTANCE. Eugene D. Jacobson (intr. by David E. Bass). U.S. Army Research Institute of Environmental Medicine, Natick, Mass.

Agents which influence gastric secretion are vasoactive in other circulatory areas. It is not known to what extent they are active in the gastric circulation. The effects of agents which accelerate (histamine, acetylcholine) or inhibit (norepinephrine) gastric secretion were investigated in the vascular bed of the perfused canine stomach. Blood flow to the stomach was maintained constant with a pump, and pressure changes were measured in the gastric vascular circuit in response to a wide range of doses of histamine, acetylcholine and norepinephrine. The agents were continuously infused, both locally and systemically, and the dose was calculated as a drug concentration in the blood perfusing the stomach per minute. Histamine induced a 40 percent fall in gastric vascular resistance in the dose range 0.01 to 0.40 ug per ml per minute. Vascular resistance declined 20 percent in response to acetylcholine infusion in the dose range of 0.03 to 1.00 ug per ml per minute. Norepinephrine administration in the dose range 0.01 to 1.00 ug per ml per minute was followed by a 50 percent increase in gastric vascular resistance. There was no appreciable difference in the dose-response relations of histamine or norepinephrine when the local route of administration was compared with the systemic; however, acetylcholine was more effective when it was administered locally. It appears that agents which stimulate the stomach to secrete also decrease vascular resistance in the stomach, and an agent which depresses the rate of gastric secretion vasoconstricts the gastric vascular bed.

PULMONARY BLOOD FLOW IN THE FETAL AND NEWBORN LAMB. H.N. Jacobson*, L.B. Strang*, C.D.Cook, P.A. Drinker*, and H. Levison*. The Department of Obstetrics and Gynecology, the Department of Pediatrics, Harvard Medical School, and the Hydrodynamics Laboratory, Massachusetts Institute of Technology.

Pulmonary blood flow in the fetus is about 10 to 20 per cent of the cardiac output and it increases abruptly when ventilation begins. Previous work suggested that this increase is due to a change in vascular resistance secondary to changes in pulmonary mechanical forces developed with ventilation of the lung. Factors controlling pulmonary blood flow of lambs delivered by caesarean section were re-investigated using separately ventilated lungs with direct measurement of flow at constant vascular pressure gradients. Measurements were made during stepwise inflation and deflation of the fetal lung and the effects of changing the inspired gas composition were measured in relation to the onset of ventilation. Evidence was found that pulmonary blood flow was controlled by active vasomotor responses induced by changes in alveolar gas composition. These affected blood flow in the initial change at the onset of breathing as well as after ventilation was established.

THE COMPRESSIBILITY OF ALVEOLAR GAS AND ITS EFFECT ON THE WORK OF BREATHING. M. J. Jaeger* and A. B. Otis. Univ. of Florida, College of Medicine, Gainesville, Fla.

The alveolar gas is compressed and expanded during every breathing cycle. The tidal volume measured with a body plethysmograph indicating chest movement (V_{chest}) is therefore larger than the tidal volume measured at the mouth (V_m). The ratio V_m/V_{chest} is inversely proportional to the square root of an expression which includes the breathing frequency, the airway resistance and the compressibility of alveolar gas. In normal subjects the ratio is nearly equal to unity, but in patients with obstructive emphysema, for instance, the high airway resistance and the large lung volume contribute to make V_{chest} much larger than V_m. In some cases V_{chest} is twice as large as V_m, and the work of breathing is underestimated if it is based on determinations of V_m, because appreciable work has to be done to compress and dilate alveolar gas. Furthermore, the work done to overcome tissue elasticity has to be computed from measurements of V_{chest}.

MECHANICAL FACTORS AFFECTING GASTRIC EMPTYING. N.C. Jefferson, Y. Kuroyanagi*, and H. Necheles. Dept. of Gastrointestinal Research, Medical Research Institute of Michael Reese Hospital, Chicago, Illinois.

Fixation of a small area of the stomach to the abdominal wall of dogs or establishment of a gastric fistula shortened gastric emptying time significantly. Attachment of metal washers to gastric mucosa, submucosa, or serosa did not affect gastric emptying. These results may have implications both for the research worker and the clinician. Supported by USPH Grant A-6078.

THE TERMINAL MEMBRANE CONDUCTANCE OF THE MUSCLE SPIKE POTENTIAL. Howard Jenerick. Emory University, Atlanta, Georgia.

Following analytical procedures already reported from this laboratory (Nature, 191, 1074-76, 1961) it has been possible to reconstruct the instantaneous relationship between membrane voltage and membrane ionic current during the spike potential of Rana pipens sartorius muscle. It seems clear that slopes at various points or regions of such a current-voltage plot can be identified as membrane conductances. It has been observed that the ionic current is linear with membrane voltage between the second inflection point and the initial portion of the afterpotential. The membrane conductance therefore is constant during this terminal phase and has been measured under various experimental conditions of pH and ionic concentrations. It should be mentioned that this portion of the spike has a duration in the order of a millisecond and represents a significant fraction of the total spike activity. Fibers in normal Ringer's fluid show a terminal conductance in the order of 10-20 millimhos/cm^2 (over 100 measurements). Similar values are found in fluids with Ca^{++} raised to 10 mM (from 1 mM) or K^+ altered from zero to 12.5mM. Replacement of chloride by sulfate does not significantly alter the conductance. On the other hand, the conductance is increased about 25% by Ringer's fluids at pH 9-10, and decreased about 50% at pH 5-5.5. The possibility that these shifts may reflect alteration of net charge on surface protein layers was tested by tryptic digestion with negative results to date.

EFFECT OF INFUSION OF BILE ACID UPON GASTRIC SECRETION IN DOGS. P. H. Jordan, Jr. and J. A. Kreager, Jr.* Dept. of Surgery, Univ. of Florida, Gainesville, Florida.

The cause for increased gastric secretion following portacaval transposition in dogs is unknown. Disruption of the enterohepatic circulation of bile acids following an external biliary fistula increases daily bile acid production as much as 100 fold. This suggested that portacaval transposition, acting as an internal biliary fistula, might cause an increase in circulating bile acids thus stimulating gastric secretion. The effect of intravenous administration of bile acids upon gastric secretion was therefore studied. Seven dogs, prepared with Heidenhain pouches, were given sodium taurocholate intravenously in doses of 0.4 gm., 1.0 gm., and 2 gm. All infusions required 80 minutes. These doses were comparable to the amount of bile acids expected to enter the intestine during a meal. Gastric collections made every 20 minutes were titrated for free acid. Controls were run on all dogs using normal saline. Two gm. of bile acids increased volume and free acidity of the gastric secretion in each of 15 experiments. One gm. resulted in increased volume of gastric secretion in 9 of 11 experiments and increased free acid in 7 of 11 experiments. The 0.4 gm. dose was followed by an increase in volume and free acidity in 4 of 6 experiments. The magnitude of the responses varied from dog to dog but reflected dose-response curves for the individual dog. Intravenous infusion of sodium taurocholate increased gastric secretion from Heidenhain pouches in dogs. The relation between this fact and the hypersecretion following portacaval transposition is being explored.

CONTRACTIONS OF THE ANTENNAL PULSATILE ORGAN OF THE AMERICAN COCKROACH, PERIPLANETA AMERICANA L. Stanley R. Joseph* and Jack Colvard Jones. Dept. of Ent., Univ. of Md., College Park, Md.

The antennal pulsatile organ of intact P. americana nymphs contracts 10 times in 7.2 to 22.6 seconds, with means of 9 to 12.5 seconds. In freshly severed heads examined in saline, the pulsation rates rapidly decrease and completely stop in 6 to 10 minutes. When the pulsatile organ is isolated in saline it contracts 10 times in 8.2 to 16.6 seconds (average 10.6 seconds). (Supported by N.I.H. Grant H-5193; Miscellaneous Publication Number 463, Contribution Number 3378, of the Maryland Agricultural Experiment Station, Department of Entomology).

RESPONSE OF NORMAL MEN TO INFUSED NOREPINEPHRINE BEFORE AND AFTER CHRONIC COLD EXPOSURE. Robert J. T. Joy (intr. by George Clark) USA Research Institute of Environmental Medicine, Natick, Massachusetts

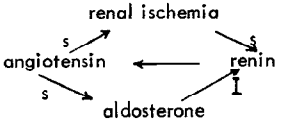
Norepinephrine has been suggested as a mediator of non-shivering thermogenesis in the cold acclimatizing rat, with a decline in shivering accompanied by an increase in vasopressor and calorigenic responses to exogenous hormone. In cold exposed man there is a decline in shivering with maintainence of heat production. This is a study of mechanisms of physiological cold acclimatization in man. Nine healthy males were infused with norepinephrine (0.15 ug/Kg/min) for 20 minutes before and after five 40 hour weeks of semi-nude exposure to 5°C. All infusions were given in the basal state, in a quiet room at 27°C (subjects nude), after a 30 minute period of control measurements. Rectal temperatures and respiratory rates were unchanged either by the drug or the intervening cold exposure. The drug increased respiratory minute volumes and tidal volumes and decreased heart rates, but equally so in both experiments. Mean skin temperatures were unaffected by the drug but were significantly ($p<.025$) higher after cold exposure (mean 1°C). The drug-induced increase above basal of systolic and diastolic blood pressures was significantly lower ($p<.025$) after cold exposure. Oxygen consumption was the same in both basal periods and was unaffected by the drug before cold exposure. After cold exposure, norepinephrine produced a significant ($p<.025$) increase in oxygen consumption (mean 18 cc/min/M^2). These results show a changed sensitivity to norepinephrine in cold exposed man, with a decrease in vasopressor response and the development of a calorigenic response. The data suggest that in man norepinephrine may be a mediator of a non-shivering thermogenesis occurring with cold acclimatization.

REVERSAL OF EPINEPHRINE EFFECTS ON PLASMA NEFA IN FASTED RATS. John Kabal* and Estelle R. Ramey, Georgetown Univ. School of Med. Wash., D.C.

Epinephrine is known to elevate plasma NEFA and glucose levels in fed rats. We have found that this is not the invariable effect of this agent. Normal fed rats treated with 1 mg/kg epinephrine in oil subcutaneously show a simultaneous elevation of plasma NEFA and glucose which reaches its peak at 1 hr. and is back to normal at 5 hrs. If the epinephrine is administered to rats fasted for 16 hrs., the plasma glucose is elevated as usual but the plasma NEFA actually is depressed from a level of 0.995 meq/l to 0.601 meq/l. The lowest NEFA level is reached after 1 hr. and restoration to normal fasting levels is achieved after 5 hours. Thus, the time course of the epinephrine effect is the same as in the fed animals but the direction of the change of the plasma NEFA is reversed. Similarly, rats treated with 1 mg/kg epinephrine in oil daily for 7 days, do not respond with the elevation of plasma NEFA seen in control rats. There is instead a drop in NEFA levels in response to epinephrine. The blood sugar level is unaffected. These results suggest that fasting which produces a shift from glucose to increased lipid utilization also alters the response to epinephrine. It may be that under these conditions the epinephrine induces more marked increases in hepatic uptake of NEFA and peripheral utilization of lipids which override the increased mobilization of lipids from the depots. The inhibition of glucose utilization by epinephrine is consistent with this hypothesis.

THE INTER-RELATION OF ANGIOTENSIN AND ALDOSTERONE ON KIDNEY RENIN. Yale J. Katz, Sol Bernick*, Paul R. Patek*, Rolando de Hoyos*, and Raymond S. Moore*. University of Southern California School of Medicine, Los Angeles, California.

Angiotensin (but not epinephrine) when given subcutaneously to rats, causes at first an increase and then a decrease in the juxta-glomerular index and the renin content of the kidney. Because angiotensin stimulates aldosterone secretion it seemed possible that aldosterone might be involved in the secondary decline in the JG index and the kidney renin content. In support of this notion we find that 2 μg angiotensin t.i.d. for seven days causes a 2 to 3 fold increase in the kidney renin in the normal rat and an 8 to 10 fold increase in the kidney renin in the adrenalectomized rat. When 2 μg aldosterone is given along with angiotensin to the normal rat no increase in kidney renin occurs and only a partial increase in renin occurs in the adrenalectomized rat. These findings coupled with previous studies lead us to suggest the following relationships:



where "s" = stimulation and "I" = inhibition

INDUCTION OF "PARADOXICAL" SLEEP BY CONDITIONAL STIMULATION IN THE RABBIT. M. Kawakami* and Charles H. Sawyer. Dept. of Anat. and Brain Research Institute, UCLA, Calif.

"Activated" or "paradoxical" sleep occurs naturally as part of an afterreaction to coitus in the female rabbit (Endocrinology 65: 622, 1959; Fed. Proc. 21: 354, 1962). Under appropriate hormonal conditions this peculiar electroencephalographic (EEG) and behavioral response can be evoked by low frequency electrical stimulation of the brainstem via chronically implanted electrodes, especially in hypothalamic or rhinencephalic areas. In the present study this type of stimulation (30-60 sec trains of 30-100 μA pulses of 0.5 msec duration at a frequency of 5 cps) served as the unconditioned stimulus (US). Four estrogen-treated rabbits were selected for their low threshold and short latency of response (1-5 min). A tone of 500 cps about 20 decibels above room noise was used as the conditional stimulus (CS). After the US threshold of paradoxical sleep had been determined, the rabbit was habituated to the CS (about an hour). Then the tone was paired with the electrical stimulus. Following as few as 10 repetitions of positive short latency paradoxical sleep responses to the paired stimuli over the course of 4-6 hours, the response was evoked by the tone alone; the latency was the same as that following paired CS-US stimulation. The conditioned response was quickly extinguished if the CS was not reinforced.

GRAPHICAL ESTIMATION OF SURVIVAL TIME OF IN VIVO LABELLED RAT ERYTHROCYTES. Bergene Kawin (intr. by Joseph Meites). VA Hospital, Fort Howard, Maryland.

Early rapid decrease of erythrocyte Cr-51 concentrations following intravenous sodium radiochromate injection into rats may indicate very transient adsorption and loss of Cr-51 from labelled cells. This is accompanied by a slower and more extended rate of Cr-51 decrease. Based on this rate the erythrocyte survival half-time was about 23 days. Evidence from related preliminary studies suggest that this value may have been influenced in some proportion by the initial amount of chromium Cr-51 label as well as by the actual rate of loss of the erythrocytes themselves. This interpretation, which accords with in vivo labelling procedure, is contrasted with an alternate interpretation which suggests possibility of re-utilization of chromium eluted from erythrocytes labelled by in vitro methods.

NA AND K CONCENTRATIONS IN NECTURUS PROXIMAL TUBULE. Raja N. Khuri*, David A. Goldstein*, David L. Maude*, Charles J. Edmonds*, and A. K. Solomon. Biophysical Laboratory, Harvard Medical School, Boston, Mass.

Micro-electrodes of cation sensitive glass (Eisenman, G., Rudin, D. G., and Casby, J. U., Science, 126, 831, 1957) have been used to measure the Na and K activities in droplets of fluid collected from the most distal regions of the proximal tubule in the Necturus. The results are reported in terms of the ratios of the cation concentration in glomerulus to that in serum (G/S) and the cation concentration in the tubule compared to that in glomerulus (T/G). In the case of Na, the G/S ratio is 1.00 $\pm$ 0.02 (std. error), and the T/G ratio is 0.99 $\pm$ 0.01 in a series of 4 animals. In another series of 3 animals in which the measurements were made by direct micro-puncture of tubules, the G/blood ratio was 0.96 $\pm$ 0.04 and the T/G ratio was 1.03 $\pm$ 0.05. In the case of K, measurements made in droplets collected from 6 animals gave a value of 1.11 $\pm$ 0.31 for the G/S ratio. This number is not significantly different from 1.0. In a separate series of 9 determinations on 5 animals, the T/G ratio was found to be 1.9 $\pm$ 0.1 which differs significantly from 1.0 at the 0.001 level. This latter figure is in good agreement with the value of 1.7 previously determined with the flame-photometer by Oken and Solomon (Proc. 1st Int. Cong. Nephrol., Geneve, 1961, p. 52) in 12 collections from the most distal segment of the proximal tubule.

The Minimal Air of Dogs, L. Kleinman*, D. Poulos*, and A.A. Siebens, University of Wisconsin, Madison, Wisconsin.

The term "minimal air" has been used in referring to the volume of air remaining in the lungs after the chest has been opened and the lungs allowed to collapse. This abstract concerns experiments for measuring this volume, comparing it to other lung volumes and testing the hypothesis that it represents gas "trapped" distal to collapsed airways. Anesthetized mongrel dogs were placed on an operating table in the supine position. An endotracheal tube was inserted and sealed in position by an inflatable cuff. The sternum was exposed in such a way that longitudinal midsternal thoracotomy could be quickly performed with a cast cutter. Nitrogen was displaced from lungs during a period of oxygen breathing. Functional residual capacity was measured in triplicate by helium dilution. The thorax was entered and the air expelled by the lungs collected in a carefully counter-balanced spirometer from which carbon dioxide cannister had been removed. Minimal air was obtained by subtracting the expelled air from the functional residual capacity. The mean of 18 measurements on dogs weighing between 8 and 16 kilograms was 262 $\pm$ 71ml. The mean FRC was 472$\pm$ 137ml. The mean ratios minimal air/FRC, minimal air/dry lung wgt., and minimal air/dog wgt. were .57 $\pm$ .086, .095 $\pm$ .029 and .218 $\pm$ .042, respectively. Correlation coefficients of minimal air with FRC, animal wgt. and dry lung wgt. were .79 ($P<.01$), .70 ($P<.01$) and .67 ($P<.05$). Minimal air was more than twice the volume of "anatomical" dead space (nitrogen single breath), suggesting this volume fills alveoli as well as airways. Cardiac contractions and oxygen consumption continued for from 10 to 20 minutes following thoracotomy and cessation of ventilatory movements, indicating patency of airways between alveoli and spirometer.

RENAL SODIUM REABSORPTION AND OXYGEN CONSUMPTION DURING WATER AND MANNITOL DIURESIS. F. G. Knox* and D. W. Rennie. Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

The Na/O_2 ratio (EqNa reabsorbed/M suprabasal O_2 consumed) is constant in mammalian kidneys under many conditions. However, mannitol reportedly reduces net Na reabsorption without affecting renal oxygen consumption, possibly because inward diffusion and reabsorption of non-filtered Na is augmented by mannitol (Kiil, F., K. Aukland, H. Refsum, Am. J. Physiol. 201: 511, 1961). We have studied the Na/O_2 relationship in anesthetized dogs during water diuresis followed by mannitol diuresis. Renal O_2 consumption ($\dot{V}_{O_2}$) was computed from I-131 diodrast clearances and an O_2 electrode. Filtered Na Load was varied by increasing ureteral pressure. O_2 consumption of the non-filtering kidney (basal $\dot{V}_{O_2}$) was extrapolated from the linear relationships between total $\dot{V}_{O_2}$ and Na reabsorption. There was a significant positive correlation between Na reabsorption and total $\dot{V}_{O_2}$ in each diuresis, supporting the theory that $\dot{V}_{O_2}$ is dependent upon Na reabsorption. However, in 60 determinations the Na/O_2 ratio was reduced from 40 Eq/M during water diuresis to 20 Eq/M during mannitol diuresis due to decreased net Na reabsorption not accompanied by decreased $\dot{V}_{O_2}$. Thus, the overall relationship between Na reabsorption and $\dot{V}_{O_2}$ is not as constant as heretofore supposed. Basal $\dot{V}_{O_2}$ was the same in both types of diuresis; therefore it seems unlikely that augmented recirculation of Na is the mechanism that sustains renal $\dot{V}_{O_2}$ during mannitol diuresis. A significant positive correlation between the Na/O_2 ratio and filtration fraction may be important and will be discussed. (Supported by a grant from the Life Insurance Medical Research Fund.)

ENHANCEMENT OF RENAL Na^+ TRANSPORT BY DILANTIN. Alan Koch, Robert Higins*, Merle Sande*, Jerome Tierney*, and Robert Tulin*. Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine, Seattle.

Anesthetized mongrel dogs were maintained on a solute diuresis by continuous infusion of isotonic solutions of either NaCl or $NaHCO_3$ at rates between 10 and 20 ml/min. Under these conditions, Na^+ reabsorption was generally less than 90% of the filtered load. The anticonvulsant drug diphenylhydantoin (Dilantin) was administered, and the renal transport of Na^+, K^+, Cl^-, and HCO_3^- was followed. An immediate increase in the reabsorption of Na^+ and Cl^- were invariably noted. Effects on renal Na^+ transport were evident within 5 min and were maximal within 15 min. The action waned with a half-time of about 20 min. The response was graded; large doses caused complete reabsorption while smaller doses caused proportionately less increase. The dose-effect relation was quite variable; in different animals equi-effective doses differed by as much as a factor of 5. Concomitant with the decrease in Na^+ excretion, K^+ excretion usually fell, but the ratio of K^+ to Na^+ excretion increased markedly. When the control condition was frank HCO_3^- excretion, Dilantin caused an increase in HCO_3^- reabsorption as well as affected Na^+ and Cl^- transport. Thus, the drug appears to enhance all facets of active Na^+ transport in the kidney. (Supported by grant H4469 from the National Heart Institute, National Institutes of Health, Department of Health, Education and Welfare.)

CHANGES IN THE MEMBRANE POTENTIAL AND PERMEABILITY OF MUSCLE FIBERS IN CA-FREE SOLUTIONS. **K. Koketsu, R. Kitamura* and H. Kimizuka*. Dept. of Psychiatry, Univ. of Ill. Coll. of Med., Chicago, Ill.**

For the purpose of analyzing the mechanism of membrane depolarization in calcium-deficient media, the changes in the membrane potential and resistance of frog's sartorius muscle fibers were studied immediately after the calcium ions were removed from the bathing solution (pH: 6-9, Temperature: 22-24°C). The changes in the outflux of sodium, potassium and chloride ions, as well as calcium ions, were studied using radioactive tracers under similar experimental conditions. The membrane potential started to drop within a few seconds after the calcium ions were removed from the bathing Ringer's, Na-free choline or sucrose solutions. The membrane resistance, however, remained unchanged, or even increased during initial depolarization. If a chelating agent was added to the Ca-free solution, membrane depolarization was enhanced; a marked increase in the membrane resistance was observed during initial depolarization in the Ca-free choline solution containing EDTA. The rate of the K^{42} outflux increased within a minute upon withdrawal of the external calcium ions, particularly with the addition of a chelating agent. Results obtained from studies on the Ca^{45} outflux indicate that the initial loss of tissue calcium is rapid and transient. It is suggested that the dissociation of calcium, bound to some anionic sites in the membrane, is the actual cause of the changes in the membrane potential, resistance and ion movement, such as those observed in the present experiment. (Supported by USPHS Grant NB 01650-05).

IMPROVEMENT OF HYPERTENSIVE AND UREMIC STATES IN DOGS WHEN SUBJECTED TO CHRONIC LYMPHATIC SHUNTS. S. N. Kolmen* (intr. by C. R. Allen). The Carter Physiology Laboratory, University of Texas Medical Branch, Galveston, Texas.

Fourty-two dogs were subjected to one of the three following procedures: uninephrectomy alone, uninephrectomy plus gauze encapsulation of the contralateral kidney, uninephrectomy plus partial constriction of the renal artery to the contralateral kidney. The dogs in the latter two groups became hypertensive and/or uremic. One week later, thoracic duct fistulas were instituted in all dogs. The lymph flow was either returned to the external jugular vein, shunted into the esophagus, or allowed to escape from the body. The latter two fistulas, when patent, were effective in lowering the induced hypertension and uremia. Cessation of flow in the shunts resulted in the resumption of the hypertensive and uremic state. (Supported by USPHS Grant AM-3695(03).

UREA TRANSFER ACROSS THE SWEAT GLANDS. G. K. Komives*, S. Robinson, F. R. Meyer*, C. H. Ts'ao*, and J. T. Roberts*. Anatomy-Physiology Dept., Indiana University, Bloomington.

The effects of varying the plasma urea level and the rate of sweating on the concentration of urea in the sweat were studied on men walking on a motor-driven treadmill in a hot, dry environment in which sweat evaporated from the men as it was formed. Hourly sweat rates were measured as the net weight losses of the men, and analyses were made of the sweat residue washed from the skin at the end of each hour with a measured volume of distilled water. This method makes possible the collection of sweat from the whole body under normal physiological conditions. When plasma urea was raised 4-fold (150 mg%) by the ingestion of urea, the urea level of the sweat always remained the same as that of the plasma. The sweat and plasma concentrations also remained the same despite an almost 2-fold variation in the sweat rate. This relation was unaffected during adaptation of the men to salt deficiency in which the sweat glands were forced to increase their osmotic work. These results were interpreted to mean that sweat urea arises from the extracellular fluid by a process of passive diffusion across the sweat glands. Since the urea level in the plasma and sweat were the same, it was concluded that when the skin is functioning under normal atmospheric conditions the amount of urea cleared by the sweat glands depends entirely upon the sweat rate. In one series of experiments, the kidney urea clearance was 45 ml/1.73 m^2/min while that of the sweat glands was 17 ml/1.73 m^2/min at a sweat rate of 15 ml/1.73 m^2/min. (Supported by U. S. Army Medical Research and Development Command, Grant DA-MEDDH-60-10.)

THE TIME OF ONSET OF VASODILATATION FOLLOWING A BRIEF CONTRACTION OF THE FOREARM MUSCLES. Gabriel T. Koroxenidis,* Adrian Corcondilas,* and John T. Shepherd. Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

With the use of Whitney mercury-in-rubber strain-gauge plethysmographs, an attempt was made to time the onset of vasodilatation in the forearm following single short contractions of the forearm muscles of 0.25 to 0.35 second duration. An increase in blood flow to the forearm can be detected within a second following the end of the contraction. The brachial artery pressure did not change except for a fall in diastolic pressure confined to the beat concomitant with the contraction. Since the rate of increase in forearm volume with venous occlusion is linear over 6 seconds, it is concluded that the increase in flow is due to dilatation of forearm muscle vessels. The same response is present in the sympathectomized forearm, and since no changes are seen on the control side in normal subjects, the vasodilatation is considered to be locally mediated. The flow is at its maximum immediately after contraction and subsides rapidly to the resting level. Over the range of contractions examined, there is an approximately linear relationship between the strength of the contraction and the increase in flow. The speed of onset of the dilatation resulting from this local mechanism makes it unnecessary to postulate a dilatation mediated by the central nervous system to account for the immediate circulatory adjustments that occur in muscles at the onset of exercise.

RECURRENT FACILITATION OF FROG MOTOR NEURONS. Kisou Kubota* and John M. Brookhart. Dept. of Physiology, Univ. of Oregon Medical School, Portland, Oregon.

The existence of recurrent facilitation of spinal motor neurons has been confirmed in the frog. In isolated spinal cord preparations, stimulation of VR9 or VR10 may induce discharge in the adjacent root having a latency of 3.3 msec. (15-17°C). This phenomenon has been studied using intracellular recordings. In a population of 200 identified motor neurons, stimulation of the adjacent root induced an EPSP in 66%; in 33% discharge was initiated. The mean characteristics of the EPSP were: latency, 2.2 msec; rise time, 1.4 msec; decay time constant, 3.4 msec; amplitude, graded. The amplitude of antidromic spikes was not altered during the EPSP. Intracellular polarization did not influence the EPSP. Threshold to intracellular stimulation was reduced during the EPSP. Repetitive stimulation induced minimal summation of EPSPs which were poorly sustained. These characteristics suggest a dendritic termination of excitatory collaterals. The hypothesis undergoing test is that recurrent collaterals facilitate synergic motor neurons in such a manner as to promote synchronous firing. (Supported by USPHS NINDB Grant B385.)

EFFECT OF NEGATIVE PRESSURE LUNG INFLATION ON LEFT ATRIAL PRESSURE AND PULMONARY VASCULAR RESISTANCE. Kizuku Kuramoto, (intr. by S. Rodbard). University of Buffalo Chronic Disease Research Institute, Buffalo, N.Y.

Pulmonary vascular resistance was studied in thoracotomized dogs enclosed in a respirator. The lung was inflated by negative respirator pressure, the trachea being open to atmospheric pressure. Blood flow through the lung was held constant. At end-inspiration, "intrapleural" and left atrial pressures fell equally; the pulmonary arterial pressure fell to a lesser extent. Calculated resistance increased during the mid-inspiratory phase and became maximal at end-inspiration and early expiration. Negative pressure lung inflation had only small effects on resistance at minimal negative respirator pressures; resistance increased markedly as "intrapleural" pressure became more negative. Resistance returned to control values at each end-expiration, regardless of the previous degree of negative pressure inflation. Resistance increased in isolated lungs under constant perfusion when pulmonary venous and intrapleural pressures oscillated together; resistance fell when pulmonary venous pressure was held constant with respect to atmospheric pressure. The results suggest that previous disagreements on pulmonary vascular resistance may have been due to failure to evaluate the effect of "intrapleural" pressure on left atrial pressure. The increased resistance during negative pressure inflation may result from a negative transmural pressure in the collapsible vessels of the lung.

CHRONIC VAGUS STIMULATION OF STOMACH. Y. Kuroyanagi*, N.C. Jefferson, T. Geisel* and H. Necheles. Dept. Gastrointestinal Research, Medical Research Institute, Michael Reese Hospital, Chicago, Illinois.

In mongrel dogs, both vagus nerves were attached to the surface of the heart muscle, with the idea of chronic stimulation of the stomach by the cardiac action potentials. In 20% of the animals gastric lesions appeared within weeks to months, such as ulcers, extensive hemorrhage in the antrum, and gastritis. No lesions were observed following sham operations. In a number of animals, the sutures appear to have destroyed nerve conduction in the vagi, and in other dogs, stimulation of the vagus in the chest may not have reached motor fibers.

Supported by USPH Grant A-6078.

GASTROVASCULAR FLUID OF THE PORTUGUESE MAN-OF-WAR, PHYSALIA.
Charles E. Lane, D. G. Anderson,* and Kenneth Hines.*
Institute of Marine Science, University of Miami, Miami, Florida.

Although it is a biological truism that coelenterate gastrovascular fluid serves many of the functions of blood, little analytical work appears to have been done to support this conception. Gastrovascular fluid in Physalia, the Portuguese Man-of-War, may be aspirated from any of several extensions of the gastrovascular cavity. It is isosmotic with sea water but differs from sea water in ionic composition. It contains approximately 3 gr./l. of protein and amino acid. The chromatographic spectrum of these nitrogen-containing substances is remarkably constant from animal to animal regardless of size, season, or nutritive state. Both copper and iron occur in gastrovascular fluid in concentrations several thousand times greater than in ambient sea water. The light blue color of gastrovascular fluid is discharged in a reducing atmosphere and is restored on oxygenation. When gastrovascular fluid is dialyzed against distilled water, however, some copper is lost through the dialysis membrane. Iron distribution follows that of copper in dialysis. The concentration of phosphorus in gastrovascular fluid exceeds that of ambient sea water by several hundred times. It is suggested that the coelenterate gastrovascular cavity contains the first extracellular fluid of constant composition to appear in the phyletic series and that it qualifies admirably as a blood.

FINGER AND SUBLINGUAL TEMPERATURE CHANGE INDUCED BY MUSCULAR ACTIVITY.
E. M. Larsen. Dept. of Physiology, University of Wisconsin, Madison.

The effect of brief muscular activity on finger and sublingual temperatures as indications of peripheral vascular reaction was studied in 24 young adults. The subjects were dressed in street clothes and had not been active, ingested food, fluid, or smoked immediately prior to the experiment. Each subject sat comfortably relaxed without talking in a quiet room. Temperatures were determined by thermistor-thermometer and surface banjo type probe placed underneath tongue and held between thumb and index finger. During 2 to 3 minutes the subject briskly climbed stairs to 5th floor and down to laboratory. Sublingual and finger temperatures were immediately redetermined. After activity both temperatures decreased in 21 subjects, finger decreased and sublingual increased in 1, finger increased and sublingual remained unchanged in 1, and both temperatures increased in 1 subject. Finger temperature decreases ranged from 0.1 to 14.0° F. with an average of 6.1° F. Sublingual decreases ranged from 0.5 to 4.0° F. with an average of 1.3° F. There was a highly significant difference in finger temperature and a significant change in sublingual temperature induced by brief strenuous muscular activity. The mechanism involved probably consists essentially of nerve impulses initiating muscular activity and increasing peripheral vasoconstriction. The increased vasoconstriction may be maintained or augmented by reflex stimulation of the vasomotor center from multiple areas including active muscles. The temperature decreases obtained in this study confirm the concept of increased peripheral vasoconstriction during strenuous muscular activity.

THE EFFECT OF pH ON THE RATE OF OXYGEN DISSOCIATION FROM THE RED BLOOD CELL. W.H. Lawson, Jr. (intr. by A.H. Woodcock). U.S. Army Research Institute of Environmental Medicine, Natick, Mass.

It has been reported that decreasing temperature markedly decreases the rate of O_2 dissociation from the red blood cell in vitro; and suggested that red cells, during the time they spend in the capillary, may not have time to equilibrate with the oxygen tension of cold tissue (Fed Proc 1962). Because pH would be an important variable in oxygen exchange between red cell and tissue, we have measured its effect at 22°C in blood from 2 normal humans. Blood was diluted 1:50 in saline-phosphate-bicarbonate buffer and aliquots equilibrated with gases containing various concentrations of CO_2 and sufficient O_2 to maintain oxyhemoglobin saturation around 95%. The diluted blood was then reacted with an equal volume of deoxygenated isotonic buffer at about the same pH and pCO_2 and containing $Na_2S_2O_4$ which for practical purposes instantly reduces and maintains the oxygen tension outside the red cell at zero. The measurements were made by differential photocolorimetry in a stopped flow system and results are given as time in seconds for reaction to go to half completion, t 1/2. For reference t 1/2 at 37°C pH 7.3 and pCO_2 43 is .04 sec. The reaction constant, K_c (fractional change per sec.), equals .695/t 1/2.

pCO_2 (mm Hg)	0	10	21	43	74	149	505
pH	8.8	7.8	7.5	7.2	7.0	6.7	6.2
t 1/2 (sec)	.63	.33	.20	.16	.12	.10	.08

These results indicate that the rate lowering produced by decreasing temp. from 37° to 22°C at pH 7.3 is only partially reversed by marked decreases in blood pH produced by altering pCO_2.

THE ROLES OF CITRATE AND POTASSIUM ION IN CARDIAC ARREST. Y.C.P. Lee, H.G. Richman,* and M.B. Visscher. Dept. of Physiol., Univ. of Minn., Minneapolis, Minn.

This report concerns studies on the relationship of Ca^{++} and K^+ in myocardial arrest. Isolated rabbit hearts were perfused with buffered salt solution by the Langendorf method. Various levels of $[Ca^{++}]$ and $[K^+]$ were utilized. Mechanical contraction was recorded by a tension gage and electrical activity by bipolar electrodes. The heart could be effectively arrested by removal of the calcium from the extracellular space without changing the potassium concentration. Chelating or calcium binding agents as Na-citrate, K-citrate, Na-EDTA and Na-oxalate were effective. Arrest could be maintained by continuous perfusion with the salt solution excluding calcium. By perfusion with various levels of Ca- and Na-citrate, the maximum $[Ca^{++}]$ for the onset of cardiac arrest was found to be 0.09 mM/l, about 5% of the normal level. Doubling the $[K^+]$ during arrest perfusion was necessary to provide a complete recovery if the calcium level was lower than 0.09 mM/l. Raising the $[K^+]$ could also induce arrest, however, the amount of potassium required was dependent on the $[Ca^{++}]$ concentration. The arrest ratio of Ca/K was found to be linear in the range of $[Ca^{++}]$: 0.09-1.45 mEq/l and $[K^+]$: 2.7-55 mEq/l. At higher levels of $[Ca^{++}]$ an exponential increase in potassium was required to induce complete arrest. At the higher levels of $[Ca^{++}]$, the recovery of the heart arrested by large amounts of potassium may be complicated by fibrillation. In the heart arrested by chelating agents an action potential remained long after the disappearance of mechanical contraction whereas in potassium arrest, disappearance of mechanical contraction was associated with a corresponding diminution of electrical activity.

CARDIAC EFFECTS OF CORTICOSTEROIDS IN THE INTACT DOG
Allan M. Lefer, Thomas C. Bianco, and Duane C. Sutfin. (intr. by C. L. Prosser). Univ. of Illinois, Urbana, Ill.

Acute effects of aldosterone and cortisol were studied in anesthetized (sodium pentobarbital) closed chest male mongrel dogs (15-20Kg). Intravenous (IV) injections of d-aldosterone in aqueous solution in doses ranging from 0.001 to 100μg exerted no detectable effect on the heart rate, left ventricular contractile force (LVCF), femoral arterial blood pressure (FABP), electrocardiogram, intrathoracic pressure (ITP), or femoral arterial blood flow. Mean control values in 22 anesthetized postoperative dogs with resealed chests are as follows: FABP; systolic (mm Hg) = 149±3, FABP; diastolic (mm Hg) = 94±3, LVCF; systolic (Gm) = 59±2, LVCF; diastolic (Gm) = 16±1, Heart rate; (beats/min.) = 145±5. Su 4885 (an 11 β-hydroxylase inhibitor of corticosteroid biosynthesis) was administered orally (75mg/Kg) two hours prior to anesthesia and was followed by a slow IV infusion of 50-75 mg/Kg Su 4885 bitartrate during thoracotomy. In these adrenocortically inhibited animals, intracoronary injection of aldosterone exerted a positive inotropic effect in doses of 0.01-0.08μg. LVCF increased 23 per cent above control levels in 70 per cent of the injections, while FABP decreased 7 mm Hg. The time to maximum response was 66 seconds, and the total duration of the effect was 150 seconds. Heart rate and ITP were unchanged. Corresponding doses of aldosterone given rapidly IV and by IV infusion were ineffective. Cortisol succinate appeared to be less effective under similar conditions. Su 4885 IV infusions (1-6 mg/Kg/min.) resulted in a marked negative inotropic effect, bradycardia and decreased FABP. This cardio-inhibition was temporary; magnitude of change and recovery time were dose-dependent.

MYOCARDIAL GLUCOSE UPTAKE, IN VITRO. Eugene A. Lentini and Richard I. Park* Dept. of Physiology, Univ. Of Oregon Medical School, Portland, Oregon.

The glucose uptake of trabeculae carneae from the rat's left ventricle was determined at various glucose concentrations. The investigations were designed to determine the glucose uptake during a non-stimulated period and then during a succeeding period of isometric contractions of one per second. The oscillographic recording of the developed tension was accomplished by using a strain gage transducer. The muscles were placed under a total resting tension of one gram and bathed in a Ringer's glucose solution aerated with 95% O_2 + 2% CO_2 + 3% N_2. The glucose uptake was calculated from differences in the glucose concentrations of the bathing fluid during the experimental period. It was noted that the total glucose uptake was not related to the dry weight of the preparation. The time course of the mean cumulative glucose uptake was alinear during the experimental period irrespective of the glucose concentration. The mean developed isometric tension was directly related to the concentration of the glucose in the muscle bath. It was found that the cumulative glucose uptake occurring during specific portions of the experiment could be related to both the developed tension and the glucose concentration present in the muscle bath. This finding was supported by a multiple correlation analysis.
(Supported by grants from NIH (H-4562) and the Medical Research Foundation of Oregon.)

THE EFFECT OF EPINEPHRINE AND 3',5'-AMP ON PERFUSED RABBIT LIVER. F.M. Levin*, F.S. Elliott* and W.C. Shoemaker. Michael Reese Hosp., Chicago, Ill.

Responses to 2 ug and 20 ug epinephrine and 2 mg 3',5'-AMP were studied in the in situ perfused rabbit liver under normothermic and hypothermic conditions. Hepatic venous outflow rate increased after both epinephrine and 3',5'-AMP. The increased flow after 2 ug epinephrine occurred within the first 20 sec in normothermia, but was markedly delayed in hypothermia. The potassium concentration of the perfusate leaving the liver and the net rate of hepatic potassium output increased in response to both epinephrine and 3',5'-AMP. Maximum potassium levels were reached within 30 sec after epinephrine administration in both normothermia and hypothermia. However, the return to control levels was delayed in hypothermic experiments. Chloride concentration of the perfusate increased after epinephrine in the hypothermic liver. Administration of epinephrine in doses 20 ug produced an increase in perfusate pH, HCO_3^- and total CO_2 concentrations. Both epinephrine and 3',5'-AMP produced an increased hepatic glucose output. After epinephrine the maximum rate hepatic glucose output in hypothermia occurred later than in normothermia. The time sequence, obtained by rapid sampling, suggested the following order: increase K^+ output, increased flow, increased output of Cl^-, HCO_3^- and CO_2 together with an uptake of H^+, and finally an increased glucose output.

Response of Intestinal Vasculature to Regional Vasoconstrictor Nerve Fiber Stimulation. David H. Lewis, Björn Folkow,* and Stefan Mellander.* Dep't Physiol., Univ. Göteborg, Göteborg, Sweden

Observations were made on a short segment of jejunum in chloralose-urethane anesthetized cats. Rt. adrenal gl. was ligated and lt. denervated at hilus. Measurements were made of art. bl. press. intestinal venous outflow (drop recorder), and changes in intest. tissue volume (plethysmograph). Both splanchnic nerves were cut and stimulated supramaximally at freq. of 0.5 to 16/sec. In 15 cats, low freq. (0.5-2) incr. resist. 1.5-2 times, which was well maintained for duration of stimul. There was an initial vol. decr (capacitance vessel response) of 10-15% of contained bl. vol., followed by steady vol. decr. indicating inward filtration of extravascular fluid. After stimul. there was slight reactive hyperemia and return of vol. to control. High freq. stimul. (8-16/sec) incr. resist. 6-10 times, but this faded away to approx. 20% of peak response in 1-2 min. Initial vol. decr. was 30-40% of contained bl. vol., but as resist. response declined, vol. tended to incr. and could exceed control. After stimul. there was marked react. hyperemia and additional vol. incr. With normal portal flow, nerve stimul. (8-16/sec) could raise portal vein press. 1-2 mmHg. It is suggested that low level sympathetic activity is compatible with maintained intest. resist. incr. and a shift of blood and extravasc. fluid away from this region. Max. sympath. activity is very much counteracted by local factors. The incr. in vol. suggests a relatively better maintained postcapillary resist. response than precapillary and with the large intest. capill. filtration coefficient (some 10 times larger than skeletal muscle) could account for large losses of circul. fluid vol. This would be aggravated by an incr. in portal vein press.

CATION SELECTIVITY OF BIOLOGICAL MEMBRANES. B. D. Lindley* and T. Hoshiko. Dept. of Physiol., Western Reserve U. Sch. of Med., Cleveland Ohio.

The orders of effectiveness of the alkali metal ions in maintaining some bioelectric and secretory phenomena were studied. At the outer surface of bullfrog skin., Rb, Cs and K were poor compared to Li or Na in sustaining the potential. This selectivity order was unaltered by vasopressin. At the inner surface, high K or Rb but not Li, Na or Cs depressed the potential. Secretion of frog skin glands required NaCl and was partially sustained by Cs or KCl, but not by Rb or LiCl. Electrical activity of isolated frog ventricle persisted in Li or Cs Ringer at least 6-10 min., compared to 4 min. in Na-free isotonic sucrose. In either K or Rb excitability was lost in less than 15 sec. After soaking in sucrose neither Cs nor Li was able to restore excitability. The above orders of selectivity are tabulated together with those determined in "Ringer's" for a Na-selective glass electrode (Beckman 78178 V). These observations serve as a restraint upon theories of ionic selectivity in biological systems.

Membrane	Selectivity Order
Skin outer surface, in sulfate Ringer	Na:Li:Rb:Cs/K
Skin inner surface, in sulfate Ringer	K:Rb:Li:Na:Cs
Skin gland, R. pipiens, in Cl-Ringer	Na:Cs/K:Li/Rb
Frog heart muscle, resting membrane	K/Rb:Cs/Li/Na
Frog heart muscle, excited membrane	Na:Li/Cs
Glass electrode in Cl-Ringer	Na:Li:K/Cs/Rb
Glass electrode in sulfate Ringer	Na:Li:Rb/K:Cs

THE REGULATION OF INTRAGASTRIC HYDROGEN ION CONCENTRATION IN MAN. A.E. Lindner*, N. Cohen*, and H.D. Janowitz. Mount Sinai Hospital, New York, N.Y.

Intragastric mechanisms which regulate H ion concentration were studied by instilling isotonic hydrogen-containing solutions and a dilution indicator (phenol red) into the stomachs of 17 human subjects. Solution I contained H and Cl (160 mEq/L). Solution II contained H (100 mEq/L), Na (60 mEq/L), and Cl (160 mEq/L). Osmolality and electrolyte concentrations were determined in samples recovered at 15 minute intervals over one hour periods. From the phenol red data the volume of fluid added by secretion and that lost through the pylorus were calculated. Similar results were obtained with both solutions. In all experiments H declined linearly with time. Decline in H conc. was correlated directly with fall in osmolality (r 0.98 for Solution I and 0.90 for Solution II) and inversely with rise in Na conc. (r-0.88 for Solution I and -0.62 for Solution II.) K entered the gastric fluid in progressively increasing concentrations. Cl conc. declined less steeply than H. Results of calculations suggest that several mechanisms may be responsible for the lowering of H concentration of instilled (and presumably secreted) acid: (1) entry of a fluid free of H and containing bicarbonate (alkaline component) with consequent fall in osmolality; and (2) an exchange diffusion mechanism (Na for H) which is required to account for the results in nearly 1/3 of the experiments. The striking fall in osmolality (mean 55 mOs., range 16-89 mOs. for Solution I; mean 50 mOs., range 28-81 mOs. for Solution II) cannot be accounted for quantitatively by these mechanisms. The entry of K is correlated with the rate of gastric secretion (r 0.86).

SOME OBSERVATIONS ON MUSCLE ELECTROLYTES AFTER ISOTONIC CONTRACTION IN VIVO. C. T. Liu (Intr. by R. R. Overman). Clin. Physiol. Lab. Univ. of Tenn. Col. of Med., Memphis, Tennessee.

The maintenance of concentration gradients for Na^+ and K^+ as well as Ca^{++} and Mg^{++} across the cell membrane is based upon an active process within the cell. In order to investigate the electrolyte changes after an increase of cellular activity, studies were made following prolonged in vivo isotonic muscular contraction in a group of 4 normal male mongrel dogs varying in weight from 12 to 14 Kg. Both hind limbs of the supine anesthetized dogs were suspended vertically by attaching a string from the animal's toes to a horizontal bar. One of the hind limbs of each animal was further connected with a muscle lever to which a 300 gm. weight was attached. The sciatic nerve of the same side was cut and the peripheral end of the nerve was stimulated at a rate of 92/min. for 3 hours with a Tektronix square wave stimulator. The strength of the stimulus was 50 v. and the stimulation duration was 60 msec. During the period of muscular contraction, a tracing of the movement of the leg was recorded on a kymograph, and also a series of blood samples were taken from the femoral vein of the stimulated side for pyruvic and lactic acid determinations. At the end of the experiment two pieces of gastrocnemius muscle from both legs were excised for electrolyte and glycogen determination. The data revealed that there was no change in tissue Ca^{++} and Mg^{++} concentrations either in intracellular or in extracellular compartment. Although no changes in plasma electrolyte concentrations were found an accumulation of intracellular Na^+ which corresponded with a reduction of intracellular K^+ was observed in the stimulated muscle without any appreciable water displacement. Thus, it is suggested that the release of energy from ATP for the performance of muscular work may involve the process of exchange of extracellular Na^+ and intracellular K^+ in the muscle cells.

PRIMARY AND RECURRENT MYOCARDIAL INFARCTION: SURVIVAL AND CAUSES OF DEATH IN 177 PATIENTS FOLLOWED 10 YEARS. A. R. Lorimer*, R. M. Hagstrom*, C. Constantinides*, J. M. Merrill, F. T. Billings*, C. O. T. Ball* and G. R. Meneely. Vanderbilt Univ. School of Med., Nashville, Tenn.

All white patients hospitalized in 1950-51 with acute myocardial infarction have been followed to death or current cardiac class (American Heart Association). Seventy-six males, mean age 56, 43 females, mean age 66, sustained a primary and 42 males, mean age 56, 16 females, mean age 67, a recurrent myocardial infarction. The 30 day mortality was 28% for primary and 40% for recurrent attacks. Lower mortality for primary attacks persisted after 6 months, 1, 5 and 10 years. Mortality in men under 55 at time of recurrence was significantly higher ($p<0.05$) at all times than in their primary attack counterparts. After 10 years the mortality rate for men over 55 at primary infarct was 75% and for men under 55 was 48%. After recurrent attacks, the comparable mortality rates were 87% and 84%. Three-fourths of deaths were due to arteriosclerotic heart disease. In those surviving, two-thirds were in cardiac class I or II. Twenty-seven per cent of the 177 patients survived 10 years, comparable to the 23% in 1821 patients reported by Biörck (ACTA MEDICA SCANDINAVIA 168:245, 1960). (Support from Federal Aviation Agency, Light Research Foundation, Middle Tennessee Heart Association, United Fund of Chattanooga.)

BRONCHIAL PRESSURES AND DIAMETERS DURING FORCED EXPIRATION. P.T. Macklem*, R.G. Fraser*, M.R. Becklake* and D.V. Bates. The Joint Cardio-Respiratory Service and Department of Radiology, Royal Victoria Hospital, McGill University, Montreal, Quebec.

The functional significance of bronchial diameter changes during forced expiration was assessed by the direct measurement of bronchial pressure, esophageal pressure, and airflow at the mouth during cinebronchography. As each frame of the cinebronchogram was exposed, a signal was recorded. From the cinebronchogram, bronchial diameters could be measured by the technique of Fraser (1) and compared to the simultaneous measurements of the other variables. From the data, pressure gradients down the bronchial tree and bronchial compliance can be measured. In 3 normal subjects, narrowing of the large bronchi was one of the factors limiting expiratory flow. In 3 patients with emphysema collapse of large bronchi occurred on forced expiration due to an increase in their compliance. This played a major role in airflow limitation.

1. Fraser, R.G. Measuromont of the Calibro of Human Bronchi in Three Phasos of Respiration by Cinebronchography. J. Can. Assoc. Radiol., 12, 1961.

CENTRAL INHIBITION OF TONIC SYMPATHETIC ACTIVITY ON THE CAT'S HEART. J. W. Manning and M. deV. Cotten*. Department of Physiology, Emory University, Atlanta, Georgia.

The aim of this study was to assess the role of tonic sympathetic activity in depressor responses obtained by central nervous stimulation. Arterial blood pressure, heart rate and cardiac contractile force were measured in 31 cats anesthetized with 50 mg/Kg of alpha chloralose. Low intensity stimulation of the septal area between the lateral ventricles elicited a 20 to 70 mm Hg fall in mean arterial pressure with a simultaneous reduction in heart rate and contractile force. The same changes were observed when stimulation was repeated after vagotomy or injection of cholinergic blocking drugs. Alpha adrenergic blocking agents abolished mainly the vasodepressor reactions, whereas beta adrenergic blocking agents abolished mainly the cardiac depression. The centrally induced decrease in cardiac force and rate was still observed when an aortic resistance was adjusted to prevent the fall in systemic arterial pressure. Extirpation of the sympathetic supply to the heart blocked the evoked cardiac depression but not the fall in blood pressure. Thus, excitation of the septal area in the cat markedly reduced sympathetic tone to heart and blood vessels. The cardiac depression did not result from hemodynamic alteration. The pharmacological findings also suggest that two types of adrenergic receptors mediate the resting vasomotor and cardiac tone. (Supported by USPHS Grant B-2645).

CONTROL OF BETZ CELL EXCITABILITY BY DIRECT CORTICAL STIMULATION. M. Matsunaga*, H. Suzuki*, and S. Ochs, Dept. Physiol., Indiana University School of Medicine, Indianapolis, Indiana.

Recordings were made from Betz cells in the anterior sigmoid gyrus near the cruciate sulcus. Insulated metal electrodes with exposed tip less than 1 μ and glass microelectrodes were used from extracellular recording. Pes peduncular stimulation was used to antidromically excite the Betz cells identified by their short latency of 1-2 msec. While recording from a Betz cell, the cortex was excited by a brief 10 μsec pulse applied to the surface 0.3--3.5 mm from the site of the recording electrode. This stimulation gave rise on the surface to a direct cortical response (DCR) as recorded from a surface electrode over the Betz cell. At high strengths a discharge appeared in the Betz cell with no apparent latency while at moderate and lower strengths, discharges were found with a latency varying from 2-5 msec. In the latter case, at any given strength, some variation in latency from trial to trial was seen. Excitability was also studied by adjusting pes peduncular stimulation to just below threshold and pairing it with a cortical stimulus at various time intervals. The effect of the cortical conditioning pulse was determined at each interval between it and the antidromic pes peduncular test pulse by the number of Betz cells facilitated to discharge in 10 trials. The curve of facilitation started with a latency of 2-8 msec; it lasted 10-20 msec and then gradually returned within another 10 msec. The time course of facilitation suggests a relationship to the DCR.

Supported by USPHS Grants B-1993-C3 and M-4815.

A Potent Intestinal Stimulant for Pancreatic Secretion (other than Secretin or Pancreozymin). John Maylock*, M.H.F. Friedman, and Ronald Green*. Department of Physiology, Jefferson Medical College.

Extracts of intestinal mucosa prepared with soap solutions, but not with non-saponic alkaline reagents, yield a potent pancreatic secretory stimulant effective only on systemic or portal intravenous administration (Friedman, Maylock, Green, 1959). Potent secretory preparations devoid of vasodilator action have been prepared. Present studies show that calcium, magnesium and tungstate ions inactivate the extract. Potency of neutralized extracts is lost after storage at $4^{\circ}C$ for 24 hours but frozen preparations maintain potency for at least 2 weeks. The active principle can be concentrated into the liquid core of frozen preparations. No choline has been found in potent extracts. Spectrophotometry, paper and thin layer chromatography, and electrophoresis have shown a component which remains to be identified. Activity has been associated with a 10-carbon compound, probably lipid in nature. Hydrolysis of potent fractions yield products which are not similar to those obtained from secretin.

STRUCTURAL REQUIREMENTS FOR CONNECTIVE TISSUE STIMULATING ACTIVITY IN POLYSACCHARIDES. Esther L. McCandless and Judith Lehoczky-Mona*. University of Buffalo Chronic Disease Research Institute, Buffalo, New York

The physiological significance of the effect of carrageenan on the growth of collagenous connective tissue was studied by investigation of the effect of subcutaneous injection of 50 mg. of analogous polysaccharides in the guinea pig. Growth was obtained after administration of the following straight chain polymers of galactose: lambda carrageenan and unfractionated carrageenans from a number of species of seaweed, with sulfate substitution in different positions: agar; agarose. An uncharacterized polygalacturonic acid was effective also. Minimal growth occasionally obtained after kappa carrageenan injection was thought to be due to contamination with the lambda polymer. The branched chain galactan pectin, and an uncharacterized polygalactose caused no growth. Polymers of glucose, fucose, and mannuronic acid were ineffective: laminarin, laminarin sulfate, dextran, dextran sulfate, fucoidin and alginic acid. Sulfate appears to be unnecessary for activity since sulfate-free agarose and polygalacturonic acid caused growth. Effective polymers thus far have been essentially linear galactans linked through carbons 1 and 3. Tissue produced by alpha and beta linked polymers were distinguishable chemically and histologically by a higher collagen content in the former, and by the presence of foreign body giant cells in the latter. (Supported by grant A-4216 from US PHS.)

DIET AND ABNORMAL MUSCLE ACTIVITY. A.R.McIntyre and Thomas Toft*. Univ. Nebraska Coll. of Medicine, Omaha, Nebraska.

Hyperirritability and spontaneous electrical activity has been observed and recorded in the skeletal muscles of rabbits when maintained for periods of 10 days to two or more weeks on a diet of carbohydrate alone supplemented with brewers yeast extract and α-tocopheral. The abnormal electrical activity resembled that seen in rabbits and hamsters as a result of vitamin E deficiency, but in contrast could neither be prevented nor abolished by the administration of α-tocopherol. The abnormal electrical activity consisted of spontaneous fibrillation and "dive bomber" bursts similar to those seen in dystrophia myotonica in man and mouse and previously described by this laboratory (1). Studies indicate that complete starvation with access to water ad libitum does not produce this abnormality until late in starvation, when deranged electrolyte distribution may result in complicating factors. Restoration of a normal diet will, in most instances, restore the muscles to normal. These findings are discussed and may possibly be correlated with the finding of low cholinesterase activity in dystrophic mice previously reported (2).

1. Muscle Dystrophy in Mice of the Bar Harbor Strain. An Electromyographic Comparison with Dystrophia Myotonica in Man. A.R.McIntyre, A.L.Bennett, and J.S.Brodkey. A.M.A. Arch. J. Neurol. and Psych. 81:678,1959.

2. Cholinesterase Activity of Dystrophic and Denervated Muscles. James A. McFarland, and A.R.McIntyre. The Pharmacologist, Vol. 3, No 2, 1961.

FURTHER STEPS TOWARD STANDARDS FOR COCHLEO-TYMPANIC REFLEX TESTING. E. S. Mendelson. Air Crew Equipment Laboratory, NAMC, Phila. 12, Pa.

The ease and adequacy of acoustic reflex testing by tympanomanometry vary among subjects widely and unpredictably. A number of factors in this relation, which involve specific individual differences in reflex reactions and evident modifications in resting and reflex activity, have been defined in previous communications to the Society. Short term and long term auditory conditioning influences have been implicated, as suggested by correlations with acute experimental treatment and with previous chronic auditory experiences. In more recent experiments, two other models of experimental conditioning have been explored briefly, one acoustic, the other non-acoustic: (1) Using repetitive alternation of a tone and a noise as stimuli, reflex reactions have been recorded at intensity levels which had ordinarily appeared ineffective; the tone elicited responses, although the latencies were irregular. (2) When the subject's hands were then immersed in cool water (18°C) and the test repeated, the noise appeared to become the effective stimulus. The findings are consistent with the hypothesis under which the tests had been designed, namely, that both auditory and autonomic neural regulatory mechanisms determine the character of the middle ear muscle reflexes. It had already been concluded that three broad types of middle ear muscle activity had to be distinguished, corresponding (a) to the resting state, (b) to unconditioned, i.e., protective, reflex responses of short latency, and (c) to conditioned, i. e., accommodative, muscular responses which may occur sporadically under certain stimulus conditions, and that the indications of each type varied subjects. The present report shows the feasibility of modifying the stimulus-response relationships experimentally at several levels in the third of these types.

ALTERATION OF HUMAN SERUM CHOLESTERYL ESTER FATTY ACIDS WITH DRUGS. Joseph M. Merrill. VA Hospital and Vanderbilt University, Nashville, Tenn.

Administration of different hypocholesterolemic drugs will decrease the linoleic acid content of human serum. This decrement is caused principally by a decrease in serum cholesteryl esters. (Fed. Proc. 21:290, 1962). To investigate the possibility that an additional mechanism may contribute to this decreased serum linoleic acid, total lipids have been extracted from serum and separated by silicic acid column chromatography. Examination of the cholesteryl ester fatty acid patterns by gas liquid chromatography revealed the following changes in response to drug administration: (1) a decrease in linoleate of 3-22% (2) an increase in oleate of 3-31%. These changes were produced by administration of nicotinic acid, ethinyl estradiol, the d-isomer of triiodothyronine and to a lesser extent by MER-29. The percent change observed was roughly proportional to the decrease in serum cholesterol. These changes in linoleate and oleate are in the direction of those reported in patients with liver disease (Fed. Proc. 21:299, 1962). This raises the possibility that the normal cholesterol esterifying mechanism is altered by administration of these diverse hypocholesterolemic drugs.

THE REGULATION OF THE SWEATING RESPONSE TO WORK IN MAN. F. R. Meyer*, S. Robinson, J.L. Newton*, C.H. Ts'ao*, and L.O. Holgersen*. Anatomy-Physiology Dept., Indiana University, Bloomington.

A study was made of the time relations of the sweating responses of men in exercise with corresponding changes of temperature at various locations in the body. A series of 50-minute treadmill work experiments was carried out on men in which sweating was determined at frequent intervals by net weight loss, and temperature was recorded by thermocouples in the femoral vein, long saphenous vein, gastrocnemius muscle, rectum, esophagus, tympanum, and at 7 points on the skin. When the intensity of work was varied from experiment to experiment and room temperature held constant (25°C), the acceleration of sweating and the steady state attained during work, as well as the decline of sweating following work are all more closely related to changes of temperature in the working muscles and in the femoral veins draining blood from the leg muscles than to temperature changes in any of the other locations studied. When work was constant (4.5mph/9% grade) and the environmental temperature varied from experiment to experiment (15, 25, 34, 40°C), mean skin temperature varied with the environmental temperature, but the rectal, femoral vein, and muscle temperature were about the same in all of the 3 cooler environments. In this series sweating increased with the increments in skin and environmental temperature without corresponding changes in the deep body temperatures. Results suggest that sweating was regulated in these experiments by reflex effects originating from thermal receptors in the working muscle or in the veins draining the muscles, summated with reflexes originating from cutaneous thermal receptors, both acting through the hypothalamic center, the excitability of which was increased in proportion to its own temperature. (Supported by U. S. Army Medical Research & Dev. Command Grant DA-MEDDH-60-10.)

THERMAL RESPONSE IN THE DOG EXPOSED TO MICROWAVES. S. M. Michaelson, R. A. E. Thomson* and J. W. Howland. University of Rochester School of Medicine and Dentistry, Rochester, New York.

The thermal response of the dog exposed at 165 mw/cm^2 2880 Mc pulsed microwaves is characterized by an increase in rectal temperature followed by a period of stabilization above normal. A secondary rapid increase in rectal temperature occurs, which may be followed by collapse and death of the animal if exposure is prolonged. Insensible water loss is an accurate index of exposure. Repeated exposures to microwaves result in greater tolerance that resembles thermal adaptation. Hydration, alteration in environmental temperature, premedication with central nervous system depressants or previous exposure to ionizing radiation influence the thermal response and sensitivity.

HYPO-,HYPERCAPNIA AND VENTILATION IN CROSS-CIRCULATED DOGS. C. C. Michel*, S.S. Mei* and F.F. Kao. Department of Physiology, Downstate Medical Center, State University of New York, Brooklyn, N.Y.

Ventilatory responses to hypo-,hypercapnia were studied in 11 pairs of cross-circulated dogs (A.J.P. 202:1024,1962). Hypercapnia of the donor dog was produced by means of CO_2 inhalation (3,5,7% CO_2 in 40% O_2 and balance nitrogen) and hypocapnia by artificial hyperventilation. The arterial blood of the donor perfused the head of the recipient via its vertebral arteries. A rectilinear relationship between total ventilation of the recipient and arterial Pco_2 of the donor dog's hypercapnic blood was seen. However, when the donor dog was artificially hyperventilated, ventilation of the recipient dog was maintained at or below its resting level and this ventilation was independent of the Pco_2 changes of the arterial blood perfusing its head. Similar findings were obtained after the removal of both carotid sinuses and bodies of the recipient dog. The magnitude of this "maintained" ventilation of the recipient was correlated with the slopes of its CO_2 response curves. Upon discontinuation of hyperventilation in the donor, apnea occurred in the donor (with or without cervical bilateral vagotomy), but not in the recipient. Further observations were made when the hind limbs of the recipient dog were induced to exercise. Under these conditions artificial hyperventilation of the donor reduced the ventilation of the recipient considerably before its ventilation became independent of the Pco_2 perfusing its head.
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TOPOGRAPHY OF ESOPHAGEAL PRESSURE AS A FUNCTION OF POSTURE IN MAN. J. Milic-Emili,* J. M. Turner* and J. Mead. Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

Esophageal and mouth pressures have been determined at various fixed lung volumes in four normal subjects in various postures. Esophageal pressure was measured by means of a catheter-balloon system. The balloon was 2 cm in length and 3.5 cm in perimeter and contained 0.2 ml of air. As a result of the small volume of air used, the contribution of esophageal elastance was negligible. In the upper part of the esophagus (tip of balloon at a distance of less than about 30 cm from the nares) changes in intrapulmonary pressure and head posture produced considerable pressure variations which were clearly unrelated to changes in pleural pressure. As the balloon was placed at progressively lower levels, esophageal pressure in the standing subjects increased by about 0.35 cm H_2O per cm. This gradient, which is roughly comparable to the gradient in lung surface pressure observed by Krueger et al (J. Appl. Physiol. 16: 465, 1961), was reversed as the subjects were tilted head down. Since the magnitude of the gradients did not change appreciably when lung volume was varied from 20% to 80% of VC, the gradients are independent of lung density and hence unrelated to any fluid-like behavior of lung tissue. The observed gradients, however, appear to be gravity dependent. To what extent they may reflect differences in pleural pressure along the esophagus or mediastinal factors, is not clear.

EFFECT OF EXERCISE ON THE OXIDATION OF FREE FATTY ACIDS. H. I. Miller, B. Issekutz, Jr. and K. Rodahl. Division of Research, Lankenau Hospital, Philadelphia, Pa.

Experiments were carried out on dogs with indwelling arterial and venous catheters. The exercise consisted of a 20 min. run on a treadmill. O_2 uptake and CO_2 output, blood lactate acid level, and plasma FFA were measured. $NaHC^{14}O_3$, 1-C^{14}-palmitic or oleic acids were infused before, during and after exercise, for 3 hours. The specific activity of the expired $C^{14}O_2$ was measured by means of a Liquid Scintillation Counter using Hyamine as CO_2 absorbent. Experiments with labeled $NaHCO_3$ revealed that during exercise the $C^{14}O_2$ output rapidly rises and follows the changes of the blood lactic acid level. The decrease of the body bicarbonate pool may be the cause of the rise of the RQ in the first 10-15 minutes of work. After exercise a slow refilling of the bicarbonate pool may explain the low RQ observed during recovery. The corrected RQ suggests an intensive participation of fat oxidation in the energy supply during work. This conclusion was further supported by the finding that exercise increased 2-3 fold the corrected $C^{14}O_2$ output derived from labeled palmitic or oleic acid.

EFFECT OF HYPOPHYSECTOMY IN THE RAT ON THE REACCUMULATION RATE OF GASTROCNEMIUS MUSCLE GLYCOGEN. Vivian B. Millington* and Leslie L. Bennett. Dept. of Physiol., Univ. of California, San Francisco.

Following a reduction in the gastrocnemius muscle glycogen by sciatic nerve excitation, glycogen reaccumulation rates were compared in hypophysectomized and unhypophysectomized female rats of the Long-Evans strain. Significantly less glycogen was found in the non-excited muscle of the hypophysectomized rat. Excitation for 30 sec. resulted in the glycogen concentration being reduced by about 50% in the unhypophysectomized rat, a loss which was significantly greater than that in the hypophysectomized animal. In the unhypophysectomized rat, reaccumulation rates over 10-, 20- and 30-minute recovery periods were more rapid, and the glycogen concentrations reached at the end of each of these periods were significantly higher than in the hypophysectomized rat. However, the glycogen level reached at the end of each of the three recovery periods was less than the corresponding non-excited control value by statistically the same amount in both the hypophysectomized and unhypophysectomized groups. The venous blood glucose concentrations were consistently lower in the hypophysectomized rat, and attempts to increase the reaccumulation rates by markedly increasing the blood glucose levels were not successful. Exogenous ACTH, while it raised the glycogen concentration of the non-excited muscle in the hypophysectomized rat to levels in excess of the unhypophysectomized animal, did not change the reaccumulation rates. From these results and within the limits of the methods used, a possible factor that may partially or fully account for the slower glycogen reaccumulation rate in the hypophysectomized rat could be the significantly smaller glycogen loss which occurred on excitation of the muscle.

THE LOCATION OF MEDULLARY CO_2 CHEMOSENSITIVITY IN CATS. R.A. Mitchell*, B.W. Richardson* and J.W. Severinghaus. Cardiovascular Research Inst., Univ. of Calif. Med. Center, San Francisco, California

Perfusion of the subarachnoid space about the medulla with mock C.S.F. containing high Pco_2 and H+, dilute nicotine, or acetylcholine produces hyperpnea. We attempted to localize the chemosensitive area by direct application of these agents to the surface of the medulla of lightly anesthetized cats.

Pledgets saturated with normal mock C.S.F. equilibrated with high CO_2 or containing nicotine or acetylcholine produced hyperpnea when applied to the ventrolateral surface of the medulla within a bilateral zone bounded medially by the pyramidal tracts, laterally by the 8th to 11th cranial nerves, rostrally by the pons and extending 6 mm caudad. The hyperpnic responses, which began in 3 seconds, resembled those obtained by perfusion of the subarachnoid space. They were not observed from other areas on the medulla or 4th ventricle. Since Loeschcke and co-workers have suggested that the chemosensitivity resides in the respiratory afferents in the cranial nerves, we sectioned the 7th to 12th cranial nerves unilaterally in 6 cats; this did not alter the chemosensitivity on the ipsilateral side. Unilateral, intracranial, extradural section of the 7th through 12th cranial nerves in 2 cats two weeks before study did not alter the chemosensitivity on the side of section. These studies suggest that chemosensitivity in the medulla to H+ in the C.S.F., which has been shown to play a role in the respiratory response to inhaled CO_2, resides in the ventrolateral medulla.

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POST-TETANIC CHANGES IN THE LATERAL GENICULATE NUCLEUS. Noel L. Morlock*, Wade H. Marshall, and Anthony F. Bak*. Natl. Insts. of Health, Bethesda, Md.

The effect of barbiturate on the post-tetanic changes in the lateral geniculate nucleus (LDG) of cats has been contested. To resolve this, chronic cats with implanted electrodes positioned in the optic tract and LDG were used. In the unanesthetized animal, tetanization of first order fibers at 400 per second for 20 seconds resulted in the typical short (15-30 seconds) first subnormality of the post-synaptic response in the LDG. Subsequently, little if any post-tetanic potentiation (PTP) was noted and no second subnormality. When given Nembutal (25-35 mg/K), the geniculate response in these same cats was depressed from control levels and tetanus resulted in marked PTP and prolonged second subnormality lasting until anesthesia began to wear off. Post-tetanic potentiation was greater when the tetanus was given while geniculate response was in a second subnormality produced by a previous tetanus. Thus depression of geniculate response and production of subliminal fringe most probably are responsible for PTP found in the LDG of Nembutalized animals. Also the prolonged second subnormality is related in an as yet unknown way to effects of barbiturate anesthesia. Additionally, in a series of acute experiments using Nembutal anesthesia impedance measurements were made in the LDG following tetanization of the contralateral optic nerve. A pair of platinum black depth electrodes in a bridge circuit were used. With use of relays and good electrical isolation impedance and lateral geniculate response records were obtained. During tetanization impedance increased 0.25-0.5% and remained increased during PTP, returning to control with return of the response to control level. Also it was noted that Nembutal increases impedance of brain tissue.

THE CONCENTRATION DEPENDENCE OF SODIUM EFFLUX FROM MUSCLE. L. J. Mullins and A. S. Frumento+. Department of Biophysics, University of Maryland School of Medicine, Baltimore, Md. +Fellow of the Argentine National Board for Scientific and Technical Research. Present address: Departamento de Ciencias Biologicas, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires.

Frog sartorius muscles subjected to overnight loading with Na^+ in K-free Ringer in the cold were subsequently labelled with Na^{24} and then immersed in choline Ringer and the efflux of Na^{24} followed for 4 hours. The initial efflux of Na^+ appeared to be 17 pmole/cm^2 sec. and was constant with time. This rate changed very abruptly to about 9 pmole/cm^2 sec. and this latter rate was maintained for the first 40 minutes of efflux. The efflux then declined gradually with time and reached values of the order of 0.1 pmole/cm^2 sec. The back addition of counts lost from muscles enabled one to calculate the relationship between efflux and $[Na]_i$ for muscle. This is an S-shaped curve with a value at half saturation of about 17 mM per liter of fiber water.

ARTERIAL CONSTRICTION IN THE DIVING SEAL (PHOCA VITULINA). H.V. Murdaugh, Jr., W.W. Pyron*, J.K. Brennan*, and W.L. Mitchell*. Mt. Desert Island Biol. Lab., Salisbury Cove and Dept. Med. Univ. Alabama Med. Center, Birmingham.

Atropine will block the bradycardia and arterial constrictor response (ACR) to diving in harbor seal (Clin. Res. 9:18, 1961). Further evaluation of the ACR of the seal was conducted using oxygen tension of extradural vein blood and observation of webb artery as indices. Hexamethonium Chloride would not prevent the ACR. Tetraethylammonium chloride (2mgm/lb IV) impaired bradycardia but not the ACR, but when 3 mgm/lb was given I.V., bradycardia was prevented and oxygen tension at 3 minutes of dive decreased to as low as 19 mm Hg. When pilocarpine (0.2 mgm/lb IV) was administered before the larger quantity of TEAC the oxygen tension at 4 minutes of dive did not fall below 94 mm Hg. Pilocarpine caused bleeding from small webb artery to cease at onset of salivation. It is suggested that the ACR of the seal is an example of cholinergic arterial constriction.

EFFECT OF SPLANCHNIC ADRENERGIC BLOCKADE ON MESENTERIC HEMODYNAMICS AND SHOCK PROTECTION. Dennis L. Murphy,* Nawzad Fadhel* and James J. Smith. Dept. of Physiology, Marquette Univ. School of Med., Milwaukee, Wis.

Pretreatment with adrenergic blocking agents such as phenoxybenzamine and maintenance of intestinal blood flow during shock by perfusion of the mesenteric artery are two methods of diminishing the lethality of experimental shock procedures. Since hemorrhagic intestinal mucosal lesions similar to those in shocked dogs are characteristically found after prolonged epinephrine infusion, and since plasma epinephrine levels in shock exceed 40-70X normal values, the possibility was suggested that intestinal perfusion and adrenergic blockade were shock-protective thru a common pathway of the mesenteric vascular bed. This was investigated by a comparison of canine mesenteric blood flow, blood pressure and portal venous pressure responses to i.a. epinephrine after either systemic (i.v.) or local superior mesenteric (i.a.) injection of 0.7 mg/kg phenoxybenzamine. While control mesenteric flow and resistance were not significantly altered by phenoxybenzamine alone in either group, mesenteric reactivity to epinephrine and to hemorrhagic hypotension showed significant differences between the two groups. A subsequent hemorrhagic shock survival study yielded 5/10 survivors in dogs with a localized splanchnic adrenergic blockade, 4/10 survivors in the dogs with a systemic adrenergic block and 0/10 survivors in the control, saline-injected group. Bleeding volumes and circulatory responses were similar in all groups; autopsies revealed typical hemorrhagic intestinal lesions in the entire control group but only infrequent (4/20) and minimal lesions in the other groups. These findings indicate that (1) localized adrenergic blockade is as effective as systemic blockade in modifying the lethality of hemorrhagic shock, and (2) shock protection by adrenergic blockade does not correlate well with mesenteric vascular reactivity to epinephrine.

FACTORS AFFECTING FOCAL DISCHARGES OF EPILEPTOGENIC CORTEX. F. S. Musgrave*, M. Sanaman* and D. P. Purpura (intr. by P. F. A. Hoefer). Columbia University, New York.

The production of a 4mm-diameter cold lesion in suprasylvian gyrus of adult cats is immediately associated with a 12-36 mV local negative cortical D. C. (injury) potential which disappears in 15-30 mins. Focal epileptogenic discharges develop at variable times during and after the injury potential. Characteristic 1/sec focal discharges commence after disappearance of the injury potential. Complete or partial neuronal isolation of the area involved in the lesion does not alter the basic 1/sec discharge pattern or the cyclic variations in discharge characteristics observed in many instances. Changes in frequency of focal discharges in intact or isolated cortical areas are associated with similar steady potential variations. Epileptogenic lesions in isolated cortex generally exhibit one variety of paroxysmal activity but multiple independent discharges result from subsequent splitting of the lesion site. The amplitude but not the frequency of focal discharges in intact or isolated cortex is affected by systemically administered nembutal (40-60 mg/Kg). Minimal alterations in 1/sec discharge frequency are observed at levels of hypoxemia sufficient to abolish spontaneous electrocortical activity. Topical GABA, KCl, and procaine produce polarity changes in focal discharges but fail to alter discharge-frequency. Topical TEA augments the amplitude and frequency of focal discharges whereas barium suppresses focal activity. The results suggest that the basic periodicity of focal discharges in freezing lesions of cortex is not attributable to synaptic drives originating outside the lesion site.

EFFECTS OF CO_2 ON GASTRIC K^+ EFFLUX. A. Naitove (intr. by F. G. Carpenter). Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

The separate and interacting effects of variations in alveolar CO_2 and O_2 tensions on K^+ flux into the stomach during continuous histamine stimulation were studied. Experiments were performed on unanesthetized, trained dogs with chronic Heidenhain gastric pouches. The patterns of gastric K^+ efflux observed when the animals were breathing room air resembled those reported by others. Periods of hypercapnia (P_{ACO_2} = 56 mm Hg) were associated with significant decreases in gastric K^+ efflux. Both the volume and the K^+ concentration of secretions decreased. These values returned towards normal as the alveolar gas tensions returned to normal. Changes in alveolar O_2 tensions over a range of 60-140 mm Hg did not influence the responses associated with high, normal or low CO_2 values. Further experiments suggest that extracellular pH changes during the periods of hypercapnia may have played a role in modifying the gastric K^+ efflux.

SECRETIN, PANCREOZYMIN, AND CHOLECYSTOKININ. H. Necheles, A. Bridgwater*, Y. Kuroyanagi*, and T. Geisel*. Dept. Gastrointestinal Research, Medical Research Institute, Michael Reese Hospital, Chicago, Illinois.

Secretin and pancreozymin - cholecystokinin were administered via portal or systemic vein to anesthetized dogs with ligated pylorus, external bile drainage, catheter in gallbladder, and cannulated pancreatic duct. Effects on pancreatic secretion were significantly decreased when secretin and pancreozymin were given via portal vein, but effects of cholecystokinin on gallbladder pressure did not appear to be different when given by either route. An enzyme isolated from liver and kidney destroys secretin; it may be a cathepsin-like enzyme with optimal pH 3-5. Human plasmin also destroys secretin. It is doubted whether a specific secretinase exists.

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ASANGUINEOUS TOTAL BODY PERFUSION. W. A. Neely, M. D. Turner, and J. L. Haining*. Departments of Surgery and Biochemistry, University of Mississippi School of Medicine, Jackson.

Boerema has reported bloodless survival depending upon the increased solubility of oxygen in plasma at three atmospheres. Wolf et al. found that the upper limit of survival is about 10 minutes after total cessation of cerebral blood flow. A procedure has been devised to remove blood from animals and perfuse the body with a anaerobic-buffered-glucose-colloid solution for periods up to 30 minutes. The perfusate was discarded after one pass. At the end of the perfusion period blood was replaced. Five of ten animals have survived this procedure with prompt and permanent return of normal cardiopulmonary function after reinfusion of blood. Three of five permanent survivors had detectable neurological deficits some of which have subsided. Lactic acid was produced and appeared in the discarded perfusate. The pH of the discarded perfusate was not lower than 7.29. It would appear that the upper time limit of anoxic survival is greater than previously reported. This study emphasizes the possible importance of accumulated metabolic acids in hemorrhagic shock. (Supported by National Institutes of Health Grants RG-7181 and AH-4568).

AN ANALYSIS OF THE DISPERSION OF INJECTED INDICATOR AFTER ONE COMPLETE CIRCULATION. K. K. Nicholes*, A. F. Toronto*, E. H. Wood, and H. R. Warner. Latter-day Saints Hospital, Salt Lake City, Utah and Mayo Foundation, Rochester, Minnesota. (Supported by NIH grant no. H-4664)

The time-course of concentration of indicator measured at a site downstream from a point of a sudden single injection of this indicator is characterized by a large primary hump followed by one or more smaller humps. With a wide variety of injection and sampling sites and after correction for distortion due to the sampling system the primary hump of this curve can be described by

Equation 1 $$C = \frac{K}{\sigma} e^{-.5\left(\frac{t-t_1}{\sigma}\right)^2} - T\,dc/dt$$

where C is concentration, t is time, and T, K, σ, and t_1 are constants. Let h(t) be the expected time-course of dye concentration after one complete transit of indicator if the dye were sampled at the same point at which it was injected as an impulse. On the assumption that h(t) has the form of equation 1, the principle of superposition was used to derive the parameters of h(t) with the help of a digital computer from analysis of the contour of the first and second humps of an indicator-dilution curve. Such an analysis has been performed on curves recorded simultaneously from the pulmonary artery and ascending aorta of dogs and humans following injection into the superior vena cava and left heart. From these studies h(t) was found to be independent of the point of injection and sampling and of the characteristics of the sampling system. With the subjects at rest from .3 to .5 of the injected indicator could be accounted for as contributing to the second hump of the indicator-dilution curve, while during exercise, this fraction rose to 0.95. Exercise also caused marked changes in the parameters of the calculated h(t) function.

CHANGES IN RAT LIVER MITOCHONDRIA AFTER THYROIDECTOMY. Thomas W. O'Brien* and Howard M. Klitgaard (intr. by Alvin F. Riecker). Department of Physiology, Marquette University School of Medicine, Milwaukee 3, Wisconsin.

Other investigators have shown that the swelling of rat liver mitochondria is related to the thyroid status of the animal. The changes in rat liver mitochondria occurring 36 days after thyroidectomy were studied using the following parameters: $\bar{W}$, mean mitochondrial area; K_A, ratio of total mitochondrial area to cytoplasm area; and K_N, number of mitochondria per cytoplasm unit. Mitochondrial and cytoplasm areas were determined by planimetry on photographic enlargements of liver cell electronmicrographs. The shotgun method and the spider method, both modifications of Chalkley's random-point method, and the area-by-weight technique yielded results within 5% of those obtained by planimetry. Analysis of a limited number of micrographs showed no apparent difference in mean mitochondrial area between the controls ($\bar{W} = 0.419\ \mu^2$) and rats 36 days after thyroidectomy ($\bar{W} = 0.398\ \mu^2$). The K_A decreased from the control level of 0.348 to 0.297 in the thyroidectomized animals and the K_N similarly decreased from 0.854 μ^{-2} to 0.750 μ^{-2}. These results suggest an increase in extramitochondrial cytoplasm in rat liver 36 days after thyroidectomy. This study is being extended to follow the complete time course of mitochondrial changes after thyroidectomy. These mitochondrial changes will be correlated with the previously determined tissue oxygen consumption and enzyme activities.

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INTRARETINAL RESPONSES OF THE MONKEY RETINA TO ELECTRICAL STIMULATION. Thomas E. Ogden* and Kenneth T. Brown. Dept. of Physiol., Univ. of Calif. Medical Center, San Francisco, Calif.

The retinas of Cynamolgus monkeys, under light pentothal anesthesia, were electrically stimulated by brief current pulses; these were passed between a small intraocular cathode, pressed lightly against the retina, and a retro-bulbar anode. Intraretinal responses were recorded by penetrating tungsten microelectrodes located at distances of up to 2 mm. from the cathode. The retinal response to direct electrical stimulation included four major components, as follows: (1) Antidromic responses of optic nerve fibers; (2) A positive wave with a latency of 4-5 msec. and a duration of about 3 msec., recorded with maximum amplitude in the ganglion cell layer; (3) A negative wave with a latency of 4-5 msec. and a duration of about 3 msec., recorded with maximum amplitude near the outer plexiform layer; (4) A negative wave with a long latency (over 20 msec.) and a duration of 20-50 msec., recorded with maximum amplitude in or near the inner nuclear layer. The early slow potentials (2 and 3) have not been described previously. Responses (1) and (2) could be evoked equally well by stimulation of the optic nerve. Present evidence indicates that response (2) is a postsynaptic response of ganglion cells and is mediated by small centrifugal fibers. Responses (3) and (4) were not found in the central fovea, and were abolished by occluding the retinal arteries while leaving the choroidal circulation intact. Hence the site of origin of these potentials cannot be distal to the outer plexiform layer. (Supported by PHS grant B-1903)

ACTH IN DOG BLOOD. N. Ohsawa* and E. S. Redgate. Western Reserve University School of Medicine, Cleveland, Ohio.

Dog plasma, incubated 12 to 16 hours at 37° C, contained no detectable quantity of ACTH. U.S.P. Reference Standard was added, the plasma dissolved in 5% acetic acid and heated to 70° C for 30 minutes. The solution was applied to an XE-64 resin column (Dixon, Liddle). ACTH was eluted with 50% acetic acid and the eluant lyophilized. The dry powder was dissolved in acid-saline (0.01 N HCl in 0.9% NaCl) and assayed in hypophysectomized rats by the adrenal ascorbic acid depletion method. When compared with Reference Standard dissolved in acid-saline, recovery was 145% (mean of five experiments). Dog plasma was processed as described above and ACTH added to the lyophilized eluant. Potency was 180% as compared to ACTH in acid-saline. ACTH added to unprocessed dog plasma or to bovine serum albumin (Fraction V) was more potent than ACTH in acid-saline (160 and 180%, respectively). When corrected for "potentiation", recovery by the XE-64 method is about 80%. By this method, blood ACTH levels in dogs under deep pentobarbital anesthesia have been shown to range between less than 1.5 to 7.5 milliunits for 100 ml whole blood. The elevation in the level of ACTH in blood from the carotid artery, induced by hemorrhage, was unexpectedly as great as that in blood from the jugular vein. (Supported by U.S.P.H.S. Grant No. B3238 and U.S.A.F. Contract No. AF AFOSR 62-3.)

MAMMALIAN CELL WATER EXCHANGE IN RESPONSE TO EXTRACELLULAR OSMOTIC GRADIENTS. Edwin G. Olmstead, Dept. of Medicine, Univ. of N. Dak., Grand Forks, N. Dak. When mammalian cells are placed in hypertonic solutions in Vitro water is transferred from the cell and at equilibrium $\pi_T^{in} = \pi_T^{ex}$ where π_T = total osmotic pressure; or,

$$\phi_E^{in} RTm_E^{in} + \phi_P^{in} RTm_P^{in} = \phi_E^{ex} RTm_E^{ex}$$

the ϕ_E, ϕ_P, m_E, m_P are the osmotic coefficients and molal concentrations of dissolved electrolyte (E) and protein (P). $\frac{d\phi_E^{in}}{dm_E^{in}}$ and $\frac{d\phi_E^{ex}}{dm_E^{ex}}$ are constant (K) over pathological variations of π_T^{ex}, but $\frac{d\phi_P^{in}}{dm_P^{in}} \neq K$ as ϕ_P^{in} increases sharply with increase m_P^{in}. Therefore, at equilibrium with hypertonic extracellular solutions.

$$\frac{\partial \pi_T^{in}}{\partial m_E^{in}} + \frac{\partial \pi_T^{in}}{\partial m_P^{in}} > \frac{d\pi_T^{ex}}{dm_E^{ex}}$$

and less H_2O is transferred from the cell into hypertonic solutions than is transferred to the cell from hypotonic solutions removed equidistant from cellular isotonicity. (Supported USPH grant H-6387)

BRONCHOCONSTRICTOR RESPONSES OF EACH LUNG TO IPSILATERAL AND CONTRALATERAL EFFERENT VAGAL STIMULATION IN THE DOG. C. R. Olsen*, H. J. H. Colebatch*, and J. A. Nadel. Cardiovascular Research Inst. Univ. of Calif. School of Med., San Francisco.

We measured total resistance of each lung in 5 dogs anesthetized with sodium pentobarbital (32 mg/kg), paralyzed with gallamine triethiodide, and artificially ventilated. This was accomplished with a tracheal divider, two respiratory pumps, and simultaneous measurement of flow and transpulmonary pressure for each lung. Electrical stimulation of the peripheral end of the right vagus nerve in the neck caused an average maximal 8-fold increase of resistance in the right lung (avg control resistance 4.9 cm/L/sec) but only a slight change in the left lung (avg +35%; control resistance 5 cm/L/sec). Stimulation of the left vagus produced an average 14-fold maximal increase of resistance in the left lung (avg control 4.2 cm/L/sec) but only a slight increase (avg +64%; control 4.7 cm/L/sec) in the right lung. Prostigmine (50 or 100 µg/kg) augmented the contralateral change in 3 dogs during left vagal stimulation (avg +168%) and in 1 dog during right vagal stimulation (+158%). It was not possible to demonstrate crossover of the right vagus in two dogs and of the left vagus in one. When both lungs were ventilated by a single pump (2 dogs), ventilation shifted away from the lung whose vagus was stimulated. These findings indicate that in the dog the principal parasympathetic motor innervation of the airways is via the ipsilateral vagus nerve. However, a slight response to stimulation of the contralateral vagus can be obtained, indicating the presence of some crossover of vagal efferent fibers. (Supported by USPHS grant H-6235 and a Junior Fellowship from the San Francisco Heart Association.)

TEMPERATURE COEFFICIENT OF WATER EXCHANGE I N BEEF RED BLOOD CELLS. C. V. Paganelli. Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

Washed, concentrated beef red cell suspensions (hct. ratio .8 - .9) were incubated briefly with an isotonic buffer containing tritiated water (HTO) and mixed rapidly with non-labeled buffer. The efflux of HTO from the cells was followed by use of a modified Hartridge-Roughton flow tube. The efflux could be described by a single exponential function with a rate constant of $74 \pm 9(\text{s.d.})\text{sec}^{-1}$ at 25°C. Data from experiments performed in the temperature range 5-30°C permitted calculation of an activation energy of 5400 cal/mol from a standard Arrhenius plot. The activation energy for self-diffusion of HTO given by Wang et al (J.A.C.S. 75: 466, 1953) is 4600 cal/mol, whereas activation energies for processes presumed to involve interaction between membrane components and transported substances are commonly in the region of 10,000 cal/mol. The relatively low activation energy for water exchange and its closeness to the activation energy for self-diffusion of water suggest that it crosses the red cell membrane by a process of restricted diffusion through aqueous channels. (Supported by USPHS Grant RG 6696.)

THE ASSESSMENT OF THE DEGREE OF AORTIC INCOMPETENCE BY A PULSATING CUFF TECHNIQUE.

J. F. Palmer* and I. F. S. Mackay. University of the West Indies, Jamaica, West Indies.

The principle of the technique is that of applying an intermittently arterial occlusive pressure to a pneumatic cuff placed around the arm. The pressure, which is rapidly applied and released, is triggered from the R-wave of the electrocardiogram. This was applied to patients suffering from aortic incompetence in such a way that the regurgitant flow in the brachial artery was captured and the resulting increase in forward flow measured plethysmographically. This increase in flow was used to assess the backflow in the brachial artery and was employed as an index of the degree of aortic valvular incompetence. (See Mackay and Palmer, J. Physiol. 161:37P, 1962). Twenty-two patients, whose degree of aortic incompetence had been clinically assessed with the aid of the Braunwald and Morrow[1] Dye Technique as "Slight", "Mild-Moderate", "Considerable" or "Severe", were found to have, respectively, backflows measured by this technique of 5-15%, 15-35%, 30-35% and 40-55%.

The Relationship of Respiratory Dead Space on Comparative Diffusing Capacity of Patients with Pulmonary Disease. L. J. Pecora and G. El Samra* Veterans Administration Hospital and Kettering Laboratory, Cincinnati, Ohio.

This study was made to observe the effect of increased anatomic dead space on the determination of pulmonary diffusing capacity and the effect of using the measured dead space value in the calculations. Dead space, increased experimentally by 200 ml in normal subjects, increased minute ventilation by CO_2 stimulation. The minute ventilation was increased about 50%, chiefly due to increased tidal volume. Alveolar ventilation was reduced. Ten patients with chronic emphysema and 7 patients with other pulmonary diseases, most of whom had increased dead space and poor mixing, served as the study group. The diffusing capacity of each patient was measured by the steady state and single breath methods. Since the rebreathing method gave results comparable to the single breath method in our hands, the study was limited to the single breath and steady state methods. On the same day, the anatomic dead space was measured by Bohr's CO_2 method and pulmonary mixing was measured either by the seven minute nitrogen washout or by the single breath nitrogen washout methods. All subjects were tested while seated. The diffusing capacity was calculated using both the assumed dead space (body weight in lb. plus valve DS) and also the measured dead space. The mean anatomic dead space was 249 ml. The mean diffusing capacity measurements were: SS (assumed DS) 4.9; SS (measured DS) 5.8; and SB 16.5. It is interpreted from these data that although the use of the measured dead space in the calculations by the steady state method increases the values about 15%, the steady state method still remains about 30% of the single breath measurement in these patients.

MAMMALIAN RESPIRATION OF PRESSURE-OXYGENATED SOLUTIONS. J. Pegg, T. Horner, and E. Wahrenbrock (intr. by J. W. Severinghaus), Cardiovascular Research Inst. and Dept. of Anesth., Univ. of Calif. Med. Center, San Francisco.

Rats, tracheostomized under ether anesthesia and immersed within a pressure chamber in isotonic solutions at 37°C equilibrated with oxygen at 5-20 atmospheres absolute, survived up to 4 hours breathing the solution spontaneously and during this time responded to stimuli and showed normal motor activity. During immersion heart rate was 60% of normal, respiratory frequency 40% of normal and expiration was labored and prolonged. After 30 minutes at 10 atmospheres in an essentially unbuffered solution, arterial oxygen saturation was 76%, Pco_2 174, and pH 6.61. After 30 minutes at 17.5 atmospheres in a solution buffered with 0.4% THAM, oxygen saturation was 93%, Pco_2 45, and pH 7.28. These values imply that alveolar ventilation was roughly half normal. On return to room air the rats were active briefly but death usually occurred within 15 minutes despite administration of 100% oxygen or intermittent positive-pressure breathing. The lungs contained sero-sanguinous fluid and were atelectatic. Lung extracts had a minimum surface tension greater than 18 dynes/cm. Continuous positive pressure breathing at 15 cm H_2O pressure prolonged life up to 5 hours and with O_2 up to 21 hours. The lungs of those surviving more than 7 hours had hyaline membranes; controls given continuous positive pressure breathing with 100% oxygen died, but their lungs had no hyaline membranes. Certain similarities exist in the lungs of these rats and of infants dying with respiratory distress syndrome.

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OBSERVATIONS ON THE ROLE OF THE STOMACH IN HUNGER. S. B. Penick, G. P. Smith, K. Weinecke, and L. E. Hinkle (intr. by E. L. Becker). Dept. of Medicine, N. Y. Hospital-Cornell Medical Center, New York, N. Y.

To study the relation between gastric contractions and hunger, experiments were carried out on hungry men after a 5 hour fast. Their sensations were reported on a pre-arranged check list at 30 minute intervals. 8 subjects in 24 experiments swallowed a type 430 transensor capsule which measures intraluminal pressure and broadcasts an externally monitored signal. Gastric motility was monitored for 2 hours. The mean rate of contraction (types II & III) was 1.3 ± 1.1 per hour. There was no correlation between degree of "hunger" as reported by subjects and the number of gastric contractions. In 7 experiments, a balloon was passed on 4 of these same subjects and was filled with 50 cc of water. Gastric motility was monitored for 90 minutes. Contractions occurred at a mean rate of 13.5 ± 2.45 per hour, significantly more frequent than the mean rate of 0.7 ± 0.88 per hour recorded using the transensor alone ($p<.001$). In 4 of these 7 experiments, the transensor also was swallowed and most contractions were recorded simultaneously by both devices. In 3 subjects, a gastric balloon was inflated in 4 steps of 25 cc each over 20 minutes. During glucagon-induced anorexia, contractions did not occur until a volume of at least 75 cc had been obtained, and the mean total contractions during the inflation period and for 20 minutes thereafter were 3.3 ± 2.5 After placebo, contractions occurred at a volume of less than 50 cc and the total mean contractions were 10.3 ± 4.9, significantly greater than after glucagon ($p<.02$). These experiments suggest that spontaneous gastric contractions are infrequent in fasting individuals and that they bear little relation to the sensation of hunger. Rather, hunger is characterized by increased gastric irritability, defined as a propensity to contract promptly and frequently upon any object perceived as a bolus.

MEASUREMENT OF pO_2 IN EXCISED HUMAN SKIN WITH THE BECKMAN MICRO-ELECTRODE. Raymond Penneys. Vascular Sect., Robinette Fdtn., Hosp. Univ. Penna., Phila.

These experiments were done to see if a Clark-type oxygen electrode, recently miniaturized to an external diameter of 1mm by the Beckman Instr. Co., would provide absolute pO_2 measurements in human skin, as it does in liquids and "soft" tissues, such as brain. We first placed the electrode inside an 18 gauge Riley needle, as is usually done to protect the membrane, but soon discarded this method because it required too deep a puncture for skin. We then tried a Riley needle with a blunt end to allow a more superficial insertion but also discarded this because the pO_2 of dead skin (Montgomery and Horwitz, J. Clin. Invest. 29, 1120, 1950), so measured, did not come into equilibrium with that of the surrounding saline; we suspect that this was due to entrapment of an air bubble at the tip of the needle. We finally inserted the electrode, unprotected by any needle, directly into skin that had been punctured to a depth of about 1mm by an 18 gauge needle. Now, the pO_2 of dead skin equaled that of the saline (0-740mm Hg, 14 expts.), demonstrating that the barrier to the diffusion of oxygen presented by skin does not appreciably affect the electrode. To prove that the electrode tip was completely inside the skin, and not in the saline, the pO_2 of excised, living skin was measured in the same manner and was found to be much lower than that of the saline (9 expts.). In addition, the day-to-day calibration of the electrode showed that its behavior was not adversely affected by its use in skin. The Beckman microelectrode thus provides absolute pO_2 measurements in excised, human skin and probably in other "firm" tissues. (USPHS H-4906-C2)

SLOW MUSCLE FIBERS IN THE SUPERIOR OBLIQUE OF THE CAT. G. Pilar and A. Hess (intr. by A. R. Martin). Dept. of Physiology, University of Utah, Salt Lake City, Utah.

Glass micropipettes were used to obtain intracellular records from individual fibers in the superior oblique muscle of the cat. Two types of muscle fibers were found: 1) fibers with resting potentials of 70 - 90 mV which responded to motor nerve stimulation with action potentials; 2) fibers with resting potentials of 45 - 60 mV which responded to nerve stimulation with local junctional potentials similar to the 'small junctional potentials' seen in the slow fibers of frog muscle. In the latter the junctional potentials could be graded by varying the stimulus applied to the motor nerve, and individual components of the response could be seen to have different amplitudes and time-courses, suggesting that the nerve terminals were distributed along the fibers. Such responses could be obtained regularly near the peripheral tendon insertion of the muscle. Isometric tension recordings from partially curarized muscles suggested that these 'slow' fibers respond to repetitive nerve stimulation with a maintained contracture. When the muscles were stained for cholinesterase, 'en plaque' and 'en grappe' endings were seen on separate muscle fibers. However, in the region from which the small junctional potentials were recorded only 'en grappe' endings were found, these being distributed along the fibers. Morphologically, 'Felderstruktur' and 'Fibrillenstruktur' muscle fibers could also be distinguished.

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THE EFFECT OF HYPERTONIC MANNITOL ON VENTILATION.
W.S. Ploski*, G.G. Nahas, B.R. Fink and M. Verosky*. College of Physicians and Surgeons, Columbia University, New York, N.Y.

Six dogs were anesthetized with nembutal and nephrectomized. After intubation, they breathed from a spirometer containing 100% oxygen. Following a control period during which V_E increased, 1.5 M mannitol was infused at a rate of 0.8 ml/kg./min. for 30 minutes, an amount calculated to increase the osmolality of extracellular fluid by 50 mOsm. Twenty minutes after the infusion, $[H^+]$ and pCO_2 in arterial blood were 21×10^{-9} M/L and 11 mm Hg above normal, while $[HCO_3^-]$ had decreased 1.8 mEq/L, and the average V_E was 25% less than the control. In contrast, in the cerebrospinal fluid, $[HCO_3^-]$ was increased by 0.5 mEq/L, pCO_2 by 2.2 mm Hg and $[H^+]$ by 1.4×10^{-9} M/L. Blood $[H^+]$, pCO_2, $[HCO_3^-]$ and V_E subsequently returned toward control values. The observed fall in V_E could be attributed to an intracellular alkalosis caused by an osmotically induced shift of water from intracellular to extracellular space, probably resulting in an increase in intracellular buffer concentration and a decrease in intracellular $[H^+]$.

CORTICOSTERONE SECRETION IN RATS WITH HYPOTHALAMIC LESIONS. John C. Porter. Univ. of Texas, Southwestern Med. School, Dallas, Texas.

Corticosterone secretion was investigated in rats with diabetes insipidus caused by electrically induced lesions in the anterior hypothalamus. Forty-two to fifty-two hours after placement of lesions, the left adrenal vein was cannulated and the effluent blood collected. The corticosterone content of this blood was determined by a double isotope derivative procedure. Corticosterone secretion from the left adrenal of rats with intact hypothalami was 12.8, 11.2, 12.2, and 11.5 μg corticosterone during the first, second, third, and fourth 15-minute interval, respectively, of a 60-minute collection period. Rats with anterior hypothalamic lesions secreted 1.8, 2.7, 3.6, 6.1, 9.0, 10.7, 11.1, and 10.6 μg corticosterone in the first through the eighth 15-minute interval, respectively, of a 2-hour collection period; and removal of the pituitary from lesioned rats reduced the secretion of the steroid to 0.3 μg. One hundred mU arginine vasopressin given every 30 minutes to rats with hypothalamic lesions and hypophysectomized rats with lesions did not significantly change the rate of secretion, while 5 mU ACTH given at half-hour intervals to rats with lesions greatly increased the rate of corticosterone secretion, suggesting that the low rate during the first 15-minute collection period was not due to an unresponsive adrenal. Blood flow through the adrenal vein and arterial blood pressure were similar in all groups of lesioned animals.

PRESERVATION OF INSULIN EFFECT ON FFA MOVEMENT IN HYPOPHYSEAL-ADRENOCORTICAL-DEPENDENT INSULIN RESISTANCE. D. Rabinowitz* and K. L. Zierler. Dept. Med., Johns Hopkins Univ. and Hosp., Baltimore, Md.

During studies of insulin effect in patients with disturbance of the hypophyseal-adrenocortical axis it was discovered that although there was insulin resistance with respect to glucose uptake by muscle, there was either normal or increased responsiveness to insulin with respect to other metabolic events. Six patients with active acromegaly, three with Cushing's syndrome and three normal subjects in whom endogenous growth hormone activity had been stimulated by a 66-hour fast were studied by continuous close intra-arterial injection of insulin to achieve a concentration of about 300 μunits per ml brachial arterial plasma. In all, glucose and potassium uptake by forearm in response to insulin was less than half normal. Insofar as arterial-superficial venous concentrations measure metabolism of forearm adipose tissue, insulin effect on glucose and potassium uptake by adipose tissue was reduced but there was probably less inhibition than there was of uptake by muscle. In normals, insulin decreases release of free fatty acids from adipose tissue. This effect of insulin was unabated or enhanced in all these patients. These studies apparently dissociate the effect of insulin on potassium and on glucose uptake from its effect on FFA release; that is, they make difficult a unitary explanation of insulin action.

(Supported by ONR, MDAA INC. and NIAMD (A-750 and A-5524)

THE ELECTROPHORETIC SERUM PROTEIN PATTERN IN DIABETES AND ITS RELATION TO HYPOTHYROIDISM. Elaine P. Ralli. New York University School of Medicine, New York City, New York.

Serum electrophoretic patterns were done on 42 diabetic and 19 hypothyroid patients. In the diabetic patients the alpha globulin fraction was elevated in 14 cases, the beta fraction in 13 and the gamma fraction in 13. In the hypothyroid patients the alpha globulin was elevated in 9 cases, the beta fraction in 5 and the gamma fraction in 9. Diabetes and hypothyroidism have several laboratory and clinical findings in common, i.e., changes in the distribution of the serum globulins, elevation of the serum cholesterols and carotene, neuropathy and sensitivity to injected insulin. The latter finding is demonstrated in the "brittle diabetic". Therapy with Triiodothyronine in patients with diabetes decreased the tendency to insulin shock, decreased the serum cholesterol levels and tended to restore the serum globulins to normal. The findings suggest that a lack of thyroid hormone may be responsible for the sensitivity to insulin, the hypercholesterolemia and the changes in serum globulins that occur in some diabetic patients.

AREA-VOLUME CHANGES OF HEMOLYSING SINGLE ERYTHROCYTES. R.P. Rand*, D. van der Baaren*, and A.C. Burton. Department of Biophysics, University of Western Ontario, London, Ont.

In hemolysis by osmotic swelling, the critical factor might be a critical increase of volume, or a critical surface area. Mean values for suspensions of cells cannot settle which. Single red cells, in low concentration in their own plasma, were photographed on edge, in a hanging drop enclosed by oil. The tonicity of their environment was reduced by the use of micropipettes and a micromanipulator. The profile of 64 cells from 2 normal subjects and of 16 cells from a patient with spherocytosis were photographed initially and at the moment of hemolysis, detected by a sudden decrease in optical density. Hemolysis occurred after the cell reached a spherical shape. The initial and final areas and volumes were calculated, with the individual shape factor, i.e. area/volume$^{2/3}$. With decreasing shape factor, i.e. more sphericity, the area at hemolysis increased from +14% for the group of 'thin' cells to +28% for the spherocytes, while the increase of volume fell from +117% to +89%. Thus the 'thin' cells, which suffered a greater increase in volume before hemolysis, had a smaller critical area. The results are not conclusive as to whether an area or volume is critical, but would be consistent with the area being crucial, if, in addition, changes of ionic concentration affect the membrane permeability to hemoglobin.

Supported by the Life Insurance Medical Research Fund.

THE EFFECT OF THE HOMOLOGOUS SERIES OF ALCOHOL ON THE BLOOD BRAIN BARRIER. **Stanley I. Rapoport* (intr. by Wade H. Marshall). Natl. Insts. of Health, Bethesda, Md.**

Following an i.v. injection of 0.9N $NaHCO_3$, there is an acid response at the arachnoid surface of the cerebral cortex of the Nembutalized, Flaxedilized cat. It has been suggested that this follows passage of CO_2 but restriction of HCO_3^- from the CSF (cerebrospinal fluid) by the "cerebral membranes" (Gesell and Hertzman, Am. J. Physiol. 78: 610, 1926). The effect on this response of the homologous series of normal alcohols (and some isomers) was determined. A filter paper pledget, saturated with a particular alcohol, was applied for 10 minutes to a region of the arachnoid where the magnitude of the normal response had been recorded with a pH electrode. After its removal, the response was retested. Topical saline was a control. Complete reversal of the initial acid reaction was taken to mean breakdown of the bicarbonate-restricting barrier. This breakdown leads to immediate pH equilibrium between CSF under the electrode and the just-alkalinized blood. Alcohols below C=5 gave breakdown, and differed significantly ($P<.05$) from controls; alcohols above C=5 did not. Water, saturated with n-butyl alcohol, did not give breakdown. In a two phase system (alcohol/bicarbonate-restricting phase) in chemical equilibrium, the chemical activity, by the Gibb's Phase Rule, should be identical for butyl alcohol molecules in the bicarbonate-restricting phase whether aqueous-saturated or pure alcohol be applied. It follows that the pure butyl may act by solvation of the bicarbonate-restricting phase. The ineffectiveness of the relatively water insoluble higher series of alcohols suggests, however, that an aqueous or polar barrier may hinder penetration. A study of reversibility might elucidate these points. Alcohol breakdown resembles that of surface active agents but not that of metabolic inhibitors.

CARDIAC PERFORMANCE DURING EXERCISE IN DOGS WITH BANDED PULMONARY ARTERY. G. C. Rastelli,* F. J. Hallerman,* H. J. C. Swan. Mayo Clin. and Mayo Found., Rochester, Minn.

The cardiovascular response to exertion of the recently stressed right ventricle is not known. Seven dogs with induced right ventricular hypertension resulting from banding of the main pulmonary artery were studied 2 to 3 months after the operation. Exercise of graded severity was induced up to the maximal effort the dogs would perform. The right ventricular systolic pressure, which averaged 86 mm. Hg at rest, increased during the maximal exercise by an average of 90%. In one dog a peak pressure of 228 mm. Hg was reached. Frequently during exercise an alternating right ventricular pressure pulse occurred which was not accompanied by electrocardiographic changes. The right atrial systolic pressure increased from rest values of 0 to 2 mm. Hg to an average of 17 mm. Hg. The systemic arterial pressure was insignificantly affected by exercise. The average cardiac index increased by 130% compared with control values; this increase was due principally to an increase of the heart rate (100%). The stroke work increased from a rest value of 11.5 gm.M. to 23 gm.M. Total right ventricular work increased by a factor of 3.8. It is concluded that the recently hypertrophied right ventricle is capable of generating pressures and developing work levels of an order similar to that of the left ventricle. Elevated filling pressures and increased contractility contribute to the achievement of such levels of performance.

DIFFERENTIAL MEASUREMENT OF PULMONARY COMPLIANCE IN DOGS. Christen C. Rattenborg, John R. Benfield, Salvatore L. Nigro, Otto Gago and William E. Adams, (Intr. by Duncan A. Holaday). University of Chicago, Dept. of Surgery and Sec. of Anest.

The compliance of each lung was determined during artificial ventilation. A bronchial divider was placed with the aid of bronchoscopy, fluoroscopy and a "carina finder". Both lungs were inflated simultaneously with a square flow adjusted to produce the same rise in pressure on each side. The compliance (C) was determined by measuring the slope (S) of the rectilinearly rising pressure curve from the dogs. This slope was compared with a curve from a lung model (LM) with a known compliance inflated with the same flow ($\dot{V}$). $C_L=k\cdot\Delta V/\Delta P=k\cdot\dot{V}\cdot t/\Delta P=(k\cdot\dot{V})\cdot(t/\Delta P)=K/S_L$, $K=C_L\cdot S_L$, also $K=C_{LM}$ or $C_L=C_{LM}\cdot S_{LM}/S_L$. Both lungs of 3 normal dogs had a compliance of 0.045 l/cm H_2O (0.041-0.058) with the left lung representing approximately 40% of the total and the right representing about 60% of the total. The compliance of the experimental lungs is expressed as percent of the predicted value based on these control studies. The results are summarized in the table:

EXPERIMENTAL LUNG	No. of Dogs	COMPLIANCE Left	Right	l/cmH_2O Total	In % of predicted	TIDAL VOLUME normal =100%
Reinflated (L)	5	0.010	0.027	0.037	68%(54-79)	68%(59-85)
"Denervated"(R)	2	0.019	0.018	0.037	82%(79-84)	77%(76-78)
Reimplanted(R)	3	0.022	0.022	0.044	83%(79-87)	68%(50-90)

A simple method to perform comparative differential compliance measurements has been developed and applied to three groups of dogs each having one experimental lung and a contralateral normal lung. In every instance the decreased compliance of the experimental lung correlates well with bronchospirometric data. (Supported by The John A. Hartford Foundation, Inc., New York and the Burroughs Wellcome and Co. Inc.)

ALTERATION OF CAROTID SINUS BARORECEPTOR REFLEX EXCITABILITY FOLLOWING DECEREBRATION OR ELECTRICAL STIMULATION OF MESENCEPHALON AND DIENCEPHALON IN CAT. D. J. Reis* and M. Cuenod* (intr. by P. D. MacLean). Natl. Insts. of Health, Bethesda, Md.

Changes of mean BP as for example in sleep or in anticipation of exercise suggest the hypothesis that baroreceptor reflex excitability may be reset by the CNS. Experiments were performed to test this. Cats, chloralosed or decerebrated, vagotomized and with one Herring's nerve (HN) cut were used. Test stimuli were carotid occlusion (CO), or sinus stretch (SS) induced by introduction of saline under pressure into the innervated sinus. The resulting rise or drop of mean aortic BP was measured. Decerebration from anterior hypothalamus to pontomesencephalic junction resulted in a 30% fall in BP and in bradycardia. The BP rise to CO was reduced and the BP fall to SS augmented. Evidence that the reduced response to CO was due to tonic inhibition by structures below the mesencephalon was the return of the response after cerebellectomy and the reduction or absence of the usual rise of BP following section of the vagi and HN in decerebrated animals. Changes of reflex excitability also occurred with electrical stimulation of the mesencephalic reticular formation and posterior hypothalamus. Stimulation at intensities producing little or no change in mean BP were associated with augmentation of the reflex rise to CO during the stimulation and inhibition following. Long-lasting inhibition of the rise to CO was seen with slow frequency stimulation. Inhibition was abolished by Pentothal. In some animals pontomedullary section resulted in a paradoxical reflex rise to SS. It is concluded that carotid sinus reflexes are tonically and phasically influenced by supramedullary structures.

RENAL BLOOD FLOW, O_2 CONSUMPTION AND SODIUM REABSORPTION DURING O_2 BREATHING AT HIGH AMBIENT PRESSURE. D. W. Rennie and F. G. Knox*. Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N.Y.

Incidental to other studies we have observed that O_2 breathing at high ambient pressure reduces renal blood flow but not GFR. The observations provide evidence for the dependency of renal O_2 consumption ($\dot{V}_{O_2}$) upon Na reabsorption rather than renal blood flow. Dogs anesthetized with chloralose were placed on O_2 in a Navy recompression chamber. Ambient pressure could be increased to 3 atm and regulated to $\pm$ 25 mm Hg. The right renal vein and ureter were cannulated. Renal blood flow was computed from whole blood clearance of I-131 diodrast; GFR, from creatinine clearance. Arterial and renal venous P_{O_2} were measured with a polyethylene-covered, calibrated O_2 electrode placed in the chamber. Mean renal blood flow of 6 dogs decreased from 325 ml/100 g/min at 1 atm O_2 to 200 ml/100 g/min at 3 atm O_2 ($P < .01$). The mechanism is not known. However, GFR and net reabsorbed Na diminished only 10% ($P > .10$). Renal A-VO_2 difference increased from 1.9 ml/100 ml to 3.6 ml/100 ml ($P < .01$) and $\dot{V}_{O_2}$ did not change significantly. Therefore, $\dot{V}_{O_2}$ in these experiments paralleled Na reabsorption, not renal blood flow. The Na/O_2 ratio remained constant at 28 EqNa/M suprabasal O_2 consumption. (Supported by a grant from the Life Insurance Medical Research Fund.)

VENTROMEDIAL HYPOTHALAMIC LESIONS WITHOUT HYPERPHAGIA. R. W. Reynolds (intr. by O. A. Smith, Jr.) Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine, Seattle.

Radio frequency current and electrolysis were used to place ventromedial hypothalamic lesions in rats. In general the two types of lesions differed in their effects on weight gain, water intake and emotionality. Radio frequency destruction failed to produce the hypothalamic hyperphagia which follows electrolytic lesions. It is suggested that the symptoms of hyperphagia resulting from electrolytic lesions are irritant effects rather than the results of simple tissue elimination. (Supported by grants MY-4003 and 2-B5082 from the National Institutes of Health, Department of Health, Education and Welfare.)

THE RESIDUAL VOLUME OF THE LEFT VENTRICLE OF CATTLE. E. A. Rhode, J. P. Holt and H. Kines. Univ. of California, School of Veterinary Medicine and Heart Research Laboratory, Univ. of Louisville.

In awake standing cattle with catheters placed in the left ventricle and ascending aorta left ventricular end diastolic pressure (EDP), end systolic pressure (ESP), and aortic pressure were measured and end diastolic volume (EDV), end systolic volume (ESV), and stroke volume were determined by means of an electric conductivity method described earlier by one of us (J.P.H.). In some experiments a second measure of stroke volume was made from a site in the abdominal aorta. In one cow typical of the group, a 270 Kg female whose heart weight was 1210 Gm., the average of four values at the time of the original determinations were Stroke Volume 225 ml., EDV 490 ml., ESV 265 ml., Residual Fraction 54.0%, ESP 171.0 mm. Hg and heart rate 75.9 beats per minute. Four weeks later a second series of measurements were made with average values, Stroke Volume 229 ml., EDV 566 ml., ESV 337 ml., Residual Fraction 59.4%, ESP 163 mm. Hg and heart rate 95.8 beats per minute. (Supported by USPHS Grant H 5622)

EFFECT OF OPENING THE THORAX ON CARDIAC OUTPUT AND OTHER FACTORS. T. Q. Richardson,* J. D. Fermoso,* and A. C. Guyton (intr. by W. L. Williams). Dept. Physiol., Univ. Med. Center, Jackson, Miss.

The effect of opening the thorax on cardiac output, arteriovenous oxygen difference, rate of oxygen consumption, right atrial pressure, and mean arterial pressure has been determined in ten mongrel dogs. Cardiac output, arteriovenous oxygen difference, and rate of oxygen consumption were measured with a continuous cardiac recorder which has been described previously. Both right atrial pressure and mean arterial pressure were monitored with Statham strain gauges. After control cardiac output, arteriovenous oxygen difference, rate of oxygen consumption, right atrial pressure, and mean arterial pressure were determined with the thorax closed, a large incision was made in each side of the thorax at the level of the fourth intercostal space. Opening the chest caused cardiac output to fall an average of 19 per cent $\pm$ 1.07 per cent standard error of mean. The right atrial pressure rose from -0.27 mm Hg to 2.8 mm Hg when the thorax was opened, and the arteriovenous oxygen difference increased from 7.2 volumes per cent to 10 volumes per cent. There was a slight decrease in mean arterial pressure, and oxygen consumption showed little change. After collecting the data, the effect of opening the chest on cardiac output and venous return was analyzed by equating cardiac output and venous return curves. Upon equating the respective cardiac output and venous return curves for the closed and open-chest dogs, the analysis showed that the cardiac output would be expected to decrease in the manner demonstrated in these experiments. Also, the analysis showed that the basic cause of the decrease in cardiac output was a shift of the cardiac output curve to higher right atrial pressure levels, this shift resulting from the change in intrathoracic pressure.

THE TRANSFER FUNCTION OF ARTERIAL PRESSURE RECEPTORS. J. D. Ridges*, W. S. Topham*, and H. R. Warner. Biomedical Computer-Simulation Laboratory, Latter-day Saints Hospital, Salt Lake City, Utah.

Although it has been known since the work of Bronk and Stella (1932) that the frequency of action potentials on the carotid sinus nerve is determined not only by the pressure in the carotid artery but also by the rate of change of pressure, as yet no quantitative description of this relationship has been published. To describe this relationship, Warner (1958) suggested

$$\text{Equation 1} \qquad f = a\frac{dP}{dt} + b(P-P_o) \quad ,$$

where a and b are constants, P is arterial pressure, P_o is the minimum static pressure capable of exciting action potentials and f, the frequency of action potentials on the pressure-receptor afferent nerves, is limited, of course, to positive values. The present study was designed to test the validity of this model and investigate the effect of various physiological maneuvers on a, b, and P_o. Afferent action potentials from pressure receptors in the aortic arch and carotid sinus were recorded at 60 inches per second (ips) on one channel of magnetic tape and aortic or carotid arterial pressure was recorded on another channel. These signals were then reproduced at 3 3/4 ips and fed to an analog computer where the frequency of action potentials was measured and displayed continuously as an analog signal on a multichannel oscilloscope. The time-course of this measured frequency was compared to the frequency predicted by the computer from solution of Equation 1 using the recorded arterial pressure as input. This equation satisfactorily describes pressure receptor behavior and provides a useful framework upon which to express the effect of certain physiologic disturbances on these organs.

EFFECTS OF HISTAMINE AND INSULIN HYPOGLYCEMIA ON SIMULTANEOUSLY RECORDED GASTRIC MOTILITY AND ACID OUTPUT IN SPIDER MONKEYS.
P. T. Ridley* and F. P. Brooks. Department of Physiology, University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania.

Acid output and motility were measured simultaneously in 4 monkeys equipped with chronic gastric fistulae following subcutaneous histamine and intravenous insulin. Gastric contractions were measured by a balloon fixed in the pyloric antrum connected via a strain gauge to a direct writing recorder. Gastric juice was collected by dependent drainage. Animals were fasted for 18 hours, and restrained in a chair. Subcutaneous histamine injections of 0.05-0.2 mg base/kg body weight were given hourly. Motility was recorded and gastric content collected for a 4 hour period in 7 experiments. Histamine increased acid output in all experiments, but showed no significant effect on gastric motility. Insulin hypoglycemia was produced by 0.25, 0.5, and 1.0 U/kg body weight in 8 experiments. At 0.5 U/kg no significant increase in gastric secretion was found; however, a significant increase in the number of type II contractions (greater than 10 cm of H_2O pressure) was noted. At 1.0 U/kg there was a significant increase in both acid output and motility. Simultaneous recording has revealed a dissociation between secretion and motility at 0.5 U/kg of insulin. This has significance for studies on the vagal control of gastric secretion and motility. (Supported by Grant RG5007(C5) from the National Institutes of Health.)

ELASTIC PROPERTIES OF TISSUES AND AUTOREGULATION OF BLOOD FLOW. R.L. Riley, S. Permutt, and B. Bromberger-Barnea, Johns Hopkins University, Baltimore, Md.

Certain features of organ blood flow can be simulated in a simple mechanical model. Fluid flows from an "arterial" reservoir to a "venous" reservoir through an elastic "artery", a fixed resistance, and collapsible "capillaries" and "veins" which are in a rigid fluid-filled box or "tissue" compartment. The model has the following properties: 1) Perfusion does not occur unless the pressure in the "arteries" (PA) is greater than the pressure in the "veins" (PV) and "tissue" (PT). 2) When PA > PV > PT, increasing PA with PV held constant leads to a linear increase in flow ($\dot{Q}$) and a gradual increase in PT. When PT becomes $\geq$ PV, $\dot{Q}$ remains constant regardless of PA ("autoregulation"). 3) "Autoregulation" occurs at a lower $\dot{Q}$ whenever there is an increase in the fluid content of the rigid box ("extra-vascular fluid volume"), an increase in the compliance of the "arteries", or a decrease in the diameter of the "arterioles". The model was analyzed also for conditions where the "tissue" compartment had varying degrees of elasticity. A simple form of graphical analysis was developed which demonstrates that "arterial" and "venous" pressures and "arteriolar" resistance alone are not sufficient to predict $\dot{Q}$. One also must have information about the elastic properties of the "tissue" and the "arteries". It is suggested that any organ in which an increase in arterial pressure leads to an increase in tissue pressure shows the same properties as the model.

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THE RELATION BETWEEN METABOLISM, BODY TEMPERATURE AND AGE OF RATS. G. C. Ring, G. Dupuch* and D. Emeric*. University of Miami School of Medicine, Coral Gables, Florida.

The metabolism (Cal/day/kg$^{\frac{2}{3}}$) of female Fischer rats when measured monthly at an environmental temperature of 30° C decreased until they were 6 months old and, thereafter, increased. (See Weiss, A. K., Fed. Proc. 21, 219, 1962.) In the males the minimal metabolism was reached somewhat later. The body temperature measured in the colon following the metabolic determinations was found to be quite variable. It appeared to be correlated with the level of metabolism in young rats. The Q_{10}, calculated from changes in body temperature of about 1° C, was found to be 1.6 for female rats up to 15 months of age. This is lower than the figure of 2.3 calculated by Du Bois for human subjects. In older rats there appeared to be no correlation between body temperature and metabolism. The body temperature was usually found to be lower in old than in young animals.

ANTI-CONVULSIVE AND NEUROCHEMICAL EFFECTS OF AMINO-OXYACETIC ACID. P. Dante Roa*, J. K. Tews* and W. E. Stone. Depts. of Neurology and Physiology, University of Wisconsin, Madison, Wisconsin.

Amino-oxyacetic acid (AOAA), which is known to inhibit conversion of gamma-aminobutyric acid (GABA) to succinic semialdehyde, was given i.v. to dogs prepared for recording of cortical electrographic activity and for freezing of the brain *in situ*. At 20 mg./kg., AOAA had little effect on cortical activity; at higher doses there was some depression. AOAA showed an inhibitory action on seizures induced by two convulsants. Normally a dose of 20 mg./kg. thiosemicarbazide or 15 mg./kg. pentylenetetrazol induced a severe seizure; a several-fold increase in the dose of convulsant was required for this response after 20 mg./kg. AOAA. Cerebral tissue was analyzed for 22 free amino acids and related substances by ion exchange chromatography, and for ammonia, glutamine, and citrate. At various dosages and time periods AOAA induced large increases in brain GABA, ammonia, glutamine and tyrosine, small increases in alanine and lysine, and a decrease in aspartic acid. Convulsant doses of thiosemicarbazide alone induced a decrease in GABA and small increases in ammonia and alanine (observed during the seizure). With large doses of thiosemicarbazide after AOAA, the chemical pattern during the seizure was essentially the same as with AOAA alone. Hence the seizure cannot be attributed to low GABA or other observed chemical changes. Convulsant doses of pentylenetetrazol alone induced small increases in ammonia; GABA did not decrease, and other constituents measured did not change significantly. With large doses of pentylenetetrazol after AOAA, the chemical pattern during the seizure was like that with AOAA alone. (Supported by U.S.P.H.S. Grants B-3360 and NB-00818.)

LUNG VOLUME CHANGES AND RATE OF CHANGE FOLLOWING TRACHEAL OCCLUSION AS A FUNCTION OF INSPIRED OXYGEN. W. G. Robertson* and L. E. Farhi. Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N.Y.

Lung volume changes and rate of change following tracheal occlusion were studied in rats pre-breathed with one of several O_2-N_2 mixtures. (1) The total change in volume is linearly related to F_{IO_2}, but is less than the volume of O_2 present in the lungs at the time of occlusion due to the accumulation of CO_2 which reaches a partial pressure of 100 to 120 mm. (2) The rate of lung volume change is constant on 100% O_2 but when N_2 is present in the inspired gas it decreases with time. The initial rate is a function of F_{IO_2} between 0.2 and 0.5. Above this it is the same as when O_2 is breathed. Whereas when O_2 has been inspired, P_{AO_2} remains high during collapse; but when N_2 is present P_{AO_2} decreases with time, due to dilution, and limits the diffusion of O_2, hence $\dot{V}_{O_2}$. Since N_2 is not readily absorbed, it provides a remaining lung volume into which CO_2 can accumulate. (Supported by the U.S. Air Force.)

ADJUSTMENT OF MYOCARDIAL OXYGEN UPTAKE TO VENTRICULAR LOAD. Simon Rodbard. Public Health Research Institute for Chronic Disease of The State University of New York at Buffalo.

Data on 15 anesthetized dogs have shown a high correlation between myocardial tension T calculated as the product of mean arterial pressure P and the cube root of the stroke volume $V^{1/3}$, with active oxygen uptake qO_2-b/aFG in which qO_2 is oxygen uptake per minute, F is heart rate, G is heart weight, and a and b are derived constants. a is considered to be the efficiency of conversion of oxidative energy to tension while b is the noncontractile energy cost. Active oxygen uptake per beat was independent of F. The foregoing correlation suggests that the number of contractile units which shorten in a given beat is determined by the conditions of loading, rather than by the state at end-diastole. Thus, after depolarization establishes permissive conditions for contraction, a mechanical servomechanism comes into operation in which tension on the wall triggers the shortening of a contractile unit; the ventricular contents are compressed thereby, increasing wall tension slightly and triggering a second unit which produces more tension. When wall tension is sufficient to lift the load, triggering ceases and the remaining myocardial units remain uncontracted. Energy derived from oxygen uptake used in re-elongation of the shortened units is proportional to tension. This approach can account for the adjustment of power development in a given beat to the imposed mechanical load, as well as for the correlation between myocardial oxygen uptake and tension development.

THE POSSIBLE ROLE OF A LIPID ACCEPTOR PROTEIN IN LIPOPROTEIN FORMATION. Paul S. Roheim and Howard A. Eder*. Albert Einstein College of Medicine, New York, N.Y.

Our previous data indicated that perfusion of livers from cholesterol-fed rats resulted in release of lipid into a perfusate of Ringer's solution. This release was enhanced several times when normal rat plasma was the perfusate but after 100 minutes of perfusion, no further release could be observed. Changing the perfusate resulted in the same increase of lipids. It was established that the release occurred primarily into the very low density (D1.019-1.006) lipoprotein fraction. These observations suggested that there is a factor present in normal rat plasma which stimulates lipid release. Further studies showed that this factor is present in the lipoprotein free portion (D>1.21 fraction) of the rat plasma. Two possibilities were considered; (1) the D>1.21 fraction of normal rat plasma enhances lipoprotein formation either by stimulation of lipoprotein synthesis de novo, or (2) by a component protein acting as an efficient precursor for lipoprotein formation. The effect of the D>1.21 fraction on lipoprotein synthesis was studied by measuring incorporation of C^{14}labeled amino acids into the lipoproteins by the perfused rat liver. It was shown that D>1.21 does not stimulate lipoprotein synthesis de novo from amino acids. Therefore, the presence of a lipid acceptor protein (LAP) in the lipoprotein free rat plasma was postulated. Under these conditions, according to our hypothesis, LAP preferentially combines with lipid to form very low density lipoproteins. Further work is being conducted on the isolation and characterization of the LAP and it's role in physiological fat transport.

OXYGEN LACK AS A CAUSE OF POST-OCCLUSION HYPEREMIA. J. M. Ross,* H. M. Fairchild,* and A. C. Guyton. Univ. Med. Center, Jackson, Miss.

Two hypotheses have been proposed to account for the reactive hyperemia that occurs following a period of occlusion of arterial blood vessels. One is that vasodilator metabolites accumulate during the occlusion and cause dilation when the occlusion is released. The other is that lack of oxygen per se causes reduced muscle tone in the blood vessel walls, which causes an increase in blood flow upon release of the occlusion. The present experiments were designed to determine which of these theses is more likely correct. Control flow in perfused hindlimbs of four dogs was established using 100 per cent oxygen saturated blood. The arterial supply was then occluded for 5 minutes, following which the blood flow rose an average of approximately four fold and then returned to the control value within a few minutes. This same procedure was then performed again, this time allowing 0 per cent saturated blood to flow into the limb after termination of the occlusion. The blood flow, after release of the occlusion, rose again an average of about four fold but did not return toward the control level at all. Instead, it remained elevated at the maximal post-occlusion flow rate as long as the 0 per cent saturated blood was infused into the limb. These results make it unlikely that accumulation of vasodilator metabolites is the cause of the post-occlusion hyperemia, because in the second experiments they should have been at least partially washed out of the limb after release of the occlusion, and the flow should have returned at least partially toward normal. On the other hand, the results can be explained very well on the basis of the oxygen lack theory of vasodilation.

CHANGES IN EFFICIENCY AND METABOLISM OF THE MYOCARDIUM IN DOGS EXPOSED TO 25°C FOR 24 HOURS. C. Russ and J. C. Lee.* Dept. of Pharmacology, Univ. of Pittsburgh School of Medicine, Pittsburgh, Pa.

In a previous investigation we observed a decline in cardiac output in dogs as hypothermia (20°-25°C) was prolonged. The decline in cardiac output was accompanied by an increasing arteriovenous oxygen difference which appeared to be associated with an increase in plasma transaminase activity. Almost all dogs dying during the late hours (18-24) of cooling did so after cardiac output had decreased markedly. On the basis of these observations, our attention in this report is directed to changes in myocardial efficiency and metabolism in dogs exposed to prolonged cooling. Supported by AF 41(657)-417.

OXYGEN TRANSPORT DURING BREATH-HOLD DIVES TO 90 FEET. K. E. Schaefer and Charles R. Carey*. USN Medical Research Laboratory, USN Submarine Base New London, Groton, Connecticut.

The CO_2 and O_2 content (STPD) in the lungs at various depths was calculated from the measured gas tensions and volumes of mixed expired and alveolar air, the known volume of residual air and the total dry gas pressure in the lungs. The CO_2 content decreases during descent to 90 feet in a linear fashion and increases again during ascent. The O_2 content of the lungs changes stepwise. During the 15 seconds of effortless descent to 25 feet, 250 ml of O_2 are transferred from the lungs while the estimated O_2 consumption (based on resting O_2 uptake) is 59 ml during this period. No further O_2 transfer occurs during descent from 25 to 90 feet. Climbing up the line during ascent results in another decrease in O_2 content which does not cover the O_2 cost during this period. Towards the end of the dive, the O_2 transfer is reduced to minimal values. There is no indication of a reversed O_2 gradient during ascent.

INHIBITION OF SECRETIN MECHANISM WITH LOCAL ANESTHETICS, Herbert Schapiro* and E. R. Woodward. Univ. of Fla. Col. of Med., Gainesville, Florida.

Pancreatic secretin is liberated when HCl contacts upper intestinal mucosa. Cell of origin and mechanism has not been determined. Gastrin mechanism of pyloric antrum is inhibited by topical application of anesthetics, indicating importance of submucous plexus in this hormonal mechanism. Present study evaluates a possible role of intrinsic nervous tissue in secretin formation or release. Four dogs prepared with Thomas duodenal cannulas opposite major pancreatic duct and a Thiry fistula of distal duodenum. Pancreatic juice collected by cannulating pancreatic duct, while Thiry loop perfused with N/10 HCl 0.25 cc per minute for thirty minutes. Thiry loop treated with cocaine, oxethazaine, xylocaine, or pontocaine, and HCl perfusion repeated. In fourteen experiments, five per cent cocaine and two per cent oxethazaine inhibited pancreatic secretion by eighty per cent or more. Lesser concentrations were correspondingly less effective. Xylocaine and pontocaine (2%) caused thirty to sixty per cent inhibition. It is concluded that intramural nerve plexuses may play a role in secretin mechanism. This would compare with importance of submucous plexus in gastrin mechanism.

OXYGEN DEPENDENCY OF ION TRANSPORT IN ISOLATED TURTLE BLADDERS. T. P. Schilb*, W. A. Brodsky, A. K. Spafford*, D. Waller*, and A. Primack*. Dept. of Med., Univ. of Louisville School of Med., Louisville, Kentucky.

Anoxia was induced in turtle bladders immersed in Na Ringer's by gassing ambient solution with 99% N_2-1% CO_2. In four experiments, the rate of water and salt transport (from mucosa to serosa) was reduced to 1/2-3/4 that found in paired hemi-bladders gassed with 99% O_2-1% CO_2. In other tests, electrical potential (75-90 mv, serosa positive) decreased by 10-20 mv in 30 minutes, after shifting from O_2 to N_2, while electrical resistance (250-300 ohms) increased by 50-100 ohms. P. D. was sustained at 30-60 mv for over three hours under conditions of nitrogen anoxia. When bladders were interposed between choline Ringer's solutions, electrical potential reversed, serosal side becoming 20-30 mv negative to mucosal side; while electrical resistance was 600-700 ohms for each cm.^{2}, or twice that of the bladder in Na Ringer's. Transport of water and chloride in the choline system were 1/5-1/3 that of bladders in Na Ringer's. Shifting from O_2 to N_2 in choline reduced trans-bladder potential to zero. Returning from N_2 to O_2 caused a sharp increase in magnitude of potential in either Na or choline Ringer's. Transient spikes of P. D. occurred after changing gasses in Na Ringer's. In changing from O_2 to N_2, P. D. spiked in the positive direction by 10 mv preceeding the decline during the next 60 minutes; in changing from N_2 to O_2, P. D. spiked in the negative direction by 10 mv preceeding its rapid return to control levels. Data can be analyzed by assuming the existence of two ion pumps-Na^+ and Cl^- The Na^+ pump, apparent in bladders surrounded by Na Ringer's, is relatively insensitive to lack of oxygen. The Cl^- pump, apparent in choline Ringer's, is highly oxygen dependent. (Supported By Grant No. A-461, N. I. H.)

EFFECT OF PRESSOR AGENTS ON RENAL HEMODYNAMICS AND SODIUM EXCRETION IN UNANESTHETIZED DOGS. Herman E. Schmid, Jr. (Intr. by H. D. Green). Bowman Gray School of Medicine, Winston-Salem, N. C.

Angiotensin II, epinephrine and other pressor agents were infused intravenously for 2-6 hour periods into trained unanesthetized dogs. Continuous measurement of systemic blood pressure was made via femoral artery catheter. Clearance measurements of inulin, PAH, sodium and potassium were conducted using standard technics. Approximately equi-pressor infusions of angiotensin II and norepinephrine produced different effects on renal hemodynamics and sodium excretion. Angiotensin II (0.5-1.0 μgm/min) reduced glomerular filtration rate (C_{In}), markedly reduced renal plasma flow (C_{PAH}) and resulted in an elevation of filtration fraction. Sodium, and urine flow paralleled the change in glomerular filtration rate. Norepinephrine (2.0-8.0 μgm/min) usually produced no change or a slight increase in glomerular filtration rate, had a minimal effect on renal blood flow and resulted in an increased filtration fraction. Again, sodium, and urine flow appeared dependent on the glomerular filtration rate. A bradycardia associated with both drugs was more pronounced with norepinephrine. This work demonstrates that alterations in sodium and water excretion by the kidney during infusion of pressor agents can be influenced by alterations in renal hemodynamics. (Partially supported by research grant H-5948, training grant HTS-5392 from the National Heart Institute).

IMMUNOLOGIC STUDIES ON THE MECHANISM OF ACTION OF ERYTHROPOIETIN. John C. Schooley and Joseph F. Garcia.* Donner Lab., Univ. of Calif., Berkeley, California.

We have previously shown (Proc. Soc. Exp. Biol. & Med., 109:325, 1962) that serum obtained from rabbits immunized with human urinary erythropoietin neutralizes the erythropoietic activity of human urinary erythropoietin. Injections of such sera into normal mice markedly decreased their 24 hr Fe^{59} incorporation into red blood cells and their peripheral reticulocyte counts. The present experiments indicate that injections of the serum into normal mice results in an erythroid aplasia of the bone marrow. Injections of the serum into polycythemic mice 24 hr to 44 hr after initiating a wave of erythropoiesis with erythropoietin has no effect on the magnitude of the erythropoietic response, although injections one hr before or at the same time the exogenous erythropoietin was administered completely abolished the erythropoietic response. These findings support the contention that the erythroid aplasia is the result of the neutralization of the biological activity of erythropoietin as a result of an antigen-antibody reaction and not the result of a cytotoxic action of the immune serum on erythroid cells. The fact that injections of the immune serum results in an erythroid aplasia in normal mice and does not directly effect erythroid cells supports the concepts that erythropoietin is involved in the normal regulation of red cell production and that this regulation is the result of the effect of erythropoietin on the differentiation of stem cells and not on the maturation of erythroid cells.

THE EFFECT OF HELIUM AND THE RARE GASES ON CELLULAR GROWTH. H. R. Schreiner, J. A. Lawrie, and R. C. Gregoire (intr. by H. Rahn). Research Laboratory, Linde Company, Tonawanda, New York.

The gases of the helium group are characterized by complete chemical inertness, yet are capable of producing pronounced biological effects, e.g. narcosis, and are able to protect animal and plant cells against the oxygen-dependent component of radiation injury.

The growth rate of the fungus Neurospora crassa was selected as a model system for the exploration of its responses to the chemically inert components of its gaseous environment. A special incubator capable of maintaining at predetermined levels temperature, system pressure, humidity, pO_2, pCO_2 and gas circulation rate was constructed for these studies.

At one atmosphere pressure the gases of the helium group (helium, neon, argon, krypton, and xenon), in the presence of 5% oxygen, exert a systematic effect on the cellular growth of N. crassa which can be related to the molecular weight of the chemically inert gas present by the empirical equation: rate of linear hyphae growth (mm/hr) at 30°C = $3.88 - 0.1785 \sqrt{\text{molecular weight}}$. The growth response of N. crassa to a variety of gaseous environments can be predicted by this equation. Studies employing the chemically inert gas SF_6 indicate that molecular size cannot account for the observed biological effects. Evidence will be presented which is compatible with the view that states of "subcellular hypoxia" are produced when chemically unreactive gases physically displace oxygen from cellular sites for which they have a high degree of affinity.

Sulfur-Sulfur Linkage of Insulin to Muscle, Liver and Adipose Tissue. I. L. Schwartz and P. M. Edelman* Dept. Physiol., U. of Cinc. Coll. Med.

The chemical attachment of insulin to rat diaphragm muscle, liver and adipose tissue was studied with I^{131}-insulin. All tissues were shaken for 10 min. at 37°C. in 5 ml. Krebs-Ringer HCO_3^- buffer (95% O_2 - 5% CO_2, pH 7.4) containing 0.5 to 1.0 μc of I^{131}-insulin (I/insulin mole ratio = 2/1; sp. act. = 1 μc/unit) and then boiled in ethanol or water containing 10^{-3}M N-ethylmaleimide (to inhibit SH-SS interchange reactions during denaturation of the tissue proteins) and either electrodialyzed or washed repeatedly in 0.15M NaCl, 0.15M Na acetate buffer (pH 4) and 8 M urea (to remove adsorbed and otherwise electrovalently-bonded radioactivity). Thereafter additional radioactivity was released on exposing the tissues to mild conditions which split SS bonds but do not hydrolyze peptide bonds (0.1 M cysteine, pH 8; 0.05 M sulfite in 6 M urea, pH 7; 0.05 M sulfite in sat. phenyl mercuric hydroxide, pH 9). Aliquots of I^{131} insulin were resolved into A and B chains by 3 methods (Biochem. J. 76, 146, 1960; Biochem. Preps. 8, 70, 1960; JACS 77, 4927, 1955). It was found that the SS bound radioactivity which was released from the labeled tissues exceeded that which could have been obtained by complete cleavage of the phenylalanine chain from its linkage to the A chain in the intact hormone molecule, and/or from direct SS linkage to tissue. In the case of liver, similar evidence for SS bonding of hormone to tissue was obtained only in an experiment involving hepatic tissue obtained from an animal which had been fasted for 24 hours. These findings indicate that (1) a covalent (SS) bond is involved in the attachment of insulin to target tissues, and (2) that this attachment involves the A chain cyclic disulfide or both interchain disulfides, the latter alternative implying an initial cleavage of the hormone molecule followed by SS bonding of the A and B chains to separate tissue sites.

THE ROLE OF TRANSMURAL PRESSURE IN REACTIVE HYPEREMIA. J. B. Scott* and F. J. Haddy. University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

The most likely causes of vasodilation during arterial occlusion are accumulation of vasodilating metabolites, reduction of oxygen tension, and fall of transmural pressure. In this study, the possible role of transmural pressure was investigated by comparing pre- and post-occlusion resistances when intraluminal pressure during occlusion was a)allowed to fall and b) held near the pre-occlusion level. In 26 dog forelimbs, the brachial artery, brachial vein, cephalic vein, and nerve supply were isolated. All other structures were included in an arterial tourniquet. The brachial artery was perfused with 76 ml. arterial blood per minute while measuring perfusion pressure. Pressures before, during, and immediately following interruption of flow for 20 seconds (n=10) were 115,37, and 96 mm. Hg, for 30 seconds (n=27) were 124,27, and 97 mm. Hg, and for 60 seconds (n=4) were 141,41, and 114 mm. Hg. Corresponding pressures when the limb was packed with blood by occluding the veins shortly before interrupting arterial inflow for 20 seconds (n=10) were 115,67, and 125 mm. Hg, for 30 seconds (n=36) were 129,59, and 138 mm. Hg, and for 60 seconds (n=4) were 140,70, and 152 mm. Hg. The results were essentially the same in the acutely denervated limb. These studies show that in this preparation the post-occlusion resistance decrease is abolished when the bed is kept filled during occlusion and suggest that reactive hyperemia following short-lived occlusion results largely from myogenic relaxation subsequent to fall in transmural pressure.

ATRIAL CONTRIBUTION TO STROKE VOLUME IN DOGS WITH CHRONIC CARDIAC DENERVATION. F. J. Sellers*, D. E. Donald and E. H. Wood, Mayo Foundation, Rochester, Minnesota.

The relatively small changes in stroke volume and atrial pressures associated with the change from effective atrial systole to ineffective systole observed in closed-chest dogs with chronic heart block may be due to the damping effects of neural cardio-regulatory mechanisms. Dogs whose hearts were denervated several weeks previously by the technic of Gilbert and colleagues were studied under morphine-pentobarbital anesthesia without thoracotomy. Two electronically coupled pacemakers connected to electrode catheters were used to stimulate the atria and ventricles either simultaneously (ineffective atrial systole) or in normal sequence with an A-V delay of 0.06 to 0.1 second. Observations were made at stimulated rates of 120 to 200 beats/minute, which exceeded the stable spontaneous rate of 110-120 beats/minute of the denervated heart. Stimulation of the atria only at these rates was followed by normally conducted ventricular contractions. A striking inversion of the T wave closely similar to that seen with simultaneous A-V stimulation served as an index of effective electrical stimulation of the ventricles. Cardiac output was determined by dye dilution. The change from effective to ineffective atrial systole caused a decrease in cardiac output of about 15 per cent. This effect was similar over the heart range of 120 to 180 beats/minute. The associated increase in mean right atrial pressure of approximately 1.5 cm. of H_2O at 120 was somewhat greater at the higher rates. Spontaneous and electrically driven atrial contractions were equally effective. Conducted ventricular contractions appeared somewhat more effective than electrically driven contraction, however, the effect of unavoidable differences in A-V interval in the two circumstances could not be adequately controlled.

TOTAL RESPIRATORY INERTANCE IN NORMAL AND OBESE PERSONS
J.T.Sharp, S.K.Sweany*, J.P.Henry*, R.J.Pietras*, and W.R.Meadows*. Hines VA Hospital, Hines, Illinois.

Total respiratory inertance was estimated in eight normal and twelve excessively obese subjects including four patients with the obesity-hypoventilation (O.H.) syndrome. Inertance was calculated using the physical formula relating natural frequency, compliance and inertance and assuming a "lumped" physical system. Total respiratory compliance was measured by the mid-position shift method of Heaf and Prime and the natural frequency by Mead's modification of the oscillatory method of Dubois et al. The mean inertance value in normals was 0.0046 ± 0.0006 (S.E.) cm. $H_2O/L/sec^2$, a value reasonably close to that of Dubois et al. of 0.0058 cm. $H_2O/L/sec^2$. The natural frequency in our normals averaged 7.5 ± 0.3 c.p.s. The obese normals had an average inertance of 0.0130 ± 0.0017 cm. $H_2O/L/sec^2$ and a natural frequency of 5.3 ± 0.1 c.p.s. The O.H. patients had an average inertance of 0.0172 ± 0.0020 cm. $H_2O/L/sec^2$ and a mean natural frequency of 6.0 ± 0.4 c.p.s. Differences in inertance and natural frequency between normals and both obese groups were significant ($p<.001$). Total inertance correlated well with body weight ($r=+0.79$). Since lung and airway gas volumes were less in the obese than in the normal subjects, their increased inertance must represent added inertance of the thorax and abdomen rather than increased lung (gas) inertance. Accelerations encountered during maximal breathing capacity maneuvers (approximately 500 L/sec^2) required acceleration pressures of 2.3 cm. H_2O in normals and 8.0 cm. H_2O in obese subjects. These are small compared to pressure components required to overcome elastic and frictional resistances during comparable respiratory maneuvers.

GLUCOSE AND FRUCTOSE ABSORPTION IN THE UNANESTHETIZED DOG. William C. Shoemaker, Howard M. Yanof*, L. Newton Turk* and T. Hastings Wilson. Dept. of Surgical Research, Michael Reese Hosp. and Med. Ctr. Chicago, and Dept. of Physiology, Harvard Medical School. Boston.

Dogs were prepared with catheters in the portal vein, hepatic vein and splenic artery and allowed to recover from the operation for 3-6 days. Glucose, lactic acid and ketose concentrations were measured in arterial, portal and hepatic venous blood in a control period and at intervals after oral feeding of 50 gm of glucose or fructose. Hepatic and splanchnic blood flow was measured by a modified bromsulphalein method and by a trapezoidal wave electromagnetic blood flowmeter. The rate of hepatic and nonhepatic splanchnic outputs or uptakes were calculated by multiplying the concentration difference by the concomitent flow value. Following ingestion of 50 gm of glucose or fructose the portal vein plasma glucose concentration, portal venous-arterial concentration differences, and the rate of glucose output from the gut, rose rapidly and remained high for about 1 hr. Estimation of absorption indicated 84% of the glucose was recovered as nonhepatic splanchnic glucose output. With glucose absorption there was an increased rate of lactic and production by the gut and a decreased rate of clearance by the liver. After fructose feeding 42% of the carbohydrate was absorbed by the gut and released into the circulating plasma appeared as ketose while the remainder was absorbed as glucose.

ONTOGENETIC STUDIES OF SOME EVOKED RESPONSES OF CEREBELLAR CORTEX. R. J. Shofer* and D. P. Purpura, Columbia U., N. Y.

Local surface responses to stimulation of cerebellar cortex prior to the 2nd postnatal week (p. n. w.) in kittens consist in brief diphasic spikes succeeded by variable duration (20-60 msec) surface-positivities. By the 3rd-5th p. n. w. 10-20 msec negativities develop immediately after spike-like components but these negativities are 'swamped' by surface-positivity elicited with strong stimulation. The surface-negativities evoked in this period rapidly attenuate during low-frequency (5-10/sec) surface-folial stimulation. Superficial negative responses of cerebellar cortex (SCbR) evoked in adult cats are obtained after the 5th-7th wk. Then such SCbR's augment during repetitive stimulation and succeeding surface-positivities are rarely observed. Surface-positive afferent responses of cerebellar cortex undergo progressive decreases in latency and increases in amplitude during postnatal development. The ontogenetic changes in cerebellar responses to surface stimulation appear to be related to two features of the postnatal morphogenesis of cerebellar cortex; progressive "disappearance" of elements constituting the external granular layer and invasion of the molecular layer by Purkinje cell dendrites. The development of the SCbR is referable to synaptic activation of Purkinje cell dendrites which have attained superficial zones of the molecular layer whereas the surface-positivities elicited in young kittens ($<$ 3 weeks old) reflect activity of elements below the external granular layer. Sub-surface synaptic pathways involved in afferent responses of cerebellar cortex are relatively well developed at birth in the kitten.

THE ANALYSIS OF CUTANEOUS SENSIBILITY WITH AN ANALOG CROSS-CORRELATOR. R. Siminoff, J.U. Casby and T.R. Houseknecht (intr. by G. Ling). Woman's Med. Coll. and East. Penna. Psychiatric Inst., Phila.

Activity was recorded from an intact cutaneous branch of the tibial nerve in response to "natural" stimuli which were defined as; "hair"- stroking only the hairs with a wisp of cotton, "touch"- actual stroking of the skin with a stiff brush, and "pressure"- application of a steady pressure to the skin. "Pain" was defined as either pin prick, clamping the skin with a hemostat or burning. "Touch" was the most effective stimulus for activating "A" fibers. With "hair" stimulus only fast adaptation was seen but with "pressure" a fast adapting component showing the typical on-off response was seen as well as a slow adapting component. "Pain" was the most effective stimulus for activating "C" fibers although there was a "C" fiber group responding to the three mechanical stimuli. "C" fibers showed the properties of fatigue and after-discharge. The response as recorded on the peripheral nerve to any given "natural" stimulus was three peaks corresponding to the alpha, delta and C groups and furthermore there was no overlapping of the three peaks. Therefor the data presented by the cross-correlation technique was compatable with present day knowledge of peripheral nerve physiology and the analog cross-correlator has been shown to be a valuable tool in the analysis of peripheral nerve activity in response to physiological stimuli.

A CARDIOVASCULAR DEPRESSOR REFLEX FROM THE EPICARDIUM OF THE DOG. Peter Sleight (intr. by J. H. Comroe, Jr.). Cardiovascular Research Inst., Univ. of Calif. Sch. of Med., San Francisco.

Thirty-two anesthetized open-chest dogs and 3 intact conscious dogs with implanted pericardial catheters were studied. The coronary chemoreflex initiated by left atrial or left coronary injections of veratridine or nicotine was abolished on its afferent side by application of 2 ml of 0.1% procaine to the epicardium of the ventricles for 45 sec, but not by 2 ml of 1.0% procaine intravenously. Intrapericardial injections of 5-10 μg of veratridine caused hypotension and bradycardia in all of 10 animals. In 27 of 29 dogs, 7-33 μg of nicotine (1/60,000) applied to the ventricular epicardium produced similar reflex hypotension and bradycardia, which was abolished by epicardial procaine or vagotomy. One cm^2 of nicotine-soaked filter paper (2-3 μg nicotine) applied to the left ventricle elicited the reflex in 6 of 8 dogs. The response from areas rich in large coronary vessels was no greater than from epicardium overlying muscle. No response could be obtained from nicotine placed on the right ventricle. No reflex effects resulted from applying nicotine to the parietal pericardium or by stretching it. In the conscious animals 7 μg of nicotine intrapericardially led to pronounced depressor effects with no respiratory effects or obvious distress. None of these reflex effects influenced pulmonary artery pressure except by an increase in pulse pressure resulting from bradycardia. These results suggest that the receptors for the coronary chemoreflex are located largely in the epicardium of the left ventricle. (Supported by a Wellcome Foundation Travel Fellowship, a San Francisco Heart Association Junior Research Fellowship and USPHS Grants H-6285 and HTS-5251.)

The Effect of Serotonin and Histamine on Gastric Blood Flow
H. Sosin, M. D. *, E. F. Bernstein, M. D. *, E. T. Peter, M. D. * and O. H. Wangensteen, M. D. Department of Surgery, University of Minn. Minneapolis, Minnesota

Serotonin has previously been shown to enhance histamine stimulated gastric secretion of HCl from canine Heidenhain pouches, while no secretion was observed with serotonin administration alone. Serotonin increased gastric blood flow by 67%. In these experiments gastric blood flow was measured during administration of histamine alone, histamine plus several dosages of serotonin, and serotonin alone to determine whether serotonin affects gastric blood flow in the presence of histamine. The origin of the left gastric artery was exposed in 12 adult mongrel dogs via a left subcostal approach. Left gastric artery flows were measured with a Medicon FM-6 gated sine wave electromagnetic flowmeter. Central aortic pressure was monitored with a Sanborn 267B strain gauge. Both were recorded on a Sanborn 150 Polyviso recorder. Stable control flows were established for at least 30 minutes. Histamine 4 μ/min., histamine 4 μ/min. plus serotonin in doses of 10, 20, 40 and 60 μ/kg/min., and serotonin alone in doses of 20 and 40 μ/kg/min. were administered intravenously. Flows, expressed as mean % change of control were: histamine 4 μ/min. +9%, histamine 4 μ/min. plus serotonin 10 μ/kg/min. → +25. 6%, histamine 4 μ/min. plus serotonin 20 μ/kg/min. → +43%, histamine 4 μ/min. plus serotonin 40 μ/min. → +87%, histamine 4 μ/min. plus serotonin 60 μ/kg/min. → 189%. Results indicate a directly proportional relationship between left gastric artery flow and increasing doses of serotonin in the presence of histamine.

RELATIVE RESPONSIVENESS TO ANGIOTENSIN OF ISOLATED SMOOTH MUSCLE OF ARTERIES AND VEINS. H. Sparks, Jr.* and D. F. Bohr. Dept. of Physiol., Univ. of Mich., Ann Arbor.

This investigation confirms and quantifies previous in vivo evidence of a differential effect of angiotensin on arteries and on veins (Folkow, B., B. Johansson and S. Mellander. Acta Physiol. Scand. 53: 99, 1961). In view of this evidence, and because of the current use of angiotensin and steroids in the treatment of shock, the effect of desoxycorticosterone (DOC) on the contractile response of normal isolated vascular smooth muscle to angiotensin was explored. Helical strips were cut from radicles of dog superior mesenteric artery (1 mm outside diameter) and their companion veins, and suspended in a common bath of bicarbonate Krebs solution at 37° C. Arteries and veins stimulated with synthetic val-5-angiotensin II showed different dose response curves; the threshold concentration for response for the vein was at least 100 x that for the artery. Thresholds for norepinephrine were similar in artery and vein. It has been observed that DOC potentiates the response of aorta to catecholamines and in this study this has been confirmed with small vessels. However, DOC introduced into the bath before angiotensin stimulation did not cause the vein to act more like the artery and did not protect either the vein or the artery from tachyphylaxis to angiotensin. This study indicates that angiotensin, even with steroids, is a poor drug for increasing venous tone and thus decreasing the pooling of blood in the venous system. Perhaps the beneficial effect of steroids in conjunction with angiotensin is due to the potentiating effect of steroids on the vascular response to endogenous catecholamines. (Supported by a grant from the American Heart Association.)

IN VITRO INTESTINAL TRANSPORT OF IMINO ACIDS. Richard P. Spencer, Ted M. Bow,* Mary Anne Markulis,* Kenneth R. Brody,* Department of Biophysics, Univ. Buffalo, and Radioisotope Service, V.A. Hospital.

Imino acid and amino acid transport by everted hamster intestinal sacs have been compared with respect to site of transport, mutual interference, temperature coefficient, response to low Na medium, effect of NaCN, $CH_3.CH_2.CN$ and ascorbic acid. Responses of the two classes of compounds are practically identical. Imino acids of the non-ring form $X.NH.CH_2.COOH$ are transported against a concentration gradient if X = H or CH_3, but not C_6H_5, $CH_2.COOH$ or $NH_2.C{=}NH$. Ring type imino acids with the formulation $(CH_2)n.NH.CH.COOH$ (n=1,2,3,4) are being investigated; transport definitely occurs when n=3 or 4. Studies of L-proline analogues showed that: 4 OH- and 4 ring -S- both transported; 5 C_6H_5- not transported; 5 CH_3- and 5 O=, if they are transported are below the 2% level; 4,5-dimethyl not transported. The 5 position is thus a key point in proline transfer. When coupled with the transport of the non-planar 4-OH-proline, this allows an estimate of the minimal channel size for imino acid transport. The effect of unsaturation on the transport of imino acids and their analogues was investigated; 3,4-dehydroproline underwent accumulative transport, as did allylglycine. There was also transport of imidazole-5-carboxylic acid. No transport was found for the following: pyrrole-2-carboxylic acid, 3,5-dimethyl-4-acetyl-pyrrole-2-carboxylic acid, orotic acid, picolinic acid, pyrimidine-4-carboxylic acid, and indole-2-carboxylic acid. These results must be analyzed in terms of the spatial conformation of the molecules and the pK values of the substituents. (Supported by Grant A-4887 (C1) from the U.S. Public Health Service).

FURTHER OBSERVATIONS ON PCO_2, pH, AND THYROID BINDING. Myron Stein, Milton W. Hamolsky,* and A. Stone Freedberg. Dept. of Med., Beth Israel Hosp. and Harvard Med. Sch., Boston, Mass.

Studies performed in our laboratory have suggested that PCO_2 and pH are important factors in controlling the distribution of thyroid hormone between specific plasma binding proteins and peripheral tissues. In 30 patients with elevated PCO_2, in vitro uptake of I-131 triiodothyronine (T_3) by their own erythrocytes was elevated to hyperthyroid levels returning to normal when hypercapnia could be normalized. Matching hypercapneic plasma to eucapneic red cells resulted in elevated erythrocyte uptakes; eucapneic plasma to hypercapneic cells in normal uptakes. The in vivo turnover of infused I-131 thyroxine (T_4) was similarly increased in 8 of these hypercapneic subjects. The production of myxedema in one hypercapneic subject resulted in erythrocyte uptakes that were elevated for the severity of myxedema but decreased in relation to the severity of hypercapnia. Short term in vivo alterations of blood pH and PCO_2 in dogs caused striking changes in T_4 and T_3 plasma binding. Respiratory or metabolic alkalosis produced decreased erythrocyte uptake of I-131 T_3 as well as decreased turnover of infused I-131 T_4. Respiratory and metabolic acidosis increased both the erythrocyte uptake and I-131 T_4 disappearance. The effects in the dog appeared to be related to pH alone as CO_2 retention with maintenance of normal pH did not produce changes in erythrocyte uptake or I-131 turnover.

(Supported by PHS grants A-140 and OH-39).

CONTRACTILITY OF IN SITU GENETIC DYSTROPHIC MOUSE MUSCLE. Sheldon A. Steinberg (intr. by S.Y. Botelho). Graduate School of Medicine, U. of Pa., Phila., Pa.

Studies of contractility of in vitro genetic dystrophic mouse muscle and in situ human dystrophic muscle (pseudohypertrophic muscular dystrophy) show certain differences. In order to determine if technical factors alone could be responsible for the reported differences in contractility, we performed studies upon in situ genetic dystrophic mouse muscle as follows: Normal and dystrophic mice, 2-4 months of age, were anesthetized with nembutal. Isometric tension and electrical activity of the Triceps Surae muscle, evoked by stimulation of the transected Sciatic nerve, were recorded. As in the previously reported in vitro studies, the results indicate that the in situ dystrophic muscle: 1. develops less single twitch and tetanus tension than normal, 2. is stiffer than normal and 3. has a longer than normal single twitch relaxation period (dys. 25.3-98.3 msec; norm. 13.2-42.1 msec). With repetitive activity (6/sec/2sec and 60/sec/1sec) the relaxation period is shortened. The active tension-length curves are uniformly flattened in the dystrophic mice. It is apparent from the data reported here and by others, that both in vitro and in situ genetic dystrophic mouse muscle differ from in situ muscle of patients with pseudohypertrophic muscle dystrophy with respect to stiffness and the effects of repetitive activity.

THE BASAL FOREBRAIN SYNCHRONIZING SYSTEM IN THE CAT. M. B. Sterman*, W. Wyrwicka* and C.D. Clemente. Departments of Anatomy and Psychology, UCLA Medical Center and Veterans Administration Hospital, Sepulveda, California.

Electrical stimulation of a discrete basal forebrain area in the cat results in the sudden onset of EEG synchronization in both acute, immobilized and chronic unrestrained preparations. In the latter, synchronization is accompanied by the effective induction of behavioral sleep. Recent electrophysiological studies have indicated that the intralaminar nuclei of the thalamus and the structures of the limbic system are directly related to this basal forebrain area, and involved in the mediation of its influence. Very low voltage stimulation exerts a tonic synchronogenic influence upon the intralaminar system of the thalamus, which appears in relation to the diffuse and rhythmic aspects of the induced EEG response. Higher voltages (2-3 volts), additionally, will evoke activity in limbic structures, accompanied by potential and EEG synchronization and by conspicuous somatic autonomic effects. Behavioral conditioning experiments have demonstrated that a neutral sensory stimulus can induce EEG synchronization and sleep preparatory behavior when paired with basal forebrain stimulation. The facility with which conditioning is achieved indicates important functional interaction between the basal forebrain synchronizing system and the cerebral cortex. These findings suggest that mechanisms involving basal forebrain, thalamic, and limbic structures may be responsible for active behavioral inhibition, in contrast to generalized excitation associated with the reticular activating system of the brain stem.

THERMOREGULATORY RESPONSES IN MAN FOLLOWING SUDDEN CHANGES IN ENVIRONMENTAL TEMPERATURE. J.A.J. Stolwijk*, J. D. Hardy and R. O. Rawson. J. B. Pierce Foundation Laboratory and Department of Physiology, Yale University, New Haven, Connecticut.

Thermoregulatory responses in human subjects in the resting state were studied before and for two hours after a sudden transfer from neutral or cool environments to warm or hot environments. Transfers were made from 20°C and 28°C to 33°, 38°, 43°, and 48°C. Continuous records were obtained of metabolism measured as 0_2 consumption, evaporative heat loss measured as continuously recorded weight change, and average skin temperature, rectal temperature and tympanic membrane temperature. All data were obtained with a time resolution of better than five minutes. Upon transfer from 28°C to a warm environment sweating, measured as an increase in the rate of weight loss, started within 20 minutes, with an increase in the heat conductance of the body occurring even earlier. Under these conditions such responses occur before the rectal temperature or the tympanic membrane temperature show any measurable deviation.

CHEMICAL CHANGES IN THE BRAIN DURING INSULIN HYPOGLYCEMIA AND RECOVERY. W. E. Stone, J. K. Tews* and S. H. Carter*. Dept. of Physiology, University of Wisconsin, Madison, Wisconsin.

Chemical changes in the brain have been studied by the technique of liquid air fixation in situ (dogs). Cerebral constituents measured included 22 free amino acids and related substances by ion exchange chromatography, and ammonia, glutamine, citrate, malate, lactate, acid-soluble phosphates, acetylcholine, glycogen and true glucose. After insulin injection, cortical electrographic records showed remarkably little change during the initial 2-hour period of rapid fall in blood sugar. Subsequently the activity became progressively depressed while blood sugar was dropping only slightly. In deep "shock" the cortex was nearly isoelectric. Only one convulsion was observed; in this instance clonic jerking movements of the body were associated with groups of 3 to 5 large spikes in the cortex. In profound hypoglycemia, brain glucose was reduced to 0.4 to 4 mg. per 100 g. Glycogen, lactate and citrate decreased. Ammonia showed a great increase; this change may play a role in the development of "shock" and convulsions. Aspartic acid and lysine increased, while alanine, gamma-aminobutyric acid, glutamic acid and glutamine decreased. Creatine phosphate decreased and nucleoside triphosphates showed partial conversion to diphosphates, with release of inorganic phosphate. Acetylcholine tended to decrease, but was inconsistent. During recovery (11 to 60 min. after glucose injection) some of these changes were reversed (glucose, citrate, ammonia, glutamic acid and phosphates), some even going past the normal levels to opposite abnormal levels (lactate, aspartic acid, alanine, gamma-aminobutyric acid and acetylcholine). Others showed no recovery (glycogen and glutamine); lysine showed a further increase, and leucine also increased. (Supported by U.S.P.H.S. Grant No. NB-00818.)

A FUNCTIONAL ANALYSIS OF LARYNGEAL AND PHARYNGEAL SENSORY UNITS IN THE CAT. Arthur T. Storey. (intr. by L. T. Rutledge). Dept. of Physiol., University of Michigan, Ann Arbor, Mich.

In decerebrate cats unit discharges to peripheral stimulation were studied in strands of the distal end of the cut superior laryngeal nerve. Receptors were identified as tactile, pressure, water, and proprioceptive. Many mechano-receptors responded to more than one stimulus. Some discharged readily to cold, .5 M saline or 25% ethanol. A distinction could usually be made between pressure and proprioceptive receptors, the former showing increased firing to cold and 25% ethanol and often giving an "off" discharge. The latter frequently slowed to a cold stimulus, evidenced no adaptation and no "off" discharge. The time course of adaptation was not the same for all units. Tactile receptors adapted depending upon the stimulus cendi-tions. A light touch with one or two hairs within the unit's receptive field could elicit a discharge of 300 per sec. with no after discharge whereas at discrete points in the same field a tactile stimulus elicited the high frequency discharge followed by a slowly adapting after discharge. Water receptors were of two types. About half discharged only to moving water and the rest fired also to tactile stimulation. The multimodality laryngeal and pharyngeal receptors are in contrast to receptors in cutaneous areas but are similar in some respects to those found in the oral cavity.

ORGANIZATION OF REFLEX PATHWAYS FROM SEMI-CIRCULAR CANALS TO EXTRA-OCULAR MUSCLES. J. Suzuki and B. Cohen. (Intr. by S. Shanzer). Neuro. Dept., Mt. Sinai Hosp., N.Y.

By stimulating vestibular nerve branches to semi-circular canals with pulse trains, synaptically linked eye muscles were activated. Anterior canal stimulation excites ipsilat. superior rectus and contralat. inferior oblique. Smaller potentials occur in contralat. sup. rectus, a 'co-working' muscle. Lateral canal stimulation activates ipsilat.medial rectus and contralat. lat.rectus. Post.canal stimulation activates ipsilat.sup.oblique and contralat.inf.rectus with ipsilat.inf.rectus a 'co-working' muscle.Simultaneous bilateral ant. canal stimulation produces conjugate upward and bilat. post. canal stimulation conjugate downward movements. Simultaneous stimulation of both lat.canals or one ant. and contralat. post. canal causes inhibition of extra-ocular muscle potentials and no eye movement. Thus, inhibition of antagonists accompanies excitation and predominates when muscles are both excited and inhibited. Stimulating ant. and post. canals on one side causes conjugate rotatory movements and sup. and inf. rectus potentials are blocked. Stimulation of one lat. and either ipsilat. or contralat. ant. or post. canal produces oblique movements in one eye and rotatory oblique movements in the other. The degree of obliqueness is controlled by varying the strength of the lat. or vertical canal stimulus. These data indicate that ampullary nerves function independently to produce particular eye movements. When stimulated simultaneously, the resultant eye movement is a summation of their vectors.
Supported by USPHS Grant B-294.

THE ROLE OF THE LIVER IN RENAL HYPERTENSION. Richard D. Sweeney Gordon N. French, Ward D. O'Sullivan (intr. by William C. Foster) Misericordia Hospital, Philadelphia, Penna.

Pressor substances have been demonstrated in the renal venous blood with renal hypertension but these are almost absent by the time the blood is in the peripheral veins. The portacaval transposition is a common experimental procedure to spare gastrointestinal hormones from deactivation by the liver. This study attempts to evaluate the liver's capacity to deactivate the renal pressor substances by using the portacaval transposition to pass the renal venous blood through the liver after having previously produced renal hypertension by renal artery stenosis. Some animals have shown an impressive remission of their renal hypertension following a portacaval transposition with ligation of the inferior vena cava below the renal veins. One animal underwent a subsequent correction of its transposition and promptly developed its hypertension again.

EARLY METABOLIC EFFECTS OF GROWTH HORMONE IN HYPOPHYSECTOMIZED AND HOUSSAY RATS. Norbert I. Swislocki* and Clara M. Szego, Department of Zoology, University of California, Los Angeles.

Male S.-D. rats, 150-170 gms, were maintained on a tube-fed diet for 6-8 days following hypophysectomy. At 24 hrs after the last feeding, an I.P. injection of 3 mg bovine growth hormone (GH; NIH-916) was given. Controls received saline. Observations were made through a 6 hour period. At 30 and 60 minutes after GH, the following were statistically significant: Plasma non-esterified fatty acids (NEFA) fell from 350 ± 22 μeq/l (S.E.) at 0- time to 197 ± 44, $P < 0.01$ at 30 min and 224 ± 20, $P < 0.01$ at 60 min; blood amino acid nitrogen (BAN) dropped from 12.1 ± 0.33 mg % to 10.6 ± 0.49, $P < 0.05$ (marginal) at 30 min and 10.0 ± 0.32, $P < 0.001$ at 60 min; blood sugar (BS) decreased from 93 ± 5.5 mg % to 57 ± 9.5, $P < 0.01$ at 60 min. The expected elevation of NEFA frequently reported by others, was also found in the present study at 4-6 hrs. Partial (95%) pancreatectomy, which rendered the rats mildly diabetic (fed BS 284 mg % ave., range 159-477) was performed 3-5 days prior to hypophysectomy. This failed to interfere with the metabolic responses measured at 60 min after GH: Plasma NEFA diminished from 286 ± 29 μeq/l to 216 ± 9, $P < 0.05$ (however, $P < 0.001$ w.r. to 60 min saline pancreatectomized control of 343 ± 12); BAN from 14.7 ± 0.70 mg % to 11.1 ± 0.82, $P < 0.01$; and BS 97 ± 3.4 mg % to 60.0 ± 2.5, $P < 0.001$. These data indicate that the effect of GH in promoting fatty acid mobilization from adipose tissue, as seen by increased circulating NEFA levels 4-6 hours after treatment, appears to be secondary to the reduction of these values induced by the hormone at 30-60 minutes. They also suggest that these actions of GH do not require the presence of an intact pancreas. Aided by USPHS predoctoral fellowship GF-9912-C2, by grant CY-1488 from the N.I.H. and by Cancer Research Funds of the University of California.

DEPLETION OF ACETYLCHOLINE FROM MUSCLES TREATED WITH HC-3. R. E. Thies. Dept. of Physiology, Washington Univ. School of Med., St. Louis, Mo.

In cats HC-3 inhibits acetylcholine (ACh) synthesis and thereby blocks synaptic transmission presynaptically; yet in guinea pigs its curare-like action can cause postsynaptic neuromuscular (n-m) block. If HC-3 inhibits ACh synthesis in guinea pigs, then prolonged indirect stimulation after treatment with HC-3 should reduce ACh content. Anesthetized guinea pigs and cats were injected with HC-3, which caused n-m block. Left serratus muscles were stimulated at 20/sec for 32-37 min; right serratus muscles were unstimulated. Muscle pairs were rapidly excised and extracted for ACh content. Extracts were purified on ion exchange resin columns and assayed by their depression of the rat's blood pressure. About two-thirds of standard ACh solutions were recovered after such purification. Any depressor activity remaining after responses to ACh were blocked by atropine was subtracted from initial activity; such residual activity was largely due to histamine.

ACh Content of Muscles after Neuromuscular Block by HC-3

Species:	Expt:	Assayed ACh Content: (ng/g) [unstimulated]	[stimulated]	Depletion [u-s/u] by HC-3 plus Stimulation: (%)
Cat	1	16	4	75
	3	31	7	77
	4	26	5	81
Guinea	2	27	23	15
pig	5	34	22	35
	6	21	13	38

ACh depletion after stimulation without HC-3 has not been tested; MacIntosh found it to be about 25% in cat muscles. The small depletion of ACh from HC-3 treated guinea pig muscles supports previous experiments that did not show a presynaptic action of HC-3 at g. pig n-m junctions. (partial support: Muscular Dystrophy Assoc. & Myasthenia Gravis Found.)

THE INFLUENCE OF INTRALUMINAL PRESSURE ON MEMBRANE POTENTIAL AND NET WATER MOVEMENT IN ISOLATED CANINE ILEAL LOOPS IN SITU.

C. S. Tidball and J. K. Lawrence*. Physiology Department, The George Washington University, Washington, D. C.

A balanced physiologic saline was perfused through the lumen of ileal loops in the anesthetized dog at a rate of 2 ml/min. When there was no restriction to outflow from the lumen, the intraluminal pressure ranged from -3 to 16 mm Hg. Under these conditions the initial membrane potentials were within a few millivolts of zero and varied little from animal to animal. However the initial net water movements varied considerably and were not correlated with either the membrane potential or the intraluminal pressure. In subsequent 20 min periods absorption decreased spontaneously while no significant change in membrane potential was observed. The tendency for the water movement to shift from absorption to secretion with time was eliminated in some experiments and reduced in others by bilateral cervical vagotomy which did not alter the membrane potential and only decreased absorption to a small extent. In these animals adjusting intraluminal pressure to 10 mm Hg by restricting perfusion outflow brought about increased absorption and made the membrane potential more negative. When intraluminal pressure was increased above 15 mm Hg the membrane potential became increasingly negative but absorption fell to levels below those under conditions of minimal pressure. Therefore in the vagotomized, anesthetized dog increases in intraluminal pressure from 10 to 40 mm Hg produce concomitant increases in negative membrane potential, whereas pressure induced increases in absorption are restricted to the range below 15 mm Hg.

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EFFECTS OF TEMPERATURE ON THE ISOMETRIC CONTRACTION OF RAT MUSCLE.

X. T. Truong,* B. J. Wall,* and S. M. Walker. Dept. of Physiology, Univ. of Louisville School of Med., Louisville, Ky.

The effects of temperature on the isometric tension of tetanus, the frequency of stimulation required for complete tetanus, and the rate of tetanic tension development and relaxation were studied in the rat triceps surae. Male albino rats were anesthetized with sodium barbital and the triceps surae mounted with circulation intact, in a torsion-rod isometric myograph. The muscle was stimulated both through the sciatic nerve and directly with rectangular pulses of 0.25 msec at frequencies of 1, 30, 60, 120, 200, and 250 cps. For each of these frequencies of stimulation, isometric mechanomyograms were obtained at different muscle temperatures varying from 15°C to 40°C. Isometric tension of the complete tetanus is found to increase with an increase in muscle temperature, being highest at 40°C, the highest temperature used in this study. The frequency of stimulation required for complete fusion and maximum tension development of the tetanic contraction varies with the muscle temperature, being higher when the temperature is increased. At a frequency of stimulation producing incomplete tetanus, a decrease in temperature improved fusion and raised the tension. The rate of tension development and tension relaxation in the complete tetanus is increased by an increase in temperature. The main effects of a rise in temperature on the isometric contraction of rat triceps surae thus appeared to be an increase in the magnitude of tetanic tension and an increase in the rate of tetanic tension development and relaxation. (Supported by the Natl. Inst. of Neurological Diseases and Blindness, Grant H-697(C12) from the Natl. Heart Inst., and the Amer. Heart Assn.)

UNITARY RESPONSES IN THE MEDULLA OBLONGATA RELATED TO CAROTID SINUS RECEPTOR FUNCTIONS. A. Trzebski,* L. H. Peterson, F. Attinger*, A. Jones* and R. Tempest*, Univ. of Penna. Medical School and Graduate School of Medicine, Philadelphia, Pa.

Single unit activity within the solitary tract and lateral and caudal medullary reticular formation has been recorded via microelectrodes oriented stereotaxically in anesthetized intact dogs. Relationships between alterations in carotid sinus pressure and such single unit activity were sought. A stereotaxic instrument designed to permit rotation from supine to prone position allowed recording of medullary and Hering's nerve activity simultaneously. Respiratory activity, E.C.G. and arterial blood pressure were also recorded. Only a small proportion (<5%) of the total tested single medullary units exhibited direct alterations in electrical activity obviously associated with contralateral, ipsilateral or bilateral carotid sinus receptor variations. Three types of associated responses were, however, noted in this small proportion (i) decrease or cessation of the rate of discharge after occlusion of the carotid artery with the rebound after re-opening while distention of the carotid sinus resulted in an increased frequency of discharge; (ii) increase in rate of discharge after occlusion and decrease during distention of the carotid sinus; (iii) change in the spatial distribution of the spikes.

The patterns of activity of particular units following alterations in intra-sinus blood pressure due to carotid occlusion or distention were dissimilar to the patterns resulting from similar pressure alterations due to intravenous injections of nor-epinephrine and acetylcholine.

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THE INFLUENCE OF TEMPERATURE ON RESPIRATION IN EXERCISING MEN. C. H. Ts'ao, F. R. Meyer, B. E. Epperson, L. O. Holgersen. (intr. by D. B. Dill). Anatomy-Physiology Dept., Indiana University, Bloomington.

Experiments were conducted to determine the influence of changes in body temperature on respiration in exercise. Continuous recordings of pulmonary ventilation and of rectal, gastrocnemius muscle, femoral vein, and skin temperature were made during a series of four 10-minute periods of exercise, each followed by a 5-minute recovery period. The experiments were performed under two different environmental temperatures (25° and 40°C) and at three intensities of treadmill work (3.5, 4.0, and 5.3 mph all up a 9% grade). The time required to accelerate ventilation to the steady state during each 10-minute bout of exercise was much shorter than corresponding elevations of temperature even in the gastrocnemius muscle and femoral vein. In the 5-minute recovery following each bout of work, rectal temperature continued to rise, and the deceleration of ventilation was much more rapid than the temperature decline in either the gastrocnemius muscle or the femoral vein. In hard work experiments in the cool environment, the steady states of ventilation in the successive 10-minute bouts of exercise tended to go down or remain the same while the corresponding deep body temperature tended to rise. From these data we may conclude that temperature contributes little to the rapid respiratory responses to short periods of vigorous exercise. On the other hand, in the steady state of prolonged moderate work, a rise in body temperature produced by increasing environmental temperature, increased ventilation of men by 20 to 40% per degree centigrade rise in rectal temperature. (Supported by National Science Foundation Grant G6230.)

EVOKED SLOW WAVE AND UNIT RESPONSES IN THE HYPOTHALAMIC VENTROMEDIAL NUCLEUS. Takashi Tsubokawa and Jerome Sutin (intr. by A. Brodish). Yale University School of Medicine, New Haven, Conn.

The effect of mesencephalic reticular formation stimulation upon slow wave and unit responses evoked in the ventromedial nucleus by septal and amygdaloid single pulse stimulation was studied in locally anesthetized, Flaxedil immobilized, cats. Medial mesencephalic stimulation increased the amplitude of the septal-ventromedial evoked slow wave and suppressed the amygdaloid-ventromedial response. Forty-one per cent of the units recorded in the ventromedial nucleus were activated by amygdaloid stimulation, thirty-three per cent by septal stimulation and twenty-two per cent were fired by both afferent pathways. The remaining four per cent were fired by mesencephalic stimulation. The units discharged by septal or amygdaloid stimulation were found most readily in the caudal half of the ventromedial nucleus. Neurons activated by septal stimulation were generally observed more dorsally within the nucleus than those fired by amygdaloid or both amygdaloid and septal sources. Seventy per cent of the amygdaloid-ventromedial units were inhibited by medial mesencephalic R.F. stimulation. Thirty per cent of the septal-ventromedial units were facilitated by midbrain reticular formation stimulation, but the majority were not affected. The latency range for amygdaloid-ventromedial units was 7 to 43 msec. with the mode around 12 msec. Septal-ventromedial units had a range of 5 to 32 msec. with modes at 10 and at 20 msec., correlating with the peaks of the bimodal slow wave evoked response.

DISTRIBUTION OF LUNG SURFACE PRESSURE AS A FUNCTION OF POSTURE IN DOGS. James M. Turner (intr. by Jere Mead). Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

A gradient in lung surface pressure has been demonstrated by Krueger, et al (J. Appl. Physiol. 16: 465, 1961) in dogs held in the vertical position. The magnitude of the gradient was consistent with the hypothesis that air-filled lung tissue has the properties of a homogeneous fluid of the same mean density as that of the lungs at FRC. With the use of a technique similar to theirs in which a polyethylene catheter with a 2-2½ cm long balloon halfway along its length is inserted into the pleural space at the apex and withdrawn just above the diaphragmatic insertion 12-14 cm from the mid-line, repeated measurements of pressure are obtained as the balloon's position is changed by 0.5 cm steps. In the present study a gradient roughly comparable to that found by Krueger has been observed, the sign of which is reversed when the dog is tilted from the vertical to the head-down position. However, the gradient does not diminish with increasing lung volume as would be predicted from the associated change in lung density. Moreover, the gradient is not uniform and in general is more marked over the upper two-thirds of the lung than over the lower third. This appears to correlate with observed differences in curvature of the lungs in the two regions. In addition, traction applied to the trachea altered the distribution of pressures. These observations suggest that the observed gradients may reflect differences in supporting forces applied to the surface of the lung rather than fluid-like behavior of lung tissue.

IN VIVO RETARDATION OF PROTEIN BIOSYNTHESIS IN SUBCELLULAR COMPONENTS DURING ACUTE HYPOXIA.* M.D. Turner, Anne C. Turner, W.J. Lovell, and E.L. Whitfield. University of Mississippi School of Medicine, Jackson, Mississippi.

As the diffusion pressure of oxygen from arterial blood to tissue declines during hypoxic states the chief mechanism for cellular energy production is impaired. A correlation of the degree of functional impairment of subcellular organelles with the severity of total body hypoxia is not known. In the present study one group of rats were exposed to a pO_2 of about one atmosphere(154 mm. Hg) and a second group to a pO_2 of 34 to 37 mm. Hg for two hours. The animals remaining at the given oxygen tension, then received injections of glycine-2-C^{14}. At intervals after injection the pancreases were removed and the specific activities of the protein fractions of microsomes, mitochondria, zymogen granules, and cell sap were determined. Specific activities of cell sap and plasma amino acids were also obtained. During hypoxia the rate of amino acid incorporation into mitochondria, microsomes, and cell sap proteins was reduced fourfold whereas a twofold reduction occurred in the zymogen granules. The data indicate that at least a part of this inhibition may be due to decreased transfer of the tagged amino acid into the tissue cells.

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EFFECTS OF PROLONGED INFUSION OF ANGIOTENSIN II IN UNRESTRAINED DOGS. J. Urquhart*, J. O. Davis, and J. T. Higgins, Jr.*, NIH, Bethesda, Md.

Seven normal female dogs were infused with angiotensin II intravenously by a Rose osmotically driven pump, worn by the animal, which permitted uninterrupted infusion of 1-2 ml/day for 4-11 days. Two rates of angiotensin infusion were given, 15 and 80 ug/kg/day. Each rate of infusion produced a 2 to 8 fold increase in urinary aldosterone excretion throughout the infusion period in the four dogs studied. Neither rate of infusion significantly altered arterial pressure in four trained dogs in which measurements were made daily throughout the infusion. The initial effect of the lower infusion rate on Na balance was retention for 1-2 days, followed by restoration of balance for 1-2 days; thereafter a natriuresis lasting 1-2 days occurred in three of the dogs, followed by further retention. The fourth dog in this group failed to show a natriuresis during the infusion, but resumed Na retention, accompanied by a progressive rise in plasma Na concentration from 145 to 160 mEq/L. The higher rate of infusion initially produced a natriuresis of 60-80 mEq, followed by Na retention. The lower infusion rate produced kaluresis concomitant with Na retention in two of four dogs. The higher infusion rate uniformly produced kaluresis initially, with concomitant hypokalemia. Urine volume increased to 2-4 L/day during the higher infusion rate; smaller increases occurred at the lower rate. RPF and GFR were each increased approximately 30% in two of the three dogs in which these measurements coincided with a natriuresis. No changes in GFR or RPF were detected during Na retention or Na balance. These studies indicate that angiotensin II stimulates aldosterone secretion with resultant increased mineralocorticoid activity at rates of infusion too low to influence arterial pressure. However, angiotensin has transient renal hemodynamic effects which appear to influence electrolyte excretion directly.

FAMILIAL HYPOTHALAMIC DIABETES INSIPIDUS IN RATS. Heinz Valtin*, Henry A. Schroeder, and Kurt Benirschke*. Departments of Physiology and Pathology, Dartmouth Medical School, Hanover, N. H.

Familial hypothalamic diabetes insipidus has arisen as an apparently spontaneous mutation, along with a mutation for albinism in some of the affected animals, from a pure strain of Long-Evans hooded rats being bred for an unrelated research problem not involving radioactivity. In one of the adult female rats weighing 260 Gm, urine flow and urine osmolality ranged from 250 ml/24 hours and 125 mOsm/kg respectively in the untreated state, to 8 ml/24 hours and 2450 mOsm/kg after a subcutaneous injection of 0.5 pressor unit of vasopressin tannate in oil. While six hours of dehydration in this rat caused reduction in urine flow of about 50%, urine osmolalities did not rise above 250 mOsm/kg. These periods of dehydration were accompanied by a mean weight loss of 7.5% of body weight. The pars nervosa of the pituitary gland of this rat showed a reduction in neurosecretory material to about one-third of normal, when stained by the aldehyde fuchsin method. Urines were negative for reducing substances, and the rats had a normal non-fasting blood glucose concentration of 103 mgm%. The mode of inheritance has not been fully defined, but it is neither a simple dominant nor sex-linked. There is a high degree of semisterility and a high incidence of stillbirths and runts. Thus far the pedigree includes 17 affected females and 10 affected males; of these, 4 females are albinos. The albino trait without co-existent diabetes insipidus has been carried into the F2 generation and is inherited as an autosomal recessive. (Supported by U.S.P.H.S. Grant H-6181.)

A COMPARISON OF THE SOLUBILITY CHARACTERISTICS OF AN EXTRACT OF KIDNEY CONTAINING SODIUM WITH SODIUM SALTS OF PHOSPHOLIPIDS. J. C. Vanatta. Univ. of Texas, Southwestern Med. School, Dallas, Texas.

The purpose of this work is to compare the solubility characteristics of the Na salts of phospholipids with the purified extract of dog kidney containing Na (I) reported by Vanatta and Zimmerman (Fed. Proc. 21:144, 1962) in order to test whether I could be a Na salt of a phospholipid or a mixture of such salts. Extract I dissolves in CCl_4 in concentrations of 25 mg/cc. Na salts of phosphatidylserine, cephalin or lecithin would not dissolve in CCl_4 in this concentration. Dog kidneys were extracted by the procedure of Hokin and Hokin (J. Biol. Chem. 233:805, 1958) and the Na salts of the phospholipids obtained were prepared by washing a solution of this extract in petroleum ether with 0.1 N NaOH, and then washing with water until the washings were pH <7.0. The extract (II) then contained 2.04×10^{-4} meq Na/mg solids. On distribution between equal volumes of CCl_4 and 75% dioxane-water, 75% of I and only 36% of II were in the dioxane-water phase. 70 mg of dioxane soluble material from II was then subjected to countercurrent distribution in a 2 tube, 11 transfer system using the single withdrawal technique, with CCl_4 as the stationary phase, and 1,2 propanediol cyclic carbonate as the moving phase. No solids from II were detected in the zero tube CCl_4 phase, whereas this contained over 70% of the solids of I. Two additional extracts prepared as II were tested. One of these had no weight in the zero tube, the other had less than 1% of the total weight and contained only 1.40×10^{-4} meq Na/mg solids, which is less than 10% of the value for I. The dissimilarities support the concept that the Na in extract I is not in the form of a simple salt of a phospholipid. (Supported by PHS Research Grant HE-01574 09 from NHI.)

EFFECT OF TREATMENT OF ENDOTOXIN SHOCK ON RENAL HEMODYNAMICS AND SURVIVAL. J. A. Vick*, J. W. LaFave* and L. D. MacLean. Ancker Hospital, St. Paul and Department of Surgery, University of Minnesota, Mpls.

Renal plasma flow (RPF) and glomerular filtration rate (GFR) were determined in 28 dogs using clearance of creatinine and PAH before and at intervals following a lethal dose of E. coli endotoxin. Arterial blood pressure and urine output were continuously monitored and the influence of the following treatments on all variables noted: 1) Metaraminal bitartrate, 25 mgm in 250 ml of sterile saline was infused in amount sufficient to maintain arterial blood pressure at 100-120 mm.Hg. 2) Hydrocortisone sodium succinate 200 mgm., 3) Phenoxybenzamine hydrochloride (Dibenzylene) .5-1.0 mg/Kg. diluted in 100 cc. saline. Treatments were started 60-90 minutes after administration of endotoxin at a time when shock or anuria had developed. The RPF, GFR, urine output and extraction ratios for PAH (Epah) all fell sharply after endotoxin and remained markedly depressed for 8 hours or until death. Treatment with metaraminal or hydrocortisone did not significantly alter these results. However, treatment with Dibenzylene resulted in an increase in RPF, GFR, Epah and urinary output to normal or near-normal levels. The influence of Dibenzylene on survival was assessed in an additional 22 animals. All dogs received a lethal dose of endotoxin; eleven were treated after the onset of shock with Dibenzylene. All untreated animals died in 11.8 hours (mean). Ten of 11 treated animals survived.

DYNAMIC ANALYSIS OF RHINENCEPHALIC SLOW WAVES SEEN DURING TRAINING. Donald O. Walter. Brain Research Institute, University of California, Los Angeles.

The digital amplitude and phase "meter" recently developed by N. Goodman (J. Franklin Inst., 1960) provides a statistically best estimate of integrated frequency and its amplitude, in any oscillatory phenomenon. Applied to digitized EEGs from the hippocampus and entorhinal cortex of cats being trained in a discriminative approach task (Adey, Walter & Hendrix, 1961), it shows that the coordinated wave trains are most regular during actual locomotion toward the goal; that they are often subject to a gradual acceleration (e.g., from 5.5 to 6.5/sec) during this approach; and that the two wave trains are largely modulated together, both in amplitude and phase. Formal testing shows the statistical significance of these conclusions, even for results of a single approach. The frequency of the entorhinal lead is consistently different from the hippocampal one, however, implying that their coordination is not due to passive wave transmission. A new hypothesis of wave transmission between hippocampus and entorhinal area is suggested by these results: that what is transmitted is not primarily the series of impulses defining the successive waves of a train, but a tonic "impulse to wave", whose slight modulation by the phasic wave is only a secondary modifier of the evoked train. The same hypothesis can also explain evocation of hippocampal theta waves by arousing stimuli. (Supported by Grant B-1883, USPHS)

THE ROLE OF PERIPHERAL RESISTANCE IN CONTROLLING CARDIAC OUTPUT DURING EXERCISE. H. R. Warner, W. S. Topham,* and K. K. Nicholes.* Biomedical Computer-Simulation Laboratory, Latter-day Saints Hospital, Salt Lake City, Utah.

The regulation of cardiac output during exercise is accomplished by the arterial pressure receptors. In a particular exercise run arterial pressure may be maintained just above or below resting level depending upon the extent to which the animal is aroused by the exercise. This arousal phenomenon by itself will cause only a minor rise in cardiac output during exercise if peripheral resistance does not fall. To test this hypothesis, chronic dogs were prepared with an electromagnetic flowmeter implanted around the ascending aorta with a cannula inserted through the flowmeter into the aorta for pressure measurements. Two weeks after this operation, a plastic cuff containing a balloon was implanted around the descending thoracic aorta. Inflation of this balloon compressed the aorta against the plastic cuff and increased resistance to outflow from the central arterial bed. As the dog exercised on the treadmill, the pressure and flow signals were fed directly to an analog computer where peripheral resistance calculated at the end of each systole was compared with a reference voltage. If the calculated resistance differed from the reference voltage, one of two solenoid valves was opened (depending on the sign of the error signal) allowing air to enter or leave the balloon. In this way peripheral resistance could be artificially controlled as the dog exercised. With resistance so controlled, heart rate and cardiac output increased less than 10% during exercise at 4 m.p.h. at 10% grade, while with no artificial control and the same amount of exercise, heart rate and cardiac output doubled as resistance decreased to one-half the resting value. Thus, it appears that the decrease in peripheral resistance that occurs with exercise constitutes the major determinant of cardiac output.

EFFECT OF CHANGES OF IONIC ENVIRONMENT ON SOME MEMBRANE PROPERTIES OF AN ISOLATED NERVE CELL. Yoshiaki Washizu*, Charles Edwards and Carlo A. Terzuolo. Dept. of Physiology, University of Minnesota, Minneapolis, Minnesota.

The membrane potential and membrane resistance of the isolated nerve cell of crayfish stretch receptor organs were measured following changes in external K^+, Na^+, Ca^{++} and Cl^- ion concentrations. The ensuing effects on the action potential and the generator potential were also studied. The external solutions were exchanged while the cell was impaled with a microelectrode. For resistance measurements, the electrode was one of the arms of a Wheatstone bridge. The principal results to be presented and discussed are: 1) The resting potential decreased in Ca^{++} free solution by 1/3 to 1/2 of its resting value. Membrane resistance in this condition became less than 0.5MΩ (normal value, 2 to 5MΩ). Substitution of Cl^- with glutamate or acetate ions did not alter the above results; 2) In normal or elevated $[Ca^{++}]_o$ the relationship between the resting potential and log $[K^+]_o$ was approximately linear for increases up to 10 fold, and the slope was 40-50mV per 10 fold change of $[K^+]_o$. If $[Ca^{++}]_o$ was increased 5 fold, five fold increase of $[K^+]_o$ reduced the membrane potential, but the membrane resistance was not significantly altered. Thus, under these conditions the membrane potential and membrane resistance behaved independently.

VASCULAR SMOOTH MUSCLE CONTRACTIONS INDUCED BY EPINEPHRINE IN CHLORIDE-DEFICIENT ELECTROLYTE MEDIA. William H. Waugh, Dept. of Med., Univ. of Kentucky Coll. of Med., Lexington, Ky.

The effects of usually less penetrating anions than chloride were studied on contractions of vascular smooth muscle. Dog intestinal arterial segments were perfused with solutions containing 140 mM NaCl, 5mM "Tris", 7mM acetate, and physiologic concentrations of K, Ca, Mg, HPO_4, and glucose, at pH 7.4. Isosmotic replacement of all the Na and Cl in the perfusate by NaI, NO_3, or Br and by sodium butyrate, β-hydroxybutyrate, acetate, or pyruvate markedly potentiated tension responses induced by l-epinephrine (l-epi). These results were of quick onset and were rapidly reversed by chloride-rich perfusate. Replacement of NaCl by sodium isethionate, acetylglycinate, ferrocyanide, thiosulfate, sulfate, or succinate did not likewise potentiate l-epi-induced contractions. However, the active state induced by brief l-epi-stimulation was mildly prolonged by most of the latter anions. The chloride substitutions did not contract quiescent arterial muscle. The above findings suggest that certain organic as well as inorganic anions increase the active tension of arterial smooth muscle responses by an action neither directly related to the relative membrane impermeability of the anion nor to delayed repolarization. Rather, the action appears related to anion adsorption affinity, ion-pair formation, and/or lipoid-solubility in the muscle cell membrane.
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THE EFFECTS OF INSULIN ON REGIONAL CHOLESTEROL METABOLISM Lucille J. Wedel,* David H. Elwyn* and William C. Shoemaker, Michael Reese Hosp. and Med. Ctr., Chicago, Ill.

The net rate of cholesterol metabolism in the liver and nonhepatic splanchnic area (gut) was measured in the intact unanesthetized dog by a previously reported system (Am. J. Physiol. 196; 311, 1959) involving catheterization of the hepatic vessels and measurement of hepatic blood flow with BSP. The effects of insulin and glucose administration were compared with a postabsorptive control period in a series of 6 normal and 7 diabetic dogs. There was an increased rate of hepatic uptake of free cholesterol and output of esterified cholesterol after insulin in the normal dog. After glucose there was an increased hepatic output of free and uptake of esterified cholesterol. The uptake of free cholesterol by the gut increased, but the esterified cholesterol uptake changed abruptly to an output after insulin. The output of esters further increased after glucose administration. In general these trends were also observed in the diabetic dog. However, the response to insulin was more variable and dependent in part upon the nutritional state of the diabetic animal; most striking was the increased ester output by the gut after glucose. The effects of insulin on the gut and liver are in opposite directions. The effects on free and esterified cholesterol are likewise in opposite directions.

SYMPATHETIC FUNCTION AND THE DEVELOPMENT OF TEMPERATURE REGULATION. David R. Wekstein (intr. by E. F. Adolph). Department of Physiology, University of Rochester, Rochester, New York.

What is the role of the sympathetic nervous system in the maturation of temperature regulation in the preweanling rat? Animals 6 to 16 days of age were placed in an environment of 15°C air. The time required for the animal's colonic temperature to drop from 30 to 20°C was taken as an index of cooling rate. Reserpine, pentolinium and nerve-growth-factor antiserum (Levi-Montalcini and Booker, Proc. Nat. Acad. Sci. 46:384,1960) were used to assay autonomic function. None of these blocking agents influenced the rate of cooling of the 6 day old animal. In the 16 day old animal the same agents had a pronounced effect, such that control animals did not cool, while animals that had received reserpine cooled in 54 minutes, animals that had received pentolinium cooled in 134 minutes and animals that had received the antiserum for the first five days of life cooled in 74 minutes. This study as well as studies of the effect of reserpine on the developing heart rate and the change of heart rate when the animal is exposed to an air temperature of 40°C show that most sympathetic functions develop during the early postnatal period of the rat.

TACTILE DISCRIMINATION IN HEMIDECORTICATE CATS. Bernice M. Wenzel, R. D. Tschirgi and J. L. Taylor*. Univ. of Calif., Los Angeles and Univ. of Ill. Coll. of Med., Chicago.

Can normal cats learn to associate a rapidly flashing light with a tactile stimulus on one foreleg and a slowly flashing light with a tactile stimulus on the other foreleg? Can this task be performed better by hemidecorticate cats (operated at nine days of age) by virtue of decreased ambiguity in tactile information arising from symmetrical points? The subjects were two hemidecorticate cats, two normal littermates, and two surgical controls. Testing was done in a box containing two lucite feeding cups, mounted one above the other. A light inside each cup could be flashed at either of two rates. Electro-tactile stimuli could be delivered to the upper part of either foreleg through topical electrodes. The cats were first trained to associate a stimulus on one side with one flash rate. Whenever the electro-tactile stimulus was presented, the lights went on in the two cups. If the cat licked the cup with the correct flash rate, food was immediately delivered. If the other cup was licked, no food was given. The correct light was varied randomly between the two cups. Twenty trials a day were given until performance was 95% correct in one session. Three weeks later the same procedure was followed with the stimulus presented to the other side of the cat and the other light correct. After another three weeks, sessions were held with both stimuli presented in random order. Although the cats had previously reached criterion with each stimulus-light pair independently, they were all unable to respond at that level of proficiency when both pairs were presented in the same session. It is concluded that normal cats cannot learn the task described and that hemidecorticate cats are unable to perform better than normals.

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THE INCORPORATION OF GLUCOSE-1-C^{14} AND FRUCTOSE-U-C^{14} INTO GLYCOGEN IN REST AND CONTRACTING RAT DIAPHRAGM MUSCLE. George W. Wermers,* H. Mead Cavert, and Carrill F. Quello*. Physiol. Dept., Univ. of Minn., Minneapolis.

A whole rat diaphragm similar to that used by Kipnis and Cori (JBC 224:681, 1957) was incubated for 2 hours in a Ringer-bicarbonate medium (pH = 7.45) and the incorporation of C^{14}-labeled glucose and fructose into glycogen was studied. To produce contractions, supramaximal stimuli were applied directly to the muscle at a rate of 15/min. The percentage of final glycogen which was derived from glucose-1-C^{14} ranged from 6 to 13 in resting muscle (N = 6) and from 8 to 26 in contracting muscle (N = 6). When insulin was present the percentage of final glycogen derived from glucose-1-C^{14} ranged from 50 to 83 for resting muscle and from 40 to 74 for contracting muscle. After 2 hours of incubation with fructose-U-C^{14} and insulin, 21 to 47% of final glycogen in resting muscle and from 8 to 66% of final glycogen in contracting muscle were derived from labeled substrate. Data obtained from carbon by carbon degradation of glycogen isolated from resting (N = 4) and contracting (N = 3) muscles which had been incubated with glucose-1-C^{14}, show that from 93 to 100% of the radioactivity found in glycogen resided in the carbon 1 position. These results suggest that (1) the pathway (or pathways) for the incorporation of glucose into glycogen is not altered by repetitive contraction and (2) the incorporation of glucose into glycogen occurs with relatively minor redistribution of radioactivity in the hexose chain. (Supported by USPHS Grant GM-07305-03).

LIMITATIONS TO OXYGEN TRANSFER BY THE LUNG DURING EXERCISE AT AN ALTITUDE OF 19,000 FEET. John B. West (intr. by H. Rahn). Dept. of Physiol., The Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

During the Himalayan Scientific and Mountaineering Expedition, 1960-61, the diffusing capacity of the lung for carbon monoxide was measured at 19,000 ft. (5,800 m; P_B approx. 380 mm Hg) at work levels of 300 and 900 Kgm/min. With the subjects breathing air, a change in diffusing capacity of less than 20% was found compared with the sea level values, and this could be wholly accounted for by the increased rate of reaction of carbon monoxide with hemoglobin due to hypoxia. Measurements of arterial oxygen saturation by ear oximetry gave an average resting value of 67% which fell to 63 and 56% respectively for the 2 work levels. Several readings of less than 50% saturation were recorded on severe exercise. The progressive fall in arterial oxygen saturation as the work level was raised occurred in spite of an increasing alveolar oxygen tension, and the resulting large alveolar-arterial oxygen differences can be explained by the diffusion limitations of the lung under these conditions. (Supported in part by the Medical Research Council of Great Britain.)

CARDIOVASCULAR RESPONSE OF THE CHICKEN TO HYPERTHERMIA. G. C. Whittow, P. D. Sturkie and G. Stein. Physiology Section, Rutgers University, New Brunswick, New Jersey.

During hyperthermia, the mean respiratory rate of fourteen female chickens increased to a maximum of 194 respirations/min. at a mean rectal temperature of 43.2°C. While the respiratory rate was increasing, the cardiac output increased in twelve out of the fourteen birds. The mean maximal percentage increase of cardiac output was 57.4%. The increased cardiac output was usually the result of an increase both in stroke volume and in heart rate. Following the decrease in respiratory rate, the cardiac output decreased progressively until death occurred. The diminution in cardiac output was associated with a decrease of stroke volume but the heart rate increased further during this period. In general, the arterial blood pressure and calculated total peripheral resistance decreased during hyperthermia. However, towards the end of the heating period (mean rectal temperature 44.4°C), when cardiac output and arterial blood pressure both decreased, there was usually an increase in calculated total peripheral resistance.

ESSENTIAL FATTY ACID DEFICIENCY IN THE MOUSE. J. Walter Wilson and Elizabeth H. Leduc. Brown University, Providence, Rhode Island.

The development of EFA deficiency in mice has presented some problems apparently not encountered in rats. This is due to the fact that weanling mice may weigh from 1/3 to 1/2 adult weight. The young attain nearly adult size before the symptoms appear and then only if the diet is completely free of EFA. Also, the skin symptoms previously described do not appear typically if the humidity of the mouse room is relatively constant and the mice are free of ectoparasites. Our purpose was to study the effect on the liver cell with the light and electron microscope. The only striking change was in the mitochondria which may be much enlarged and have a large number of additional cristae. We attribute this to the fact that the EFA in the bond that couples oxidative phosphorylation to the main electron transport chain in the mitochondrial membranes is gradually replaced by polyunsaturated fatty acids that are synthesized in the body. This makes the bond ineffective and leads to uncoupling. This accounts for the high rate of metabolism and high food intake of the intact mouse. Changes in the mitochondria and some, if not all, other symptoms of the deficiency may be due to the decreased ATP production. (Supported by U.S.P.H.S. Grant C-510.)

INFLUENCE OF CO_2 ON THORACIC COMPLIANCE. Sabbo Woldring (Intr. by Werner K. Noell). Dept. of Neurosurgery, Roswell Park Memorial Institute, Buffalo, N. Y.

Thoracic compliance has been studied at different alveolar CO_2 levels. The experiments were done on anesthetized cats and rabbits. The animal was placed in a plethysmograph, breathing outside air through a tracheal cannula which perforates the wall of the plethysmograph. A recording spirometer connected to the plethysmograph measures changes in lung volume. The EMG of diaphragm and external oblique muscle is recorded simultaneously. An increase in alveolar PCO_2 was obtained by having the animal breathe oxygen through an increased dead space. Reduction of $P_A CO_2$ was achieved by passive hyperventilation. Thoracic compliance was measured by having the animal breathe from a reservoir in which the pressure has been increased or reduced; the resulting changes in lung volume are plotted against the applied pressures. In cats distinct differences in compliance were observed at different alveolar CO_2 tensions; during hypercapnia the compliance decreases, whereas in hypocapnia it is augmented. Reverse changes are observed in the activity of the expiratory muscles. In rabbits expiratory muscle potentials are difficult to obtain during anesthesia and changes in compliance at different $P_A CO_2$ are minor or absent. The effects of CO_2 on expiratory muscle activity and compliance disappear entirely on bilateral vagotomy. The results are interpreted as evidence of a tonic influence of CO_2 on the respiratory reflexes which control the volume of the lungs. (Supported by N.I.H. Grant RG-9034)

Adrenocortical Function in the Primate Infant

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A period of adrenal hypofunction has been reported to exist in the human infant during the first week of life. The present study was made to determine if this hypofunctional period is demonstrable in another newborn primate, the rhesus monkey. Plasma concentrations of 17-hydroxycorticosteroids (17-OHCS) were determined prior to and following ACTH administration in two day old and adult rhesus monkeys. In contrast to the human infant, no significant difference in resting steroid levels was observed between infant and adult monkeys. Although the administration of ACTH elicited a marked increase in 17-OHCS concentration in all animals, the response of infant monkeys was significantly greater than that of adult animals. Thus, four hours following a single injection of ACTH, the 17-OHCS levels of infant monkeys was 180 ugm% while that of adult animals was only 93 ugm%. The greater response of the infant could not be ascribed to a prolongation of corticosteroid metabolism since the half life of administered 4-C-14 cortisol was the same in both age groups.

THE EFFECT OF SODIUM PENTOBARBITAL ON GASTRIC CONTENT OF THE SPIDER MONKEY. C. Y. Woo* and F. P. Brooks. Dept. of Physiology, School of Medicine, Univ. of Pennsylvania, Philadelphia 4, Pa.

Three female spider monkeys (ateles), weighing 3-5 kg., equipped with chronic gastric fistulas (Thomas), were used in this study. The animals were fasted for 16 to 18 hours before beginning the experiment. Gastric content was collected by dependent drainage with the animal restrained in a chair over a 3-hour period. The volume, pH, Na^+, K^+, Cl^-, the concentrations of acid titrated to pH 3.5 and 7.0 and pepsin were determined. After control values were established, single intraperitoneal injections of 15 mg. sodium pentobarbital per kg. of body weight were given at the beginning of the second hour. The animals lost corneal reflexes within 15 minutes after injection and remained in a lightly anesthetized state for about an hour. Ten experiments were done for control values, and eight for barbiturate studies on different days. Comparisons of the values of the 2nd-hour collections indicate that light anesthesia with sodium pentobarbital had no significant effect on volume, acid secretion, electrolyte concentrations, and peptic activity. (Supported by Grant RG5007(C5) from the National Institutes of Health.)

INTERACTIONS OF CORNEAL EPITHELIUM AND STROMA: SULFATE REDUCTASE. B. Wortman. Washington Univ. School of Med. St. Louis, Mo.

Reduction of sulfate to sulfite and its subsequent assimilation into a larger molecule, such as taurine, has been observed in the intact chick embryo as well as in extracts, Lowe and Roberts, J. Biol. Chem., 212, 477(1955), and a possible mechanism for this reaction has been proposed, Chapeville and Fromageot, Biochim. Biophys. Acta, 26, 538(1957). Sulfate reductase had been thought to occur only in plant and bacterial cells and has not been described in mammalian cells. An enzyme system has been found in beef cornea epithelial extracts which will catalyze the reduction of sulfate in 3'-phosphoadenosine 5'-phosphosulfate with the production of measurable amounts of 3'-phosphoadenosine 5'-phosphate. Sulfite ions are not detected but are incorporated into another molecule which is heat stable and found in the epithelial extracts. The enzyme is dependent upon pyridine nucleotides for its activity and both reduced di- and tri-phosphopyridine nucleotides serve equally as well.

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THE EFFECT OF DISTAL NEPHRON DAMAGE ON THE EXCRETION OF AMINO ACIDS AND PEPTIDES. Leebert A. Wright* and T. Frederick Nicholson. University of Toronto, Toronto, Canada.

The pattern of amino acids and peptides excreted in the dog's urine from both normal and damaged kidneys was determined by high voltage electrophoresis followed by paper chromatography. When the distal segments of the nephrons of one kidney in the dog were damaged by the retrograde ureteral injection of 0.05% mercuric chloride the urine from the damaged kidney showed an increased excretion of neutral and acid amino acids and a markedly decreased excretion of peptides. The simultaneous decrease of peptides and increase of amino acids suggests that free amino acids in the tubular fluid are involved in peptide formation by the distal parts of the nephron and that part of the increased amino acid excretion observed in certain renal lesions may be due to decreased peptide formation rather than decreased amino acid reabsorption.

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EFFECT OF RELAXIN ON THE MYOMETRIUM OF THE RABBIT. Shotetsu Yamada, M. R. Callantine, and M. X. Zarrow. Dept. of Biol. Sciences, Purdue University, Lafayette, Indiana.

The *in vitro* effect of relaxin was studied on the estrogen and progesterone dominated rabbit myometrium. Uteri were obtained from immature Dutch-belted rabbits treated with PMS and HCG or from mature animals at various times after mating. The tension developed by the myometrium was recorded under isometric conditions (Endocrin. 69:1088). An electrical stimulus (60 cycle A.C.) of 2 v/cm longitudinal field with a duration of 5 sec. and frequency of 1 stimulus every 45 sec. was used. The stimulus was applied by suspending a segment of muscle in Krebs solution between two Ag.AgCl wire ring electrodes. The addition of relaxin to the Krebs solution containing uteri of rabbits treated with PMS and HCG caused a 20-60% increase in uterine tension when a negative staircase was present. Relaxin caused either no change or a decrease in tension in uteri exhibiting a transient or positive staircase. Comparable results were obtained in early pregnancy but in midpregnancy and later (i.e., after placental development) relaxin had either no effect or decreased uterine tension even in the presence of a negative staircase.

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EFFECTS OF BRONCHOACTIVE AGENTS ON STATIC PRESSURE-VOLUME CHARACTERISTICS. S. Yoshida* and S. Rodbard. University of Buffalo Chronic Disease Research Institute, Buffalo 14, N.Y.

Static pressure-volume characteristics of the lung during continuous infusion of bronchoactive agents into the bronchial or pulmonary arteries of the thoracotomized dog have been studied. Airway pressures during histamine or acetylcholine infusion were higher for comparable volumes at less than 20 mm Hg on inflation than in the controls. However, on nearly full expansion of the lung the airway pressures were essentially similar during drug infusion and control experiments. This pressure difference was greater during inflation from the collapsed state; the difference was smaller when inflation was begun from the end-inspiratory level. During deflation the pressure-volume curve nearly retraced that of the control; pulmonary compliance calculated from the middle third of the deflation curve showed little change. The pressure-volume curve following the release of bronchoconstriction by a single injection of tripelennamine hydrochloride or atropine exhibited still greater pressures for smaller volumes in some tests than in the control; the following pressure-volume characteristics were similar to the controls. These findings suggest that the increase in pressure may be accounted for by closure of some of the pulmonary spaces by surface tension forces during bronchoconstriction, so that the number of units sharing a given air volume is decreased. Epinephrine or norepinephrine infusions into the pulmonary artery did not alter the static pressure-volume characteristics.