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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

EFFECTS OF HEMORRHAGE ON PERIPHERAL BLOOD FLOW. F. L. Abel* and Q. R. Murphy. Dept. of Physiol., Univ. of Wisconsin Med. Sch., Madison.

The immediate effects of moderate hemorrhage on the distribution of blood flow were investigated. Dogs were bled rapidly an amount equal to 5% of their calculated blood volume (5 ml. per kg.). The bleedings were repeated four times at intervals of ten minutes. Blood flow was measured by the electromagnetic flowmeter in the renal, superior mesenteric, and common iliac arteries. Peripheral resistance was calculated for these beds. The results show marked constriction in the iliac and mesenteric beds following loss of 5% and 10% of the blood volume, but little change in resistance of the renal bed. Following the loss of 20% of the blood volume, there was a sharp increase in resistance of the iliac and renal beds which was not accompanied by a corresponding increase in resistance of the superior mesenteric bed. It is concluded that the renal flow is maintained after small blood losses at the expense of muscle, skin, and intestine; but that flow to the intestine remains relatively high following more severe bleeding.

OXYGEN TENSION OF HUMAN CEREBRAL GRAY AND WHITE MATTER. John E. Adams* and John W. Severinghaus, Cardiovascular Research Institute, U. of Calif. Med. Center, San Francisco.

A new polarographic membrane-covered needle oxygen tension electrode 1 mm in diameter (Beckman) appears to have less than 5% error in unstirred materials. It has been used in 23 neurosurgical procedures to estimate both surface and deep P_{O_2}. 3 patients were awake and 20 were under N_2O-barbiturate anesthesia; some were supplemented with halothane. P_{O_2} was surprisingly consistent, and not measurably affected by distance from surface vessels, in contrast to results reported with bare platinum electrodes. The mean values and ranges of P_{O_2} in mm Hg were: cerebral cortical surface 13 (4-20), cerebral white (depth ca. 5 mm) 30 (11-38), contused cortex 31 (20-58), surface which had been coagulated 54 (22-66). Several readings taken within cortical gray agreed with surface readings ($\pm$ 3 mm Hg). In one subject comparative blood values were: Pa_{O_2} 139, Pa_{CO_2} 45; jugular venous P_{O_2} 50, P_{CO_2} 50; cortical surface vein draining test area P_{O_2} 60; 3 gyri of frontal lobe, surface tissue P_{O_2} 4-6 mm. During hypothermia (29°C) both carotids and both vertebrals were occluded for 3 minutes. P_{O_2} on temporal cortical surface fell very slowly (from 25 to 15 mm Hg). We conclude that actively metabolizing neural tissue has a much lower oxygen tension than had been assumed from studies of venous blood.

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CYCLICAL NATURE OF TEMPERATURE VARIATIONS IN THE VENOUS SYSTEM.

S. Afonso*, J. F. Herrick, G. G. Rowe, and C. W. Crumpton. Dept. of Med. and Cardiopulmonary Research Laboratory of the U. of Wisconsin School of Medicine, Madison 6, Wisconsin.

The function of the circulatory system to distribute the heat generated by cellular activity and to equalize the body temperature is well known. This function has been studied extensively by very competent investigators over a period of many years. The literature, however, seems to contain limited experimental data on oscillatory patterns of the dynamic thermal variations existing in the venous system. The thermistor has proven to be a convenient and reliable device for studying the small but significant variations in temperature of the flowing blood. These variations are keyed to certain bodily processes, one of which is the breathing frequency. At higher body temperatures, the variation synchronized with the breathing frequency appears to modulate a slower type of variation in temperature which is not so evidently related to physiological variation. Records of these variations will be presented. Final conclusion must await further investigations.

ELECTRICAL STIMULATION OF THE HUMAN THALAMUS AND GLOBUS PALLIDUS. W. Watson Alberts, Elwood W. Wright, Jr., Grant Levin, and Bertram Feinstein (intr. by Benjamin Libet). Mount Zion Hospital and Medical Center, San Francisco, Calif.

In 3 cases of intractable pain, portions of the posterior ventral lateral and posterior ventral medial thalamic nuclei were explored by electrical stimulation prior to thermal lesion production. Brief (~1 sec.) trains of 1-msec. square pulses of alternating polarity, 60 p.p.s., at threshold strength (0.3-2.5 ma. with 2-3 mm. electrode tip), elicited contralateral sensations. The generally known topographic relationships were verified (face, medial; arm, intermediate; leg, lateral). The sensations included not merely paresthesia (tingling and electric shock) but also warmth, drawing or constriction, pain, vibration, and the feeling of motion without contraction, as well as occasional contraction. Pain, when elicited, was in the area of the patient's own pain. By comparison, 146 threshold stimulations (0.5-7.5 ma. with 5-10 mm. electrode tip, 5-10 sec. trains, other parameters as above) in 62 Parkinson patients produced mainly contralateral tremor in two lateral ventral thalamic targets (70%, 88% of responses) and in two pallidal targets (53%, 65%). Muscle contraction, sensation (but only of the paresthesia type), and other responses including cessation of tremor, nausea, apprehension, etc., were also found.

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CARDIAC PERFORMANCE AND SURVIVAL TIMES OF RABBITS WITH SEVERE AORTA CONSTRICTION. N. Alexander, M. DeCuir*, T. Goldfarb* and D.R. Drury. Physiol. Dept., School of Med., Univ. of Southern Calif., Los Angeles, Calif.

A modified Sarnoff heart-lung technique was used to study cardiac performance (c.p.) in 43 rabbits 4 to 120 days after severe constriction of the abdominal aorta proximal to the superior mesenteric artery. The peak pressure developed by the heart when pumping only coronary flow was taken as indicator of c.p.. In 17 normals, this ranged from 120 to 170 mm Hg, aver. 145. Four to 20 days after aorta constriction peak pressures were normal in 12 of 13 animals; 21 to 30 days, 4 of 7 had pressures of 185-250 mm Hg; and 31 to 120 days, 20 of 23 had pressures of 190 to 290 mm Hg. About half of all the animals had hypertrophied ventricles but of these only half had a high c.p.. A study of survival times of aorta constricted rabbits showed that 90% of them, after the rapid development of hypertension, died with signs of congestive heart failure and ventricular hypertrophy within 33 days. This correlated well with the heart-lung results that it took approximately 30 days for a high c.p. to develop. Survival beyond this critical period was increased from 10% to 60% if the circulatory system was stressed, e.g., by a mild hypertension or regional restriction of blood supply, for several weeks before the stricture was applied.

AN IMPROVED METHOD FOR THE BIOASSAY OF ANTI-INFLAMMATORY ACTIVITY OF ADRENO-CORTICAL STEROIDS IN RATS. Ralph W. Alexander and I.E. Bush (intr. by Natalie Alexander). U. South. Calif. School of Med. and Radcliffe Infirmary, Oxford, England.

In 1950 a cotton pellet assay was introduced for assessing anti-inflammatory activity of cortisone-like steroids in rodents. Although simple to carry out we found the precision of this assay to be rather low due to the shallow slope of the log dose - response plot. "Carrageenin", a water soluble polysaccharide extracted from Irish moss (seaweed) has been shown to cause a striking granulomatous response to guinea pigs. We therefore incorporated this polysaccharide into cotton pellets and produced large, easily dissectable granulomata in adrenalectomized rats. In several assays using 1-6 mgs cortisone acetate and 1-4 mgs cortisol acetate we found that the precision using "Carrageenin" impregnated cotton pellets was twice that obtained with plain cotton pellets. The reason for the increased precision was the steeper log dose-response slope obtained. λ, the index of precision, ranged between 0.10-0.17.

RELATIONSHIP BETWEEN CHANGES IN CARDIAC OUTPUT AND PERIPHERAL BLOOD FLOW DURING EPINEPHRINE INFUSION IN MAN. M.J. Allwood,* E.W.O. Keck,* R.J. Marshall* and J. T. Shepherd. Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

Cardiac output (C.O.) was measured by the indicator-dilution technic in seven healthy men aged 30-35 years, lying supine. Forearm blood flow (F.F.) was determined by venous occlusion plethysmography using the Whitney strain gauge. Epinephrine bitartrate ("Suprarenin"-Winthrop) was infused intravenously at 2.5 to 15 μg. per minute. The onset of changes in blood pressure, heart rate (H.R.) and F.F. was not always synchronous. Control values for F.F. were 4.0 (range 2.1-8.7) ml./100 ml./min. and for C.O. 7.2 (range 4.9-8.7) L./min. With 10 μg./min. infused for 5 min., F.F. initially reached a peak of 15.9 (8.0-26.1) ml. and the C.O. was 10.7 (8.8-13.0) L./min. After a transient decrease the F.F. was 6.5 (4.0-9.9) ml. and the C.O. was 10.0 (6.6-12.3) L./min. With longer infusions (20 min.) in four subjects the F.F. and C.O. showed a further slight increase. In the three subjects with the largest increase in C.O. (70 per cent), oxygen consumption was increased by 11 per cent. Thus the increase in C.O. is not wholly due to increased metabolism. The initial increase in C.O. was largely due to an increase in H.R. Subsequently, increases in H.R. and stroke volume were of about equal importance; this contrasts with a similar increase in C.O. during supine exercise which was achieved mainly by an increase in H.R.

A QUANTITATIVE EVALUATION OF NON LACTATE HYDROGEN ACCEPTORS IN ANOXIC RAT LIVER SLICES. Norman R. Alpert, Richard Chenoweth* and Richard Winzler*. University of Illinois, College of Medicine, Chicago, Illinois

Anaerobic muscle produces large quantities of lactate. Under these conditions pyruvate serves as a hydrogen acceptor, facilitating the oxidation of DPNH, and thus allowing glycolysis to continue. Liver, in contrast, produces very little lactate during anoxia. For this tissue, fat formation has been implicated as a possible substitute hydrogen acceptor system. Experiments were carried out to evaluate the quantitative significance of this and other non-pyruvate hydrogen acceptors in anaerobic liver slices. It has been assumed that in liver slices under anaerobic conditions all carbohydrate which traverses the glycolytic pathway and does not appear as lactate may be involved in a non-pyruvate hydrogen acceptor transformation. The total carbohydrate which disappeared anaerobically per gram of liver slice incubated in a high K medium for 90 min. and 120 min. was 21.8 and 38.1 mg while the lactate which appeared was .5 and 1.7 mg. Thus a considerable amount of carbohydrate is not accounted for as lactate. In addition anoxic liver uses glycogen as a substrate in preference to the exogenous glucose. A Pasteur effect of 10% at 90 min. and 25% at 180 min. was observed. This work was supported in part by USPHS Grant H2345.

EFFECT OF ATRIAL SEPTAL DEFECTS ON HEMODYNAMIC ALTERATIONS CAUSED BY ACUTE PARTIAL OBSTRUCTION OF THE PULMONARY ARTERY. D. S. Amorim,* H. W. Marshall,* D. E. Donald* and E. H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Systemic and pulmonary blood flows and pressures in a series of 10 anesthetized dogs with closed chest and atrial septal defects created 1 to 15 months previously were measured before, during and after graded degrees of obstruction of the main pulmonary artery by a balloon at the tip of a cardiac catheter. Similar observations were made in dogs with intact cardiac septa. Obstructions of the main pulmonary artery to elevate the right ventricular systolic pressure to more than 80 mm. Hg in dogs with atrial septal defects caused right-to-left shunts through the defect of up to 55 per cent of systemic flow and decreased the magnitude of the left-to-right shunts. No systematic changes in mean aortic pressure and insignificant to slight increases in mean right atrial pressure occurred. In contrast, in dogs with intact septa lesser degrees of obstruction producing increases in right ventricular systolic pressure to more than 60 mm. Hg were associated with increases in mean right atrial pressure and striking decreases in mean aortic pressure and cardiac output. The hemodynamic status of these normal dogs deteriorated rapidly in contrast to that of the dogs with atrial septal defects that were capable of maintaining right ventricular hypertension over periods longer than 30 minutes without significant decrease in systemic arterial pressure. It is concluded that under these conditions the presence of an atrial septal defect is associated with a considerable increase in resistance to the hemodynamic effects associated with right ventricular hypertension caused by acute partial occlusion of the pulmonary artery.

THE EFFECT OF CENTRAL BODY THERMAL STATES ON THE COLD INDUCED VASODILATION RESPONSE. R. D. Anderson*, W. G. Boettcher*, G. J. Grossbeck*, R. L. Harrington* and R. F. Kapelowitz* (intr. by T. Adams). Dept. of Physiology & Biophysics, Univ. of Washington Sch. of Medicine, Seattle.

The central body thermal state (CBTS) is recognized as an important variable in the determination of the pattern of the cold induced vasodilation (CIVD) response, but quantitative data on these relationships have not been available. The effect of a modified CBTS on the CIVD response of normal subjects was therefore studied. A thermocouple was taped to the digital pad of the right index finger and a mercury in rubber (Whitney) strain gauge was placed at the nail base to record relative finger volume and blood flow. The finger was immersed in a stirred 0° C water bath. The data obtained did not necessarily indicate a direct time relationship between pulse and finger volumes and surface temperature during cycling. When the CBTS was decreased by exposure of the whole body to 7° C for 1 hour, the time for cycling was longer than at a "normal" CBTS and the rate of temperature rise was reduced. When the whole body was exposed to 40° C for 1 hour, the time for cycling was shorter than "normal" and the rate of temperature rise was higher. Observations during which the finger was maintained at a constant temperature of about 34° C while the CBTS was modified indicated that finger temperature per se is a relatively unimportant influence on the pattern of the CIVD response. The more potent variable affecting the temperature cycling and the general pattern of the local circulatory response under these conditions appears to be the CBTS.

METABOLISM OF FREE FATTY ACIDS (FFA) BY FOREARM TISSUES IN MAN. R. Andres, M. Baltzan* and K. L. Zierler. Dept. Med., Johns Hopkins Univ. and Hosp. and Baltimore City Hosps., Baltimore, Md.

Forearm metabolism was measured as previously described (J. Clin. Invest. 35: 671, 1956 and 36: 723, 1957). The R.Q. of deep tissues in 45 normal subjects was 0.76 ± 0.018 (SEM). Only 16 ± 4.6% of oxygen consumption could be accounted for by glucose uptake (corrected for lactate production). The missing substrates for oxidation would be expected to be substances yielding an R.Q. of 0.71, i.e., fatty acids. We were not able to demonstrate with consistency that the FFA fraction (Gordon's and Dale's methods used) was a major substrate. Results in 47 subjects were as follows: in 1/3 of the subjects, half or more of the O_2 uptake could be accounted for by uptake of FFA; in 1/3, less than half of the O_2 uptake was accounted for; and in 1/3, the A-V difference was negative, that is, an apparent output of FFA from deep tissues occurred. Forearm venous blood from superficial tissues had higher concentrations of lactate, O_2 and FFA and lower concentrations of glucose and K than deep venous blood, implying metabolic difference between fat and muscle. FFA output occurred in 85% of the superficial veins. Analysis of data from those deep veins which showed large FFA output revealed that the total metabolic pattern resembled that of a superficial vein. We conclude that blood collected from a catheter which anatomically lies in a deep forearm vein may actually be sampling predominantly blood from deep-lying adipose tissue or may be collecting blood from superficial tissues via venous intercommunications. These factors may have obscured the detection of FFA uptake by muscle. A sex difference in FFA metabolism has also been demonstrated: female subjects have higher arterial concentrations and greater uptake of FFA by deep tissues than males.
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CHOLINESTERASE/MONOAMINE OXIDASE RATIOS IN THE AVIAN CENTRAL NERVOUS SYSTEM. M.H. Aprison, T.L. Folkerth* and K.M. Hanson*. Indiana Univ. Med. Center, Indianapolis, Ind.

Some investigators think that acetylcholine (ACh) and serotonin (5-HT) act as neurohumors. Cholinesterase (ChE) and monoamine oxidase (MAO), the enzymes which keep these two important compounds at physiological levels are widely distributed in the central nervous system (CNS) as well as in other parts of the body. However, it is extremely interesting that in the CNS, high ChE activities usually are found where MAO levels are low. Davison (Physiol. Rev. 38, 729, 1958) summarized some human tissue data and showed that ChE/MAO ratios for caudate nucleus and putamen were over 100 whereas the cortex was under 10. These findings suggest that each system may be selectively involved in a specific brain part, or may interact with each other under certain physiological conditions. Several investigators have shown that 5-HT can inhibit ChE in vitro. Aprison (Fed. Proc. 19, 275, 1960) reported 50% inhibition of brain ChE activity when ACh and 5-HT were present in equal molar concentrations ($3x10^{-3}M$). Further studies in which the brain ChE and MAO activities are compared in other species seem in order. Since we are using pigeons in a neurochemical-behavioral project, it was decided to determine the ChE(μMACh/gm/hr)/MAO(μM NH_3/gm/hr) ratios in specific brain parts. The ChE/MAO ratios for the cortex, caudate nucleus, mid-brain, cerebellum and medulla-pons are 85, 135, 174, 415, and 76 respectively. When compared with a peripheral organ such as liver (14), the brain ratios are much higher.

DETECTION OF RETROGRADE PASSAGE OF INDICATOR FROM AORTA TO LEFT VENTRICLE IN DOGS. Egas Armelin,* Leon Michaels,* H. W. Marshall,* D. E. Donald* and E. H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Detection of indicator in the left ventricle immediately after injection into the root of the aorta is proof of retrograde passage across the aortic valve and can be used to assess aortic regurgitation. Dilution curves of indocyanine green were recorded simultaneously from the left ventricle and femoral artery of 26 control dogs and 38 dogs with experimental aortic regurgitation, all with closed chests. The effects of variation in sampling site in the left ventricle and injection site in the aorta and time of injection in the cardiac cycle on the ratio of the areas of the immediately appearing portion of the left ventricular curve to the femoral curve (regurgitant fraction, RF) were studied. Synchronization of injection period to coincide with systole or diastole caused little variations in RF. However, the RF values from short duration injections (40 msec.) were time sensitive; RF values were minimal with injections in late diastole and early systole and maximal, in late systole and early diastole. Physiologic regurgitation was detected in normal dogs during a short, sharply delineated period just at the end of systole apparently related to valve closure. The correlation coefficient between RF values from nonsynchronized injections extending over several cardiac cycles and percentage regurgitation from back perfusion studies at necropsy was 0.85. This was superior to other indicator dilution and pressure pulse methods studied.

A NEW THEORY OF THE REGULATION OF BREATHING. B.W.Armstrong, H.H.Hurt, Jr., J.M.Workman and R.W.Blide. U. of Md. School of Med., Baltimore, Md. (intr. by D.B.Dill, Army Chemical Center, Edgewood Arsenal, Md.)

During muscular exercise the mixed venous P_{CO_2} ($P\bar{v}_{CO_2}$) and acidity ($H^+\bar{v}$) as well as arterial acidity (H^+a) are greater than at rest while the Pa_{CO_2} remains essentially constant. The relationship between ventilation ($\dot{V}$) and each variable, except Pa_{CO_2}, is statistically significant. These considerations suggest that the hyperpnea of muscular exercise can be explained if the classic concept that humoral control of breathing is mediated only by receptor mechanisms in the arterial blood stream (the respiratory center, the carotid and aortic bodies) is expanded by postulating a chemoreceptor, probably in the pulmonary artery, whose activity is related to $P\bar{v}_{CO_2}$ and $H^+\bar{v}$. This concept has been tested in dogs by measuring alterations of P_{CO_2} and H^+ of arterial and mixed venous blood, produced by injections of lactic acid or sodium bicarbonate solutions, by CO_2 inhalation, and by muscular exercise. The resulting hyperpneas cannot be explained on the basis of arterial or mixed venous changes; they can be explained if both arterial and mixed venous changes are considered. Harvard Fatigue Laboratory data (J. Physiol. 66:9,1928, 69:18,1930), from normal men at rest and exercise, have been used to quantitate the concept. Some relationships found are:

$\dot{V} = 1.1\ H^+a + 2.3\ P\bar{v}_{CO_2} - 140.$ SE: 10.0 L/min.

r $\dot{V} \cdots H^+a \cdot P\bar{v}_{CO_2} = 0.92$; P: < 0.001.

Ventilatory responses to diabetic acidosis, shock, CO_2 inhalation, NH_4Cl and $NaHCO_3$ administration agree well with the $\dot{V}$ "predicted" by this equation; it also "predicts" the $\dot{V}$ of exercising subjects reported by Mitchell et al (J. Clin. Invest. 37:1693,1958). The Glomus pulmonale recently described by V. Krahl (Bull.U. of Md. Sch. of Med. July 1960) may be part of the postulated mixed venous chemoreceptor mechanism.

A MICRO METHOD FOR DETERMINING THE ACID-BASE VALUES OF BLOOD. Poul Astrup (intr. by J. W. Severinghaus). Department of Clinical Chemistry, Rigshospitalet, Copenhagen, Denmark.

A micro-method, suitable for capillary blood, is described for determining pH, PCO_2, standard bicarbonate, base excess and buffer base of blood.

The method requires measurement of actual pH and pH after equilibration with carbon dioxide at two known tensions. For this purpose a new micro equipment has been developed, involving a capillary glass electrode (for 25 μl samples) and a device for equilibration of micro quantities of blood (30-50 μl) with gases.

Capillary blood is drawn from ear or finger. For the actual pH, about 20-25 μl is sucked directly into the capillary electrode and the reading is made immediately, or it is sucked from blood drawn anaerobically into a heparinized capillary glass tube. About 80-90 μl of blood from two capillary glass tubes is divided between two of the chambers of the equilibration apparatus. This is shaken mechanically (2600 RPM) and after 3 minutes the pH values in the two samples are measured. By using these two values and the known gas PCO_2, the rectilinear pH/log PCO_2 line is drawn and the PCO_2, standard bicarbonate and base excess can be calculated. The method is highly accurate, as the 3 values can be found with an error of less than $\pm$ 2%.

CENTRAL ROUTES TAKEN BY REGENERATING OPTIC FIBERS. Domenica G. Attardi* and Roger W. Sperry. Calif. Inst. of Tech., Pasadena, Calif.

There is good physiological evidence that regenerating optic fibers of fishes and amphibians find their original place of termination in the optic lobe. Whether the course taken by the growing fibers in regaining their central terminals is a random one or is selective was investigated. Histological studies were made in which section and regeneration of the optic nerve was combined with retinal lesions in goldfish and other species. The results suggest definite preferential selection by the fibers for their original central pathways: evident in the choice of medial or lateral tracts, in the point of entrance into the tectum, and later, the point of entrance into the plexiform layer within the tectum. Neuronal specificities thus appear to operate in the patterning of fiber pathways of the central nervous system as well as in the details of the synaptic interconnection.

CORONARY BLOOD FLOW AS A CRITICAL DETERMINANT OF CARDIAC PERFORMANCE AND SIZE. M. Bacaner, J. Connelly, D. Bruns (Intr. by E. L. Dobson), Donner Lab., Univ. of Calif., Berkeley, Stanford Univ. Hospital, San Francisco.

Starling's "Law of the Heart" relating the strength of contraction directly to diastolic size is still held to express the primary mechanism regulating in vivo performance although it has been shown that stroke output and size vary both independently and inversely with each other. Because cardiac metabolism is fundamentally influenced by coronary blood flow (CBF), cardiac circulation was studied to define its role as a regulating and limiting factor of cardiac performance and size through its effect on heart metabolism. Graded pulmonary artery constriction (PAC) was used to provoke heart failure and shock. After establishing heart failure, blood was shunted from the inferior vena cava to a reservoir then pumped into a femoral artery to raise blood pressure. CBF was determined by the disappearance of Na^{22} injected into the left ventricular myocardium, cardiac output by the arterial dilution curve. It was found that (1) PAC caused a progressive decrease in myocardial contractility and increase in size as CBF fell, (2) V-A shunting caused a progressive return of working capacity and decrease in heart size as CBF was augmented (while the pulmonary artery remained constricted). These data indicate that the strength of contraction, size and adaptive mechanisms to increased work loads may be critically determined by the coronary circulation and independently of the work load.

ON THE NATURE OF THE UNCHANGING DIAMETER IN ISOLATED MICROSCOPIC VESSELS UNDER PRESSURE VARIATION. Silvio Baez and Harold Lamport. Dept. Anesthesiology, N.Y.U. Medical Center, New York and Dept. Physiology, Yale Univ. School of Med., New Haven, Conn.

Our studies of the effects of pressure in isolated microscopic vessels have disclosed two constant characteristics unique to the smallest blood vessels; (a) a selective closure of precapillary sphincters at positive pressures; and (b) an unchanging vessel diameter (plateau) under considerable pressure variation.

The nature of the latter vascular feature (b) has been further analyzed by the following experimental approach: 1. The effect of static pressure was tested on isolated arterioles, ranging from 34 to 42 micra in diameter, using various perfusion fluids: rat plasma and serum, 25% gelatine, 3% dextran, 3% albumin solutions and kerosene. Although dextran and gelatine solutions show increased apparent viscosity at lower ranges of pressure as determined by the Oswald Viscometer, no significant difference appears in plateau formation with all 5 fluids employed. 2. In another set of experiments, the responsiveness to topical epinephrine of the isolated vessels under decrement and increment of static pressure was determined, keeping vessel diameter constant. The results indicate that the log of the dose of epinephrine required to produce a given change in the vessel radium is proportional to the original tension of the vessel. The results of these experiments warrant, for the present, the following conclusions: (a) that plateau formation is not due to lack of pressure transmission but is inherent in the nature of the vessel wall; and (b) that the shorter plateau described for innervated preparations may be related to circulating neuro-humors or tissue mediators.

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SIMULTANEOUS T-1824 AND RISA TIME-CONCENTRATION CURVES IN SPLENECTOMIZED DOGS. Carleton H. Baker. Dept. of Physiology, Med. Coll. of Georgia, Augusta.

Time concentration curves of several tag-protein complexes were determined over a period of five hours in chronically splenectomized dogs anesthetized with morphine and sodium pentobarbital. T-1824 blue dye in distilled water, human albumin solution tagged in vitro with T-1824, or autologous dog plasma tagged in vitro with T-1824 were injected at the same time as I^{131}-tagged human serum albumin (RISA) or in vitro I^{131}-tagged dog fibrinogen. The T-1824 solutions contained 1.5 mg. of dye per ml. of solution. Sufficient dye was injected to have an optical density of about .500 in the dog's plasma and enough radioactive I^{131}-tagged compounds so there were approximately 3000 counts/min./ml. of plasma at 10 minutes post injection. Arterial samples were taken at 5, 10, 15, 20 and 30 minutes post injection and then at 20 minute intervals thereafter. It was noted that the disappearance rates of the I^{131}-tagged proteins are the slowest of the various complexes and the semilogarithmic slopes are smooth and linear. However, the disappearance rate of the various T-1824 solutions is an essentially non-linear one with many abrupt changes in concentration. It also appears that the disappearance rate of the in vitro tagged T-1824 protein complexes was less than that of the distilled water solution of T-1824, but not as low as the I^{131}-tagged compounds. (Supported by USPHS grant H-4573).

CELLULAR SITE FOR SYNTHESIS OF HUMAN PROTHROMBIN AS REVEALED BY FLUORESCENT ANTIBODY. William J. Baker * and Marion I. Barnhart. Dept. Physiology and Pharmacology, Wayne State University, Detroit, Michigan.

The objective of this investigation was to identify the specific cells engaged in synthesis of prothrombin utilizing immunocytochemical techniques. Purified human prothrombin was used in rabbits to elicit potent antiprothrombin sera. A single injection of human prothrombin (1-4 mg/Kg) was mixed with $Al(OH)_3$ as an adjuvant and injected IM into a rabbit. Antisera were obtained 10 days later which were of comparable strength to those produced using Freund's adjuvant which required considerably greater amounts of antigen, 3 injections and about 5 weeks to harvest. These antisera did not form precipitin bands with purified human fibrinogen nor exhibit any common antigenic components with antiprothrombin sera to dog or bovine prothrombin. The described immunologic evaluation was made with the Wilson modification of the Ouchterlony agar gel diffusion technique run at several concentrations. Gamma globulin concentrates were prepared by Ethodin fractionation of the antiprothrombin serum and conjugated with lissamine rhodamine B 200. Such rhodamine labelled antihuman prothrombin provided the fluorescent tag for the study of human liver imprints. Liver parenchymal cells containing adequate concentrations of prothrombin attracted fluorescent antibody and produced patches of brilliantly fluorescing cells. Not all liver cells react with the specific antiprothrombin. This may mean that the liver parenchymal cell is specialized or that there is cyclic prothrombin synthesis (Supported by the Michigan Heart Association).

CHRONIC AWAKE DOGS WITH TOTAL CARDIAC DENERVATION. Basdeo Balkissoon* and Edward Hawthorne. Howard Univ. School of Medicine Washington, D. C.

Total cardiac denervation compatible with chronic survival in dogs was accomplished by a surgical technique involving right thoracotomy and right sided cardiac denervation followed in two weeks by left sided denervation. On both sides all branches of the thoracic vagus above the cardiac apex were sectioned and all thoracic sympathetic ganglia through the eighth were excised. At thoracotomy, mercury in rubber strain gages were placed around the ascending aorta and the middle of the left ventricle for recording aortic circumference (AC) and ventricular circumference (VC) changes in the awake dogs. Bradycardia was characteristically absent following administration of epinephrine (0.05 mg I.V.) in seven chronic, denervated dogs. This response was unaltered by atropinization (0.02 mg/kg). Awake, normal dogs characteristically showed a bradycardia after epinephrine in this dosage and this effect was blocked by atropinization. Semicontinuous monitoring of AC, VC, and heart rates over 24 hours (two minutes every half hour) revealed a remarkable constancy of heart rate in denervated as compared to normal dogs. Rapid (one to four minutes) infusions of a blood-dextran mixture into a peripheral vein of standing denervated dogs increased end-diastolic VC and stroke volume as indicated by the VC gage. This was accompanied by an increase in systolic and diastolic AC. Infusions in awake, intact dogs only caused an increase in heart rate. Awake dogs with denervated hearts appear to obey Starling's Law of the heart.

SURVIVAL OF RATS CHRONICALLY EXPOSED TO SULFUR DIOXIDE:(1)
C. O. T. Ball,* R. M. Heyssel,* O. J. Balchum(2),* G. O. Elliott* and G. R. Meneely. Vanderbilt University School of Medicine, Nashville, Tennessee.

Three hundred and five male rats were randomly assigned to constant temperature humidity controlled exposure chambers chronically breathing 0, 1, 2, 4, 8, 16 and 32 ppm SO_2. The rats are transferred daily to clean, serviced cage racks, are carefully examined and weighed weekly with hematologic studies quarterly and pathologic studies at death. Incidence and degree of wheezing, eye opacities, loss of fur and scaley tails are associated with sulfur dioxide concentrations. The control group maintains the best weight. White blood cell counts, per cent neutrophils and hemoglobin are elevated in the SO_2 exposed groups. After 8 months, all of the control group, 93% of the 1-16 ppm groups and 82% of the 32 ppm group were alive. At 12 and 16 months the corresponding per cent survivals were 91 and 75% among the controls; 84 and 68% in 1-16 ppm SO_2 groups and 58 and 44% in the 32 ppm SO_2 group.

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THE PREPARATION AND CHARACTERISTICS OF A HIGHLY PURIFIED MgACTIVATED MUSCLE ATPase. Iris Maggiolo Barbato* and Norman R. Alpert. University of Illinois, College of Medicine, Chicago, Illinois.

Kielley and Myerhof reported the isolation of a particulate muscle ATPase, different from actomyosin which was activated by Mg and inhibited by Ca. In our initial studies of this preparation we found an extremely rapid initial ATPase rate which was altered within the first minute to a much slower more stable rate. This was comparable to the initial and secondary rates observed for actomyosin ATPase. With the thought that an impurity might be responsible for the inactivation further purification of the enzyme was attempted. This purification consisted of a series of extractions with 1% digitonin and subsequent precipitation with 70-90% ammonium sulphate. The optimum activity of the purified enzyme was found at 40° C and pH 7.0 at a ATP: Mg ratio of 4:1. Electron microscopy of the purified sample indicated the absence of particulate matter. Micro quantitative methods for lipids showed the presence of phospholipids but the absence of cholesterol. The high initial rate was still present in the purified enzyme. Km values calculated for the first and fifth minute are 8×10^{-3} and 5×10^{-3} respectively. This research was supported in part by USPHS Grant H2345.

PURIFICATION AND PROPERTIES OF MITOCHONDRIAL MONOAMINE OXIDASE FROM BEEF LIVER. Libero Barbato* and L. G. Abood. University of Illinois Medical School, Dept. of Psychiatry, Chicago, Illinois.

Mitochondria from beef liver have been extracted three times with a 0.5% (final conc) Triton solution, respectively at pH 7.5, 8, 8.5. The last extraction gives a clear solution, with a 5-fold increase in specific activity. A final twenty-fold purification is obtained by treating the solution with calcium phosphate gel first at pH 8.5, then at pH 7, and eluting the activity from the gel several times with 0.2 M K_2HPO_4. The Michaelis constant (Km.) of the crude mitochondrial Triton solution is 6.1×10^{-3}M and that of the purified enzyme 8×10^{-3}M. Activity is measured either manometrically, with tyramine as substrate, or spectrophotometrically, with benzylamine as substrate. The activity of a crude mitochondrial solution is not linear with time, while the activity of the purified enzyme is linear during the first two minutes. p-chloromercurobenzoate gives 100% inhibition at a final concentration of 3×10^{-4}, 90% at 1×10^{-4} and 65% inhibition at 2×10^{-5}. This inhibition does not seem to be competitive. The activating effect of KCN and the inhibitory effect of iproniazid have been confirmed using as substrate kynuramine. The enzyme appears to be also activated by incubating in phosphate buffer at pH 8 at 25°. The effect of phenantroline has been studied both with benzylamine and with kynuramine. With benzylamine as substrate complete inhibition occurs at 3×10^{-4}M and with kynuramine, 3×10^{-3}M gives only 50% inhibition. The enzyme shows an optimum at pH 8.5 and an inflection point at pH 8, which could not be resolved in another maximum. (Supported by ONR)

MODIFICATIONS OF PROTHROMBIN SYNTHESIS IN THE DOG USING FLUORESCENT ANTIBODY. Marion I. Barnhart and Gordon F. Anderson*. Dept. Physiology and Pharmacology, Wayne State University, Detroit, Mich.

Immunochemical procedures have identified liver parenchymal cells as sites for the synthesis of prothrombin. The present study is concerned with the dynamic aspects of prothrombin synthesis and makes use of agents known to modify the prothrombin function of the liver. A correlative study was made on circulating levels of various plasma proteins and the cellular state of the liver following coumarin drugs and vitamin K_1 therapy. Coumadin (3 mg/Kg) was given I.V. and 24 hours later the plasma prothrombin was essentially zero while the circulating fibrinogen remained normal. Fluorescent microscopy and specific fluorescent antiprothrombins were used in the cellular evaluation of liver function. Coumarin derivatives appear to interfere directly in the synthesis of prothrombin rather than promote storage and inhibit the release of prothrombin from the hepatic cell. Vitamin K_1 administration produced renewed synthesis of prothrombin as indicated by brightly colored patches of fluorescent cells. Even though normal circulating plasma levels of prothrombin were reached within 5 hours liver cells were not as brilliant in their fluorescence as in the normal pre-treatment animal. Also, not all of the liver parenchymal cells reacted uniformly with the fluorescent antibody. The questions of specialization of function or cyclic production of prothrombin by liver parenchymal cells still remain to be clarified. (Supported by the Michigan Heart Association)

THE ROLE OF THE VEINS IN THE CARDIOVASCULAR RESPONSE TO CAROTID OCCLUSION. H.J.Bartelstone and H.H.Wang (intr. by S.C.Wang) Dept. of Pharmacology, College of Physicians & Surgeons, Columbia Univ., New York City.

It was reported previously that carotid occlusion resulted in an increase in venous return of venous origin. By preventing this increase in venous return from reaching the heart the pressor response to carotid occlusion was markedly diminished. In the present study further investigation of this venous contribution to the carotid occlusion response was carried out. In anesthetized, thoracotomized, vagotomized dogs the following measurements were made: venous, arterial and left intraventricular end-diastolic (EDP) pressures with Statham guages; cardiac contractility with a Walton guage, and cardiac output with a rotameter. Carotid occlusion produced: little change in central venous pressure; increase in cardiac contractility, EDP and arterial pressure; maintenance or increase in cardiac output and considerable increase in total peripheral resistance (TPR). When, during subsequent carotid occlusion, the increase in venous return of venous origin was aspirated from the inferior vena cava, the following changes ensued: reduction of the increases in contractility and EDP; marked reduction of the arterial pressure rise, and a precipitous fall in cardiac output. The increase in TPR was not modified. The decrease in cardiac output was much greater than that which could be accounted for by the volume of venous blood aspirated. Re-infusion of this volume at the "aspiration rate", during the same carotid occlusion run, re-established typical carotid occlusion responses. Of significance is the fact that removal of arterial blood, in an identical manner, had an insignificant effect on cardiac output. The ability of the competent heart to respond to carotid occlusion by maintaining or increasing cardiac output is dependent upon reflex venoconstriction and the resultant increase in venous return of venous origin. (Supported by a grant from USPHS B 31C)

HYPOCAPNIA AND ERYTHROPOIESIS. R. G. Bartlett, Jr. and N.E.Phillips.* U. S. Naval School of Aviation Medicine, Pensacola, Fla.

The unfailing correlation between hypoxia and erythropoiesis accompanying altitude acclimatization seems to have given rise to an unquestioned cause-effect relationship. However, accompanying a noticeable hypoxia there is also a hypocapnia produced by the respiratory loss of carbon dioxide stores. Therefore, hypocapnia also is positively correlated with erythropoiesis, and such a correlation raises the obvious question of a possible cause-effect relationship. Experiments were designed to ascertain whether or not the hypocapnia accompanying altitude acclimatization might be a factor in the increased erythropoiesis observed. There was a significantly lesser percentage of reticulocytes in the tail blood of mice subjected to a carbon dioxide rich but oxygen poor atmosphere (5% CO_2, 10% O_2), as compared to animals exposed to a similarly low oxygen atmosphere without added carbon dioxide. There was also a lesser weight loss in the animals breathing CO_2. During the first few hours of exposure the hypocapnic animals were definitely less active than were the normocapnic animals. From these preliminary observations, then, it is evident that the hypocapnia accompanying altitude acclimatization may be a contributing factor in the erythropoiesis and other factors observed.

INDIVIDUAL BLOOD DIFFERENCES IN THE OXYGEN DELIVERY RATE OF ERYTHROCYTES STUDIES POLAROGRAPHICALLY. J. P. Baumberger, Helen C. Leong* and Kathleen Bardwell*. Physiology Dept., Stanford University, Stanford, California.

The current produced at a dropping-mercury-electrode cathode in a polarographic circuit is much greater in whole blood than in buffer saturated with the same gas mixture. The ratio of the two currents is a measure of the Oxygen Delivery Rate (ODR) by the erythrocytes. This functional characteristic is related to the degree of reduction of the hemoglobin and in general shows the following relationship: (100/Hb%) (Bound O_2 /Dissolved O_2) = 42.3 (ODR-3). Although the Bound O_2 /Dissolved O_2 changes 60% in going from 25% to 94% oxyhemoglobin, the ODR changes from 12 to 4, that is, the ODR at a low saturation is much greater than at a high saturation and this serves as a compensating factor in hypoxia. The blood of different individuals have ODRs which are different. In some bloods the ODR is of a different magnitude, e.g. at 25%, 50% and 75% saturations, respective ODRs are 4.6, 5.9 and 8.75 in one individual and 7.05, 9.5 and 11.95 in another. While in others the change in ODR with saturation is more marked than usual, e.g. 10.3, 17.5, 24.7. We do not know the basis of these individual differences but will assume the working hypothesis that they depend on differences in erythrocytes oxygen permeability or on hemoglobin-polymer oxygen interchange reactions or on rouleau behavior of the blood. Conclusions: 1) Oxygen delivery rate increases with reduction. 2) Individual bloods differ in the delivery reduction relationship a) as to magnitude and b) as to relative change.

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ACETOACETIC ACID METABOLISM BY SKELETAL MUSCLE FIBERS FROM CONTROL AND DEPANCREATIZED RATS. C. H. Beatty, A. Marco,* R. D. Peterson,* R. M. Bocek* and E. S. West.* Dept. of Biochemistry, Univ. of Oregon Med. School, Portland, Oregon.

Previously we have demonstrated that at substrate levels of 4 mM/L acetoacetate, both diaphragm and adductor fibers from fed alloxan diabetic rats take up less acetoacetic acid than diaphragm and fibers from fed control rats. In the present investigation, with a substrate level as low as 1 mM/L acetoacetate, there was a decrease of over 50% in uptake by fibers from fasted depancreatized rats (0.15 $\pm$ 0.02 SE mg/g/hr wet wt, n = 7) as compared to the fasted control series (0.32 $\pm$ 0.03 mg/g/hr, n = 8). In the presence of 4 mM/L acetoacetate, fibers from fasted depancreatized rats (0.22 $\pm$ 0.04, n = 6) again took up less than half as much acetoacetate as did fibers from fasted controls (0.50 $\pm$ 0.04, n = 6). It was possible to demonstrate low acetoacetate uptakes by fibers from depancreatized rats in both phosphate and bicarbonate buffered media. Since muscle comprises about 40% of the body weight and liver only about 5%, the 50 to 60% reduction in uptake of acetoacetate by muscle from diabetic rats would have an effect on ketonemia comparable to the 4.8-fold increase in production of ketone bodies reported for diabetic liver slices. The experiments discussed above were done in the presence of 150 mg % glucose. However, the addition of this amount of glucose to the medium had no effect on acetoacetic acid uptake (-0.01 mg/g/hr for the control series, +0.03 mg/g/hr for the diabetic series). The addition of glucose plus insulin (0.47 units/ml) increased uptake by 30% in the control (+0.15 mg/g/hr), and by 100% in the diabetic series (+0.22 mg/g/hr). No data was considered significant unless the P value was $< .02$. The addition of glucagon (20 ug/ml) had no effect on acetoacetic acid uptake.
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THE USE OF PERMANENTLY VISUALIZED ORGANS IN STUDYING THE EFFECTS OF "G" FORCES IN DOGS. E. L. Beeding* and F. R. Steggerda. Holloman Air Force Base, New Mexico.

In 1937, Steggerda and Gianturco demonstrated that the colon of cats can be made permanently opaque to X-rays by injecting Thorium Dioxide (Thorotrast) into the walls of this organ. In the present experiments attempts were made to visualize other organs in the abdominal cavity and then to record distortions of these organs under varying "G" forces in the apparently normal unanesthetized dog. Organs successfully visualized with this technique include the colon, urinary bladder, kidneys, stomach and diaphragm. The liver and spleen also may be visualized quite satisfactory by injecting the opaque material directly into the blood stream. A suspension of finely ground particles of $BaSO_4$ (Micropaque) has in some cases been substituted for Thorotrast. By using a Micronex X-ray machine, the tube of which was mounted over a decelerated sled on which the animal was positioned, X-ray pictures were made of the amount of organ displacement in comparison to organ position noted before the start of the experiment. Adjustments were so made that the X-ray picture was taken at the point of maximum deceleration. The X-ray machine is capable of giving exposure times as short as 1/2000 of a second and thus affords a clear outline of the edges of the organs visualized.

EFFECT OF REMOVAL OF OLFACTORY BULBS ON TASTE DISCRIMINATION IN NORMAL AND BRAIN OPERATED RATS. R. M. Benjamin, Neurophysiology Laboratory, Univ. of Wisconsin Medical School, Madison 6, Wis.

Ablation of the cortical taste area produced transient impairment of taste discrimination (quinine hydrochloride) and coagulation of the thalamic taste nucleus produced permanent impairment of taste discrimination as measured by the traditional preference technique. Additional removal of the olfactory bulbs had no effect on thresholds measured in this fashion. Different results were obtained if thresholds were measured by a conditioned avoidance technique using electric shock. Normal thresholds were lower than by the preference method, both cortical and thalamic removals were followed by only a temporary loss of discrimination which returned to normal levels with further training, and finally, removal of the olfactory bulbs at this stage produced a marked and permanent increase in "taste" thresholds. These results suggest that quinine solutions have an olfactory component which is not used in the preference situation but which can become a conditioned stimulus in a shock avoidance situation. Thus if the animals are motivated by shock they will avoid a quinine solution on the basis of its olfactory properties at concentrations too weak to taste. (Aided by grant 3-1932, NINDB, USPHS.)

CIRCADIAN PHYSIOLOGIC RHYTHMS AND LOWERED BLOOD 5-HYDROXYTRYPTAMINE IN HUMAN SUBJECTS WITH DEFECTIVE MENTALITY. Heinz W. Berendes*, Egon Marte*, Robert J. Ertel*, J. A. McCarthy*, John A. Anderson*, and Franz Halberg. Cambridge State School & Hospital, Cambridge, Minn. and Medical School, University of Minnesota, Minneapolis 14, Minnesota.

Circadian (about 24-hr.; circa, dies) periodic changes were mapped for 5 phenylketonuric patients with verified high blood phenylalanine levels ($\bar{X}$=24.9±0.54 mg.%), 5 mongoloids and 5 medically normal subjects. On the 10 patients, rectal temperatures were determined at 6-hr. intervals for several months. These longitudinal temperature profiles revealed periodic components that were synchronized with the 24-hr. routine of institutional life. Beats on the temperatures record of some cases suggested the interaction of additional free-running though circadian periodicity. Blood profiles with 4-hrly. sampling during a 24-hr. period also were obtained for WBC, eosinophils (chamber count), cortisol (Mason) and 5-hydroxytryptamine (Davis). Circadian periodicity was ascertained in such transversal profiles, with significant phase differences among the variables studied. The blood profiles provide a refined standard of reference, revealing e.g. increases to 10,000 or more WBC/mm^3 at peak-time ($\bar{X}$ for mongoloids at 17:00 = 11,300/mm^3). Moreover, in both groups of patients blood 5-hydroxytryptamine levels were significantly lower by comparison to normals, living on the same diet ($P < .05$); the mean values were .140±.041 µg/ml for phenylketonurics, .209±.024 µg/ml for mongoloids and .316±.016 µg/ml for normals. The finding of lowered blood 5-hydroxytryptamine levels in these patients with defective mentality is strengthened by the periodicity approach which rules out possible differences brought about by sampling in different stages of circadian rhythm.

BEHAVIOR OF THE NON-EMBOLIZED VESSELS ACCOMPANYING GRADED DIFFUSE PULMONARY EMBOLISM. Theodore Bernthal, Alan Horres*, and Joseph T. Taylor, III* Department of Physiology, Medical College of South Carolina, Charleston, S. C.

The vascular bed of the left lower lung lobe in dogs was embolized *in situ* in steps with 75u glass beads during auto-perfusion with arterial blood at several perfusion pressures and the effects upon left lobar pulmonary artery blood flow measured. Changes in shape of the derived flow-pressure and resistance-pressure curves and in value of the ratio $\frac{\text{flow at high perfusion pressure}}{\text{flow at low perfusion pressure}}$ were analyzed. Such analyses indicate that, aside from the obstruction of blood flow occurring in the embolized vessels in the perfused lobe, the non-embolized vessels there also offered progressively increasing resistance to blood flow as embolization proceeded and with characteristics suggesting that this was due to moderate progressively increasing vascular tone. (Supported by Grant H-1320, National Institutes of Health, USPHS)

EFFECT OF HYPOPHYSECTOMY ON THE ADRENOCORTICAL RESPONSE TO BILATERAL CAROTID CONSTRICTION. E. G. Biglieri* and W. F. Ganong, Metabolic Unit and Dept. of Physiology, School of Medicine, University of California, San Francisco 22, Calif.

To determine whether the reported rise in aldosterone secretion following bilateral common carotid constriction is dependent on ACTH, 5 hypophysectomized dogs were studied. Adrenal venous blood was collected 1 and 1½ hours after hypophysectomy. The common carotid arteries were then constricted and samples obtained 15 min.(2 dogs), 30 min.(3 dogs), and 60 min. thereafter. The constriction lowered lingual blood pressure to an average of 55/51 mm. Hg.; systemic blood pressure rose, then fell slowly to control values by the end of the experiment. Aldosterone was measured by the double isotope dilution technique and 17-hydroxycorticoids by the Silber-Porter method. 17-hydroxycorticoid secretion remained unchanged at < 1.0 µg/min. Aldosterone values (mean ± Standard error) were: Control 1, 30 ± 7.8 mµg/min.; Control 2, 26 ± 8.5 mµg/min.; 15 min. after constriction 11 mµg/min.; 30 min., 10.0 ± 2.1 mµg/min.; 60 min., 6.0 ± 1.8 mµg/min. In similarly studied normal dogs, a rise in aldosterone secretion occurred after constriction. The data suggest that any rise in aldosterone secretion following carotid constriction is dependent on pituitary secretion, presumably of ACTH. (Supported by Commonwealth Fund).

THE RESPONSE OF THE ABDOMINAL MUSCLES IN CAT TO POSITIVE PRESSURE BREATHING. Beverly Bishop (intr. by F. R. Griffith, Jr.). The Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

Electromyographic experiments on dial-anesthetized cats have revealed that the abdominal muscles assume an active expiratory role during continuous positive pressure breathing (4 to 20 cm H_2O). That this abdominal muscle expiratory response to positive pressure is not mediated exclusively as a segmental stretch reflex has been demonstrated by the persistence of the response when the abdomen is completely opened and by abolition of the response when the spinal cord is transected at the thoracic level. Bilateral sectioning of the dorsal roots from L_1 to L_4 also eliminates the response. Thus, local afferent inflow would seem necessary but insufficient for maintaining the positive pressure response. Cervical vagotomy initially eliminates the response indicating the importance of vagal afferent impulses. Differential blocking of the vagi with novocaine or compression suggests that the vagal afferent impulses subserving this positive pressure reflex are initiated by receptors distinct from lung stretch receptors. Future experiments should reveal the type and location of the receptors involved.

NEURAL CONTROL OF SODIUM EXCRETION. William D. Blake. Univ. of Maryland School of Med., Baltimore, Md.

Despite reports to the contrary "denervation diuresis" is generally held to result from increased glomerular filtration rate (GFR) in the denervated kidney. The following studies were undertaken to demonstrate the importance of variables other than GFR in promoting excessive excretion of sodium from the denervated kidney. Following acute, unilateral, renal denervation in pentobarbital anesthetized dogs, clearance studies were used to estimate renal function in the separate kidneys. Ratios of function, denervated/innervated kidney, during intravenous infusions of hypertonic NaCl, urea or mannitol indicated that excessive excretion of sodium by the denervated kidney was exaggerated by NaCl infusion or independently by increased GFR and diminished concomitant with increasing water and solute excretion. Depth of anesthesia was not a variable in these experiments. The nature of the stimulus evoking sodium conservation by the innervated kidney was not defined, but the failure of the denervated kidney to respond was clearly demonstrable and attributable, in part, to a defect in sodium "reabsorption". (Supported by a grant from the Life Insurance Medical Research Fund.)

THE RENIN AND ANGIOTENSINASE CONTENT OF THE KIDNEY OF NORMAL AND RENAL HYPERTENSIVE RATS. Pedro Blaquier*, David F. Bohr, Alberto C. Taquini,Jr*, and Sibley W. Hoobler, Departments of Physiology and Internal Medicine, University of Michigan, Medical School, Ann Arbor, Michigan.

Renin and angiotensinase concentrations of the kidneys were determined in the following groups of rats: 1) 7 normal; 2) 12 with renal hypertension produced by unilateral clipping of the renal artery; 3) 11 unilaterally clipped, which failed to develop hypertension; 4) 22 with renal hypertension produced by clipping of the renal artery and contralateral nephrectomy; and 5) 7 unilateral clipped with contralateral nephrectomy which failed to develop hypertension. Kidney extracts were assayed for renin by two different methods: 1) direct intravenous injection into a rat sensitized by ganglionic blockade, and 2) the in vitro production of angiotensin which was subsequently assayed in a similar manner. Angiotensinase was determined by incubating the kidney extract for two hours at 37° with a known amount of synthetic angiotensin. Renin content was reduced in kidneys of all groups of rats with renal artery clips. The greatest reduction occured in the rats that failed to develop hypertension. The reduction in the untouched kidney was greater than that in the clipped kidney. One gram of the normal kidney is capable to inactivate 1 mg. (3000 Dog Units) of synthetic angiotensin under the conditions described above and no change in its concentration was observed in the different experimental groups. There was no significant difference between the weights of the kidneys in the normotensive and hypertensive groups. (Supported by a grant from the Michigan Heart Association.)

EFFECT OF ZYMOSAN ON PROPERDIN TITERS OF DOGS SUBJECTED TO HEMORRHAGIC SHOCK. B. Blattberg* and M. N. Levy.
St. Vincent Charity Hosp., Cleveland, Ohio.

Dogs were injected subcutaneously with 50 mgm. zymosan incorporated in adjuvants. Control animals were also selected but did not receive zymosan. After 2-3 weeks, all animals were subjected to oligemia at 35 mm. Hg arterial pressure for 150 minutes, then all shed blood was returned to the dog. Periodically, blood samples were drawn and properdin titers were determined by the phage neutralization assay. The zymosan injected dogs had considerably increased properdin levels at the time of hemorrhage. In all dogs, the titers remained constant during oligemia and fell in the post-transfusion period. Properdin titers fell to a greater extent in the injected dogs than in the control dogs, but rarely fell below the dog's control level.

THE AFFERENT MECHANISM OF THE BAINBRIDGE REFLEX. Clark M. Blatteis (intr. by Steven M. Horvath). U. S. Army Medical Research Laboratory, Fort Knox, Kentucky.

The effective stimulus for the Bainbridge reflex was studied in 36 morphine-premedicated (0.5 mg/kg), chloralose-anesthetized (100 mg/kg), closed-chest dogs by ivc, right atrium, right and left ventricles and pulmonary artery catheterization. Two different stimuli were used: the caval ostia and the right atrium were in the first instance perfused with 500 cc/min and 1000 cc/min of whole blood for 15 seconds, in the second instance distended by balloon and prong-catheters for 3 minutes. Heart rate (ECG), blood pressures and oxygen consumption were measured continuously; cardiac outputs were determined before and during each stimulus. The observatinns were made on 3 preparations: intact, carotid sinus baroreceptors bilaterally procaine-blocked, and bilaterally vagotomized dogs. The Bainbridge reflex was not elicited by an increase in the rate of flow or the volume of venous return; in the intact dogs the heart rate was slowed rather than increased during the perfusions, and it was not affected in the denervated preparations. Venous and arterial systolic pressures were increased in all the preparations, but least in the vagotomized dogs. Central venous hypertension alone likewise did not induce reflex cardiac acceleration since localized caval and right atrial distension produced no heart rate and blood pressure changes in any of the preparations used. Cardiac outputs were increased during perfusion, but not changed during distension. The heart accommodated to increased filling by increasing systolic discharge.

THE EFFECT OF CERVICAL SYMPATHETIC STIMULATION ON CEREBRAL OXYGEN TENSION. (Preliminary Observations) Byron M. Bloor and George C. Stevenson (intr. by J. W. Severinghaus) Dept. of Surgery, Western Reserve Univ., Cleveland, Ohio.

Quantitative pO_2 determinations have been carried out with platinum micro electrodes stereotaxically placed in the cortex, white matter, ventricle and cisterna magna of the African Green Monkey (Cercopithecus-sabaeus). The effect of cervical sympathetic and vertebral nerve stimulation has been studied. Unequivocal pO_2 changes have been produced in all loci with bilateral sympathetic stimulation and with bilateral sympathetic and vertebral nerve stimulation. Prompt decreases in oxygen tension were usually observed. In some instances, however, a sharp increase in brain pO_2 was observed concomitantly with a drop in cisternal oxygen tension.

EVOKED ACTIVITY IN THE SOMATOSENSORY CORTEX OF THE OPOSSUM. C. W. Bodemer* and A. L. Towe (intr. by N. B. Everett). Depts. of Anatomy and Physiology & Biophysics, Univ. of Washington Sch. of Medicine, Seattle.

Since the opossum is a primitive mammal, it presents an opportunity to study the phylogenetic as well as the ontogenetic aspects of evoked cortical activity. Both the distribution of evoked primary responses in the somatosensory cortex and the patterns of activity of individual neurons within it were investigated. Adult Didelphys virginiana were anesthetized with α-chloralose or Dial-urethane and paralyzed with decamethonium bromide or d-tubocurarine chloride. One cerebral hemisphere was exposed, the dura was reflected and the pial surface was bathed in saline or mineral oil. Gross potentials and single unit activity were recorded by standard methods. All evoked discharges were produced by stimulation of the palmar surface or individual digits of the forepaw contralateral to the recording site. Primary evoked responses occurred in a restricted patch of cortex 24 to 28 square mm. Usually, they were initially positive, diphasic waves measuring up to 2.5 mV in peak-to-peak amplitude. At maximal stimulus intensity the response began 9.0 to 9.5 msec after stimulation; the positive phase lasted about 9 msec and the negative about 11 msec. As the stimulus intensity was decreased toward threshold, the response began later, the change between threshold and minimum latency being about 7 msec. The amplitude of the primary response dropped rapidly to zero toward the periphery of the responsive cortex; the rate of change of peak voltage with distance was greater than in cat or monkey. Individual units were isolated within this active tissue at depths of 400 to 1200 μ below the pial surface. Their recorded behavior was similar in every respect to that of somatosensory units in the cat or monkey. (Supported by grant B 396 from the National Institute of Neurological Diseases and Blindness.)

A DIRECT RECORDING OF TENSION FROM ISOLATED ARTERIOLAR SMOOTH MUSCLE. David F. Bohr and Patricia L. Goulet*, Dept. of Physiology, University of Michigan, Ann Arbor.

Previous studies on isolated vascular smooth muscle have been limited to the use of large arteries and veins. These vessels are not significantly involved in control of resistance to blood flow, and it is probable that there are differences between this smooth muscle and that of the smaller muscular vessels that do control resistance. The current study was designed to obtain an isolated smooth muscle preparation from these smaller vessels. Arterioles of the rabbit mesoappendix have been used. After freeing the vessel of fat and connective tissue, a snugly fitting steel rod (150 to 300 μ diameter) is threaded through a 3 mm length of the vessel. With the arteriole in a mid-position on the rod, the two ends of the rod are mounted in synchronously driven chucks of a jeweler's lathe. The sharp edge of a piece of razor blade (clamped in the slide rest) is then pressed firmly against the steel rod at an end of the arteriolar segment to which a thread has been tied. When the rod turns the blade slices a helical strip (50 to 150 μ wide) from the arteriole. After a strip approximately 1 mm long is obtained, the rod is cut just distal to the 'strip end' of the arteriole. The other end of the rod is removed from the chuck and mounted in a Grass strain gauge transducer. The thread is tied to a fixed point in a bath of Krebs solution and the position of the transducer is adjusted with 150 mg tension on the arteriolar strip. After a 2-hour period in the bath at 37°, the strip responds reproducibly to epinephrine for an additional 8-hour period. Numerous observations have been made which indicate that there are basic differences between the contractile machinery of this smooth muscle and that of smooth muscle obtained from larger arteries. (Supported by grant H-3756 C1 from the National Heart Institute, PHS.)

CRITICAL DAMPING IN NORMAL BLOOD GLUCOSE REGULATION. Victor W. Bolie* and J. M. Crismon. Iowa State University, Ames, Iowa and Stanford Univ., Stanford, California.

Recent refinements in insulin bioassay procedures have led to new experimental results (Metz, R. Diabetes. 9:89-93, 1960) of quantitative importance in glucose homeostasis. A parallel development is the recent formulation (Bolie, V.W. Glucose-insulin feedback theory. Proceedings of the Third International Conference on Medical Electronics. London, 1960) of a set of equations which simultaneously interrelate the various roles of the primary organs of glucose regulation, utilization, and excretion. The present paper deals with extensions of these results to the case of limited (Physiological) variations in the concentrations of insulin and glucose in the blood stream. It is shown from experimental data that the normally functioning glucose homeostatic mechanism exhibits physiological coefficients which approximate the well-known critical damping criteria of servomechanism theory, which quantitatively expressed the "optimum" compromise between excessively slow response and an inclination toward oscillatory instability. Using a distribution volume of 14 liters for the 70 kg adult, it is shown from experimental data that the regulatory coefficients for the actions of insulinase, the pancreas, the liver and tissue response to insulin, and the liver and tissue response to glucose are α = 0.92/hour, β = 0.24 unit/hour/gram, τ = 6.25 gram/unit/hour, and δ = 3.0/hour. From critical damping considerations, the corresponding coefficients are found to be α = 0.80/hour, β = 0.30 unit/hour/gram, τ = 4.8 gram/unit/hour, and δ 3.2/hour. Curves are presented to illustrate the effects of changes in the "organ-sensitivity coefficients" on the responses to standard glucose and insulin injection tests. On theoretical grounds the half-life of insulin is found to be approximately 53 minutes.

RESPIRATORY COMPRESSION OF THE ESOPHAGUS BY MEDIASTINAL STRUCTURES. Stuart Bondurant, Milton Carlson, Richard Hawley and Eugene Klatte (intr. by John B. Hickam). I. U. Med. Center, Indianapolis, Indiana.

Respiratory intraesophageal pressure change (IEP) may be caused by extrinsic compression as well as by intrathoracic pressure change (ITP). To study the cause and the magnitude of extrinsic compression, esophageal pressure has been measured with a multi-balloon system composed of three matched 7 cm. balloons arranged end-to-end and an adjacent 21 cm. balloon. Tidal volume was measured simultaneously. Ten normal males were studied seated, supine, and leaning forward before and during acute central vascular engorgement induced by inflation of an aviator's G suit. RESULTS: Seated; the previously reported greater apparent elastance measured in the lower esophagus was confirmed (Group Mean 4.6 cm./L upper balloon, 8.2 cm./L lower balloon, $p<.01$). Elastance measured with the long balloon was not significantly different ($p>0.1$) from that of the middle small balloon despite different pressure-volume relationship and frequency response of the balloons. Seated to leaning forward; Elastance decreased in all balloons, most markedly ($p<.05$) in the lower two small balloons (5.8 to 5.1 and 8.2 to 6.1). Seated to supine; Elastance measured with the small balloons did not change ($p>.1$), that measured with the long balloon increased from 6.1 to 7.2 ($p<.02$). Cineradiographic study of radio-opaque balloons revealed esophageal distortion which changed with respiration to be minimal in the seated position, to be increased with central vascular engorgement, to vary with the individual and with position, and to be caused by: aorta, pulmonary artery, left main bronchus, left atrium, right atrium, or left ventricle. There is evidence of extrinsic compression throughout, more marked in the lower esophagus. The unqualified use of IEP to estimate ITP would seem unjustified.

VARIATIONS IN EXCITABILITY OF DORSAL COLUMN FIBERS OF FROG SPINAL CORD. Stella Y. Botelho and B. H. C. Matthews*. Physiology Departments, Graduate School of Medicine, University of Pennsylvania, Philadelphia and Cambridge University, England.

During the course of studies which were designed to elucidate further the phenomenon of intermittent conduction (Barron and Matthews, J. Physiol. 85:73, 1935), we noted that single antidromic test impulses in the dorsal columns could be enhanced by conditioning volleys which originated at various sites distant from the site of the test stimuli. Experiments were performed upon decerebrated, curarized frogs. Test stimuli were applied to the surface of the dorsal columns through a silver ball electrode. Antidromic test impulses were recorded either from the nerve segment, which consisted of fibers of medial and lateral peroneal nerves or from dorsal roots. Conditioning stimuli were applied to peripheral nerves and to ventral and dorsal roots. The results indicated that enhancement of test potentials occurred with conditioning impulses which arose from: 1. electrical stimulation of contra- and ipsilateral sciatic and brachial nerves, 2. electrical stimulation of dorsal column fibers at the same site to which test stimuli were applied, and 3. pressure on any of the limbs. There was some indication that the enhancement occurred only when the preparation was reflexly active and was dependent upon adequate circulation and impulses arriving in sensory fibers. Supported in part by grants from the U.S.P.H.S. National Institutes of Neurological Diseases and Blindness (Special Traineeship BT-327 and B-1981).

A STUDY OF DIFFUSION OF ATP THROUGH GLYCEROL-TREATED MUSCLE USING ADP AND MYOKINASE-INDUCED CONTRACTION. W. J. Bowen and H. L. Martin.* Natl. Insts. of Health, Bethesda, Md.

Investigation of muscular contraction by use of glycerol-treated (g-t) muscle has suffered from lack of information concerning the diffusion of contraction-inducing ATP into the bundles of fibers and into individual fibers. We have studied this problem by replacing the ATP with ADP after the ATP-induced tension of a fiber remained constant for one or more minutes. The fiber bundles were treated with 0.4% myokinase solution to make the amount of dismuting enzyme constant. All g-t muscle contains myokinase but the amount varies. When ADP was applied, wide fiber bundles developed more tension. Narrow ones did not. The contraction is the result of ADP diffusing without the interference of dephosphorylation as occurs with ATP and then being dismuted to ATP and AMP. Thus ATP is formed in areas where there would be none by diffusion. The amount of extra tension developed was correlated directly with the cross section of the bundles. The maximal cross-sectional area of bundles which did not develop further tension in 0.5 to 2.0 x 10^{-3} M ATP was 0.02 mm^2 and the width 175 μ. This indicates that ATP had completely diffused through the narrow bundles and their fibers and that the diffusion constant through individual myokinase-treated fibers is greater than 3 x 10^{-8} cm^2/sec., the value found by Hasselbach in longitudinal sections of g-t muscle. Since ADP formed from the dephosphorylation of ATP also diffuses and up to half of it is dismuted to ATP, it is concluded that dispersal of ATP through g-t muscle is increased by myokinase.

RELATIONSHIP OF PARIETAL CELL MASS TO AGE AND WEIGHT IN NORMAL WISTAR RATS. S. P. Bralow, M. D.*, S. A. Komarov, M. D., H. Shay, M. D. Fels Research Institute, Temple University Med. Center, Philadelphia, Penna.

The parietal cell mass was estimated in 4 groups of healthy Wistar rats from our colony. Each group consisted of 3 animals of comparable age (1, 1 1/2, 2 and 3 months) and fasting weight (55, 85, 171 and 270 gms.). The technique of Cox and Barnes (Proc. Soc. Exper. Biol. and Med. 60:120, 1945) was modified in that the strips of mucosa were cut at approximately right angles to the antral margin. Included in each strip were the transitional antral zone and the body of the glandular portion of the stomach to the greater curvature. The parietal cells were stained according to Marks and Drysdale's modification of Zimmermann's differential stain of the gastric mucosa (Stain Tech. 32:48, 1957). The mean parietal cell count per unit area (6.98 x 10^{-6} sq. cm.) of glandular mucosa was corrected for shrinkage and nuclear overestimate. The count per unit area did not depend on age or weight of the animal and was estimated to be 42.6 ±1.41. The distribution of parietal cells (counts per unit area) was not uniform within the strips. The maximal concentration of parietal cells occurred in the mid-body of both the anterior and posterior walls and appeared to be related to mucosal thickness. The means of counts in the 6 strips per animal were not significantly different in 9 of 12 animals. The estimated parietal cell mass ranged from 25.94 million in the 1 month old group to 51.58 million in the 3 month old group. There was a highly significant ($P < 0.001$) positive correlation between estimated parietal cell mass and age ($r = 0.98$) as well as between cell mass and body weight ($r = 0.95$).

BLOOD FLOW IN THE HEPATIC VEINS OF THE RAT (MOTION PICTURE). R. W. Brauer, R. F. McElroy, Jr.* and G. F. Leong*. U. S. Naval Radiological Defense Laboratory, San Francisco 24, California.

To visualize blood flow in the hepatic veins of the rat, a contrast medium (Urokon) was injected under controlled pressures by way of transhepatically inserted needles. Injected by this route, the contrast medium enters directly into one of the major hepatic veins with very little filling of sinusoidal channels. Under such conditions, it is possible to observe not only the shape of hepatic veins but also the relative rate of blood flow in these vessels. The picture to be presented will show a series of such experiments demonstrating the fact that in the pentobarbitol anesthetized rat hepatic vein flow is intermittent, being maximal during the peak of expiration and virtually nil during inspiration. The effects of artificially increasing intrathroracic pressure, and of orthostatic circulatory failure will likewise be demonstrated.

FROM ELASTICITY OF THE HEART. Gerhard A. Brecher, H. Kolder* and Alan D. Horres*. Department of Physiology, Emory University, Atlanta, Georgia.

Freshly excised dog hearts were submerged in Ringer's solution of constant temperature. Inside and outside pressures of the cannulated ventricle (either right or left) were equilibrated so as to measure the ventricular volume at zero transmural pressure. Under such conditions the ventricular wall is considered to be in an "elastic equilibrium state". Pressure volume curves were determined before the onset of rigor mortis. Using the changes in volume distensibility as a criterion for the beginning of rigor mortis, it was found that at temperatures above 37 degrees C stiffening of the ventricles occurred within the first hour after removal of the heart. At 10 degrees C rigor mortis changes did not appear before six hours, and at 1 degree C not before 66 hours. Measurements of the right and left ventricular volumes before rigor mortis onset showed that in the elastic equilibrium state of the ventricles, the left ventricle had a volume of 22 ml ± 3 ml per 100 grams of ventricle weight and the right ventricle 18 ml ± 2.8 ml per 100 grams of ventricle weight. The results imply that under dynamic conditions any reduction of the ventricular volume below the volume in elastic equilibrium state probably stores potential elastic energy which in turn facilitates the filling of the ventricle during diastole.

CHEMOCEPTOR REFLEXES IN SWINE. H.E. Bredeck, R.A. Herin and N.H. Booth. (intr. by C.A. Maaske). Colo. State Univ., Ft. Collins, Colo.

Respiratory reflexes originating from chemoceptors in the carotid body have not been previously demonstrated in swine. These investigations indicate the carotid sinus areas of pigs possess chemoceptors sensitive to potassium cyanide and lobeline. Stimulation of these chemoceptors causes a reflex stimulation of the respiratory center and hyperpnea. The sensitivity of the chemoceptors to potassium cyanide is apparently enhanced by vagotomy, whereas this procedure does not reduce the threshold to lobeline. Intravenous injections of cyanide reflexly stimulate the respiratory center if one or both carotid sinus areas are intact. Following bilateral vagotomy and denervation of the chemoceptors in the carotid sinus regions, no respiratory response is elicited by intravenous injections of potassium cyanide.

THE INFLUENCE OF INCREASED PERITUBULAR OSMOTIC ACTIVITY ON REABSORPTION IN THE KIDNEY. Emanuel H. Bresler, M. D. and John F. Monroe, M. D. (intr. by J. K. Hampton, Jr.). Veterans Administration Hospital and Departments of Medicine and Physiology, Tulane University, New Orleans, Louisiana.

Radioisotope studies reveal that sodium and other electrolytes may diffuse across the wall but it is not known whether this diffusion is markedly limited by comparison with water. If the diffusion of sodium and other electrolytes is markedly restricted, then the combined osmotic activity of glucose and protein in the peritubular area should not importantly effect the volume of reabsorbate. On the other hand, if such diffusion is essentially free, then variation in peritubular osmotic activity should influence the degree of tubular reabsorption. In an attempt to determine whether significant amounts of filtered fluid are passively reabsorbed in the renal tubule in answer to external osmotic forces generated by glucose, a steady state of urinary flow was established in dogs by an initial challenge of 150 cc of 5% NaCl followed by maintenance infusions of 0.85% NaCl. Glucose was added to the N-saline during two half hour periods in amounts designed to raise the plasma glucose up toward but not exceeding Tm values. In the periods preceeding the establishment of a steady state, large variations in salt and water output occurred independent of changes in plasma glucose revealing, as would be expected, the influence of other prepotent factors. When satisfactory steady states were established, a rise in plasma glucose produced a fall in salt and water output unassociated with consistent directional changes in inulin clearances. These results suggest that the reabsorption of glomerular fluid may be importantly effected by the osmotic activity generated by glucose transport.

KINESIOLOGY OF THE ABDOMINAL COMPRESSION REACTION. D. I. Briggs*, B. Landau*, K. Akert and W. B. Youmans. Department of Physiology and Department of Anatomy, University of Wisconsin, Madison.

A type of activity described as the abdominal compression reaction (ACR) is seen when strong steady state activity of abdominal muscles rhythmically is interrupted by breathing (Am. Jour. Physiol. 196: 1160, 1959). The ACR is elicited by procedures which cause a decrease in central blood volume (Fed. Proc. 19: 376, 1960). Electromyographic records from the diaphragm and intercostal muscles and oscilloscopic records from single fibers in the central stump of the sectioned phrenic nerve in dogs which had received sodium pentobarbital (30 mg/kg) show that the diaphragm is not activated as a part of the ACR. In some instances the intercostal muscles show no action currents; in other cases they show a burst of activity during inspiration and again during the ACR. The steady state contraction of the external oblique abdominal muscle commonly begins to develop while expiration is in progress (as observed by Gesell) and strengthens to reach a maximum after completion of expiration. Whether the steady state contraction is sustained until just before the next inspiration, or increases or dies out during the interrespiratory period, or is absent depends upon a number of factors the most important of which are the level of pulmonary ventilation and the volume of blood in the heart and lungs. When a strong ACR is present the initial phase of inspiration is the movement of the diaphragm posteriorly related to sudden inhibition of the ACR and the corresponding decrease in intraabdominal pressure. The diaphragm begins to move posteriorly because of less pressure on the abdominal side and continues to move as a result of its contraction.

GASTRIC JUICE IN SPIDER MONKEYS WITH INNERVATED POUCHES AND FISTULAE. F.P. Brooks, G.P. Smith*, R.A. Davis*, and G. Bjotvedt*. Dept. of Physiol., Univ. of Pennsylvania, Philadelphia, Pa.

Two spider monkeys weighing 2 and 3 Kg were equipped with gastric fistulae and gastric pouches that were innervated as shown by an increased acid output after insulin hypoglycemia. Food was offered routinely at 9 A.M. and 1 P.M. Collections between 9 A.M. and noon while the animal was restrained in a chair after a 16 Hr fast and without the usual morning feeding showed little or no titratable acidity to a pH of 3.5. in the pouch but concentrations up to 70mEq/L in the main stomach. One monkey was studied over a period of 12 days with balloons attached to the pouch while "free" in his cage or on a leash. During the period from 9 A.M. to 5 P.M. the mean total acid output from the pouch was 3 mEq., while from 5 P.M. to 9 A.M. it was 0.3mEq. When the animal was fed after 5 P.M., the night secretion rose to an output of 3.5mEq of total acid. Mean volumes and total acid concentrations were 40 ml and 69 mEq/L during the day and 31 ml and 8 mEq/L during the night. Pepsin activity of juice secreted by the pouch and diluted 1:10 was the same in both night and day specimens, k = 0.05 (Riggs and Stadie). (Supported by Grant No. RG5007 C3, National Institutes of Health.)

EFFECTS OF NICOTINE IN PRODUCING ABNORMAL GROWTH OF ANIMLA CELLS THROUGH LOWERED OXIDATION STATES. MATILDA M. BROOKS. DEPART. OF PHYSIOLOGY,UNIVERSITY OF CALIFORNIA, BERKELEY, CAL.

Solutions of nicotine in concentrations of .00001% to .000003 % in sea water.produced abnormal growth in the larvae of Strongylocentrotus purpuratus, resembling that produced by other reagents not chemically related, and analyzed by Brooks elsewhere as reducing reagents. The larvae produced resembled the original "lithium larvae" of Herbst,known as exogastrula. Brooks showed that in each case studied inhibition of one of the essential enzyme systems of the oxidation-reduction scale was inhibited, thereby producing a block which is reflected in its ratio of oxidants to reductants up to the final stage of the activation of oxygen for energy production. Since a correct ratio of oxidants to reductants of the various enzyme systems is necessary for normal energy relations and growth, any change produced by a lowering of the redox potential to a more negative value, either through the application of reducing reagents or through the absence of an essential element, such as calcium, will change this ratio. Nicotine was found to be such a reducing reagent. Continuous application of nicotine to living cells,either through ingestion or inhalation,would prevent the growth of cells to maturity, and only undifferentiated embryonic cells can be formed at the lowered oxidation state.Filters in cigarettes must also filter out nicotine.

PLASMA POTASSIUM RISE DURING RESPIRATORY ACIDOSIS IN THE ABSENCE OF THE LIVER. E.B. Brown, Jr., and David M. Long, Jr.* Depts. of Physiology and Surgery, Univ. of Minnesota, Minneapolis, Minnesota.

The early transient rise in plasma potassium in cats, which is produced by breathing CO_2 concentration greater than 20%, has been attributed to stimulation of the sympatho-adrenal system resulting in a release of potassium from the liver. In order to determine whether the gradual and continuous rise in plasma potassium that accompanies severe hypercapnia in dogs is produced by this mechanism, the liver was removed following a porto-caval shunt operation or as part of a total abdominal evisceration. In both cases plasma potassium rose in response to acidosis just as it does with the liver intact. It would appear, therefore, that the liver is not the source of the extra plasma potassium appearing in response to severe respiratory acidosis in dogs.

CONDITIONED RESPONSES IN THE GAMMA EFFERENT SYSTEM. Jennifer S. Buchwald* and Earl Eldred, Univ. Calif., School of Medicine, Los Angeles 24, Calif. and Long Beach Veterans Adm. Hosp., Long Beach, Calif.

The development of a conditioned response in the gamma efferent system has been studied in acute experiments performed on cats immobilized by Flaxedil. Activity in gamma efferent fibers was monitored in fine filaments of ventral roots L6 or L7. The conditioning procedure consisted of pairing a 1000 c/sec tone of 1.5 sec duration with an overlapping, 0.5 sec shock to the ipsilateral hind paw. Frequently, gamma unit discharge was accelerated or slowed with initial presentation of the tone alone. These responses were habituated with repeated presentations of the tone. Units used for conditioning either showed no initial response to the tone or were habituated to it before the conditioning trials. Conditioned acceleration of gamma fiber discharge was obtained as early as the fifth trial. This response in the gamma system is believed to represent true conditioning as: 1) the response was not present before CS-US pairings, developed during the pairing of CS and US, and could subsequently be elicited by the CS alone; 2) after a conditioned response was obtained and extinguished, it could be brought back with fewer CS-US trials than were originally required to establish it; 3) the conditioned response occurred with presentation of the CS, but was not evoked by a tone of different frequency; and 4) presentations of unpaired CS and US in alternating sequence produced no response, whereas paired CS-US for the same number of trials evoked a response to the CS.

INHIBITION OF CAUDATE INDUCED "SPINDLING" BY STIMULATION OF THALAMIC AND BASAL GANGLIONIC STRUCTURES. N. A. Buchwald, G. Heuser, C. Lauprecht, and E. J. Wyers (Intr. by C. D. Clemente). Univ. of Calif., School of Med., Los Angeles, Calif., and Veterans Administration Hosp., Long Beach, Calif.

Single shocks delivered to the head of the caudate nucleus in cats evoke two temporally distinct electrographic events in cortex and thalamus. A short latency potential is followed in 230-250 milliseconds by rhythmic "spindling" of 10-12 cps frequency. Inhibition of this "caudate-spindling" can be accomplished by 300 cps stimulation of the basal ganglia and of many of the thalamic nuclei. In general the caudate itself, the globus pallidus, including the nucleus endopeduncularis, and the more lateral thalamic structures, e.g., the nucleus ventralis anterior, block spindling induced by stimulation of the ipsilateral caudate nucleus only. Spindling induced by excitation of either caudate nucleus is blocked by unilateral stimulation of the posterior medial thalamus including the central median nucleus and by a small midline area in the rostral thalamus. No blockade of "caudate-spindling" can be produced by stimulation of structures contiguous with the pallidum and caudate (the internal capsule and the medial basal amygdala). On the other hand, stimulation of hypothalamic sites, and stimulation of the midbrain reticular formation, at intensities beyond those required for EEG desynchronization, block or inhibit spindling induced by excitation of either caudate nucleus. Although "caudate-spindling" can be inhibited by thalamic excitation, the converse is not always true. For example, spindling produced by stimulation of the central median nucleus is not affected by 300 cps excitation of the caudate nucleus.

ELECTRICAL AND DIFFUSIONAL RESISTANCE OF HUMAN STRATUM CORNEUM CONJUNCTUM. Konrad J. K. Buettner. Departments of Meteorology and of Physiology, University of Washington, Seattle, Washington.

This part of the horny layer can be separated by stripping with adhesive tape. The layer seems to be identical with the str. lucidum and seems to contain most or all of the barrier against transfer of water, electricity, drugs and poisons. The resistance to water vapor transfer and to electrical current in vitro is much higher at low relative humidities. It is irreversibly changed by exposure to relative humidities above 96°/o. The in vitro data correspond to those on living forearm skin. The transfer in vivo and in vitro of solvents and their vapors as well as that of water solutes will also be discussed. The diffusion resistance is not altered by exposure to ethyl ether in vivo or in vitro. The barrier function seems independent of the skin pump which seems responsible for skin water intake.

DEPENDENCY OF THE HYPOXIC HEART RATE RESPONSE TO AMBIENT TEMPERATURE. R.W. Bullard and G.E. Funkhouser. (Introduced by E.E. Selkurt) Indiana University School of Medicine, Indianapolis, Indiana

Mammalian species which hibernate are more tolerant of hypoxia than are non-hibernating species. Studies were done in an attempt to explain these differences. Thirteen-lined ground squirrels (hibernators) and white rats were exposed to varying degrees of hypoxia (5% and 10% O_2 in N_2) at different ambient temperatures. At an ambient temperature of 35°C rats on 10% O_2 and ground squirrels on 10% and 5% O_2 showed marked cardiac acceleration. The rats on 10% O_2 showed cardiac deceleration at an ambient temperature of 10°C which seemed related to the concurrent body temperature depression (Q_{10} = 2.5). In the ground squirrel on 5% O_2 and at 15°C very marked cardiac deceleration occurred which was not body temperature dependent but coincided with a marked O_2 consumption decrease. The direction of the cardiac response to hypoxia depended on the ambient temperature in both species. The direction of the response may be related to the metabolic requirements of the animal. Marked cardiac and metabolic depression may be of survival value in hypoxic exposure.

A COMPARISON BETWEEN THE NITROUS OXIDE METHOD AND ELECTROMAGNETIC ROTAMETER IN THE MEASUREMENT OF UTERINE BLOOD FLOW IN THE PREGNANT DOG
by Ralph Burrows* and Vincent Glaviano, Univ. of Ill. College of Medicine, Chicago, Illinois.

Despite widespread use of the N_2O method for measuring uterine blood flow, the technique has never been compared with another method for measuring blood flow. Employing a modification of the N_2O method, uterine blood flow was recorded on 16 pregnant dogs late in gestation. These results were compared with measurements simultaneously made with a Shipley-Wilson electromagnetic rotameter. The inflow end of the rotameter was inserted into the left common carotid artery, while the outflow tubing was connected to the paired uterine arteries. The ovarian arteries were bilaterally tied-off at the rostral end of the uterine horns. Our results demonstrate that (1) in 13 dogs, the average uterine blood flow with the N_2O method was 9.1 ml./100 gm./min. (S.E. = 1.7), while the average rotameter flow was 5.7 ml./100 gm./min. (S.E. = .7) during the same period, (2) the two methods were found to be significantly different ($P < .05$), (3) equilibrium between uterine tissue and venous outflow did not usually occur at the end of a 30 minute period, (4) at the end of a 30 minute period, simultaneous samplings of blood from different uterine veins yielded dissimilar levels of N_2O. (Supported by a grant from the National Institutes of Health, H-3686).

THE RAT'S TAIL IN TEMPERATURE REGULATION. Alan C. Burton, Tom Ing* and Peter Rand*. Univ. of Western Ontario, School of Medicine.

The laboratory rat has been much used in studies of acclimatisation, yet its normal mechanisms of temperature regulation are not fully known. The blood flow of the tail was measured, by venous-occlusion plethysmography, at a range of environmental temperatures. A very abrupt increase from less than 2 mls/100/mls tissue/min occurs at about 27°C. to a high value of 30 to 40. The heat loss of the tail was measured by a gradient calorimeter and showed a similar abrupt increase, up to 25% of the total heat production. Vasodilation in the tail is an important part of defence vs heat in the rat. In 3 rats after acclimatisation to 11°C. or to 30°C., the 'critical environmental temperature' for the abrupt increase shifted by several degrees. This suggests a change in sensitivity of peripheral thermal receptors related to a change in thermal properties of the skin after acclimatisation.

Supported by a grant from the Defence Research Board of Canada.

ENZYMATIC DETERMINATION OF ATP DURING GROWTH AND CELL DIVISION OF TETRAHYMENA. John Byfield*, Krikor H. Seraydarian, and Otto H. Scherbaum. Dept. of Zoology and Heart Association Ressearch Laboratory, UCLA, Calif.

The nucleoside-triphosphate content in normal and synchronously dividing Tetrahymena has already been reported by Plesner (Biochim. Biophys. Acta, 29:462, 1958), but nothing was known about the changes in ATP concentrations during the synchrony-inducing temperature treatment. We have followed up this problem. Exponentially growing mass cultures of Tetrahymena were exposed to seven temperature cycles (29°-34°C, half an hour each) and sampled at one hour intervals, before, during, and after the treatment. The cells were collected, washed, and homogenized at about 0°-5°C, extracted with 10 per cent perchloric acid. The acid extract was then neutralized and aliquots used for the estimation of ATP with firefly luciferin-luciferase system in a fluorometer; on the same samples the protein content was estimated by the Lowry method. To obtain reproducible results, it was found imperative to make the enzymatic determination immediately after the neutralization step. More than 50 per cent of the ATP activity is lost upon aging of the extract at 5°C for three hours. The ATP content of about 10 millimicro-moles per milligram protein in exponentially growing cells decreases during the first shocks to about 60 per cent, within the first hour of the treatment, and remain at this level for several hours. Upon release from the treatment the ATP-protein ratio increases to values comparable to that of the untreated cells. A considerable reduction of ATP content was similarly observed in cells of the early stationary phase when cell growth and cell division have practically ceased. (This work has been supported by NSF grant #G-9082).

SOME PHYSIOLOGICAL AND ANATOMICAL COMPARISONS BETWEEN BRAINS OF CAPYBARA (HYDROCHOERUS) AND GUINEA PIG (CAVIA). G. B. Campos* and W. I. Welker. Laboratory of Neurophysiology, Univ. of Wisconsin School of Medicine, Madison, Wis.

Among closely related genera larger animals typically have larger and more convoluted brains. It was the purpose of this study to obtain information which might shed light upon the causes of such differences. To this end, the brain of capybara (Hydrochoerus), the largest living rodent, was compared with that of guinea pig (Cavia), a member of a related family. Somatic-sensory, auditory, and visual regions of the cerebral cortex of capybara were outlined using the evoked potential method. Results were obtained on 5 animals under sodium pentobarbital anesthesia. Volumetric measurements of various nuclei of the brains of capybara and guinea pig were made by means of planimetry. The cerebral cortex of capybara is highly fissured whereas that of guinea pig is not. The brain weight of capybara is at least 14 x that of guinea pig. The cortical face area occupies about 85% of SI in capybara and 60% in guinea pig. Sulci within and around SI appear to be limiting sulci, a fact which agrees with similar findings in primates and carnivores. The locations of somatic-sensory, visual, and auditory regions is homologous with those previously obtained in guinea pig (Zeigler and Woolsey, unpublished) which has a brain of similar general morphological configuration. (Aided by grant M-2786, NIMH, USPHS.)

THE INFLUENCE OF ENVIRONMENTAL TEMPERATURE ON THE OXYGEN CONSUMPTION OF NEWBORN MICE SUBJECTED TO PROGRESSIVE HYPOXIA. S. Cassin and A. B. Otis, Dept. of Physiol., Coll. of Med., University of Florida, Gainesville.

Newborn mice were subjected to progressive hypoxia at 20°C, 25°C, 30°C and 35°C and their oxygen consumption measured. Oxygen consumptions were determined on individual animals in modified Warburg vessels using standard manometric methods. Hypoxia was produced by replacing the oxygen consumed by the animal with pure nitrogen. Animals breathing room air at 25°C and 30°C showed an oxygen consumption greater than that found at 35°C. Those cooled to 20°C showed an oxygen consumption which was markedly less than that at 35°C. During progressive hypoxia critical oxygen pressures (oxygen partial pressures below which oxygen consumption progressively falls) were 70 mm Hg at 35°C, 105 mm Hg at 30°C, 90 mm Hg at 25°C and 85 mm Hg at 20°C. These results suggest that the metabolism of the newborn mouse, in contrast to that of the newborn rat (Adolph, E. F., Quart. Rev. Biol. 32,89,1957), is stimulated by mild hypothermia (25°C and 30°C). Hypoxia appears to interfere with this metabolic stimulating effect of hypothermia. (Supported by Contract AF 41(657)-102 with the School of Aviation Medicine.)

EPSILON-AMINOCAPROIC ACID (EACA) AS INHIBITOR OF VARIOUS COMPONENTS OF THE FIBRINOLYTIC SYSTEM. D. R. Celander* and M. M. Guest. Univ. of Texas Med. Branch, Galveston, Texas.

EACA has been reported previously to be a potent inhibitor of activators of the fibrinolytic system with little effect (at comparable concentrations) on fibrinolysis itself. This communication describes its ability to inhibit the streptokinase-elicited activator of human and canine plasma, urokinase, and canine and bovine fibrinolysin in one stage systems. Two stage procedures have been used in the further evaluation of its effect on urokinase and in studies of its effect on staphylokinase. Ninety per cent inhibition of streptokinase-human activator, streptokinase-canine activator, and urokinase requires concentrations of EACA of 6.25×10^{-4} M, 1.25×10^{-4} M, and 6.25×10^{-3} M respectively. In a two stage procedure which minimizes EACA inhibition of formed fibrinolysin, 1×10^{-3} M EACA inhibits urokinase less than 25%. As much as 50% of the urokinase activity remains in the presence of 1×10^{-2} M EACA. Under similar conditions, the action of staphylokinase on canine profibrinolysin is markedly delayed by as little as 5×10^{-4} M EACA, but it is not abolished by EACA in concentrations as high as 1×10^{-2} M. Concentrations of EACA of 6.25×10^{-4} M and 1.25×10^{-3} M inhibit canine fibrinolysin 45% and 65% respectively and bovine fibrinolysin 60% and 80% respectively. The bovine system is thus more sensitive. It is concluded: 1) The degree of sensitivity of activators to EACA is not uniform, both urokinase and staphylokinase being markedly less sensitive than the streptokinase-elicited human or canine activators. 2) The concentration of EACA required to inhibit fibrinolytic activity varies with species of origin and overlaps concentrations inhibitory to activator. 3) Use of EACA in the in vivo control of activator or fibrinolytic activity must be approached with caution.

TEMPERATURE AND HUMIDITY IN THE LOWER TRACHEA OF THE DOG. John L. Chapin. Department of Physiology, University of Colorado School of Medicine, Denver, Colorado.

This study was undertaken to determine the validity of the assumption that the upper airways warm and wet inspired air to body temperature and to 100% relative humidity. A psychrometer consisting of matched thermocouples encased in a plastic tube which permitted a 3 meter/sec. air flow and which could be inserted into the trachea from the mouth was used to measure temperature and relative humidity in the upper airways of anesthetized dogs. The relative humidity at the bifurcation of the trachea was found to be between 99 and 100% on inspiration. On expiration about a ½° rise in dry bulb temperature was found suggesting that further warming and wetting of inspired air occurs in the broncheal tree and that a small water transfer from this site to the upper respiratory tract occurs as expired air is cooled in the airway.

ANGIOTENSIN EFFECTS ON PULMONARY AND SYSTEMIC HEMODYNAMICS. John E. Chimoskey*, Pedro C. Blaquier*, Alberto C. Taquini, Jr.* and David F. Bohr. Dept. of Physiology, University of Michigan, Ann Arbor, Mich.

Using catheterization and strain gauge transducers with direct writing oscillographs, pulmonary artery pressure, right atrial pressure and femoral artery pressure changes in response to single injections of 2.0 mcg/Kg of synthetic (Val 5) angiotensin II were studied in 6 morphine-urethan anesthetized dogs. Mean femoral pressure rose from 93 to 132 mm Hg immediately following the injection, pulmonary artery pressure rose from 14.2 to 19.2 mm Hg and heart rate fell from 115 to 89 beats/min. Right atrial pressure remained unchanged. Currently the response to 30-minute continuous intravenous infusions of angiotensin, 0.6 and 0.4 mcg/Kg/min., are being studied. Pressures are recorded as above as well as left ventricular end-diastolic pressure. Dye dilution cardiac output is measured using indocyanine green and cuvette densitometer. Studies on 5 dogs have demonstrated elevated systemic arterial pressures and depressed heart rates with unaltered right atrial and left ventricular end-diastolic pressures. There has been no consistent response in pulmonary arterial pressure or cardiac output to the larger infusion. Pulmonary arterial pressures and cardiac outputs are unaltered by the 0.4 mcg/Kg infusion, demonstrating no change in pulmonary vascular resistance in the presence of an elevated systemic vascular resistance. (Supported by grants from the Michigan Heart Association and the National Heart Institute, PHS.)

FRACTIONATION OF PROTEIN, RIBOSE, AND PHOSPHATES IN NORMAL AND SYNCHRONOUSLY DIVIDING CELLS. Shao-Chia Chou* and Otto H. Scherbaum, Dept. of Zoology, U.C.L.A., Los Angeles, California.

The relationship between polyphosphates and ATP, with respect to cell division in microbial systems, has frequently been considered (Sall T. et al, J. Bacteriol. 76:640, 1958; Katchman, B.J. et al, J. Bacteriol. 77:331, 1959). One hypothesis (Scherbaum, O. H., Ann. Rev. Microbiol. 14, 1960) is being tested on the ciliate Tetrahymena, which has been synchronized by application of temperature cycles. The cells are grown in 7 liter cultures and sampled in the following stages: (1) normal exponential multiplication; (2) at the end of the synchrony treatment, during which cell growth occurs, but division is halted; (3) just prior to the first synchronous division; and (4) in the maximum stationary phase, when cell growth and cell division have ceased. The collected cells were extracted with 70 per cent ethanol at -70°C., followed by extraction with 10 per cent trichloroacetic acid. These fractions were analyzed for proteins, inorganic phosphate, labile phosphate, and ribose content. A flow sheet will be presented showing the distribution of these compounds in the various fractions during the four growth stages mentioned above. The acid labile phosphate fractions show a similar pattern to that found with adenosine triphosphate, when the latter is enzymatically estimated, (as reported separately at this symposium). The polyphosphate fraction recently reported in yeast cells could not, as yet, be detected in Tetrahymena. (This work has been supported by U.S.P.H. grant #RG-6461).

LIPIDS IN SYNOVIAL FLUID FROM RHEUMATOID AND OSTEOARTHRITIC PATIENTS. A. C. Chung, J. R. Shanahan, and E. M. Brown, Jr. (intr. by A. R. Behnke). The Lankenau Hospital, Philadelphia, Pa.

Synovial fluid from knee joints of patients with rheumatoid and degenerative arthritis was extracted with chloroform and methanol mixture. After separation of the aqueous layer, the following lipids were determined in the chloroform: total cholesterol, triglyceride and phospholipids. Silicic acid column chromatography was used to separate phospholipids into the following major classes of phosphatides: cephalin, lecithin, sphingomyelin and lysophosphatides. In some cases, serum and synovial fluid were obtained simultaneously from each patient; and these samples were subjected to electrophoresis, using starch as the supporting medium for the separation into α and β lipoproteins. Synovial fluid, after incubation with hyaluronidase, migrated to similar positions observed in serum. In the cases studied, the amount (in mg. per 100 ml synovial fluid) of cholesterol, phospholipids and triglyceride ranged from 106-200, 83-111 and 32-85 respectively. The distribution of phosphatides in synovial fluid, when compared with values reported in normal serum by other investigators using the same silicic acid column, showed a somewhat higher value in sphingomyelin and lower value in lecithin fraction. Although the α / β ratio for cholesterol and phospholipids found in fluid was different from α / β ratio in serum from the same patient, the distribution of phosphatides in α and β lipoproteins of the fluid generally followed the distribution of the α and β lipoproteins of the serum.

CIRCULATORY ACTION OF A QUINIDINE ANALOGUE. H. L. Conn, Jr. and R. J. Luchi* Univ. of Pa., Dept. of Med., Philadelphia, Pa.

Four metholyl 6 methoxy quinoline is quinidine without the quinuclidine ring. This drug was synthesized as a part of our study of the nature of quinidine binding to protein. 4OH 6M quinoline competes in this reaction although the association constant for the reaction with albumin is only one-third as great. Its structural and binding similarities to quinidine led us to test its action on the circulation. In the anesthetized dog a marked hypotension was produced by 200 mg./Kg. IV but cardiac force and output, heart rate, and EKG were unchanged. Atropine failed to reverse the effect but large doses of hypertensin and norepinephrine did. In the anesthetized cat the drug failed to block ganglionic transmission. In the dog isolated hind limb a direct, marked peripheral vasodilatation was produced. The constrictor effects of 3γ/Kg. of epinephrine and norepinephrine were blocked. Conclusions are that 4OH 6M quinoline in this dose exhibits the hypotensive but none of the cardiac effects of quinidine and that its action results from some form of competition with adrenergic substances at a peripheral vascular site.

EVALUATION OF COLLATERAL CIRCULATION IN OCCLUSIVE DISEASE. Margaret C. Conrad[x] and Harold D. Green. Bowman Gray School of Med., Winston-Salem, N. C.

Skin temperature, blood flow, and pulse volume were measured simultaneously in normals and in patients with occlusive disease and patients with vasospasm, in a room maintained at 20C. After equilibrium they were given 120 cc ethyl alcohol to induce vasodilation. The relationship between skin temperature and flow was similar to that previously reported. The plethysmographic measured flow rose and fell with a series of spikes, or peaks and dips during the rise and fall of skin temperature. The tone of the vessels varied markedly with minor psychic stimuli. The relationship between flow and pulse volume was compared in the normals and in patients with spastic or occlusive disease. In normal subjects the ratio of flow/pulse volume remained within a relatively constant range from subject to subject and in the dilated and constant state. In subjects with occlusive disease, the ratio was increased in proportion to the development of collateral circulation and serves as a useful index of the extent of the collateral circulation developed about a segmental occlusion. Supported by HTS 5392 and A. H. A.

IS INCREASED VASOMOTOR TONE PRESENT IN HYPERTENSION? James Conway (intr. by C. R. Brassfield). Depts. of Medicine and Physiology, University of Michigan, Ann Arbor.

Many studies have shown blood flow to most tissues to be normal in hypertension, but it has never been possible to determine whether the increased resistance, which therefore must be present, is due to an increased vasomotor tone or to some other changes. This has been due to the absence of satisfactory methods for comparing the levels of vasomotor tone in one animal with another. If the peripheral resistance in a fully dilated vascular bed is used as a reference point the change in resistance produced by the activity of vascular smooth muscle can be used for a measure of vasomotor tone in different animals. When such comparisons are made between normal and hypertensive subjects it can be shown that in this disease there is an increase in the resistance in the maximally dilated vascular bed, the severity of which varies with the level of blood pressure. This suggests that there is a non-myogenic element in the increased peripheral resistance in hypertension. Although the increased non-myogenic resistance was considered to be a structural change, it is capable of variation with some antihypertensive drug suggesting that there might be a hitherto unsuspected mechanism controlling vascular resistance.

THE EFFECTS OF HYPNOTIC SUGGESTION ON RENAL FUNCTION IN HUMAN SUBJECTS. Samuel A. Corson, Elizabeth O'Leary Corson*, Harold Rosen*, William G. Reese* and Roscoe A. Dykman*. Yale Univ. School of Med., Johns Hopkins Univ. and Univ. of Ark. Med. Center.

Experiments were performed on patients with indwelling urinary bladder catheters after a 14-18 hr. period of food and water deprivation. In one series of experiments, following control urine collections, hypnotic suggestion of drinking water was made to hydropenic patients. This often led to a diuresis. In most cases, the response did not have the characteristics of a water diuresis. The urine osmolarity did not decrease; U_{Na}, U_{Cl} and U_{K} often increased. The quality of the diuretic responses appeared to be similar to that of the conditioned diuretic responses we observed in dogs. In another series of experiments the patient was given a breakfast consisting of 4 glasses of milk. After the diuresis was well under way, hypnotic suggestion of thirst was made. This often produced an antidiuresis accompanied by a marked increase in urine osmolarity (from 350 mOs/L to 650 mOs/L) and in urine electrolyte concentrations. Our preliminary data suggest that the central nervous system of human subjects under hypnosis may respond preferentially to verbal symbols of hydration and mobilize the physiologic mechanisms designed to increase water excretion in spite of the fact that the organism is actually water-deprived and requires water conservation. Conversely, verbal symbols of dehydration may invoke physiologic water conservation mechanisms in a well hydrated subject when water excretion would represent the appropriate physiologic response.

RENAL FAILURE IN THE ALLIGATOR. R. A. Coulson* and T. Hernandez. Biochem. Dept., La. State Univ. Sch. Med., New Orleans, Louisiana.

The injection of 10 m Moles of D-serine into small alligators produced a renal dysfunction of several weeks duration. The nature of the disorder was quite similar to that seen when comparable alligators were kept at 6° C. for several days. The decreased tubular production of NH_3 and CO_2 was accompanied by an increased excretion of NaCl with little change in the osmotic pressure of the urine. Glucose, which is normally absent from the urine, appeared in considerable amounts. In the normal alligator, phosphate and uric acid are secreted by the renal tubules. In the animals in renal failure caused by D-serine, the clearances of these substances were greatly reduced. The alligator does not produce urea and therefore azotemia was manifest in a rise in blood uric acid from 2.5 mg % to levels as high as 70 mg %. No other NPN derivatives were altered significantly from the normal. In the recovery period there was a gradual rise in both NH_3 and CO_2 excretion and a fall in NaCl output. Glucose reabsorption and uric acid and phosphate excretion were resumed and the animals appear to have recovered completely. The data support the view that ammonia and CO_2 are produced by the tubules and that these ions function in salt conservation. The alligator has the ability to excrete as much as one half the ingested nitrogen in the form of NH_3 if the renal tubules are intact and if enough water is available. In dehydration and in renal disease uric acid becomes the only end product of nitrogen metabolism.

HYPERVENTILATION, BREATH HOLDING, AND DROWNING. Albert B. Craig, Jr., Dept. of Physiology, University of Rochester School of Medicine and Dentistry, Rochester, New York.

Several incidents of losing consciousness while swimming underwater are known to the author. All survivors reported that they had hyperventilated before swimming. Deaths due to drowning have occurred under circumstances which suggest that the victim's first problem was passing out. Experiments were designed to answer the question, how can this happen? Four types of breath holding were executed: (a) at rest, (b) after hyperventilation, (c) during mild exercise, and (d) after hyperventilation and during mild exercise. Breath holding began after a maximal exhalation followed by maximal inhalation. At the breaking point the subject made a maximal expiration, and the end tidal air was analyzed for O_2 and CO_2. It was found that when the breaking point was reached the P_{CO_2} was higher and the P_{O_2} lower during exercise than at rest. The lowest P_{O_2} was observed after the subject had exercised following hyperventilation; the P_{O_2} was 34 mm or below in four of the twelve subjects, a degree of hypoxia often associated with unconsciousness. Other experiments support the conclusion that loss of consciousness after hyperventilation and during exercise is possible and is probably due to hypoxia.

RETINAL RESPONSES TO DIRECT ELECTRICAL STIMULATION.
Donald R. Crapper* and Werner K. Noell. The Univ. of Buffalo Sch. of Med., Buffalo, N. Y.

Ganglion cell responses were recorded in rabbits from the retinal surface after removal of cornea and lens. A single brief electrical stimulus applied to either the retina or the vitreous evoked 1 - 2 bursts of spikes per ganglion cell. The time of occurrence of these bursts ranged from 4 - 60 msec; it varied with the latent period of the ganglion cell to a flash of light but was always shorter. Macroelectrode recording typically showed a sequence of several bursts. Stimulus intensity determined the number of spikes per burst but did not markedly alter latency. Optic nerve sectioning failed to abolish burst activity. Light stimulation depressed responses to electrical stimulation and vice versa depending upon relative stimulus strength. A second electrical stimulus was without effect when applied during the burst activity following the first stimulus but at other times evoked the typical response. The findings provide evidence for an intricate intraretinal network system responsive to electrical stimulation.

THE RATE OF THE BOHR SHIFT IN RED CELL SUSPENSIONS. Margot R. Craw*, Joseph A. Morello* and R. E. Forster. Depts. of Physiology and Anesthesiology, Grad. Sch. of Med., Univ. of Penna., Phila., Penna.

We have estimated the rate at which O_2 is displaced from intracellular HbO_2 upon the addition of CO_2 to a suspension of human red cells at 37°C. The speed of this process was measured in a modified Hartridge-Roughton rapid reaction apparatus, in which two motor driven syringes were used to deliver to the mixing chamber at constant known speeds, (a) a buffered saline suspension of red cells (whole blood diluted 1:50) and (b) an isotonic solution containing CO_2, both (a) and (b) having a pO_2 of 30-35 mm Hg. By this means red cells at a pCO_2 of 4-5 mm Hg are suddenly exposed to a pCO_2 of 60-66 mm Hg, with no change in pO_2. The mixture leaves the mixing chamber and travels at a constant rate along a 1.7 mm bore observation tube. At serial positions along this tube the O_2 tension is determined by means of a teflon covered 0.005 cm platinum electrode. (Staub, Bishop & Forster, Fed. Proc. 18: 152, 1959). In these experiments the average initial rate of decrease of HbO_2 was 130%/sec. This reaction rate must depend on a series of processes:

(1) Diffusion of CO_2 into the red cell
(2) The intracellular reactions involving CO_2
(3) The simultaneous dissociation of HbO_2 and diffusion of O_2 out of the cell.

The rate of dissociation of HbO_2 combined with the rate of diffusion of O_2 out of the red cell, under reasonably similar conditions, was significantly faster than the overall combined rate of the above processes, suggesting that the rates of processes (1) and (2) are slow enough to be important in blood gas exchanges.

ACETYLCHOLINE PRODUCTION BY ISOLATED FROG SPINAL CORD. Paolo Crepax* and John M. Brookhart. Dept. of Physiology, Univ. of Oregon Medical School, Portland.

Information concerning chemical mediation of synaptic excitation is being sought through the use of the isolated spinal cord of the frog. Motor neurons of isolated cords, bathed in recirculated nutrient Ringer's have been activated antidromically, polysynaptically through dorsal root fibers, and through simpler connections from descending fibers in the lateral column. The eserinized perfusate has been assayed for acetylcholine using the heart of Venus mercenaria. A substance having some actions of 5-hydroxytryptamine appeared irregularly in the perfusate with all forms of excitation and with the preparation at rest. Acetylcholine appeared in the perfusate in greater quantity during lateral column stimulation than during dorsal root or antidromic stimulation. A role of acetylcholine as a synaptic transmitter agent can only be inferred if a quantitative relation between acetylcholine production and motor neuron excitation can be established. Experiments directed to this objective are in progress. The preparation also offers the opportunity to determine whether the acetylcholine is produced by the terminals of the lateral column fibers or by indirectly activated interneurons.

THE ROLE OF CARBON DIOXIDE TENSION IN PULMONARY ARTERY BLOOD IN THE CONTROL OF RESPIRATION. Gerd Cropp*, and J. H. Comroe, Jr. Cardiovascular Research Institute, Univ. of Calif. Med. Center, San Francisco.

Because systemic arterial blood P_{CO_2} does not correlate well with pulmonary ventilation during muscular exercise, some investigators have suggested that respiration may be regulated by mixed venous P_{CO_2} acting on pulmonary arterial chemoreceptors. We have tested this hypothesis by increasing and decreasing abruptly the P_{CO_2} in pulmonary arterial blood of dogs and cats. Using synchronized injection-withdrawal techniques so that venous pressure and flow were not changed, we injected blood at 37°C equilibrated with 93% CO_2-7% O_2 into the right atrium while withdrawing equal volumes of blood from the intrathoracic inferior vena cava. We were able to increase pulmonary arterial blood P_{CO_2} 7-50 mm Hg, depending upon the rate of exchange. We measured tidal volume and end-tidal P_{CO_2} continuously and systemic and pulmonary arterial P_{CO_2} every few seconds during and immediately after the infusion period. Ventilation did not increase until sufficient time had elapsed for systemic arterial blood P_{CO_2} to rise. There was poor correlation between pulmonary arterial P_{CO_2} and ventilation, although the animals had a normal ventilatory response to inhaled CO_2 in air. These observations do not support the theory that there are important chemoreceptors sensitive to P_{CO_2} in the precapillary portion of the pulmonary circulation.

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CORONARY VASOMOTOR TONUS AND EXTRACORONARY FACTORS AS DETERMINANTS OF CORONARY BLOOD FLOW. Cecil E. Cross*, P. Andre Rieben‡, Erich Wagner* and Peter F. Salisbury. St. Joseph Hosp., Burbank, Calif.

Coronary flow (CF)(right heart bypass), arterial and coronary venous oxygen contents, left ventricular (LVP) and aortic (AP) pressures were measured. Arterial O_2 (oxygenator), blood temp., blood pH were kept constant. Arterialized venous return was injected either into the pulmonary artery (LV pumping entire systemic flow)or into a femoral artery (machine pumping systemic flow). LVP paralleled AP regardless of systemic flow. LVP could be dissociated from AP by inflation of an intracavitary LV balloon. Variance analysis was performed on the following parameters: CF, cardiac oxygen consumption ($\dot{V}_O$), "mean coronary driving pressure" (CDP) (the integrated difference between AP and LVP per unit time). When the hearts had not been manipulated CF was a strict linear function (mean r 0.952) of CDP, irrespective of systemic blood flow. In the same hearts lesser correlations were observed between CF and $\dot{V}_O$. During or after overdistension (LVdiastP above 15 mm Hg), electrical countershock or other "cardiac injury" CF was again a strict linear function of CDP but with a much steeper slope. CF and $\dot{V}_O$ of injured hearts were not related. Even in uninjured hearts CF and $\dot{V}_O$ could be made to vary in opposite directions at will. Pitressin decreased the regression line (uninjured hearts). Conclusions: CF is adapted to mechanical activity of uninjured hearts by purely mechanical pressure differentials without changes of coronary vasomotor tonus. Coronary vasomotor tonus decreases after cardiac injury and increases after pitressin. Slopes of regression lines $f_{(CF-CDP)}$ express coronary vasomotor tonus numerically. Neither CF nor coronary vasomotor tonus are influenced by cardiac oxygen consumption.

A PHYSIOLOGICAL FACTOR AFFECTING DEFIBRILLATION OF THE HEART. J. W. Crowell. Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

The hearts of twenty dogs were fibrillated by applying 15 volts thyratron discharge at 60 cycles per second. After a varying period of time, cardiac massage was instituted. The arterial blood pressure was measured by a citrate manometer system attached to the femoral artery. The records show that cardiac massage could raise the arterial pressure only to 30 to 40 mm. Hg during the first 30 seconds after massage had begun. Then the pressure in each instance rose very rapidly to near control levels and remained high for approximately 3 minutes. After the 3 minute interval, the arterial pressure decreased to 40 to 80 mm. Hg. Concomitant with the sudden increase in pressure, the tone of the heart changed from a flabby tone to a firm tone, and fibrillation became more pronounced. Furthermore, it was extremely difficult to defibrillate the heart during this period, though after the 3 minute interval was over, electrical defibrillation was easily effected. It is believed that these effects are all caused by epinephrine secreted during the period of circulatory arrest by the sympathetic nervous system but failing to reach the heart because the blood is not flowing. With the institution of cardiac massage, this epinephrine reaches the heart to exert the above effects. Since epinephrine is known to be detrimental to defibrillation of the heart, this could explain the difficulty in cardiac defibrillation that has been encountered by others soon after cardiac massage is begun.

ANTRAL INHIBITION OF GASTRIC ACID SECRETION. Ivan E. Danhof. Dept. of Physiol., Univ. of Texas Southwestern Medical School, Dallas, Texas.

In anesthetized mongrel dogs of both sexes, fasted 24 hours, the stomach was isolated by ligatures at the cardiac and pyloric regions. The veins along the lesser and greater curvatures were ligated at the incisura angularis and cannulated at the pylorus. In groups I and II, solutions of pH 7.0 and 1.0, respectively, were placed in the antral area of the stomach with only mild distention (pressure < 8 cm. H_2O). Blood collected from the veins draining the antrum was collected in an ice bath for periods up to two hours, dialyzed against distilled water in the cold for 24 hours, lyophilized, and resuspended in saline. The material was infused over a 1/2 to 1 hour period in unanesthetized, antrectomized, gastro-jejunostomized, gastrostomized dogs. Through the gastrostomy were placed at the time of infusion a Beckman pH probe and a catheter for continuous gentle suction (to prevent elaboration of intestinal inhibitors). Consecutive 15 minute secretory samples were measured and titrated with N/10 NaOH using Topfer's reagent and Phenolphthalein as indicators. Rectal temperatures were measured. Infusion of group I materials into an assay animal caused a substantial increase in gastric HCl elaboration while the infusion of saline caused no change in the small spontaneous secretion. Infusion during histamine-induced gastric HCl secretion produced no change. Infusion of group II material inhibited spontaneous gastric HCl secretion within 1/2 to 1 hour and histamine-induced gastric HCl secretion within 1/2 to 2 1/2 hours. The inhibition lasted 15 to 45 minutes. The inhibition could not be related to the presence of hyperthermia-induced autonomic discharge. The data presented are evidence for the presence of a gastric HCl inhibitor released from the antrum when bathed by acid.

EFFECT OF TEMPERATURE ON MUSCLE TENSION PRODUCTION BY THYROIDECTOMIZED AND THYROXIN TREATED RATS. George D'Asaro (intr. by Neena B. Schwartz) Institute for Psychosomatic and Psychiatric Research and Training of Michael Reese Hospital, Chicago.

Previous work has shown (A.J.P., 198:456, 1960) that when muscle temperature is uncontrolled, thyroxin treated rats show higher temperatures and lower tensions, at subtetanic frequency than controls. In the following experiments the effect of both uncontrolled and controlled temperatures was studied. In vivo isometric tension of rat gastrocnemius muscle was measured at a stimulation frequency of 30/sec. in 56 rats pre-treated with thyroidectomy (X), thyroxin (T), or saline (S). Muscle temperatures were measured by means of a needle thermistor and controlled by heating or cooling externally the whole body of the barbitalized rat. In the first experiment the muscles were at first stimulated with no attempt to control temperature. The T muscles had the highest temperature (34.4°C) and the lowest tension, while the X muscles had the lowest temperature (32.3°C.) and the highest tension. Upon bringing the muscles to 33°C., the tension differences, although reduced, were still significant. In the second experiment, tension was measured for each rat at three muscle temperatures: 28, 33, and 38°C. The tension decreased with increasing temperature (Q_{10} of -2.14). Clonus amplitude increased with increasing temperature. Although tensions of T rats were not different from S rats, the tensions of X rats were significantly greater. Thus when temperature is uncontrolled, the slight temperature differences among groups cause great differences in tension owing to the high Q_{10}. When muscle temperature is controlled, treatment differences are reduced, but still present. (Supported by a research grant, B 1510, from the Nat'l. Inst. of Neurological Diseases and Blindness, PHS).

RETROGRADE FLOW IN SMALL VEINS BEFORE AND DURING SYMPATHETIC STIMULATION. D. L. Davis and W. F. Hamilton. Med. Coll. of Georgia, Augusta.

In earlier observations (Am. J. Physiol. 196: 1316, 1959) maximal sympathetic stimulation of the blood vessels of the dog paw markedly increased and maintained digital vein pressures for the duration of the stimulus, even though arterial inflow had stopped. This observation must imply that blood was unable to drain either downstream (proximally) or upstream (distally-toward the capillaries) from the digital vein. To decide whether flow toward the capillaries was prevented by constrictive closure or by closure of small vein valves a technique was employed in which blood from a large vein on the opposite leg was perfused into a small plastic catheter loop inserted into the digital vein. The blood pressure of this circuit was regulated by an occluding cuff on the opposite leg. During the unstimulated states a retrograde flow in the digital veins was possible whenever the perfusion pressure exceeded the digital vein pressure, and proved that collateral channels unguarded by valves did exist. With a normal arterial inflow this retrograde flow probably extended backwards as far as the first unguarded collateral venous channel, and then flowed centrally again. When the small artery inflow was stopped the retrograde flow extended back as far as the small arteries. During maximal sympathetic stimulation small vein constrictive closure prevented flow in either direction in the digital vein until perfusion pressures of approximately 100 mm Hg. were employed. (Supported by the Life Insurance Medical Research Fund and USPHS grant H-240).

EFFECTS OF APPLIED PRESSURES ON CSF EXCHANGE. George D. Davis and James A. Wall (intr. by A. Sidney Harris). La. State Univ. School of Med., New Orleans, La.

Formation and removal of fluid from the cerebrospinal system has been studied in the anaesthetized dog. This was done by means of a conventional spinal needle, inserted into the cisterna magna, and connected to a manometer. Simple apparatus was then used to measure the inflow of Locke's solution under conditions of increased applied pressure to a maximum of 60 cm. H_2O. Additionally, the same needle was used to measure outflow of fluid from the cistern with increasing amounts of negative pressure. The positive pressure (inflow) results agree closely with previously published work, and, yield a graph showing a direct relationship between fluid inflow (reabsorption by the vascular system) and applied pressure. With negative pressure, however, the outflow from the system increases only to a certain point (-20 to -30 cm. H_2O) and then remains constant in spite of negative pressures of as much as -60 cm. H_2O. The maximum rate of fluid output from the medium sized dogs used was remarkably constant at 12 cc./hr. Arterial blood pressure and respiration rate were not affected by these procedures. It would seem that these experiments offer strong support for the active secretion explanation of CSF production.

NATURAL COLD ACCLIMATIZATION IN MAN IN THE SUBARCTIC. T. R. A. Davis and R. J. T. Joy (intr. by J. R. Blair). U. S. Army Medical Research Laboratory, Fort Knox, Kentucky.

A 10 man squad was attached to a company of soldiers undergoing combat maneuvers in Alaska for a total of 52 days during January and February 1960. Before and after this period, shivering, oxygen consumptions, rectal and skin temperatures were measured in response to a standard cold exposure of 12°C for 2 hours. Finger cooling rates were measured in response to a local standard cold exposure of -15°C still air. During the period in Alaska immediate climatic conditions were measured 3 to 4 times daily. Daily calculations of fluid intake, physical activity, amount of sleep, and amount of cold exposure were also recorded. There were 3 consecutive periods during the maneuvers consisting of camp, field and camp. Fluid intake was decreased 30% during the field period. Activity increased 40% in the field and there was no significant difference in the mean daily amount of sleep obtained during the three periods but cold exposure increased 50% during the field period. The total period in Alaska produced a 50% decrease in shivering, a 30% decrease in oxygen consumption and no significant change in the rate of finger cooling. The rate of change in shivering was the same as the change seasonally effected in another group studied in Kentucky during the same period of the year but much less than the 80% change produced in a group acclimatized in the nude in a cold chamber for 30 days.

MATURATIONAL CHANGES IN THE NORMAL MONKEY EEG. Marisa I. Robert Ramirez de Arellano (intr. by W. F. Windle). Lab. Perinatal Physiol., NINDB, NIH, USPHS, DHEW, San Juan, P. R.

Periodic serial EEGs, 425 recordings, were made between birth and 2-1/2 years on 49 rhesus monkeys of known gestation, delivered vaginally or by section. Restraint reduced movement artifacts with minimal disturbance. Electrodes were applied over frontal, parietal, occipital, and temporal areas. Monopolar, using ears as reference, and bipolar recordings were made while awake and during spontaneous sleep without drugs. Photic stimulation also was used. Maturation changes in activity were related to animal's physiological state. Dominant frequency, amplitude changes, and type of rhythm of different areas, were considered. Waking EEG during 1st month showed low voltages in all areas, most marked in occipitals, 50-60 μv average, increasing to maximal voltage about 3rd month, with amplitudes 2-3 times higher. As the animal matured (1 year), a trend toward lower voltages occurred. Frequencies of 3-6/sec during 1st month gradually increased to 8-10/sec after 3rd. Sleep showed development of striking patterns; voltages were generally higher than while awake, especially in the parietal and frontal. On 1st day we observed bursts of high voltage, 5-6/sec sinusoidal waves, most marked in the parietal leads, and considered them to be sleep spindles. After 2nd week, paroxysmal bursts acquired such a "spiky" appearance that they could be misinterpreted as seizure discharges. Spindle formations of occipital cortex was observed in some monkeys.

THE EFFECT OF NALORPHINE ON RESPIRATORY PATTERN AND BLOOD PRESSURE IN DOGS WITH VARIOUS LEVELS OF BRAIN TRANSECTION. S. Deavers*, H. E. Hoff and R. A. Huggins. Department of Physiology, Baylor Univ. College of Medicine, Houston, Texas.

Nalorphine in unanesthetized dogs exhibited a morphine like action by producing a) deep sigh immediately upon administration b) increase of sighing breathing c) post-sigh-inhibition of eupnea and d) tachypnea. The chief differences from morphine are a reduction in degree of action and regularity in sighing suggesting that nalorphine does not have the same depressing effect on the cortex. Nalorphine produces effects similar to morphine at all levels of brain transection by increasing the rate and amplitude of eupnea and enhancing sighing respiration. However these effects are less marked than for morphine. There was no evidence of nalorphine antagonizing either the respiratory or circulatory effects of morphine.

LOCALIZATION OF HYPOTHALAMIC CENTERS REGULATING APPETITE. A.P. Debons*, L. Silver*, B.P. Cronkite, G. Brecher, H.A. Johnson* and I.L. Schwartz. Medical Research Center, Brookhaven National Laboratory, Upton, N. Y.

The glucostatic theory of appetite regulation rests heavily on the assumption that gold thioglucose produces lesions in the "satiety center" of the ventromedial hypothalamus. It is contended (Metabolism 6: 435, 1958) that the toxic gold moiety of this compound destroys the satiety-integrating neurones after being selectively accumulated by virtue of the special affinity of these cells for glucose. We have obtained critical evidence in support of this hypothesis by activation with thermal neutrons of Gold^{197}, $Au^{197}(n,\gamma)Au^{198}$, and Sulfur^{32}, $S^{32}(n,p)P^{32}$. These activation products were identified by β and γ spectrometry and radioautography. The radioautographs show that the gold and probably the sulfur moieties of gold thioglucose are accumulated in well-defined areas of the ventromedial hypothalamus in all animals that developed hyperphagia and obesity, but in none of the control animals. The technique of neutron radioactivation, as employed in this study, constitutes a new and unique method for the combined functional and anatomical localization of a neuronal integrating center.

EFFECTS OF "LIMBIC SYSTEM" LESIONS ON REPRODUCTIVE FUNCTIONS OF FEMALE RATS. J. deGroot and V. Critchlow*. Univ. California, San Francisco and Baylor University, Houston, Texas.

The effects of electrolytic brain lesions on mating and other aspects of reproduction were studied in 81 mature, female Holtzman and Long-Evans rats (200-250 gram B.W.). Sixteen animals, including 5 sham-operated rats, were used as controls. Complete destruction of the medial habenular nuclei (13 rats) was followed by 1) frequent matings during the "diestrus" of normal cyclicity or the "anestrus" of gestation as evidenced by the presence of sperm in the vaginal smears; 2) a high incidence of infertility; 3) significant decreases in litter size at birth ($P=0.01$) and at weaning ($P=0.001$). Similar results were seen with large bilateral lesions in the amygdaloid complex or stria terminalis (14 rats). In contrast, these aberrancies in reproduction were not observed in rats bearing unilateral lesions in these structures or in groups (3-6 rats each) with bilateral lesions in the lateral habenular nuclei, septum, fornix, olfactory bulbs or mammillary nuclear complex. The abnormal matings associated with the lesions in the medial habenula and amygdala may be related to the 'hypersexuality' observed in other species following lesioning of the amygdaloid complex. (Supported by USPHS grants B-1743, B-2293, SF-364 and SF-322).

SELECTION OF A VENTILATORY REGIME AND THEORY OF MINIMUM WORK. Pierre Dejours (intr. by W. O. Fenn). Lab. de Physiol., Faculte de Med. et Centre Marie Lannelongue, Paris, France.

It has been postulated by others that the alveolar ventilation requirements are satisfied in such a manner that the work done by the respiratory muscles is nimimal. Certain observations to be discussed do not fit well in this concept since (1) the ventilation pattern differs among various subjects to such an extent that one may speak of "ventilatory personalities," and (2) in the same subject, at a given alveolar ventilation, the pattern may vary, depending upon the physiological circumstances which determined the ventilation. The functional properties of the ventilatory system (respiratory centers, motor pathway, thoracic and respiratory proprioceptive pathways) together with the pattern of the ventilatory stimuli determine the type of ventilation in a given subject. The economy of the respiratory muscles should be considered as one of the elements in the functional properties of the ventilatory circuit.

THE EFFECT OF LIVER IRRADIATION ON DIFFERENT TYPES OF R.E. SYSTEM STIMULATION. Ernest L. Dobson, Lola S. Kelly and Caroline R. Finney*, Donner Lab., University of Calif., Berkeley.

Phagocytic function of the R.E.S. is stimulated by estradiol or bacterial endotoxins. We have shown (Am. J. Physiol. 198, 1134, 1960) that stimulation by estradiol is accompanied by marked proliferation of R.E. cells in the liver. The functional stimulation by endotoxin is equally great but the increase in cell proliferation (DNA synthesis) is very much lower. Howard (J. Path. and Bact. 78, 465, 1959) has shown a change in staining and acid phosphatase content of R.E. cells of liver following endotoxin administration. Experiments reported here show that radiation interferes with stimulation by estradiol but not with stimulation by endotoxin, in agreement with the hypothesis that estradiol stimulates primarily through R.E. system proliferation while endotoxin stimulates primarily through activation of existing cells. Phagocytic function was measured in mice by the clearance of colloidal carbon from blood. Irradiation, approximately 3,000 rads in 10 days, was administered with colloidal $CrP^{32}O_4$ (Dobson and Jones, Acta Med. Scand. 144 Supl., 273, 1952). Despite this high radiation dose, estradiol stimulation was not completely suppressed. The irradiated mice were stimulated half as much as the controls. Endotoxin stimulation on the other hand was essentially not affected by the irradiation.

EFFECT OF EXERCISE ON SERUM THYROXINE-BINDING. J.T.Dowling and J.T.Nicoloff, (intr. by D. H. Simmons). VA Center and UCLA Med. Center, Los Angeles, California.

The human thyroid gland is notable for its constant function during a variety of alterations in bodily economy. In view of the intimate relationship of thyroid hormone to widespread metabolic processes this stability is paradoxic. Recently it has been found that the interaction of circulating thyroxine (T_4) with its specific transport proteins, the T_4-binding globulin (TBG) and T_4-binding prealbumin (TBPA), is altered in a number of physiologic states. The significance of these changes is uncertain. The hypothesis was raised that acute reductions in T_4-binding of extracellular fluids might temporarily increase the availability of hormone to the tissues. Since it places abrupt and profound demands on energy metabolism, exercise was employed to test this hypothesis. Five subjects ran distances from one-quarter to three miles. Sera were obtained at varying intervals before, during and following exercise. T_4-binding was assessed by electrophoretic and ion-exchange resin technics. Marked depression of T_4-binding by TBPA was observed after as little as 100 yards, and was maximal at distances of one-quarter to one mile. Whereas the control T_4-capacity of TBPA averaged 100 ug.per cent, exercise values were reduced to below 50 ug.per cent. Changes in T_4-binding by TBG did not occur. These alterations were remarkedly consistent between individuals and in replicate studies performed thus far. Binding capacities returned to control levels as soon as one-hour after exercise. Although the physiologic significance of these observations is not established, acute changes in the circulating transport of T_4 may be a sensitive means for altering the tissue availability of the hormone.

THE MANNER OF EXC TION OF CO_2 IN URINE, Douglas R. Drury and Mary Almen*, Physiology Dept., University of Southern California, Los Angeles.

There are two theories about the origin of the bicarbonate that is excreted in alkaline urines. One view represents bicarbonate as being actively reabsorbed by the tubules so that what is excreted is what was filtered and not reabsorbed. Another view looks on CO_2 as highly diffusible in the kidney as it is elsewhere, and that the bicarbonate of the tubular fluid exchanges with intracellular CO_2 all the way down the nephron. We have studied this problem by two methods. In one we injected $NaHC^{14}O_3$ by constant infusion until the specific activity (S.A.) of respired CO_2 became constant. At this time we found the S.A. of urine CO_2 definitely lower than that of respired CO_2. In the other method we produced an osmotic diuresis, then injected simultaneously ferrocyanide and $NaHC^{14}O_3$ and collected urine in 5 second periods. Labeled bicarbonate appeared almost immediately in the urine whereas ferrocyanide appeared only after 40 seconds or more. The results with both procedures indicate that CO_2 exchanges very readily between cells and tubular fluid.

UNILATERAL COLD-ADAPTATION TO RECURRENT ICE-WATER IMMERSION. C. J. Eagan (intr. by J. P. Hannon). Arctic Aeromedical Laboratory, Ladd AFB, Alaska.

Evidence for a topical adaptation to recurrent cold exposure has been sought in a study of the cold-induced vasodilation (CIVD) reaction of the finger. One middle finger of each of 2 subjects was immersed in ice water, for at least 5 min, 6 times per day, for 17 consecutive days. The corresponding, contralateral finger served as control in 20 min test immersions (to a depth of 2.8 cm in $1 \pm 0.5^{\circ}C$ water), done simultaneously on the 2 fingers, before, during, and after, the exposure period. Plethysmography, calorimetry, and thermometry, applied concurrently, showed no differences in the vascular responses of the 2 fingers. However, minute-by-minute comparisons of pain sensation, using a 5-unit scale, showed that at the end of the exposure period there was a marked reduction in pain from the test finger. Comparisons of CIVD reactions of the fingers, done serially, supported the above conclusions; pulse rate comparisons confirmed the subjective estimates of pain. The method of simultaneous bilateral testing, subsequent to unilateral cold exposure, using 3 separate criteria of vascular reactivity, could detect local circulatory adaptations, had they occurred. Since only pain sensation was changed, it is considered that central "habituation" (Glaser et al., J. Physiol. 146: 152, 1959), rather than local adaptation, is involved. The failure to find a circulatory adaptation, as other workers have reported, is attributed to the method of testing, which obviates mistaking the results of behavioural changes for physiological adaptation.

CARDIOVASCULAR CHANGES INDUCED BY ELEVATED INTRACRANIAL PRESSURE
H. E. Ederstrom and Oliver Wiger*. Univ. No. Dakota School of Med., Grand Forks, N.D.

The cardiovascular responses to increased intracranial pressure (ICP) have been ascribed to anoxemia of the CNS, and to stimulation of a receptor that reflexively induced neural and humoral pressor effects. For the purpose of differentiating vasomotor constrictor responses of neurogenic origin from humoral effects, a group of dogs were subjected to unilateral lumbar or thoracic synpathectomy, or to motor denervation of the leg. Following recovery, blood flow in the legs was measured under anesthesia while ICP was held at 200mm Hg for 2 minutes. The typical vagal effects on the heart and vasopressor responses were found. Blood flow was measured in the cannulated femoral artery during ICP and an average rise of 50% found, indicating that increased cardiac output occurs during this procedure. In the normal leg vasoconstriction occurring during ICP reduced venous outflow to about one-half the control level. When one leg had been sympathectomized less than one hour previously it had control blood flows about double those of the unoperated leg. During ICP flow decreased in the operated leg to about one-half the control level. Following chronic lumbar or thoracic sympathectomy, or motor denervation, similar reductions in flow were observed in both operated and normal legs. The results suggested that ICP elevation released blood-borne pressor substances that could account for the intense vasoconstriction, and that vasomotor stimulation was not necessarily involved in the response. (Supported by Am. Heart Assoc. Grant)

EFFECT OF PANCREATIN ON NITROGEN AND FAT METABOLISM IN THE PANCREATIC DEFICIENT RAT. L.E. Edwards and A.C. Brehme*, Department of Physiology Medical College of Virginia, Richmond, Va.

Since pancreatin added to the diet of pancreatic duct-ligated rats restores growth in these animals, it was thought that metabolic studies should be carried out in relation to the digestion of fat and protein. Duct-ligated rats were placed in metabolism cages and the urines and feces were collected and pooled for three two-week periods. The first period consisted of a control diet containing no pancreatin, the second period consisted of a diet containing 1% 3X pancreatin and the third period consisted of the control diet again. Pancreatin markedly increased the digestion of fat and protein in the duct-ligated rats but seemed to impair to some extent the digestion of fat in the normal rat. Growth is restored in the pancreatic deficient rat by pancreatin and this is tied in with the improved protein and fat digestion.

HISTAMINE-INDUCED ELEVATION OF PRESSURE IN THE SUPERIOR SAGITTAL SINUS IN DOGS. Charles H. Ellis and Honora M. Noonan*. The Wellcome Research Laboratories, Tuckahoe, New York.

Intravenous injection of 5 to 10 microgram/kg of histamine diphosphate into anesthetized dogs results in a transient marked rise in superior sagittal sinus pressure. Inhibition and potentiation of the response can occur without observable changes in either amplitude or duration of the classic fall in systemic arterial pressure. The histamine-induced rise in sagittal sinus pressure can be blocked by ergotamine tartrate, by dihydroergotamine methane sulfonate, by dibenamine and by hexamethonium; it is enhanced by phloroglucinol, by the serotonin antagonist, B.W. 57-301 [2-amino-4-(N'methyl-N-piperazino) 5-(4'chlorophenylmercapto)-pyrimidine hydrochloride], and by iproniazid [Marsilid]. The antihistaminic compound, chlorcyclizine [Perazil] blocked the response although the arterial pressure fall was only partially inhibited. After adrenalectomy the response of sagittal sinus pressure to histamine is abolished; the fall of arterial pressure more protracted. An indirect mechanism via a sympathetic discharge of catecholamines is postulated for the histamine-induced rise in sagittal sinus pressure.

ROLE OF THE THYROID IN PULMONARY FUNCTION. Lois T. Ellison and Robert G. Ellison (intr. by W. F. Hamilton). Medical College of Georgia, Depts. of Physiology and Surgery (Thoracic), Augusta, Ga.

Considerable evidence in the literature suggests an intimate association between thyroid function and a variety of pulmonary disorders. Therapeutic benefit from I^{131} induced hypothyroidism has been observed in patients with obstructive emphysema and abnormal peripheral utilization of thyroid hormone in hypercapnia has been reported. Patients receiving inorganic iodine may develop myxedema and sudden withdrawal of the iodide may be followed by severe pulmonary insufficiency in emphysematous patients. Both aminosalicyclic acid and isoniazid are antithyroid drugs and diamox is said to lower I^{131} uptake. This plus other similar information prompted us to study pulmonary function in patients with hyper and hypothyroidism. Results in 8 hyper and 5 hypothyroid individuals indicated that in the former respiratory rate and tidal volume were significantly greater than in the latter. Nevertheless, the alveolar PO_2, although usually within normal limits in both types, tended to be higher in patients with hypothyroidism. Arterial PO_2 and PCO_2 were below normal in both and remained the same after exercise. Oxygen removed/liter ventilated was decreased below normal in hyper and hypothyroid cases, but in the former became markedly abnormal on exercise. Two patients of each type, restudied after adequate therapy, showed changes toward normal. Findings may be explained by physiological adjustments of the body to meet its metabolic demands. It would seem that respiratory function in patients with chronic pulmonary insufficiency would be further embarrassed by an increase in thyroid activity whereas certain aspects of decreased function might theoretically be beneficial. (Supported by USPHS Grant H-2562, Ga. Heart Assoc. and LIMRF).

CHEMORECEPTOR ACTIVITY IN THE CAROTID BODY OF CAT. C. Eyzaguirre and J. Lewin*. Dept. of Physiology, University of Utah College of Medicine, Salt Lake City.

The sinus and carotid body were excised together with a stretch of Hering's nerve and mounted in a flow chamber. Locke's solution (37°C, pH 7.4), equilibrated with varying concentrations of O_2 (10-100%) in N_2, was flowed through the chamber at 4 ml/min. Action potentials were recorded from the nerve. Pressoreceptor discharges were eliminated by removing the adventitia of the sinus. Chemoreceptor discharges were present in 100% O_2 and increased as O_2 was reduced. Whenever O_2 was decreased (e.g. from 50-20%) afferent frequency rose to a peak in several secs. showing a slight decline shortly afterwards. When the preparation was bathed with a solution equilibrated with a given pO_2 (e.g. 50%) an increase in temperature above 38°C markedly increased chemoreceptor discharge. This increase in frequency was followed by a decrease although temperature remained unchanged. Experiments performed in intact animals (37-38°C rectal) under gallamine and controlled ventilation showed: 1) progressive reduction in inhaled O_2 (100-10%) increased chemoreceptor frequency; 2) when O_2 was kept constant, inhalation of 6% CO_2 significantly increased chemoreceptor impulses; 3) relatively small changes in ventilation or blood pressure markedly changed chemoreceptor activity. In summary, carotid body chemoreceptors respond to a wide range of O_2 changes and this effect is influenced by temperatures above 38°C; relatively small increases in CO_2 also stimulate these receptors.

This work was supported by a Senior Research Fellowship, SF-260, US Public Health Service and by a grant from the National Science Foundation; one of us (J.L.) supported by a Rockefeller Foundation Fellowship.

FACTORS DETERMINING SPEED OF CO_2 STORES CHANGES. **Leon E. Farhi (intr. by H. Rahn). The Univ. of Buffalo Sch. of Med., Buffalo, N. Y.**

Determination of the CO_2 storage capacity (slope of the CO_2 dissociation curve) of the whole body has yielded results scattered over a wide range. In order to ascertain factors which could account for this discrepancy, the body has been described in terms of a multiple compartment system in which each compartment (tissue or organ) has its own capacitance (storage capacity) and resistance (inversely related to blood flow). An analogue was programmed using the specific values available for man. The computer results were found to duplicate very well existing physiological data. By varying some of the parameters it was possible to determine the most important factors in body CO_2 stores reequilibration. These are: (1) time, (2) perfusion of the muscle mass, and (3) alveolar ventilation. The time required for readjustment is always of several hours' duration. Analysis of the literature reveals that most of the data were probably obtained before equilibration had been completed. (Supported by the Wright Air Development Command, Wright-Patterson Air Force Base, Ohio.)

HYPERTROPHY AND INCREASED PROTEASE IN THE PANCREAS IN GASTRECTOMY IN THE RAT. S. E. Feldman, M. D. Poultry Husbandry Department, University of California, Berkeley, and Department of Surgery, Mount Zion Hospital, San Francisco.

Rats were gastrectomized and kept for prolonged periods of time (6 weeks to 6 months or more) on the standard rate diet 1. Anemia appeared in practically all the gastrectomized rats with an average of 8.4 grams hemoglobin per 100 grams of blood while those of normal rats were 14.3 grams hemoglobin. It is suspected that the anemia is due to Bartonella infection but this has not been established with certainty. Marked responses to the gastrectomy were found in the pancreas. It hypertrophied and the increase varied from group to group, the pancreas in some cases increasing two fold over that of normal rats, when calculated as weight of the pancreas per 100 grams weight of the rat. The increase in the weight of the pancreas was in part due to protein since the percent of nitrogen increased markedly. Along with the increase in the protein content of the pancreas there was an increase in the proteases of the pancreases of the gastrectomized over that of normal rats calculated as protease activity per gram of pancreas or as protease activity per 100 gram weight of rat. Some increase of amylase activity also occurred in the gastrectomized rats but it was not so marked nor did it always occur. The lipases responded to the gastrectomy in a manner similar to that of the amylases. The data may be interpreted to mean that the stomach plays a role in the function of the pancreas. It is probably due to the external secretion of the stomach but its internal secretion may also play some role in the influence the stomach exercises upon the function of the pancreas. This investigation was supported in part by Research Grant #A-1805 from the National Institutes of Health.

INCORPORATION OF C^{14}-VALINE INTO LIPIDS BY SLICES OF ADIPOSE TISSUE. D. D. Feller and E. Feist*. Veterans Administration Hospital and University of Washington School of Medicine, Seattle, Washington.

This study was undertaken to determine whether propionic acid was formed from valine in adipose tissue, and, if so, whether the propionic acid was consequently converted to fatty acids. Inguinal adipose tissue obtained from male Swiss mice fed an adequate diet ad libidum was sliced and incubated in the presence of C^{14}-valine. Saponifiable lipids were recovered by standard procedures and C^{14} content determined in this as well as in the CO_2 fraction. Organic acids were isolated and identified by paper chromatography. Radioactivity associated with the compounds on paper was determined by radioautographic procedures. Results demonstrate conversion of C^{14}-valine to lipids, CO_2, propionic acid and methylmalonate. Addition of carrier propionate or, independently, methylmalonate at 0.01M concentrations effected conversion of C^{14}-valine to fatty acids. The results show that valine is a precursor in the biosynthesis of lipids in adipose tissue. The data indicate that propionate and methylmalonate may be intermediates in the path of valine to fatty acids and follow an overall scheme common for conversion of isoleucine, acetate and propionate to fatty acids in adipose tissue.

POTASSIUM-WASTING NEPHROPATHY INDUCED BY VITAMIN D. Thomas F. Ferris*, Howard Levitin*, and Franklin H. Epstein. Dept. of Int. Med., Yale Univ. School of Med., New Haven, Conn.

The finding of hypokalemia in patients with hypercalcemic renal disease has occasionally been reported and infusions of calcium are said to increase the excretion of potassium in animals. In an effort to determine the effect of hypercalcemia on potassium conservation, a group of rats were placed on a low K diet for six days at the end of which time K excretion was minimal. They were then made hypercalcemic by the daily injection of 200,000 units of vitamin D for four days. This dosage of vitamin D consistently raised the serum calcium to levels between 12-14 mg % without a significant rise in serum urea. Urinary potassium excretion increased in response to the development of hypercalcemia so that by the tenth day it had reached a level of four times that of pair fed controls. Urinary losses of K were not secondary to adrenal stimulation, since the same response was observed in adrenalectomized rats maintained on DOCA. The increase of renal potassium excretion was not a consequence of the phosphate diuresis induced by vitamin D, since when normal animals, excreting minimal amounts of potassium, were given a buffered sodium phosphate load no increase in K excretion was observed.

CHANGES IN MECHANICAL PROPERTIES, APPEARANCE AND SURFACE ACTIVITY OF EXTRACTS OF ONE LUNG FOLLOWING OCCLUSION OF ITS PULMONARY ARTERY IN THE DOG. T. N. Finley*, E. W. Swenson*, J. A. Clements, R. E. Gardner*, R. R. Wright*, and J. W. Severinghaus. Cardiovascular Research Institute, Univ. of Calif. Med. Center, San Francisco.

The immediate response of one lung to occlusion of its pulmonary artery is a decrease in compliance (C), an increase in airway resistance (R) and a decrease in resting volume (V) causing a reduction in ventilation ($\dot{V}$) to that lung. This response was reversed by the inhalation of 6% CO_2 in 15% O_2. The chronic changes were followed in 8 dogs, sacrificed at intervals from 3 hours to 6 months. During the first week following ligation, the lung with the occluded pulmonary artery was filled with bloody, serous fluid, C and V were markedly reduced and $\dot{V}$ fell to zero. Following this period these values began increasing. At 4 weeks they were 50% of normal, and were not affected by the inhalation of 6% CO_2; the lung was still small, had a bluish appearance, was firm and difficult to inflate. Histologically it showed scattered PAS-positive hyaline membranes lining the alveolar ducts and alveoli. There was no evidence of infection. For the next 5 months, C, V, and $\dot{V}$ increased to about 70% of normal. At 6 months, the lung appeared normal though slightly reduced in size; histologically it showed only a few scattered areas of interstitial fibrosis. The earliest measurement (3 hours) of extractable surface active material from the lung with the occluded artery showed a decrease of 30% in the ratio of change in surface tension over average surface tension compared to the other lung. This decrease was found at 2, 4, and 6 weeks but not at 6 months. This decrease in surface activity could account in part for the changes in mechanical properties that were observed. (Supported in part by H-4247, USPHS.)

RAPID CHANGES IN HEART RATE INDUCED BY TILTING. John G. Fletcher* and Frank Girling, Environmental Physiology Group, Defence Research Medical Laboratories, Toronto, Canada

It is well known that changes in posture alter heart rate, and that holding a relaxed man in a head-up position can produce fainting. The effect of different positions on the heart rate is not clear, nor has it been determined how rapidly heart rate responds to change in position. Experiments were performed at 70°F and 55% R.H., the subjects being normal, physically relaxed human males whose physiques ranged from "lean with well-developed musculature" to "obese and poorly developed". Each subject was exposed for 30 seconds at each of 8 positions, multiples of 45° to the vertical. Each position followed every other in a systematic design of 64 position changes per experiment. Not less than 5 experiments were done with each man. Heart rates were monitored continuously; a cardiotachometer recording the number of beats per 5 seconds, and a cardiochronograph operating from separate chest electrodes. It was found that the resting heart rate was related to body position and the relationship was the same in all subjects. Heart rates were highest in the vertical head-up position, lowest in the head-down and intermediate in the 2 horizontal positions. In both 45° head-up positions the rate was higher than in the horizontal; in both head-down 45° positions the rate was lower than in the horizontal. The time taken to move from one position to another did not exceed 3 seconds. It was found that the heart rate changed very rapidly after tilting, the maximum time taken to achieve a new steady rate being less than 15 seconds. Deceleration of the heart rate appeared to be a more rapid process than acceleration; changes from high to low rates occurred in less than 5 seconds. The results show that rapid alterations in heart rate follow changes in posture. The mechanisms effecting these alterations will be discussed.

APPLICATION OF DIRECT BLOOD NITROUS OXIDE ANALYSIS TO THE MEASUREMENT OF CORONARY BLOOD FLOW IN DOGS. I. Forte, A. Jane Williams, J. E. Schmitthenner and H. Neal (Intr. by J. H. Hafkenschiel). Division of Research, Lankenau Hospital, Philadelphia, Pa.

Analysis of blood nitrous oxide has been carried out for a period of seven years by direct measurement using an infrared analyzer. These measurements have been applied to the determination of coronary blood flow in dogs according to the Fick principle with respect to nitrous oxide desaturation of arterial and coronary sinus blood. Since it was necessary to anesthetize the animals before blood flow determinations could be made, the rates of flow under two types of anesthesia (pentobarbital sodium, and a combination of morphine, dial-urethane, pentobarbital sodium) have been compared. Rates of flow have been determined during pharmacodynamic stimulation with various adrenergic like drugs such as nicotine and "hypertensin". This direct method of nitrous oxide analysis appears to be accurate and reproducible, and the coronary blood flow determinations, although limited by an indirect method of measurement over a period during which an unsteady state may possibly exist, are, nevertheless, quantitative. Slower blood flows obtained using the combined anesthesia are more accurately measured than the faster flows under pentobarbital sodium anesthesia. Supported by grant H1817C5 from P. H. S.

THE EFFECT OF THE DIETARY LIPID LEVEL ON TISSUE MAGNESIUM. William C. Foster and Julia A. Rehm‡ Laboratory of Physiology Research, Misericordia Hospital, Philadelphia, Pa.

High levels of dietary magnesium have been reported to reduce the deposition of lipids in the arterial endothelium of rats when placed on diets high in cholesterol and cholic acid. The experiments reported in this study were undertaken to determine the effect of the dietary lipid level on the magnesium content of various tissues in the rat. Groups of Wistar-strain albino rats were placed on diets of low and high magnesium, with low and high lipid content, for 30 days. After sacrifice, the magnesium content of skeletal muscle, liver, kidney, brain, and blood was determined by the method of Neill and Neely. It was found that high levels of dietary lipid caused a reduction in the magnesium content of all tissues studied. Likewise, the tissues of rats fed high levels of magnesium showed similar reductions in the content of magnesium when placed on a high lipid diet. However, these reductions started from a higher level. (Studies supported by a grant from the National Institute of Dental Research.)

UTERINE RESPONSE TO ESTROGEN IN THE ALLOXAN-DIABETIC RAT. Diane D. Fowler and Sherwin H. Sloan (intr. by Clara M. Szego). University of California, Los Angeles.

As part of a long-term exploration of early parameters of estrogen action on the uterus, an investigation was conducted on the influence of alloxan diabetes on the Astwood uterine water imbibition response to estradiol-17β, 14-16 days after ovariectomy, in adult rats. Alloxan (20 mg/100 g B.W.) was injected S.C. to a number of these animals 3 days prior to estrogen administration. Only those rats having a blood sugar of over 300 mg % were used. Estradiol-17β in olive oil (0.5 μg/100 g B.W.) was administered S.C. 6 hrs. before autopsy. Estradiol treatment of non-diabetic castrates resulted in a uterine water content of 84.8 ± 0.4 % (S.E.), a significant increase ($p < 0.001$) over oil-injected controls (79.6 ± 0.5 %). The same dose of estrogen elicited no response in alloxan-diabetic castrates (79.0 ± 1.6 %). Insulin, 0.5 U/100 g B.W., I.P. 3 hrs. before autopsy, a dose which did not influence responsiveness to estrogen in controls (84.8 ± 0.4 %), substantially counteracted the diminished sensitivity of alloxan-diabetic rats (83.4 ± 0.5 % -- $p < 0.05$). Adrenalectomy performed concomitantly with alloxan administration abolished the reduced estrogen sensitivity observed with alloxan alone (85.1 ± 0.4 %). The results indicate that at least a portion of the estrogen insensitivity of the alloxanized rat may be ascribed to adrenocortical hypersecretion. The relationship of the results to metabolic derangements of diabetes, or to failure of the estrogen-induced histamine release mechanism described earlier from these laboratories (Spaziani and Szego, Endocrinology 63, 669, 1958) is being explored. Aided by a grant from the National Cancer Institute of the National Institutes of Health (CY-1488).

SPATIAL SEPARATION OF SEQUENTIAL PORTIONS OF THE INSPIRATE IN THE NORMAL LUNG. Charles W. Frank (intr. by M.H.Williams Jr.). Albert Einstein College of Medicine, New York.

The arterial saturation was monitored during a 25 second period of breatholding at a constant lung volume in normal subjects. There was no fall of arterial saturation when breatholding was accomplished after inspiration of 1900 ml of air from the residual lung volume.. However, when the 1900 ml of inspired gas was divided into its two major components, and the 400 ml of pure O_2 were inspired first, followed by 1500 ml of pure N_2, the arterial saturation exhibited a slight (avg. 2.5%) but consistent fall. This fall was not observed when the separate gases were inspired in the order N_2 (400 ml)-O_2 (1100 ml) or N_2(800 ml)-O_2 (400 ml)-N_2 (700 ml). In all combinations, the inspired O_2 concentration was approximately 21%, and the mean O_2 tension in the samples expired after breatholding was similar for all of the inspired gas mixtures, and for air. These findings indicate that the filling of the normal lung from the residual volume occurs in a sequential pattern; the first portion of the inspired mixture apparently goes disproportionately to a space which is soon filled and which is poorly perfused. Examination of the N_2 composition in the expirate following breatholding indicates that this first filled space is last emptied during a forced expiration.

FUNDAMENTAL DIFFERENCES BETWEEN ACETYLCHOLINE- AND POTASSIUM-INDUCED CONTRACTURES. **George B. Frank. Dept. of Pharmacology & Therap., Univ. of Manitoba Faculty of Med., Winnipeg, Canada.**

Since both acetylcholine and potassium initiate contractures by depolarizing skeletal muscle, it is generally assumed that a fundamentally similar mechanism of action is involved. In a previous study of the role of calcium ions in excitation-contraction coupling, it was found that potassium-induced contractures of frog's skeletal muscle could be eliminated completely by keeping the muscle in a calcium-free solution for a few minutes. In these experiments the solutions contained choline in place of sodium and 10^{-4} g/ml d-tubocurarine. In similar experiments with solutions containing sodium rather than choline and no d-tubocurarine, the contractures could not be eliminated completely even after the addition of EDTA (5 mM/l) to the calcium-free solutions. Since d-tubocurarine eliminated this residual response, it was thought to be produced by acetylcholine released from nerve endings by potassium. The residual response did not appear in muscles denervated 14 days or more before testing. On the other hand, a residual response could be produced if the devervated muscle was treated for a few minutes with 10^{-4} g/ml acetylcholine before testing with potassium in a calcium-free solution. Replacing chloride with bromide in the solutions increased the size of contractures produced by 25 mM potassium 4 to 12 times in different muscles. In contrast, contractures produced by acetylcholine were at most doubled in size and were usually essentially unaltered. (Supported by the National Research Council of Canada and the Canadian Muscular Dystrophy Association.

A COMPARISON OF SEVERAL METHODS FOR MEASURING FLOW RESISTANCE IN SUBJECTS DURING EXPOSURE TO SO_2. Robert Frank,* Jere Mead, Mary O. Amdur* and J. L. Whittenberger. Harvard School Public Health, Boston, Mass.

Three methods were used to measure respiratory flow-resistance in nine healthy volunteers exposed to SO_2 (average concentration 13 PPM) while seated in a body plethysmograph. Measurements were made during a control period and starting 10 minutes after the onset of exposure. Included were the esophageal pressure method for estimating lung tissue viscous and airway resistance (quiet and rapid breathing), the DuBois method for estimating airway resistance (rapid breathing), and a third method for estimating total respiratory resistance (rapid pressure oscillations applied at a rate of 7 cycles/sec.)* Average values for control and exposure were: esophageal pressure method, quiet breathing 1.54 and 2.46 cm H_2O/L/sec. (S.D. of paired differences: 0.59 cm H_2O/L/sec.; $p<.01$); same method, rapid breathing: 1.23 and 1.73 cm H_2O/L/sec. (S.D. .44 cm H_2O/L/sec.; $p<.01$); DuBois method: 1.08 and 1.55 cm H_2O/L/sec. (S.D. .39 cm H_2O/L/sec.; $p<.01$); method for measuring total respiratory resistance: 1.68 and 1.96 cm H_2O/L/sec. (S.D. .31 cm H_2O/L/sec.; $p<.05$). In another experiment 10 volunteers were exposed to SO2 (average concentration 11 PPM) for the same interval. Flow-resistance was measured by the esophageal pressure method (quiet breathing) and by the Clements' interrupter method (continuous expiration from a point of maximal inspiration). Average control and exposure values for the first method 1.48 and 2.46 cm H_2O/L/sec. (S.D. .97 cm H_2O/L/sec.; $p<.01$); the interrupter method showed no significant increase during exposure. From these observations it appears that the change in flow-resistance induced by a respiratory irritant is inversely related to the frequency at which a method operates.

* The volume-history of the lungs was nearly the same for all measurements.

ASPECTS OF THE PHYSIOLOGICAL RESPONSE TO WHOLE-BODY VIBRATION
T.M. Fraser, G.N. Hoover, and W. F. Ashe (intr. by E. T. Carter).
RCAF, and The Research Foundation, The Ohio State Univ., Columbus 10, Ohio.

Unrestrained seated human subjects were exposed to harmonic sinusoidal vibration in all combinations of 4 frequencies, 4 amplitudes, and 3 planes. Concurrent records of heart rate and pattern, respiration rate and pattern, and immediate post-vibration blood pressure were obtained, along with an assessment of transmissibility. The results demonstrated a relationship to frequency of vibration such that at 2 cps and all amplitudes there was a tendency towards decrease in the respective values, whereas with increasing frequency an increase occurred related to the amplitude at the frequency concerned. The increase is compatible with the response of an untrained subject to sub-maximal exercise. The frequency of maximum transmissibility was observed to vary with the plane of vibration. Reasons for this are discussed.

CORRELATION OF EEG OF OLFACTORY CORTEX WITH MOTOR RESPONSE. Walter J. Freeman (intr. by S. F. Cook). Dept. of Physiology, Univ. of California, Berkeley.

Previous measurements of the amplitude of prepyriform electrical activity in cats demonstrated a positive relation with sensory input, but only during anticipation and not (on the average) during work performance. Statistical correlation of measurements of amplitude made during work with the rate of work showed a positive correlation after short periods of food deprivation (3-9 hours) and a negative correlation after long periods (48-72 hours). Sufficient measurements have now been made to show a graphic correlation between amplitude and rate of work at each of 2 periods of deprivation (24 and 48 hours). When rates of work for each cat are plotted in order of increasing magnitude, it is found that for values below the mean rate of work for each cat the amplitude of prepyriform electrical activity increases, so that for every 3% increase in rate of work there is a 1% increase in amplitude. For values above the mean rate of work the amplitude decreases, so that peak amplitudes tend to occur with rates of work near the mean. Maximal amplitudes also occur in association with unusually high rates of work, i.e. those 2.0 S. D. or more above the mean. Similar correlations exist between rate of work and the amplitude of the prepyriform potential evoked by direct electrical stimulation of the cortex at constant intensity. It is concluded that the amplitude of electrical activity in primary olfactory cortex is as closely related to the motor output as it is to the sensory input to the brain.

HEAT PRODUCTION AND HEAT LOSS OF THYROIDECTOMIZED AND ADRENALECTOMIZED RATS EXPOSED ACUTELY TO COLD AIR. M. J. Fregly and P. F. Iampietro, Department of Physiology, College of Medicine, University of Florida, Gainesville and Physiology Branch, QM Research and Engineering Center, Natick, Massachusetts

Thyroidectomy (propylthiouracil treatment) and adrenalectomy increased rate of cooling of rats restrained in air at 5° C. At the same colonic temperature during cooling, both thyroidectomized and adrenalectomized rats maintained higher skin temperatures than control rats. Heat production (measured by oxygen consumption) was determined for thyroidectomized and control rats only. At the same colonic temperatures during cooling, thyroidectomized rats had the same metabolic heat production as controls. However, calculated heat loss at a given colonic temperature during cooling was greater for thyroidectomized than for control rats. The inability of thyroidectomized rats to tolerate cold as well as control rats is almost entirely due to a more rapid loss of body heat. The cause of failure of heat conservation may be related to changes in vascular reactivity induced by the hypothyroid state. Supported by Contract AF(657)-171 with The School of Aviation Medicine, Brooks Air Force Base, Texas.

THE ROLE OF THE LIVER AND THE INFLUENCE OF ANESTHESIA ON PANCREATIC AND LIVER SECRETIONS DUE TO SECRETIN. M.H.F. Friedman and Ann M. Ambromovage,* Dept. of Physiology, Jefferson Medical College, Phila., Pa.

Experiments on unanesthetized dogs with chronic cannulated fistulas of the stomach and intestine as well as acute experiments under anesthesia were performed. Pancreatic juice was obtained by intubation of the pancreatic duct through the duodenal cannula. Liver bile was similarly obtained from cholecystectomized dogs. Secretin was given either by systemic vein or by portal (splanchnic) vein. Pancreatic and biliary secretions were measured by a pressure-equilibrium drop recorder. In the unanesthetized animal wide variations between dogs were encountered in pancreatic and biliary responses to standard doses of secretin as well as to intestinal instillation of acid. In each dog, however, the responses fluctuated only within narrow limits. The ratio between secretin response and acid response was constant and characteristic for each dog. Under anesthesia the standard dose of secretin elicited a constant response from both pancreas and liver, but the secretion resulting from acid instillation was poor and inconsistent. The ratios between secretin-provoked and acid-provoked secretions for both pancreas and liver fluctuated widely. In pancreatic as well as bile secretions there were no statistically significant differences between the effects of secretin given by systemic route and by portal route. It was concluded: 1. the effect of secretin on liver secretion parallels that on pancreatic secretion; 2. the liver plays little if any role in inactivating secretin of endogenous origin; 3. anesthesia depresses the formation or elaboration of secretin by acid in the intestine.

INHIBITION OF ACTIVE SODIUM TRANSPORT BY CHOLERA TOXIN. Geraldine J. Fuhrman* and Frederick A. Fuhrman. Basic Medical Sciences Laboratories, Stanford University School of Medicine, Palo Alto, California.

In small intestine and colon sodium is transported actively from lumen to blood, but water transfer depends upon gradients of water activity and is a passive process. Net absorption of water, therefore, is dependent upon active sodium absorption. If active sodium transport across intestinal mucosa were decreased or abolished, one would predict excretion of abnormally large amounts of water and sodium from the intestine, i.e., diarrhea. This hypothesis was tested by determining the effect of a cholera filtrate on active ion transport in the frog skin and gastric mucosa. The potential difference across the membranes, the current produced at zero potential, and the influx and outflux of Na^{22} were measured. Cholera filtrate clearly decreases net Na flux and sodium influx; i.e., active sodium transport in the skin. The filtrate did not have this effect when applied to gastric mucosa. Since gastric mucosa does not actively transport sodium, the toxin may be rather specific. The nature of the active component of cholera filtrate is not known, but after dialysis through cellophane the active material is present in the dialysate, and heating for one hour at 80°C. does not measurably decrease the activity. Its properties therefore resemble those of the cholera endotoxin and differ markedly from those of receptor destroying enzyme (RDE). The effect on sodium transport is consistent with our hypothesis for the diarrhea of cholera.

A METHOD OF ISOLATED HEAD PERFUSION IN THE DOG. P. M. Galletti and M. A. Hopf (intr. by P. A. Stewart). Dept. of Physiology, Emory University, Atlanta, Ga.

A method of external perfusion of the isolated head of the dog by means of a pump-oxygenator has been developed. The leading ideas of the surgical technique proposed are to prevent temporary cerebral ischemia during the period of preparation, and to avoid the use of a donor dog and of homologous blood. Carotid and jugular vessels are prepared and one pair of vessels is first connected to the external circuit (Pulmo-Pak^{R}) for partial perfusion. The other pair of neck vessels is then cannulated, the chest is opened and the superior vena cava and the vertebral arteries are clamped intrathoracically. The heart remains active, and can take over the head circulation again when the external perfusion is later stopped. In acute experiments, the heart is arrested, the animal exsanguinated and the lower part of the body surgically removed from the perfused head.

CHANGES IN BLOOD ACTH LEVELS FOLLOWING ADMINISTRATION OF SU-4885 TO ADRENALECTOMIZED DOGS. W. F. Ganong and E. M. Gold*, Department of Physiology and Metabolic Unit, School of Medicine, University of California, San Francisco 22, California

The increased pituitary ACTH secretion associated with administration of SU-4885, an inhibitor of adrenocortical 11-β-hydroxylase, has been attributed to lowered circulating cortisol levels secondary to decreased cortisol production. To determine whether this agent causes ACTH release independent of its effects on the adrenal, SU-4885, 10 mg./kg./hr., was infused intravenously for four hours to pentobarbital anesthetized adrenalectomized dogs maintained on desoxycorticosterone trimethylacetate. Blood ACTH (Nelson and Hume, Endocrinology 57:184, 1955) was measured at the end of the infusion. It was also measured after four-hour control infusions of saline, and in some cases, before the infusions were started. Circulating whole blood ACTH levels (mean ± standard error) were 7.5 ± 2.7 mu% before infusion (11 dogs), 12.6 ± 2.2 mu% after saline (10 dogs), and 22.9 ± 5.4 mu% after SU-4885 (9 dogs). Six of 10 dogs had values of 10 mu% or less after saline infusion, while 8 of 9 dogs given SU-4885 had values of 13 mu% or more. Circulating corticoids were undetectable in all adrenalectomized dogs, using a method which detects both cortisol and 11-desoxycortisol (Gold, Serena and Cook, J. Clin. Endocrinol. & Metab. 20:315/1960). The data suggest that in the dog, SU-4885 can increase blood ACTH levels by a pathway independent of its action on the adrenal cortex. (Supported by Commonwealth Fund.)

AN ACTION IN VITRO OF ADRENAL CORTICOSTEROIDS UPON FLUID MOVEMENT ACROSS THE ISOLATED INTESTINAL EPITHELIUM. Carmia Ganz-Borek* and C. Adrian M. Hogben. Physiology Department, The George Washington University School of Medicine, Washington, D.C.

Net movement of fluid across the isolated bullfrog intestinal epithelium can be easily followed over a 6 hour period using a technique previously reported (Proc. Soc. Exp. Biol. and Med. 99:746, 1958). In this technique, net movement of water is determined by weighing sacs of small intestine which are incubated at room temperature. The sacs are not everted and both surfaces are exposed to the same saline solution. When adrenal corticosteroids were added to the outside medium bathing the serosal surface, they stimulated the absorption of fluid. Hydrocortisone acetate 10 mg/l - 10 experiments and 5 mg/l - 5 experiments; desoxicorticosterone acetate, 5 mg/l - 3 experiments; and aldosterone acetate, 0.5 mg/l - 3 experiments; all increased the net fluid absorption significantly. Hydrocortisone acetate 1 mg/l - 5 experiments did not significantly alter fluid movement.

A SYSTEMATIC FRACTIONAL PROTEIN EXTRACTION OF BRAIN AND ITS SUB-MICROSCOPIC PARTICLES. **Alexander Geiger and Iris Maggiolo Barbato. University of Illinois College of Medicine, Department of Psychiatry, Chicago, Illinois (intr. by L. G. Abood).**

It has been found that when C^{14} labeled glucose is perfused into cats' brains, most of the activity incorporated into proteins is found in the particulate matter. A technique has been developed for a systematic extraction of brain proteins, the first step of which consists in homogenization of the tissue with 0.3M sucrose followed by separation by differential centrifugation of the nuclei, mitochondria, and microsomes. The sucrose supernatant contains about 28% of the total proteins of the brain. Nuclei, mitochondria, and microsomes contain 13, 50, and 9% respectively. These three particulate sediments were suspended separately in 20% NaCl by homogenization. The NaCl extracts about 50, 25, and 60% respectively of the nuclear, mitochondrial, and microsomal proteins. Triton X-100 (0.5%) a non-ionic detergent at pH 8.5 was used for a third extraction of the residual particles giving a solubilization of 8, 10, and 3% of the proteins of the nuclei, mitochondria, and microsomes. By this procedure, which permits further fractionations of the obtained supernatants, 90% of the total protein activity can be recovered.

POST-TETANIC POTENTIATION AND RECURRENT INHIBITION OF MONOSYNAPTIC REFLEXES IN DOGS WITH EXPERIMENTAL HIND-LIMB RIGIDITY. S. Gelfan and I. M. Tarlov.* N. Y. Med. College, New York City.

The marked disturbance of functional organization of the spinal cord in experimental hind-limb rigidity, due to anoxic destruction of interneurons, has been further analyzed by means of post-tetanic potentiation and recurrent inhibition testing. The observed alterations in course and duration of post-tetanic potentiation of the monosynaptic reflexes in rigid animals must be due to altered excitability of the "spastic" motoneurons. We previously proposed that this excitability alteration is due to extensive motoneuron denervation. Such motoneurons, however, are still subject to recurrent inhibition. Activity, attributed by some to Renshaw cell discharges, has been recorded in rigid dogs when antidromically stimulated. When recurrent inhibition of monosynaptic reflex is pitted against post-tetanic potentiation, the net result, again, takes a different course from that in the normal dog. This inhibition is clearly less effective against the potentiated state in rigid animals. The relation of this modified effect to the hypothetical Renshaw cells will be discussed.

ELECTRICAL RESPONSE OF MAMMALIAN SMOOTH MUSCLE TO STIMULATION OF THE EXTRINSIC SYMPATHETIC AND PARASYMPATHETIC NERVES. J. S. Gillespie (intr. by F. Brink, Jr.). Rockefeller Institute, New York.

The response, recorded with an intracellular microelectrode, of mammalian smooth muscle cells to drugs, to stretch and to changes in the ionic environment have been reported. The response of such cells to stimulation of the extrinsic nerves has not. Using a preparation of the rabbit colon retaining the two extrinsic parasympathetic (pelvic) nerves and the sympathetic (lumbar colonic) nerves it has been possible to do so. The preparation shows spontaneous rhythmic activity; associated with each contraction there is a short burst of spike activity. Between bursts there are slow waves of depolarisation which initiate the bursts of spikes. Stretching the preparation prolongs the period of spike activity producing finally a continuous spike discharge whose frequency fluctuates with rhythmic variations in tension. Single electrical stimuli to the sympathetic (inhibitor) nerve are ineffective. Low frequencies of repetitive stimulation (2/sec) have two effects. The rate of depolarisation during the slow waves is reduced so that the time taken to reach the firing level is increased, and the correlation between spikes and contraction is lost. Spikes are seen when mechanical inhibition is complete and small contractions are seen without spikes. At higher frequencies (20/s-50/s) there is complete mechanical inhibition with suppression of both spikes and slow waves. Hyperpolarisation is seen only rarely. Stimulation of the motor (pelvic) nerves at frequencies up to about 2/sec will "drive" the preparation; each nerve stimulus is followed by a "local response" which if large enough initiates a spike and an increment in tension. Above 2/sec there is maintained depolarisation. Spikes are superimposed but diminish in amplitude and eventually disappear leaving irregular low amplitude slow waves. The muscle remains in tetanic contraction.

DELAYED RESPONSE PERFORMANCE OF SPLIT-BRAIN MONKEYS WITH UNILATERAL PREFRONTAL ABLATION AND OPTIC TRACT SECTION. M. Glickstein*, H. Arora*, and R. W. Sperry, Div. Biol., Calif. Inst. of Tech., Pasadena, Calif.

Bilateral (but not unilateral) prefrontal lesions markedly impair delayed response performance of monkeys. Moreover, in bilateral operates this deficit is classically accompanied by hyperactivity and distractability. Seven Rhesus monkeys are being tested on the delayed response following seriatim ablation of one optic tract, one prefrontal area, and corpus callosum along with anterior and hippocampal commissures. Of three cases completed to date, two with prefrontal lesions ipsilateral to the cut optic tract were relatively unaffected by the commissurotomy. One case with prefrontal ablation contalateral to the cut tract showed marked impairment of delayed response performance after the commissurotomy. Moreover the latter deficit appeared to be unaccompanied by the classical frontal symptoms of hypermotility and distractability found after bilateral ablations. Supported by U.S.P.H. Grant No. 2546.

DEEP HYPOTHERMIA BY VENO-ARTERIAL COOLING. Frank Gollan, Mark W. Wolcott*, Curtis G. Wherry* and Bernard Sigel*. VA Hospital and Univ. of Miami School of Medicine, Coral Gables, Florida.

With the aid of a pump-oxygenator the inadequate perfusion of internal organs during ice immersion can be overcome and overoxygenation of venous blood results (Gollan, F., Blos, P. and Schuman, H.; J. Appl. Physiol. 5:180, 1952.) This study shows that it is possible to utilize overoxygenated venous blood during partial cardiac bypass without an oxygenator and to produce hypothermic cardiac arrest. Nineteen dogs were pretreated with 30 mg quinidine/kg by slow i.v. drip to prevent ventricular fibrillation. Venous blood from the right atrium was withdrawn by gravity at a flowrate of about 30 ml/kg/min., passed through a heat exchanger and pumped into a femoral artery. Animals breathing 100% oxygen had venous pO_2 as high as 120 mm Hg; this rose to 360 mm Hg when 5% CO_2 in oxygen was used. The heart rate-temperature curve and left ventricular pressures resembled those observed in cooling with artificially oxygenated blood. After 30 minutes at about 13°C the venous pO_2 of dogs breathing 5% CO_2 in oxygen decreased to about 100 mm Hg and of dogs breathing 100% oxygen to about 50 mm Hg. On slow rewarming myocardial depression manifested itself in failure of the left ventricular systolic and end-diastolic pressure, as well as heart rate, to return to the same values at corresponding cooling temperatures. This myocardial weakness during the early rewarming phase of deep hypothermia by veno-arterial cooling could be overcome by the i.v. administration of 8-16 mcg of l-arterenol/min. Thus, the simple procedure of veno-arterial blood stream cooling (Ross, D.N. Guy's Hosp. Rep. 103:97, 1954) can be extended to the range of deep hypothermia.

POSTNATAL DEVELOPMENT OF THE TRANSCALLOSAL RESPONSE.
Bernice Grafstein, (intr. by A. S. V. Burgen), Dept. of Physiology, McGill Univ., Montreal, Canada.

In the two-day old cat (unanaesthetized cerveau isolé preparation) the transcallosal response recorded with monopolar leads from the surface of the cortex consists of a focal positive-negative potential change, similar in configuration to that observed in the adult, but smaller in amplitude and lasting about twice as long. Most striking is the long latency, about 40 msec. in the two-day old animal, compared with 2-3 msec. in the adult. Up to about 4 weeks of age, the latency of the response decreases continuously and its amplitude increases, but there is no change in its configuration. Between 27 and 32 days, however, there is an abrupt decrease in the latency, corresponding to the appearance of an early positive deflection. The positive phase of the response thus appears to have two peaks, until about 7 weeks, when they fuse to produce a response resembling that in the adult, although still somewhat longer in latency and duration. No corresponding changes occur in the negative component of the response. It has been possible to measure the conduction velocity of the callosal fibres by stimulating eccentrically in the corpus callosum and comparing the transcallosal responses produced in the two hemispheres. It has thus been established that the appearance of the early positive deflection may be correlated with the onset of activity in a fast-conducting group of callosal fibres. (Supported by a grant from the Cerebral Palsy Foundation)

IS THERE A ROSTRAL HYPOTHALAMIC "SLEEP CENTER"? Ronald Grant and Lorraine B. Emery*. Dept. of Physiology, Stanford University.

An attempt has been made to confirm the finding of W.J.H. Nauta (J. Neurophysiol. 1946: 9, 285-316) that, in rats, transections in the suprachiasmatic region of the hypothalamus abolish sleep. An L-shaped knife was used to incise the rostral hypothalamus, sparing the thalamus following Nauta's method, in 75 rats. In 4 rats, a broad knife was used to incise the full depth of the brain for 3 mm on each side of the midline. In 42 rats the suprachiasmatic hypothalamus, also the preoptic area, septum and variable amounts of other anterior brain stem structures, were removed by suction. Gross post-lesion disturbances included hyperthermia, hyperactivity, diabetes insipidus, aphagia, adipsia, pulmonary edema with secondary infection and edema of the eyes with excessive lachrymation. Many animals showed greatly reduced sleep and some were never seen to sleep during several days of post-lesion survival. But some periods of sleep were observed in all rats in which post-operative difficulties were successfully controlled by use of antibiotics, tube-feeding, environmental control of hyperthermia (sometimes supplemented by barbiturate sedation in the early, extreme phase) and other nursing measures. Histological check showed that in 5 rats the lesions corresponded closely to those described by Nauta in sleepless animals: all of these rats were seen to sleep. Many other animals had laterally more extensive lesions including the critical zone. We conclude that the relatively sleepless state of rats with lesions in the rostral hypothalamus is a transient condition and that the effects of such lesions should not be considered to show that integrity of this area is essential for sleep behavior.

The Evaluation of a New Analgetic Agent in the Rodent, Dog, and Human in Experimental Pain. L. C. Greene and H. Wendel*
Smith Kline & French Laboratories, Philadelphia, Pennsylvania.

The correlation between laboratory results in analgesic testing in animals and experimental pain in humans in relation to clinical efficacy of analgetic agents is constantly being re-evaluated. The present communication is concerned with our experience in evaluating a potentially useful analgetic agent, SKF 1340, N,N-dimethyl-3-phenyl-indanamine hydrochloride, in the rat (D'Amour-Smith and Randall Selitto Techniques), in the mouse (Eddy Hot Plate) and in the dog (Hardy Wolff Goodell Technique). The results from these studies have been compared with each other and with the results obtained in a double blind study in experimental pain in humans (Harris Tooth Pulp Technique - unpublished data of Dr. Stanley Harris). While the means for producing pain (noxious stimulation) varied from procedure to procedure, as well as the type of endpoint indicating pain, the results obtained in the rat and the mouse suggest that the compound has analgetic activity somewhat greater than codeine. The dog data, however, suggests analgetic activity which is about equal to or somewhat less than codeine. The latter studies in the dog have been confirmed in experimental pain in a human tooth pulp study. While the results obtained by the other techniques are not unrealistic, the results obtained in the dog are in good agreement, as far as potency of the compound is concerned, with our present clinical findings. These results are suggestive of a good correlation between the reaction threshold in the dog using thermal radiation and experimental pain in the human using electrical stimulation.

STIMULATION OF ACID SECRETION BY DISTENTION OF THE FUNDIC PART OF THE STOMACH. **Morton I. Grossman. Veterans Hospital and Univ. of California, Los Angeles.**

In dogs, the distal end of the stomach, including the entire pyloric gland area as verified hitologically, was resected and continuity was restored by gastrojejunostomy. A large bore cannula was placed in the residual stomach. In 15 tests on 3 dogs, following a one hour basal collection in which no free acid was found, a balloon was inflated with 300 ml of air in the residual stomach. Flow of acid began within 15 minutes and reached a mean peak rate of 0.8 mEq per hour which was sustained during the 2 hours that distention was maintained. Within 30 minutes after deflation of the balloon the juice became anacid. Acid secretion in response to gastric distention is known to involve gastrin release from the pyloric glands. The present experiments indicate that an additional mechanism operates from the fundic region, probably vago-vagal in character. The mechanism here described probably plays an important role in the normal acid secretory response of the intact stomach to a meal. **(Supported in part by a grant from the U. S. Public Health Service.)**

THYROID HORMONE SECRETION RATE AND LACTATION IN THE RAT. Clark E. Grosvenor, Dept. of Physiology, University of Tennessee, Memphis, Tenn.

Thyroid secretion rate (TSR) obtained from primiparous lactating rats during the first 14 days of lactation averaged 1.93ug/100g/day L-thyroxine or 130% more than obtained from non-lactating female rats of the same age and strain. A significant positive correlation existed between TSR and the amount of milk obtained from the mothers on day 14 of lactation. TSR obtained from the same rats during a second 14 day period of lactation (during which time each nursed a foster litter) was significantly reduced to an average of .98ug/100g/day L-thyroxine. A significant reduction in milk yield on day 28 accompanied the reduction in TSR. The reduction in intensity of milk secretion during the second 14 days of lactation resulted in slower growth of the foster litters. Maternal body weight was unaltered. In a second experiment the average TSR of 2.1ug/100g/day obtained during the first 14 days of lactation for 10 rats fell to .75ug/100g/day during a subsequent 14 day period of non-nursing. These data indicate that the intensity of lactation is associated with the intensity of thyroid hormone output and suggests that inadequate thyroid hormone secretion may be an important factor in the decline of milk secretion. (Supported by a Senior Research Fellowship (SF-365).

FIBRINOLYTIC ACTIVITY IN EXERCISE. M. Mason Guest and D. R. Celander*. Carter Physiology Laboratory and Department of Biochemistry, University of Texas Medical Branch, Galveston, Texas.

During exercise at 75% of capacity for 15 minutes on a treadmill fibrinolytic activity as measured by the cold fibrinolytic potential analysis as well as other tests increases significantly in all male subjects (age range 22 to 78 years). Furthermore urokinase is increased in urine samples taken following exercise when compared with urine samples, immediately preceding exercise. Conditioning during the initial 2 to 3 weeks (daily exercise on the treadmill for 15 minutes at 75% of capacity) results in a continuing rise in fibrinolytic activity and urokinase excretion. No significant changes have been found in blood clotting factors during exercise or conditioning. These results together with the data of other workers are suggestive that the fibrinolytic enzyme system plays an important role in the circulatory adjustments in exercise.

NEGATIVE PRESSURE IN THE INTERSTITIAL SPACES. A. C. Guyton, G. G. Armstrong*, and J. W. Crowell. Department of Physiology & Biophysics, University Medical Center, Jackson, Mississippi.

The methods used for many years to measure tissue pressure have all been questionable, and in most tissues the measured pressures have ranged between 0 and a few mm. Hg positive. Almost without exception the methods used would not have been able to measure negative pressures accurately even if such should have existed. Therefore, we implanted in the thigh muscle and in the subcutaneous tissue of the axillary space, the abdomen, and the leg plastic capsules one inch long and one-half inch in diameter, the walls of which were drilled with a hundred or more small holes. Within two to four weeks, granulation tissue grew through the holes, forming a layer of tissue approximately 2 mm. thick on the inner walls of the capsule. A cavity about one-fourth inch in diameter remained indefinitely in the center. A needle could then be inserted through the skin and through one of the holes of the capsule to measure the pressure inside the cavity. The pressures after complete healing have been negative in about 100 measurements and positive in only one instance, averaging -5 cm. of water when referred to the level of the capsule itself. Injection of a small amount of isotonic saline or removal of an equal amount of interstitial fluid was followed within 15 minutes by asymptotic return of the pressure to the same negative value. Since the fluid chambers in the capsules are actually tissue spaces that cannot be collapsed by the surrounding atmospheric pressure, it is assumed that, if we could measure the pressures in the minute interstitial spaces without distorting these spaces, the pressures there would also be negative.

MEASUREMENT OF STROKE AND MINUTE VOLUME IN INTACT CONSCIOUS DOGS WITH AN ELECTROMAGNETIC FLOWMETER. A. Guz, J. Hoffman, W. L. Weirich, and R. R. Spotts, (intr. by Karlman Wasserman). Cardiovascular Research Institute and Department of Surgery, Univ. of Calif. Med. Center, San Francisco.

We have placed a miniaturized coreless Kolin "probe" about the pulmonary artery in 4 dogs and then made continuous observations of their right ventricular stroke and minute volumes in the intact, conscious state after complete recovery from the surgical procedures; a modified Kolin 400 cycle sine wave electromagnetic flowmeter was used. We obtained the necessary zero flow base line by injecting acetylcholine I.V. and causing cardiac arrest for 3-7 seconds. The flow meter was calibrated in vivo by comparing its records with simultaneously performed dye-dilution curves over a wide range of cardiac outputs, cardiac frequencies and maximal velocities; isoproterenol was used to vary these. The areas under the flow curves per minute correlated closely with dye-dilution cardiac outputs and the regression line passed through zero; this calibration is valid for volume flow and for velocity because the flow meter measures velocity of blood flow through a cross sectional area made constant by the rigid walls of the pulmonary artery "probe".

This technique has been used in conscious animals to study sudden and longer-lasting changes in stroke and minute volume, e.g., changes occurring with feeding, respiration, exercise, and change of posture.

Supported in part by USPHS Grant H-4029.

INFLUENCE OF PYRAMIDAL TRACT UPON POSTERIOR COLUMN NUCLEI[1]. Carlos Guzman-Flores and Frederick P. Gault (introduced by Donald B. Lindsey). University of California at Los Angeles and Veterans Administration Hospital, Long Beach, California

Anatomical studies by Kuypers (1958) have revealed corticifugal connections to the Posterior column nuclei via the pyramidal tract. The present study in encephale isole cats has explored the functional significance of these connections by observing: a) the response in the posterior column nuclei evoked by pyramidal tract excitation and b) the interaction of this response with the response of the posterior column nuclei elicited by shocks to the dorsal column at C-1. Cortical augmenting responses, elicited by stimulation of the thalamic nucleus VPL, induced the pyramidal tract excitation. The response of the posterior column nuclei evoked by pyramidal tract excitation appeared only after cortical augmenting responses reached a critical amplitude and both displayed subsequent recruitment. With appropriate timing, both facilitative and occlusive interaction was displayed in the response of posterior column nuclei to pyramidal tract and to dorsal column excitation. The responses of the posterior column nuclei evoked by pyramidal tract excitation were abolished by lesion of the cortical areas displaying the augmenting response, or by interrupting pyramidal tract fibers in the cerebral peduncle. Both of these findings oppose the possibility that antidromic conduction from the nucleus VPL produced these effects or that some subcortical relay might be responsible.

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The Effect of Hyper- and Hypotonic Solutions on Small Vessel Resistance in the Dog Forelimb. **F.J. Haddy, and H.W. Overbeck* VA Research Hospital and Northwestern University Medical School. Chicago, Illinois.**

It has been reported by several authors that intra-vascular infusions of hypertonic solutions generally cause a decrease in peripheral vascular resistance. (Circ. Res. 8:538, 1960; Am.J.Physiol. 197:951, 1959). This study, utilizing previously reported techniques (Minnesota Med. 41:162, 1958), was undertaken to determine the mechanism of that response. A total of 230 intra-arterial infusions, 0.5 to 4.0 vol.%/min. in a constant forelimb blood flow, were made in 36 dogs. Agents studied were hypertonic dextrose, urea, NaCl, Na_2SO_4, and Na_2HPO_4. All infusions resulted in decrease of limb small vessel resistance, accompanied by a striking decrease in limb weight, a decrease in limb venous hematocrit and hemoglobin, and a decrease in calculated mean corpuscular volume. The viscosity of limb venous blood during infusions, determined with a glass viscometer, increased during hypertonic dextrose but remained unchanged during other infusions. All hypertonic solutions studied were found to diminish vessel responsiveness to norepinephrine and mecholyl. There was no change in small vessel resistance across the forelimb during infusion of hypotonic NaCl (0.44%) at a rate of make up of 23% of total limb flow, as contrasted with a decrease of 0.11 PRU with equal infusions of isotonic NaCl and isotonic dextrose. Limb weight increased to a slightly greater extent during the hypotonic solution infusions. These data indicate that the hypertonic solutions studied increase water movement from intra- to extracellar spaces while evoking an increase in limb small vessel caliber. The latter may be passive, due to dehydration of vessel walls, or active, possibly due to changes in intracellular ion concentrations. In contrast, the hypotonic solution studied appears to decrease the calibers of small vessels.

IN VITRO STORAGE OF RABBIT MORULAE IN GELLED MEDIA AT 10°C. FOR 72 HRS. E. S. E. Hafez. Dept. Anim. Sci., Wash. State Univ., Pullman, Wash.

A suitable medium for storage of ova is of academic and practical importance for ova transfer techniques. Selected healthy rabbit morulae (459) were stored at 10°C. in gelled or liquid media for 4, 24, 48 and 72 hrs. Sterile autologous serum was obtained by heart puncture. Gelled media were made of 7% gelatine (final conc.) in 1 serum:1 saline. Liquid media (control) were 1 serum:1 saline mixture. Synchronous pseudopregnant recipients were used. In each recipient, morulae stored in gelled media were transferred in one Fallopian tube and morulae stored in liquid media were transferred in the other tube. Laparotomy was performed 8 and 15 days p. c. Morphologic changes such as coarse granulation of cytoplasm and indistinguishable blastomeres were more pronounced in morulae stored in gelled media than in the control. At 8 days p. c., percentage implantations of ova stored in gelled media were 75, 56, 35 and 49 respectively. Percentage implantations of morulae stored in liquid media were 66, 45, 31 and 42 respectively. Implantation rate was 7 percentage points higher for morulae stored in gelled media than those in liquid media. Average survival of implantations at 15 days p. c. was 62% in gelled media and 55% in liquid media. Cell division was inhibited during storage. Morulae were susceptible to cold shock prior to storage. Morulae from different donors varied in their ability to survive storage indicating the importance of potential integrity of ova. Morulae of the same donor varied in their ability to be implanted in different recipients indicating unknown specific interactions between morulae and maternal environment.
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ABILITY OF LiCl TO SUBSTITUTE FOR NaCl IN DCA INDUCED HYPERTENSIVE CARDIOVASCULAR DISEASE. C. E. Hall, R. W. Ware*+, E. Cross* and O. Hall.* Carter Physiology Laboratory, Univ. of Texas Med. Br., Galveston, Texas.

The ability of desoxycorticosterone acetate (DCA) to cause hypertensive disease is abolished if sodium is eliminated from the diet. In rats, the onset of DCA-induced hypertension is speeded and the accompanying vascular pathologic alterations enhanced in proportion to the sodium intake over a wide range of concentrations. LiCl can substitute for NaCl in a number of physiological processes and has been used as a "salt substitute" in the control of human hypertension. Hence it was of interest to ascertain whether LiCl would sensitize or desensitize rats to cardiovascular disease induced in the rat by DCA. Female rats averaging about 100 gm were sensitized to steroid treatment by unilateral nephrectomy. Groups were then given LiCl or NaCl solution of like concentration. Half of each group received 1 mg/day of DCA by subcutaneous injection. It was found that hypertension was not induced by either electrolyte alone although each was about equally effective in sensitizing to the hypertensive action of DCA. Vascular lesions in the heart and kidney were equally severe in hypertensive animals receiving LiCl or NaCl, although splanchnic periarteritis was more prevalent in the former. It is concluded that LiCl can substitute for NaCl in sensitizing to DCA and, in the amounts consumed, exhibits no antihypertensive properties insofar as mineralocorticoid hypertension is concerned. (Supported by Grant H-4327 from the USPHS) +Captain USAF (MC).

APPLICATION OF GAS CHROMATOGRAPHY TO ANALYSIS OF GASES IMPORTANT TO RESPIRATORY PHYSIOLOGISTS. Lyle H. Hamilton and Josef R. Smith*. Wood Veterans Administration Hospital and Marquette University School of Medicine, Milwaukee, Wis.

A modified Fisher Gas Partitioner and a specially designed zero-suppression selector have been applied to the quantitative analysis of gases important to respiratory physiologists. The zero-suppression selector was considered to be essential for achieving maximum accuracy with peak height measurements. Correction factors for argon in expired air samples have been developed--a necessary technique since argon is not separated from oxygen by currently practical techniques. With this system the standard deviation for its accuracy was ± 0.024 vol. % for O_2 and approximately 0.002 vol. % for CO_2 in respiratory gas samples. The system has been demonstrated to have sufficient sensitivity and reproducibility to be used for the determination of lung diffusing capacity (D_L) and membrane diffusing capacity (D_M). It has been applied to the measurement of Ne, SF_6, He and CO in expired air samples. It has also been applied to the measurement of N_2O and C_2H_2 in the mixtures, useful for the determination of pulmonary capillary blood flow. Desirable combinations of some of these gases can be analyzed with a single 5.0 cc sample introduction, a time-saving and sample-saving feature. All the gases used to determine $D_{L_{CO}}$ can be analyzed within about 7 minutes; single components, such as N_2O, He, SF_6 or C_2H_2 can be analyzed within about 2 minutes.

INFLUENCE OF VAGOTOMY ON EXPERIMENTALLY INDUCED PULMONARY HYPERTENSION. J. W. Hampton*, W. E. Jaques*, and R. M. Bird. University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

Pulmonary hypertension developed promptly in dogs given an intravenous infusion of amniotic fluid (A.M.A. Arch. Path., 69:248, 1960) or a suspension of very small glass beads (Federation Proc., 19:56, 1960). The hypertension developed within 5 to 15 min., remained elevated for an hour or more and was not associated with significant changes in systemic pressures. The speed and character of this pulmonary response, the non-specificity of the stimulus and the morphological changes observed in the lungs, all suggested the involvement of a neural mechanism in the genesis of the pulmonary hypertension. The present study is based on 9 dogs which were anesthetized to facilitate cardiac catheterization. After base-line pulmonary artery pressures were obtained, bilateral vagotomy was done. The vagotomy caused no significant changes in the pulmonary pressures. Next, each animal was infused. In 7 dogs the infusion was 15 to 50 ml. of human or dog amniotic fluid. In one dog a rise in mean pulmonary pressure of 10 mm. Hg. was followed in 20 min. by a fall to half the pre-infusion level. The other dogs showed no pulmonary hypertension. In 2 dogs the infusion was a saline suspension of glass beads (0.2 mg./kg., circa 450 microns diameter). No pulmonary hypertension developed. These results contrast sharply with the hemodynamic changes evoked by similar infusions into dogs with intact vagi. It is inferred that the pulmonary hypertension experimentally produced by infusions of particulate matter is dependent for its development on an intact vagal mechanism.

AN APPARATUS FOR RAPID MEASUREMENT OF ONCOTIC PRESSURE IN SMALL SAMPLES. A.Tybjærg Hansen(intr.by Victor T.Wilson). Rockefeller Institute,New York,and Rigshospitalet,Copenhagen,Denmark.

The method is based on the feasibility of measuring pressure by means of an electric capacitance manometer with a minimum of liquid displacement as described by the author(Act. Physiol.Scand.Vol.19.Suppl.68,1950).The pressure chamber of the manometer is separated from the sample in which the oncotic pressure is to be measured by a semipermeable cellulose membrane.The movement of the water from the manometer into the sample caused by the osmotic forces builds up a negative pressure in the pressure chamber at a rate of 1 mm of Mercury per $3x10^{-6}$ ml. Within 1-5 minutes an equilibrium is reached between the opposing forces and the numerical value of the pressure indicated by the manometer is then equal to the oncotic pressure of the sample.The pressure can be read on a calibrated voltmeter or is more conveniently recorded.Determination of the oncotic pressure in solutions of ox serum albumin of known concentrations give results as to be expected if the Donnan effect is taken into consideration. Determination of the oncotic pressure in human and animal sera agree with the results obtained by earlier investigators and with protein determinations by other methods. A sample of 0.2 ml is ample,0.02 ml may suffice. In one hour between 10 and 15 measurements can be carried out. The osmotic effect of heavy water and other solutions of molecules which are small enough to penetrate the membrane can be shown.

THE BOHR INTEGRAL, AS APPLIED TO THE PROBLEM OF CARBON MONOXIDE ELIMINATION. J. T. Hansen and N. Pace. Dept. of Physiol., Univ. of California, Berkeley, California.

In order to more fully appreciate the rate-limiting effect of diffusion on the elimination of carbon monoxide from the circulation, it is necessary to determine the gradient conditions existing across the alveolar membrane. A major obstacle to such an endeavor is the determination of the carbon monoxide tension in the alveolar capillary.Haldane's First Law, $M(Pb_{CO})/(Pb_{O_2}) = (COHb)/(O_2Hb)$, states the dependence of the carbon monoxide tension, (Pb_{CO}), on oxygen tension, (Pb_{O_2}), carboxyhemoglobin, (COHb), and oxyhemoglobin, (O_2Hb), concentrations under equilibrium conditions. No direct approach for solving this relationship for the alveolar capillary exists. It is possible to apply the Bohr Integral for the purpose of obtaining an approximate solution. Using this approach,and knowing the arterial and venous$(O_2Hb)$and(Pb_{O_2}), the$(O_2Hb)$and(Pb_{O_2})may be determined at all points along the alveolar capillary. Under normal conditions carbon monoxide elimination proceeds so slowly that it is possible to assume a negligible change in(COHb) during alveolar transit.The Haldane expression may then be applied to obtain the(Pb_{CO}). Using this approach, the carbon monoxide tension has been shown to rise during alveolar transit in response to the rising(Pb_{O_2}) and(O_2Hb). The result of this rise is seen in an arterial (Pb_{CO}) which may be double that of the mixed venous blood.Thus,an analysis of the relationship between carbon monoxide elimination and the alveolar-capillary gradient must rest on a determination of the mean capillary tension. In this determination, the oxygen tension and oxyhemoglobin concentration of the mixed venous blood are of primary interest. Thus, under conditions of mildly depressed respiration, the venous carbon monoxide tension may be lower than the alveolar carbon monoxide tension, resulting in a momentarily reversed gradient. (Supported by O.N.R.)

SUBSTRATE METABOLISM AND OXYGEN CONSUMPTION OF KIDNEY SLICES. R. W. Hanson*, R. H. Lindsay* and S. B. Barker. Univ. of Ala. Med. Center, Birmingham, Alabama.

Previously we have reported an increased QO_2 and maintenance of rat kidney slice oxygen consumption by the addition of proline. With thyroidectomized rats this maintenance was enhanced by the addition of thyroxine. A net production of glucose, ammonia nitrogen and glutamate occurred with slices incubated in proline. Current studies attempt to account for the oxygen consumed by kidney slices from thyroidectomized rats incubated at 37° in Ringer, Ringer glucose, Ringer proline and Ringer glutamate media. In Ringer, 40 to 50% of the oxygen consumed was accounted for: 2 to 4% resulted from oxidation of endogenous glucose, assuming complete oxidation to CO_2, and 35 to 45% from endogenous nitrogen metabolism. The addition of UC^{14}-labeled glucose, although slightly increasing oxygen consumption, had little effect on the total balance. Production of $C^{14}O_2$ from the C^{14}-glucose accounted for a maximum of 16% of oxygen consumed with oxidation of endogenous nitrogen-containing substrates accounting for 35 to 45%. In a 9-hour period proline or glutamate tripled the oxygen consumption over that in a glucose medium but gave a complete accounting for the oxygen. Addition of UC^{14}-labeled proline appeared to completely obliterate endogenous oxygen consumption since 93 to 114% of the oxygen consumed was accounted for by C^{14} recoveries. As much as 70% appeared as $C^{14}O_2$, up to 25% as glucose synthesis and the remainder as production of glutamate. The addition of glutamate to Ringers gave a similar balance, up to 70% accounted for by production of NH_3 plus CO_2 and 20 to 22% from either glucose synthesis or oxidation. (Supported by USPHS Grant No. A-3241.)

VASCULAR PRESSURE RELATIONSHIPS IN RABBITS' FEET FOLLOWING FREEZING INJURY. E. Hardenbergh and R. F. Coniff*. Nav.Med.Res.Inst.,Bethesda, Md.

Blood pressures in several kinds of vessels in the rabbit's foot were measured (Haddy et al.,Am.J.Physiol.176:355,1954) before and after freezing injury to observe how the relative pressures changed in severely damaged tissue. Central pressure was measured from the carotid artery(1), and four pressures in the hind foot, from: a branch of the saphenous artery at ankle level(2), a toe artery(3), a collecting vein on the dorsum of the foot cannulated distad(4) and proximad(5). The usual control pressures were 90 to 110 mm Hg at site (1), 60 to 90 at (2), 40 to 60 at (3), and 10 to 20 at sites (4) and (5), with (4) running 3 to 8 mm higher than (5). After freezing and thawing, the carotid pressure remained unchanged; pressures in the foot arteries were higher than during the control period. The distal venous pressure started to rise immediately, as soon as the foot was thawed, and reached levels sometimes as high as 60 mm Hg; proximal venous pressure also rose but not immediately and not as high. Of the total pressure loss from carotid to proximal vein in the foot the percentage loss across the arterial side of the system, (1) to (3), was less after injury than before, that across the arteriolar-capillary-venular bed, (3) to (4), was about the same, and that across the veins, (4) to (5), considerably increased. Pressure changes caused by injection of vasoactive drugs were different before and after freezing. The data are consistent with microscopic observations of others that in tissue injury of this kind vasoconstrictor activity is lost and dilated arterial vessels allow blood to flow through to the capillaries and venules under a high pressure head. This rapidly filters fluid through the injured vessel walls, leaving within them a concentrated blood which becomes increasingly resistant to flow.

EFFECT OF TEMPERATURE ON AUTOREGULATION OF RENAL BLOOD FLOW. Rodney B. Harvey, Dept. Physiology, Univ. Utah, Salt Lake City, Utah.

Isolated dog kidneys were perfused with arterial blood from a heparinized dog using a modification of previously described methods. Renal artery pressure, kidney weight, renal vein flow and temperature, urine flow, concentration of inulin and Na, and freezing point depression (O.A.) of urine and plasma were measured. In preparations with blood flows of 3.5 - 8.0 ml/gm/min the process of autoregulation was repeatedly demonstrable. Each stepwise change in arterial pressure was accompanied initially by a nearly proportional change in vein flow. However within 90 sec vascular resistance changed so as to bring renal flow to the previous value. If the transient period of 90 sec following each change is excluded nearly complete regulation of blood flow occurred. Each stepwise increase in arterial pressure increased vascular resistance, urine flow, C_{In}, U/P Na, and kidney weight while U/PIn and U/P O.A. decreased. A stepwise decrease in pressure reversed all of these changes. Cooling to 10°C reduced the autoregulation of blood flow but did not always abolish it. Changes in blood flow, kidney weight, urine flow, and C_{In} occurred when arterial pressure was changed at low temperature. Warming the preparation reversed the changes produced by cooling. Autoregulation at low temperature followed a similar time course as at 37°C suggesting that it is not due to smooth muscle action. Kidney weight changes and autoregulation were poorly correlated temporally or in magnitude in many instances. Because glomerular filtration rate is less well regulated than blood flow and because kidney weight changes are poorly correlated with vascular resistance changes it is suggested that autoregulation is produced by some mechanism such as localized extravascular compression acting on vessels efferent to the glomerulus.

METABOLISM OF VERY LOW DENSITY LIPOPROTEIN TRIGLYCERIDES IN BLOOD PLASMA OF RABBITS. Richard J. Havel, James M. Felts, and Charles M. Van Duyne*. Cardiovascular Research Institute and Departments of Medicine and Obstetrics and Gynecology, University of California Medical Center, San Francisco, California.

Labelled triglycerides contained in very low density lipoproteins (VLDLP) were prepared by injecting palmitic acid-1-C^{14} complexed to human albumin intravenously into donor rabbits. After 30 minutes, serum was obtained by exsanguination and centrifuged at 100,000 x g for 16 hours. The VLDLP which floated to the top of the centrifuge tube were injected intravenously into recipient rabbits under chloralose anesthesia and serial samples of blood and expired air were obtained. The disappearance of radioactivity from plasma VLDLP (99% C^{14} in triglycerides) was rapid, with initial half times of 7-14 minutes. Specific radioactivity of plasma free fatty acids was maximal 2-5 minutes after injection and maintained a constant ratio to circulating VLDLP triglyceride fatty acids. It was calculated that approximately 0.05 μM free fatty acids per ml plasma were derived from circulating triglyceride fatty acids. Specific radioactivity of expired carbon dioxide was maximal in the sample collected during the first 5 minutes after injection and 14-35% of the dose injected was collected in 2 hours. No significant differences were observed in any of these measurements between rabbits fasted for 24 hours and fed rabbits infused with glucose for one hour before and during the experiment.

WEIGHT GAIN IN WEANLING ANIMALS FOLLOWING INITIAL PERIODS OF PARTIAL CALORIC RESTRICTION. F.W. Heggeness. Dept. of Physiol., Univ. of Rochester Sch. of Med., Rochester, N.Y.

Weanling but not older animals fed 60% carbohydrate diets show a transient self-limiting elevation in oxygen consumption that obligates approximately 10% of the caloric intake. This phenomenon persists for the first week of feeding. This metabolic response can be averted by "adapting" animals to the high carbohydrate diet by feeding for 6 days amounts of diet just sufficient to maintain body weight. In such adapted animals no calorigenic response accompanies the initiation of ad libitum feeding and dietary intake and efficiency of food utilization are greater than in unadapted animals. Body composition studies suggest that the adapted animals have a greater rate of fat accumulation. The duration of the response appears to be variable. In one group studied, body composition of unadapted and adapted animals was not different at 12 days. Other growth study experiments suggest that in some cases the effect persists for a longer period of time. Accelerated rates of weight gain can be sustained during ad libitum feeding if adapted animals are resubjected to periods of adaptation alternating with periods of ad libitum feeding. Further nutritional studies indicate that adaptation is incomplete in 3 days. Increasing the period of adaptation to 9 days does not significantly alter the response following 6 days. (Supported in part by a grant from the National Institutes of Health.)

THE PHYSIOLOGICAL FRACTIONATION OF PITUITARY GONADOTROPIC FACTORS CORRELATED WITH CYTOLOGICAL CHANGES. A. A. Hellbaum, L. G. McArthur,* P. J. Campbell,* and J. C. Finerty.* Department of Pharmacology, Oklahoma University School of Medicine, Oklahoma City, Okla., and Department of Anatomy, University of Miami School of Medicine, Coral Gables, Florida.

Through the removal of estrogen or androgen influence or the controlled administration of gonadal steroids, the concentration of pituitary follicle stimulating (FSH) and luteinizing (LH) factors can be regulated. The pituitary glands of adult female rats with intact gonads contain small amounts of both LH and FSH, whereas those of male rats contain relatively little LH. Gonadectomy in both sexes results in a marked increase in both LH and FSH in the pituitary as well as a corresponding increase in the "red" and "purple" (PAS-Methyl blue staining) pituitary basophil "gonadotropes." The administration of the equivalent of 3 micrograms of estradiol benzoate per day over a 45-day period stimulates depletion of LH. FSH is also markedly decreased. The cytological picture shows very few "red" but some "purple" gonadotropes. The administration of equivalent of 3 milligrams of testosterone propionate per day over a 45-day period also depletes the LH but the FSH content remains high and the correlated cytological findings show a corresponding decrease in the "red" gonadotropes, but with little effect on the "purple" ones.

GLYCINE ACCUMULATION AND K FLUXES IN THE EHRLICH ASCITES TUMOR CELL. H.G. Hempling, Dept. of Physiology, Cornell Univ. Medical College, N.Y., N.Y.

Experiments to define the relation between the maintenance of glycine gradients and steady-state K fluxes were performed with Ehrlich mouse ascites tumor cells. Cells were equilibrated with glycine to permit concentration gradients to develop. Steady-state fluxes were then measured with K^{42}. At 25°C., without glucose, external glycine concentrations were varied between 0 and 18.5 meq/l. At the lowest external glycine concentration studied (3.8 meq/l.), glycine could be concentrated up to 8 times its environment. Both K efflux and influx increased as much as twice that of controls. If K efflux is coupled to glycine accumulation, as proposed by Riggs, Walker, and Christensen (JBC 233:1479, 1960), then an independent path for K influx must be postulated, which also increases when glycine is accumulated. Cells will increase their water content by 20% in response to the accumulation of osmotically active glycine, and therefore cell swelling may also be a factor which contributes to the increase in K fluxes observed. (Supported by USPHS grant (C-3690).

HYPOTHALAMIC LESIONS AND PITUITARY LUTEOTROPIN SECRETION IN RABBITS. J. Hilliard*, C. K. Haun*, S. Kanematsu*, H. M. Radford*, and C. H. Sawyer. Univ. of Calif., School of Med., Los Angeles, Calif., and Veterans Administration Hosp., Long Beach, Calif.

Lesions in the basal tuberal region of the hypothalamus, including the arcuate nucleus and posterior median eminence, induce lactation in estrogen-primed rabbits (Anat. Rec. 136: 208, 1960). This area of the brain is identical to that in which electrical stimulation induces release of pituitary ovulating hormone and electrolytic lesions block copulation-induced ovulation. In the present experiments ovulation was induced by chorionic gonadotropin administered at the time of stereotaxic placement of the lesion. In rabbits whose hypothalamic damage was subsequently found to lie outside the critical tuberal area, the corpora lutea of pseudopregnancy were quite atrophic three weeks after ovulation. Rabbits with posterior median eminence lesions maintained corpora lutea in an active state for three-four weeks and sustained varying degrees of lactation in spite of the ovarian steroids. Hypothalamic lesions did not appear to enhance or inhibit the maintenance of corpora lutea by exogenous estrogen. The results are consistent with the hypothesis that pituitary lactogen-luteotropin secretion is chronically suppressed by nervous influences emanating from the hypothalamus. (Supported by USPHS Grant B-1162.)

TONOTOPIC ORGANIZATION OF AUDITORY CORTEX IN CATS WITH CHRONICALLY IMPLANTED ELECTRODES. J. E. Hind, W. I. Welker, G. B. Campos* and M. A. Gilmore*. Laboratory of Neurophysiology, Univ. of Wisconsin School of Medicine, Madison, Wis.

The object of this study was to map the spatial distribution of cortical potentials evoked by tone pulses in unanesthetized cats and to compare the results with the patterns observed in the same animals under pentobarbital anesthesia. The animals were implanted with electrode arrays oriented along an anterior-posterior axis through the center of AI. Stimuli were tone pulses of 16 msec. duration which were presented at a rate of 2 per second. To facilitate rapid sampling of response magnitudes an apparatus has been assembled which consists of two time gate selector circuits, a saw-tooth generator, two electronic counters, and a digital printer. Peak or average potential magnitudes at selected latencies are printed as two or three-digit numbers as the responses occur. A sample of 100 successive responses has been obtained at each electrode for various stimulus frequency-intensity combinations. Analysis has been confined to the early surface positive component which is prominent in both the unanesthetized and anesthetized states. Data have been expressed both as plots of the average evoked potential along the electrode array and as histograms of the individual response amplitudes. The spatial gradient of potential observed for a given frequency and intensity in the unanesthetized, drowsy cat is similar to that seen under pentobarbital anesthesia. In some cases the magnitude of the positive component falls to half its focal value at electrode locations 2 mm on either side of the center of the focus for a given stimulus frequency for intensities as great as 80 db above detectable response threshold. (Aided by grant B-896, NINDB, USPHS.)

ALTITUDINAL EFFECTS ON ENDURANCE RUNNING IN THE DEER MOUSE. Raymond J. Hock. White Mountain Research Station, Univ. California, Big Pine. The deer mouse, Peromyscus maniculatus sonoriensis, is found from the floor of Death Valley to the top of White Mountain Peak (14246 ft). Endurance studies were made on populations from the Owens Valley and Barcroft Labs. at 4000 and 12470 feet respectively. Treadmill speed was 41 m/min with slope of 22.5°. Mean of 25 valley mice performances was 15.8 min, while mean of 22 mountain mice performances was 7.5 min. Ambient temps. were 16 to 20°C, with a few at higher levels. Oxygen tensions at the two altitudes are 138 and 100 mm Hg, while arterial blood pO_2 is 85 and 50 mm Hg. The difference in performance is greater than these differences in oxygen account for, so it appears that the temperature variation between the two altitudes is also a factor. Effect of test ambient temperature may be different on the two groups, due to the different temperatures at which they live. In addition, there may be differences in insulation and in the critical temperature of metabolic response.

TIME COURSE OF CHANGES IN RIGHT VENTRICULAR STROKE VOLUME AFTER INTERFERENCE WITH FILLING. J. Hoffman*, A. Guz*, W. L. Weirich* and R. R. Spotts*, (intr. by I. S. Edelman). Cardiovascular Research Institute and Department of Surgery, Univ. of Calif. Med. Center, San Francisco.

Right ventricular (RV) stroke volume of the closed-chest anesthetized dog was metered with a sine wave electromagnetic flowmeter and a probe around the main pulmonary artery. When RV filling was altered by introducing steady positive pressure into the airway, the stroke volume diminished by the next beat. Restoration of normal airway pressure caused an immediate increase in stroke volume. A similar time course of stroke volume change occurred after inflation and deflation of an inferior vena caval balloon.

These studies, which were done in dogs with normal RV and right atrial pressures, were repeated on one dog who 2 weeks later had a RV pressure of 80/0 mm Hg. Positive airway pressure of the same extent and duration as that given previously caused only minor decrements of stroke volume. After balloon occlusion of the inferior vena cava, stroke volume did not alter for 4-6 beats and then decreased slightly; after balloon deflation, stroke volume took 3-4 beats to return to normal. Autopsy disclosed pulmonary artery stenosis beneath the probe and a dilated RV.

It is suggested that, with the development of RV outflow tract obstruction, there was an increase in the "central volume" available for the RV in the absence of elevated central venous pressures.

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THE EFFECT OF BODY POSITION ON STROKE VOLUME DURING EXERCISE IN NORMAL SUBJECTS. Alf Holmgren, Sture Bevegard and Bengt Jonson, (intr. by M. B. McIlroy). Dept. Clin. Physiology, Karolinska Sjukheset, Stockholm, Sweden.

10 healthy young men were studied at rest and during exercise (600 and 900 kgm per min increasing V_{O_2} > 2000 ml/min and pulse rate to between 140-170 beats/min), in the sitting and in the supine positions. The pulmonary artery was catheterized with a double lumen catheter and pulmonary blood flow was determined with the direct Fick technique. Blood gas analyses were performed with spectrophotometric technique. Pressures were measured in both positions, the reference levels being 5 cm below the sternal angle in the supine position and at the insertion of the fourth rib in the sitting position. Each subject was first studied in one position and after one hour of rest in the other. To eliminate the influence of the preceeding work test the order of the positions was varied. The results may be summarized as follows. 1. The stroke volume at rest was markedly lower in the sitting position than in the supine position. 2. During the transition from rest to work and during work with increasing loads in the supine position the stroke volume remained unchanged. 3. During transition from rest to work in the sitting position the stroke volume increased markedly. 4. During continued work in the sitting position the stroke volume remained unchanged. 5. The arterio-venous oxygen difference was markedly higher at rest and during work in the sitting than in the supine position. 6. No significant difference in pressure level or change could be demonstrated.

FACTORS INFLUENCING VOLUME AND DISTRIBUTION OF HEPATIC BLOOD FLOW. C.R. Honig (intr. by W.D. Lotspeich). Dept. of Physiol., Univ. of Rochester School of Med. & Dentistry.

Control of the complex and abundantly innervated hepatic circulation is still poorly understood. In anesthetized dogs hepatic arterial flow was measured simultaneously with flow in either portal vein or terminal aorta. Oxygen sensing micro-electrodes were used to detect change in regional "nutrient blood flow at a deep and superficial site within the liver. Concordant and discordant fluctuations in regional pO_2 occurred spontaneously, with or without parallel change in arterial or total inflow. Capacity for reflex vasodilatation was studied using constant intravenous infusions of epinephrine as stimuli. Hepatic arterial resistance fell markedly with doses between 0.01-0.5γ/kilo/min., but uniformly exceeded control above 2γ/kilo/min.. Stimulus-response relationships for hepatic and non-splanchnic arterial resistances were significantly different. Vagotomy modified the hepatic arteriolar dilatation produced by epinephrine but did not abolish spontaneous rhythmic fluctuations in total and regional "nutrient" blood flow. Epinephrine regularly increased portal venous flow and resistance in both intact and vagotomized animals. These and supporting observations indicate: 1) Hepatic vasomotor tone may not be inferred from change in pressure and regional flow. 2) Liver pO_2 varies with the distribution as well as volume of arterial or total inflow. 3) Both sympathetic nerves and the vagi participate in normal reflex control of the hepatic circulation.

GROWTH AND METABOLIC RESPONSES OF RATS EXPOSED TO WHOLE-BODY VIBRATION G.N. Hoover, W.F. Ashe*, and L.B.Roberts*. The Ohio State Univ., Columbus 10, Ohio

Assuming that the unrestrained rat must perform physical work to protect itself from vibration injury, the extra energy required must be made up by extra food intake or a decrease in body mass. To test this hypothesis, litters of weanling rats were divided into control and test groups. The test group was exposed to vibrations of 0.25 inch single amplitude at frequencies of 5, 10, 15, and 20 cps. The exposures were given for 1, 2, and 6 hours per day, 5 days per week until the animals weighed about 200 gms. Also 3 groups of 6 rats each were placed in metabolic cages. Food intake, water intake, fecal output, urine volume, and body weight were measured daily. After a period of adjustment and a short control period, 3 animals of each group were exposed to vibrations of 20cps, one-half hour per day for 7 days. This was followed by a 3 day recovery period. Urine samples were analyzed for steroids and creatinine excretion. In no group was the growth rate of the vibrated rats found to be different from that of their controls. Food intake, fecal output and body weights were not altered. Water intake showed a tendency to decrease over the test period, as did the urine volume. Creatinine excretion was not altered by vibration, and in only one group was an increase in steroid excretion observed. Since from other studies it is known that there is an increase in oxygen uptake and definite changes in circulating enzymes in the carbohydrate metabolism system, one must conclude that the duration and intensity of exposures used in these studies were not great enough to measure work load by these methods. This, in turn, raises the question as to the nature of the work involved in protecting oneself from vibration.

THE EFFECTS OF CORONARY PERFUSION ON VENTRICULAR VOLUME DISTENSIBILITY
Alan D. Horres, Francis Brown, Robert Denes and H. Kolder (Introduced by Gerhard A. Brecher). Department of Physiology, Emory University, Atlanta, Georgia.

It has been suggested without sufficient supportive experimental data that the filling of the coronary vasculature could cause a negative intraventricular pressure by expanding the ventricular walls. To test this hypothesis, ventricular pressure-volume measurements were made in the freshly excised dog heart with and without coronary perfusion while the heart was submerged in Locke's solution. It was found that at the "elastic equilibrium state" (zero transmural pressure) the ventricle could accommodate a greater volume during coronary perfusion than without perfusion. At small ventricular volumes the intraventricular pressure was negative and it became more negative during coronary perfusion. At large ventricular volumes the intraventricular pressure was positive and, above plus 30 mm of water, it became more positive during coronary perfusion. It is concluded that through engorgement of the vessels coronary perfusion stiffens the ventricular walls. This results in greater ventricular filling at low intraventricular pressures (below plus 30 mm of water and at negative pressures) but in a decrease in ventricular filling capacity at higher ventricular pressures.

EVIDENCE FOR AN INTERACTION BETWEEN Mg^{++} AND A NUCLEOTIDE RING.
Ken Hotta and Jerzy Brahms (intr. by M.F. Morales). Department of Biochemistry, Dartmouth Medical School, Hanover, N.H.

For some years it has been reasonable to assume [e.g., J. Blum, Arch. Biochem. Biophys., 55, 486 (1955)] that in the myosin catalysis of nucleoside triphosphate hydrolysis there occurs an interaction between the 6-position on the nucleotide ring and the cofactor, Mg^{++}; however, no direct evidence for this assumption has been obtained. Such evidence is now the following. The 6-OH group of inosine triphosphate has been shown by direct titration and spectrophotometrically to ionize with a pK of 9.25 (25° C, .2M KCl). At 249.5 mμ the difference in absorbance between unionized and ionized forms is nil, and at 263 mμ it is maximal. At constant pH, addition of excess $MgCl_2$ to the unionized form (e.g., pH 8.0) causes no spectral shift at 249.5 mμ, but at 263 mμ it causes quantitatively the same shift as total proton ionization. (This work was supported by National Heart Institute Grant H-3598 and by U.S.P.H.S. Training Grant 2G-174).

UNIT RESPONSES IN OPTIC NERVE OF SPIDER MONKEY. David H. Hubel and Torsten N. Wiesel* Harvard Medical School, Boston, Mass.

Single nerve fibers were recorded in the spider monkey's optic nerve with tungsten microelectrodes. Receptive fields were mapped out with small spots of light using a projection method. White light was obtained with a tungsten lamp, and colored stimuli with interferance filters. In the light adapted state all fields mapped with white light had a concentric arrangement similar to that of cat retinal ganglion cells, with a sharply demarcated center region giving 'on' or 'off' responses (excitatory or inhibitory responses), and a surrounding region stimulation of which tended to suppress the center responses. The smallest receptive field centers were found near the fovea, and the size of centers tended to increase with increasing distance from the fovea. The smallest center had a diameter of 4 min. of arc (corresponding to about 20μ on the retina), and was located 4° from the fovea; the largest center had a diameter of 2°. Some ganglion cells responded in a specific way to colored stimuli. In these cells light of short wavelength gave an 'on' response and light of long wavelength produced inhibition followed by an 'off' response. Transition between the two types of response occurred at about 500 mμ; light of this wavelength gave only feeble 'off' responses. Very weak responses were obtained to white light, presumably due to the antagonism between light of short and long wavelengths.

CHARACTERISTICS OF RECEPTORS FROM FLEXOR DIGITORUM LONGUS (F.L.D.) AND THE ADJOINING INTEROSSEOUS REGION OF CAT. C.C. Hunt and A.K. McIntyre*. Dept. Physiology, Univ. Utah, Salt Lake City, Utah.

An analysis of fiber diameter and receptor characteristics of 275 isolated afferent fibers from F.L.D. and associated interosseous nerves has shown that muscle spindle fibers have a bimodal diameter distribution, with modes in Groups I (12-22μ) and II (4-12μ), while fibers from tendon organs have a unimodal distribution in the Group I range. Receptors of the majority of fibers in the interosseous nerve were of 3 principal types: 1) slowly adapting receptors responding to pressure applied through the pretibial muscles or to squeezing the tibia and fibula together. Their fibers were mainly confined to Group I. 2) Vibration receptors, which were rapidly adapting and often extremely sensitive, responding to vibration at frequencies between 40 and 700/sec. Their fibers were largely in the 9-13μ range. Many such receptors were so sensitive that a slight tap on the floor or lightly brushing the skin would evoke discharge, although the most effective stimulus was vibration applied to bone. These receptors are probably concerned with vibration sensibility. 3) Tap receptors responding to brief tap on the tibia, with fibers in the same diameter range as 2). These may be high threshold variants of vibration receptors.

Digital Vascular Distensibility by Chester Hyman, James Arthur, Don Trotter and Travis Winsor. Departments of Physiology and Medicine, University of Southern California, Los Angeles.

The relationship between the volume of the blood vessels and the distending pressure has been studied in isolated vascular segments and in larger proximal portions of the extremities, but not in the digits because of certain technical difficulties. We have developed a method which minimizes the large irregular volume changes due to spontaneous arterial and arteriolar activity. This method measures fingertip volume when all of the vessels are distended to a uniform pressure. The increase in finger volume following local venous occlusion is first measured with any appropriate plethysmograph. When the finger shows no further systematic increase in volume, arterial flow is acutely stopped by occlusion of the upper arm. If the limb is above heart level, the pressure in the vascular bed distal to the arterial occlusion cuff tends to equalize at a value close to zero, due to the redistribution of blood. The high pressure part of the vascular bed of the fingertip will empty its blood into the arm, until the pressure in all vessels distal to the venous occlusion cuff falls to a uniform level related to the venous occlusion cuff pressure, achieving a fixed volume, A. Release of the venous occlusion cuff permits all of the blood vessels in the fingertip to come into equilibium with the pressures in the vessels of the arm to give a measure of the volume contained at the low pressure, volume B. The difference between these two volumes (A-B) represents the distention the entire vascular bed of the fingertip for the pressure difference between the occlusion and the final static pressure level. When subjects are exposed to a cold environment, distensibility of the fingertip vessels decreases, with evidence for involvement of both high and low pressure vessels.

COMPARISON OF CARDIAC OUTPUT AS MEASURED BY THERMAL DILUTION AND DYE DILUTION METHODS. C. J. Imig, Eugene Evonuk* and Wilbert Greenfield*. Dept. of Physiology, State Univ. of Iowa, Iowa City, Iowa.

A thermal dilution method was used for estimating the cardiac output employing room temperature saline as the indicator for recording time concentration curves. Measurements of cardiac output were made simultaneously with the thermal dilution and the dye dilution techniques and statistically compared. The data collected show a coefficient of correlation between the outputs as measured by the two methods of 0.96 ± 0.084. The average percent difference was 3.3 with a standard deviation of 9.7. Measurements of cardiac output made simultaneously from the right and left heart employing the thermal dilution method showed a mean percent difference of 1.6 with a standard deviation of 4.5. The thermal dilution technique employing room temperature saline as the indicator provides a convenient method for estimating the cardiac output in the intact animal.

OBSERVATIONS OF REGIONAL BLOOD FLOW AND CARDIAC OUTPUT IN CONSCIOUS DOGS. Juro Iriuchijima and Alexander Kolin (intr. by James V. Maloney) Department of Biophysics, School of Medicine, University of California, Los Angeles, California.

Electromagnetic flowmeter probes energized by sinusoidal currents were implanted at the common carotid and femoral arteries as well as at the aorta of dogs to measure blood flow in the conscious and non-restricted state. Presentation of food was shown to produce nearly instantaneous increase in carotid blood flow by a factor of three or more. The effect of muscular exertion upon blood flow in the femoral artery was studied. The greatest increases in femoral flow were observed immediately following relaxation of the muscular exertion. The early diastolic back flow, which had been described in anesthetized animals, was also frequently observed in conscious animals. To differentiate between blood flow changes caused by changes in cardiac output and by local vasoconstriction or vasodilatation, blood flow was recorded concurrently at the root of the aorta and the peripheral artery or at two peripheral arteries simultaneously. (Supported by Grant #H-3092 of the U. S. Public Health Service and by the Office of Naval Research.)

STUDIES ON RESPIRATORY QUOTIENT IN EXERCISE. B. Issekutz, Jr. (intr. by K. Rodahl). Lankenau Hospital, Philadelphia, Pa.

O_2 consumption and CO_2 output of healthy men (20 to 60 yrs. of age) were continuously recorded by means of a Noyons diaferometer, while working on the bicycle ergometer at different work loads. The following observations were made: (1) after start the RQ invariably decreases to 0.7 - 0.8. The lighter was the work load the longer lasted this low RQ. (2) The RQ rises from this low level and reaches a steady state (ΔRQ). The rate of increase and ΔRQ depend on the work load and on the physical work capacity of the subject. In the same individual ΔRQ increases approximately logarithmically with the work load. (3) The partial correlation (which eliminates the work load as common cause) between excess CO_2 ($=\Delta RQ \times O_2$ uptake) and blood lactic acid level was found to be significant ($p<0.001$). In the same individual the excess CO_2 plotted against blood lactate a regression line was obtained, the coefficient of which was significant ($p<0.001$). The work load which induces a ΔRQ of about 0.4, represents the maximal O_2 consumption of the subject (35 men and 8 women). This offers a possibility to assess the aerobic work capacity on the basis of measurements at submaximal work. It is concluded that the rise of RQ is due to the unbalance in the rate of formation and elimination of acids during exercise.

NON-METABOLIC FACTORS IN GLUCOSE APPETITE. Harry L. Jacobs (intr. by E.F. Adolph). Dept. of Physiol., Univ. of Rochester Sch. of Med. and Dentistry, Rochester, N.Y.

Observations on the ingestion of glucose available in dry food (Harper and Spivey, Am. J. Physiol. 193:483,1958) and in hypertonic solution (McCleary, J. comp. physiol. Psychol. 46:411,1953) have suggested that glucose-induced osmotic dehydration is an important factor in short term food satiation. The present studies are part of a series on the physiological regulation of glucose appetite in free-choice feeding situations. The work reported here evaluates the role of glucose-induced osmotic dehydration by comparison of glucose intake in normal and dehydrated rats. Intragastric loads of 2M glucose or 1M NaCl were administered to water-satiated or 24-hour water-deprived animals. The subsequent intake of .75M or 2M glucose solution or water was measured in two-choice tests. In water-satiated animals, the glucose load lowered glucose intake without affecting water intake. The response in dehydrated animals was different. Dehydration, induced by NaCl loads or by water deprivation, increased water intake without changing glucose intake. Volume intake of glucose solution during the 6 hr. test period resulted in a constant glucose intake, regardless of the concentration offerred for choice, the presence of intragastric loads, or of water deprivation. Conclusions: (1) The satiety value of glucose ingesta is independent of its colligative properties and is a function of its chemical-specific properties (taste and/or metabolic). (2) The independence of glucose and water intake under these conditions suggest separate regulatory mechanisms.

BASIC TYPES OF PROTOPLASMIC MOVEMENT. Theodore L. Jahn, Department of Zoology, University of California, Los Angeles, California.

Recent investigations of the foraminiferan Allogromia (Jahn and Rinaldi, 1959) and of the mycetozoan Physarum (Jahn, Rinaldi, and Brown, 1960; Jahn, 1960) have demonstrated that these members of the Sarcodina possess either of two basic mechanisms of protoplasmic movement. These mechanisms are distinct, at least at the visual level of information. Allogromia possesses single pseudopodia which may be several hundred microns long and only one micron in diameter, extensible in any direction in the medium. Each pseudopodium has two-directional streaming at all times, and moving granules reverse direction at the tips of the pseudopodia. These granules may also be seen to move in criss-crossing pathways through nodes of the anastomosing pseudopodial net. Movement seems to be caused by an active shearing mechanism acting longitudinally between two portions of a single filament of gel which is bent upon itself at the tip. Physarum has an outer tube of gel which contracts, thereby exerting pressure on the sol which flows because of differential hydraulic pressure, as in Amoeba. Existence of these two types of movement serves as the basis for a new major taxonomic dichotomy of the Sarcodina (Jahn, Bovee, and Small, 1960). The active shearing system also exists in plant cells (Nitella, Chara) which exhibit cyclosis (Kamiya, Jarosch) and possibly in striated muscles (Huxley and Hanson). It is possible that these two basic mechanisms may be similar on a molecular basis.

A COMPARISON OF THE PENETRATION RATE OF C_{14} LABELLED HYDROCORTISONE INTO NORMAL AND PATHOLOGICAL EYES. Ralph G. Janes and James F. Stiles.* State University of Iowa, College of Medicine, Iowa City, Iowa.

Hydrocortisone-4-C_{14} was used as a 0.5% solution and contained 0.5 μc in 0.25 ml. One-fourth ml was applied topically to one eye of each adult rabbit of the following groups. One group of animals had normal eyes, another group a severe conjunctivitis produced by cinnamon or clove oil, while the last group had multiple corneal ulcers produced with small pox vaccine. The animals were studied 30 and 60 minutes after receiving the hydrocortisone. Radio-labelled material was found in all parts of the eye at both time intervals but was concentrated particularly in the structures of the anterior segment. Preliminary results indicate that the rabbits with a conjunctivitis had larger amounts of radio-labelled material in their eyes than did the normals and that there was no appreciable difference between the values for normal and ulcerated eyes. When study was made to determine how much of the radio-labelled material was absorbed into the blood stream and distributed to other parts of the body, relatively large amounts of the radio-labelled material were found in the blood plasma, liver, bile and urine.

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VARIATIONS IN GLYCOGEN DISTRIBUTION THROUGHOUT THE VENTRICLES AND SEPTUM OF THE RABBIT HEART. Lillian A. Jedeikin (intr. by Nancy M. Buckley). Department of Physiology, Albert Einstein College of Medicine, New York.

When the heart is analyzed for glycogen from the endocardium to the epicardium, a wide gradient of glycogen concentration is observed, varying as much as seven-fold. For this study, the rabbit was stunned by a blow on the head, and the heart immediately removed. Cardiac arrest was produced immediately by placing the heart in ice water, and the ventricles and septum were removed as quickly as possible. Each wall was divided into three regions: apex, mid and base, and then slices were made from each of these regions going from the endocardial to the epicardial layers by means of a Stadie-Riggs slicer. After all the slices were prepared and weighed, they were placed in individual test tubes containing KOH and heated. Glycogen was precipitated by a micro method similar to that of Osterberg, A.E., (J. Biol. Chem. 85, 97, 1929), and determined by the anthrone method of S. Seifter et al. (Arch. Biochem. 25, 191, 1950). In the freshly excised heart, there was no appreciable difference in glycogen concentration in right ventricle, left ventricle and septum. There was a reproducible decrease from apex to base. The most striking gradient was observed from endocardial to epicardial layers.

Action Potentials Of Accessory Respiratory Muscles In Dog. Jefferson, N. C., T. Ogawa*, J. E. Toman, Th. Chiles*, A. Zambetoglou*, and H. Necheles
From the Department of Gastrointestinal Research, Medical Research Institute of Michael Reese Hospital, Chicago, Illinois.

We have reported previously that anastomosis of the central stump of an intercostal nerve to the peripheral stump of a phrenic nerve resulted in resumption of normal respiratory action of a diaphragm. Similar anastomosis between a long thoracic nerve and a phrenic nerve was successful in only one out of 4 experiments. Subsequently we tested the long thoracic nerve for respiratory impulses and found that only an occasional nerve would show weak respiratory action potentials. In the course of this work, a number of nerves and muscles were tested for the presence of respiratory impulses, and results are reported previously. Among 30 so-called accessory respiratory and other muscles tested for the presence of rhythmic respiratory impulses, these were found in 12. Both, expiratory and inspiratory impulses were detected in certain muscles, in others only in-or expiratory ones. The muscles with most frequent inspiratory impulses were the intercartilageous intercostal muscles, the intrinsic m. of the larynx and the nostril; those with expiratory impulses were abdominis, ext. and int. oblique, transversus abdominis, scalenus ant., and lower interosseous intercostal muscles.

VASCULAR RESPONSES TO INCREASED INTERNAL PRESSURE. P. C. Johnson. Ind. Univ. Sch. of Medicine, Indianapolis, Indiana.

Previous studies of the elevation of arterial pressure (Pa) and venous pressure (Pv) in the intestine have led to the conclusion that the resistance vessels are myogenically activated by an increase in transmural pressure. In the present study, a preparation of terminal ileum was used in which blood flow, large and small artery pressure, and weight were continuously determined. Small artery pressure was determined by a catheter or glass capillary inserted into an artery about 0.5 mm. in diameter. In almost all preparations, the small arteries and arterioles rapidly constricted both with Pv and Pa elevation. In most preparations, the large arteries dilated with Pa elevation but constricted with Pv elevation. The Pv effect on the large vessels clearly cannot be a myogenic response since these vessels dilated with Pa elevation and the effect of Pv on large artery pressure was small. In some instances, the constriction of the large arteries occurred 30 to 60 seconds after the small artery response, a delay which seems too long for a reflex mechanism. It is suggested that venous pressure elevation causes myogenic constriction of the small arterial elements, with subsequent passage of this response up the arterial tree by some intramural mechanism, possibly of syncytial nature. Elevation of Pa also produces a myogenic response of the small vessels but the increased pressure in the large arteries probably prevents their constriction. (Supported by Indiana Heart Association.)

RED CELL FALL OUT IN THE CLOTTED BLOOD OF PATIENTS WITH POLYCYTHEMIA VERA. Shirley A. Johnson, Thomas N. James* and Raymond W. Monto*. Henry Ford Hospital, Detroit, Michigan.

The percentage of hemoglobin falling out of a 24 hour specimen of clotted blood is significantly greater than normal in polycythemia vera. The mechanism of the fall out phenomenon is unknown. In this study it was found that the platelets of patients with polycythemia vera contain reduced amounts of platelet factor 3. Since this activity cannot be released by sonic disintegration of these platelets, it appears that the megakaryocytes may not produce platelets containing normal amounts of platelet factor 3. The amount of platelet factor 3 does not increase quantitatively when the platelet count is reduced to normal so the defect cannot be explained on the basis of insufficient amounts of factor 3 to meet the demands of overproduction of platelets by the megakaryocytes. According to the clot retraction assay of Hartman and Conley, clot retraction of platelets from patients with polycythemia vera is at least as rapid as normal platelets. In our investigation clots from platelet-high plasma with a determined number of platelets were examined histologically. Striking differences appeared between normal and polycythemia vera platelet-fibrin structures. The platelet clumps were larger, appearing to consist of more platelets and the fibrin strands were irregularly formed as compared to the normal. The possibility of abnormal platelet-fibrin structure playing the dominant part in the red cell fall out phenomenon is suggested.

This investigation was supported (in part) by a research grant H-3636 (C2) from the National Heart Institute, Public Health Service.

STUDIES ON 5-HYDROXYTRYPTAMINE, 5-HYDROXYINDOLE ACETIC ACID AND IPRONIAZID IN EXPERIMENTAL HYPERTENSION. G. Kaley* and B.W. Zweifach. Dept. of Pathology, N.Y.U. Sch. of Med., New York City.

The concentration of 5-hydroxyindole acetic acid (5HIAA) was measured in the urine of normal, renal hypertensive and DOCA hypertensive rats. No significant difference in the amount of urinary 5HIAA was found among these three groups of animals. When 5-hydroxytryptamine (5HT) was injected in a single large dose, there were significant differences in 5HIAA excretion between normal and renal hypertensive animals - the hypertensives excreting less of the 5HT metabolite. Chronic, daily, intraperitoneal administration of increasing doses of the precursor of 5HT, 5-hydroxytryptophan, iproniazid (a monoamine oxydase inhibitor) and the combination of these two agents for a period of 11 weeks produced a slight initial drop in the blood pressure of renal hypertensive animals. The blood pressure of normal animals was not affected. Hypertensive animals treated for this period of time showed no further reduction in blood pressure after the initial drop. The treated animals developed a degree of tolerance for 5HT as shown by the decrease in intensity of the toxic effects. (Supported by a grant from the American Heart Association).

MECHANISMS IN THE PRODUCTION OF HIPPOCAMPAL SEIZURES. E.R. Kandel and W.A. Spencer (intr. by W.H. Marshall). Nat. Insts. of Health, Bethesda Maryland.

Tetanization of either the deafferented or intact fornix triggers the seizure prone hippocampus into convulsive activity. During these seizures simultaneous cortical surface and intracellular recordings were obtained from neurons in CA_2 and CA_3 in anesthetized cats. In the deafferented fornix preparation (DFP) the most prominent feature of the intracellularly recorded seizure was a period of maintained synaptic hyperpolarization. This was preceded and/or followed by small depolarizing oscillations (synchronized with surface potentials) which occasionally reached the critical threshold for spike generation. Surface clonic phases were associated with either pyramidal cell excitation or inhibition. In the intact fornix preparation (IFP) afterdischarge began with a prolonged and profound membrane depolarization (15 to 30 mv) and consisted primarily of large depolarizing oscillations (synchronized with the surface record) with absent or abortive spike generation, and ended with a brief phase of hyperpolarization. The fact that, in the DFP, seizure begins with inhibition and terminates with a return of the resting firing pattern suggests that the cells sampled behave as follower neurons which are being driven by an active pacemaker located elsewhere. In the IFP these same cells undergo an excessive depolarization and abnormal spike generation. The shift in behavior of this cell population from inhibition to excitation is consistent with several alternative explanations. One of these is that, in the IFP, these cells are more directly involved in a pacemaker circuit.

THE INTEGRATED ELECTROMYOGRAM OF THE DIAPHRAGM AS AN INDEX OF VENTILATION. R. L. Katz*, B. R. Fink* and S. H. Ngai. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia Univ., N.Y.C.

The purpose of this study is to correlate the electrical activity of the diaphragm with inspiratory flow and tidal volume. The electromyogram (EMG) was recorded from the diaphragm of midcollicular decerebrate cats. An unipolar electrode was introduced into the diaphragm transabdominally under direct vision. After appropriate amplification the action potentials were rectified and integrated electronically. The average activity of the diaphragm during each breath was calculated. The inspiratory flow and tidal volume were measured in seven cats with a pneumotachogram and in seven other cats with a servospirometer. These parameters were measured during a progressive increase in ventilation produced by rebreathing. Linear relationships were found between the integrated EMG and flow and between the integrated EMG and tidal volume. The correlation coefficient was greater than 0.8 in the majority of the experiments. This close correlation indicates that the electrical activity of the diaphragm is a valid measure of relative changes in inspiratory flow and tidal volume. It is suggested that the integrated EMG may be used as an index of ventilation when other quantitative methods are impractical. (Supported by Grant No. RG-4717, USPHS)

EFFECTS OF GAMMA AMMINO BUTYRIC ACID, ACETYLCHOLINE AND TWO BRAIN EXTRACTS ON NEURONS OF THE TRIGEMINAL MOTOR NUCLEUS AND THE HYPOGLOSSAL NUCLEUS OF THE CAT. Yojiro Kawamura* (intr. by R.E. Smith). Dept. Physiol., Osaka Univ. Dental School and Dept. Physiol., Univ. of California School of Med., Los Angeles.

Our previous studies have shown that stretching any jaw muscle induces acceleration of the discharge frequency of neurons of the motor nucleus of the trigeminal nerve concomitant with deceleration of the discharge frequency of neurons of the hypoglossal nucleus. The possibility of an activating substance exciting the trigeminal motor nucleus and the same or some other substance inhibiting the hypoglossal nucleus was investigated in this experiment. Gamma ammino butyric acid (GABA), acetylcholine (Ach), a saline extract of dog brain tissue (S.A.) and an ethanol extract of the same tissue (S.I.) all of pH 7.2 were micro-injected into cats' trigeminal motor nuclei and hypoglossal nuclei, and alterations of the discharge frequency of neurons adjacent to the sites of microinjection were recorded. The discharge frequency of the trigeminal motor nuclei was increased by injection of S.A. and of Ach but was decreased by injection of S.I. Conversely the discharge frequency of hypoglossal nuclei neurons was greatly increased by injection of S.I. and only mildly increased by injection of Ach and S.A. Injection of GABA decreased the discharge frequency of both sets of neurons. The significance of these results with respect to the neurogenesis of jaw movements is discussed.

EFFECT OF ATROPINE ON THE CARDIOVASCULAR RESPONSE TO EXERCISE IN THE DOG. E. W. O. Keck,* M. J. Allwood,* J. T. Shepherd and R. J. Marshall,* Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

Cardiac output was measured by the indicator-dilution technic in five dogs that had been taught to run at graded speeds on a treadmill. Cardiac output at rest averaged 4.0 L./min. After intravenous doses of atropine (1.0-2.6 mg.) cardiac output averaged 3.5 L./min., the heart rate increased from 120 to 236 per minute and the stroke volume decreased from 33 to 15.5 ml. The blood pressure after atropine, both at rest and during exercise, was not significantly different from that before atropine was given. During control exercise the output increased by 90 per cent, the heart rate by 74 per cent and the stroke volume by 11 per cent. During exercise in the atropinized dog the output increased by 101 per cent, the heart rate by 8 per cent and the stroke volume by 87 per cent. Thus, while the increased output during exercise is normally achieved by a change in heart rate, in other circumstances a similar increase may be attained by a change in stroke volume.

INFLUENCE OF RADIATION DOSE RATE ON HEMATOPOIETIC TISSUE AND HOMOGRAFT REACTION. Lola S. Kelly and James McRae*, Donner Lab., Univ. of California, Berkeley.

Recent reports have indicated that the LD_{50} is greatly affected by a variation in the radiation dose rate in the range of 50 r/min. to 0.2 r/min. (Logie et al. Rad. Res. 12, 349, 1960). Current experiments are concerned with the changes in hematopoietic tissue when the radiation dose rate is varied within these limits. For example: a group of mice given 840 r in 1 hour with no other treatment all died within 14 days. At this dose rate all the mice in a second group accepted rat bone marrow grafts. On the other hand, a third group given the same radiation dose spread uniformly over a 17-hour period all survived the acute radiation syndrome without further treatment. A fourth group treated with rat bone marrow after the low-dose rate exposure rejected the graft promptly. The hematological picture was in agreement with the survival data, i.e., nearly complete recovery by 2 weeks. Studies on DNA synthesis, Fe^{59} metabolism and other indeces of radiation damage and recovery are in progress and will be reported.

CARDIOVASCULAR REFLEXES ORIGINATING IN THE ATRIA AND PULMONARY SYSTEM OF TOTALLY PERFUSED DOGS. J. E. Kendrick (intr. by R. C. Wolf). Department of Physiology, University of Wisconsin, Madison.

Systemic and pulmonary circulations in the dog were maintained by a perfusion pump. Coronary blood flow was supplied from a side tube off the cannula in the aorta. In this manner it was possible to maintain the heart in a viable condition. Systemic and pulmonary arterial blood pressure were continuously measured. Venous return was drained from the atria by special atrial cannulae. Atrial stretching was accomplished without affecting venous return by inflating a cuff around the atrial cannula. Right or left atrial pressure could be increased in a stepwise manner by partial occlusion of the drainage tubing. Occlusion of the tubing from the left atrium caused a rise in left atrial pressure and a concomitant rise in pulmonary arterial pressure. Inflation of the cuff within either atrium alone produced no predictable or significant changes in pulmonary or systemic arterial pressure. Partial occlusion of the right atrial drainage tube similarly produced no change in these pressures. Partial occlusion of the left atrial drainage tube produced a significant fall in systemic arterial pressure (15-50 mm Hg). Under the conditions of these experiments the depressor response observed apparently arises from receptors in the pulmonary system and not from atrial receptors. Vagotomy abolishes the response.

CONTRIBUTION OF PYRAMIDAL TRACT (PT) NEURONS TO SURFACE PRIMARY EVOKED RESPONSE IN CAT. Thelma T. Kennedy, A. L. Towe and H. D. Patton. Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine, Seattle.

The surface primary evoked response and the concomitant single unit activity produced in the cerebral cortex by electrical stimulation of each central footpad were examined in cats anesthetized with α-chloralose. One cerebral hemisphere was exposed for recording; the bulbar pyramids were exposed for antidromic activation of those cortical units whose axons project into the medullary pyramids (PT neurons). Recordings were made from three separate 3 mm^2 areas of tissue centered (1) just behind and (2) just in front of the lateral end of the cruciate fissure and (3) midway between the anterior ectosylvian and suprasylvian fissures in area II. The primary evoked response following contralateral forepaw stimulation consisted of (1) a small negative, large positive, small negative wave in the precruciate cortex, (2) a large positive-negative wave in the postcruciate cortex and (3) a large positive and large, prolonged negative wave in area II. Among the units isolated, 30% of 316 units in the precruciate cortex, 25% of 527 units in the postcruciate cortex and 4% of 75 units in area II were PT neurons. Most units could be fired by stimulation of any limb. Of the non-PT neurons, 74% in the precruciate cortex, 63% in the postcruciate and 24% in area II responded reliably to all four inputs. Of the PT neurons, 88% in both the precruciate and the postcruciate cortex responded to all inputs. However, the surface primary responses produced by stimulation of the hind paws or the ipsilateral forepaw were uniformly very small, having little or no negative component. These data indicate that the postsynaptic response of PT neurons contributes negligibly to the surface primary evoked response. (Supported by grants B395 and B396 from the National Institute of Neurological Diseases and Blindness.)

REGULATION OF CORONARY FLOW DURING TREADMILL EXERCISE IN THE DOG. E. M. Khouri,* D. E. Gregg, R. J. Hall,* and C. R. Rayford.* Dept of Cardiorespiratory Dis., Walter Reed Army Institute of Research, Wash. 12, D. C.

The mechanisms whereby the myocardium augments its blood supply during physical activity are being investigated. Phasic flow measurements are made in the main left coronary artery at its origin, or in the left circumflex coronary artery anastomosed to a systemic artery, and in the ascending and descending aorta, simultaneously with aortic pressure. The electromagnetic flowmeter (Kolin type) is used for the flow measurements. Transducers are implanted for periods of up to 8 weeks, and the aortic pressure is obtained by means of a carotid loop or an indwelling, aortic plastic catheter. Exercise is mild to moderate (12 to 15 km/hr. for 3 to 5 min.). Within 20 to 30 seconds, the elevations in coronary flow, cardiac output and blood pressure are essentially complete and do not change during further exercise. Calculations show that the coronary flow per heart beat is generally not significantly altered and, hence, the mean flow increase is mostly on the basis of increase in heart rate. Similarly, the left ventricular stroke volume does not contribute significantly to the increase in mean cardiac output.

MECHANISM OF CHLORIDE IMPOVERISHMENT DURING ABSORPTION. Venard R. Kinney* and Charles F. Code. Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

Burns and Visscher demonstrated that the concentration of chloride declined when an isotonic solution of Na_2SO_4 and NaCl was placed in the bowel of the dog (chloride impoverishment). We have confirmed their finding, as have others. To elucidate the mechanism, we have determined, in acute experiments, the membrane potential and the bidirectional movement of labeled water, Na and Cl in isolated loops of ileum in dogs during chloride impoverishment. Solutions containing 80 mEq. Cl (as NaCl) with and without Na_2SO_4 were placed in the gut. The rates of exsorption of Cl and water were little affected by the presence of SO_4; the rates of insorption, however, were reduced. Application of Ussing's formula to the ion flux data and the membrane potential indicated that Cl was actively transported; measurement of osmolarity and water fluxes indicated that water was osmotically retained by the SO_4 in the contents. Changes in the concentration of Cl in the solution in the gut depended on the relationship between the ratios of Cl to water in the insorbed and exsorbed fluids. When SO_4 was present, the concentration of Cl in the net absorbed fluid exceeded that in the fluid in the gut and, as a consequence, the concentration of Cl in the contents declined (chloride impoverishment).

IDENTIFICATION OF A TRANSPORT ADENOSINE TRIPHOSPHATASE ACTIVITY IN GUINEA PIG KIDNEY. C. R. Kinsolving* and R. L. Post, Dept. of Physiology, Vanderbilt School of Medicine, Nashville, Tenn.

The participation of ATPase activity in active sodium and potassium transport has been shown in erythrocytes by Hoffman (Fed. Proc. 19: 127), Tosteson et. al. (Fed. Proc. 19: 128), and Post et. al. (J. B. C. 235: 1796). This activity requires sodium and potassium ions simultaneously as well as magnesium ion, and is inhibited by cardiac glycosides. A similar activity is reported here from kidney. The specific activity is fifteen times greater and the background activity one-fifth as large as in erythrocyte membranes. A fraction from a kidney homogenized in 0.001 M histidine at pH 7.2 was isolated by differential centrifugation between 700 x g and 10,000 x g, washed twice with the same solution and lyophilized. The concentrations which produced a half-maximal effect were 0.040 M for sodium in the presence of potassium, 0.003 M for potassium in the presence of sodium, and 2 x 10^{-7} M for ouabain in the presence of both ions. Ammonium ion substituted for potassium ion but not sodium ion. The above features correspond closely with those of erythrocyte membrane transport ATPase activity. *Fellow of the National Heart Institute. This project was supported by a grant (H-1974-C5) from the National Heart Institute, U.S.P.H.S.

PRESSURE-FLOW RELATIONS IN THE PULMONARY ARTERY WEDGE SEGMENT IN THE DOG. Arthur H. Kitchin* and H.J.C. Swan. Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

In dogs under pentobarbital anesthesia cardiac catheters of large bore were wedged in pulmonary-artery branches and the resistance to flow of the wedged segments was studied by perfusion with normal saline solution and with arterial blood. Two methods were used: stepwise changes in flow rate from a constant-speed syringe, and falling rates of flow from a standpipe. The pressure gradient was estimated from the pressure at the proximal end of the catheter, the static wedge pressure and the catheter flow-resistance. In 12 wedge segments in six animals an approximately linear relationship between flow and pressure was found with saline perfusion. With blood, "resistance" increased at low rate of flow. An approximate figure for compliance of vessels of the wedge segment was obtained in six wedge segments by a stop-flow method. With perfusion at constant flow, a decrease in resistance with inspiration and phasic changes of resistance with the cardiac cycle were observed. Carotid occlusion caused no change in resistance; aortic occlusion, with raised left atrial pressure, caused a decrease in resistance.

TRANSINTESTINAL VOLTAGE AS A FUNCTION OF NA^+ AND CL^-. Alan Koch, Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle.

Bullfrog duodenum was mounted in a lucite chamber and separate solutions were pumped past the two sides of the tissue. In any experiment the two solutions were identical. The voltage between the solutions was measured through calomel half cells, with a high impedance amplifier. Measurements were referred to the external solution. The composition of the solutions was varied by substitution of Na_2So_4, $Na_4Fe(CN)_6$ or choline chloride for NaCl. The voltage had a stable component and a transient, which followed any change of solution. The stable voltages were quite small, between $\pm$ 5 mV. The voltage was positive at zero Na^+, zero Cl^-. With increasing Na^+, the voltage fell and became negative, reaching a minimum at about 55 mM. It then rose toward zero. With increasing Cl^-, the voltage rose until 30 to 50 mM and then fell toward zero. The transient voltages were often quite large, attaining values in excess of 50 mV. They were generally single exponentials with time constants between 0.14 and 0.23 min^{-1}. The initial values depended on the changes in the concentrations of Na^+ and Cl^-. The findings are compatible with an active extrusion of both Na^+ and Cl^- from the mocosal to the serosal side. (Supported by a grant, H4469, from the National Institutes of Health.)

THE EFFECTS OF INSULIN AND GROWTH HORMONE ON THE BLOOD LEVEL AND VOLUME DISTRIBUTION OF GALACTOSE IN THE HYPOPHYSECTOMIZED RAT.
N. Kokka* and L. L. Bennett. Dept. of Physiology, School of Medicine, Univ. of California, San Francisco, Calif.

Fasted normal and hypophysectomized rats were functionally eviscerated and nephrectomized under light pentobarbital anesthesia and glucose was infused intravenously at rates which maintained a nearly constant blood glucose concentration. Single injections of galactose were given which produced an equilibrium concentration at 90 minutes of 247 ± 30 mg. %. Under these experimental conditions, the peripheral distribution of galactose in hypophysectomized rats was demonstrated to be hypersensitive to insulin by two criteria: (a) Significant decreases in the blood galactose concentration of hypophysectomized rats were observed with small doses of insulin which had no effect in normal rats; (b) After comparable doses of insulin, the changes in the blood levels and volume distributions of galactose were greater in hypophysectomized rats than in their normal controls. In neither normal nor hypophysectomized rats did the prior administration of growth hormone alter either the volume distribution of galactose or the insulin hypersensitivity. The results are interpreted as demonstrating that hypophysectomy enhances the insulin expansion of the galactose space in eviscerated-nephrectomized rats, and that this increased insulin sensitivity is not diminished by growth hormone.

STUDIES ON BASAL GASTRIC SECRETION IN CHRONIC FISTULA RATS. Effect of Urethane and Chlorpromazine. S.A. Komarov,M.D. and S.P. Bralow, M.D.*, Fels Research Institute, Temple University Med. Center, Philadelphia, Penna.

Two types of chronic gastric fistulae in rumen of Wistar rats were developed in our laboratory: 1) gastrostomy with artifical sphincter; 2) Pavlov's type stainless steel cannula. The following experiments were done: on basal secretion and on the effect of; a) intracolonic administration of normal saline; b) intracolonic administration of 5% urethane; c) chlorpromazine administered subcutaneously (0.2 mg., 0.1 mg./100 gm. body weight). The basal secretion varied with respect to volume, acid and pepsin output from hour to hour in the same experiments as well as between experiments. Smaller range of variation occurred with animal at rest or sleeping. In active animals (movements, chewing etc.) the variations were wider. In saline experiments there was an increase in volume (12% not significant) and total acid output (22%) and pepsin output (18%) both significant. In urethane experiments there was a 19.4% decrease in volume of secretion ($P < 0.01$); and also 12.3% decrease in acid output and 13.8% decrease in pepsin output--both not significant. Diminution in volume was the result of observed decrease in salivary contamination and that was likely due to suppression of cerebral cortical activity. Chlorpromazine (0.2 mg.dose) produced a highly significant depression of volume by 36% of that in control basal, total acid output by 40% and pepsin by 44%. Smaller doses produced smaller and less significant depression of volume and acid output while results on pepsin output were not consistent.

THE EFFECT OF VASOPRESSIN ON SALIVATION. Leon Kraintz, Univ. of Texas Dental Branch and Baylor Univ. College of Medicine, Houston, Texas

The effect of commercial pitressin and purified arginine vasopressin on salivary flow was studied in a series of dogs anesthetized with sodium pentobarbital. Prior to the initiation of salivation the dogs were given water 20 ml/kg via stomach tube. Salivation was induced by the administration of pilocarpine hydrochloride 0.33 mg/kg in one group of dogs. Electrical stimulation of the chorda tympani and the auriculotemporal nerves was used to elicit salivation in another series. Parotid and submaxillary saliva was obtained by intra-oral catherization of the respective ducts with polyethylene tubing. Salivary flow was recorded by means of a combination drop counter and weighing cup. A large dose of pitressin (5 units) I.V. suppressed submaxillary and parotid flow for 15-20 minutes. A detectable decrease in salivary flow from both glands was obtained with as little as 0.05 units of pitressin. The pitressin was more effective in decreasing salivation evoked by electrical stimulation than that produced by pilocarpine administration. Purified arginine vasopressin was equally effective in diminishing salivary flow.

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ELECTROPHYSIOLOGIC STUDIES OF CHICK EMBRYO HEARTS. V. Krespi* and W. Sleator, Jr. Dept. Physiology, Washington Univ. School of Medicine, St. Louis, Mo.

An investigation of the ontogenesis of the action potential has been undertaken using intracellular electrodes on chick embryo hearts in vivo and chick embryo cultures. In vivo, embryos from 9 to about 29 somites (approx. 35-55 hrs. incubation) exhibited AP's similar in shape to those obtained by Meda and Ferroni (Experientia, 15:427-428, 1959). The maximum size AP obtained was 70 mV. This was recorded as early as 13 somites. In early embryos, most of the AP's are of small amplitude. Sometimes small AP's start from a much larger negative resting potential indicating that they are not due to poor impalement. Also, some of these intracellular AP's were negative deflections starting at intracellular potentials of -30 to -100 mV. Both these effects could be explained on the assumption that these cells have a very high Na^+ content, as reported by Klein (Fed. Proc. 19:130, 1960). The more caudally along the cardiac tube the AP was obtained, the more diastolic depolarization was recorded. The younger the embryo, the longer was the duration of the AP's. Chick embryos incubated 26.5 hrs., in which no contractile cardiac tissue was observed, developed rhythmically contracting areas after 46-85 hrs. in culture. Action potentials of 70 mV (overshoot 20 mV) were recorded from these areas of the cultures. (Supported by U. S. P. H. Grant B-937)

CONTINUOUS RECORDING IN VIVO OF RESPIRATORY AIR O_2 TENSION AND DETERMINATION OF ALVEOLAR PO_2. F. Kreuzer, Department of Physiology, Dartmouth Medical School, Hanover, N.H.

The development of the catheter PO_2 electrode by Kreuzer and Nessler (Science 128: 1005, 1958) has provided the opportunity for a continuous recording in vivo of respiratory air PO_2 and for the continuous determination of alveolar PO_2. In order to follow the full possible range of respiratory frequencies, a sufficiently short response time is necessary. By refining the construction of these electrodes, a response time of 1 sec for full deflection and for a change between nitrogen and 100 % O_2 has been achieved. The electrodes were first calibrated in vitro at 37°C. Then they were incorporated into a tracheal tube and inserted into the trachea of dogs anesthetized with pentobarbital 25 mg/kg, spontaneous respiration being suppressed by anectine. The dog was breathed with a Harvard respiration pump with constant tidal volume and variable rate of respiration. Continuous tracings with a Minneapolis-Honeywell Visicorder 906 were obtained for O_2 mixtures of 10, 21, 60 and 100 % O_2 and for respiration rates from 7 to 40 per minute. The readings for the inspiratory and end-expiratory (alveolar) levels were plotted against the % O_2 obtained by Scholander analysis. All these points coincided with the in vitro calibration curve with an average error of - 3 mm Hg (S.D. = 3 %). This proves that the electrodes are able to follow the respiratory excursions of PO_2 and provide the correct alveolar PO_2 on any level of O_2.

(Supported by Grant H-2830-C3 from the National Heart Institute of the National Institutes of Health).

ORGANIZATION OF THE DORSAL COLUMN NUCLEI AND SPINAL NUCLEUS OF THE TRIGEMINAL IN THE CAT. Lawrence Kruger, Robert Siminoff and Paul Witkovsky (Intr. by J. D. Green). Department of Anatomy, School of Med., Univ. of Calif. at Los Angeles.

The present investigation consists of an analysis of 713 single units which were classified in terms of receptive fields, modality, adaptation properties and nuclear organization. In the dorsal column complex the body wall is represented with caudal parts of the body medially and successively more rostral portions laterally. The limb apices project dorsally and the trunk is represented in a smaller proportion of nuclear volume at the ventral surface. This pattern occurs at all levels of the rostro-caudal plane. The tactile pattern for the face in the spinal root of V is also undifferentiated in the rostro-caudal plane but the mandibular division is represented dorsally and the ophthalmic division ventrally. The modalities represented are predominantly hair and light touch but with a significant number of pressure and joint units also present. There is no evidence of modality segregation in any part of these nuclei nor evidence of pain representation in the spinal root of V.

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SPONTANEOUS VARIATION OF SKIN POTENTIALS AND CENTRAL NERVOUS SYSTEM. Roongtam Ladpli* and G. H. Wang. Univ. of Wisconsin, Madison, Wis.

Spontaneous potential waves from the four paws of unanesthetized cats, normal or with lesions of the central neuraxis, have been recorded with an electroencephalograph. The following results are obtained: normal and striatal cats show synchronized waves in the four paws; decerebrate cats show no waves in any paw; high spinal cats (cord transected between D_1 and D_2) show desynchronized waves in the four paws; low spinal cats (cord transected between D_9 and D_{10}) show synchronized waves in the forepaws, but desynchronized waves in the hindpaws. Previous workers have proved that spontaneous potential waves are abolished from the cat's hindpaw by section of the ipsilateral sciatic nerve. These facts indicate: spinal sympathetic motoneurons controlling sweat secretion in the footpads constantly send, unless inhibited, impulses to the sweat glands in the footpads; these impulses are synchronized by descending excitatory and inhibitory impulses from the brain; most inhibitory impulses come from the hindbrain; most excitatory impulses probably come from the interbrain.

THE EQUIVALENCE OF RIBOFLAVIN AND 6-ETHYL-7-METHYL- OR 6-METHYL-7-ETHYL-9-(1'-D-RIBITYL)-ISOALLOXAZINE FOR THE GROWTH OF THE RAT. John P. Lambooy. Dept. of Physiol., Univ. of Rochester, Rochester, New York.

The average values for different analyses of bioassay data for the activity of 6-ethyl-7-methyl- and 6-methyl-7-ethyl-flavins were found to be 47% and 36% respectively of the activity of riboflavin. These values were used to determine the level of flavin to be added to otherwise identical diets which were fed to groups of animals by the paired feeding technique. The riboflavin, 6-ethyl-7-methyl-flavin and 6-methyl-7-ethyl-flavin diets contained 5γ (suboptimal), 10.6γ and 13.9γ per gram respectively of the three flavins. Growth rates of the groups were essentially identical, showing the equivalence of these three flavins for the stimulation of growth and the utilization of food in the rat. (Supported in part by Grant No. CY-2940, NIH, Cancer Institute.)

ELECTRICAL STUDIES ON THE INNERVATION OF THE DIAPHRAGM. Barbara R. Landau*, and Konrad Akert. Depts. of Physiol. and Anat., Univ. of Wisconsin, Med. Sch., Madison.

In continuing work of Adrian and Bronk (1928), Gesell, et al, (1941) and Pitts (1942), electrical activity of efferent units in C5 and C6 phrenic nerve roots was studied in dogs under nembutal or chloralose-urethane anesthesia. Normal inspiration is associated with large and small fiber activity, which is recruited throughout the course of the bursts, and breaks off abruptly. The discharge rate of the individual units increases during the burst, but rarely exceeds 20 per second. An appreciable number of small nerve fibers may be active during the entire respiratory cycle, firing at very low rates in the interval between inspiratory bursts. This interval activity is augmented by inflating the thorax and by stimulating the Head zone of the phrenic nerve. After section of the vagi such spinal reflex activity, particularly that elicited by cutaneous afferents, is notably released, and may appear as short trains of high frequency spikes. (Supported in part by NINDB grant no. B-2617).

STUDIES OF THE FUSIMOTOR SYSTEM IN MAN. W.M.Landau, R.A. Weaver*,and T.F.Hornbein*.Divisions of Neurology and Anesthesiology, Wash. Univ. School of Med., St. Louis, Mo.

Fusimotor fibers are more sensitive to local anesthetic spinal block than larger fibers, both efferent and afferent. Differential block in normal subjects severely depresses patellar reflexes and hypotonia develops, while quadriceps strength and proprioceptive and touch sensations are preserved. This confirms other evidence that position sense is not mediated by muscle receptors. Pain and temperature sensations (delta and C fibers) are always much decreased. No signs simulating those of cerebellar lesions are observed; fusimotor depression does not explain cerebellar symptoms. In spastic and rigid patients hypertonic reactions to passive movement disappear pari passu with tendon reflexes. Parkinsonian tremor is also diminished. In other nerve block studies the H reflex from direct stimulation of the popliteal nerve is compared with the ankle jerk and gastrocsoleus strength. Though the tendon jerk is severely depressed, the H reflex is always decreased to a lesser degree. This central effect is inferred to be due to diminution of tonic spindle afferent potentiation, due in turn to fusimotor blockade. Since the relative degrees of such peripheral and secondary central effects are the same in normal, spastic, and rigid subjects,we can neither support nor reject the hypothesis that hypertonic states are due to excessive fusimotor activity. Preliminary studies in man and animals indicate that fusimotor hypofunction is related to the stretch reflex depression of spinal shock.(NIH Grant B-882).

THYROID FUNCTION FOLLOWING ACUTE, MASSIVE HEMORRHAGE IN THE RAT. S. Lang and G. Wool*. Dept. Surgical Research, Research Institute, Jewish Hospital of St. Louis and Dept. Physiology, School of Medicine, Washington University, St. Louis, Mo.

Various parameters of thyroid gland function and of thyroid hormone level regulation in the serum have been investigated in the rat after acute, massive hemorrhage. It was found that there was a slight, but significant depression of the protein-bound serum iodine (SPBI) 4 to 6 hours after hemorrhage. It was concluded that this depression of SPBI was not associated with release of additional amounts of thyroid stimulating hormone. The conclusion was based on the observations that thyroidal iodine release was inhibited and thyroxine disappearance from the plasma was unchanged following hemorrhage. The T:S ratio was, however, increased at 6 hours after hemorrhage. Loss of iodine into the bile was depressed but rapidly returned toward control values. Nevertheless, it was still below control values 2 hours after hemorrhage.

COMPARISON OF THE PAROTID SECRETION OF RUBIDIUM AND POTASSIUM. L. L. Langley and R. S. Brown.* Dept. of Physiology, Univ. of Alabama School of Dentistry, Birmingham, Alabama.

The metabolism of rubidium and potassium have been reported to be very similar. Previous investigations have shown that the parotid secretion of potassium in the dog has many unique features. The aim of this study was to learn if rubidium is secreted in a similar manner. Rb-86 was used. A stop-flow procedure indicated the location of transfer from plasma to saliva in the gland. The relationship of saliva concentration to rate of flow, and the relationship between plasma and saliva concentrations were determined. Following the injection of K-42 into the ipsilateral carotid artery there is a rapid appearance of the isotope in the saliva by virtue of duct transport. The saliva concentration curve shows a unique descending limb. Rb-86 is transferred at the same location and has a similar descending limb. At very low saliva flows the saliva concentrations of both K and Rb increase sharply. There is a similar straight line relationship between the plasma and saliva concentrations of both elements. It is concluded that the same parotid mechanism is responsible for both rubidium and potassium secretion. (Supported by NIH Grant No. D-329-C3).

FUNCTIONAL DIFFERENCES IN APICAL VERSUS DIAPHRAGMATIC LOBES FOLLOWING PULMONARY RESECTION IN THE DOG. M.T. Lategola and J.A.Schilling. Univ. of Okla. Med. School, Okla. City, Okla., and C.A.R.I., P.A.A.,Okla.City,Okla.

Four groups of dogs were used. Control measurements were made under,supine, anesthetized conditions. Each group was consequently resected in each of the 4 chest quadrants. The apical resections amounted to 17.2% and 15.4% and the diaphragmatic resections amounted to 41.1% and 26.3% of the total lung weight. The functional adaptation of the lobes remaining within the operated hemi-chest was studied at intervals during the next 160 days. Anatomical adaptation was studied at sacrifice. Thus, the assayed parameters reflect the changes which occurred in the areas of mechanics, gas exchange, hemodynamics and anatomy. The remaining upper lobes showed the largest increases in weight and volume (FRC) while the lower lobes showed small weight changes and large decreases in FRC. The anatomical differences were qualitatively and quantitatively reflected in function, The greatest displacements occurring in the upper lobes of the operated hemi-chest. Remarkable return of function normward occurred by the 160th day in these upper lobes. Since these are resting-condition measurements, it is not possible at this time to estimate the degree of loss in the maximal reserves of the parameters studied.

INFLUENCE OF URANIUM NITRATE-INDUCED NEPHROSIS ON FLOW AND COMPOSITION OF RENAL LYMPH. S. J. LeBrie* and H. S. Meyerson. Tulane University, Physiology Department, Tulane University Station, New Orleans, Louisiana.

Acute nephrosis was induced in dogs by subcutaneous injection of uranium nitrate (4mg./k). Renal capsular lymphatics were cannulated between 2 to 7 days after the injection and the flow and composition of renal lymph studied before, during and after mannitol diuresis induced by intravenous infusion of 20 ml. per kilogram body weight of 12.5 p.c. mannitol at a rate of 10 ml. per minute. From a single capsular lymphatic, the average flow in control animals was 0.00329 ml/min. The average flow in nephrotic animals was almost 15 times greater (.042 ml/min.). Control animals given mannitol showed an average increase in renal lymph flow of 542 p.c. In nephrotic animals, the average increase in renal lymph flow was approximately 1000 p.c. Calculated on a 24 hour basis, this is equivalent to a flow of 642 ml from a single lymphatic. The renal lymph to plasma ratio for sodium in control and nephrotic animals was approximately the same (1.139 and 1.119 respectively). Control animals showed no significant change during mannitol diuresis but the ratio was reduced in nephrotic animals to 1.012, a reflection of a fall in renal lymph sodium levels toward those in plasma. All nephrotic animals showed a significant proteinuria at the time of experiment. Their initial urine flows were about half those of the controls. During mannitol diuresis, flows increased about 5000 p.c. in healthy dogs but only approximately 400 p.c. in nephrotic dogs. The data appear to be consistent with the histologic findings of primary damage to the distal segment of the proximal tubule.

EXTRAVASATION AS A CAUSE OF EXPERIMENTAL COMA. S. A. Leonard* and L. M. N. Bach. Department of Physiology, Tulane University, School of Medicine, New Orleans, Louisiana.

Several investigators have found that production of experimental coma does not depend merely upon removal of large parts of the mesencephalic tegmentum. We suspected that electrolytic lesions might produce some toxic substance peculiar to burned tissue. Mechanical techniques were devised to remove the tegmentum in cats anesthetized with nembutal. These techniques involved stereotaxic placement and aseptic implantation of hypodermic needles of various gauges which permitted aspiration. Lesions produced in this manner compared easily in dimension and location with those customarily produced by electrolysis. Only rarely did animals exposed to the aspiration technique develop coma. Careful examination of the histological evidence revealed that, in those few instances, extravasation of erythrocytes could be demonstrated in residual intact tegmentum. A review of other series of animals in which coma had been produced by the standard electrolytic procedure revealed that coma usually occurred and was always correlated with evidence for extravasation. A few animals in which electrolytic lesions had failed to cause coma were each without evidence of extravasation. The usual thrombi within the electrolytic lesion were not consistently correlated with production of coma. It appears that whole blood contains some factor which is highly toxic to the tegmentum, at least. This factor is possibly ordinarily partitioned away from brain tissue by the brain-blood "barrier".

PYRAMIDAL INFLUENCES ON UNIT ACTIVITY IN POSTERIOR COLUMN NUCLEI OF CAT. M. Levitt*, M. Carreras*, W.W. Chambers and C.N. Liu* [1]
Inst. Neurol. Sciences and Dept. Anat., Univ. of Penna., Phila.

Extracellular recordings were taken from over 300 units isolated in the posterior column nuclei (P.C.N.) of cats under light pentothal-d-tubocurare anesthesia. A large percentage of units isolated were influenced by peripheral mechanical and electrical stimulation; hair bending or light touch was the adequate stimulus for over 80% of these. Peripheral receptive fields varied in area and locus; and they were somatotopically represented in the P.C.N., in accordance with classical neuroanatomy. The response properties of these units were similar to those of units in VPL, VPM and SI, as described by others. Ipsilateral and bilateral afferent inhibition was observed. Chemical or electrical stimulation of the first somatosensory cortex influenced the activity of many P.C.N. units; the motor cortex or the anterior lateral gyrus were ineffective. Cortical influences were chiefly contralateral, and the somatotopic relations were preserved. Most tactile P.C.N. units were driven by cortical strychnine spikes or brief single cortical shock (6v. 0.1 msec.). These could follow high rates of repetitive cortical stimulation, with subsequent lasting block of spontaneous discharges; however, response to peripheral stimuli persisted. Other units were not excited by cortical stimulation, but their spontaneous discharges were markedly reduced or abolished during repetitive cortical stimulation. In some of these, peripherally induced discharges were also blocked during and long after repetitive cortical stimulation. Contralateral cortical effects were abolished by section of the contralateral bulbar pyramid. Bilateral bulbar pyramidal section abolished all cortical effects. Large uni- and bilateral lesions of the midbrain reticular formation and also intercollicular decerebrations, sparing the peduncles, failed to abolish these cortical effects.

1. Supported by USPHS MF-8256 (C1)

THE EFFECTS OF INDUCED UNEVEN VENTILATION ON MEASUREMENTS OF DIFFUSING CAPACITY BY STEADY STATE AND REBREATHING METHODS. Benjamin M. Lewis, Akio Furusho* and L. C. Reed, Jr.*. Dept. of Medicine, Wayne State University and Detroit Receiving Hospital.

In 7 normal subjects simultaneous measurements of uneven ventilation by nitrogen washout (J. Clin. Invest. 31:40, 1952) and steady state diffusing capacity for CO (D_{LCO}) using an alveolar sample technique (J. App. Physiol. 11:277, 1957) were made, followed by measurement of D_{LCO} by rebreathing (J. Clin. Invest. 38:2073, 1959). Histamine and methacholine were given by aerosol and the studies repeated. In 4 subjects, N_2 clearance delay increased from 25.4% to 96.6%, steady state D_{LCO} fell from 22.5 to 10.5 ml/mmHg x min., rebreathing D_{LCO} was 31.0 before and 31.8 ml/mmHg x min. after the aerosol. In 3 subjects, N_2 clearance delay fell slightly (40.3% to 35.4%), steady state D_{LCO} changed from 26.5 to 22.5 ml/mmHg x min., rebreathing D_{LCO} was 37.6 before and 37.5 ml/mmHg x min. after the aerosol. In 3 subjects, histamine and methacholine were given, the above studies done and then Isuprel^R was given and the studies repeated. N_2 clearance delay fell from 109.1% to 29.1% while steady state D_{LCO} rose from 12.2 to 21.6 ml/mmHg x min. when uneven ventilation was relieved.

WATER AND SALT SAVING IN THE PREGNANT RAT. I. J. Lichton (intr. by J. P. Baumberger). Dept. of Physiol. Stanford Univ. Stanford, Calif.

Water and sodium are cumulatively stored in every human pregnancy, especially towards the end of gestation. Measurements have been made to determine whether the rat also stores water and sodium and if so, how much and in what relative proportions. Daily intake and urinary output of water and sodium were determined before and throughout gestation in 14 Wistar and Long-Evans rats kept in individual metabolism cages. In the last seven days before term the rats accumulated 60 (12-137) ml of water and 5.6 (1.5 - 10.4) meq of sodium; these figures were obtained by subtracting apparent water and sodium accumulation in the last seven days before mating from that in the last seven days before term. The rats consistently saved water and sodium in a fixed proportion; this amounted on the average to 93 meq of sodium per liter of water saved. At weekly intervals a dose of 5 per cent of the body weight of isotonic saline solution was given by stomach tube and recovery of administered water and sodium within 6 hours was noted. Before mating, the rats excreted in the urine an average of 76.0 per cent of the water and 82.8 per cent of the sodium given. At term they excreted 50.1 per cent of the water and 74.8 per cent of the sodium. These represent the means of the per cent recoveries for each rat. It is concluded that rats do store water and sodium towards the end of gestation and that there is a marked tendency to save hypotonic fluid.

BODY TEMPERATURE REGULATION IN HYPOXIA. Thomas P. K. Lim and Ulrich C. Luft. Department of Physiology, Lovelace Foundation, New Mexico.

The effect of moderate hypoxia (tracheal P_{O_2} = 65 mm Hg) on thermoregulation was studied under neutral (27.5° C, R.H. 30%) cold (4.0° C, R.H. 30%) and hot (40.5° C, R.H. 80%) conditions over a period of two hours in six healthy male subjects on different days with similar control periods breathing air. Neither the course of rectal and mean skin temperatures was significantly affected nor was the metabolic rate altered by hypoxia. The intensity of shivering estimated from O_2 consumption was the same (2.5 times control level) in the cold with or without hypoxia. Weight loss due to perspiration was essentially equal (I.4 Kg) breathing air or the hypoxic gas. Marked differences were observed in cardiorespiratory response to heat and cold during hypoxia. In the heat with hypoxia the heart rate increased in synergistic rather than additive fashion and the diastolic pressure was much lower. In the cold with hypoxia total ventilation was also greater than the sum of metabolic and hypoxic hyperpnea from the controls. (Supported in part by Contract AF41(657)-200, monitored by the Arctic Aeromedical Laboratory).

THE EFFECT OF HEADWARD ACCELERATION ON CARDIAC OUTPUT. Evan F. Lindberg,* William F. Sutterer,* Hiram W. Marshall,* Robert N. Headley* and Earl H. Wood. Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

Measurements of cardiac output by dye dilution and of heart rate, stroke volume, mean arterial pressure at heart level, and systemic vascular resistance were made in six subjects in the seated position during a total of 51 1-minute exposures to 2, 3, and 4 g levels of headward acceleration produced by a human centrifuge. Comparison of the average values obtained 20 to 40 seconds after the onset of acceleration with data from 31 interspersed control determinations when the centrifuge was stationary revealed decreases of 7, 18, and 22 per cent in cardiac output and of 24, 37, and 49 per cent in stroke volume; systemic vascular resistance increased 17, 41, and 59 per cent during accelerations of 2, 3, and 4 g, respectively. Inflation of an anti-g suit to a pressure of 200 mm. of mercury during accelerations had no systematic effect except for an average increase in mean arterial pressure of 15 mm. of mercury above the values obtained without inflation. In five of the same subjects acceleration was lengthened to 10 minutes and measurements were made at 2-minute intervals 25, 24, and 17 times at the levels of 2, 3, and $3\frac{1}{2}$ g, respectively. After the initial effects of these exposures, systematic alterations from the values obtained during the first minute were not observed.

MEASUREMENT OF COMPLIANCE OF THE HUMAN COLON. Martin Lipkin and Thomas P. Almy. Department of Medicine, Cornell University Medical College, and Second (Cornell) Medical Division, Bellevue Hospital, New York, New York

The motility of the human colon, customarily indicated by the recording of spontaneous phasic variations in intraluminal pressure, may be further defined in terms of compliance or resistance of its wall to distention. Pressure (P) and volume (V) of a segment of colon were recorded simultaneously, during water distention of a balloon lying in the segment. Elastic distortion of the balloons was minimized, since their diameter was larger than the maximum diameter of the viscus. P/V relationships in normal subjects have been measured which are similar to those previously noted following distention of urinary bladder. Following injection of morphine, alteration in the P/V values indicated increased resistance of the colonic wall to distention. The onset of visceral pain has been regularly noted in an area of the P/V curves where the limit of distensibility of the viscus is approached. The effects of other pharmacologic agents on P/V relationships and visceral pain are also being studied.

Thyroxine and epinephrine interrelationship. H. J. Lipner and Horace K. Sawyer*, Division of Physiology, Department of Biological Sciences, Florida State University, Tallahassee, Florida.

There still exists doubt as to whether the thyroid hormone is capable of acting directly on tissues independently of intervening materials such as the catechol amines: epinephrine and nor-epinephrine. The subcutaneous administration of epinephrine in oil at a dose level of 40 µgm per 100 gm body weight to rats that were athyroid, intact controls or athyroid and treated with 3, 10, or 30 µgm of d,l thyroxine per 100 gm body weight caused both a hyperglycemia and an elevation in oxygen consumption above the basal level. Completeness of thyroidectomy was confirmed by radioautography with I^{131}. The hyperglycermic response in comparison with basal levels indicated elevations in blood sugar of 33, 26, 26, 27 and 24% for the groups enumerated above. The increase in oxygen consumption above basal levels for these same groups was 26, 18, 17, 11 and 11%. Dihydroergotamine (DHE) (40 µgm per 100 gm body weight) caused a slight depression of both parameters of metabolic activity. Oxygen consumption and blood sugar levels, determined 90 min. after the administration of DHE followed by epinephrine, remained at basal levels. Since the DHE completely blocked a dose of epinephrine secretion (3.5 µgm per kilo per min.) it is assumed that the DHE also could block the endogenously secreted hormone. The failure to obtain depressions of oxygen consumption greater than 5% does not support the idea that oxygen consumption in thyroxine treated rats is dependent upon the presence of epinephrine.

LUNG VENTILATION IN EXPERIMENTALLY INDUCED ACIDOSIS AND ALKALOSIS IN MAN. H. H. Loeschcke, B. Katsaros and D. Lerche (intr. by L. L. Bennett). Physiologisches Institut der Universität Göttingen, Germany.

In human subjects, acidosis was induced by oral administration of NH_4Cl or $CaCl_2$ or acetazolamide. Whole blood buffer base was diminished 6.0, 4.8 and 6.3 meq/liter respectively. Alkalosis was induced by $NaHCO_3$ orally. Whole blood buffer base was augmented 8.6 meq/liter. The ventilatory response to inhaled CO_2 was determined. Blood samples were taken from the femoral artery. CO_2 content, O_2 content, O_2 capacity and pH were determined. Whole blood buffer base and CO_2 tension were calculated. End-tidal CO_2 tension was determined with a fast infrared analyzer. Ventilation was plotted against alveolar or arterial P_{CO_2}. In these curves the P_{CO_2} values for ventilations of 10, 20 and 30 liters per minute were interpolated. These data were averaged for all subjects of one group and used to construct isoventilatory lines in a P_{CO_2}-pH-whole blood buffer base diagram. This diagram allows a more specific analysis of the dependance of ventilation upon acid base parameters. Its main advantage is that the partial effects of alveolar (arterial) P_{CO_2} and arterial pH can be read directly. The partial effects of P_{CO_2} on ventilation were similar in the alkalotic and acidotic range. The partial pH effect, however, was significantly smaller in the alkalotic range (0.8 liters per minute per -0.01 pH or 20% of the total response to inhaled CO_2) compared with the acidotic range (1.7 liters per minute per -0.01 pH or 38% of the total response to CO_2). The latter figure is in agreement with the prediction of Gray and the results of Lambertsen, Smyth, Semple and Gelfand (Fed. Proc. 17:92, 1958).

PSEUDOSYNCHRONOUS CELL DIVISION IN THE YEAST SACCHAROMYCES CEREVISIAE. Allan L. Louderback*, Otto H. Scherbaum and Theodore L. Jahn. Department of Zoology, U. C. L. A., California.

The exposure of exponentially growing cultures of S. cerevisiae to a low dose of irradiation (α,γ, and X-rays) or the addition of triethylene melamine, or nitrogen mustard to the growth medium results in the formation of a large number of paired, enlarged yeast cells (Katchman et al. J. Bacteriol. 77:331, 1959). A similar cytological effect has been induced by the application of temperature cycles by the present authors. Yeast cultures in the early stationary phase of growth contain less than 6 per cent budding cells. If such a culture is transferred into fresh medium and is exposed to temperature cycles (25 min. at 33°C and 5 min. at 49.5°C) for 6 hours, the buds grow to the size of the mother cell and the number of paired yeast cells increase in the course of the treatment up to more than 95 per cent. Upon release from the treatment a division lag of 2.5 hours follows; then the culture enters gradually into the exponential phase of multiplication, similar to the positive growth acceleration phase upon inoculation of a normal microbial culture. This observation is quite different from temperature-induced synchrony of Tetrahymena (Scherbaum & Zeuthen, Exptl. Cell Res. Suppl. 3, 312, 1955), as the yeast cells seem to be arrested in their development at the same stage of their reproductive cycle, but do not show synchronized metabolic behavior ("pseudosynchrony"). A several-fold increase in polyphosphate occurs in these cells subjected to the temperature cycle treatment. However, it is not yet clear if and how the polyphosphates are implicated in pseudosynchrony. Growth curves, protein, phosphate and nucleic acid content of such cultures will be presented to illustrate the metabolic aberration induced in these "cytologically" synchronized yeast cells. (This work has been supported by NSF grant #G-9082).

ESKIMO 24-HOUR METABOLISM BY INDIRECT CALORIMETRY GRAPHICALLY ANALYSED. MacHattie, L.A., D.W. Rennie and Pierre Haab*, Dept. of Physiology, University of Buffalo School of Medicine, Buffalo, N.Y. Eskimo metabolism under conditions of village life was studied by 24-hour indirect calorimetry. Five men of Anaktuvuk Pass, Alaska were studied for 9 subject days in August, 1959, by measurements of O_2 consumption, CO_2 production and urinary N excretion, correlated with records of activity. The data were analysed by means of a new graphical system, from which the following metabolic quantities can be read off, given known values of any three of them: carbohydrate, fat, protein (or urinary N), heat, O_2, CO_2 and H_2O of oxidation. Mean 24-hour heat production was 3120 kcal., ±340 (s.e.m.), of which on the average 36 ±3% was derived from carbohydrate, 44 ±2% from fat, and 20 ±2% from protein. 24-hour metabolism was subdivided into night ("basal") and day fractions. Night metabolism averaged 40% above Boothby-Sandiford standards for basal metabolism of white subjects. There was no correlation between rate of Eskimo night metabolism and the composition of metabolic fuel; thus factors other than specific dynamic action of food may be implicated in the genesis of the elevated resting metabolism of these people.

INITIATION OF MAMMARY SECRETION IN RATS BY ELECTRICAL STIMULATION OF NERVOUS SYSTEM. M. Maqsood* and J. Meites. Michigan State Univ., East Lansing, Mich.

Recent studies in this laboratory have shown that electrical stimulation of the uterine cervix can initiate mammary secretion in estrogen-primed rats. Other areas of the body were similarly stimulated by electric current to determine whether this would induce lactation. Mature female rats of the Carworth strain were injected subcutaneously daily with 10 μg estradiol for 10 days to develop their mammary glands. For the following 5 days, groups of 5 rats each were electrically stimulated for 30 seconds twice daily in the regions of the head, lumbar vertebra, nasal mucosa and nipples. Ten control rats were injected twice daily with saline for 5 days. On the 16th day, the rats were killed and the right inguinal mammary glands were removed for histological preparation. The mammary glands of the controls regressed to a bare duct system, whereas almost all of the electrically-stimulated rats showed maintenance of the mammary lobule-alveolar system and initiation of lactation. Mammary secretion was most pronounced in the rats stimulated in the regions of the nasal mucosa and lumbar vertebra. These results suggest that electrical stimulation of the CNS induces release of prolactin and ACTH from the anterior pituitary, since both hormones are required to induce mammary secretion in the estrogen-primed rat. (Supported by NIH grant C-3448 to J. Meites).

EFFECT OF CERTAIN AMINES, AMINO ACIDS AND AMMONIA AFTER INTRAVENTRICULAR INJECTION. D.O. Marsh*, M.D. Turner*, and E.L. Gasteiger. Depts. of Physiology and Biochemistry, Univ. of Rochester Sch. of Med. and Dentistry, Rochester, New York.

A special ventricular cannula was developed and used for aspiration of cerebrospinal fluid from, and the injection of substances into the lateral and third ventricles of the unanesthetized dog. The design included a length adjustment device. These cannulae were satisfactorily implanted for periods of up to six months. Behavior, EEG, EKG, respiratory rate and intracranial pressure were recorded. Tryptamine in doses of 20-175 μg was followed by sleep and characteristic sleep EEG; larger doses produced transient nystagmus and pronounced hyperpnea without sleep. 5-Hydroxytryptamine, 5-hydroxytryptophan and DL-tryptophan, in doses of 20-300 μg appeared to initiate sleep, a sleep EEG and hyperpnea. D-tryptophan, 20-200 μg was followed by sleep, whereas after L-tryptophan, 20-200 μg there was moderate restlessness. With ammonium acetate, 2.4 mg, sleep, a sleep EEG, hyperpnea and weakness ensued. Glutamine, 10 mg, was followed by sleep. (Supported by a Buswell Fellowship, D.O. Marsh; and the Muscular Dystrophy Association of America.)

BLOOD GLUCOSE INCREASE IN ANESTHETIZED RATS GIVEN DEXTRAN. Louise H. Marshall and Charles H. Hanna.* Natl. Insts. of Health, Bethesda, Md.

The reaction of rats to parenteral dextran administration includes edema formation and decreased arterial blood pressure. In addition, a significant rise in blood glucose (approximately 45 mg%) was found in rats anesthetized with sodium pentobarbital and given dextran (60 or 600 mg/kg) rapidly by vein. This occurred when the pre-injection glucose level was normal (100-120 mg%), as well as when it was low (40-60 mg%) due to pretreatment with insulin. Conscious rats did not show this increase. The volume of the forefoot was measured by a displacement method, affording a semiquantitative measure of the amount of edema formed subsequent to increased capillary permeability. Arterial blood pressure was continuously recorded, and hematocrit values and glucose concentration (Park-Johnson micromethod) estimated from blood samples 30, 60 and 120 minutes after dextran injection. There was no correlation between the severity of the reaction to dextran typical of this species, and the magnitude of the increase in blood glucose.

THE EFFECT OF DIFFERENTIAL CHANGES IN PERIPHERAL BLOOD FLOW ON THE CONTOURS OF INDICATOR-DILUTION CURVES. Robert J. Marshall (intr. by J. T. Shepherd). Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

When peripheral sampling sites are used the contours of indicator-dilution curves (I.D.C.) can be altered by inducing differential changes in the volume and velocity of peripheral blood flow. These changes can be shown best when sampling and detecting systems with high dynamic response (Edwards et al, The Physiologist. 2:35, 1959) are used, but are still apparent with slow systems. During exercise the peak concentration of I.D.C. recorded from peripheral sites is much less than at rest. However, with central sampling sites, peak concentration is scarcely altered from rest to severe exercise; in contrast, increased blood volume of the heart and lungs, caused by overtransfusion, is accompanied by reduced peak concentration. Equal increments of cardiac output may be achieved by epinephrine infusions and by leg exercise. However, since the distribution of the increased systemic flow differs in these two circumstances, the corresponding I.D.C. are dissimilar. With epinephrine the recirculation phase is slurred, while with exercise it is tall and peaked simulating the findings with peripheral arteriovenous fistulas. Increasing the velocity of blood flow to the sampling limb in normal resting subjects by reactive hyperemia or external heating sharpens the contours of I.D.C. In patients with shunts a similar maneuver may be used to improve definition of the distortion due to the abnormally circulating blood.

THE EFFECT OF CERTAIN STEROIDS IN SODIUM TRANSPORT IN THE ISOLATED FROG SKIN. Robert D. McAfee, Ph.D. and William Locke, M. D. (intr. by L. M. N. Bach). Radioisotope Laboratory, Veterans Administration Hospital, Biophysics and Physiology Departments, Tulane University, and Oschner Clinic, New Orleans, Louisiana.

Two - methyl - 9 alpha - flurohydrocortisone and hydrocortisone sodium succinate increase both the rate and duration and therefore total quantity of ion transported in the isolated short circuited frog skin measured over a 24 hour period. The ion transport is directly related to the bio-electric current generated, and based on Ussing's work, is assumed identical to the net flux of sodium ion. It is thought that these steroids may make available transport energy which is not available to the untreated skin half by rerouting enzymatic pathways, or by lowering the resistance of the membrane to ion transport and thereby more efficiently utilizing the energy available for transport.

PLASMA FREE-FATTY ACID RESPONSE TO HYPOXIA. William T. McElroy, Jr., and John J. Spitzer. Dept. of Physiology, Hahnemann Medical College & Hospital, Philadelphia, Pa.

Anesthetized dogs were studied for response of plasma free-fatty acid (FFA) to short periods of a stress (low pO_2 of inspired air) reported to excite the sympathetic nervous system. Animals were made hypoxic for periods of ten to twenty minutes by administration of 8% O_2 in N_2 via tracheal cannulae. Other animals were open chest preparations to allow sectioning of the splanchnic nerves. In this group, the gas mixture was given from a rate-tidal volume controlled respirator. Both groups showed an increase in femoral arterial and venous plasma FFA coincident with other changes usually attributed to sympathetic effects; an increase in plasma glucose, hematocrit, blood pressure and heart rate. Since ventilatory volume and rate were controlled in open chest preparations, the FFA change was not merely due to the dyspnic efforts during hypoxia. Occlusion of adrenal glands from the circulation decreased or completely prevented the FFA change during hypoxia as compared to control responses in the same animal, thus indicating adrenal participation in the response. Bilateral splanchnic nerve section also prevented the FFA increase. During hypoxia, more FFA as well as glucose is made available to tissues, the FFA increase due to adrenal medulla release of amines. (Supported by a grant from AMD division, PHS.)

THE INFLUENCE OF POSTURE ON CARDIAC OUTPUT DURING EXERCISE. M. McGregor, W. Adam,* P. Sekelj,* R. Peel,* G. Peters,* A. Pierer,* R. Potteray.* McGill University, Royal Victoria and Children's Hosps., Montreal, Canada.

The cardiac output at rest has been found to be higher in the supine than in the upright posture. It was not known whether steady exercise of the lower limbs would abolish this. Twenty comparisons were made of cardiac output in the supine and upright postures during steady exercise on a bicycle ergometer. Output was measured with an ear oximetric method using Coomassie blue dye. In the upright posture there was an increase of pulse rate (6%) and ventilatory equivalent (20%) while there was a fall of cardiac output (12%) and stroke volume (17%). All changes were significant at the 95% level. It was concluded that during exercise the postural changes in cardiac output were maintained or augmented and that ventilatory changes were likely secondary to the changes in output.

SOME PHYSIOLOGICAL MEASUREMENTS IN SECONDARY DISEASE.
James McRae (Intr. by Lola S. Kelly), Donner Lab., Univ. of California, Berkeley.

The pathogenesis of secondary disease and the cause of the severe weight loss which follows the transplantation of incompatible mesenchymal cells is still obscure. A number of studies have been made in sublethally irradiated $F_{(1)}$ mice injected with parent spleen cells. Measurement of the food intake of wasting animals showed a difference from the controls, the experimental animals chewing an increased amount of mouse pellets but dropping a large fraction to the bottom of the metabolism cage. The actual food intake was somewhat decreased. To determine if wasting mice had a defect in liver function despite the frequently normal histological appearance, the sleep time following a standard dose of sodium pentobarbital was measured. A marked increase in sleep time was found indicating that derangement of liver function contributes to the syndrome. In addition, the function of the reticuloendothelial system was measured by the rate of removal of colloidal carbon from the blood. The reticuloendothelial function was markedly increased above that of the irradiated controls and this increased function persisted when the anemia was severe.

WHOLE BODY POTASSIUM MEASUREMENTS IN HUMANS.(1)
G. R. Meneely, R. M. Heyssel,* J. L. Ferguson,* O. C. Parrent * and R. L. Weiland.* Vanderbilt University School of Medicine, Nashville, Tennessee.

By means of a large, single-crystal, low-level, whole-body, human, gamma ray spectrometer, similar in design to the Argonne Instrument of Marinelli, Miller and Rose, it is possible to determine the identity and the quantity of trace amounts of gamma emitting radioisotopes in the human body. K^{40}, a naturally-occurring radioisotope of potassium presents a unique and convenient means of measuring total body potassium in humans. The amount of potassium is obtained by multiplying the count rate at the K^{40} photopeak by a calibration factor, the factor differing from subject to subject, depending largely on the person's height and weight. Determination of this factor for potassium was approached by means of a plastic manikin filled with a known amount of potassium, by use of bottles of various sizes filled with known amounts of K^{40} and K^{42}, and by injection of K^{42} into human volunteers. The data indicate that small subjects give more counts per μc than do large individuals, the best single relationship noted thus far being surface area. Also, whole body potassium content seems to be proportional to basal heat production, this investigation being suggested by the potassium concentration curves of Anderson & Langham.

(1) Supported by AEC AT-(40-1)-2401 & MRDC-DA-49-007-MD-995.

FURTHER STUDY OF EFFECTS OF HEPARIN ON SERUM LIPIDS AND BODY TEMPERATURE FOLLOWING INTRAVENOUS ADMINISTRATION OF FAT EMULSION IN MAN. H.C. Meng, Y.W. Cho, R.J. Ho and B. S. Sparkman, Vanderbilt U., Med. Sch., Nashville, Tenn.

It is known that heparin administration increases the rate of removal of serum lipids in alimentary lipemia or lipemia induced by intravenous infusion of fat emulsion in laboratory animals and in man. Furthermore, the low-grade rise in body temperature observed following intravenous infusion of fat emulsion is reduced in patients receiving heparin. In the present study each individual patients were given 3 consecutive infusions of 500 ml Lipomul I.V., a 15% cottonseed oil emulsion: first and third infusions without and second with heparin. Serum lipid fractions were determined and body temperature was measured at intervals. It was found that 1. the serum total fatty acids was significantly lower at the end of infusion and in most instances returned to the preinfusion levels in 3 hours when heparin was given; heparin did not significantly affect serum cholesterols and phospholipids. 2. The increase in plasma unesterified fatty acids determined at the end of infusions was much greater with heparin. 3. The mean elevation of body temperature of 10 patients measured 3 hours after the completion of infusion when the maximal rise occured was 1.3° F for the first infusion, 0.8° F for the second (with heparin) and 1.3° F for the third. It seems apparent that heparin accelerated the rate of removal of the intravenously infused triglyceride presumably due to increased lipolysis. The nature of the temperature-lowering effect of heparin is under investigation.

Method for Measuring Local Changes in Cerebral Circulation and Metabolism. John S. Meyer and F. Gotoh (Intr. by R. Bing). Dept. of Neurology, Wayne State University, Detroit, Michigan.

Combined PO_2-PCO_2 tissue measurements are made with plastic covered (5-10 mu. thick) polarograph (PO_2) and pH (PCO_2) electrodes in 0.0005 N $NaHCO_3$ solution. The 3 mm. electrode has initial response of 3 secs., equilibrium of 30 secs. Oxygen polarography does not significantly alter pH of electrolyte (52 mm. Hg. change of PO_2 induces 1 mm. Hg. PCO_2 change). Experiments in cat and monkey indicate: 1) Local blood flow is controlled by local metabolism through CO_2 production. 2) Light nembutal anesthesia (barbiturate bursts) causes slight (2 mm.) decrease in cortical CO_2. Deep narcosis causes marked depression of CO_2 production and O_2 utilization. 3) Hypoglycemia reduces cortical metabolism and circulation prior to EEG change. Normoglycemia restores cortical blood flow and metabolism. Metabolic changes prior to EEG changes explain the synergism of hypoglycemia and hypoxia. 4) Adaptation prevents an absolute threshold for CO_2 narcosis but EEG slowing or inhibition of seizures occurs between 70-100 mm. Hg. Repeated hypercapnia raises the threshold. 5) Seizures followed by isoelectric EEG show rises in brain CO_2 and fall in brain O_2 during fits. EEG flattening is due to anoxia aided by hypercarbia. 6) Nitrogen breathing causes first EEG activation with cortical CO_2 increase, later cortical depression with cortical CO_2 decrease. 7) Cerebral embolism produces a catastrophic fall in blood flow and oxygen tension with increased cortical CO_2.

THE RESPONSE TO A COLD PRESSOR TEST DURING PHYSICAL TRAINING. Ernest D. Michael, Jr., Arthur Gallon and Adran Adams (intr. by S. M. Horvath). Univ. of California, Santa Barbara, Goleta, Calif.

Members of the 1958-59 varsity basketball team at Santa Barbara and a control group of physical education majors not in training were tested each 3 weeks during a 17 week season of basketball competition. The two groups were tested on their response to a step test and to a cold pressor test. The results indicated significant step test recovery pulse rate changes were made with the basketball players after 3 weeks of training. Maximum changes were found to occur after 17 weeks of training. The diastolic pressure response to the cold pressor test increased significantly (7 mmHg) after 6 weeks of training and this was maintained for 17 weeks. The systolic pressure response did not change significantly. The results indicated that increased sensitivity of the peripheral vessels resulted from physical training.

STUDY OF INTRACARDIAC THROMBOSIS USING PLASTIC MATERIALS. V. Mirkovitch, M.D.*, Tetsuzu Akutsu, M.D.*, and W.J. Kolff, M.D. Department of Artificial Organs, Cleveland Clinic, Cleveland, Ohio.

To elucidate thrombus formation on artificial heart valves, plastic patches have been inserted into the right atrium or suspended between the right atrium and right ventricle in 46 dogs. Plastics used were: polyurethane VC (Estane #5-CS1842 Goodrich), silastic (Dow Corning, X-3-0146), knitted teflon (U.S. Catheter), marlex (Polyethylene, Philips), and collagen on a dacron skeleton (Ethicon). Thrombosis appeared where the plastic was in direct contact with the points of fixation, suture lines, or walls of atria or ventricles. Patches of smooth material, such as silastic, suspended in the bloodstream by stainless steel (Elgiloy) wires remained free of thrombus, but patches of rough material, such as knitted teflon, polyurethane sponge, or collagen, were still covered with thrombus even when suspended in the bloodstream. Thrombi filled in irregularities. On exposed rough surfaces, the amount of thrombus was inversely related to the apparent velocity of the bloodstream. Some thrombus formation is desirable when a plastic is used to close a septal defect, but not when it develops on valve leaflets where it is subjected to repeated trauma or rubbing off, and leads to growing together of the valve leaflets or to embolus formation. General heparinization or administration of fibrinolysin (Actase-Ortho) reduced the amount of thrombus formed on teflon patches in the atria of dogs. The heparin dose was 3.5 mg of lipohepin/Kg/q.8 h. subcutaneously. The doses of fibrinolysin proved to be critical. In each of six dogs 2000 U/Kg/day for 4 days greatly reduced the amount of thrombus on the teflon patch, but either more or less fibrinolysin in each of 5 dogs enhanced thrombus formation.

FETAL BRAIN OXYGEN, G.A. Misrahy, A. Beran*, J. Spradley*, and V.P. Garwood*. Deafness Research Laboratory, Children's Hospital, Los Angeles.

Fetal tissue oxygen in utero was measured polarographically with 'Siliclad' coated platinum electrodes during acute and chronic experiments in cats, rabbits, and guinea pigs. Guinea pig brain oxygen was measured continuously during labor and delivery. In the quiescent uterus, under physiological conditions, fetal brain oxygen corresponded closely (± 2%) to maternal brain oxygen. Maternal inhalation of pure oxygen or an oxygen- carbon dioxide mixture increased maternal and fetal brain oxygen. Maternal inhalation of a low oxygen mixture decreased maternal and fetal brain oxygen. Both uterine contractions and manually applied pressure to the fetal head selectively lowered fetal brain oxygen. Intravenous injections of adrenalin, apresoline, levophed, pitressin and pitocin produced complex changes in fetal brain oxygen. Changes in fetal brain oxygen during labor and delivery will be described. The relative merits of the 'Siliclad' coated electrode will be discussed.

DETERMINATION OF SURFACE TEMPERATURE WITH THERMOCOUPLES. G. W. Molnar, J. C. Rosenbaum, Jr.* and G. B. Millar*. U. S. Army Medical Research Laboratory, Fort Knox, Kentucky.

Mathematical derivation of a formula for the calculation of the true surface temperature from a thermocouple measurement is difficult because: 1) couples are of irregular shape; 2) their area of contact with the surface (therefore heat input) is usually increased with increase of height; 3) heat transfers from the sides as well as from the endface of a couple; 4) the adhesive cement or tape interposes another set of thermal properties; 5) air temperature has a gradient (linear within 1 to 2 mm.) from surface to ambient. The possibility of deriving an empirical formula from experimental data was therefore investigated. Ten thermocouples were cemented along the side of a horizontal glass model of a finger with uniform heat input. Couple height above surface was measured with a gauge graduated to 0.01 mm. Heights ranged from 0.20 to 0.88 mm. The steady state temperature differences between couples and ambient air were plotted against couple heights. The trend was linear with negative slope; r = 0.95. It seems reasonable to consider the Y-intercept to be the true temperature difference between surface and ambient air. If so, then for a couple 1 mm. high the error of couple temperature is 7.2 C° in still air when the true surface to ambient air temperature difference (obtained by extrapolation) is 30C°. An added layer of adhesive tape did not change the error. The error varies with couple height, surface-to-air gradient, and wind velocity. By adding corrections thus determined to measured couple temperatures, true surface temperatures can be approximated.

THE OXYGEN COST OF THE ASCENDING AND DESCENDING LIMBS OF THE VENTRICULAR PRESSURE PULSE. R. G. Monroe (intr. by J. L. Whittenberger) Harvard School of Public Health, Boston, Mass.

An isolated heart preparation was devised which permitted the determination of myocardial oxygen consumption while the ventricle performed work by compressing air. By an electronically operated solenoid valve the air compressed by the ventricle could be rapidly released and the ventricular pressure pulse repeatedly interrupted at a specific point during its cycle. When the pressure pulse was cut off at its peak there was a 10% increase in peak pressure that appeared in the subsequent 4-5 beats. When the pressure pulse was cut off at various points during its ascent to peak pressure, myocardial oxygen consumption could be correlated with both the pressure at which it was cut off and the area under the cut pressure pulse. When the myocardial oxygen consumption of a heart developing a full pressure pulse was compared with that of a heart in which the pressure pulse was cut off at its peak - and when the peak systolic pressures of the two compared pulses were equal - then the oxygen consumed by the heart when the pulse was cut averaged 91% of that when the pulse was full. These results indicate that by the time the pressure pulse has reached its peak, myocardial oxygen consumption has been largely determined, and that the oxygen cost of the descending limb of the pressure pulse is small.

THE INITIATION AND MAINTENANCE OF AURICULAR FIBRILLATION IN NORMAL YOUNG AND ADULT CATTLE. E. Neil Moore*, G. Fischer*, D. K. Detweiler, and G. K. Moe. Dept. Physiol., S.U.N.Y., Coll. Med., Syracuse, N. Y. and Coll. Vet. Med., U. Penn., Philadelphia, Pa.

Fibrillation can be induced in the atria of the dog by a brief burst of repetitive electrical stimuli, but will not usually persist except during vagal stimulation or infusion of acetylcholine. It has also been shown that fibrillation does not sustain itself in small fragments of cardiac tissue except upon the addition of very large concentrations of acetylcholine. It has recently been proposed that auricular fibrillation consists of random "wandering" of numerous small independent wavelets, and that the persistence of the phenomenon is a function of the number of such wavelets. According to this hypothesis the number of wavelets should be directly related to the mass of the tissue, and inversely related to the duration of the refractory period. This hypothesis was tested comparing large adult cattle with small young calves. In the normal adult cattle electrical stimuli to the atria initiated auricular fibrillation which was maintained in several animals for over 36 hours and, in one, for over two months. Similar results were obtained using adult horses. The young calves, with a correspondingly smaller atrial mass, were never observed to fibrillate longer than one or two minutes except for a single instance in which the arrhythmia persisted for 47 minutes. Adult goats and sheep in the same weight range as the calves also failed to exhibit sustained fibrillation suggesting that the observed difference between young and adult cattle is more likely a function of atrial mass than of age.

BILATERAL ORGANIZATION OF THE SOMATIC AFFERENT SYSTEM IN LOWER VERTEBRATES. George P. Moore* and Robert D. Tschirgi. Dept. Physiol., Univ. of California School of Med., Los Angeles.

In a series of frogs and alligators, evoked unit and gross electrical responses to peripheral tactile and electric shock stimuli were recorded from the medulla, tectum, thalamus and forebrain. While various subcortical areas responded to tactile stimulation, only electric shock stimuli applied to the skin or peripheral nerve trunks produced evoked potentials at the surface of the tectum or the alligator cortex. With unilateral recording in midbrain and forebrain areas, alternate contralateral and ipsilateral stimulation of symmetrical peripheral regions produced closely similar responses, indicating a high degree of right-left afferent convergence. At specific points on the alligator cortex, closely similar evoked responses were obtained from contralateral and ipsilateral forelimbs and hindlimbs indicating a generalized afferent convergence at the cortical level from the body surface. These results are consistent with the general hypothesis that somatic transmission above the level of the medulla in lower vertebrates occurs largely, if not exclusively, through the forerunner of the mammalian spinothalamic system. Furthermore, they suggest the hypothesis that positional information allowing right-left discrimination between symmetric somatic areas does not ascend beyond the medulla in amphibians and reptiles.

VASOMOTOR RESPONSES IN PLAQUES OF PSORIASIS AND APPARENTLY UNINVOLVED SKIN TO RAPID CHANGES OF ENVIRONMENTAL TEMPERATURE. Anthony P. Moreci, Ph.D., Eugene M. Farber, M. D. and Margaret Heinz, M. D. (Intr. by J. Garrott Allen, M. D.). It has been reported that a dysfunction of cutaneous blood vessels exists at some distance from visible lesions in patients with psoriasis. The present study was designed to compare the responses of blood vessels in plaques of psoriasis and apparently uninvolved skin to rapid changes in environmental temperature. Changes in the rate of blood flow in test areas were determined indirectly by thermometric means. Measurements in these areas were obtained in sequence at ambient temperatures of 25, 15, 40 and 15 degrees Centigrade. At an environmental temperature of 25 degrees Centigrade psoriatic plaques were found to be warmer than the surrounding uninvolved skin. Following a rapid decrease or increase in ambient temperature, the rate of temperature change of plaques was lower than that of the normal appearing skin. Results of this investigation indicate that resistance blood vessels in the apparently uninvolved skin of patients with psoriasis respond to environmental temperature changes in a manner similar to that of subjects without disease. On the other hand, the data indicate that resistance blood vessels in plaques of psoriasis are chronically dilated and fail to respond normally to a rapid decrease in environmental temperature. The available evidence supports the view that pathology of the peripheral circulation in psoriasis is limited to the diseased areas.

GROWTH RATE OF FLY LARVAE DURING EXPOSURE TO 12.25 CM. MICROWAVE IRRADIATION. William J. Moressi*, Charles C. Wunder, Charles J. Imig. Dept. of Physiology, College of Medicine, State Univ. of Iowa, Iowa City, Iowa.

The results support the general concept that the biological effect of the irradiation is primarily of a thermal genesis. The larvae of Drosophila melanogaster were cultured in specially-adapted chambers which held the temperature constant at 28°C. during the period of exposure. During the first 24 hours of one watt/cm^2 irradiation the average growth rate of the larvae differed from non-irradiated controls by +10±11%. This irradiation was of sufficient intensity to cause a 50% mortality within a period of 10 minutes when the chamber temperature was not prevented from rising above 28°C. At 28°C. larvae doubled in size each day exhibiting an exponential growth from which growth constants can be obtained and compared. Larvae have been exposed to power densities of 0.3 watts/cm^2 for as long as 4 days without any significant effects on the growth constants. However, preliminary work with increased intensity and duration of irradiation suggests a possible acceleration of the growth.

Aphagia and Adipsia in Rats With Extra-Hypothalamic Lesions in the Globi Pallidi and Pallido-Fugal Fiber Systems. P. J. Morgane (intr. by J.P. Quigley). Physiology Dept., Univ. of Tenn. Med. Units, Memphis, Tenn.

Paleo-striatal components, including certain pallido-fugal fiber systems, have been subjected to differentiative bilateral stereotaxic lesions and full sham procedures. Anatomical studies in the rat have shown that pallidal efferents (ansa lenticularis and lenticular fasciculus) pervade, via pallido-hypothalamic ramifications, the far lateral hypothalamic area (L.H.A.) and subthalamic regions. Earlier studies in rats (Morgane, Fed. Proc. 19/292, 1960) have shown the medial forebrain bundle not to be a crucial system in the effectuation of spontaneous feeding. Since lateral hypothalamic full sham procedures have resulted in permanent aphagia and adipsia, transversely trajecting fibers of pallidal origin might well be implicated in the functional organization of these "centers". Dorsal lesions in the internal divisions of the pallidi or in the lenticular fasciculi with complete sparing of the L.H.A. resulted in consistently reproducible aphagia and adipsia in rats without other patent behavioral deficits. The comportment of these animals mimicked that of rats in previous studies in demonstrating the phenomena of rapid metabolic deterioration, abbreviated survival periods, and, in isolated instances, aphagic "escape". Anatomical control showed that animals with permanent adipsia and aphagia sustained severe damage to the globi pallidi or to components of their efferent dispersing systems, whereas "escapees" showed less degeneration in pallido-fugal fibers and inextensive pallidal lesions. It is suggested that the hypothalamic "feeding center" per se may be a nonentity and that lesions in this area merely disjoin direct or relaying trajectories of pallidal origin. These systems, playing some fundamental role in viscero-metabolic and autonomic activities, have long been neglected in considering the mode of operation of protomorphic, so-called hypothalamic "centers".

TEMPORAL AND SPATIAL CHARACTERISTICS OF THE PRIMARY EVOKED RESPONSE IN THE SOMATOSENSORY CORTEX OF CAT. R. W. Morse* and A. L. Towe (intr. by T. C. Ruch). Dept. of Physiology & Biophysics, University of Washington School of Med., Seattle.

Cats were anesthetized with α-chloralose and paralyzed with decamethonium bromide. The primary evoked response (PER) from the pericruciate cortex was recorded by means of silver-ball electrodes and KCl-filled micropipettes as the central footpad of the forepaw was stimulated electrically. The latency of PER, measured from the shock artifact to the beginning of a deflection (either positive or negative), was studied as a joint function of stimulus intensity and recording site (both at the pial surface and in depth). At any recording position, PER latency varies inversely with stimulus intensity from threshold to 3 times threshold; at higher latencies, no additional change in latency occurs. The size of the latency change (8 to 15 msec) varies with the recording position, as does the waveform. Along the posterolateral border of the cruciate fissure, the PER is positive-negative. As the recording electrode is moved radially from this position, PER latency increases until a cortical region yielding initially negative PERs is reached. Here, PER latency abruptly shortens to a value 1.0 to 2.5 msec earlier than the earliest initially positive PER; this relationship holds from threshold to maximum stimulus intensities. Farther radially, the latency of the initially negative PER increases and its waveform changes from triphasic to diphasic (still initially negative). If the cortex just behind the cruciate fissure is penetrated, PER latency is found to shorten until a depth of about 600 μ is reached; thereafter, a complexity of changes appear. (Supported by Grant B 396 and PHS-2G260 from the National Institutes of Health, U. S. Department of Health, Education and Welfare.)

RELATION OF LUNG VOLUME HISTORY TO AIRWAY RESISTANCE. Jay A. Nadel and Donald F. Tierney. (intr. by J. H. Comroe, Jr.) Cardiovascular Research Institute, U. of Calif. Medical Center, San Francisco.

We used the body plethysmograph to measure the effects of lung volume history on airway resistance in two normal subjects after the inhalation of substances capable of increasing airway resistance and in two patients with obstructive pulmonary emphysema. In normal subjects, airway resistance, measured during panting at F.R.C., increased after the inhalation of cigarette smoke, SO_2 (28 p.p.m.) or 6% histamine phosphate by aerosol. After a maximal inspiration and relaxation to the original lung volume, the airway resistance decreased significantly in each case ($p<0.01$). Subsequently, over a period of two minutes of tidal breathing, the airway resistance gradually increased. Before inhalation of "bronchoconstrictor" substances, there was no significant decrease in airway resistance after a maximal inspiration and subsequent relaxed expiration. We believe that a maximal inspiration temporarily decreases smooth muscle tone and that this explains the temporary decrease in airway resistance after a maximal inspiration. In two patients with obstructive pulmonary emphysema, the airway resistance increased significantly ($p<0.01$) after a maximal inspiration and subsequent relaxed expiration and returned to control levels over a period of two minutes of tidal breathing. We are investigating the cause of this. Thus, lung volume history must be considered in the measurement of airway resistance. Since deep inspiration may temporarily change airway resistance, methods that require a prior deep inspiration cannot be expected to give true values for airway resistance that obtains during normal breathing.

Supported in part by grants from USPHS (H4029) and Calif. State Dept. of Public Health.

THE INFLUENCE OF ORAL ADMINISTRATION OF 6-METHYL-17-ACETOXYPROGESTERONE ON FOLLICULAR DEVELOPMENT AND ESTROUS BEHAVIOR IN HEIFERS. J. E. Nellor and J. E. Ahrenhold (intr. by W. D. Collings). Michigan State Univ., East Lansing, Mich.

The progestational action of 6-methyl-17-acetoxyprogesterone was determined when the compound was administered, as part of the normal ration, to mature beef heifers at various stages of the estrous cycle. Estrus and follicular development were inhibited during a 15 day treatment period with .6 mg of 6-methyl-17-acetoxyprogesterone per pound body weight daily, by twice-a-day feeding. Estrus occurred 5 to 6 days after the end of progestational treatment in 80% of the heifers. Heifers not bred or not conceiving at the controlled estrus returned to estrus 21 to 24 days later. The injection of 1500 I.U. of equine gonadotropin, 24 hours after the end of progestational treatment did not result in multiple ovulations. (Supported in part by a grant from The Upjohn Company, Kalamazoo, Mich.)

INTRACELLULAR RECORDINGS FROM CAT INFERIOR COLLICULUS. P. G. Nelson and S. D. Erulkar (intr. by K. Frank). Natl. Insts. of Health, Bethesda, Md. and Univ. of Pa. Medical School, Philadelphia, Pa.

Resting and spike potentials, and excitatory and inhibitory postsynaptic potentials have been recorded from single neurons in the inferior colliculus of cat. EPSPs evoked by clicks to either ear may produce spikes up to 20mV in amplitude; a hyperpolarizing PSP is frequently seen following the spike discharge. In some cells clicks elicited EPSPs whose magnitudes were different for ipsilateral and contralateral stimulation. In one cell contralateral click produced an EPSP and ipsilateral click an IPSP and in a given cell PSPs sometimes showed different latencies for ipsilateral and contralateral click. It was not uncommon to see an EPSP rising abruptly from an IPSP or vice versa. Considerable variability in the PSPs produced by equal click stimuli was sometimes noted, and sometimes maintained tonal stimulation would diminish or abolish the PSP produced by click. The intracellular technique has revealed a greater prevalence and power of inhibitory input to collicular units than might be suspected from other methods of study.

THE EFFECT OF DAMAGE TO VARIOUS PARTS OF THE TUBULES OF THE DOG'S KIDNEY ON THE EXCRETION OF SULFATE. T. Frederick Nicholson. Department of Pathological Chemistry, University of Toronto, Toronto, Ont.

The first third of the proximal tubule in the left kidney in dogs was damaged by the infusion through the kidney of a 7 mg.% solution of potassium dichromate. The last two thirds of the proximal tubule were damaged by the infusion of 1% dl sodium tartrate and the distal parts of the nephron were damaged by the retrograde injection of 0.05% mercuric chloride up the left ureter. Damage to both parts of the proximal tubule resulted in increases in sulfate excretion indicating that sulfate reabsorption takes place along the whole of the proximal segment. Damage to the distal segment was followed by a reduction in sulfate excretion from the damaged kidney of up to 85%. This suggests the possibility that sulfate is actively excreted by the distal tubule, as are potassium and phosphate.

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SEROTONIN ON DIRECT CORTICAL RESPONSES. S. Ochs, H. Booker* and M.H. Aprison. Ind. Univ. Med. School, Indianapolis, Ind.

Serotonin is present in the cerebral cortex and has been considered by some to be a neurohumor. Although only a small amount crosses the blood-brain barrier when injected systemically (Costa & Aprison), it has been shown to change behavior and to diminish the transcallosal cortical response when injected via the carotid artery (Marrazzi). Because of the possibility that systemic administration could affect responses through secondary effects, topical application to the exposed cerebral cortex was investigated. Negative wave direct cortical responses (DCR's) were elicited from two sites on the exposed cortices so that the effect of serotonin on the stimulated or the recording site could be studied. Serotonin (0.5-1.0%) placed on the recording site in cats and in rabbits greatly diminished or eliminated the DCR's. A feature of the diminution was the prolonged effect; recovery took at least 30 min. and in some cases did not return in over 1 hour. Serotonin also diminished the DCR when placed on the stimulated site; recovery occurred in approximately 10-20 minutes after removal and wash. Apical dendrites are believed to be electrically excited to give the DCR (Ochs & Booker) and the results indicate a generalized membrane effect of serotonin on apical dendrites of pyramidal cells. This conclusion is in accord with the report that serotonin has a direct action on neurons in cell culture (Geiger).

Acute Effects of Na^+, K^+ and Ca^{++} on Vascular Resistance in the Dog Forelimb. H. W. Overbeck* and F. J. Haddy. VA Research Hospital and Northwestern University Medical School. Chicago, Illinois

We have previously reported (Circ. Res. 8:57, 1960) that infusions of 10% solutions of K^+, Na^+, and Mg^{++} salts into the dog brachial artery cause active limb arteriolar dilatation, whereas Ca^{++} salts cause arteriolar constriction. It has been suggested (Am.J.Physiol. 197:951, 1959) that some changes observed may be due to solution hypertonicity rather than specific ion effects. This study, utilizing previous techniques, was undertaken to separate specific ion effects from those of tonicity. A total of 111 intraarterial infusions were made in 29 dogs. Isotonic KCl and $CaCl_2$ consistently decreased and increased, respectively, limb small vessel resistance. Isotonic NaCl had no effect at similar infusion rates, but did not significantly change serum $[Na^+]$. Infusions of hypertonic solutions of KCl produced 3 times the decrease in small vessel resistance produced by equally hypertonic solutions of dextrose, whereas $CaCl_2$ at equal hypertonicity definitely increased resistance. Hypertonic solutions of NaCl, Na_2SO_4 and Na_2HPO_4, infused to equally increase limb venous serum $[Na^+]$ irrespective of tonicity, evoked different decreases in limb vascular resistance, paralleling tonicity. Equally hypertonic infusions of dextrose, Na_2SO_4, and NaCl, irrespective of amount of Na^+ supplied, evoked equal decreases in small vessel resistance. Limb venous serum $[Na^+]$ was lowered approximately 23% by rapid infusions of isotonic dextrose and evoked decreases in small vessel resistance equal to those of control isotonic NaCl infusions. These studies indicate that acute increases in limb serum $[K^+]$ and $[Ca^{++}]$ within physiological ranges have specific peripheral small vessel dilatating and constricting effects independent of tonicity, but suggest that, in contrast, Na^+ may have little or no independent effect.

USE OF AEROSOLS TO SEPARATE FACTORS INFLUENCING INTRAPULMONARY MIXING OF GASES. E. D. Palmes and Arnold J. Kaminer . Inst. of Indust. Med., New York University Medical Center, New York, N. Y.

Intrapulmonary mixing of gases is accomplished by a combination of molecular diffusion and mechanical blending of the inspired gas with the functional residual gas. Use of a very poorly diffusing gas would permit the measurement of the latter factor with very little contribution by the former. A triphenylphosphate aerosol made up of 0.5 micron diameter particles behaves like such a gas. It has an estimated "diffusion constant" approximately 10^{-4}-10^{-6} that of gases. The transfer of this aerosol from tidal to expiratory reserve air is thus considered to be an index of the mechanical blending component. To determine this index an apparatus for rapid measurement of the quantity of aerosol in the reserve air as well as that lost from the tidal air has been developed. It has been used on 30 normal subjects in single breath experiments at tidal volumes of 1200 and 500 ml with the forced exhalation of an additional 900 ml at the end of each breath. The tidal portion of the breath is inhaled from and exhaled into one container and the additional 900 ml is exhaled into a second container; the aerosol content of each container is then determined. Present results indicate that there is good breath to breath consistency in individuals and the results on the same subject are reproducible from day to day. The results are consistent with the existence of a normal distribution of mechanical mixing abilities in the group measured.

This investigation was supported in part by PHS Research Grant, RG 5587.

SIMULATION AS A MEANS OF STUDY OF REFLEX PHENOMENA. Lloyd D. Partridge. Yale University School of Med. (Intr. by D.L. Kline) When a system is composed of several parts, each of which has been well studied it still is possible that the effect of the individual parts on the whole system might not be clear. For example the stretch reflex which has been long studied is composed of a receptor whose response to stretch is well known, the extensively studied monosynaptic reflex, and muscle the response of which to nerve activity is one of the oldest topics of physiological study. The difficulty of altering independently such factors as receptor adaptation, muscle wave summation, or reflex sensitivity leaves us with relatively little knowledge of how these individual factors contribute to the response of the total system. Electronic simulation techniques provide us with the means of building models of the responses of as many of the individual parts of the reflex as we choose to study. Interconnection of the proper parts provides a model of any hypothetical reflex composition and this model can be tested against known animal responses. By this modeling method we have demonstrated that in the usually conceived stretch reflex, adaptation is essential for stable operation, wave summation in the muscle tends to cancel the adaptation effect and the frequency of a tremor generated by the stretch reflex is not set by the conduction delay of the reflex. This method has proven quite profitable as a means of testing hypotheses but like any other method of analysis can not correct for invalid assumptions. Supported USPHS grant B-2355.

PRELIMINARY STUDIES ON PROPERTIES OF THE INHIBITORY FACTOR IN HUMAN GASTRIC JUICE. Lorraine Peissner and Jordan Tang (intr. by Stewart Wolf). Psychosomatic and Neuromuscular Section, Oklahoma Medical Research Institute, Oklahoma City, Oklahoma.

The activity of the gastric secretion inhibitor was established by a dose-response study carried out by a modification of the Shay rat technique. Volume of secretion was used as an end point. Rats injected with 4 mg of dialyzed, lyophilized gastric juice pooled from healthy subjects and dissolved in normal saline secreted 87% less gastric juice than did the control group; those receiving 2 mg secreted 73% less than control rats, and those injected with 1 mg secreted 58% of control values. Precipitation with 66% acetone did not destroy the inhibitory activity. Activity was likewise retained by precipitation with 66% ammonium sulphate. However, no purification was achieved by fractionation with different concentrations of either acetone or ammonium sulphate. Gastric juice subjected to 30-min. boiling or to trypsin digestion also retained its inhibitory property undiminished. When the material was treated with charcoal, the inhibitory activity remained in solution. Treatment with 10% hydrogen peroxide for 20 minutes at 4^{0}C resulted in a decrease in inhibitory activity of about 50%.

CORRELATION OF THE OXYTOCIC ACTIVITY OF THE PITUITARY OF SCYLIORHINUS CANICULUS WITH ENVIRONMENTAL CONDITIONS AND SECTION OF THE PRE-OPTICO-HYPOPHYSEAL TRACT. A.M.Perks and M.H.I.Dodd (Intr. by A.B.Otis). Dept. of Physiol.,Coll.of Med.,Univ. of Florida, Gainesville and Gatty Marine Laboratory,Univ. of St. Andrews, Scotland.

Following the demonstration of an oxytocin-like principle in the elasmobranch neurohypophysis attempts were made to correlate the level of oxytocic activity of the neurointermediate lobe of Scyliorhinus caniculus with asphyxia and trauma, with immersion in hypertonic solutions, and with section of the pre-optico-hypophyseal tract. 0.25% acetic acid extracts of acetone dried neurointermediate lobes were assayed on the isolated rat uterus. Neither experimental asphyxiation nor trauma during capture resulted in depletion of oxytocic activity. Immersion of animals for up to 7 hours in oxygenated sea water enriched to 5% or 10% NaCl failed to result in consistent depletion. Section of the pre-optico-hypophyseal tract appeared to result in approximately 95% depletion by 3 weeks after operation. Tract-sectioned animals maintained for 10 weeks were the only elasmobranchs found to be devoid of detectable activity. Control, saline-immersed, and asphyxiated animals showed a rough inverse relationship between the dry weight of the neurointermediate lobe and oxytocic activity in m.u./mg acetone dried powder; tract-sectioned animals did not conform to this general relationship. It appears that asphyxia and severe conditions of capture do not decrease the oxytocic activity in the neurointermediate lobe (in contrast to "stress" effects in mammals) but that the activity is dependent on an intact pre-optico-hypophyseal tract, thus correlating the pharmacologically demonstrable activity with the neurohypophyseal system. (Supported by Nuffield Foundation.)

DISCHARGE OF FLEXOR MOTONEURONS TO GRADED CUTANEOUS AND MUSCLE NERVE VOLLEYS. Edward R. Perl, Dept. of Physiology, Univ. of Utah, Salt Lake City 12, Utah.

The response of individual biceps femoris posterior and semitendinosus (BST) motoneurons to graded volleys in BST nerve, sural nerve (S), and deep peroneal (DP) or triceps surae (TS) nerves has been studied in unanesthetized, decapitate cats. Estimated probability of response (firing index or Fi) was determined by recording from filaments isolated by ventral root dissection. The cells studied had monosynaptic firing indices to maximal Group I BST volleys ranging from 100 to 0 (the latter units were included in the BST pool if monosynaptic discharge occurred during the course of post-tetanic potentiation of BST nerve). Those motoneurons which discharged monosynaptically with a high firing index to small Group I BST volleys, responded with polysynaptic timing, also with a high Fi, to relatively small volleys in S and Group II volleys in TS or DP. Such motoneurons frequently discharged repetitively to large volleys in BST, S, TS or DP with as many as 4 - 5 impulses occurring at intervals of 3 to 8 msec. On the other hand, BST motoneurons with a low monosynaptic Fi discharged only to larger volleys containing small afferent fibers in S or TS nerves and rarely discharged repetitively. Many of the cells studied were "spontaneously" active; such activity being greatest in cells with the lowest threshold to evoked activity. It is concluded that in this pool of motoneurons, monosynaptic and polysynaptic excitability are highly correlated functions.

THE EFFECT OF LUNG SIZE ON PULMONARY CIRCULATION IN VIVO. S. Permutt,* B. Bromberger-Barnea, and H. N. Bane.* Div. of Research and Laboratories, National Jewish Hospital, and Dept. of Physiology, Univ. of Colorado School of Med., Denver.

The effect of increasing the size of the lungs on pulmonary vascular resistance in vivo has been difficult to interpret due to the complicating effects on venous return of changes in intrapleural pressure and pulmonary stretch reflexes. In an attempt to determine the effects of increasing the size of the lungs per se on pulmonary vascular resistance, experiments were carried out on closed-chest, anesthetized dogs in which the size of the lungs as determined by transpulmonary pressure could be varied independently of intrapleural pressure by using combinations of varying expiratory pressures and counterpressures to the thorax. In addition, venous return was varied independently by increasing or decreasing the blood volume. At constant transpulmonary pressure, cardiac output fell and pulmonary vascular resistance increased as intrapleural pressure was increased. When transpulmonary pressure at end expiration was changed from approximately 15 mm Hg to 5 mm Hg by applying counterpressure to the thorax, there was an increase in cardiac output and a fall in pulmonary vascular resistance even though intrapleural pressure rose considerably. At constant intrapleural pressure, pulmonary vascular resistance increased as transpulmonary pressure increased. At constant intrapleural and transpulmonary pressure, increasing the blood volume caused an increase in cardiac output and a fall in pulmonary vascular resistance. It is concluded that increasing the size of the lungs causes an increase in pulmonary vascular resistance, but that this effect can be modified by changes in venous return.

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FATTY ACID SYNTHESIS FROM GLUCOSE-C^{14} IN HIBERNATORS AND NON-HIBERNATORS DURING ACUTE HYPOTHERMIA. W. S. Platner and J. L. Shields*. University of Missouri School of Medicine, Columbia, Mo.

A low R.Q. in hypothermic animals has implied lipid utilization. (Finney, Dworkin and Cassidy; Horvath; Benedict and Lee.) The source of lipid has not been defined. The present study was designed to determine the synthesis rate of total fatty acids (TFA) as reflected in serum and liver from injected glucose-C^{14}. Rats and hamsters were anesthetized with pentobarbital (40 mg/Kg) and exposed to cold until the rectal temperature reached 15°C. The animals were subsequently maintained at this temperature for 60 minutes. All animals were previously fasted for 18 hours. At the beginning of the 60 minute period glucose-1-C^{14} was injected I.P. TFA concentration and specific activity of the TFA was determined in serum and liver. Results indicate that TFA increased in both tissues of the rat but that synthesis from carbohydrate was not increased. From these data it was concluded that the hyperlipemic response to hypothermia resulted from mobilization of lipids from sources other than glucose. The most likely source would be fat depots. Comparative studies of these parameters in the turtle are in progress.

ETHIONINE DURING PREGNANCY: SELECTIVE ACTION ON FETUSES. W.R. Proffit* and L. E. Edwards, Medical College of Virginia, Richmond, Va.

Previous investigators have reported much fetal death but little apparent effect on surviving fetuses when ethionine is administered during pregnancy; it was felt that perhaps a more complete histological-histochemical examination of the fetuses would reveal previously unnoticed effects. Seven female Wistar rats were injected intraperitoneally with 50 mg./day dl-ethionine on the 11th-14th days of pregnancy; eight were fed 0.5% ethionine ad libitum in the diet from the 8th-15th day, consuming an average of 240 mg. total; eight served as untreated controls. Fetuses were removed by Caesaerian section at term; pancreas and liver were taken for freeze-substitution, and the palate was removed and formalin-fixed. In the experimental group, 73 viable young and 23 dead and partially resorbed fetuses were found at section; it was evident that other fetuses had died early and been completely resorbed. No gross defects were noted in either the young from the 15 treated mothers or in the controls, though the average number of live births per litter in the ethionine group (4.9) is considerably below normal, confirming the earlier reports. Histologic examination of the pancreas of the surviving fetuses revealed occasional slight cytoplasmic loss in the acinar cells, but in all cases the DMAB reaction for zymogen granules was heavily positive. Minimum liver damage was noted, and serial sectioning of eleven palates failed to reveal evidence of interference with palate closure. The selective action of ethionine in causing fetal deaths seems the more remarkable in view of the few effects of the drug found in the surviving and apparently normal fetuses.

EFFECT OF THERAPUTIC DOSES OF PSYCHOTROPIC DRUGS ON CLINICAL SYMPTOMATOLOGY AND URINARY AMINES. G. R. Pscheidt, G. W. Brune* and H. E. Himwich. State Research Hospital, Galesburg, Illinois.

Previous studies of ours have related the urinary excretion of indole compounds to changes in the mental condition of schizophrenic patients. This report concerns an additional six mental patients given theraputic doses of reserpine (4 mg/day) and isocarboxazid (30 mg/day), either singly or in combination. They were kept on a constant protein diet and given daily examinations including psychiatric interviews and various physiological parameters were evaluated. The 24 hr. urine specimens were collected and analyzed for total catechol amines, tryptamine and 5-hydroxyindoleacetic acid. The six patients were chosen with respect to their clinical symptomatology. There were two well adjusted mental defective patients without signs of anxiety, two schizophrenics with marked signs of anxiety, and two schizophrenics free of anxiety states but whose psychoses became easily activated if not controled by tranquilizing drugs. Differences in the clinical symptomatology were reflected in the biochemical findings. There was association of increased catechol amine excretion with anxiety states, with or without accompanying activation of psychotic states. In confirmation of our previous findings an activation of psychosis in two patients was preceded and paralled by an increased urinary output of 5-hydroxyindoleacetic acid.

ACTIVATION OF PROTHROMBIN TO THROMBIN-E AND THROMBIN-C WITH PROTEINASES. Geraldine M. Purcell * and Marion I. Barnhart. Dept. of Physiology and Pharmacology. Wayne State University, Detroit, Michigan.

Prothrombin activates to yield thrombin under a wide variety of conditions. The purpose of this study was to follow the activity of proteinase developed thrombin from its affinity for the two substrates fibrinogen and TAMe. Accordingly thrombin ratios of clotting to esterase activity (C/E) were determined for prothrombin activation by trypsin, papain and cathepsin B. Trypsin activated purified prothrombin in 50% glycerol solution to varying extents dependent upon the concentration of trypsin and the pH of the incubation mix. A C/E ratio of one was obtained when trypsin was present without activators or stabilizers. In this case 60% of the initial prothrombin activity was converted to clotting thrombin over a period of three hours. Under these conditions the thrombin had a comparable affinity for TAMe. C/E ratios less than one were produced by trypsin when cysteine and $CaCl_2$ were present and pH varied from 5-8. Papain with cysteine produced small amounts of thrombin esterase. Using quantities of papain from 7-140 γ clotting thrombin was not detected during incubation although prothrombin activity was lost rapidly. Cathepsin B was studied over the pH range 3.6-8 and did not activate prothrombin to clotting thrombin. However, small amounts of esterase thrombin formed accounting for about 5% of the initial activity. Similar results were obtained when cysteine and $CaCl_2$ were present with cathepsin B. Cathepsin B partially activates prothrombin to a derivative(s) which can once again yield prothrombin activity under appropriate conditions. (Supported by USPHS Grant H-3447 NIH)

A THEORETICAL ANALYSIS OF THE EFFECT OF UREA EXCRETION ON THE RENAL CONCENTRATING MECHANISM IN RATS. Edward P. Radford, Jr. Harvard School of Public Health, Boston, Mass.

According to present views, under maximum ADH stimulation urine is equilibrated with hypertonic papillary interstitial concentration. With increasing solute excretion rate (L_{OSM}) produced by a variety of solutes except urea, urine volume (V) may be expressed most simply as:

$$V = \frac{L_{OSM}}{D_{OSM}\ (1 + Q/L_{OSM})}$$

where D_{OSM} is the osmolality of the distal tubular fluid as it enters the concentrating process. Q is a function of (a) the active solute transfer rate from tubules to interstitial space, (b) counter-current flow of blood and tubular fluid in the medulla, and (c) the rate of passive transfer of urea from collecting ducts to papilla. At a constant rate of urea excretion, Q appears to be constant in rats. When different ratios of urea to non-urea solutes were fed to rats, changes in Q observed cannot be explained solely by alterations of passive urea transfer. Thus urea excretion may modify urine concentration by altering renal hemodynamics, or because it is an actively transported solute in the papillary counter-current mechanism.

EFFECT OF BILE DEPRIVATION ON ABSORPTION AND LYMPHATIC TRANSPORT OF DIETARY SOAPS AND TRIGLYCERIDES IN THE DOG. Alfred J. Rampone and John D. Sigurdson (intr. by B. B. Ross). Dept. of Physiology, Univ. of Oregon Medical School, Portland.

The present study was undertaken to provide more information on the mechanism of action of bile as it relates to the lymphatic transport of absorbed lipids. Seven-day fecal balance studies in 12 normal mongrel dogs revealed that 94% of both triolein and sodium oleate were absorbed when fed at rates ranging from 22 to 69 grams per day. Depriving these same animals of bile reduced the absorption to 47% in the case of triolein and 57% in the case of sodium oleate. In a second group of 10 normal dogs 90% of fed triolein and 84% of fed sodium oleate were recovered from the thoracic duct as lymph lipid. In a third group of 6 biliary fistula dogs only 8% of fed triolein was recovered in lymph compared to 40% of fed sodium oleate. Results indicate that in the absence of bile both triolein and sodium oleate are absorbed in significant quantities, but only in the case of fed sodium oleate do significant quantities of the absorbed lipid appear in the lymph.

SPECIFIC RESISTIVITY OF CEREBRAL CORTEX. J. B. Ranck, Jr. and W. E. Crill*. Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle.

Nonstimulating current pulses were passed through the cortex of the rabbit with an electrode assembly which was 1 cm in diameter and contained a guard system to reduce current divergence. The voltage gradient perpendicular to the cortical surface was measured at 100 μ intervals by a differential double microelectrode with a vertical tip displacement of 0.25 to 0.85 mm. No significant change in voltage gradient was observed throughout the depth of the cortex. At the level of the white matter the voltage gradient increased two to four times, even though current divergence could have occurred at this depth. The voltage gradient per unit applied current was converted to specific resistivity by comparing the values for the cortex with measurements of solutions of known resistivity. The mean specific resistivity of five measurements on three rabbits was 480 ohm-cm (range 350 to 630). If it is assumed that 5% of the cortex is blood, the resistivity of the non-vascular cortex is 630 ohm-cm. This value is consistent with a hypothesis that the applied current flows entirely in the extracellular space, which is 10% of the cortical volume. (Supported by grants 2B-5082, B752, 2B-5289, B395 and B396 from the National Institutes of Health.)

CANNULA IMPEDANCE TO PULSATILE FLOW. James E. Randall. Dept. of Physiology and Pharmacology, University of Missouri, Columbia, Mo.

The Navier-Stokes hydrodynamic equation has been evaluated using Womersley's tabulations for the flow of blood in rigid tubing of the sizes used in cannulating the peripheral arteries for flow measurements. These evaluations are in the form of a ratio of sinusoidal pressure to sinusoidal flow as a function of the frequency of the fluctuations, representing the impedance to sinusoidal pulsatile flow. At the frequencies present in the peripheral pulse this pulsatile impedance of a cannula can be as much as three times the opposition to steady flow, with the pressure leading the flow by about 60°. The low-pass hydraulic filter action of a length of this tubing attenuates the flow pulse to a greater extent than it attenuates the mean flow and may account for the lack of an observed back-flow in many direct-cannulation preparations. Knowledge of the exact dynamic character of these cannulae would permit one to correct for their presence. (This investigation was supported by U.S.P.H.S. Grant H-2464 from the National Institutes of Health.)

ATRIAL DYNAMICS DURING SYMPATHETIC CARDIAC NERVE STIMULATION. Walter C. Randall and Richard Ulmer*. Dept. Physiology, Stritch School of Med. and Graduate School of Loyola Univ., Chicago.

The influence of the sympathetic cardiac nerves on ventricular dynamics has been described in considerable detail, and myocardial excitability, conductivity and contractility shown to be significantly increased during stellate stimulation. A more complete analysis of myocardial activity requires that pressures be recorded from all four chambers of the heart during these stimulation experiments. The amplitude of atrial contractions increases concurrently with ventricular contractions under these circumstances, thus establishing atrial augmentation as an important corollary of ventricular augmentation. However, due to a concomitant decline in atrial diastolic pressure, mean atrial pressure may decrease and thus establish a steeper gradient from veins to atrial chamber. Augmentation of atrial contraction was more prominent in the right atrium whereas declining mean pressure was more pronounced in the left atrium The possibility that increased amplitude of pressure waves in the atria was due to back pressure (related to more forceful eversion of the A-V valves) induced by profound ventricular augmentation was ruled out by the following observations: both electrical and mechanical activity in the atria preceded that in the ventricle and direct recordings from atrial force gages conclusively demonstrated increased force of contraction by these chambers.

INTESTINAL TISSUE BLOOD FLOW IN DOGS IN EXPERIMENTAL SHOCK DUE TO HEMORRHAGE, ENDOTOXIN AND EPINEPHRINE INFUSION. R. R. Rayner*, L. D. MacLean and E. Grim. Ancker Hospital, St. Paul, Minn. and Univ. of Minnesota, Minneapolis, Minn.

Isolated loops of ileum from control animals and the three experimental groups were perfused at 135 mmHg. with blood containing approximately 2% deuterium oxide. Total venous outflow was measured. Samples of the component tissues, mucosa, submucosa, muscularis, and mesentery of the intestine were collected and analyzed for D_2O. Blood flow to each of the component tissues was calculated on the basis of the assumption that distribution of the D_2O was blood flow limited. In the dogs subjected to lethal hemorrhagic shock and retransfusion, both the total and individual tissue blood flows were identical to those for the controls. In the dogs given a lethal dose of endotoxin, the total flow was unchanged but the mucosal flow was reduced to about 50% of control. In dogs receiving an epinephrine infusion of 16 to 17 microgram/Kg./min for 2 hours, the total flow was unchanged but the mucosal flow was increased to about 140% of controls. Two sub-groups of dogs submitted to endotoxin shock were pretreated, one with hydrocortisone and the other with dibenzyline. The marked reduction in mucosal flow seen in dogs receiving endotoxin alone was prevented by hydrocortisone. This reduction was not prevented by a vasodilator (Dibenzyline).

BLOOD FLOW AND BLOOD PRESSURE RELATIONSHIPS IN THE NON-ISOLATED MANDIBULAR ARTERY OF DOGS. David R. Redden*, Jack G. Bishop, James L. Matthews*, and Homer L. Dorman*. Department of Physiology, Baylor University College of Dentistry, Dallas, Texas.

The pressure-flow relationships in the mandibular artery of 14 mongrel dogs were determined using the perfusion technique. The dogs were anaesthetized with sodium pentobarbitol, 33 mg./kg., and the blood was rendered noncoaguable with herapin, 5 mg./kg. Pressure was recorded by the use of a Statham P-23AA strain gauge, Brush amplifier, and ink writing recorder. The back-pressure effect on the shape and position of the pressure-flow curve was determined. The resulting curves, with and without back-pressure were concave to the flow axis. Critical closing pressures (CCP) of this vascular bed were determined by extrapolation of pressure-flow curves and by recording the point of stabilization of asystolic gradients. The mean CCP were found to range from 3.0 to 8.6 mm. Hg. and appear to be a direct function of the perfusion pressure. Thorotrast injections at increasing perfusion pressures indicated that there were anastomoses of the left and right mandibular arteries. These anastomoses occurred across the symphysis as well as with other arteries which entered the lingual side of the mandible.

T-1824 DISAPPEARANCE CURVES WITH SUCCESSIVE DYE INJECTIONS IN NORMOVOLEMIC DOGS. J. W. Remington and C. H. Baker. Dept. of Physiology, Medical College of Georgia, Augusta.

We have shown that repeated injections of T-1824 in the same dog give plasma volumes successively greater than the initial. Inspection of the dye disappearance curves suggests 3 factors which might be involved. 1) A steady logarithmic decline in concentration has proven the exception rather than the rule. Transient concentration changes at inconsistent times during the 70 min. sampling period, unrelated to plasma specific gravity changes, make the determination of a best fit slope a subjective affair. Such fluctuations are seen with either morphine-sodium pentobarbital or sodium barbital, anesthesia, or in unanesthetized dogs. They are as common with successive injections as with the first. The deviations are also seen in dogs given 20 mg./kg. Dibenamine. 2) When the spectrophotometer is nulled against a blank sample containing dye prior to a new dye injection, i.e. subtracting a constant dye concentration, the succeeding disappearance slope is steeper. This is due to continued disappearance of residual dye as well as that newly injected. Reading all samples against a blank standard corrects in most part this steepening, but the error in plasma volume estimation is no better for one technique than the other. 3) The overestimation of plasma volumes with successive injections seems to lie mostly on the finding that the dye concentration at 10 min. after injection, and thus for the whole recorded disappearance curve, was less than that expected. (Supported by USPHS grant H-4573).

TECHNIQUE FOR REPEATED CORRELATION OF EKG AND CENTRAL PULSE PRESSURE WAVES. Ernest Retzlaff, Joan Fontaine, Henry Besch (Intr. by C. D. Leake) Columbus Psych. Inst., Cols., Ohio

Correlation of nervous system function and cardiovascular system change as a function of aging in the albino rat is highly dependent upon a suitable technique for the direct measurement of the blood pressure wave form from an artery of suitable size in the non-anesthetized animals. Preliminary results of studies utilizing two techniques by which the aortic pulse wave is recorded indicate that despite certain obvious alterations caused by the surgical procedure, a reliable index of cardiac function may be obtained. The methods used include: 1) "T" cannulae of thinwall stainless steel 18 gage tubing, permanently inserted into the abdominal aorta; 2) cannulation of renal artery with PE 160 polyethylene tubing, following unilateral nephrectomy. Analysis of the pulse wave obtained by use of these two methods indicates that either is suitable for chronic studies over a period of many months. Correlation of the EKG, both before and after surgery, with the recorded pulse wave indicates that the animal has suffered little physiological damage either by the slight narrowing of the aortic lumen when the first method is used, or by the loss of one kidney when the second method is employed. Experience indicates that either one of these methods gives reliable data in correlation of EKG and central pulse pressure waves.
Supported in part by NIH Grant H3084.

THE EFFECT OF THE PERICARDIUM ON VENTRICULAR TRANSMURAL PRESSURE. E. A. Rhode*, H. Kines* and J. P. Holt. Heart Laboratory, Univ. of Louisville.

In anesthetized open-chest and closed-chest dogs subjected to plethora and hemorrhage, pressures were measured simultaneously in the right atrium, right ventricle, left ventricle, pleural and pericardial spaces. Right and left ventricular transmural pressure is the difference between intraventricular pressure and the pressure in the pericardial space. An elevation of ventricular end-diastolic pressure above approximately 1 mm. Hg. was associated with a nearly equal elevation in pericardial pressure at the end of diastole and a rise but to a lesser degree in pericardial pressure at the end of systole. The ventricular transmural pressure at the end of diastole has a value no more than 2 or 3 mm. Hg. under all except the most abnormal circumstances. The practice of defining "effective" ventricular end-diastolic pressure as the difference between ventricular and intra-pleural pressure gives erroneous results when ventricular end-diastolic pressure is elevated above a few mm. Hg. in an animal with an intact pericardium. When ventricular end-diastolic pressure is elevated the measured ventricular end-systolic pressure, as a measure of the pressure developed by muscular contraction, is in error because the pericardial pressure is elevated. This error may be relatively large for the right ventricle and is relatively small for the left ventricle. (Supported by USPHS Grants #1534 and #2075; The Ky., Louisville and Jefferson County Heart Assns.)

OBSERVATIONS ON THALAMO-CORTICAL RECRUITING IN CHRONIC RABBIT, CAT AND MONKEY. Franco Rinaldi (intr. by R. K. Richards). Abbott Laboratories, North Chicago, Illinois.

The characteristics of recruiting cortical responses evoked by low-frequency stimulation of intralaminar and midline thalamic nuclei have been studied in animals with implanted stimulating and recording electrodes. The animals were freely moving (cats and rabbits) or mechanically restrained (rabbits); monkeys were studied in the usual movement-limiting chair. Waveform, latency of the main negative component, cortical distribution, threshold, occurrence of repeated cycles of waxing and waning (recruiting-derecruiting) upon prolonged stimulation are the parameters which were considered in relation to the varying spontaneous behavioral state and cortical electrical activity and to the site of thalamic stimulation. Spontaneous sleep with "spindling" EEG facilitates recruiting because it lowers the threshold even by 100% comparatively to the alert state, causes enlargement of the area of cortical distribution including introduction or enhancement of bilaterality, and facilitates the repetition of waxing and waning upon prolonged stimulation. Waveform and latency are mainly related to the site of thalamic stimulation. As the recruiting response waxes and wanes its latency changes very little in cat and monkey. In the rabbit the latency of each response progressively increases with the size of it and conversely shortens as the response wanes. This latency variation is of the order of 10 msec. In the rabbit the recruiting-derecruiting cycle repeats regularly upon sustained stimulation with the rather fixed periodicity of 3.0-3.5 seconds when the spontaneous EEG exhibits "spindling" activity. In cat and monkey recruiting from stimulation of the N. centrum medianum prolonged for long periods often induces behavioral and EEG sleep which outlasts the stimulation.

PULSE PRESSURE, BLOOD FLOW AND SOUNDS IN VESSELS CONNECTED BY INTRALUMENAL IMPLANTATION OF A CUT ARTERY INTO AN ARTERY OR VEIN, A SIMPLE METHOD OF ANASTAMOSIS FOR USE IN DISASTERS. Joseph T. Roberts. Veterans Admin. Hosp., Univ. Buffalo School of Med., Buffalo, N.Y.

By a very simple quick cheap method blood vessels have been connected in 220 animals by implanting cut proximal end of artery into lumen of distal artery or vein. Recordings of pressure showed transmission of arterial pulse into peripheral vessels beyond anastamosis, confirming flow of blood as shown by seeing dye in peripheral artery or vein after injection in proximal artery. At times flow beyond connection was as active as proximally. Sounds recorded were often a continuous machinery-shop murmur as over an A-V fistula, although it must be stressed that this is a technic for arteriolization of a vein rather than A-V fistula effect. To assure this, proximal venous limb was tied and cut. In some, especially if artery was less than 1 mm. diameter, thrombosis or calcified occlusion might occur. Other vessels, when larger, stayed open and normally functional as long as 16 months before sacrifice. By this simple method, carotid, jugular, femoral, subclavian, internal mammary, coronary arteries and veins have been well connected. Venous or Teflon segments served as bridges between longer separations between cut ends of arteries, as in cases of cut thoracic or abdominal aorta. This revives interest in arteriolization of coronary sinus as introduced by J.T.Roberts, 1938-43 and popularized later by C.S.Beck, 1948. Simple household items can be used for this simple technic and often only one knot suffices.

THE REGULATION OF THE PULMONARY VASCULAR RESISTANCE. Simon Rodbard. University of Buffalo Chronic Disease Research Institute, Buffalo, N.Y.

Experiments were designed to evaluate sites of pulmonary vascular resistance (R). R remained unaffected by adrenalin, aminophylline, tetraethylammonium, histamine, acetylcholine, or by changes in alveolar or blood oxygen or carbon dioxide content. Variations in pulmonary arterial pressure did not affect R. R increased on obstruction of one main pulmonary artery; previous interpretations that R decreases are shown to be in error since pulse contour analysis demonstrates that the pulmonary vascular bed is perfused normally during only a small part of the cardiac cycle; calculations of R must take this into account. Negative pressure inspiration reduced R, suggesting that pulmonary vessels widen as they elongate. R increased with insufflation pressure. Elevation of pulmonary venous pressure reduced R, as in collapsible tubes (Circ. Res. 11:280, 1955). These data can be interpreted as indicating that R is primarily at the capillary where intrapulmonary air pressure, via bronchomotor tone, may be the controlling factor.

PHYSIOLOGICAL STUDIES ON THE ISOLATED ARTIFICIAL HEART-LUNG PERFUSED RABBIT KIDNEY. Sheldon Rosenfeld* and Alvin Sellers. Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, California.

When anesthesia of the kidney donor rabbit was obtained by transection of the cervical spinal cord, relatively normal levels of renal function were obtained in better than 90% of experiments as compared to only 40% when intraperitoneal alcohol was used as described originally (Am. J. Physiol. 196:1155, 1959). Average values for 12 experiments are: observed renal plasma flow = 1.70; creatinine and p-aminohippuric acid (PAH) clearance = 0.28 and 1.3 ml./min./g.kidney weight; PAH extraction = 75%; and U:P ratios for creatinine and glucose = 26:1 and 0.1:1. Autoregulation of renal blood flow was demonstrated in a completely denervated kidney perfused with whole blood but was abolished when alcohol anesthesia was used in the kidney donor rabbit. Ouabain exerts a direct effect upon the kidney, producing an immediate increase in renal vascular resistance, which subsides after 20 minutes and is followed by a marked diuresis and natruresis. It has been demonstrated that the renal tubular reabsorption of filtered endogenous phosphate and glucose is over 98%.

THE RADIOPROTECTIVE ACTIVITY OF YEAST RIBONUCLEIC ACID ON ISOLATED CELLS IN VITRO. Donald E. Rounds (intr. by C. M. Pomerat). Pasadena Foundation for Medical Research, Pasadena, California.

Yeast ribonucleic acid was tested as a possible radioprotective agent, using established cell strains in tissue culture. Increased concentrations of yeast RNA in the medium during exposure of amnion cells to 700r gamma radiation from a Cobalt-60 therapy unit indicated a maximum protective effect around 0.1 mg. RNA per ml. of medium. The survival response of seven cell types showed a wide variation in the degree of RNA protection. Four cell strains of nonmalignant origin showed significant numbers of surviving cells when pretreated with yeast RNA as compared with untreated cultures. Three cell strains of malignant origin showed no protective response.

THE EFFECTS OF A PERIPHERAL ARTERIOVENOUS FISTULA ON CORONARY BLOOD FLOW, CARDIAC WORK AND CARDIAC EFFICIENCY. **G. G. Rowe, R. J. Botham*, H. P. Gurtner*, C. J. Chelius*, J. Lopez*, S. Afonso*, C. W. Crumpton.**
Dept. of Med. and Cardiopulmonary Research Laboratory, U. of Wis. Med. School, Madison 6, Wisconsin.

In mongrel dogs an arteriovenous fistula was created surgically between the femoral artery and vein and the animals permitted to recover for several weeks from the operation. Cardiac output (Fick) and coronary blood flow (N_2O) were determined with the fistula open and closed by compression of the area by a clamp applied to the extremity over the fistula. Studies were varied so that in half of the experiments the first study was done with the fistula open and in half with the fistula closed. When the fistula was open the systemic and pulmonary arterial pressure was decreased ($p<0.001$), the pulse rate and cardiac output elevated ($p<0.02$), and calculated total systemic ($p<0.01$) and pulmonary ($p<0.001$) vascular resistances decreased. Comparing the "fistula open" and "closed" state left and right ventricular work did not change significantly, nor did coronary blood flow or myocardial oxygen consumption. When the fistula was open coronary vascular resistance was significantly reduced ($p<0.02$) and calculated cardiac efficiency decreased slightly but not significantly.

ZOOTOXICOLOGIC EFFECTS OF CROTALUS VENOMS. Findlay E. Russell and Bryan A. Michaelis*. Lab. Neurol. Res., College of Medical Evangelists, Los Angeles, Calif.

Crotalus venom produces deleterious changes in the mammalian cardiovascular, respiratory and urinary systems. The present study was initiated to determine certain relationships between the changes in the cardiovascular system and those in the respiratory and central nervous systems following intravenous injection of the crude venom. Cats were used in all experiments and most measurements were made simultaneously. The venoms of C. adamanteus, C. atrox and C. viridis helleri produced a precipitous fall in systemic arterial pressure and flow, a rise in systemic venous pressure, pulmonary artery pressure and cisternal pressure concomitant with changes in respiration and the electrocardiogram and electroencephalogram. These changes were only slightly modified by epinephrine. Studies were made on isolated heart preparations. (Supported by grant H-3443, N.I. H., P.H.S.)

PRESSURE-FLOW RELATIONSHIP IN THE ISOLATED, PERFUSED DOG HEAD WITH REFERENCE TO CEREBRAL ISCHEMIC PRESSOR RESPONSE. Kiichi Sagawa (intr. by A. C. Guyton). Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

In order to find out the eliciting mechanism of the powerful pressor response generated by the vasomotor center in response to cerebral ischemia; the pressure-flow relationship was studied in dogs whose cerebral arterial blood supply was isolated from the systemic circulation. Mechanical flowmeters were used because repeated determinations in a short period of time were required. To exclude extracranial flow from measurements, an anatomical study of the connections between the cerebral arteries and extracranial arteries was made by means of vascular cast preparations using dyed latex or vinyl acetate solution. The cerebral blood flow was around 60 to 70 cc/100 gm/min. at a perfusion pressure of 100 mm. Hg. The pressure-flow relationship was found to be roughly linear* and the systemic blood pressure rose markedly only when the CBF decreased to extremely low levels.

*over the perfusion pressure range of 0 to 140 mm. Hg.

FACTORS INFLUENCING CORONARY BLOOD VOLUME AND MYOCARDIAL INTERSTITIAL FLUID CONTENT. P.F.Salisbury, C.E.Cross*, P.A.Rieben*, K. Katsuhara* and E. Wagner*. St. Joseph Hospital, Burbank, Calif.

Recent data (Circ. Res. July 1960) correlating myocardial elasticity and cardiac dynamics with changes of coronary blood volume and myocardial fluid content suggested direct analysis of these parameters. The left coronary artery of an isolated dog heart was cannulated at the ostium and perfused from an adjustable reservoir with blood from a donor dog or oxygenator. Right atrium and ventricle were opened. An air-filled balloon (for distention) and a water-filled balloon (for pressure registration) were placed into the the left ventricle (apex). The mitral valve was occluded to confine the balloons. Heart rate (HR) was regulated (pacemaker). The system was placed on a wire frame suspended from a bonded strain gage which recorded its weight simultaneously with coronary artery pressure (CAP) and (inaccurate) left ventricular pressure (LVP). Venous blood dropped into a funnel and was returned. Electrically recorded weight change was verified by direct weighing on a balance. Changes of CAP, HR or LV distention caused new steady states of the heart weight within 30-60 seconds. Increased "steady state" weights were observed after increasing CAP or after ventr. fibrillation. Increasing HR, more forceful contraction or increased LV distention caused heart weight to decrease to new plateaus. Above changes of heart weight are believed to reflect coronary blood volume. Osmotic transients caused striking changes. After episodes of acidemia or certain other experimental maneuvers the heart weight did not reach a plateau but continued to increase with a measurable slope, indicating progressive myocardial edema. Myocardial edema formation was influenced by CAP, colloid osmotic pressure (plasma), drugs and ions.

MITOCHONDRIAL CHARACTERISTICS IN VARIOUS AREAS OF THE BRAIN. F. E. Samson, W. M. Balfour* and R. J. Jacobs*. Univ. of Kansas, Lawrence.

The mitochondrion (M) appears to be the powerhouse of the cell in the brain as in other organs. Although the regulation of energy metabolism is probably a function of substrate levels, the M must determine the boundaries of power-output capacity. Differences in M capacity in various areas of the brain might be expected. The question is: How does the M power capacity in various areas of the brain compare? Brains were removed from rats and quickly divided into 3 major regions: cerebral hemispheres, "midbrain", and cerebellum. M were prepared by homogenization and differential centrifugation in 0.25 M sucrose. The M in all fractions were counted with phase-microscopy. The dry weight and protein of the "mitochondrial fraction" were determined. The number of M per g. in the various areas was as follows: cerebral hemispheres, $(34.9)(10^{10})$; midbrain, $(30.9)(10^{10})$; cerebellum, $(27.5)(10^{10})$. The calculated mean mass of a M in $\mu\mu$g: cerebrum, 0.239; midbrain, 0.243; cerebellum, 0.255. The protein content of a M in $\mu\mu$g: cerebrum, 0.106; midbrain, 0.124; cerebellum, 0.133. The number of M per cell (based on DNA analysis): cerebrum, 2918; midbrain, 2158; cerebellum, 464. Based on succinic dehydrogenase activity, the mitochondrial power output capacity is highest in the cerebrum and lowest in the cerebellum. (Aided by PHS Grant B-1151.)

HYDROGEN ION BINDING IN RELATION TO SODIUM AND POTASSIUM BINDING BY CELLULAR MEMBRANE MATERIALS. Hisashi Sanui, Arselio Carvalho* and Nello Pace. Department of Physiology, University of California, Berkeley.

Previous investigations have demonstrated that the membrane materials from rat liver cells and human and dog erythrocytes exhibit exchange binding of sodium and potassium. The binding is sharply dependent on hydrogen ion concentration in the physiological range, suggesting that H^+ competes with the alkali cations for binding sites. The H^+ pK for sites binding sodium and potassium was calculated to be in the range of 5.5 to 7.5. Acid titrations carried out over the range of pH 3.0 to 8.3 show that for all of these membrane materials there appear to be three major hydrogen ion binding components, with pK of 7.1, 6.1 and 3.3. The total H^+ capacity is in the range of from 7.1 to 8.5 meq./gm. N. The pK 7.1 and 6.1 components appear to be those involved in sodium and potassium binding and have capacities of 0.3 and 0.7 for rat liver microsomes, 0.5 and 1.7 for human erythrocyte ghosts, and 1.2 and 1.6 meq./gm. N for dog erythrocyte ghosts, respectively. Differences in Na^+ and K^+ binding characteristics among the membrane materials can be explained by the relative differences in binding capacities of the two components. The most obvious difference between human erythrocyte ghosts and dog erythrocyte ghosts is in the binding capacity of the pK 7.1 component, which is more than double for the latter. It appears probable that the previously demonstrated binding of sodium and potassium is not by groups such as carboxyl, primary phosphate, ammonium and sulfhydril, but is by groups with H^+ binding pK in the range of 5.5 to 7.5 such as imidazolium of histidine and secondary phosphates of phospholipids, phosphoproteins and other phosphate-containing compounds. (Supported by the National Science Foundation).

MULTICHANNEL RECORDS OBTAINED DURING VENTRICULAR FIBRILLATION. A. M. Scher. Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle.

The onset of fibrillation induced by a single electrical stimulus was studied in 6 feline and 10 canine hearts. Simultaneous records were taken from eight or more points distributed widely around the ventricles. A unipolar record was obtained at one location and bipolar records at the others. On the beat following the stimulus, the wave of excitation followed an extrasystolic pattern which was characteristic of the particular stimulus site. The same general pattern of excitation reappeared for several beats, but this pattern was gradually modified until frank fibrillation occurred. The modifications consisted of a gradual change in the time of activation of one or more recording points with reference to the other points. This modification often continued over several beats. Also, some points at times were not activated during a particular beat or even during several successive beats. As fibrillation developed, conduction velocity decreased, activity at the various points studied being separated by greater and greater time intervals; there was also a decrease in the duration of the depolarized period in the unipolar action potential, indicating a shortening of the intracellular action potential. Although no clear circulating wave was demonstrated, it appears that the decreases in velocity and in the duration of the intracellular action potential result in a situation where a wave can actually "catch its own tail." These results accord with the circus theory as originally stated by Lewis and with other observations and theories, particularly some stated by Wiggers (Am. Heart J. 10:399, 1940). (Supported by grant H1315 from the National Heart Institute and a grant from the American Heart Association.)

CARDIOVASCULAR RESPONSE TO EXERCISE IN ORTHOSTATIC HYPOTENSION. Alexander Schirger,* R. J. Marshall* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Eight patients were studied by means of a strain-gauge manometer to measure radial artery pressure and the indicator-dilution technic for cardiac output. The zero reference point for pressure measurement was the mid-chest level when supine and the third intercostal space when upright. The cardiac output and stroke volume were abnormally low during standing but increased to a normal degree during mild exercise on a horizontal treadmill. The blood pressure, which had fallen to 75/45 mm. of mercury or less with standing, failed to increase with exercise. With supine leg exercise in the horizontal position, the systolic and diastolic blood pressures in four of six subjects fell by an average of 49 and 33 mm. of mercury respectively. During comparable exercise with the head of the table tilted 15 degrees downward, the pressure fell by an average of 50/29 mm. of mercury. Since with supine exercise venous pooling is minimized, it is unlikely that this accounts for the fall in blood pressure. The fall may be due to a failure of compensatory constriction of other vascular beds.

AUTORADIOGRAPHIC OBSERVATIONS OF PLASMA CELL PROLIFERATION IN THE LYMPH NODES OF MICE. John C. Schooley (intr. by H. B. Jones). Donner Lab., University of Calif., Berkeley.

On alternate days 60 Swiss mice were antigenically stimulated with three subcutaneous injections of dog serum and Freund's adjuvant. One day after the last injection of antigen the specific DNA precursor, H^3-thymidine, was administered (1 μc/gm body wt., 360 mc/mM). Animals were sacrificed at various intervals after injection and autoradiographs made of smears and sections of the stimulated lymph nodes, blood, lymph, and bone marrow. The temporal pattern of the percentage labeling of immature (plasmoblasts and proplasmocytes) and mature plasma cells as well as the changes in the number of silver grains over the labeled cells was determined. One hour after H^3-thymidine about 80% of the immature plasma cells were labeled whereas no labeled mature forms were found. By about 12 hours 80% of the mature plasma cells had become labeled indicating a mean-life of this order for mature plasma cells. The decline in the mean-grain count over the immature forms indicates that the maximum generation time of these cells is about 12-16 hours. By 3-4 days none of the cells in the plasmocytic series show detectable labeling indicating again the marked proliferative activity among the immature cells and a relatively short life for the mature plasmocytes. It appears from preliminary data following the administration of H^3-cytidine and H^3-leucine that the synthesis of RNA does not occur in mature plasma cells and protein synthesis in these cells is minimal.

OBSERVATIONS ON THE DEPRESSANT ACTION OF MESCALINE ON INDIRECTLY STIMULATED SKELETAL MUSCLE. Robert T. Schopp. Dept. of Physiology, University of Colorado School of Medicine, Denver, Colorado.

Dogs anesthetized with pentobarbital sodium (30-35 mg/Kg) were used in this study. The tibialis anticus muscle was stimulated via the peroneal nerve at a frequency of 1/sec. employing supramaximal intensity. The muscle tendon was attached to a torsion band and stylus which recorded the muscle contractions on a kymograph drum. Muscle contractions depressed with curare show a further depression within a few seconds after the close intra-arterial injection of mescaline. (Mescaline is an hallucinogenic agent which is structurally similar to epinephrine and norepinephrine.) Mescaline alone in doses greater than 2-4 mg/Kg causes a decrease in magnitude of contraction. Small initial doses may result in a temporary overshoot subsequent to a transient depression. The degree of depression and the duration of action are greater with increasing doses of mescaline although this may be related in part to a cumulative effect of the drug. KCl when administered intra-arterially opposes the depressant effect of mescaline on contraction. As is the case with a partially curarized muscle the opposing action of KCl is evident for some time.

EFFECT OF STIMULATION ON THE PHOSPHORYLASE LEVELS OF EXCISED ANTERIOR TIBIAL MUSCLES OF THE MOUSE. B. A. Schottelius, D. D. Schottelius* and R. R. Rulon*. Dept. of Physiology, Iowa City, Iowa.

The magnitude of the conversion of inactive to active phosphorylase which occurs upon tetanically stimulating excised anterior tibial muscles of mice was determined. Contralateral muscles were used, one a resting control, the other stimulated. Paired excised muscles were maintained on a multiple electrode assembly in oxygenated bicarbonate Ringer buffered at pH 7.4 for 1 hour for purposes of equilibration. Supramaximal square wave pulses of 1 msec. duration and a frequency of 25/sec. were employed. Durations of stimulation used were: 1/2, 1 1/2, 3, 15 and 30 sec. Both muscles were frozen at the last pulse by rapid immersion in isopentane precooled to -160° C. Phosphorylase a, t, and a/t values were determined for both the resting and stimulated muscles. Values of a and a/t showed a progressive increase with increasing levels of stimulation. In stimulated muscles the a/t ratio (%) was increased over resting control value by the following amounts: 1/2sec., 4.3; 1 1/2sec., 7.4; 3sec., 14.5; 15sec., 19.2; 30sec., 20.2. The a/t values for the stimulated muscles are significantly greater than resting control values after 1 1/2, 3, 15 and 30 sec. No significant variation between resting and stimulated muscle t values was observed. The data suggest the development of a potential ability to mobilize glycogen for energy yielding purposes at an early period of tetanic contraction.

EFFECTS OF CARBON DIOXIDE ON PARAMECIA. D. F. Sears and S. M. Gittleson (Intr. by H. S. Mayerson). Tulane Medical School. New Orleans.

Removal of carbon dioxide from the media caused decrease in speed and increase in volume with eventual cellular disintegration of paramecia. When placed in $NaHCO_3$ solutions paramecia died in a simular fashion, but addition of carbon dioxide prolonged survival time. Organisms under pressures less than one atmosphere, applied 8 or more hours, continued to move, but there was a tendency for speed to decrease with increasing tensions. Carbon dioxide above one atmosphere always resulted in death of the animals; survival time varied inversely with pressure. The cells remained intact, even to 48 hours after death, if carbon dioxide tension was maintained. These data indicate that carbon dioxide influences shape, size and activity of paramecia.
Supported by U.S.P.H.S. Grant # RG 5713.

ACTIVATION OF PURIFIED PROTHROMBIN TO AUTOPROTHROMBIN II OR AUTOPROTHROMBIN II-A. Walter H. Seegers, Eberhard F. Mammen* and William R. Thomas.* Dept. of Physiology and Pharmacology, Wayne State Univ. Coll. of Medicine, Detroit.

Autoprothrombin II is formed when purified bovine prothrombin activates in the presence of a small amount of purified thrombin. The activation is inhibited in the presence of calcium ions, and there is a pH optimum between 7 and 8. If the solutions are not buffered during the activation they become acidic. The autoprothrombin II activity is in a fraction in which the N-terminal amino acid is proline and the C-terminal amino acid is tyrosine. A tentative value for the sedimentation constant is 3.7 Svedberg units. Autoprothrombin II anticoagulant (autoprothrombin II-A)was also obtained in fractions from prothrombin. It is a general inhibitor of prothrombin activation. Autoprothrombin II and autoprothrombin II-A are closely related. Both are proteins rich in carbohydrate content. In the case of autoprothrombin II-A the N-terminal amino acid is arginine and the C-terminal amino acid is tyrosine. Autoprothrombin II corrects the recalcified clotting time of PTC deficient plasma quite effectively and is most likely the PTC factor. Blood from hemophilia A persons clots rapidly in the presence of autoprothrombin II. The recalcified clotting time of their plasma is also brought to the normal range, but for a corresponding concentration of the purified procoagulant the clotting times were never equal to that of the normal or PTC. We believe that there is an anticoagulant component in the hemophilia A plasma.

ROLE OF INTESTINE AND LIVER IN PLASMA ALBUMIN BREAKDOWN. Alvin Sellers, Joseph Katz* and Sheldon Rosenfeld*. Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, California.

To determine the role of the intestinal tract and liver in plasma albumin breakdown, I^{131} labelled homologous plasma albumin was injected into rats whose gastrointestinal tract or liver were removed either in part, or in toto. After 15-24 hours the entire rat was ground and homogenized. The non protein radioactivity was extracted from the entire body. From the non protein activity in the excreta and in the ground animal, the percent breakdown of the injected iodoalbumin was obtained. It was found that removal of the entire gastrointestinal tract depressed albumin breakdown by 10-20% as compared to sham operated controls. Albumin breakdown was depressed by 50-80% following 95% hepat ectomy or evisceration. We conclude 1) the gastrointestinal tract plays at most a minor role in plasma albumin breakdown, 2) liver is the major site of albumin breakdown, 3) at least 25% of total exchangeable plasma albumin breakdown occurs in non-hepatic, non visceral sites.

EFFECTS OF EPINEPHRINE AND NOR-EPINEPHRINE ON REGIONAL BLOOD FLOW IN THE RAT. Tatsuro Shigei* and L.A. Sapirstein. Department of Physiology, Ohio State University, Columbus, Ohio.

Rats were infused with nor-epinephrine and epinephrine at 1 mcg per minute for two minutes. Controls received isotonic saline. After two minutes cardiac output was determined in ten animals of each group. In nine animals in each group regional blood flow was determined by fractional distribution of Rb^{86}. The cardiac output was significantly elevated by both epinephrine and nor-epinephrine but there was no difference between the effects of the two (control; 318 ml/kg/min; epinephrine 415 ml/kg/min; nor-epinephrine 435 ml/kg/min). Coronary flow fraction was doubled by both (control; 2.2%; epinephrine 4.6%; nor-epinephrine 4.6%). A significant increase in the pulmonary fraction was observed after each (control; 2.6%; epinephrine 3.8%; nor-epinephrine 3.4%). Nor-epinephrine reduced the renal fraction; epinephrine was without effect (control; 11.9%; epinephrine 11.0%; nor-epinephrine 7.9%). Both reduced the adrenal flow fraction (control; .23%; epinephrine .13%; nor-epinephrine .15%). Skin and spleen fractions were likewise reduced (skin - control; 7.2%; epinephrine 5.5%; nor-epinephrine 5.1%; spleen - control 1.28%; epinephrine .29%; nor-epinephrine .61%). Both materials elevated hepatic arterial flow fraction (control 7.3%; epinephrine 11.3%; nor-epinephrine 9.1%). The flow fraction to the bowel was decreased by epinephrine and unaffected by nor-epinephrine (control 23%; epinephrine 16%; nor-epinephrine 24%).

ABSORPTION OF COPROSTEROL FROM THE RAT'S INTESTINE. C.S.Narayana Setty* and A.C.Ivy. Dept of Clinical Science, University of Illinois College of Medicine, Chicago, Illinois.

Sterols closely related to cholesterol, such as dihydrocholesterol (cholestanol) and sitosterol, though once reported not to be absorbed, are now known to be absorbable. Coprosterol (coprostanol), the cis isomer of cholestanol has been reported not to be absorbed from the intestine of mice and man. But this report has not been confirmed and the absorbability of coprostanol has not been extended to other species. Eight female rats (200-300 gm) were fed a synthetic diet free of sterols but containing 9% oleic acid and 1% sulfasuxidine plus 0.2 streptomycin sulfate for 12 days. The feces were collected twice daily in 95% ethanol and analyzed for digitonizable sterol. The experiment was repeated by the daily addition of 28 mg of coprostanol to the oleic acid in the diet. The average absorption in the 8 rats amounted to 50%, under conditions which yielded 65% absorption of cholesterol and 22% absorption of cholestanol and sitosterols. Baldin and Favarger have recently reported an average absorption in four rats of 40% and 43%, respectively. It now appears that only sterols with a "chair" configuration are absorbed.

STEADY STATE METABOLIC KINETICS IN COMPLEX BIOLOGICAL SYSTEMS. Moris L. Shore* and A. K. Davis. U. S. Naval Radiological Defense Laboratory, San Francisco, California.

Complex metabolic steady state systems in which a central compartment (blood) exchanges compound with independent peripheral compartments (tissues), with synthesis and loss of compound occurring in the system, are examined. Factors that result in the simplification of complex biological systems into two compartment open systems are discussed. Equations are derived for the two compartment open system which allow the calculation of: compartment size for the central and the combined peripheral compartments, the total rate of exchange between these compartments, and the total rate of synthesis and loss of compound from the system. Data required for these calculations can be obtained with relative ease from the accessible central compartment. Thus, a tracer dose of labeled compound is introduced into the central compartment and the specific activity-time relations of compound are determined. Values derived by graphical analysis of this curve, and knowledge of the dose of label administered are the only primary data needed to determine the parameters of the system. Practical applications of this analysis to model and biological systems will be presented.

MYOCARDIAL PRODUCTION AND UTILIZATION OF CATECHOL AMINES. J. H. Siegel* and J. P. Gilmore. Lab. Cardiovascular Physiology, National Heart Institute, Bethesda, Md.

Experiments were undertaken employing a preparation (Fed. Proc. 19, p. 108, 1960) in which it was possible to study changes in myocardial catechol amine production and utilization resulting from direct efferent cardiac nerve stimulation or carotid sinus hypotension at a constant heart rate and stroke volume. The trihydroxyindole method of Lund as modified by Crout was employed for the determination of plasma catechol amines. The results of these experiments show a) efferent cardiac nerve stimulation increases the catechol amine concentration of coronary venous blood; b) dichloroisoproterenol appears to elicit its effect upon the heart only by receptor blockade since, after the injection of this drug, direct cardiac nerve stimulation is still accompanied by an increase in coronary venous plasma catechol amines but with little change in cardiodynamics; c) carotid sinus hypotension is accompanied by an increase in the arterial plasma concentration and a widening of the coronary arteriovenous difference of catechol amines; d) the widening of the coronary A-V difference can occur in the presence of a decreased coronary venous concentration and in the presence of minimal changes in arterial blood pressure. Data will also be discussed describing the way in which the myocardial catechol amine production and utilization during carotid hypotension is modified by bilateral stellectomy or the administration of dichloroisoproterenol.

DILUTION CURVES OF INCREASED OPTIC DENSITY OF BLOOD PRODUCED BY INJECTION OF TRANSPARENT SOLUTIONS. J. D. Sinclair,* W. F. Sutterer,* I. J. Fox* and E. H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Red blood cells scatter and reflect incidental light to render the optic density (O.D.) of whole blood 4-5 times that of hemolyzed blood. The importance of these cellular effects was demonstrated in dogs during densitometric recording of dye-dilution curves simultaneously with cine-angiograms. Injection of 1 ml. of transparent medium, sodium acetrizoate (urokon) into the cava increased the O.D. of pulmonary-artery blood, producing a curve with peak deflection of 4.7 cm., compared with 23.6 cm. from 2.5 mg. of indocyanine green in 1 ml. of urokon. Similar and increasing effects resulted from injecting 1 ml. of 5, 10 and 20 per cent NaCl (peak deflections 1.2, 3.2 and 8.2 cm.). Negative deflections (decreased O.D.) were produced by isotonic NaCl (0.2 cm.); water (0.6 cm.); 7-20 sec. inhalation of 5 per cent CO_2 in O_2 (2.0 cm.) and 50 per cent CO_2 in O_2 (6.3 cm.). Adding 25 per cent saponin; water; 5 per cent glucose; 0.9 per cent NaCl; 70 per cent urokon; 5, 10 and 20 per cent NaCl, all in 1:40 dilution, changed the O.D. of blood at 800 m by -.51, -.02, -.001, -.001, 0.09, 0.08, 0.16 and 0.25 compared with 0.39 from indocyanine green, 15.7 mg./L. Similarly O.D. was increased by hypertonic solutions of KCl, LiCl, $MgSO_4$ and glucose and decreased by urea. These observations stress that densitometry on whole blood involves measurement of small changes in a dense medium, itself subject to changes, e.g. from hematocrit, hemolysis, flow, and red cell characteristics. Instruments measuring light absorption at two wavelengths, e.g. the oximeter, can largely compensate for these nonspecific changes.

EFFECTS OF CALCIUM, ACETYLCHOLINE AND EPINEPHRINE ON ACTION POTENTIALS OF HUMAN ATRIAL MUSCLE IN VITRO. William Sleator, Jr. and Taisija de Gubareff*. Physiology Dept., Washington University School of Medicine, St. Louis.

Intracellular action potentials and contractions were recorded from pieces of human atrial muscle in Kreb's solution stimulated electrically. These preparations exhibit a new type of behavior characterized by periodic "cycling" between 2 phases: high phase contractions are 2 to 8 times those in low phase, and action potentials have 2 or more spikes (Sleator et al, Fed. Proc. 19:114, 1960). High Ca^{++} concentrations, 5 - 7.5 mM increase low phase contractions and reduce tendency to cycle; at 10 mM Ca^{++} cycling usually stops, but spikes are still multiple at low frequency. Acetylcholine at 2 to 5 x 10^{-7} gm/ml weakens contractions, reduces duration of AP plateau, and abolishes double spikes and cycling in most hearts. Experiments with physostigmine and with atropine show the existence of considerable endogenous ACh. Epinephrine at 10^{-7} gm/ml (or nor-epi at 5 x 10^{-7}) reduces period of cycling and makes low phase contraction (tho still single AP) nearly as strong as high phase. Additional epinephrine leads to AP's with bizarre shapes, and to spontaneous activity. This behavior of human atrial tissue appears to reflect intrinsic capabilities of the cell membrane of a variety not previously observed in heart cells. One hypothesis about the mechanism, suggested by the ACh effects, is that the long plateau may be due to relatively low K^+ permeability. (Supported by grants from the St. Louis Heart Assn. and U. S. P. H. S. (B-937))

EFFECT OF X-IRRADIATION OF A PLASMA-CELL TUMOR ON THE IMMUNE RESPONSE IN C_3H MICE. Falconer Smith and John Owens*. Natl. Insts. of Health, Bethesda, Md.

Serum hemolysin titers tended to drop with increased size of the transplanted plasma-cell tumors, X5563, in some C_3H/Lw mice while no hemolysin was observed in other mice of the same strain with comparable tumors after a single intravenous injection of sheep erythrocytes. Exposure of the tumors to 2000 r of 200 KVP X rays abolished the tumor effect on antibody formation in 3 of 4 mice tested 6-7 weeks after X ray. Average serum hemolysin titer for 9 mice immunized 7 days after tumor irradiation was log -2.6 and -2.4 for 6 of 9 mice (no antibody was observed in 3 mice of this group) whose tumors were irradiated 24 hours before immunization. Serum titers averaged -0.8 in 9 tumor mice and -2.7 in 16 non-tumor control mice which had not been exposed to X rays. These results suggest the possibility that irradiation of the tumors interrupted some metabolic process which was responsible for the interference with the primary immune response observed in mice with actively growing plasma-cell neoplasms.

MEASUREMENT OF DIFFUSING CAPACITY OF THE LUNG WITH GAS CHROMATOGRAPHIC TECHNIQUES. Josef R. Smith* and Lyle H. Hamilton (intr. by Ross C. Kory). Wood Veterans Administration Hospital and Marquette University School of Medicine, Milwaukee, Wis.

Methods for the measurement of the single breath diffusing capacity (D_{LCO}) have been developed with a modified Fisher Gas Partitioner. D_{LCO} for ten normal subjects have been determined with He, Ne and SF_6 as the inert gas in the breathing mixture. Twelve measurements on four subjects were made using two inert gases (Ne and SF_6) in the same breathing mixture. The findings suggested that with a breath-holding time of 10 seconds the differences in molecular weight and solubility of the inert gas did not measurably affect the calculated D_{LCO}. The values obtained from normal subjects were comparable to those reported with standard methods of gas analysis. Expected low values for D_{LCO} were found in patients having known diffusion impairment. A mixture of 0.3-0.5% Ne and 0.4% CO in air was the preferred breathing mixture for use in determining D_{LCO} because these gases are separated quickly and easily with the gas chromatograph. Advantages of the technique include: a) Accurate analysis of all required gas components with a single instrument and a simple technique; b) Adequate chromatographic response from small samples (complete analysis on a single 5.0 cc sample within about 7 minutes); c) Simple method for calculating D_L (use of peak height measurements for the calculation without conversion to percentage values or correction for interfering gases).

INFLUENCE OF AGE ON HEMATOPOIETIC RECOVERY FOLLOWING IRRADIATION. Willie W. Smith and Ilo M. Alderman*. Natl. Insts. of Health, Bethesda, Md.

It has been suggested that adaptations to a new diet and environment at weaning are responsible for the low resistance and high variability in survivorship of mice irradiated at about 4 weeks of age. Comparison of mice weaned at 21-23 days with littermates weaned 11 days later, all irradiated at age 33-35 days, revealed no differences in response to 520-680 r 3 Mev X rays (LD_{25-65}). Comparison of bone marrow, granulocytes and lymphocytes in mice 7.5 weeks old (LD_{50}=800 r) and 31 weeks old (LD_{50}=920 r) given 600 r and 700 r showed an earlier recovery of bone marrow cellularity and of circulating granulocytes in the older mice but no difference with age in lymphocyte recovery. As noted by other investigators for species differences, the lymphocyte response appeared to be dose dependent while the granulocyte response was associated with ability to survive.

VASA VASORUM OF THE PULMONARY ARTERY. Sidney S. Sobin and Wallace G. Frasher.* College of Medical Evangelists, Los Angeles, California.

In our studies of the distensible behavior of a defined segment of the pulmonary artery from its origin to the first side branch beyond the bifurcation it became necessary to characterize the vascular supply to the vessel wall. Using a specially prepared non-wettable polymer, controlled retrograde infusion into the aorta of the rabbit results in detailed filling of the microcirculation above the infusion site. The arterial and venous vasa patterns are exhibited by glycerin clearing. Arterial vasa of the pulmonary artery at its origin arise from specific branches of the right and left coronary arteries and extend up the respective side of the pulmonary artery in a characteristic pattern. These vessels freely anastomose with each other. A clearly defined arterial supply originates from a stellate group of vessels at the ligamentum arteriosum and extend proximally to join with the coronary artery branches and distally over the right and left pulmonary arteries. A major supply of the right and left pulmonary arteries arises from the rich vasculature of the contiguous trachea and bronchi and anastomose with the stellate group. The venous vasa drain to the coronary veins as well as to the adjacent ligamentum arteriosum and bronchial areas.

RAPID EFFECTS OF T.S.H. ON THYROIDAL PERMEABILITY. David H. Solomon (Intr. by Ralph R. Sonnenschein). Univ. of Calif. Med. Center, Los Angeles, Calif.

Effects of hormones on the permeability of target organs have been demonstrated in the case of the uterus and the adrenal. In the present study, TSH was administered by the intracardiac route to one-day old cockerels and its effect observed on thyroidal water content, on the uptake of P^{32}, Na^{24}, and RISA and on the release of pre-labeled thyroidal iodinated compounds. In the saline-treated chick, the distribution of Na^{24} into the thyroid gland was slow, an equilibrium concentration being attained only after 1 - 3 hours. TSH caused a striking increase in the rate of entry of Na^{24} into the gland, with onset as rapid as the effect on release of pre-labeled thyroid "hormone" (approximately 20 minutes latency). An increase in P^{32} uptake was also noted 20 min. after TSH administration; however, the maximum increase was delayed for hours, while that of Na^{24} uptake was almost immediately reached. Thyroidal water concentration was enhanced by TSH within 40 minutes, but did not become maximal until 3 - 4 hours later, at a time when the Na^{24} uptake had returned to pre-treatment levels. The volume of distribution of RISA was unaffected by TSH. Conclusions: TSH increases the rate of entry of water, Na^{24}, and $P^{32}O_4$ into thyroid tissue; the effects are probably not due to capillary dilatation per se; the Na^{24} influx is temporally related to the release of thyroid hormone.

VASODILATION IN MUSCLE DURING ACTIVATION OF THE PATELLAR REFLEX. R.R. Sonnenschein. Dept. of Physiology, Univ. of Calif. Medical Center, Los Angeles.

In mid-collicular decerebrate cats, arterial pressure and total blood flow in the external iliac artery supplying the muscles of the skinned hind leg were continuously recorded. Tension produced by the quadriceps femoris was recorded via a strain gauge coupled to the ankle, the lower end of the femur being fixed. Activation of the reflex for 1 to 2 min. by one per sec. tapping of the patellar tendon was accompanied by 30 to 100% increase in flow with usual latency of 15 to 25 sec.; arterial pressure was usually constant. Recovery to original flow rate occurred in 15 to 30 sec. after cessation of tapping. The hyperemia was not materially affected by atropine, dihydroergotamine or hexamethonium, or by block or section of the sympathetic chain. Electrical stimulation of the intact femoral nerve to elicit muscle activity comparable in frequency and intensity to the reflex response resulted in the same pattern of hyperemia. The same motor response resulting from stimulation of the centrally blocked or cut femoral nerve was accompanied, however, by little or no increase in flow; when present, the onset of hyperemia was delayed. The results suggest that the vasodilation accompanying the patellar reflex is not primarily dependent upon the direct action of local metabolites on the vessels, but instead upon a reflex which originates from the muscle during contraction and activates the vessels via vasomotor (dilator) fibers not running in the sympathetic chain. (Supported by USPHS grant B-1247).

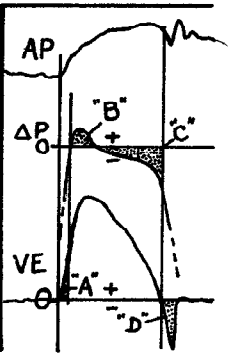
SITE OF NERVE SECTION AND ITS EFFECT ON FIBRILLATION POTENTIALS AND ISOMETRIC CONTRACTIONS OF MUSCLE BUNDLES. Louise B. Speck* and Jerome W. Gersten. University of Colo. School of Medicine, Denver, Colo.

There is evidence that high sciatic or brachial plexus injuries do not result in fibrillation potentials in the leg or forearm until two or three months after injury. This is far longer than the two or three weeks noted after more distal nerve injuries. Experiments were designed to test the hypothesis that the time intervals depend on the site of severance of axonal continuity. The sciatic nerve was sectioned close to the spinal cord on one side of a rat and close to the gastrocnemius muscle on the other side. The onset of fibrillations and the isometric tensions of glycerinated muscle fiber bundles were studied. The tension studies were made at 2, 7, 14, 21, and 30 days after section. Fibrillations and a decrease in tension appeared earlier with the low section than with the high section. An interesting increase of tension above normal level was noted with the 48 hour specimens. These results appear to validate the importance of axonal continuity.

THE SYSTOLIC PRESSURE GRADIENT ACROSS THE NORMAL AORTIC VALVE. M. P. Spencer and F. C. Greiss* Bowman Gray Sch. of Med., Winston-Salem, N.C.

It is commonly accepted that the ventricular pressure (VP) must and does exceed the aortic pressure (AP) throughout the entire systolic ejection period (vis., the cardiac cycle diagram of any standard text of physiology.) To reinvestigate this problem, we measured ventricular ejection with the square-wave non-cannulating E. M. flowmeter attached to the ascending aorta and measured VP to AP gradient (ΔP) by means of a paired gauge method (METH. IN MED. RES., Vol.8, p.341) with lateral pressure needles in the left ventricle and ascending aorta. We have found VP exceeds AP only for a brief interval in early systole.

As illustrated at "A", the initial headward acceleration of blood in the ascending aorta occurs before opening of the aortic valve by release of tension stored in the "cocked" valve leaflets. When VP exceeds AP, the valve opens and blood is accelerated to peak flow in early systole, ("B"). VP falls behind AP soon after the maximum flow and well before maximum AP. This reverse pressure gradient (AP>VP) is present throughout the remaining 2/3 of systole, and decelerates the blood slowly ("C") until valve closure. The valve is then re-"cocked" by rapid fall in VP, ("D").



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(VE) - Ventricular Ejection

EVIDENCE FOR JUNCTIONAL POTENTIALS IN MYOCARDIUM. Nick Sperelakis* and T. Hoshiko. Physiology Dept., Western Reserve Univ. School of Med., Cleveland, Ohio.

Recent work demonstrating that the myocardium is neither a morphological nor a functional syncytium suggests spread of excitation by junctional transmission between cells. In addition, the experimental induction of unidirectional propagation in a predictable direction in frog ventricular strips suggests a chemical process as the probable mechanism of junctional transmission. Therefore, the rising phase of the action potentials of frog ventricular strips was studied for evidence of exaggerated junctional potentials under conditions of impaired junctional transmission. These conditions included low Ca^{++} - high Mg^{++}, hypertonic solutions, high rates of stimulation and passage of direct current through the length of the strip. Three components were identified in the rising phase under control conditions: a slowly rising foot, a rapidly rising middle portion and a final slow rise to the peak. Upon treatment with Mg^{++} and d.c. pulses, the foot was converted to an exaggerated prepotential. The exaggerated prepotential was consistently most prominent in a given cell when the strip was stimulated from one end than when stimulated from the other. Occasionally a pronounced prepotential in isolation alternated with a prepotential plus action potential response. It is suggested that the prepotential is due to a junctional process.

EFFECTS OF THE RETICULAR FORMATION ON THE RECOVERY CYCLE OF A SPINAL REFLEX. D. Spinelli (intr. by C.A.G. Wiersma). Division of Biology, California Institute of Technology, Pasadena, California.

Stimulation of the bulbar reticular formation with 200/sec. rectangular pulses of .1 msec. duration and about seven volts intensity modifies markedly the recovery cycle of the monosynaptic reflex activity. The early facilitation of the second response (between 1.5 and 5 msec.) is strongly depressed without changes in the amplitude of the first one. The late part of the recovery cycle is also markedly affected. The reduction of the second response typical for that part of the cycle is less pronounced and the duration of the cycle is very much reduced. There can be a complete disappearance of depression at 200 msec. during reticular stimulation, whereas without stimulation the amplitude of the second response is usually about 30-40% of the first. A similar reduction of the depression of the response of the dorsal root reflex to a second stimulus has been observed. These findings suggest that higher centers may control excitatory interneuronal chains and that the late part of the recovery cycle of the monosynaptic reflex should not be ascribed to depletion of transmitter substance but to activity of inhibitory interneurones.

UPTAKE OF FREE FATTY ACIDS BY THE LIVER AND BY THE SKELETAL MUSCLE OF THE DOG. John J. Spitzer and B. Issekutz, Jr.* Dept. of Physiology, Hahnemann Medical College & Hospital, and Division of Research, Lankenau Hospital, Philadelphia, Pa.

The liver of anesthetized mongrel dogs removed plasma free fatty acids at an average rate of about 0.3 mEq/hr./100 gr, as determined from the portal-hepatic free fatty acid difference and the estimated hepatic plasma flow. Intravenously administered epinephrine or norepinephrine increased the portal-hepatic difference and the hepatic uptake of free fatty acids. Estimated hepatic plasma flow decreased after norepinephrine, but did not change consistently after epinephrine. Infusion of glucose decreased the portal-hepatic difference and the uptake of free fatty acids by the liver. The uptake of free fatty acids by the skeletal muscle was determined by simultaneously measuring blood flow through the profunda femoris veins, and arterio-venous fatty acid difference. Thigh muscles of the anesthetized dog showed only an occasional uptake of free fatty acids during rest. During direct electrical stimulation the muscles showed a consistent uptake of fatty acids on the stimulated side, whereas the non-stimulated leg continued to release fatty acids. (Supported by the National Heart Institute).

INITIATION AND ABOLITION OF THE ELECTRIC RESPONSE OF THE NERVE FIBER BY THERMAL AND CHEMICAL MEANS. Constantine S Spyropoulos. National Institutes of Health, Bethesda, Md.

Techniques were developed to produce pulses of temperature variation or pulses of variation in the chemical composition of the medium surrounding the node of nerve fibers of Bufo marinus. Application of a pulse of temperature rise during the plateau of a prolonged response resulted in abolition of the response. A pulse of rise [Ca^{++} ion] also brought about abolition. Sudden cooling or removal of [Ca^{++}] or a sudden rise in [K^{+}] during the plateau resulted in prolongation of the response. In the node at rest sudden cooling or sudden rise in [K^{+}] initiated a full-sized response in an all-or-none manner.

CONSTANCY OF OXYGEN USE BY RESTING DOG SKELETAL MUSCLE WITH INCREASED BLOOD FLOW. Wendell N. Stainsby, Dept. of Physiology, College of Medicine, University of Florida, Gainesville.

Oxygen use by the resting *in situ* gastrocnemius-plantaris muscle group of the dog was measured at spontaneous blood flow level and during increased blood flow. The oxygen use was calculated from measurement of venous outflow and arterial and venous blood oxygen contents. The blood flow was increased by reducing or removing sympathetic vasoconstrictor tone. The vasoconstrictor tone was reduced or removed by infusion of three to six hundred ml of donor dog blood, cold block of the sciatic nerve, procaine block of the sciatic nerve, or section of the sciatic nerve. Infusion of donor dog blood did not produce much blood flow elevation, but sometimes (66% of the dogs) doubled oxygen consumption. This increase in oxygen use after infusion of donor dog blood was not related to the blood flow and persisted even after the dogs were bled to 50 mm Hg arterial blood pressure. Cold block of the sciatic nerve produced a three-to-eightfold increase in blood flow and was accompanied by a two-to-fourfold increase in oxygen use. However, there was visible twitching of the muscle. Procaine block and section of the sciatic nerve produced a two-to-threefold increase in blood flow with no change in oxygen use. It is concluded that increasing the blood flow in the absence of chemical or neural stimulation of the muscle does not alter resting oxygen use. (Supported by a research grant RG 6264 from the Public Health Service.)

ON THE POSSIBILITY OF FREEZING LIVING LUNG RAPIDLY. N. C. Staub and W. F. Storey (intr. by J. M. Felts). Cardiovascular Research Institute Univ. of Calif. Med. Center, San Francisco.

To gain new insight into dynamic morphologic and physiologic events that occur simultaneously in the lung, we are attempting by rapid freeze techniques to stop motion and preserve the lung under known conditions. Recent progress in the physics of rapid freezing demonstrates that tissues must be cooled to -140°C in 40 msec to achieve the vitrified state. Except for the outer 20 micra, the lung cannot be cooled that rapidly. However, ice crystal size is submicronic if the tissue can be cooled below -20°C in a few seconds. We pour 1-2 liters of liquid propane (-180°C) over the anterior portion of the right middle lobe in an open-chest anesthetized cat. The temperature at the pleural surface decreases to -100°C in .01-.1 sec and at 2 mm depth to 0°C in 0.1-0.3 sec and to -20°C in 2 sec. Other studies show a frozen margin 1 mm deep in 0.6 sec and 2 mm in 2 sec for a plane surface. At the lobe tip, the favorable geometry greatly increases the frozen depth with time. We have determined time-temperature and time-frozen depth curves for lung tip and plane surface and for liver. After initial freezing, the pyramidal shape lobe tip (2 cm long, 1.5 cm thick at the base) is excised, further cooled to -196°C in liquid nitrogen and later transferred to fixative in absolute alcohol at -60°C for 3-6 weeks. Subsequently it is embedded in nitro-cellulose, sectioned and stained for study. Photographs of lung surface before and after freezing, and after fixation and staining do not reveal any obvious distortion. At present, we are confining our analysis to the outer 2 mm of lung although the tissue appears qualitatively the same to a depth of 3-5 mm. We believe that our cooling is rapid enough to stop reflex activity and mechanical events. (Supported in part by Contract ONR Nonr 222(55))

LOCALIZATION OF BEHAVIORAL CONTROL IN ONE CORTICAL HEMISPHERE. I. Steele-Russell* and S. Ochs. Ind. Univ. Med. School, Indianapolis, Ind.

Bures has shown that spreading depression (SD) can be used to localize a conditioned response to one or the other cerebral hemisphere of rats. Small holes were drilled through the skull on each side leaving dura intact. Cups with removable plugs were implanted on each side so that SD's could be produced at will in one or the other cortex of otherwise intact rats. A small drop of 10 or 25% KCl was used for this purpose. Naive rats learned to bar-press for food pellets while one hemisphere was made inoperative with SD during the training sessions. SD initiated by KCl depressed the cortex for 3-4 hours and each daily session lasted 1 hour. Six days were required to reach a satisfactory level of performance. The "open" cortex was shown to contain the behavioral change; when SD was initiated on that side the animal no longer showed learned behavior. SD was initiated as before on the side origionally "closed" and the learned behavior was exhibited again in full force. Localization of bar-pressing was shown by repeated switching of SD from the trained to the untrained hemisphere and back again. Animals could be studied for up to 12-15 days by means of these chronic implants to permit an investigation of localization of different schedules of behavior as well as interaction of different learning patterns and interhemispheric transfer.

THE EFFECTS OF LEGUMES ON GASEOUS VOLUME AND COMPOSITION OF THE GASTRO-INTESTINAL TRACT. F. R. Steggerda and John Dimmick.* Department of Physiology, University of Illinois, Urbana.

Isocaloric diets containing low and high contents of legumes were consumed by five adult male subjects to record effects on gaseous volume and composition of passed flatus, nitrogen balance and borborygmus. The legumes consumed were in the form of either pork and beans or canned dry lima beans, which made up either 25% or 50% of the caloric intake per day. Each dietary period was two weeks in length. The most striking result was that flatus, collected for at least eight 2 hr. periods during each two week dietary period ranged in volume from average of 17 cc/hr. on the control to 1014 cc/hr. on the bean diets. The actual % CO_2 in the flatus under corresponding conditions changed from 9% to 53%. The % of O_2, H_2 and N_2 decreased when the subjects were on beans, while the CH_4 usually showed an increase. The nitrogen balance studies showed no appreciable difference between diets high and low in legumes. Recorded borborygmus was more pronounced during the bean experimental period than when they were absent from the diet. Preliminary experiments on dogs indicate that the application of moist heat to beans before injecting them into the intestine caused a better absorption of CO_2 from the intestine and less flatulence than obtained with untreated beans.

FETAL HEMOGLOBIN IN YOUNG GOATS FED "ALTITUDE" MILK.
J. Clifford Stickney, Theadore L. Browne* and Edward J. Van Liere, West Virginia Univ. Med. Ctr., Morgantown.

Preliminary studies were made on the fetal hemoglobin (determined by the method of Visser et al, Blood 12: 1004, 1957) of 4 newborn kids fed the milk of goats exposed 4 hr daily to 22,000-25,000 ft simulated altitude in a decompression chamber. Fetal hemoglobin was also determined in 4 control kids beginning at the age of 6 weeks. Fetal hemoglobin, total hemoglobin and red blood cell counts were made on saphenous vein samples of blood. Fetal hemoglobin was found to decline in the experimental group from about 60% at the 2nd week to essentially zero between the 9th and 11th weeks. Comparison of the decline in control and experimental groups from the 6th week suggested no essential differences. This was in spite of an apparent, concurrent rise in total hemoglobin and red blood cell values in the group fed "altitude" milk. (This investigation was supported by research grant RG-5149 from Division of General Medical Sciences, Public Health Service)

EFFECT OF CIGARETTE SMOKING ON THE SERUM POTASSIUM LEVEL IN MAN.
William S. Stirewalt* and Arthur H Steinhaus George Williams College, Chicago

In ten tests on six male college students the smoking of two cigarettes within 12 minutes produced an average rise in serum potassium of 0.14 meq/L (+ 2.89%) followed by an average drop below pre-smoking level of 0.16 meq/L (- 3.37%). The differences were significant on the 0.001 level. It is suggested that the observed elevation of serum potassium levels, as a possible determinant in muscular fatigue, may explain earlier observations in this laboratory of reduced spontaneous running activity of white rats subjected to cigarette-smoke-laden air (Steinhaus, A.H, Schultz, F. and Wilson, W.C. Effect of Tobacco Smoke on Spontaneous Activity of White Rat. Fed. Proc. 11 (1), 1952.) and unreported recent observations following subcutaneous nicotine. Serum was analyzed for potassium with a Coleman Model 11 Flame Spectrophotometer.

EXCITATORY INTERACTION OF CEREBELLAR AND PERIPHERAL INPUTS TO CUNEATE UNITS. A. M. Stoiber and C. D. Barnes*. Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle.

In cats anesthetized with pentobarbital and paralyzed with decamethonium bromide, extracellular microelectrodes were used to record spikes evoked in cuneate neurons by a single test shock to the ipsilateral forepaw. The responses were conditioned by stimulation of either the ipsilateral hemisphere or the anterior lobe of the cerebellum with a single shock or a brief train of stimuli at 312/sec. Most units were excited by the conditioning stimulus (latency 2.5 to 8.5 msec), the latency varying within that range with the strength of stimulus, shortening with maximal stimulus. Those units which followed only low stimulus frequencies (less than 20/sec) were considered to be stimulated orthodromically; more rapid following rates (100/sec) may be indicative of antidromic firing. Excitation more commonly accompanied stimulation of the anterior lobe than of the hemisphere. Convergence of excitatory inputs from both cerebellum and periphery was demonstrated. Orthodromically excited units which would follow rapid rates of the test stimulus alone (100 sec) were inhibited or blocked at conditioning-testing intervals of 15 to 175 msec as previously reported (Fed. Proc. 19:288, 1960). (Supported by grants 2B-5082, B395 and B396 from the National Institute of Neurological Diseases and Blindness.)

VENTILATION OF TERMINAL AIR UNITS. W. F. Storey and N. C. Staub. (intr. by R. J. Havel). Cardiovascular Research Institute, University of California Medical Center, San Francisco, California.

We have developed a rapid freeze technique to study terminal air units at TLC and near FRC in open chest chlorolase--anesthetized cats ventilated by positive pressure respiration with tidal volumes selected at 20-25 ml/kg. A sternal splitting incision provided wide exposure of the lung lobes. Airway pressure varied between 10 cm H_2O (inflation) and 4 cm H_2O (deflation). At a selected time in the respiratory cycle, the right middle lobe tip was rapidly frozen solid by pouring over its surface 1-2 liters of liquid propane (-180°C). The specimen was immediately excised, further cooled in liquid N_2, then placed in an alcohol solution of chemical fixative at -60°C. Fixation and dehydration required 3-6 weeks at this temperature. 180 and 200μ thick serial sections of nitrocellulose-embedded lung were stained with Chromtrope 2R and Fast Green. Diameters of 110 alveolar ducts were measured in 12 sections of 3 lungs near TLC and of 112 ducts in 13 sections of 2 lungs near FRC. Mean duct diameter near TLC (293μ) was 40% greater than mean diameter (208μ) at FRC. We projected photographic film strips of serial sections for measurement of diameters of 520 alveoli in 12 sections of 3 lungs near TLC and 527 alveoli in 9 sections of 2 lungs near FRC. Mean alveolar diameter near TLC (170μ) was 30% greater than mean diameter (130μ) near FRC. The data of Macklin and Hartroft for alveolar diameter in the cat correspond with our figures, at FRC.

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DIRECT RENAL ACTION OF CERTAIN ENZYME INHIBITORS. J.C. Strickler*, R.H. Kessler, and R.F. Pitts, Dept. of Physiology, Cornell Univ. Med. College, New York, New York.

Diuretic compounds such as the organic mercurials and the chlorothiazide derivatives inhibit sodium reabsorption in the renal tubule. Their mode of action remains obscure but is possibly related to an effect upon enzyme systems concerned with ion transport. This inhibition might be effected by blocking an ion carrier directly or by interfering with energy required for active transport. Demonstration in vivo of either of these possible routes of action has failed. Recently Davies (personal communication) has proposed that the electron transport system may serve not only as a major pathway of oxidative metabolism but also as a cation carrier. Inhibition of this enzyme system in the renal tubule might therefore increase water and electrolyte excretion. In the present work agents known to affect electron transport either directly or indirectly were infused into one renal artery of saline loaded dogs. Antimycin A, a potent in vitro inhibitor of the electron transport system, produced a marked increase in sodium and water excretion when infused at a rate of 1 mg/hour. Iodoacetamide, an inhibitor of sulfhydryl containing enzymes in this and other systems, also produced diuresis at the same rate of infusion. These effects could not be attributed to alterations in renal hemodynamics. Dinitrophenol, which acts to uncouple phosphorylation from respiration, did not produce diuresis. Studies of other inhibitors are in progress. Our results suggest that inhibition of the electron transport system in the renal tubule increases water and electrolyte excretion.

STUDIES OF THE EFFECT OF VARIOUS RESPIRATORY MANEUVERS UPON THE NITROGEN ELIMINATION CURVE. Robert C. Stroud. U.S.N. Medical Research Laboratory, New London, Conn.

Alterations in the multiple breath nitrogen elimination curve may be produced by various respiratory maneuvers undertaken during the test, e.g. by a single deep breath, a valsalva maneuver or a voluntary cough. Theoretical considerations imply that the type thus produced depends largely upon the presence or absence of very poorly ventilated and/or "trapped air" spaces. On the basis of observed responses it is concluded that such tests can be of value in supplying useful pulmonary function information.

SEPTAL VERSUS HYPOTHALAMIC CONTROL OF SHIVERING. D.G. Stuart*, Y. Kawamura* and A. Hemingway. Depts. of Physiol., Univ. of California Med. School, Los Angeles, and Osaka Univ. Dental School, Japan.

Experiments from other laboratories have suggested that the septal area of the forebrain is involved in the production of shivering in that lesions of this area in anesthetized cats have inhibited shivering and electrical stimulation of this area in unanesthetized cats and goats has produced shivering. Partial and complete bilateral and unilateral stereotactic electolytic ablations of this area did not affect the shivering response of 9 cats exposed to a standardized cold stress four to six weeks post surgery. Unilateral electrical stimulation of 10 cats lightly anesthetized with alpha chloralase evoked shivering when the stimulating electrode was stereotactically placed at specific sites within the dorso-medial posterior hypothalamus. However, similar stimuli applied to the septal area of the same preparations up to 1.5 mm from the midline, 1 mm rostrad to 1 mm caudad of the anterior commissure produced piloerection without concommitant rage but did not produce shivering. In one cat stimulation of this same region inhibited spontaneously occurring shivering. Piloerection was further evoked by electrical stimulation of the septal area of 3 unanesthetized cats chronically implanted with electrodes, but additionally shivering was evoked in one such cat by stimulation at a site 3 mm rostrad to the region that inhibited shivering. It is suggested that the septal area is implicated in temperature regulation and further that it mediates both facilitory and inhibitory effects on shivering with the specific neuroanatomical pathways yet to be determined.

BRAIN TISSUE OXYGENATION BEFORE, DURING, AND AFTER SIMULATED CARDIAC ARREST. Kenneth Sugioka,M.D., Rodney McKnight,M.D., and David Davis,M.D. (Intr. by John H. Ferguson) Div. Anes., Univ. N. Carolina,Chapel Hill.

Three minutes has been given as the maximal period of time between cessation and restoration of circulation before permanent brain damage occurs. We felt that this time limit was subject to modification depending upon oxygenation of the brain prior to circulatory arrest and upon methods used to reoxygenate the brain. Oxygen tension in the cerebral cortex of dogs was studied using the Beckman oxygen micro-electrode. The brain tissue oxygen tension, the EEG, and arterial pressure were continuously recorded. Cardiac arrest was simulated by occluding venous return to the heart for a period of 3 minutes, at the end of which time the occlusion was released with prompt resumption of circulation. Before circulatory arrest the animals were given successively, room air, 10% O_2, 100% O_2 by means of an endotracheal tube and a piston type pump and then were resuscitated while being hyperventilated with 100% O_2, room air, or 10% CO_2-90% O_2 mixtures. Results indicate that the time interval between circulatory arrest and onset of cerebral anoxia is doubled when the animal is ventilated with 100% O_2 before arrest as against prior ventilation with room air or 10% O_2. Hyperventilation at the time of restoration of circulation with room air, 100% O_2 or O_2-CO_2 mixtures show little difference in the rapidity of onset of brain reoxygenation but show marked differences in the rate and amount of oxygenation of cerebral tissue. In addition to the above findings it has been possible to record at near absolute values, the brain tissue oxygen tension of the animal while breathing oxygen concentrations varying from 10 to 100% O_2. The conclusion drawn from this study is that oxygenation of the brain before circulatory arrest is a factor in determining the time available to restore circulation before irreversible brain damage occurs.

EFFECT OF PARATHYROIDECTOMY ON CALCIUM UPTAKE BY RAT FEMUR AND INCISORS
Alice P.Suiker* and D.Harold Copp. Department of Physiology,University of British Columbia, Vancouver, Canada.

Sixty female rats of the Wistar strain were parathyroidectomized by electro-cautery or sham operated at 6 weeks of age. Two days later, each animal was injected intraperitoneally with high specific activity Ca^{45} (less than 0.01 mg.Ca). Serial blood samples were taken from the tail vein. Animals were killed after 8,24 or 168 hours, and plasma,urine,feces,femur,incisors and total carcass were analyzed for Ca,P and Ca^{45}. Calcium accretion (A) and exchangeable calcium pool (E) were estimated for femur and incisors by the method of Bauer,Carlsson and Lindquist (Kgl.Fysiog.Sällsk.i.Lund Forhandl. 25:1-6,1955). The following results were obtained:

	Sham operated controls.	Parathyroidectomized
Plasma calcium	9.72 mg.%	5.29 mg.%
Femur: Calcium accretion (A)	0.118 mg.Ca/hr.	0.068 mg.Ca/hr.
Net calcium increment	+ 8.4 mg.Ca/week	+ 3.5-5.9 mg.Ca/wk.
Incisors: Calcium accretion (A)	0.067 mg.Ca/hr.	0.046 mg.Ca/hr.
Net calcium increment	+ 8.6 mg.Ca/week	+ 1.9 mg.Ca/week
Exchangeable calcium pool(femur)	5.0%	3.9%

Calcium accretion,net calcium increment and exchangeable calcium pool were all reduced in the parathyroidectomized rats. It is suggested that this may be due to the lowering of the plasma calcium level. Injection of parathyroid extract was found to have the opposite effect.

1) Aided by a grant from the Associate Committee on Dental Research, National Research Council of Canada.

THE INFLUENCE OF SODIUM AND IMPERMEANT ANIONS ON THE RENAL TRANSPORT OF POTASSIUM DURING STOP FLOW. Lawrence P. Sullivan. Dept. Physiol., Univ. of Michigan, Ann Arbor.

The influence of urinary concentrations of sodium and impermeant anions upon the potassium concentrations in serial urine samples collected following a period of ureteral occlusion in a dog undergoing osmotic diuresis was studied. First, in order to increase Na concentrations in stop-flow urine, hypertonic NaCl was infused into the renal artery of a dog shortly before and during a period of stopped flow. The presence of increased sodium concentrations in the nephron had little effect on the maximum potassium concentration achieved during stopped flow and had no effect on the minimum potassium concentration achieved. Secondly, Na_2SO_4 was infused in the same manner. The presence of the impermeant anion in the tubule during stopped flow resulted in the disappearance of any indication of potassium reabsorption and caused secretion of potassium at a site in the nephron where reabsorption ordinarily occurs. Potassium concentrations were maximal in the stop-flow samples containing minimum amounts of sodium. It is concluded that an increase in urinary sodium concentrations has little influence on the development of the potassium stop-flow pattern. Specifically, the minimum potassium concentrations achieved are not the result of decreased secretion due to a lack of sodium but rather are caused by reabsorption in the distal tubule. When Na_2SO_4 is infused, the alterations in the stop-flow potassium concentration pattern that result are caused by the presence of the impermeant anion rather than by an increase in urinary sodium concentrations. (Aid from Am. Heart Assoc.; Life Insurance Med. Research Fund; U.S.P.H.S.)

THE SIGNIFICANCE OF ADRENOCORTICAL STEROIDS ON THE STOMACH.

David C. H. Sun and Harry Shay. Samuel S. Fels Research Inst., Temple Univ. Med. Center, Philadelphia, Pennsylvania.

Opinions differ regarding any gastric secretory or ulcerogenic effect of adrenocortical steroids. A brief review of the literature on this subject will be presented. Our studies on an attempt to clarify the mechanism of action of these steroids on the gastro duodenal segment will be reported. (1) The effect of a single injection of cortisone, hydrocortisone or ACTH on output of acid and pepsin was determined in four Heidenhain pouch dogs. The results showed ACTH and hydrocortisone to be very mild stimulants for acid and pepsin secretion in two dogs and ineffective in the two others. (2) The possible potentiating or synergistic action between hydrocortisone and urecholine on gastric secretion was studied in three Heidenhain pouch dogs --- a synergistic action between hydrocortisone and urecholine on gastric secretion was found in all three dogs. (3) The effect of combined vagal and adrenal stimulation on the stomach --- esophogostomized dogs were sham fed once daily, or 20 units of ACTH Gel intramuscularly daily, or their combination for 3 to 6 months and then autopsied. Combined vagal and adrenal stimulation produced acute erosions and gastritis in the stomach of the dog treated for three months. These data suggest that the adrenal corticoids could contribute to the potential for ulcer occurrence or reactivation, not so much through the increase in secretion they alone might induce, since this is small, but of greater importance in their synergistic action with the vagal mechanism.

PRESSURE RESPONSE IN A SIMPLE ELASTOMERIC MODEL

James H. R. Sutherland. (intro. by R. P. Ahlquist). Dept. of Pharm., Medical College of Ga., Ga.

For many years the thin walled rubber tube has been used as a convenient model to gain insight into the hydrodynamic properties of large arteries. In this study single pressure pulses, uncomplicated by reflected waves, were recorded as they passed down a length of gooch tubing. The pulse was produced by a special injection device with continuously metered volume output. Pressure pulses were obtained at various rates of input and starting pressures, and at several points along the tube. On the thesis that the recorded flow will travel down the tube at the pulse wave velocity, one can easily calculate the increase in volume that will occur at a given point and time in the tube. This increase in volume is equal to the flow rate (cc/sec) divided by the wave velocity (cm/sec). This derived volume increase can then be compared with the volume increase associated with the pressure when the tube is being stretched at the same rate as with the pulse being studied. The dynamic characteristics of a short, blind length of this tube were determined by injecting recorded amounts of fluid at various rates and recording the pressure response. These pressures include viscous as well as distensibility characteristics of the wall. These dynamic distensibility curves give the volume increase that must be associated with a particular pressure level on the pulse pressure curve. The volume increases derived from the inflow-velocity relationship agree well with the volume increases read from the curves of dynamic volume-pressure characteristics of the tube. (Supported by Grant H-3514(C2) from Nat. Heart Inst., USPHS).

A COMPENSATED DICHROMIC DENSITOMETER FOR INDOCYANINE GREEN. William F. Sutterer (intr. by Earl H. Wood). Mayo Clinic, Rochester, Minnesota.

The high optical density (O.D.) of blood is chiefly due to scattering and reflection of light by red cells. Thus O.D. of blood varies with conditions altering shape and degree of aggregation of red cells such as flow, additions of nonisotonic solutions and even variations in CO_2. Good compensation for these nonspecific variations in O.D. of blood can be attained by using two photocell-filter assemblies: (1) the detecting cell, sensitive to light (800 mμ) highly absorbed by the dye and (2) the compensating cell, insensitive to light at 800 mμ and also nonresponsive to changes in light transmission of blood with variations in oxygen saturation. The compensated densitometer consists of a dichroic mirror which reflects light of 800 mμ to the detecting photocell and transmits portions of wavelengths shorter and longer than 800 mμ to a second, compensating, photocell-filter assembly. Sensitivity of this compensating photocell to light on each side of 800 mμ is adjusted so that it is nonresponsive to changes in oxygen saturation in addition to insensitivity to dye. Responses of this densitometer and a conventional densitometer were compared by recording dilution curves simultaneously from the same site in the circulation following injections of 1 ml. of indocyanine green (2.5 mg.) and solutions causing nonspecific changes in O.D. such as 10 per cent NaCl. Peak deflections (9.5 cm.) of the dye curves were equal while those following NaCl were 0.6 and 5.0 cm. for the compensated and conventional devices. Similarly, cessation of flow caused respective deflections of 0.5 and 4.5 cm. Thus a compensated densitometer can increase the reliability of densitometry in blood.

PULMONARY PERFORMANCE OF SMOKERS AND NON-SMOKERS. H. E. Swann, Jr. and T. F. Hatch (intr. by H. S. Belding). Dept. of Occupational Health, University of Pittsburgh.

A group of twelve male cigarette smokers were compared, in respect to pulmonary performance, with non-smokers of about the same ages and size. Measurements included: minute volume, breathing frequency, tidal volume and oxygen consumption, at rest, 4 and 8 kg-meters per second of exercise, together with simultaneous measurements of percentage uptake of ether, carbon monoxide and acetylene from inspired air. These test gases were used to provide indices of ventilatory efficiency, diffusion capacity and pulmonary blood flow, as contributors to overall cardiorespiratory gas exchange capacity. The two groups breathed equal volumes of air at rest and at 4 kg-m./sec. exercise. At 8 kg-m./sec., the median ventilation rate of the smokers was 10% higher than for non-smokers. Oxygen consumption was the same for both groups at all levels of activity. Tidal volumes and breathing frequencies were not sensibly different. Median vital capacity was lower in the group of smokers. Percentage uptake values for ether were slightly reduced in smokers, acetylene uptake more so and carbon monoxide uptake was reduced most of all. Converting these percentages to effective rates of ventilation, diffusion and blood flow, it is shown that the smokers have poorer ventilatory efficiency and substantially reduced diffusion capacity compared with non-smokers. These constituted no functional handicaps at rest or under mild exercise but there is evidence of the beginning need for compensatory increase in ventilation by the smokers under moderately heavy exercise.

THE METABOLISM OF PROGESTERONE BY HUMAN ENDOMETRIUM. Max L. Sweat (Intr. by I. H. Kaiser). Dept. of Obst. and Gyn., U. of Utah College of Med., Salt Lake City, Utah.

Human secretory endometrium (0.5 gm) was incubated for two hours at 37° C in 5 ml of 0.025 M Sodium phosphate buffer (pH 7.4) contain- 10,000 cpm (S.A., 5 mc/mg) 4-C-14 progesterone. Products of the incubation were extracted with lipid solvents and chromatographed in the formanide systems of Zaffaroni. Radioactive areas on the chromatogram were located by means of a strip feed counter, eluted from the strip with methanol and subsequently dried for the preparation of derivitives and rechromatography. The products were identified on the basis of the chromatographic behavior of their free, acetylated and oxidized or reduced forms. At least six products have been demonstrated. Strong evidence has been obtained for the following compounds: pregnanedione, allopregnanedione, 4-pregnene-20α-ol-3-one, 4-pregnene-20β-ol-3-one, and 6 β-hydroxy progesterone. A compound which forms a diacetate has also been isolated and is believed to be 1, 4-pregnadiene-6β, 20α-diol-3-one. The nature of the products demonstrates that endometrium either does not have the capacity to hydroxylate the 17-carbon atom or is able to carry out this reaction only to a limited extent. As it was also demonstrated in this series of experiments that androstenedione-4-C-14 was not converted to estrogens, it is evident that at least two reactions which readily occur in the metabolism of progesterone by the human ovary do not occur in endometrium. (Supported by grant RG 4720. Division of Gen. Med. Sciences. USPHS)

EFFECT OF NITRATE ION ON THE DISTRIBUTION OF SUCROSE IN THE RAT'S VENTRICLE. S. T. Taketa,* C. G. Alexander,* and G. A. Feigen. Dept. of Physiology, Stanford University, Stanford, California.

Electrically driven ventricle strips were maintained at 37° C in either chloride - or nitrate-reference solutions for periods up to 9 hours in the former case and 5 hours in the latter. Both types of solution contained sucrose in a concentration of 600 mg/100 ml. The ventricle strips were removed from the muscle baths, dried, and analyzed for sucrose by the method of Ross and Mokotoff. Since nitrate was found to interfere with the colorimetric determination of sucrose it was necessary to eliminate this anion by passing the solution through an anion exchange resin, Duolite A-101D. Both wet and dry weights were recorded to determine water content. The results show a small but significant increase in the wet weights of the nitrate-treated muscles, amounting to about 2% above those of the chloride controls. The time-course of sucrose distribution can be separated into several kinetic components: an early linear phase, 1, an early exponential phase, 2, and a late exponential phase, 3. The early exponential phase becomes asymptotic to a line parallel to the X-axis which cuts the Y-axis at roughly the value of the extracellular phase in the case of chloride. The delayed exponential phase may represent either the rate of adsorption of sucrose by some structural barrier or, more probably, its slow penetration into the cell, which can be shown by extrapolation to begin very early in the process of sucrose uptake by the muscle.

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ALTERATIONS IN BEHAVIOR AND ENDOCRINE FUNCTION IN RATS WITH HYPOTHALAMIC CONSTANT ESTRUS (CE). S. Taleisnik* and S.M. McCann. Dept. of Physiol., School of Med., Univ. of Pennsylvania, Philadelphia, Pa.

Animals with CE induced by lesions in the suprachiasmatic area showed atrophic ovaries and enlargement of uteri and pars distalis of the pituitary. Ovaries from these rats were filled with large follicles with a scarcity of corpora lutea or their remnants. In contrast to rats without lesions, CE animals failed to show detectable LH in plasma after ovariectomy (ovarian ascorbic acid assay technique). Hypophysial LH content was subnormal in these rats but increased after ovariectomy in spite of reduction of pituitary weight to normal. Rectal temperature was elevated. Their activity (measured in activity cages) was decreased and showed loss of the characteristic cyclic changes which occur in normal females. Mating activity was lost. (Supported by grants USPHS A1236 C3 and AF49(638)-685.)

LOCALIZATION OF ELECTRICAL ACTIVITY IN THE RETINA OF THE UNOPENED CAT EYE BY AN ELECTRODE STAINING METHOD. Kyoji Tasaki* and Kenneth T. Brown. Dept. of Physiol., Univ. of Calif. Medical Center, San Francisco, Calif.

Stainless steel electrodes, of the type described by Green (Nat. 182: 962, 1958), were used to record various types of electrical activity within the cat retina. The retinal depth of each kind of electrical activity was marked by electrolytic deposition of iron from the electrode tip into the tissue. The iron was then stained with ferricyanide to form a dense and sharply delimited spot of Turnbull's blue about 10-20μ in diameter. These spots were observed in histological sections. The membrane having a high electrical resistance was clearly identified as Bruch's membrane. Maximum amplitudes of both a- and c-waves were found immediately adjacent to the retinal side of Bruch's membrane. Maximum amplitudes of both the b-wave, and the dc component of the ERG described by Brown and Wiesel (Amer. J. Ophthal. 46, No. 3, Pt. II: 91, 1958), were found near the outer margin of the inner nuclear layer. The single units which yield only slow potentials in response to light stimuli were also found near the outer margin of the inner nuclear layer. All localizations of this study confirm those of Brown and Wiesel (J. Physiol. 149: 537, 1959; also above reference), who used physiological methods for determining electrode depth. Thus we have also validated their physiological methods, which are superior to histological techniques because of greater convenience and the immediate information they provide on electrode depth.

A THIRD SOMATIC TACTILE SENSORY AREA. Ronald R. Tasker. (intr. by C. N. Woolsey). Univ. of Wisconsin, Madison, Wis.

In addition to the two known cerebral cortical sensory areas SI and SII, Penfield (1954) predicted the presence of a "supplementary sensory" area on the medial hemispheral wall, and Marshall (1949) drew attention to a third area of forearm representation caudal to that of SI. This study has demonstrated in the cat, using the evoked potential technique under pentobarbital or chloralose anesthesia, that a third somatic tactile sensory area, contralateral like SI, does indeed exist. From a hind limb area adjacent to that of SI, its trunk area extends caudally on the medial wall and its forearm area turns laterally onto the convexity in the lateral gyrus where it comes to lie adjacent to the SI forearm area and to merge with the SI face area. (Aided by grant B-732, NINDB, USPHS.)

A STUDY OF THE GENERATOR POTENTIAL OF THE CRAYFISH STRETCH RECEPTOR. Carlo A. Terzuolo and Yoshiaki Washizu*. Dept. of Physiology, University of Minnesota, Minneapolis, Minn.

A study of the generator potential of the tonic stretch receptor cell of the crayfish has shown: a) that the amplitude of a subthreshold generator potential is a linear function of the length of the muscle fiber; b) that the permeability of the cell's membrane is increased as indicated by a decrease in membrane resistance. This change in resistance becomes particularly large at the level of membrane potential at which cathodal block occurs; c) that the amplitude of a subthreshold generator potential is dependent on the value of membrane potential. This was altered by means of directly applied currents. The equilibrium potential of the generator was found to approximate zero membrane potential. The amplitude of the spike potential is not significantly different when the cell is firing because of the applied stretch or when a depolarizing current is applied. This finding is taken to indicate that there is no overlap between the membrane the permeability of which is increased by stretch and the electrically excitable membrane responsible for the spike potential as recorded intracellularly from the soma. In certain conditions, which can be easily reproduced, a spike potential can be recorded intracellularly from the soma while no action potential is propagating along the axon.

KINETICS OF ACETYLCHOLINE RELEASE FROM SINGLE NEUROMUSCULAR JUNCTIONS. R. E. Thies (intr. by V. B. Brooks). Rockefeller Institute, New York.

The kinetics of acetylcholine (ACh) release were studied to determine if ACh content of motor nerve endings is significantly depleted during repetitive stimulation. ACh release per impulse was estimated from amplitudes of end-plate potentials (e.p.p.'s) and from analysis of their 'quantum content'. Excised serratus nerve-muscle preparations from guinea-pigs were stimulated indirectly at frequencies of from 12/min to 20/sec. To permit intracellular recording of e.p.p.'s, neuromuscular transmission was blocked by tubocurarine or HC-3, as well as by increased concentrations of Ca and Mg ions. In 12 trials with 5 junctions, increasing frequency 10-fold from a range of 12/min to 2/sec depressed ACh release per impulse by 1/3 within 1 to 2 seconds. When repetitive stimulation was continued at such elevated but natural frequencies (5/sec to 20/sec), ACh release per impulse declined by another 1/3 in 1 to 8 minutes. Upon return to the original frequency after 3 to 20 minutes, ACh release partially recovered within 5 to 10 seconds, and then increased slowly toward control values. The distinctive rapid and slow changes of ACh release during both depression and recovery are interpreted as evidence for two ACh compartments within nerve endings: the first, 'available' ACh, which is quickly depleted when repetitive stimulation is initiated; and the second, a 'major' ACh store, which is depleted 100 times more slowly. Initial recovery is more than 10 times faster than known rates of ACh synthesis; therefore, it may reflect a rapid restoration of 'available' ACh from the 'major' store. The ensuing gradual recovery is consistent with re-establishment of the 'major' store of ACh by synthesis. The kinetics of ACh release suggest that a limiting rate of ACh movement from the 'major' store to the 'available' store tends to conserve the total ACh content of motor nerve endings.

HYPERCORTICISM AND PHYSIOLOGICAL CHANGES IN THE PACIFIC SALMON (ONCORHYNCHUS TSHAWYTSCHA). Sydney F. Thomas, O.H. Robertson and Marcus Krupp (intr. by J.M. Crismon). Stanford University and Palo Alto Research Foundation.

A study was made of the changes occurring in a number of blood constituents during the spawning migration of the Pacific salmon (O. tshawytscha). The glucose content of the blood increased to about twice that found in salmon in the sea. Glucose tolerance tests showed a slow return of blood glucose to pre-injection levels similar to that observed in diabetes in human beings. Rarely was glucose found in the urine. The concentrations of sodium and potassium decreased, the latter to a marked degree. Cholesterol values rose during the migratory period, then fell at the time of spawning to concentrations lower than those found in sea salmon. Total proteins exhibited a pronounced diminution, including variable reduction in gamma globulins. Protein-bound iodine decreased progressively from the sea to the spawning grounds. Estimations of the number of red blood cells, hemoglobin content and packed cell volume showed fluctuations during the migration period but by the time of spawning the blood picture was in general like that of the sea salmon. Accompanying the above changes was a progressive rise in the concentration of 17-hydroxycorticosteroids to high levels at the time of spawning. Detailed comparison with the characteristic physiological and histological features of Cushing's syndrome revealed many similarities between the spawning salmon and the human patient suffering from Cushing's syndrome.

EFFECT OF CAROTID SINUS DENERVATION AND VAGOTOMY IN ENDOTOXIN SHOCK
Nguyen K. Thuong*, Lerner B. Hinshaw and Lorentz E. Wittmers*. Dept. Physiology, Univ. of Minnesota Med. School, Minneapolis, Minnesota.

The problem of bradycardia in endotoxin shock has been described by many investigators but little is known about the mechanism of this paradoxical phenomenon. The purpose of the present study was to determine the role played by the carotid sinus nerves and the vagi in this kind of shock and their possible relation with the mechanism of bradycardia. Twenty two mongrel adult dogs, anesthetized with Sodium Pentobarbital, were used and divided into five groups; control, sham, denervation of carotid sinus, vagotomy, vagotomy and carotid sinus denervation. Escherichia coli endotoxin (0.55 mg./kg.) was injected intravenously. Mean blood pressure and heart rate were followed for a period of four hours after introduction of endotoxin. In control and sham experiments, bradycardia and hypotension were observed after endotoxin. Following bilateral denervation of the sinus, the dogs presented an improvement both in blood pressure and heart rate after endotoxin. Following sinus denervation and post endotoxin vagotomy, blood pressure and heart rate increased, but the effect was dependent on the time that vagotomy was performed. After pre-endotoxin vagotomy, the animals usually showed bradycardia for a short period following endotoxin. In order to determine whether or not this bradycardia was entirely related to a nervous control, a series of isolated perfused cat hearts was undertaken. In some experiments, bradycardia was observed after endotoxin. The result of this preliminary study indicates that the carotid sinus nerves and the vagi perform an important role in endotoxin shock, but the intimate nature of bradycardia requires a neuro-humoral mechanism rather than nervous control alone.

EFFECTS OF SODIUM AND POTASSIUM CHLORIDE ON THE GROWTH OF BAKER'S YEAST.
Adelaide Tolberg and Nello Pace. Dept. of Physiology, Univ. of California, Berkeley.

Sodium chloride and potassium chloride were added to basal yeast growth medium so that salt concentrations ranged from 0.01 M to 1.0 M or higher. Growth of baker's yeast in these media was measured turbidimetrically, and growth rates were calculated for the exponential phase of growth. In appropriate concentrations either salt caused a decrease in the rate of yeast growth. However, NaCl was found to be appreciably more inhibitory than KCl or than a mixture of equal amounts of NaCl and KCl. For example, the growth rate was decreased 26-43% in cultures containing 0.4 M NaCl, but only 7-13% in those containing 0.4 M KCl, or 0.2 M KCl plus 0.2 M NaCl. The growth rate in cultures containing 0.4 M NaCl plus 0.4 M KCl was decreased 32-34%; i.e., within the range found with 0.4 M NaCl alone. Further studies have shown that addition of small amounts of KCl to the NaCl medium results in a higher growth rate, approximating that in equivalent concentrations of KCl alone. These data suggest that NaCl has a specific inhibitory effect on yeast growth which is not merely an osmotic inhibition. The reversal of NaCl inhibition by small amounts of KCl suggests that the mechanism of inhibition involves a competition of Na with K.
(Supported by the Nat. Inst. of Arthritis and Metab. Dis., U.S.P.H.S.)

LUNG VOLUME AND THE DISTRIBUTION OF VENTILATION IN NORMAL NEWBORN INFANTS. W. H. Tooley*, M. Klaus*, K. H. Weaver*, and J. A. Clements. Cardiovascular Research Institute, U. of Calif. Med. Center, San Francisco.

Lung volumes and the distribution of ventilation were measured while newborn infants were sleeping quietly in a plethysmograph. The nitrogen concentration of the inspired and expired gas was recorded continuously. Tidal volume (V_T) was recorded continuously from changes in pressure in the plethysmograph. The anatomical dead space (V_D) and tha alveolar tidal volume (VA) were calculated from the volume trace and the change in nitrogen concentration during expiration. The log end-expiratory concentration of nitrogen was plotted against the number of breaths and estimation made of the rapidly and slowly ventilated compartments. Four hundred measurements of V_A and V_D were made on 15 newborn infants. The mean value for V_D was 2.2 ml/kg (S.D. 0.6 ml/kg), for V_A 4.2 ml/kg (S.D. 1.4 ml/kg) and for alveolar ventilation ($\dot{V}_A$) 140.4 ml/kg/min (S. D. 30.7 ml/kg/min). 25 nitrogen washouts were done on 13 infants. Each washout curve could be resolved into two components: A slowly ventilated component which varied from 27 to 56% of the FRC and received 3 to 23% of the ventilation and a rapidly ventilated component of 44 to 73% of the FRC which received 77 to 97% of the ventilation. The sum of the volumes of these two components was the FRC (22 ml/kg - S.D. 6.0 ml/kg). The lung volumes (V_D, V_A and FRC), when related to body weight, were similar to normal adult values and the distribution of ventilation was comparable; however, the alveolar ventilation was about double that of resting, normal adults.

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THE INFLUENCE OF VAGAL ACTIVITY ON SYMPATHETIC CONTROL OF HEART RATE. Alan F. Toronto* and Homer R. Warner. Latter-Day Saints Hospital and University of Utah School of Medicine, Salt Lake City, Utah.

Two hypotheses have been suggested to describe the influence of efferent vagal stimulation on the heart rate response (ΔHR) to the frequency (f_1) of efferent cardiac sympathetic nerve stimulation.

Equation 1 $\Delta HR = K$ (for a given f_1)

Equation 2 $\Delta HR = K\ HR_o$ (for a given f_1)

where K is a constant and HR_o is the heart rate when f_1 is zero. HR_o will depend upon the frequency (f_2) of vagal stimulation. In experiments performed on dogs, neither of the above equations proved adequate to predict ΔHR as observed. The following equation, however, did predict ΔHR resulting from a given f_1 over a wide range of values for f_1 and f_2:

Equation 3 $\Delta HR = K(HR_o)^2$.

Although the magnitude of the change in heart rate due to f_1 was affected by vagal stimulation, the kinetics of the heart rate response to a step increase and decrease in (f_1) was unchanged.

THE MECHANISM OF THE RISE IN ARTERIAL PRESSURE FOLLOWING OCCLUSION OF ABDOMINAL ARTERIES. R. W. Torrance and J. H. Siegel (intr. by Dr. Ray G. Daggs). Lab. Cardiovascular Physiology, National Heart Institute, Bethesda, Md.

The rise of arterial pressure following occlusion of the coeliac and mesenteric arteries in the cat under chloralose has been ascribed to a pressoreceptor reflex by Sarnoff and Yamada (Circulation Res. 7: 325, 1959) and to purely mechanical effects by Boyer and Scher (Fed. Proc. 19: 98, 1960). The results of a variety of experiments which included completely isolating the splanchnic vascular bed, both with and without cross perfusion, and the recording of action potentials, indicate that both mechanical and reflex factors are operative. The occlusion of vessels per se increases the peripheral resistance. Also, blood runs off from vessels distal to the occlusion into the active circulation and so tends to increase heart output by acting as an infusion. Pressor reflex effects due to local irritation as ligatures were tightened on arteries were regularly found, but when these were excluded in cross perfusion experiments, reflex pressure changes could still sometimes be elicited by arresting the flow in splanchnic vessels. Whether pressoreceptors, chemoreceptors or ischaemic pain receptors are involved remains to be established.

INTERACTION BETWEEN EXCITATORY AND NONEXCITATORY CUTANEOUS INPUTS IN THE SOMATOSENSORY SYSTEM OF MONKEY. A. L. Towe. Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle.

Macaca mulatta were anesthetized with Dial-urethane and paralyzed when necessary with d-tubocurarine chloride. Single units were isolated in hand area I of the postcentral gyrus by conventional extracellular, KCl-filled micropipette techniques. Each digit of one hand was electrically stimulated via needle electrodes inserted into the skin of the distal phalanges. Units were identified which could be fired by some, but not all, digits. The responsiveness of each unit to the most effective digit was tested at various intervals following stimulation of a slightly excitatory or nonexcitatory digit. In each instance the probability of response was depressed for 0.1 to 0.3 second. The duration and intensity of the depression decreased with greater spatial separation of the conditioning and testing inputs. However, two types of interaction pattern were obtained. Within the first 10 to 20 msec of interaction, before response probability dropped to zero, the latency of response increased in some units, and decreased in others progressively by as much as 6 to 8 msec. Associated with these latency changes was a decrease or an increase in the number of spikes in each discharge, respectively. During recovery from the depression, response latency returned along the same path. Interaction between adjacent digits yielded the shortening-of-latency pattern; widely separated inputs yielded the lengthening-of-latency pattern. These interaction patterns are readily explained if the excitatory field gradually diminishes with distance and gives way to an inhibitory field at greater distances. (Supported by grant B 396 from the National Institute of Neurological Diseases and Blindness, Department of Health, Education and Welfare.)

PHYSIOLOGIC ASPECTS OF PROFOUND HYPOTHERMIA. M. Trede,* A. V. Foote,* and J. V. Maloney, Jr. Department of Surgery, University of California Medical Center, Los Angeles 24, California.

In this study some physiologic effects of rapidly induced profound hypothermia, total circulatory occlusion, and rapid rewarming were examined. Two series of dogs were cooled to below 10°C, using an extracorporeal heat exchanger and either autogenous lung oxygenation or a pump-oxygenator. The following parameters were monitored: arterial and venous BP, EKG, EEG, ventricular contractile force (VCF), temperature gradients between the core and periphery of the animals, arterial pH, pCO_2 and buffer base, as well as arterial and venous oxygen saturations. During cooling a metabolic acidosis developed and this was further increased during circulatory occlusion. VCF increased up to 2 times control values on cooling to 20°C, demonstrating the independence of this factor of stroke volume, as the hearts were kept empty by cardiac bypass. Below 20°C, VCF decreased in association with extreme bradycardia or cardiac arrest. The EEG became isoelectric at about 20°C; on rewarming, activity reappeared at 25°C. It is demonstrated that extreme acidosis at low body temperatures is compatible with survival. (Supported by U. S. Public Health Service grants H-2812 and HTS-5357).

SIMULTANEOUS RECORDING FROM VOMERONASAL AND OLFACTORY NERVES+ Don Tucker (intr. by L. M. Beidler.) Div. of Physiology, Florida State University, Tallahassee, Florida.

The vomeronasal (Jacobson's) organ in the tortoise Gopherus polyphemus has a small opening directed toward the naris and situated in the angle formed by the nasal septum and a lateral projection enclosing the organ. The vomeronasal nerves course obliquely up the septum, enter the cranial cavity between the olfactory nerves, and terminate in the accessary olfactory bulbs at the dorsocaudal aspect of the olfactory bulbs proper. Small twigs of the vomeronasal n. and the olfactory n. were freed in the cranial cavity and recordings made under oil. Differential responses between the two nerves to various odors were observed and were best exemplified by butyric acid for the vomeronasal n. and butyl acetate for the olfactory n. The larger number of odors tested stimulated the olfactory n. most efficiently. These included alcohols, fatty acids and their esters, oils of orange and cloves, ammonia, bromoethane, 2-furaldehyde, 2,3-butanedione, etc. Adrian (L'Annee Psychol. 50:107, 1951) has suggested that the spatial-temporal patterning of excitation in the olfactory organ may be an important basis for discrimination. The system studied in Gopherus is ideal for the demonstration of similar differences because of the extremes in geometry between the vomeronasal and olfactory parts. (Supported in part by USPHS Grant No. B-1083.)

VECTOR ORIENTATION OF P, QRS AND T AXES IN BEEF CATTLE. Wm. C. Van Arsdel III*, Hugo Krueger and Ralph Bogart*, Dairy and Animal Husbandry, Oregon State College, Corvallis, Oregon.

Electrocardiograms were obtained from seven newborn calves and for five of them again at 800 pounds body weight. Six leads were taken in each of two planes to provide frames of reference from which the x, y, and z coordinates for the vectors of the P, QRS and T axes were estimated. In the newborn calf the QRS axis is directed cephalad while the T axis is directed caudad. At 800 pounds body weight, the QRS axis is directed dorsally, the T wave axis, ventrally. These changes in orientation may in large measure be due to the anatomical alterations necessitated by the development of the rumen and other growth processes. The QRS and T waves in the electrocardiogram are usually discordant at birth and remain discordant when adult weights are reached. The P vector at birth points mainly caudad, somewhat downward and slightly to the left; at 800 pounds body weight it points similarly caudad, markedly downward and slightly to the left. The QRS shifts from a mainly forward, slightly elevated position to a position mainly dorsad. The T points initially mainly caudad and slightly downward at birth; at 800 pounds body weight it is mainly ventrad. Breed differences in the positions of the axes were noted at birth and at 800 pounds. (See Oregon Agricultural Experiment Station Bulletin 51).

ASPHYXIAL ELECTROLYTE AND WATER MOVEMENTS IN THE CEREBELLUM.

A. van Harreveld. Division of Biology, California Institute of Technology, Pasadena, California.

A movement of electrolytes from an extraneuronal space mainly into apical dendrites of the cerebral cortex was observed a few minutes after circulatory arrest. A histochemical method based on substitution fixation at -25° C in 90% alcohol saturated with silvernitrate was used to make the distribution of some of the ions visible. By manipulation of the pH of the silver solution this method can be made to reveal the presence of chloride only or in addition to chloride other ions like phosphate and carbonate. When applied to the cerebellum it was found that, whereas in the oxygenated organ the distribution of these ions is rather uniform, in the asphyxiated cerebellum a concentration of these electrolytes had taken place in the large dendrites of the Purkinje cells and in fibers which run the whole length through the molecular layer. The appearance and number of these fibers suggests them to be the Bergmann fibers which are considered to be glial elements. This was supported by the observation that the number of these fibers with respect to the number of Purkinje cells is the same as the numbers of Bergmann's fibers and cells of Purkinje in preparations treated with a glial stain. As was demonstrated for the apical dendrites of the cerebral cortex, the fibers of Bergmann increase markedly in diameter during asphyxiation, indicating that with the electrolytes water is transported into them. The importance of this finding is that the asphyxial movement of electrolytes and water is not restricted to nervous elements but can take place in glial fibers.

A STUDY OF GOITROGENS RELATED TO L-THYROXINE DEIODINATION IN THE RAT. L. Van Middlesworth, S. L. Jones* and C. E. Chapman*. Dept. of Physiology, University of Tennessee, Memphis, Tennessee.

Propylthiouracil has been shown to reduce the deiodination of L-thyroxine by the rat to 50% of control values. This deiodination was studied for the minimal effective dose of propylthiouracil in male rats weighing 250 grams and fed a complete synthetic diet plus 1% $KClO_4$ in drinking water. The animals were injected each day with 2.5 ug L-thyroxine tagged with I^{131} L-thyroxine. After isotopic equilibrium, 2 micrograms of propylthiouracil per 100 gram body weight were injected subcutaneously. The urinary I^{131} was reduced to 71% of control values by the propylthiouracil medication. Therefore, we believe that microgram quantities of propylthiouracil reduced the deiodination of L-thyroxine to 71% of deiodination which occurred in absence of propylthiouracil. Other antithyroid drugs, i.e., methimazole, and aminotriazole and perchlorate did not influence L-thyroxine deiodination. Therefore, these experiments suggest that the most sensitive effect of propylthiouracil in the rat is interference with deiodination of L-thyroxine and this interference is unrelated to the antithyroid property of propylthiouracil.

COUNTERCURRENT DISTRIBUTION STUDIES ON ETHER-SOLUBLE COMPOUNDS CONTAINING Na EXTRACTED FROM DOG KIDNEY. J. C. Vanatta. Univ. of Texas Southwestern Med. School, Dallas, Tex.

Approximately 90 gm. of dog kidney tissue was extracted with ethanol, 1:1 ether-ethanol, and with diethyl ether. The extracting solvents were evaporated and the residue reextracted with diethyl ether, and this evaporated to dryness. This residue contained Na, approximately 8 meq/kg whole kidney. The residue was washed with acetone and the acetone insoluble material dissolved in 150 ml. petroleum ether. An aliquot of this was subjected to a countercurrent distribution using 25% ethanol-water (v/v) as the second phase. A 5 tube system was used, and 35 transfers were carried out with the ethanol-water as the moving phase. The single-withdrawal technique of Craig was used (Weissberger, A. "Techniques of Organic Chemistry", Vol III, Part I, 2nd Ed., New York: Interscience Publishers, Inc., 1956, p. 181). Sodium determinations were carried out on the 31 ethanol-water samples withdrawn, and on the remaining ethanol-water, and petroleum ether phases in the 5 tubes of the system. Two major fractions of Na consistently appeared. The more polar fraction occurred in a curve with its peak in the ninth to sixteenth tube on 5 different countercurrent distributions of 3 different extracts. This curve contained 25 to 35% of the Na in the system. The less polar fraction remained in the petroleum ether phase in the original tube and contained about 45% of the total Na in the system. This would indicate that at least 2 different compounds which bind Na are in the extract. (Supported by research grant H-1574 C-6 from the National Heart Institute, U.S.P.H.)

ADRENERGIC AND CHOLINERGIC-LIKE EFFECTS OF ENDOTOXIN ON THE CARDIOVASCULAR SYSTEM OF THE DOG. James A. Vick* and Lerner B. Hinshaw. Departments of Pharmacology and Physiology, University of Minnesota Medical School, Minneapolis, Minnesota.

Parallel work in this laboratory has shown that the intravenous injection of endotoxin in intact and eviscerated dogs results in a fall in arterial blood pressure and a decrease in heart rate. The following studies were carried out to determine the etiology of the bradycardia and its possible relationship to the eventual peripheral vascular collapse following a lethal injection of endotoxin. Anesthetized intact and eviscerated adult dogs were administered E. coli endotoxin (5 mg./kg.) Heart rate and arterial blood pressure were continuously recorded. The typically observed bradycardia and hypotension after endotoxin were prevented by pre-and post-treatment with atropine. Eserinized eviscerated animals exhibited marked bradycardia and hypotension following endotoxin, with death occurring more rapidly than in the controls. Adrenalectomy facilitated the onset of bradycardia and hypotension after endotoxin, and early death occurred. Adrenalectomized dogs administered atropine showed no change in heart rate after endotoxin and died following three to four hours of progressive hypotension. These findings suggest that both parasympathetic and sympathetic nervous systems may perform crucial roles in endotoxin shock. The drug studies implicate the possible release of acetylcholine at the terminations of the vagi and at postganglionic parasympathetic nerve endings, resulting in cardiac slowing and peripheral vascular collapse. The important role of a functioning sympatho-adrenal system is also indicated.

FIBRINOGEN CONCENTRATIONS IN LYMPH AND BLOOD AS A RESULT OF INDUCED HYPOFIBRINOGENEMIA. A. E. Vita and S. N. Kolmen (intr. by E. A. Blair). The University of Texas Medical Branch, Galveston, Texas.

Hypofibrinogenemia was induced in 16 nembutalized dogs by hemorrhage (30% of blood volume). Effects of hypovolemia were avoided by simultaneous infusion of an equal volume of a red cell-serum suspension. Samples of thoracic duct lymph and femoral arterial blood were collected prior to and following the above procedure. Fibrinogen concentrations, total protein concentrations, hematocrits and lymph flow rates were measured. A state of hypofibrinogenemia without significantly lowered plasma or lymph total protein levels was produced. Both the fibrinogen concentration and total amount of fibrinogen delivered via the thoracic duct were increased following the procedure. It is suggested, therefore, that the fibrinogen which is mobilized as a result of decreased blood levels reaches the vascular bed via lymphatic channels.

EXCITATION AND INHIBITION OF SINGLE TACTILE THALAMIC RELAY NEURONS BY CORTICAL STIMULATION. Hardress J. Waller. Albert Einstein College of Medicine, New York, N. Y.

Comparison of the effects of stimulation of sensorimotor cortex on somatosensory transmission at cuneate and thalamic levels (Fed. Proc., 1960,19:302) showed greater reduction and lower thresholds for reduction of the thalamocortical than the medial lemniscal response to peripheral stimulation. Single neuron activity of the tactile thalamic relay nuclei was studied in cats under local or barbiturate anesthesia, using micropipettes 0.5-1.5 microns tip diameter. Single shocks (0.075 to 1.5 microcoulombs) to forepaw Areas I or II activated more than 75% of neurons which also responded to stimulation of contralateral forepaw. Latencies ranged from 0.3 to 10 msec., but more than 50% were between 0.7 and 2.0 msec. At a constant stimulus intensity, or when the intensity was changed, latencies of discharge of some units showed a discontinuous (bimodal) distribution. This implies synaptic mediation of the later responses. By contrast, the earliest discharges are due to antidromic invasion. Pairing of cortical conditioning and peripheral testing stimuli typically led to reduction in probability of discharge or in mean number of discharges if the cortical stimulus preceded the test response by at least 2 to 6 msec. and not more than 10 to 70 msec. However, responses of other thalamic neurons to stimulation elsewhere (face, hindpaw) were minimally influenced by stimulation of forepaw cortex. Thresholds for depressive interaction were significantly lower with some neurons and higher with others than the thresholds for excitation of the same neuron. The presence of an inhibitory mechanism is inferred because depressive interaction can occur without response of the thalamic neuron to the conditioning cortical stimulus. (Aided by USPHS grant NIH-B1603, C2.)

CALCIUM EXCRETION IN RELATION TO URINE FLOW AND URINE IONIC STRENGTH. Mackenzie Walser. Johns Hopkins School of Medicine, Baltimore, Md.

The mechanisms by which the kidney regulates calcium excretion are unknown. Several observations suggest that much of the variation in calcium excretion which can be induced experimentally is passive, being determined by the electrolyte composition of distal urine and urine flow. NaCl or $NaHCO_3$ diuresis augments calcium excretion more than water or nonelectrolyte diuresis. Na_2SO_4 or $Na_4Fe(CN)_6$ diuresis has a much more pronounced effect. During each type of diuresis, urine calcium concentration tends to be independent of flow, and urine/plasma calcium concentration ratio is largely independent of plasma calcium. During NaCl or Na_2SO_4 diuresis, U/P calcium varies with urine Cl or SO_4 concentration. Even after correction for ion-pair formation, urinary free calcium ion concentration during Na_2SO_4 diuresis increases with urine sulfate concentration. These observations suggest that calcium concentration in distal tubular fluid may be proportional to plasma calcium, the proportionality constant varying with urinary ionic strength. When U/P ratio of ionic strength is unity, U/P ratio of free calcium ion concentration, in either NaCl or Na_2SO_4 diuresis, is close to unity also. The mechanism of the effect of ionic strength is unknown, but may be related to the electrochemical gradient of calcium activity.

MAZE TRAINING FOR HIBERNATING MAMMALS. John T. Walsh* and M. L. Riedesel* (intr. by U. C. Luft). Biology Department, University of New Mexico.

Cortical electrical activity, which may be involved in learning and retention, either ceases (Lyman, 1951. EEG, Clin. Neurophysiol. 3: 255) or is reduced in amplitude (Strumwasser, 1959. Am. J. Physiol. 196:8) in deep hibernation. In this study hibernators were trained for measuring effects of hibernation on retention. A 6-choice-point T maze was found to be suitable for training Mesocrecitus auratus and tame Citellus spilosoma (Nine auratus had a mean of 19 trials for perfect score; Four spilosoma had a mean of 16 trials for perfect score). A visual discrimination box based on observed tendency of C. spilosoma and C. lateralis to seek refuge in holes provided a successful training situation. Correct discrimination of visual clues lead back to home cage. Incorrect choice to drop-out, fall and recapture.

THE EFFECTS OF ACETYLCHOLINE AND DIMETHYLAMINOETHYL ACETATE ON THE RUBIDIUM EFFLUX FROM FROG SARTORIUS. Raymond R. Walsh and John L. R. Edgar, Jr. (intr. by C. A. Maaske). Department of Physiology, University of Colorado School of Medicine, Denver, Colorado.

Both acetylcholine (ACh) and its tertiary analog, dimethylaminoethyl acetate (DMAEA), accelerate the efflux of radioactive rubidium from frog sartorii which have been poisoned with iodoacetate and cyanide. Neither ACh nor DMAEA (at pS 2.5) affect rubidium efflux from normal, non-poisoned muscles. The increase in rubidium efflux from IAA-CN treated muscle is concentration dependent: the rate is increased slightly at pS 3.0 and considerably at pS 2.5. The increased efflux at pS 2.0 is not appreciably greater than that at pS 2.5. In the case of ACh, there is no evidence of autoinhibition at pS 2.0 in contrast to the effect of ACh upon the hydrolytic behavior of acetylcholinesterase. At pH 7.2 ACh is only slightly more effective than equivalent concentrations of DMAEA in accelerating the rubidium efflux. However at pH 8.8 DMAEA is considerably more effective than ACh in increasing rubidium efflux. If the action of ACh and DMAEA herein described is upon the hypothetical membrane receptor substance, then this substance differs in several important aspects from the enzyme, acetylcholinesterase. (Supported, in part, by USPHS Grant No. B-1098.)

CARDIOVASCULAR RESPONSE TO EXERCISE IN SEDENTARY MEN AND ATHLETES.
Yang Wang *, R.J. Marshall*, H.L. Taylor, and J.T. Shepherd.
Dept. of Med. and Lab. of Physiol. Hygiene, Univ. of Minn., Minneapolis, Minn., and Mayo Clinic and Foundation, Rochester, Minn.

Cardiac output (C.O.) was measured by the indicator-dilution technic in 4 sedentary men aged 25, 27, 32 and 35, and in 3 athletes aged 18, 20 and 21 when resting supine, standing, and walking on an inclined treadmill for 3-3.5 minutes. Top work load was achieved at 4.5 m.p.h. on a 12° incline for the sedentary men and on an 18° incline for the athletes. At rest supine the sedentary men had C.O. of 6.1 to 7.5 L/min. and heart rates of 58 to 72/min.; values for the athletes were 6.9 to 8.8 L/min. and 51 to 64/min.. During the last minute of the severest exercise the sedentary men achieved C.O. of 15 to 25 and the athletes 26.5 to 29.5 L/min.; corresponding heart rates were 168 to 183, and 180 to 195/min.. In the sedentary group, the stroke index (S.I.) was 51 to 56 ml. when supine; it fell by a mean of 44% on standing, attained the value at rest supine with very light exercise, and during the severest exercise averaged 9% more than that at rest supine. The athletes had a S.I. of 63 to 73 ml. at rest supine; it fell by a mean of 45% on standing, approached the resting supine value with very light exercise, and during the severest exercise was only 8, 8, and 10% more than at rest supine. Thus although the S.I. is higher at rest in athletes than in sedentary men, the pattern of response to change of posture and to graded exercise is identical. These results strongly suggest that while athletes have a higher initial stroke volume than sedentary men, in neither athletes nor sedentary men are there large changes in stroke volume with increasing severity of exercise, the average increase in stroke volume in both groups being less than 10%.

THE CONTROL OF HEART RATE BY SYMPATHETIC EFFERENT INFORMATION.
Homer R. Warner. University of Utah, Salt Lake City, Utah.

The sympathetic and vagal nerve supply to the heart of mongrel dogs was interrupted bilaterally and the frequency (f) of efferent sympathetic action potentials controlled by electrical stimulation of the preganglionic fibers entering the stellate ganglion. A voltage proportional to f was recorded on multichannel magnetic tape along with the time-course of heart rate calculated by an analog computer from the interval between aortic pressure pulses. The computer was then employed to test the ability of several mathematical models to predict the time-course of heart rate from various patterns of variation in f. The following set of equations was found to make this prediction most successfully:

Equation 1 $A_1 = k_1 f$,

where A_1 is the concentration of noradrenalin outside the cells of the S.A. node and k is a constant.

Equation 2 $d(A_2)/dt = K_2(A_1) - K_2(A_2) - d(AB)/dt$.

A_2 is the concentration of noradrenalin inside S.A. node cells where A_2 reacts with a substance B to form compound AB according to

Equation 3 $d(AB)/dt = k_3(A_2)(B) - k_4(AB)$.

The number of B molecules is limited as shown by

Equation 4 $(AB)_{max.} = (AB) + (B)$.

Finally

Equation 5 $\Delta HR = k_5(AB)$

shows that it is the concentration of AB that determines the change in heart rate (ΔHR). The equation coefficients are empirically adjusted until the heart rate response to a step increase and decrease in f of two different magnitudes is successfully predicted. The equations will then predict the heart rate response to any subsequent pattern of variation in f.

REPETITIVE FIRING IN THE CRAYFISH STRETCH RECEPTORS. Yoshiaki Washizu* and Carlo A. Terzuolo, Dept. of Physiology, University of Minnesota, Minneapolis, Minnesota.

The physical constants of the membrane of the crayfish tonic and phasic stretch receptor cells have been measured. Rheobasic current of the phasic cell is twice the one of the tonic cell. The frequency of the firing of the latter is a log function of the tension of the muscle fiber while the relationship between the frequency of firing and the length of the muscle fiber is about linear. Direct stimulation of the impaled cell, either tonic or phasic, shows that the rate of firing is a linear function of the current's intensity up to a frequency of about 30-40/sec. Thereafter the frequency becomes a log function of current's intensity. Adaptation is prominent in the phasic cell when weak currents (twice the rheobase) are used. In the tonic receptor a repetitive firing can be recorded from the axon when a sudden stretch is applied during cathodal block. Since this result was not duplicated by means of cathodal pulses applied through the impaling microelectrode, the possibility might be suggested that the locus of spike's origin may change. The end of an anodal pulse applied during cathodal block is followed by a train of impulses. The number of spikes in the train depends on the duration and intensity of the anodal pulse. Repetition of the stimulus at short time intervals markedly increases the duration of the train which terminates in a series of oscillations.

OXIDATIVE PHOSPHORYLATION OF HEART MITOCHONDRIA AND TENSION DEVELOPMENT IN GLYCEROL-TREATED MUSCLE FIBERS. Shizuo Watanabe and Lester Packer*. Dept. of Biochem., Dartmouth Med. Sch., Hanover, N.H.

It is a current view that oxidative phosphorylation of mitochondria supplies ATP for muscular contraction. It is the purpose of this paper to present a model experiment in accord with this view.

Rabbit heart mitochondria were isolated in a medium containing EDTA and sucrose. Mitochondria were then washed with 0.33 M sucrose. Fiber bundles of rabbit muscle psoas were extracted for two days at 0° and stored for six months at about -10° in 50% glycerol-water. Fibers were then washed for one day at 0° with 0.15 M KCl buffered with 0.02 M phosphate (pH 7). It was observed that glycerol-treated fibers developed tension neither in a medium containing mitochondria and glutamate, nor in a medium containing mitochondria and ADP, but that fibers did develop tension in a medium containing mitochondria, ADP, and glutamate (0.1 M KCl buffered with 0.02 M phosphate, pH 7). Therefore, tension development was evoked by ATP produced by mitochondrial oxidative phosphorylation of ADP.

The respiration of the mitochondrial suspension was traced by a polarographic oxygen electrode. Simultaneously, the tension development was recorded by using a strain gauge transducer. It was then found that the tension development run very closely with the oxidative phosphorylation in a wide range of ADP concentrations (10^{-5} - 10^{-3} M), and that the half-maximum tension was obtained when the concentration of ADP was 2.5×10^{-4} M.

The results obtained have suggested that tension response is faster than ATP-production. This suggestion is significant in a long standing question: the ATP-binding mechanism or the ATP-splitting mechanism.

(This work was supported by National Heart Institute Grant H-3598).

POSTSYSTOLIC MYOCARDIAL AUGMENTATION: EXPERIMENTAL DEVELOPMENT AND CLINICAL APPLICATIONS. David H. Watkins and E.R. Duchesne (intr. by Clifford A. Angerer). Professorial Surgical Unit of the Denver General Hospital, Denver, Colo.

The presentation is designed to demonstrate a method, postsystolic myocardial augmentation, by which the work load of the myocardium may be electively decreased in pathological conditions while at the same time the coronary arterial flow is increased without reduction of the total circulating blood volume. The presentation will demonstrate by lantern slides the mechanical apparatus which has been designed to provide an atraumatic impulse to each unit stroke volume of the cardiac output, together with the device which synchronizes the output of the assisting mechanism with the desired phase of the cardiac cycle according to the specific need of the hemodynamic situation present and the means by which the volume, length and phase of the augmenting impulse may be varied to adapt to the hemodynamic situation present. Studies of the experimental methods involved, including a short 26 mm. movie film strip, will be shown and these will also demonstrate electrocardiographic and manometric studies of failing hearts before, during and after the application of the apparatus for postsystolic myocardial augmentation. It will be further shown how this apparatus has been used for the various clinical conditions for which it was designed. The advantages of this method over other attempted methods of assisted circulation will be discussed.

THYROID STATUS AND TISSUE OXYGEN CONSUMPTION RATES. A. Kurt Weiss. Univ. of Miami School of Med., Coral Gables, Fla.

The thyroid gland regulates the metabolic rate of the body by markedly altering the oxygen consumption levels of a few selected tissues only. Other tissues are apparently either refractory or much less responsive to the effects of alterations of the thyroid hormone level. Thus, certain types of smooth muscle, the cerebral cortex, the spleen, thymus, testis, seminal vesicle, lung and dermis from hyperthyroid, euthyroid and hypothroid rats show only very slight variations in their oxygen consumptions (Weiss, Am. J. Physiol. 188:430, 1957). On the other hand, liver, diaphragm, heart ventricle and kidney cortex preparations from hyperthyroid rats show higher oxygen consumption rates when compared with tissues from euthyroid animals. Rat epidermis falls into yet another catagory. In hyperthyroid rats, the epidermis respires either at a similar or at a slightly lower level than in euthyroid rats, while in hypothyroid rats a very marked reduction in the oxygen consumption of the epidermis is observed. This suggests that although the respiratory level of rat epidermis is at a maximum in the euthyroid rat, it is the thyroid hormone level which regulates the rate of epidermal oxygen consumption, since in the absence of normal thyroid function maximal oxygen consumption levels cannot be attained. (Supported in part by grant RG-5100 from the National Institutes of Health.)

Variations in Left Atrial Pressure Patterns in the Intact Dog A. N. Welter*, Hamilton, L. H., and Henschel*, E. O. (Introduced by A. F. Rieck), Department of Physiology, Marquette University School of Medicine and Woods Veterans Administration Center, Milwaukee, Wisconsin

Right and left atrial pressure patterns were recorded simultaneously in the closed chest dog. Left heart catheterizations were performed by either the transcarinal puncture technique (Henschel, E. O., Hamilton, L. H. and G. R. L. Rainbow. J. Appl. Physiol. 11 (2): 319, 1957) or the transseptal technique demonstrated by D. Donald at the Fall Meeting of the American Physiological Society, September 8-11, 1959, Urbana. Pressures were recorded at selected time intervals with the dogs maintained for one hour in the supine, left lateral, right lateral or prone positions. In a second series of experiments the position was changed at fifteen minute intervals and pressure patterns were recorded at regular time intervals. The mean left atrial pressure was normal and did not change during an experiment while marked variations were seen in the pressure pattern. Those patterns seen most frequently were of the following types: a) fusion of the "v" and "a" waves, b) fusion of the "a" and "c" waves, c) complete fusion of the "a", "c" and "v" waves and d) independent "a", "c" and "v" waves. Shifts in the pressure pattern occurred spontaneously, suggesting that the left atrial pressure pattern was labile.

THE EFFECT OF STRETCH ON THE OXYGEN CONSUMPTION OF FROG SARTORIUS MUSCLE. W. J. Whalen.* Dept. of Physiology, College of Med., State Univ. of Iowa, Iowa City, Iowa.

Previous experiments showed that the QO_2 of isolated strips of heart muscle increased with increasing length. It was of interest to determine whether, under the same conditions, the isolated frog sartorius muscle would respond similarly. One of a pair of muscles from a small R. pipiens was placed in a microrespirometer containing Ringers-bicarbonate solution maintained at 27.5° C. The muscle was stretched to rest length and held there to serve as a control. The other muscle of the pair was prepared in like manner but was allowed to remain at the minimum length for the first hour. In succeeding one hour periods it was stretched to rest length. The QO_2 increased as length increased, whether the muscle was resting or stimulated. (Feng, T.P., J. Physiol. 74:441, 1932). The quantitative relationships of length, tension and QO_2 will be discussed. (Supported by USPHS grant H-5390.)

TOTAL HEMISPHERECTOMY IN THE MONKEY. (16-mm. Motion Picture With Sound and Color) **R. J. White, L. H. Schreiner, C. S. MacCarty and J. H. Grindlay (intr. by E. H. Wood). Mayo Clinic and Mayo Foundation, Rochester, Minnesota.**

Although many fundamental contributions have been made in the field of experimental neurology through the study of animals from which large portions of the brain have been removed or destroyed, little experimental work has been done in primates to define the anatomic limitations of resectability compatible with consciousness or survival, nor has the functional recovery following total ablation of a cerebral hemisphere been examined extensively. To study the method and effects of total cerebral hemispherectomy in the primate, monkeys have been subjected to complete unilateral removal of all the cerebral cortex, basal ganglia, internal capsule and thalamus at one operation. This film deals with: (1) the surgical procedure, (2) the anatomic perimeters of the cerebral extirpation and (3) the resultant neurologic recovery in animals during the first postoperative year.

ACTIVITY IN THE PULMONARY EFFERENT NERVES OF THE CAT. J. G. Widdicombe. (intr. by Kenneth Brown). Dept. of Physiology, St. Bartholomew's Hospital Medical School, London.

Activity has been recorded from 51 single efferent nerve fibers in the pulmonary branches of the vagi of cats. The right thoracic vagus was first exteriorized and the chest then closed so that action potentials could be studied both during spontaneous breathing and during the vigorous movements of coughing which would disturb intrathoracic nerve recording. In eupnea, about half the efferent nerve fibers showed a discharge in expiration only. With ventilation by a pump, the discharge was usually synchronous with deflation and absent in inflation; increasing the FRC decreased the discharge. These rhythmical variations usually disappeared on cutting the left vagus. The most active discharge down the fibers was seen on making the animal cough, either by touching the laryngeal or tracheal mucosa or by inhalation of an irritant gas. After the latter procedure, and also in one cat with purulent pneumonia, spontaneous activity was synchronous with inspiration instead of expiration, presumably due to sensitization of cough receptors also excited by inflation. Hypoxia and hypercapnia increased the discharge frequency, and systemic arterial hypertension inhibited it. From the pattern of activity in the fibers it is thought most likely that they are bronchoconstrictor, and if so the results suggest that some of the bronchial narrowing in expiration is active and its inhibition during inflation may be reflex in origin from the lung.

BLOOD DISTRIBUTION DURING CARDIAC ARREST INDUCED BY HYPOTHERMIA. Paul W. Willard* and Steven M. Horvath. Dept. of Physiol., The Lankenau Hosp. and Jefferson Med. Coll., Philadelphia, Pa.

Blood volume and distribution were determined during euthermia and submersion hypothermia in rats by the Cr^{51} technique. At cardiac arrest (12°C) blood volume of the entire body, lung, spleen, liver, kidney, heart, diaphragm and gastrocnemius muscle were measured. Under hypothermia blood pooled in the lung and spleen. The liver responded by an increase in blood volume, but not by a significant amount. When the control (4.92 ml/100 gm) and hypothermic (7.89 ml/100 gm) liver red cell mass were compared an increased amount was noted, however, this may be explained by the difference in size of hematocrit of the two groups of animals. The kidney and muscle tissue showed no increase in blood volume. A preliminary study indicated that splenectomized animals had similar blood distribution to non-splenectomized animals. In splenectomized animals there was more blood accumulation in the visceral organs during cooling than in non-splenectomized animals.

ASPHYXIAL TOLERANCE BY RHESUS MONKEYS. W. F. Windle and J. B. Ranck, Jr.* Laboratory of Neuroanatomical Sciences, NINDB, NIH, USPHS, DHEW, Bethesda, Maryland.

Asphyxiation of fetal monkeys in amnio induced rhythmical gasping and slowing of the heart. They survived for 16-17 minutes, resuscitation being effected even after gasping had ceased, for the heart continued to beat for some time; all resuscitated monkeys exhibited neurological deficits and had structural brain damage. Newborn monkeys placed in N_2 survived only about 11 minutes, cardiac failure occurring within 2 or 3 minutes after gasping stopped; no brain damage was encountered in these. Young adult monkeys were asphyxiated in N_2 and 5% CO_2. One with cardiac arrest required resuscitation by opening the thorax and massaging the heart. One experienced four consecutive asphyxial episodes. The heart of the adult failed at the time respiration ceased. The animals showed neither neurological deficits nor structural brain damage. The heart of the fetus is more resistant to asphyxial damage than the brain. The reverse is true of the newborn and adult. Cardiac resistance to asphyxial damage in monkey decreases from late fetal to adult life; this may be due in some measure to reduction in cardiac glycogen reserves.

THE RELATIONSHIP OF CALCIUM UPTAKE TO CONTRACTION IN GUINEA PIG ATRIA. Saul Winegrad (intr. by A. M. Shanes). Natl. Insts. of Health, Bethesda, Md.

Heilbrunn and Wiercinski (J. Cell. & Comp. Phys. 29, 15, 1947), Bianchi and Shanes (J. Gen. Phys. 42, 803, 1959), and others have implicated Ca^{++} as a coupling agent between excitation and contraction in skeletal muscle. To test this possibility in heart muscle the uptake of Ca^{45} by guinea pig left atrial appendages at rest and during contraction was studied. The resting uptake was found to be 15 pM/(gm-sec) or 0.015 pM/(cm^2-sec), and the additional uptake per beat at a contraction rate of 30/min., 550 pM/gm or 0.55 pM/cm^2. If it is assumed that the action potential is 140 msec long and the additional Ca^{++} uptake with contraction occurs during this period, then the rate of Ca^{++} movement during the action potential is 3.9 pM/(cm^2-sec) or 260 times that at rest. The increase in the strength of contraction produced by increasing the rate of contraction (the staircase phenomenon) was accompanied by an almost parallel increase in the Ca^{++} taken up per beat. These data are consistent with the proposed role of Ca^{++} as a coupling agent in heart muscle contraction.

STEADY STATE TEMPERATURE DISTRIBUTION IN THE HUMAN. E. H. Wissler (intr. by R. G. Daggs), Dept. of Chemical Engineering, University of Texas, Austin, Texas.

A mathematical model of the physical aspects of the human thermal system has been developed. It permits: 1) different segmental (trunk, head, arms, legs) rates of heat production; 2) heat transmission by tissue conduction, blood convection, and counter-current exchange between arteries and veins; 3) heat transfer by convection and evaporation from the respiratory tract and by radiation, convection and evaporation from the skin surface. Computations predict the steady state for the nude basal man to occur in still air at 30.4°C. resulting in a trunk axial temperature of 37°C. and skin surface temperatures of 35.8° for the trunk, 36.1° for the head, 34.1° for the arms, and 34.0° for the legs. The radial temperature distribution in the trunk calculates to be nearly uniform with a drop of 1 C° across the outer fifth of the radius. In the arms and legs the distribution is nearly parabolic. These results correspond closely to published measurements. Hence the mathematical model goes far to account for the temperature distribution of the body on a purely physical basis. (Supported by a U.S. Army Contract No. DA-49-007-MD-2005).

SOMATIC AFFERENT ACTIVITY RECORDED FROM THE BRAINSTEM OF THE ALLIGATOR. Paul Witkovsky and Lawrence Kruger. Depts. of Zoology and Anatomy, U.C.L.A. (intr. by B.C. Abbott)

Single unit activity from the dorsal column nuclei and spinal nucleus of the fifth nerve has been recorded with a microelectrode in response to physiological stimuli applied peripherally. Units were classified according to modality, rate of adaptation and location and extent of receptive fields. Units responding to light touch, pressure and joint movement have been identified. Almost all units possess ipsilateral receptive fields with the limb regions being most densely innervated. The spatial pattern of response in the brainstem suggests that the hindlimb and tail are represented medially at all antero-posterior levels of the nuclei with the thorax and forelimbs being represented more laterally, respectively. A spatial organization of modalities is not apparent. Touch and pressure stimuli applied to the face evoke activity in the spinal nucleus of the fifth nerve. The spatial and modality representation of the dorsal column nuclei in the alligator does not markedly differ from that of the cat. (Supported by U.S.P.H.S. grant B-2684)

INFLUENCE OF TRIPARANOL (MER/29) ON THE BLOOD CHOLESTEROL AND CERTAIN ENDOCRINE ORGANS OF EGG-LAYING HENS. Harry Y.C. Wong, Frances M. Farrow* and Rose Y. Shim*. Dept. of Physiology, Howard University School of Medicine, Washington, D. C.

It has been reported by Blohm and associates (Arch. Biochem. 85:250, 1959) that Triparanol inhibits cholesterol synthesis in the rat and causes hypertrophy of the adrenal glands at high doses of this drug. Several groups of 37 week old egg laying hens were injected subcutaneously with 6.25, 12.5 and 25 mg. of Triparanol in olive oil per kilogram of body weight five times a week for nine weeks. There were no significant changes in the blood cholesterol during the investigation. However, it was observed that different levels of the blood cholesterol of hens were partially related to the egg-laying cycle. When the hens were laying frequently, the blood cholesterol decreased accordingly and when they stopped laying, the blood cholesterol was increased. Therefore, it seems that the egg-yolk may act as an excretory pathway for the elimination of blood cholesterol in hens. Triparanol has no influence in reducing the yolk cholesterol of eggs when compared with the hens on plain mash. The thyroid and adrenal weights of the hens injected with Triparanol were similar to the hens on plain mash. (Supported by grants from National Heart Institute, H-2420 (C3), American and Washington Heart Associations and Kerr Chickeries).

ON THE MECHANISM OF INTERCELLULAR TRANSMISSION IN RAT ATRIUM. J. W. Woodbury and W. E. Crill*. Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle.

A current flowed through a single rat atrial cell via an intracellularly placed electrode produces appreciable changes in the transmembrane potential of surrounding cells. A map of the equipotential changes for a given applied current is roughly elliptical with the long axis in the fiber direction. The decline of membrane voltage with distance is about twice as steep perpendicular to the fibers as parallel to them. If a two-dimensional equivalent of the cable equation is used, the space constant is about 130 μ in the fiber direction. Since cell dimensions are 10 μ by 20 μ by 80 μ, it follows that current flow in one cell produces potential changes in adjacent cells. Therefore, a sufficient postulate is that spread of excitation in atrium is mediated by local circuit current flow. Since current does spread efficiently from cell to cell, there must be low-resistance intercellular connections, presumably at the intercalated discs. The specific resistance of the disc membrane, calculated on the basis of the electronmicrographic spacing of about 80 Å between the opposing membranes, must be about 0.3 ohm-cm^2 if most local current flow is to enter adjacent cells instead of escaping through the fluid gap between discs. This value is so low that the surprisingly short space constant cannot be attributed to the resistance of the intercalated discs. Rather, the small space constant probably reflects the large membrane area per unit volume in cardiac tissue resulting in a low effective specific resistance of non-disc membrane. (Supported in part by grant B-1752 and 2B-5269 from the National Institutes of Health.)

EFFECT OF ALCOHOL AND HISTAMINE ON PANCREATIC SECRETION. E. R. Woodward, B. E. Walton,* and H. Schapiro,* Department of Surgery University of Florida, College of Medicine, Gainesville. Supported by NIH Research Grant No. A2372.

Alcohol stimulates pancreatic secretion indirectly, through increasing the secretion of acid gastric juice. Upon passage into the duodenum, gastric HCl activates the secretin mechanism. Histamine, however, has been considered a direct stimulant of pancreatic secretion, somewhat less potent than secretin. In present experiment, seven dogs were prepared with Thomas cannulas for the collection of pancreatic juice. Secretory responses were determined to (1) i.v. secretin 1 cl.u./kg. (2) sub-q histamine 0.1 mg./kg. (3) i.v. 5% ethyl alcohol 200 cc and (4) oral 5% alcohol 200 cc. Collections made at ten min. intervals, and volume, bicarbonate, and amylase determined. Total gastrectomy was then performed, and all studies repeated after recovery. Secretin resulted in an immediate increase in volume and bicarbonate and decrease in amylase. This response was unaltered by total gastrectomy. Histamine stimulated pancreatic secretion after a latent period of 20-40 min., the juice resembling secretin juice in composition. Total gastrectomy completely abolished the response to histamine. Oral and i.v. alcohol also produced "secretin" juice, after a latent period of 40-80 min. These responses also were entirely absent after total gastrectomy. It is concluded that histamine did not stimulate the pancreas directly. It appears that histamine, like alcohol, depends on the secretion of acid gastric juice which in turn activates the secretin mechanism when it comes in contact with duodenal mucosa. The normal response to secretin after total gastrectomy indicates the ability of the pancreas was probably not impaired.

STRAIN AND SEX DIFFERENCES IN THRESHOLD AND PATTERN OF ELECTROSHOCK CONVULSIONS IN RATS. D.E. Woolley*, M.R. Rosenzweig*, D. Krech*, E.L. Bennett*, and P.S. Timiras. Depts. of Physiology and Psychology and Lawrence Radiation Lab., Univ. of California, Berkeley.

Previous studies have shown correlated differences in adaptive behavior and brain chemistry among strains of rats. Our present objectives were to determine whether these correlated characteristics were associated with other parameters of brain function, and whether sex, body weight and brain weight influence brain excitability. Of the two strains studied, the S_1 are better learners, have higher brain cholinesterase (ChE) activity and greater acetylcholine (ACh) concentration than the S_3. In each strain 36 male and 36 female adult animals were studied. Brain excitability was assessed by the minimal electroshock seizure threshold (EST) test. Spread of excitation was determined from duration of flexor and extensor tonic components of maximal convulsions. The results indicate that the method of electroshock convulsions, largely restricted to pharmacological studies, is useful in investigating the effects of other factors on brain function: 1) EST is markedly lower in females than in males. Female higher brain excitability is tentatively attributed to hormonal influences (mostly estradiol.) 2) Each strain-sex group shows positive correlation between EST and body weight. No correlations are found with brain weight. 3) S_1 rats show higher brain excitability than S_3. 4) Duration of extensor tonic phase of maximal convulsions is shorter in S_1 than in S_3 rats. Since S_1 rats have a higher brain ACh-ChE, these findings suggest that spread of excitation is related to this chemical system. Thus, the strain superior in learning ability and higher in brain ACh-ChE, also has higher brain excitability as shown by the EST. (Supported by grants M 1292 USPHS and S-60-14 NAS)

GROWTH OF WHITE MICE DURING LIFE-LONG CENTRIFUGATION. Charles C. Wunder and Stanley R. Briney*. Dept. of Physiology, College of Medicine, State Univ. of Iowa, Iowa City, Iowa.

This study deals with long-term role of gravity in control of growth. Although increased field imposes a smaller limiting size upon mice, considerable growth is possible for individuals which can adapt. As previously reported, decreased body mass occurs during the first week of artificially increased gravity. The extent of this decrease depended upon centrifugal field intensity and age. Some skeletal structures continued to grow during this period, the initial effect being primarily upon soft tissues. These animals have been exposed to fields of from 15 to 14 G's. Age at onset of exposure varied from one to 11 weeks. In fields as intense as 7 G's, surviving mice regained the lost mass and for a period of time grew almost as rapidly as controls. For example mice weighing 11 grams, placed in the centrifuge at 5 weeks of age, attained an average mass of 19 ±1 gm. Some survived for one year. Controls attained 28 ± 1 gm. while those at 2 G's attained 22 ± 1 gm. Some of these 2-G mice lived 2 years and reproduced during centrifugation. After several weeks of exposure skeletal growth rates finally decreased as did the rates of total growth.

THE EFFECT OF COLD ON THE VASOMOTOR ACTIVITY OF AN ISOLATED SKELETAL MUSCLE. Lloyd R. Yonce. (intr. by A.T. Miller, Jr.). Univ. of North Carolina School of Med., Chapel Hill, N.C.

This study was designed to show the circulatory response of an isolated skeletal muscle to decreasing temperature. The left gracilis muscle of 17 dogs was acutely denervated and separated from the surrounding tissue. All blood vessels except the major artery and vein were ligated. The muscle was placed in a temperature-controlled oil bath and the muscle artery connected to the femoral artery by polyethylene cannulas. The arterial blood supply to the muscle was maintained at the same temperature as the oil bath. Venous blood flow was measured with a drop recorder. The circulatory resistance was calculated as the quotient of the arterial blood pressure divided by the venous blood flow per minute per 100 gm tissue. The temperature was decreased from about 37.5° C to about 15° C in 30-50 minutes. In 12 of the muscles the resistance decreased as the temperature was lowered from 37.5°, followed by a secondary rise in resistance beginning at temperatures ranging from 35° to 25° and continuing down to the lowest temperatures reached (about 15°). In 4 experiments the resistance increased steadily as the temperature was lowered. In one experiment the resistance continued to decrease when the temperature was lowered to 15°. Other workers have shown an efflux of potassium from skeletal muscle when its temperature is lowered. This increased extracellular potassium may be responsible for the vasomotor response to cold. Potassium concentration of the venous blood was measured as the temperature was decreased in 11 of the muscles. There appeared to be no correlation between the potassium concentration of the blood and the vasomotor response to temperature. (Supported by Army Contract No. DA-49-007-MD-1002).

EFFECT OF DIFFUSION IN GAS PHASE ON ALVEOLAR INHOMOGENEITY. A. C. Young and C. J. Martin*. Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine and Firland Sanitorium, Seattle.

Any lack of uniformity of alveolar gas resulting from a diffusion gradient will be erased more rapidly in helium than in oxygen since the diffusion coefficient of helium is three times that of oxygen. The degree of homogeneity of alveolar air was studied in 15 subjects who breathed a helium-oxygen mixture or 100% oxygen. The group included normal men and women and patients with tuberculosis, compensatory overdistention following pneumonectomy, bullous lung disease or obstructive emphysema. A subject's lungs were first flushed with one of the gases. He then was given a breath of the same gas containing a trace of nitrogen by means of a bellows system controlling both volume and rate. At the end of inspiration he held his breath. The duration of this breath-holding was varied to allow time for diffusion. The nonuniformity of the expired nitrogen concentration was used as a criterion of alveolar inhomogeneity. The homogeneity of the alveolar air was no greater when the lungs were filled with helium than when they were filled with oxygen. The slope of the alveolar plateau for corresponding breath-holding time was not appreciably different for the two gas mixtures. There is no evidence in these studies that a significant diffusion gradient in gas phase is present in the individual lung unit.

EFFECT OF NUTRIENT SUPPLEMENTS DURING WORK ON PERFORMANCE IN DOGS. D. R. Young* (intr. by N. Pace), Quartermaster Food and Container Institute for the Armed Forces, Chicago, Ill.

Effect of consuming fluid supplements during work on maximum aerobic work capacity has been examined. The data presented here have been drawn from a series of work tests conducted with pure-bred, male, beagle dogs; the tests followed a common plan of treadmill running at a speed of 3.63 mph and a constant work load of 202.9 kg.-m./min. Initially, systematic studies were undertaken to determine energy conversion and the nature of the changes in blood sugar during work. In the post-absorptive dog 95% of the potential energy for work was derived from the metabolism of fat. Of the fat-energy approximately 32% was oxidized directly as fat; 64% was oxidized as carbohydrate. The blood sugar declined systematically during the early phase of exhaustive running then tended to rise. In studies of the effect of nutrient supplements, whole milk with added copper and iron was used as the control to study the comparative effect on performance of providing no supplement, water, or separately pure solutions of lactalbumin, glucose, phospholipids, or water-soluble vitamins (exclusive of Vitamin C). Consumption of milk, vitamins, or phospholipids during work led to a significant reduction (-54%) in work capability. The intake of glucose or protein was neither beneficial nor detrimental. The cardio-respiratory responses and changes in blood levels of glucose, fructose, pyruvate, urea, and N.P.N. were for the most part unrelated to variations in performance. Blood lactose and galactose, however, were elevated in the milk-treated animals. Preliminary results of the effect of supplementation with fat emulsions will be presented.

RENAL REGULATION OF URATE EXCRETION IN DALMATIAN AND NON-DALMATIAN DOGS. **T.F.Yü, L.Berger*, S.Kupfer and A.B.Gutman*. Mount Sinai Hosp., New York.**

Previous reports indicate that the Dalmatian is characterized by defective tubular reabsorption of the filtered urate, and that tubular secretion of urate occurs. In the non-Dalmatian dog, urate clearance: GFR ratios are low, implying reabsorption of the filtered urate; tubular secretion of urate has not been reported. Present clearance studies in 6 Dalmatians and 11 non-Dalmatians, with appropriate urate loading and osmotic diuresis, yielded urate:GFR ratios >1.1 (maximum 2.0 and 1.7 respectively), indicating tubular secretion of urate in both Dalmatian and non-Dalmatian dogs. Stop-flow studies in 2 pedigreed Dalmatians revealed maximal net urate secretion (mean U/P urate:creatinine ratio, 1.9) in the proximal segment and a lesser peak (mean ratio, 1.6) in the distal segment. Both secretory peaks were abolished by probenecid or, in massive dosage, by PAH, resulting in U/P urate:creatinine ratios < 1, indicating some reabsorption of urate particularly in the proximal segment (mean minimal ratio, 0.6). Stop-flow studies in 13 mongrels revealed peak net urate secretion in the distal segment (U/P urate: creatinine ratios to 1.6) and maximal net urate reabsorption in the proximal segment, partially inhibited by probenecid. It is concluded that in the dog regulation of urate excretion, apart from conversion to allantoin, involves glomerular filtration, tubular reabsorption (deficient but still demonstrable in the Dalmatian) and tubular secretion (ordinarily masked in the non-Dalmatian by preponderant reabsorption). Both reabsorption and secretion of urate in the dog appear to be largely "active".