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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

LOBSTER MOTOR AXON AS A MODEL SENSE ORGAN. W. J. Adelman, Jr. and E. Pautler (intr. by H. Rahn). Dept. of Physiology, Univ. of Buffalo, Buffalo, New York.

The characteristics of repetitive firing evoked by constant current stimulation in single lobster motor axons have been analyzed in terms of a model sense organ. The following characteristics were observed: 1) the response time is an inverse function of the logarithm of stimulus intensity; 2) successive spikes in the repetitive volley also are inversely related to the logarithm of the stimulus intensity; 3) the time constant for each spike process appears as a parameter which is a hyperbolic function of the number of spikes in the volley; 4) the magnitude of the spike interval variance (σ^2) is an exponential function of stimulus duration. From these observations it is suggested that the pulse-coded response to a stimulus is determined by the stimulus intensity, but is modified by both accommodating and randomizing factors inherent in the responding system. Secondary modifications are super-normality and relative refractoriness. Simple mathematical relationships describe this model sense organ behavior. (Supported by research grant B-1314, Natl. Inst. of Neurological Diseases and Blindness, PHS.)

AMYGDALOID AND PALLIDAL INFLUENCES ON MIDBRAIN RETICULAR UNITS RESPONDING TO SCIATIC NERVE STIMULATION. W. R. Adey and N. A. Buchwald.* Depts. of Anatomy and Physiology, Univ. of California at Los Angeles and VA Hosp., Long Beach.

Microelectrodes have been used to record units in the mesencephalic reticular formation which fired spontaneously and were facilitated by sciatic stimulation. Separate stimulation of amygdala, globus pallidus and sciatic nerve was tested at repetition rates of 1-10/sec. The effects of amygdaloid-sciatic, pallidal-sciatic and pallidal-amygdaloid shock pairings (50 msec interval) have been tested at the same repetition rates. Sciatic stimulation at rates of 3/sec or faster caused a sustained rise in firing rate (around 200/sec), although at 10/sec firing was often not as fast as at 5 or 7/sec. Separate stimulations of the globus pallidus and amygdala produced variable effects, but marked facilitation sometimes occurred. Paired amygdaloid-pallidal stimuli often reduced the firing rate to a low level. Paired amygdaloid-sciatic or pallidal-sciatic stimuli modulated the high frequency firing induced by sciatic stimulation alone. This modulation was greatest in the range 3-7 stimuli/sec.

Administration of chlorpromazine (1-2 mg/kg) markedly lowered the spontaneous firing rate. Additionally the sustained increase in firing rate following sciatic stimulation was replaced by a high frequency burst with each stimulus and little or no discharge between stimuli. Amygdaloid-sciatic or pallidal-sciatic pairing of stimuli further enhanced this modulating effect. Trifluoperazine (2 mg/kg) left basic firing rates unchanged and enhanced firing rates induced by paired pallidal-amygdaloid stimulation. These findings may bear on mechanisms of tremor and abnormal movement.

STUDY OF COMPETENCY OF NORMAL PULMONARY AND TRICUSPID VALVES. D. F. Bajec,* Newton C. Birkhead,* Stefan A. Carter* and Earl H. Wood. Mayo Fndn. and Mayo Clinic, Rochester, Minn.

Recording of a dilution curve from just upstream to a cardiac valve following injection of indicator just downstream to the valve provides a sensitive method for detection of regurgitant flow. If uniform mixing of injected and regurgitated indicator is assumed, the amount of regurgitant flow is related to the ratio of the area of the forward triangle portion of the immediately appearing fraction of injected dye upstream to the valve to that of the simultaneous systemic artery curve. Dilution curves of cardio-green were recorded via a cardiac catheter just upstream to the pulmonary valve and simultaneously from a femoral artery following injection of indicator just downstream to the valve in 6 normal, anesthetized dogs and similarly from the right atrium of these dogs following injections into the inflow portion of the right ventricle. No early appearing dye was detected upstream to the pulmonary or tricuspid valves in any of these animals, indicating their high degree of competency. Similarly no evidence of pulmonary regurgitation was obtained in 10 patients with heart disease but with clinically normal pulmonary valves, as contrasted to evidence of tricuspid regurgitation in 8 out of 10 of these patients, 5 of whom had right ventricular systolic pressures over 50 mm Hg and one clinical evidence of tricuspid regurgitation. The detected fraction of regurgitated dye averaged 9(1-23) %.

REACTIONS OF SPLENECTOMIZED DOGS TO INFUSIONS OF BLOOD. C. H. Baker* and J. W. Remington. Dept. of Physiology, Med. College of Georgia, Augusta.

In a series of experiments designed to study the rapid plasma loss following serial infusions (50-100 cc each) of homologous blood, it was observed that about 40% of the dogs anesthetized with morphine and Nembutal developed urticaria, rapid labored breathing and occasionally a falling arterial pressure. The animals were usually dead within 24 hr. Cross-matching of the donor and recipient blood did not always indicate cell incompatibility but instead a plasma incompatibility is suggested. Blood volumes (BV) as determined by T-1824 and as calculated from the hematocrit changes, using the control dye volume as the baseline, remained essentially constant and equal throughout the course of the infusions in nonreacting dogs. However, reacting dogs held a constant BV as determined by T-1824 but a gradually decreasing BV as determined by the hematocrit changes until the third infusion. The calculated BV then remained fairly constant but significantly lower than the BV measured by T-1824. Dogs treated with diphenhydramine behaved in the same manner as the non-reacting dogs. Unanesthetized dogs

exhibited transient acute declines in arterial pressure, urticaria, vomiting, diarrhea and muscle twitching. The BV as calculated from the hematocrit change remained near the control value, but the BV as determined by T-1824 increased quantitatively with each succeeding infusion. (Supported by grants from the PHS (H-240) and Life Insurance Med. Research Fund.)

ALTERATIONS IN RENAL HEMODYNAMICS AND ANTIDIURETIC HORMONE RELEASE FOLLOWING ACTIVATION OF THE VOLUME RECEPTOR MECHANISM IN THE DOG. Robert A. Baratz* and Raymond C. Ingraham. Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.

There are two possible mechanisms to explain the action of the volume receptors in the control of extracellular fluid volume; 1) a direct action on renal hemodynamics or 2) a neural or hormonal control of antidiuretic hormone (ADH) release. In the experiments to be reported, simultaneous changes in renal hemodynamics and antidiuretic hormone activity of the plasma were measured under various conditions calculated to activate the volume receptor mechanism in the dog. The series studied necessarily produced little, if any, stimulation of the osmoreceptors and included hemorrhage and subsequent reinfusion, plethora with 6% dextran, positive pressure breathing and negative pressure breathing. Antidiuretic hormone was assayed using rats rendered unconscious with ethanol and under constant water load. All injections of standards and unknowns were intravenous and the criterion of potency was change in the specific gravity of the rat's urine. Hemorrhage and positive pressure breathing caused the expected decrease in renal hemodynamics plus a very significant increase in plasma antidiuretic hormone activity. The plethora series showed an increase in effective renal plasma flow and a suggestion of a decrease in the plasma level of ADH. The production of a diuresis with negative pressure breathing was inconsistent and various types and levels of anesthesia, degrees of hydration and dehydration and position of the animal were tried to produce more uniform responses.

ENHANCEMENT OF DNA METABOLISM AND MITOTIC ACTIVITY BY PITUITARY GROWTH HORMONE IN IMMATURE INTACT MOUSE LIVER. Cyrus P. Barnum* and Franz Halberg. Univ. of Minnesota Med. School, Minneapolis, and Cambridge State Hosp., Cambridge, Minn.

D_8 (Dilute Brown, Subline 8) females, 4-5 wk of age, were studied under conditions standardized for periodicity analysis (light from 06:00 to 18:00, for 1 wk prior to study). A single intraperitoneal injection of 10 μg/gm body weight of pituitary growth hormone (STH) at ~16:30 consistently raised mean mitotic activity, when the latter was studied in histologic sections from animals killed at noon on the day following injection. In animals injected at 16:30 and killed at 04:30 (peak-time of P_{32} incorporation into DNA) on the day following injection, the effect on mitotic activity was not apparent, but there was an increase in relative specific activity of DNA (as % of acid soluble P). Effects of single doses of STH upon mitosis or DNA metabolism thus may be assessed in immature liver of intact mice by the appropriate selection of the times of injection and killing. Moreover, for variables undergoing 24-hr periodic changes with defined phase differences (such as P_{32} incorporation into DNA and mitosis) effects of the same hormone (STH)

become apparent at different times (i.e. the daily peak-time of the variable). The data, of interest also to bioassay, demonstrate the temporal dependence of hormone effects upon endorgan periodicity. (STH obtained from Endocrinology Study Section, Natl. Insts. of Health.)

SYNCHRONIZATION AND DESYNCHRONIZATION IN THE CHRONIC CERVEAU ISOLÉ OF THE DOG. H. L. Batsel and R. R. Gauch (intr. by A. D. Keller). Physiology Dept., U. S. Army Med. Research Lab., Fort Knox, Ky.

In our hands the acute isolated cerebrum (prepontine transection) of the dog exhibits slow waves and "sleep spindles" (sleep pattern) as did the original preparation of Frederic Bremer, but chronic preparations exhibit an electrocorticogram characterized by low-voltage, fast activity at least similar to the normal (or waking pattern). Although the waking pattern has been found most commonly in a given chronic preparation, on certain occasions and for unknown reasons, so-called synchronized patterns have appeared. Under these conditions the "synchronized" pattern has been converted without fail to the "desynchronized" state by intravenous injection of adrenaline (5-10 μg/kg) after other attempts at arousal have failed. Latent periods for adrenaline activation have been extremely variable, ranging from 1 to 17 min. An isolated experiment suggests that adrenaline acts at the diencephalic level but the mode of action remains problematical especially in view of the numerous pharmacodynamic actions of adrenaline. These results differ from those of Bonvallet et al., and Rothballer in that our acute preparations have uniformly failed to be activated by 5 μg/kg adrenaline, whereas chronic preparations have always shown a complete and long-lasting activation.

ACID STIMULATION OF TASTE RECEPTORS. L. M. Beidler. Div. of Physiology, Florida State Univ., Tallahassee.

The summated neural activity of the chorda tympani nerve was recorded as various acids were flowed over the surface of the tongue. A flow-chamber was used to minimize the possible buffering capacity of saliva. The concentrations of 19 different organic and inorganic acids were individually adjusted to elicit the same magnitude of response as that to 5 mM HCl. The molar concentrations for equiresponse varied from 2.2 to 150 mM whereas the H^+ conc. varied from 0.7 to 6.0 in M. The greater response of organic acids over HCl at equi-pH can quantitatively be accounted for by the facilitory action of the undissociated acid which is adsorbed to the receptor according to the Langmuirs adsorption isotherm. The change in response with conc. of both organic and inorganic acids can thus be quantitatively predicted. The addition of Na acetate to acetic acid may result in no appreciable change of magnitude of response even though the H^+ conc. has decreased by a factor of 10. This is explained by an increase in acid binding to receptor when the ionic strength is increased in accordance to similar findings in the titration of wool proteins with acids.

ABSENCE OF DEFICITS IN TASTE DISCRIMINATION FOLLOWING CORTICAL LESIONS AS A FUNCTION OF THE AMOUNT OF PREOPERATIVE PRACTICE. R. M. Benjamin (intr. by K. Akert). Physiology Dept., Univ. of Wisconsin, Madison.

Albino rats were subjected to varying amounts of practice on a simple taste discrimination before ablation of the cortical receptive

area for taste. The thresholds of normal animals on first exposure to this test are generally 2-3 x higher than the stable level reached after moderate amounts of practice. If lesions are made in naive animals which are subsequently introduced to the discrimination test for the first time, their thresholds show the same decline and are never significantly different from normal. Similarly, if animals had received extended overtraining preoperatively, the lesions also had no effect; that is, these thresholds remained at normal levels. However, a marked impairment in discrimination was produced in animals with moderate amounts of preoperative training, their thresholds increasing 7-11 x normal following operation. These differential effects demand that the sensory neocortex, at least as far as taste is concerned, must play a more dynamic role in discrimination behavior than that of a simple mechanism for the analysis or elaboration of input information.

NEW METHOD FOR DETERMINING THE FREE ENERGY OR E*. Reinhard H. Beutner. Med. Res. Lab., Des Moines Still College, Des Moines, Iowa.

The energy produced in metabolism cannot be entirely converted into heat, since the mechanical and electrical energy of the organism must likewise originate from that source. This is "free" energy, or E* as Szent-Gyorgyi calls it. The actomyosin-ATP theory postulates a direct conversion of chemical into mechanical energy. However, the combining of actin, myosin and ATP has never been shown to be as rapidly reversible as it should be if muscle contraction is to be explained. In spite of much work done on it, the theory has become more hypothetical, as Szent-Gyorgyi admits himself. More recently he tried to solve the problem of E* generation by studying radiant energy. However, radiation is not known to be associated with nerve or muscle activation. Instead, nerve or muscle generates electric energy. Electrical methods should therefore be tried for studying the origin of E*. The resting potential furnishes electric energy by means of oxidative metabolism. In order to understand in which manner and by which kind of chemical reaction E* may be generated, we have devised a new apparatus, the "bio-electric energy converter," in which a conversion of chemical into electrical energy occurs. Only a few chemical reactions, such as the oxidation of unsaturated fatty acids, lend themselves to a study of the conversion of chemical into electrical energy, in this apparatus. (Supported by research grants from the Natl. Heart Inst., PHS, and the Am. Heart Assoc.)

RADIOPROTECTIVE COMPOUNDS IN DOGS AND MICE. L. T. Blouin* and R. R. Overman. Clin. Physiology Lab., Univ. of Tennessee College of Medicine, Memphis.

The compound s,β-aminoethylisothiuronium bromide (AET) has been demonstrated by this laboratory to possess protective ability against an otherwise lethal dose of whole-body x-radiation in dogs. In a paper presented at the 1957 APS Fall meeting, it was pointed out that dogs have a very low tolerance for AET when administered by parenteral routes. Sufficient AET to afford protection could be given in aqueous solution form by the oral route in unanesthetized animals. A further study of this compound and the closely related propyl compound (APT) has been undertaken in which the drugs were compounded in various forms for oral administration. In addition, para-aminopropiophenone (PAPP), an agent which produces methemoglobinemia, has been

investigated. Pilot experiments were carried out in mice to test the toxicity and protective ability of the above compounds and of various combinations. Preliminary results indicate that combinations of AET and PAPP may afford a greater degree of protection than that provided by either compound alone. Radioprotective results of combinations of AET or APT with PAPP in dogs will be discussed. In addition, AET compounded in an enteric coated pellet or capsule form has been studied, and found to be relatively non-toxic, but difficulty in predicting blood-AET levels at any given time has been experienced. Results of toxicity and radiation studies will be presented.

HEMODYNAMICS OF EXPERIMENTAL TOTAL PULMONARY VALVULECTOMY. Walter J. Brown, Jr.,* Robert G. Ellison* and William F. Hamilton. Depts. of Physiology and Surgery (Thoracic), Med. College of Georgia, Augusta.

Pulmonary valvular insufficiency was produced experimentally by complete excision of the pulmonary valves. The operations were performed under direct vision during complete inflow occlusion under either hypothermic or normothermic conditions. The dogs were then studied by repeated x-rays of the chest, electrocardiograms and cardiac output measurements (Fick). Fifty-four dogs were used in the study, 16 being under observation from one to 54 months. During the first 14 months, the dogs were in excellent clinical condition and no appreciable changes were seen by x-ray or electrocardiogram. Cardiac outputs remained normal. Thereafter, there was a progressive reduction in the resting cardiac output and the right heart shadow progressively enlarged, but without electrocardiographic evidence of axis deviation. Animals that were either killed or did not survive further experimental procedures all showed dilation and hypertrophy of the right ventricle. Early catheterization studies indicated a systolic pressure gradient across the pulmonary valve area. This gradient was confirmed by direct recording of the right ventricular and pulmonary artery pressures simultaneously at thoracotomy. An average RV-PA systolic gradient of 6 mm Hg was noted in 5 out of 10 cases. Five dogs in which surgically produced lesions brought about an increased stroke volume (atrial and ventricular septal defects, patent ducti, and arterio-venous fistulae) developed an RV-PA gradient averaging 8 mm Hg after excision of the valves. In spite of enlarged right ventricles and reduced cardiac outputs there was no clinical evidence of heart failure and all long-term survivors appeared normal. (Supported by the Life Insurance Med. Research Fund and PHS H-240.)

SOME INHIBITORY PROCESSES IN SPINAL CORD IN CATS. N. A. Buchwald and E. Eidelberg (intr. by H. W. Magoun), Dept. of Anatomy, School of Medicine, Univ. of California at Los Angeles and VA Hosp., Long Beach.

Polysynaptic and dorsal root reflexes have been studied in paralyzed, unanesthetized cats by stimulation and recording in hindlimb flexor nerves and in dorsal and ventral sacral roots. Inhibition of both dorsal root and polysynaptic reflexes was produced by brain-stem reticular stimulation and by critical pairing of shocks to the afferent roots. Subsequent administration of thiosemicarbazide resulted in loss of the inhibitory effects of reticular formation stimulation on ventral root polysynaptic reflexes, and, indeed, facilitation was often seen. By contrast the dorsal root reflex was diminished in amplitude following

administration of the same drug with little effect on inhibition following reticular stimulation. The effects of thiosemicarbazide were reversed by intravenous administration of pyridoxine. Similar results on inhibition following a conditioning shock to the dorsal root have been obtained.

CHANGES IN SELF-SELECTION OF FOOD WITH AGE IN THE FEMALE RAT. Rosemary Burke* and Esther DaCosta. Chicago Teachers College, Chicago, Ill.

Forty normal female rats, in groups of 8, ranging from 4 to 58 wk of age, were allowed to choose from 3 diets, i.e. high (54%) protein, high (48%) fat and high (81%) carbohydrate during 13 wk. During the first week more than 50% of the diet chosen by the 4- and 9-wk-old groups was high carbohydrate. During the next 2 or 3 wk the consumption of the high fat increased so that in the last 2 wk the youngest group consumed about 80% high fat and 20% high protein and the next older group about 80% high fat and 20% high carbohydrate. The 18-wk-old group chose between 40 and 50% protein the first week while the 31- and 58-wk groups chose over 50% high fat diet initially and continued this throughout the experimental period. Thus the preferred diet was the high fat except initially and during the last 2 wk in the 58-wk group. Although the preference of the high fat diet needs an explanation, the need of protein for growth in the young and the negative nitrogen balance in the older rats may explain the deviations from the preference of high fat.

MECHANISM OF THE REPETITIVE DISCHARGE OF RESPIRATORY NEURONES. B. Delisle Burns and G. C. Salmoiraghi.* Dept. of Physiology, McGill Univ., Montreal, Canada.

Neurones found in the lateral reticular formation of the medulla in cats with microelectrodes discharge repetitively during each phase of respiration. Some discharge during inspiration, some during expiration. Such bursts of action potentials appear to be due to repeated activation of each neurone through its interconnections with active neighbors, the excitation spreading away continuously and returning to the same unit by way of self-reexciting chains of neurones within the inspiratory and expiratory network, respectively. Supporting this view is the finding that a single, short-lasting shock to the medulla given during inspiration or expiration interrupts abruptly the discharge of inspiratory or expiratory neurones presumably due to simultaneous excitation followed by simultaneous refractoriness of all the neurones involved in the process of self-reexcitation. That such effect is not the result of injury is indicated by the finding that a shock of just sufficient strength to stop a discharge when given at one point of the burst fails to do so when given slightly earlier. In such case prolongation of the burst rather than arrest is induced by the shock. Fully consistent with this view also are the effects of polarization of respiratory neurones individually with cathodal and anodal current and the effects of hypercapnia. (Supported by a grant from the Natl. Research Council of Canada.)

LUNG TISSUE TENSION AND AIRWAY CONDUCTANCE. John Butler,* C. G. Caro* and A. B. DuBois. Dept. of Physiology and Pharmacology, Grad. School of Medicine, Univ. of Pennsylvania, Philadelphia.

Airway conductance ($1/R_A$) varies with lung volume (V). Further investigation of this relationship showed 1) regions of greater conductance for unit volume change ($1/R_AV$) at the extremes of the vital

capacity; 2) greater $1/R_AV$ after administration of atropine or isoproterenol. A possible explanation of these findings lay in 1) alterations in airway caliber due to traction on the airways by the varying lung compliance pressure (P_{C_L}) and 2) alterations in distensibility of the airways. Since the mean intraluminal pressure is atmospheric, the transluminal pressure gradient of the airways is determined by the mean P_{C_L} during panting. Airway conductance, thoracic gas volume and mean esophageal pressure were measured during panting at different respiratory levels throughout the vital capacity of 10 normal subjects aged 23-43 yr. $1/R_A$ showed an approximately straight line relationship to esophageal pressure. The mean change in $1/R_A$ for a 1-cm change in P_{C_L} ($1/R_AP_{C_L}$) was 0.10 1/sec/cm^2 water (range 0.050-0.140). Zero conductance intercepts lay between P_{C_L} of +1 and +10 cm water. When lung compliance was decreased by strapping the chest (ibid. Caro et al.) $1/R_AV$ was markedly increased. However, $1/R_AP_{C_L}$ was unchanged. This appeared to substantiate the hypothesis that, in an individual, $1/R_A$ was related to lung tension rather than volume. Atropine and isoproterenol administration increased both $1/R_AP_{C_L}$ and $1/R_AV$ in normals; forced expiration in asymptomatic asthmatic patients decreased both. This indicated that airway distensibility was altered by these procedures.

EFFECTS OF CHEST STRAPPING ON LUNG MECHANICS. C. G. Caro,* J. Butler* and A. B. DuBois. Dept. of Physiology and Pharmacology, Grad. School of Medicine, Univ. of Pennsylvania, Philadelphia.

To test the hypothesis that the mechanical changes in the lungs found in young kyphoscoliotic patients resulted from thoracic cage restriction, the chests of 10 healthy volunteers were strapped in full expiration with adhesive tape or rubber inner tube. Subdivisions of total lung volume and airway conductance (plethysmographic methods), static and dynamic lung pressure-volume (P-V) relationships (esophageal pressure), and the distribution of inspired gas (single breath test) were measured, sitting. The mean FRC was reduced by about 35% by either method of strapping. The mean TLC was halved by inextensible strapping, but reduced by only 1/4 with elastic strapping. Despite the reduction of lung volume mean airway conductance at the new FRC was unchanged. The distribution of inspired gas was not markedly uneven. The static P-V relationship of the lungs was consistently altered, a smaller volume change resulting from unit pressure change throughout the reduced vital capacity. Dynamic lung compliance at the new FRC was half of the control value. After removal of the strapping the P-V relationship remained altered during several tidal breaths but returned to normal via an exaggerated hysteresis-like change during a maximal inspiration. It is concluded that artificial thoracic cage restriction: 1) alters the P-V relationship of the lungs; 2) simulates the changes in the lungs found in young kyphoscoliotics; 3) permits physiologic measurements to be made at equivalent lung volumes but different transpulmonary pressures.

EFFECTS OF AMPHENONE B ON CHOLESTEROL METABOLISM. K. K. Carroll (intr. by R. L. Noble). Dept. of Med. Research, Univ. of Western Ontario, London, Canada.

Amphenone B causes a marked accumulation of cholesterol in the adrenal cortex (Hertz et al. Rec. Prog. Hormone Res. 11:119, 1955) and the present study was initiated to examine this effect in relation to the increased cholesterol levels found in rats fed erucic acid. Addition of 0.25% amphenone B (CIBA) to synthetic diets caused the expected increase in adrenal cholesterol and in addition a 2- to 3-fold increase in liver and plasma cholesterol. The effects on liver and plasma cholesterol were of similar magnitude on diets containing no fat or 15% of oleic, palmitic or erucic acids, but the effect on adrenal cholesterol was somewhat greater in the presence of erucic acid. Excretion of fecal sterol was not altered by the addition of amphenone B to the various diets.

EVIDENCE FOR INCREASED PROTEOLYTIC ENZYME IN CEREBROSPINAL FLUID DURING AUGMENTED CATABOLISM WITHIN THE CENTRAL NERVOUS SYSTEM. Loring F. Chapman and Harold G. Wolff. Depts. of Medicine (Neurology) and Psychiatry, New York Hosp.-Cornell Med. Ctr., New York City.

It was observed that cerebrospinal fluid from some subjects when incubated with globulin acquired the property of contracting smooth muscle. CSF collected from subjects with active disease of the central nervous system (recent cerebrovascular accidents, neoplasm of the central nervous system, multiple sclerosis) predictably gave such a reaction. However, CSF collected from subjects with inactive, nonprogressive or no disease of the central nervous system ("old" cerebrovascular accidents, myasthenia gravis, progressive muscular dystrophy, vascular headache during headache-free intervals) gave such reactions only rarely, under the conditions of measurement. Also, CSF from subjects with vascular headache of the migraine type, or with sustained noxious stimulation and pain arising from disease of the legs or pelvic organs, or with disease classified as chronic schizophrenia, predictably gave this reaction. The properties of the substance formed during incubation were similar to those of vasodilator polypeptides formed by the action of proteolytic enzymes on plasma proteins. Starch gel electrophoresis of whole serum indicated a diminution of the alpha 2 and beta components following incubation with active CSF.

SIMULTANEOUS RENAL TUBULAR REABSORPTION AND UTILIZATION OF METABOLITES BY THE DOG KIDNEY IN VIVO. Julius J. Cohen. Dept. of Physiology, Univ. of Cincinnati College of Medicine, Cincinnati, Ohio.

Reports of the renal tubular reabsorption of metabolites using clearance techniques have often implied that some moiety of the reabsorbate may be utilized. Further, in vitro studies with renal tissue indicate the kidney is capable of utilizing a variety of substrates. That the two processes, reabsorption and utilization, are not necessarily related is indicated by recent reports from other laboratories that glucose is not utilized during transport, while on the other hand citrate utilization exceeds citrate reabsorption. In a study of the metabolites utilized by the kidney in vivo, additional evidence for separation of utilization and transport has been found. The simultaneous net reabsorption and net utilization of substances were determined. Renal venous blood was obtained by right renal vein catheterization of anesthetized (left nephrectomy) dogs. Experiments with acetoacetate reveal that no significant utilization of this metabolite occurs. This is in contrast to the

remarkable stability of the acetoacetate reabsorptive mechanism. Similarly, for lactate only a small net utilization of this substrate is observed, which is not related to the magnitude of the simultaneous reabsorption of lactate. On the other hand, the consumption of two alpha-keto acids, pyruvic and alpha-ketoglutaric, exceeds their simultaneous reabsorptive rates.

RATE AND PATTERN OF GLUCOSE METABOLISM IN THE RETINA. Leonard H. Cohen* and Werner K. Noell. Roswell Park Memorial Inst., Buffalo, N. Y.

The mammalian retina in vitro is characterized by its high aerobic lactic acid production. In the retina of the adult rabbit, in a phosphate-buffered medium, glucose was converted to lactic acid 8 times as rapidly as it was oxidized to carbon dioxide. Respiration was nevertheless high ($Q_{O_2} = 12$), and 80% of the oxygen consumed was accounted for by the oxidation of glucose. The bulk (60%) of the carbon dioxide from glucose oxidation arose from carbons 3 and 4; less than 10% came from carbon 6. Glucose carbon 1 oxidation exceeded that of carbon 6. Addition of pyruvate stimulated the oxidation of carbon 1. Moreover, it enabled anaerobic CO_2 production by way of the hexosemonophosphate shunt. In the non-functioning retina of the 5-day-old rabbit, the hexosemonophosphate shunt was the pathway for almost all of the aerobic C-1 oxidation; anaerobic C-1 oxidation occurred without pyruvate in the medium, but at half the rate. In the presence of pyruvate, oxygen diminished the formation of $C^{14}O_2$ from glucose-1-C^{14}. Inhibition by iodoacetate of aerobic C-1 oxidation was completely reversed by pyruvate. The evidence indicates that pyruvate provides or serves as the principle electron acceptor for the hexosemonophosphate shunt. The implications of the coexistence of a high capacity hexosemonophosphate shunt and a high capacity Embden-Meyerhof system will be discussed in relation to the metabolic compartmentation of the retina. (Supported by Public Health Grant B-812.)

BLOOD AND INTERSTITIAL SPACES OF THE FUNCTIONAL ILEUM. W. D. Collings, H. G. Swann and H. F. Stegall.* Physiology Depts., Univ. of Texas Med. School, Galveston, and Michigan State Univ., East Lansing.

A mixture of red cells labeled with Cr^{51} and serum albumin labeled with I^{131} was injected continuously into the influent blood of a segment of dog ileum. The injection was made into a small branch of the mesenteric artery; its rate was about 1% of the volume flow through the segment. All effluent blood was collected by cannulating the corresponding mesenteric vein. Net blood loss was prevented by transfusion with dog blood at the same rate as blood was draining from the vein cannula. At blood flows of 0.3-0.4 ml/gm/min, the labeled albumin was found to enter the ileum at two rates, the one fast, with a half-time of about 10-15 sec and the other slowly, with a half-time of about 100 sec. Labeled red cells entered approximately at the same rate as that of the "fast" albumin rate. In interpretation, the 2 rates here observed are taken to indicate that in the living ileum, just as in the functional kidney, some plasma traverses the intravascular compartment (the fast rate) along with the red cells, whereas another plasma moiety courses more slowly through an extravascular compartment (the slow rate).

DEPRESSION OF FOREARM SWEAT GLAND RESPONSES BY REPEATED INTRADERMAL INJECTIONS OF ACETYLCHOLINE OR ACETYL-β-METHYLCHOLINE. K. J. Collins,* F. Sargent II and J. S. Weiner.* Dept. of Human Anatomy, Oxford Univ., England.

The effect of repeated intradermal injections of acetylcholine or acetyl-β-methylcholine (Mecholyl) on eccrine sweat gland activity was investigated by the plastic impression method (Thomson and Sutarman. Trans. R. Soc. trop. Med. Hyg. 47:412, 1953). Two to eight successive injections were made at 25- or 60-min intervals and the activity of the same glands followed by photometric projection. Large doses (200 μg/.05 ml) produced a marked depression of active glands after 3 or more injections. Smaller doses (10 μg/.05 ml) evoked approximately the same number of glands initially, but there was no profound reduction even after 6-8 injections. Repeated injections of N saline did not diminish the subsequent response to acetylcholine or Mecholyl. The depression was generally unaffected by the local vasodilatation produced by intradermal injections of Priscol (2 mg/.5 ml) or histamine (1 μg/.5 ml). Adrenaline (10 μg/.5 ml) causing intense local vasoconstriction rapidly depressed the response of the glands to successive injections of both large and small doses. The effects of drug-induced vasoconstriction on sweating were similar to those of ischemia (Collins, Sargent and Weiner, J. Physiol. 142:32, 1958). Inhibition of sweat gland activity by large doses of Mecholyl has been ascribed to "fatigue" of the glands (Thaysen and Schwartz, J. Clin. Invest., 34:1719, 1955). Alternative explanations may be that excess acetylcholine or Mecholyl injected intradermally induces a neurohumoral block at the neuroglandular junction or depresses sweating indirectly by local vascular impairment.

COMPONENTS OF THE PERIPHERAL RESISTANCE. James Conway, and F. Gutman (intr. by D. F. Bohr). Dept. of Physiol., Univ. of Michigan, Ann Arbor.

In the makeup of blood vessels there are 2 components contributing to the peripheral resistance: 1) their numbers and basic connective tissue structure; 2) the degree of vascular tone applied by arteriolar smooth muscle. In any preparation an observed relationship between perfusion pressure and the flow of blood will be governed by these 2 variables and an attempt has therefore been made to separate them. This has been achieved by comparing the resistance in the blood vessels of the denervated hindlimb of the dog with the resistance after the effect of smooth muscle tone had been removed by the intra-arterial infusion of acetylcholine. Pressure/flow curves for the denervated leg were curved, convex to the pressure axis (similar to those found by Green, et al., 1944) with resistance at 80 mm Hg varying from 5.1 to 13.7 PRU_{100}. Under acetylcholine the pressure flow curves were linear but did not pass through the origin and at 80 mm Hg the resistance varied from 1.3 to 2.4 PRU_{100}. Thus the resistance offered by the denervated limb was between 5 and 6 times greater than that offered by the fully dilated limb. This ratio provides a measure of the effect of smooth muscle on peripheral resistance. Some preparations with the highest peripheral resistance have also had a high structural resistance showing that the peripheral resistance in these cases was determined by the basic structure of the vessels supplying the limb, rather than a high vasomotor tone. (Supported by a grant from the Michigan Heart Assoc.)

METABOLIC RESPONSES OF THE FROG LIVER TO IODOACETATE AND EPINEPHRINE. Albert B. Craig, Jr. (intr. by W. O. Fenn). Dept. of Physiology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Epinephrine is thought to increase glycogenolysis by the activation of liver phosphorylase. It has been reported that epinephrine increases the concentration of hexosephosphates. Another method of changing the concentration of the hexosephosphates would be through the action of iodoacetate (IAA), which inhibits the dehydrogenase converting 1,3-diphosphoglyceraldehyde to its acid. Epinephrine will increase the output of glucose and promote a characteristic potassium loss from the isolated perfused frog liver. As might be expected, the ketoacid and lactic acid production is increased. IAA also enhances glucose output and potassium loss but the production of lactic acid is markedly decreased. These responses to IAA are dose-dependent. Lactic acid production was suppressed for at least 2 hr after 20 min of IAA, but potassium loss was increased only so long as IAA was administered. Epinephrine and IAA were administered in various combinations. When the dose of IAA was high, epinephrine produced no further increase in potassium or glucose losses and failed to augment the inhibited lactic acid production. With a lower dose of IAA, the addition of epinephrine did increase lactic acid formation but again failed to promote a further potassium loss. These results support our previous hypothesis that in the liver there is a potassium loss which is related to that phase of intermediary carbohydrate metabolism characterized by an increase of hexosephosphate concentration.

SERUM ELECTROLYTE CHANGES FOLLOWING HEMORRHAGE. Jerry B. Critz* and Arthur W. Merrick. Depts. of Physiology and Pharmacology, Univ. of Missouri, Columbia.

Normal serum sodium, potassium, magnesium and the hematocrit were determined in 1-day (A), 5-day (B), and 2-month-old (C) white New Zealand rabbits. A significant increase in sodium and magnesium was observed in C; the potassium level was the same in A, B and C. The hematocrit in A was significantly higher than that observed in B and C. The hematocrit changes may be associated with gross weight changes. Sodium, potassium, magnesium and hematocrit also were determined in 2-month-old rabbits subjected to a 10, 20 and 30% hemorrhage. Analyses were made 8, 24, 48, 96 hr and 1 and 2 wk subsequent to hemorrhage. Moderate blood loss in adult dogs and cats reportedly produced a sodium decrease and a potassium increase. Hemorrhage in juvenile rabbits resulted in similar sodium and potassium changes. These electrolyte changes are attributed to hemodilution by intracellular fluid. Magnesium reportedly increased or exhibited no change in adult humans, dogs and rabbits after hemorrhage. In young rabbits, a 10% blood loss had no effect upon the magnesium level while a 20 and 30% hemorrhage produced a significant decrease. Return to control level was observed at 48 hr and 1 wk respectively. Several theories are suggested for the magnesium loss. The decrease in hematocrit may be related to the severity of hemorrhage and it is suggested that no red cell reserve exists in juvenile rabbits.

OXYGEN TRANSPORT IN HEMORRHAGIC SHOCK AS A FUNCTION OF THE HEMATOCRIT RATIO. Jack W. Crowell (intr. by Arthur C. Guyton). Dept. of Physiology and Biophysics, Univ. of Mississippi Med. Ctr., Jackson.

In 75 dogs with different hematocrit ratios in which the blood pressure had been maintained at 30 mm Hg for 15 min, the oxygen consumption, arterial and venous oxygen concentration, and the arterial blood pH were measured and the cardiac output, peripheral resistance and maximum oxygen transport capacity determined. The oxygen consumption per kg increased as the hematocrit ratio increased until the hematocrit ratio reached 42. An increase in the hematocrit ratio above 42 caused a decrease in oxygen consumption. A curve produced by multiplying the oxygen concentration of arterial blood times the cardiac output showed that the oxygen available determined the oxygen consumption of the animals. The arterial blood pH was highest in those dogs with the greatest oxygen consumptions, but the pH was below limits compatible with life in the anemic animals. Total peripheral resistance increased greatly as the hematocrit ratio increased. Analysis of the data showed that the range of maximum resistance to hemorrhagic shock coincides with the hematocrit ratio range of maximum oxygen transport. Also, the rate of development of an oxygen debt determines how long the animals can remain in hypotension without developing irreversible shock.

EFFECT OF SELF-SELECTION ON THE SPECIFIC GRAVITY OF THE ALBINO RAT. Esther DaCosta and Frederick Hoelzel.* Chicago Teachers College, Chicago, Ill.

After 13 wk of self-selection in 3 diets, i.e. high (54%) protein, high (48%) fat and high (81%) carbohydrate, specific gravity determinations on 38 males and 46 females were done by under-water weighing. The males ranged from 21 to 71 wk of age and the females from 17 to 71 wk of age. The specific gravity of the total, eviscerated and skinned eviscerated animal and the skin and viscera were separately determined. Specific gravity of the eviscerated skinned carcass of the male ranged from 1.0359 to 1.0373 in the 21- and 31-wk groups and decreased to 1.0251 in the 44-wk group and 1.0202 in the 71-wk group. The specific gravity of the eviscerated skinned carcass of the female in the 17-wk group was 1.0269 and rose to 1.0431 in the 31-wk group and lowered to 1.0374 in the 71-wk-old group. The skin and viscera in general followed a reverse of the above pattern. The pattern of specific gravity change with age followed a similar pattern to that reported previously on control rats on a stock diet. However, the difference between age groups and the sexes is reduced by self-selection, as if an animal by choosing its diet can control fat deposit better than if forced to eat a stock diet.

MITOCHONDRIA IN DEVELOPING RAT BRAIN. Dennis R. Dahl* and Frederick E. Samson. Physiology Dept., Univ. of Kansas, Lawrence.

Mitochondria from whole brains of female Sprague-Dawley rats 1-50 days old were examined for relative cellular quantity and oxidative-phosphorylative capacity. The concentration of mitochondrial protein (MP) is constant during the first 5 days after birth, i.e. the rate of synthesis of MP is the same as the rate of total brain growth. This is followed by a period of accelerated MP synthesis during which the MP, initially at 12%, increases to about 20% of total cerebral protein. By the 21st day (weaning), the rapid proliferation of MP tapers off. Calculation of the relative amount of MP per cell (assume a constant amount of desoxyribose nucleic acid in each cell) reveals an increase per cell throughout the entire age range studied, with a 3-fold increase during the first 21 days. The rate of O_2 utilization per mg MP is constant

throughout the age range studied; the rate of high-energy phosphate synthesis per mg MP declines slightly. Apparently, newly formed mitochondria are fully capable of oxidative-phosphorylation. Also, the well known acceleration of O_2 utilization with brain development can be accounted for by the increase in MP. The relative gain in MP per cell during development may be a prerequisite to the greater power cost of maintaining a larger surface area as the growing cells extend into the extracellular space. (Aided by PHS Grant B-1151 and PHS Medical Student Fellowship.)

CIRCULATION TIMES THROUGH THE CORONARY AND SYSTEMIC CIRCULATIONS OF DOGS. André David* and Earl H. Wood. Mayo Fndn. and Mayo Clinic, Rochester, Minn.

Dilution curves were recorded simultaneously from the coronary sinus via a cardiac catheter and the femoral artery of 4 normal anesthetized dogs following injections of cardio-green into the pulmonary artery and similarly from the right ventricular outflow tract, superior vena cava and inferior vena cava. The average appearance and build-up times were 4.4, 3.4; 5.4, 5.3; 7.2, 10.3; 7.8, 5.4; and 7.4, 8.6 sec in the femoral artery, coronary sinus, superior and inferior venae cavae and right ventricle respectively. The respective peak deflections were 10.9, 6.8, 2.5, 1.2 and 1.9 mg/l. Similar relative relationships were obtained in human subjects. The curve recorded from the right ventricle or pulmonary artery is the resultant of the relative fractions of dye traversing the coronary and upper and lower body circulations. The contribution of dye traversing the coronary sinus to this mixed venous curve was, however, too small to allow accurate estimation of coronary flow. Although dye traversing the coronary sinus arrived at the femoral sampling site during the disappearance phase of the femoral dilution curve, the distortion produced was too small to cause a practically important error in measurement of cardiac output by the Hamilton method.

SMALL VESSEL RESPONSES OF DOG'S PAW. D. L. Davis* and W. F. Hamilton. Dept. of Physiology, Med. College of Georgia, Augusta.

Pressures and flows were measured in small veins and arteries during sympathetic stimulation to determine whether high small vein pressures previously reported (Am. J. Physiol. 190:37, 1957) were transmitted through the capillary bed by flowing blood, and hence could indicate capillary pressures high enough to produce local fluid loss. At stimulation frequencies less than 1-2/sec (reported physiological range) the constrictor response was limited to arterioles. An increase in small artery pressure with concomitant decreases in small vein pressure and in blood flow occurred. At stimulation rates from 1-2/sec to approximately 10/sec small vein pressures were progressively increased while small artery pressures and blood flows were progressively decreased. At higher stimulation frequencies flow in these very small vessels was stopped completely, and small artery pressures fell to low levels. Experiments indicated that closure of arteries occurred at the ankle and that a static column was formed which communicated with the capillaries. Simultaneously small vein pressure rose well above the oncotic level and was long maintained. This indicated that small vein walls were contracting against a static column of blood held between a strong constriction (closure?) at the ankle level and postcapillary venular valves (or constrictive closure). Since these high pressures occurred after flow had stopped they could not be relevant to transcap-

illary water shifts. (Supported by the Life Insurance Med. Research Fund and PHS grant H-240.)

SOME EFFECTS OF ELECTRICAL POLARIZATION OF THE ORGAN OF CORTI. H. Davis, D. H. Eldredge* and R. P. Gannon.* Central Institute for the Deaf, St. Louis, Mo.

The cochlear partitions of guinea pigs were electrically polarized through Cu - $CuSO_4$ electrodes connected by salt bridges to small holes drilled into scala vestibuli and scala tympani of the basal turn of the cochlea. The cochlear microphonic (CM) and the negative summating potential in response to tone bursts at 7000 cps and 100 SPL were recorded from conventional intracochlear electrodes less than a millimeter away. These bursts evoked maximal CM responses but there was no peak limiting, even at supramaximal intensities. Both summating potential and CM were increased when scala vestibuli was made more positive and reduced when it was made more negative relative to scala tympani. This supports the theory that the summating potential and CM are fundamentally similar. With bursts of 500 cps, strong enough to cause peak-limiting of CM, moderate polarization caused an increase or decrease in the voltage level of the (peak-limited) responses. With stronger polarization and particularly with continuation of polarization for a few seconds there were changes of wave form as well as in amplitude.

EFFECTS OF ACUTE AND CHRONIC HYPOTHALAMIC LESIONS ON ALDOSTERONE SECRETION IN DOGS WITH CHRONIC EXPERIMENTAL ASCITES. James O. Davis, Robert C. Bahn, Nicholas A. Yankopoulas,* Bernard Kliman,* Ralph E. Peterson* and Wilmot C. Ball, Jr.* Natl. Insts. of Health, Bethesda, Md., and Mayo Clinic, Rochester, Minn.

During acute studies of dogs with chronic ascites and high aldosterone output, adrenal vein aldosterone and corticosterone output was measured 1) in 2 dogs before and after placement of large hypothalamic lesions via the oral approach (pituitary gland not removed) and 2) in 4 dogs before and after hypophysectomy and, subsequently, following extensive destruction of the hypothalamus. In the first 2 dogs, the hypophysis was damaged and aldosterone and corticosterone secretion fell 75-85% and 80-95% respectively. In the other 4 dogs, hypophysectomy was followed by a similar marked fall in aldosterone and corticosterone output. After the hypothalamic lesions, a further drop in corticosterone secretion occurred but the effect on aldosterone was variable. In 2 dogs no change in aldosterone secretion was discernible whereas in 1 animal aldosterone became undetectable and in the remaining dog aldosterone output was 3-fold higher than during the post-hypophysectomy period. In 7 dogs with ascites and chronic hypothalamic lesions, urinary aldosterone output remained elevated and sodium retention continued unabated. The data from these acute observations show a striking dependence of the high rate of aldosterone secretion upon intact pituitary function. The evidence from acute studies on the relation of the hypothalamus to aldosterone secretion was indeterminate but chronic observations yielded consistently negative data.

NON-SHIVERING THERMOGENESIS IN MAN. T. R. A. Davis, D. R. Johnston, F. C. Bell and F. D. Jacks (intr. by J. R. Blair). U. S. Army Med. Research Lab., Ft. Knox, Ky.

In a previous report it was demonstrated that shivering levels and heat production change as a result of seasonal acclimatization. The object of the present study was to determine the effect of prolonged cold exposure upon shivering and heat production in 10 subjects. The cold exposure consisted of daily exposures of 7 hr in the nude in a cold chamber at 12°C for a total of 32 days. On the days of measurement, shivering, oxygen uptake, rectal and skin temperatures were determined after 4 hr of exposure and 16 hr of fasting. Basal oxygen uptakes were measured every 7th day after 13 hr of fasting. The results showed that 1) after 20 days of exposure, shivering levels had fallen to approximately 10% of the initial value; 2) oxygen uptake above basal during this period had fallen to only 70% of the initial value; and 3) although mean skin temperatures showed no change, rectal temperatures showed a significant fall on the 15th day. It is concluded from these results that 1) shivering disappears in man as a result of cold exposure, 2) a non-shivering thermogenesis is again demonstrated in man, 3) cold exposure lowers central body temperature as well as total heat production, 4) since skin temperature does not change, heat loss from the skin surface is the same throughout the period of exposure.

UPTAKE OF RADIOSULFATE BY MITOCHONDRIA FROM RAT KIDNEY CORTEX AND LIVER. Ingrith Deyrup and R. E. Davies. Zoology Depts., Barnard College and Columbia Univ., New York City, and Biochemistry Dept., Univ. of Pennsylvania, Philadelphia.

It has been established previously that mammalian kidney cortex slices in vitro can accumulate radiosulfate under conditions paralleling, in several respects, renal sulfate reabsorption in the intact mammal. It has now been found that mitochondria from rat kidney cortex and liver can accumulate S^{35} from media containing radiosulfate. When mitochondria, isolated and washed twice in 0.25 M sucrose at 0°C, were immersed in solutions containing $S^{35}O_4$ = (total SO_4 = 0.5 to 10 μM), rapid uptake of radiosulfate occurred, e.g. within 5 min (25°C). Ratios of virtual sulfate concentration in mitochondrial water to medium sulfate concentration of more than 200 to 1 were observed. Uptake was followed by precipitous loss (e.g. within 15 min, at 25°C) in the case of kidney cortex mitochondria. Such loss did not occur for up to 1 hr from these mitochondria at 0°C, nor from liver mitochondria at 0° or 25°C. After preincubation in 0.25 M sucrose (30 min, 37°C), kidney cortex mitochondria showed negligible S^{35} accumulation. Studies have been made of the effects upon mitochondrial sulfate uptake of temperature, pH, ionic composition and osmolarity of the medium, and of substances known to affect sulfate transport in kidney in vivo and sulfate accumulation in kidney cortex slices in vitro. (Supported by Grants H-2061 and H-2520 of the Natl. Heart Inst.)

THE SECRETIN AND PANCREOZYMIN ACTIVITY OF THE INTESTINES OF VAGOTOMIZED RATS. John E. C. Dorchester (intr. by M. H. F. Friedman). Dept. of Physiology, Jefferson Med. College, Philadelphia, Pa.

Using a simple cross over design, and rabbits as the assay animal, the secretin and pancreozymin activity of the acid extracts of the intestines of vagotomized and control albino rats was compared. Secretin activity was estimated by counting the number of drops of pancreatic juice secreted in the 30 min following the intravenous injection of equal volumes of the extracts. Pancreozymin activity was judged by both the

concentration and total amount of amylase secreted in the juice in response to the injections. It was found that vagotomy led to 1) a reduction in secretin activity and 2) an increase in pancreozymin activity. There was no significant difference in the intestinal weights. It would appear, therefore, the formation of secretin and pancreozymin extractable from the duodenum may be influenced by the integrity of the vagus nerves. (Supported by Grant A-1613, PHS.)

CONDITIONED REFLEXES ESTABLISHED BY COUPLING VISUAL AND MOTOR CORTEX STIMULATION. R. W. Doty and C. Giurgea.* Dept. of Physiology, Univ. of Michigan, Ann Arbor, and Institutul de Fiziologie, Academia R.P.R., Bucharest.

Rectangular 1-msec pulses, 50/sec, applied with bipolar electrodes at marginal gyrus as "CS" for about 4 sec initially induced no response whatever. This stimulation was paired 6-10 times/day at 3-5 min intervals with stimulation of post. cruciate gyrus as "US." As reported (Giurgea, Studii Cercetari Fiziol. Neurol. 4:41-73, 1953), specific responses to such "CS" gradually develop. Following first appearance, some response occurred on 95% of "CS" presentations and in 45% of these closely resembled the movement induced by the "US." Dog Epsilon flexed left foreleg to "US"; "CS" at 1.8 mA elicited no response for 40 pairings, thereafter flexions of right foreleg, and subsequent to 81st pairing, flexions of left foreleg to 0.6 mA. After 200 such pairings stimulation of post. ectosylvian gyrus, previously neutral, also produced left foreleg flexions though never paired with "US." Dog Beta flexed hindleg to "US"; after 65 pairings discrete flexions of this limb occurred to "CS" of 1.0 mA which initially produced no action at 2.0 mA. In Beta flexion to "CS" persists through 1 month and 85 presentations without "US" and is not made to auditory, post. ectosylvian or hyppocampal stimulation. There is no logical or experimental basis for considering "motivation" to be a factor in the foregoing phenomena. Other preparations, to be described, were not as completely successful.

EFFECTS OF A SAMPLING SYSTEM ON DYE CURVES. Philip Dow. Dept. of Physiology, Med. College of Georgia, Augusta.

Patterns of distribution of Evans Blue in water flowing in a tubular model have been varied by altering its mode of introduction, the length and size of tubing, and the flow rate. Precautions were taken to minimize disturbing discontinuities in the tubing. By a needle at the end of the model, a constant sampling of the flowing stream is drawn through a densitometer cuvette which may be placed at any spot along a 2-m length of polyethylene tubing. Thus the effects of length and flow in the sampling tube are studied separately on the different types of curves produced by variations in the model. Slug curves and both wash-in and wash-out of abrupt fronts have been studied, and the results to date seem not quite what should be expected from parabolic flow. With increasing distance, a high peak seems to disappear mostly into a broadening and bowing of the middle portions of the curve, without proportionate extension of the long tail which is a conspicuous feature in short segments of tubing. Curve areas were satisfactorily uniform and calculated mean transit times checked well with tube volumes and measured flows. Straight segments of semilog downslopes bore no consistent relation to the volumes. (Supported in part by grant H-240 from PHS, and by Life Insurance Med. Research Fund.)

ROLE OF CIRCULATING LACTATE IN THE METABOLISM OF GLUCOSE. D. R. Drury and M. C. Almen.* Dept. of Physiology, School of Medicine, Univ. of Southern California, Los Angeles.

We used C^{14}-labeled lactate and glucose to study the metabolism of these compounds in normal and in diabetic animals. Lactate is very rapidly oxidized to CO_2 in both, and within 3 hr after injection most of it has been burned. About a fourth of it is converted to glucose in the diabetic. Glucose is not as quickly burned as lactate in normals. When tagged glucose is injected in normals or diabetics the label quickly appears in the circulating lactate in considerable amounts. A large part of the glucose that is oxidized enters the pool of circulating lactate which is then directly oxidized without being reconverted to glucose.

BLOOD GLUCOSE CHANGES IN NEWBORN DOGS IN RESPONSE TO COLD AND EPINEPHRINE. H. E. Ederstrom and Alvin Larson.* Dept. of Physiology and Pharmacology, Univ. of North Dakota Med. School, Grand Forks.

Dogs of various ages were exposed to 5°C air temperature and blood glucose levels determined after 1 hr. The procedure failed to raise blood glucose over the control level in dogs aged 4 days or younger. The average blood glucose in older dogs rose as follows: 5-7 days old, 13 mg%; 8-10 days old, 15 mg%; 11-15 days old, 9 mg%; 16-25 days old, 4 mg%; adult dogs, 4 mg%. Blood glucose levels were determined after epinephrine, 0.2 mg/kg, had been given intramuscularly previous to cold exposure. This dosage gave a rise of 22 mg% in 2- to 4-day-old dogs and progressively greater effects were found as the animals grew older. At 8 days of age the glucose increase was about the same as in the adult dog, or 100 mg%. Norepinephrine in the same dosage lowered blood glucose 10 mg% in the 2- to 4-day-old animals, and gave a rise averaging 25 mg% in dogs older than this. The results indicate that changes in blood glucose in response to epinephrine vary with the age of the animal. Mobilization of glucose was not found to be an important factor in the development of temperature regulation in the young dog. (Supported by research Grant RG4580, from PHS.)

DIFFERENTIAL ACTION OF DRUGS ON INTRACRANIAL AND EXTRACRANIAL CIRCULATION IN DOGS. C. H. Ellis. Wellcome Research Labs., Tuckahoe, N. Y.

Certain vascular headaches have been ascribed to activation of stretch receptors by dilatation of the superior sagittal sinus. Other vascular headaches such as migraine are thought to be of extracranial origin. A clear distinction between intra- and extracranial circulation by techniques involving selective intra-arterial infusions cannot be made in dogs because of complex anastomosing within the cephalic arterial vasculature. Blood is drained from the intracranial bed in dogs via the large venous sinuses into 1) the spinal sinuses or 2) via the internal maxillary veins into the external jugulars. Bilateral ligation of the internal maxillary veins results in a separation of the major efferent cephalic pathways to a degree that lateral pressure measurements from the superior sagittal sinus can be considered to reflect vasomotor changes in the intracranial bed; and measurements from the external jugular changes in extracranial vascular activity. Epinephrine at 0.5 μg/kg i.v. has exhibited differential action on the 2 vascular beds. The superior sagittal sinus pressure was elevated, external jugular pressure was reduced. Vasomotor effects of epinephrine on intracranial

circulation are complex. Both decreases and increases in superior sagittal sinus pressure have been recorded in response to doses of the order of 1 μg/kg i.v. Effects of vasodilators appear to be less confusing, histamine and glyceryltrinitrate having consistently increased the superior sagittal sinus pressure. Ergotoxin reduced s.s.s. pressure.

CARDIOPULMONARY PHYSIOLOGY IN EXPERIMENTAL AND CLINICAL CONDITIONS WITH INCREASED PULMONARY BLOOD FLOW. Lois T. Ellison,* Robert G. Ellison,* Thomas Yeh,* David P. Hall* and W. F. Hamilton. Depts. of Physiology and Surgery (Thoracic), Med. College of Georgia, Augusta.

An understanding of cardiopulmonary physiology in diseases associated with high pulmonary blood flow is important, particularly in regard to the etiology of pulmonary hypertension and surgical management of patients with this condition. Effects of left to right shunts produced in dogs by staged bilateral subclavian-pulmonary artery anastomoses were studied in 34 dogs with emphasis on the alveolo-arterial (A-a) oxygen tension difference when breathing different oxygen mixtures. Pulmonary artery pressure was measured at thoracotomy and later at cardiac catheterization along with determination of quantity of shunt. Seventeen dogs are currently being studied at intervals. Before surgery the A-a difference on ambient air averaged 14 mm Hg, on 12% O_2 11 mm, and on 30% O_2 33 mm. After recovery from the second shunt these values were 17, 14 and 33, respectively. Control pulmonary artery pressure averaged 18/13 and had increased to 44/21 7-10 months after surgery. These results suggest that the slight increase in total A-a difference may be due to impaired diffusion. Similar observations were made in 6 patients with atrial septal defect and 1 patient with a femoral arterio-venous fistula studied before and after surgery. (Supported by grants from the Georgia Heart Assoc., Life Insurance Med. Research Fund, and PHS.)

METHOD FOR OBSERVING CHANGES IN LOCAL CEREBRAL BLOOD FLOW EMPLOYING SEVERAL CHRONICALLY IMPLANTED MICROTHERMISTORS. John Evans* and Loring F. Chapman. Depts. of Medicine (Neurology) and Psychiatry, New York Hosp.-Cornell Med. Ctr., New York City.

The electrical resistance of thermistors changes greatly with relatively small changes in temperature. If an electrical current is passed through a thermistor, heat is generated, and the thermistor may assume a temperature higher than that of the surrounding medium. If the temperature of the surrounding medium is constant the temperature reached by the thermistor will be dependent upon the rate of the flow of the medium since increased flow will dissipate increased amounts of heat energy. Changes in flow thus can be observed by noting changes in the resistance of the thermistor. The sensitivity of the method can be increased by employing the thermistor as one resistor in a Wheatstone bridge circuit, and measuring changes in potential difference. An apparatus employing the above principle was constructed. The apparatus allowed simultaneous recording from 4 thermistors implanted in various regions of the brain of cats. Several days after implantation by means of a stereotaxic instrument, recordings were made under several conditions of behavior, sensory stimulation, and exposure to pharmaceutical agents.

DEXTRAN AND HEMOSTASIS. Barbara J. Excell* and Robert E. Semple. Dept. of Physiology, Queen's Univ., Kingston, Canada.

Recent investigations have been primarily concerned with the way in which dextran interferes with the formation of the hemostatic plug. Clots formed, in vitro, by blood containing clinical dextrans in concentrations that were associated, in vivo, with prolonged bleeding times and often wound seepage, showed strengths that were significantly lower than controls. There was no evidence of fibrinolysis. Fibrin conversion was not significantly affected by the presence of dextran in vitro, because with dextran concentrations in the order of 3 gm/100 ml recoveries ranged from 97 to 100% of controls. Dextran, added to blood in vitro, did not promote agglutination or platelet breakdown when the blood was incubated at 37°C but did cause marked agglutination and a significant reduction in the platelet count when samples were stored at 4°C. A clinical dextran preparation and a narrow fraction high molecular weight dextran both brought about, in vitro, significant reductions in prothrombin consumption but a low molecular weight fraction (MW = 5000) did not. (Supported in part by Medical Grant 9310-15 from the Defence Research Board of Canada.)

CORONARY FLOW AND MYOCARDIAL OXYGEN CONSUMPTION IN HYPOTHERMIA. H. Feinberg,* A. Gerola* and L. N. Katz. Cardiovascular Dept., Michael Reese Hosp., Chicago, Ill.

Hypothermia was produced by cooling the blood in 15 open-chested anesthetized dogs prepared for total coronary flow measurements. Cardiac output was kept constant throughout. Blood pressure (BP) did not fall spontaneously while heart rate (HR) decreased when hypothermia developed (up to 27°C). Blood pressure was altered to modify the pressure-work in the hypothermic and control periods. The mechanical efficiency increased with hypothermia proportionately with the HR change. No significant alteration in the O_2 cost of cardiac effort, as indicated by the BP x HR index, followed hypothermia. The coronary a-v O_2 difference tended to fall with hypothermia despite an increase in arterial O_2 content—thus, a uniform decrease in percent O_2 extraction occurred. In hypothermia, the ratio coronary flow over cardiac O_2 consumption was higher than in the control period because the denominator fell while the numerator tended to remain constant. During the "steady state" of hypothermia, coronary a-v O_2 difference remains constant while coronary flow is the means by which changes in cardiac O_2 consumption are met. This is no different than in the control period.

EFFECT OF A HIGH FAT DIET ON BLOOD SUGAR OF THE RAT. Dorothy Fetter and Enid Neidle.* Dept. of Physiology, New York Univ. College of Dentistry and Brooklyn College, Brooklyn, N. Y.

Sixty female Wistar rats, 3 wk old, were divided into 2 groups of 30 each, and fed isocaloric diets, adequate in all respects. Group A had 11% of the calories as fat and 70% as carbohydrate, while group B received 69% of the total calories from fat, and 17% as carbohydrates. After 1 wk on the diets, the rats in group A averaged a blood sugar of 98 mg% while those in group B averaged 124 mg%. During the following 8 wk, blood sugar determinations showed an average increase of 20-25 mg% for the rats on a high fat diet (group B) over those on a low fat diet (group A). At the 10th wk, the determination showed that the average blood sugar for the rats on the high fat diet was only 10 mg%

higher than that for the controls. Whitney and Roberts (Am. J. Physiol. 181:446, 1955) reported, for rats on a high fat diet, a blood sugar of 6-8 mg% higher than that of the control rats. These authors used male rats whose weights were approximately 300 gm. It may be that the rise in blood sugar accompanying the high fat diet is associated with age, being more pronounced in younger animals.

AUTONOMIC INNERVATION OF THE EYE. David G. Fleming and James L. Hall (intr. by G. N. Loofbourrow). Depts. of Physiology and Anatomy, Kansas Univ., Lawrence.

A procedure was devised for studying gross and microscopic changes in the eye during stimulation of the cervical sympathetic nerve. The Richins-Hall toluidine blue method for neural activity was adapted to this investigation. In the first series of cats, the cervical sympathetic nerve on one side was stimulated continuously for 3 hr. Just before the stimulation was discontinued, lead subacetate was perfused into the anterior chamber of both eyes. This method produces instantaneous in vivo fixation of the eye. Gross examination of the eyes in midsagittal section revealed that the lens in the eye on the stimulated side was flatter than the lens in the contralateral eye. Histological examination of the ciliary region demonstrated constricted vessels only in the stimulated eye. Both, however, indicated considerable metabolic activity. In the second series, the ciliary ganglion was extirpated unilaterally. The pupil in the eye on the ganglionectomized side was extremely dilated indicating unopposed sympathetic activity. After 3-hr stimulation of the contralateral sympathetic nerve, vasoconstriction was demonstrated only in the stimulated eye. As contrasted to the preceding series, a high level of metabolic activity was seen only in the stimulated eye. The results support the hypotheses that the sympathetic nervous system affects accommodation through the vasomotor mechanism and that unilateral cervical sympathetic stimulation produces considerable parasympathetic activity in both eyes.

THYROID HORMONE IN THE BOVINE HYPOTHALAMUS. William C. Foster and Betty D. Eichner.* Lab. of Physiology Research, Misericordia Hosp., Philadelphia, Pa.

In an earlier study higher concentrations of thyroid hormone, expressed as protein-bound iodine (PBI), were found in the posterior lobe of the pituitary gland than in the anterior. Since a relationship has been found between the hypothalamus and the posterior pituitary gland it was thought important to study PBI in the former organ and other parts of the brain. The tissues were obtained at slaughter and cut for analysis with a sharp cork-borer, to insure uniform size and depth into the cortex. The tissue plugs were weighed and the PBI determined by a modification of the Chaney method. In 12 bovine brains the PBI levels are reported and expressed as mean, maximum to minimum, and standard deviations in the following areas: hypothalamus 4.6, 12.3 - 3.1, ±2.72; left frontal pole 3.1, 7.3 - 0.3, ±2.09; left superior frontal gyrus 3.2, 5.0 - 1.3, ±1.14; left occipital pole 1.8, 2.8 - 0.7, ±0.93; right frontal pole 1.8, 4.3 - 0.3, ±1.58; right superior frontal gyrus 2.5, 4.5 - 0.1, ±1.70; and right occipital pole 2.8, 5.1 - 0.4, ±1.58, respectively. PBI was found to be 32.7-61% higher in the hypothalamus than in other parts of the brain analyzed. The results suggest further study. (Supported by Grant #H-3700, Natl. Heart Inst., PHS.)

TRANSPORT OF P-AMINOHIPPURATE (PAH) FROM CELL TO LUMEN IN KIDNEY TUBULE. Ernest C. Foulkes and Benjamin F. Miller (intr. by W. D. Lotspeich). May Inst. for Med. Research, Jewish Hosp. and Med. Ctr., and Depts. of Physiology and Medicine, Univ. of Cincinnati College of Medicine, Cincinnati, Ohio.

Intracellular accumulation of various anions (phenol red, diodrast) in the rabbit kidney tubule has been well documented. The following experiments were designed to test the hypothesis that in the rabbit no further concentration step is required for the transfer of these materials from the cells into the tubular lumen. If this be the case PAH should be accumulated in the cells to the same concentration as in the proximal tubular urine. The maximum active uptake in vivo was determined by measurement of intracellular PAH in kidney cortex rapidly removed from freshly killed animals with high plasma levels of PAH. A value of about 10 μM/ml cell water was obtained. The concentration of PAH in the tubular urine was estimated during massive osmotic diuresis on the assumption that bladder urine under these conditions approaches proximal tubular urine in composition. With simultaneous PAH and mannitol loading, a concentration not exceeding 10 μM/ml proximal tubular urine was observed. The same value was calculated from results obtained by the stop-flow technique. It appears therefore that in the rabbit, an animal with a large volume of glomerular filtrate, no concentration step is required at the luminal border of the cells. The absence of such a step could explain a self-depression of tubular function at very high concentration of PAH in the plasma water filtered at the glomerulus.

ACUTE RED CELL MASS CHANGES FOLLOWING THERMAL INJURY. H. A. Fozzard and J. P. Gilmore (intr. by S. W. Handford). Naval Med. Field Research Lab., Camp Lejeune, N. C.

Although the occurrence of an acute erythrocyte loss following burn is well established, there is still some question as to its extent and immediate cause. The present study was undertaken to determine the extent of the red cell mass loss in the dog following thermal injury and to relate the changes to changes in the osmotic fragility and morphology of the erythrocytes. Measurements of the above changes were made prior to, and at 1, 3 and 6 hr following a 22 cal/cm^2 30% surface area burn. The results of the experiments indicate that following a severe burn there occurs approximately a 13% loss of the red cell mass at least half of which can be attributed to the direct destruction of erythrocytes and changes in osmotic fragility. It was also observed that the red cell mass may occasionally increase following burn and that this increase appears to be a result of splenic extrusion of sequestered erythrocytes. The results also indicate that while there is a physiologic basis for whole blood therapy following burn, the more immediate requirement is plasma volume replacement.

INFLUENCE OF PULMONARY EDEMA ON PULMONARY VASCULAR RESISTANCE IN EXCISED DOGS' LOBES. N. R. Frank and I. Gribetz (intr. by J. Mead). Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

Pulmonary vascular resistance was measured in excised lobes of dogs' lungs before and after induction of edema. Pulmonary arterial and left atrial pressures were held constant. Measurements were made of changes in vascular flow during inflation and deflation of the lobe by

fixed volume steps. Transpulmonary pressure was measured at each step from a saline manometer attached to the trachea. Six percent dextran in saline was used as the perfusate. Edema which was characterized by extensive foam was induced either by raising vascular pressures or instilling plasma (human and dog) in the airway. At most lung volumes, before the onset of edema, vascular resistance was greater during inflation than deflation. The difference corresponded roughly to the volume-pressure hysteresis of the lobe. After edema, vascular resistance was approximately the same during inflation and deflation, despite the persistence of lung hysteresis. In general, vascular resistance at a given vascular and airway pressure was lower following edema.

HEAT TOLERANCE IN RATS AND HAMSTERS. H. M. Frankel* and G. Edgar Folk, Jr. Dept. of Physiology, State Univ. of Iowa, Iowa City.

The survival time of male rats upon exposure to environmental temperatures of 40, 45, 50, 55 and 60°C was determined. In addition, the survival time of male and female hamsters to environmental temperatures of 40, 45 and 50°C was determined. Upon cessation of respiration, samples of blood were drawn from the heart for hematocrit, serum specific gravity, calcium, potassium and sodium determinations. Confinement of the animal to a small space reduced the survival time. No linear relationship existed between survival time and environmental temperature. The sex of the animal did not affect the survival time. No correlation was found between survival time and either body weight, body surface area or initial body temperature. Exposure to high environmental temperatures resulted in increased values for hematocrit, serum specific gravity and potassium. Values for serum calcium and sodium were relatively unchanged. The most common finding at autopsy was vascular engorgement and pulmonary edema in animals exposed to temperatures of 45°C and above. Speculation will be offered as to the cause of thermal death. (Aided by a Research Grant from the Natl. Science Fndn.)

CHANGES IN SELF-SELECTION OF FOOD WITH AGE IN THE MALE RAT. Homer Franklin and Esther DaCosta. Chicago Teachers College, Chicago, Ill.

Forty normal male rats, in groups of 8, ranging from 8 to 58 wk, were permitted free choice of 3 diets, i.e. high (54%) protein, high (48%) fat and high (81%) carbohydrate, for 13 wk. During the first week food consumption usually equaled about 13 gm/rat/day, but in the 18-wk-old group about 30 gm/rat/day and tapered off to about 10 gm/rat/day. During the first week the pattern to be followed throughout the experimental period was set. High fat was the preferred diet, high proteins often a close second and high carbohydrate almost neglected. However, the 18-wk-group showed a marked preference for high carbohydrate initially, but by the end of the first week ate almost exclusively high fat and in the 13th week ate 9.14 gm of high fat per rat/day with negligible quantities of the other 2 diets. The pattern of dietary choice in the male rat does not seem to reflect any remarkable physiological wisdom but rather a choice that promotes obesity and its associated problems.

PREPYRIFORM ELECTRICAL ACTIVITY ASSOCIATED WITH DRIVE. Walter J. Freeman (intr. by Robert D. Tschirgi). Dept. of Physiology, Univ. of California, Los Angeles.

The prepyriform cortex in the cat is a 3 x 12 mm strip of paleocortex

at the base of the frontal and temporal lobes. Direct electrical or afferent stimulation activates a dipole field of current; one pole lies in the molecular layer and the other in the base of the cortex. "Spontaneous" prepyriform activity arises from the same dipole and provides a large component of hypothalamic electrical activity. In this study records from chronically implanted cats demonstrated the existence of an active state in the dipole, in which the amplitude of the electrical activity increased up to 10-fold over the resting state. The active state was elicited by the odor of food or by sights or sounds associated with food in cats when hungry, but not when satiated. Single painful stimuli (e.g. pin-prick, pinch or shock) did not produce the active state; repetitive painful stimuli did so, in association with either aggressive responses or conditioned escape and avoidance responses. Direct electrical stimulation of the prepyriform cortex caused arrest of any concurrent behavioral activity, but only at intensities at which evoked prepyriform electrical activity overrode the intrinsic activity of the active state. Extensive bilateral lesions of the cortex were associated with inanition and impaired conditioned avoidance responses. It is suggested that the prepyriform cortex manifests an excitatory state, which contributes to the intensity and duration of several drives.

PRODUCTION OF HYPERTENSION IN ADRENALECTOMIZED RATS GIVEN HYPERTONIC SALT SOLUTION TO DRINK. Melvin J. Fregly. Dept. of Physiology, College of Medicine, Univ. of Florida, Gainesville.

Ten male Holtzman rats weighing 200-240 gm were bilaterally adrenalectomized. All rats were placed in individual cages in a room maintained at 25 ± 1°C and illuminated from 8 A.M. to 6 P.M. The rats were given Purina laboratory chow as food and choice between water and 0.9% NaCl solution as drinking fluids. Two weeks were allowed for post-operative recovery. During the next 3 wk, intakes of water and 0.9% NaCl solution were measured to assess completeness of adrenalectomy. Any adrenalectomized rat not showing typical NaCl appetite was replaced. At the end of the 3-wk control period, 5 of the rats were given 2% NaCl solution as the sole drinking fluid; Purina chow remained as food. The other 5 rats were given 0.9% NaCl solution as sole drinking fluid. Within 6 wk, mean systolic blood pressure of adrenalectomized rats on hypertonic (2%) NaCl solution was elevated significantly above that of control group on isotonic (0.9%) NaCl solution. By the 10th and 11th wk of the experiment, blood pressures of rats given hypertonic saline had reached 170 mm Hg or more. At the end of the 11th wk, the salt solutions were exchanged; that is, rats on 2% saline were given 0.9% saline while those on 0.9% saline were given 2% saline. Other conditions remained the same. In 3-4 wk mean systolic blood pressure of the rats switched to hypertonic salt solution reached hypertensive levels but at a relatively faster rate than the previous group. The elevated blood pressures of the original group given 2% saline have persisted for at least 11 wk after replacement of 2% saline with 0.9% saline. It is concluded that sustained hypertension can be induced in adrenalectomized rats by hypertonic (2%) NaCl solution.

CENTRAL ACTION OF ALCOHOL AS GASTRIC SECRETORY STIMULANT. M. H. F. Friedman, M. E. Jaffe* and J. H. Gans.* Dept. of Physiology, Jefferson Medical College, Philadelphia, Pa.

Experiments were performed on unanesthetized dogs equipped 3 wk

to 10 months earlier with gastric and intestinal cannulated fistulas and also Pavlov pouches of the stomach. In addition, at the time of operation the vagus nerves had been brought intact through the neck muscles and placed subcutaneously. Recovery was good and no disturbances in gastric function were noted as a consequation of vagus nerve transposition. In these animals, alcohol when administered by intestinal fistula, by rectum or by vein, stimulated gastric secretion profoundly. The composition of the juice differed from histamine-stimulated secretion principally in having a higher peptic activity. Section of the vagus nerve under local anesthesia made while the stomach pouch was secreting actively in response to alcohol resulted in an immediate cessation of secretion. Secretion, however, persisted if only one vagus nerve was severed. The rate of secretion could also be depressed by administration of atropine in doses smaller than that required to affect histamine-stimulated secretion. These experiments offer evidence that alcohol provokes gastric secretion through central vagal excitation.

SITE OF ACTION OF CARNITINE ON FATTY ACID OXIDATION. Irving B. Fritz. Dept. of Physiology, Univ. of Michigan, Ann Arbor.

We have recently shown that the addition of carnitine to either liver slices or homogenates resulted in augmented conversion of labeled palmitate to ketones (Am. J. Physiol. 190:449, 1957). The present report deals with substrate specificity and probable locus of action of carnitine on the fatty acid oxidase system. Washed rat liver particulates were incubated with carboxyl-labeled stearate, palmitate, laurate, octanoate, butyrate or acetate in the presence and absence of carnitine. The amount of activity appearing as respiratory $C^{14}O_2$ and as C^{14} in the carboxyl group of β-ketonic acids was measured. The addition of carnitine enhanced palmitate and stearate oxidation by 2-fold or more, regardless of whether albumin was added to the medium to bind the fatty acids. In contrast, the conversion rates of the shorter chain length fatty acids to $C^{14}O_2$ and ketones were not increased by the presence of carnitine. The oxidation of C^{14}-carboxyl-labeled palmityl CoA by either liver particulates or a soluble system was not influenced by added carnitine. The consistent carnitine effect on the combustion of non-esterified palmitate and stearate by liver particulates was lost when the fatty acid oxidase system was made soluble by various treatments. The facts that carnitine addition augmented the oxidation of only non-esterified, long-chain fatty acids, was effective only in particulate system, and was without effect on the oxidation of palmityl CoA suggest that the site of carnitine action is at a stage prior to the formation of palmityl CoA in an organized system.

CALORIMETRIC MEASUREMENTS OF PHYSIOLOGICAL RESPONSES OF THE CONSCIOUS DOG TO LOCAL HEATING OF THE ANTERIOR HYPOTHALAMUS. Madeline M. Fusco (intr. by J. D. Hardy). Physiology Dept., Univ. of Pennsylvania, Philadelphia.

Total calorimetric measurements of the physiological responses of a conscious dog to local thermal stimulation of the thermo-sensitive region of the anterior hypothalamus were made at cool (14°C), neutral (25°C), and slightly warm (29°C) environmental temperatures. Oxygen consumption, hypothalamic, rectal, and mean skin temperature, surface and respiratory evaporative heat loss and total nonevaporative heat loss were measured during a 5- to 6-hour run at each of the environmental temperatures. Local central heating (42.5°C at the electrodes)

was produced by application of radio-frequency energy between 2 needle electrodes implanted in the pre- and supra-optic area of the anterior hypothalamus. (I am greatly indebted to Dr. R. D. Squires for his invaluable help in the preparation of this animal.) At all 3 temperatures 2 hr of local hypothalamic heating produced a steady fall in rectal temperature from 38.1°C to 37.2°C. In each case shivering occurred on cessation of heating and was inhibited on re-application of heat. In the cool environment the lowered core temperature was effected chiefly by a slight depression of heat production relative to heat loss, shivering was depressed; there was no panting. At the neutral temperature the response was a 20-45% decrease in metabolism, no panting and slight vasodilation. In the slightly warm environment, there was no effect on metabolism, but a marked increase in heat loss through panting, and slight vasodilation.

BLOOD GLUCOSE, PYRUVATE, LACTATE AND POTASSIUM FOLLOWING INTRAPORTAL GLUCAGON, BEFORE AND AFTER DIHYDROERGOTAMINE. Giorgio Galansino,* Giuseppe D'Amico* and Piero P. Foa. Depts. of Physiology and Pharmacology, Chicago Med. School, Ill.

The pancreato-duodenal blood of a dog A treated intravenously with growth hormone (beef, Armour) manifests hyperglycemic activity when injected into the femoral vein of a test dog B. Pretreatment of dog B with dihydroergotamine (DHE) blocks this hyperglycemia, suggesting that the active principle in blood may be a sympathomimetic amine and not glucagon as previously believed. However, since normally glucagon is secreted into the portal and not into the femoral vein and since its effects on the liver are similar to those of epinephrine, there is a possibility that glucagon may act through a mediator capable of being blocked by DHE. To investigate this possibility and to study the effects of glucagon on blood pyruvate, lactate and potassium, crystalline glucagon (Lilly 0.05 mg in 0.1 cc/kg) was injected into the portal vein of anesthetized dogs (Nembutal 35 mg/kg and barbital 100 mg/kg, i.v.). In some experiments, this was done 30-40 min after the intraportal injection of DHE (Sandoz, 0.04 mg/kg). In all experiments glucagon caused a marked hyperglycemia (av. 100%) without significant changes in blood lactate, pyruvate and potassium. Pretreatment with DHE did not alter the results significantly. The results suggest that glucagon does not act through the liberation of a sympathomimetic amine. (Aided by Grant A-522 NIAMD, PHS.)

DC POTENTIAL IN THE SEMICIRCULAR CANALS. R. P. Gannon,* D. H. Eldredge,* C. A. Smith* and H. Davis. Central Institute for the Deaf, St. Louis, Mo.

We have measured the endolymphatic potentials in the ampulla of the lateral semicircular canal, relative to the surrounding perilymph. Our electrodes were glass capillaries filled with 3 molar KCL, 1 μ tip diameter, 7-10 megohms resistance. As the pipette was advanced it showed potentials of -20 to -70 mv as it penetrated the wall of the membranous labyrinth, and -30 to -70 mv as it penetrated the crista. These are presumably intracellular potentials. In no instance was a positive potential recorded as the pipette passed through the endolymphatic space between these 2 regions of negativity. This finding is consistent with our previous measurements in the utricle, i.e. not more than +5 mv. On the other hand Trincker has reported (Pfluger's

Arch. 264:351, 1957) a potential of +30 to +40 mv in the lateral semicircular canal. Perhaps the basis for this contradiction is Trincker's use of a metallic electrode (Svaetichin) for measuring DC potentials.

DEEP COOLING TO CARDIAC STANDSTILL. Maurine Giese,* M. Mason Guest, John R. Derrick* and Gunter Corssen.* Internal Medicine, Physiology, Surgery, and Anesthesiology Depts., Univ. of Texas Med. Branch, Galveston.

Since cooling the anesthetized mammal to body temperatures at which cardiac arrest occurs results in arrhythmias and fibrillation as the temperature is lowered, we have experimentally evaluated measures which have been reported to reduce the incidence of these cardiac dysfunctional states. Dogs were cooled to temperatures at which cessation of cardiac activity occurred and then the animals were resuscitated by the judicious use of warming and electrolyte control. Using cyclopropane-oxygen for induction, followed by the intravenous administration of adrenolytic drugs, cardiac standstill without fibrillation in our experimental animals has consistently been obtained. The attempt has been made to evaluate changes in the internal environment during the procedures described. The variables which were studied include oxygen, carbon dioxide and cyclopropane contents of the blood, blood pH, blood and cardiac tissue electrolytes, blood volume, hematocrit, ECG, and venous and arterial pressures.

ABDOMINAL COMPRESSION REACTION IN DOGS UNDER SODIUM PENTOBARBITAL (MOTION PICTURE). T. M. Gilfoil* and W. B. Youmans. Dept. of Physiology, Univ. of Wisconsin Med. School, Madison.

In dogs anesthetized with either sodium pentobarbital or sodium pentothal a strong contraction of the abdominal muscles may occur just after the completion of expiration. The characteristics of the abdominal compression reaction will be shown in 3 dogs and for comparison the normal type of respiration will be shown in an animal which also was anesthetized with sodium pentobarbital. The abdominal compression reaction may be seen to begin immediately after completion of (passive) expiration, and relaxation may occur before the next inspiration or the contraction may be maintained until the onset of inspiration. The phenomenon was present in varying degree in 10 of 25 dogs anesthetized with sodium pentobarbital (30-33 mg/kg intravenously). It has not been observed in dogs premedicated with morphine and anesthetized with ether or chloralose. It is apparent that the abdominal compression reaction has little effect on pulmonary ventilation, and it is suggested that its role is to promote venous return under conditions where circulation is tending to fail.

GASTRIC-ACID SECRETION IN THYRO-PARATHYROIDECTOMIZED RATS. Dale Goldsmith* and E. S. Nasset. Dept. of Physiology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Gastric-acid secretion after methacholine stimulation was studied in 4 groups of male rats by the stomach lavage technique. The groups consisted of unoperated controls (group A), and thyro-parathyroidectomized rats either untreated (group B), injected with 1 mg dl-thyroxine per kg for 4 days prior to assay (group C), or fed thyroid fraction for 4 days prior to assay (group D). The operated animals were allowed to recover 3-5 wk before use. Their metabolic rates decreased an average

of 30%. The metabolic rates of group C and group D returned to euthyroid levels after treatment with thyroxine or thyroid fraction. The secretory response of each animal was expressed as a function of the "free acid" (measured potentiometrically) secreted after several injections of methacholine. The average free acid secretions of group B and of group C were one-third to one-half that of group A. There was wide variation in the responses of members of each group. Rats in group C tended to give maximal secretion only after 4 injections of methacholine whereas animals in groups A and B responded well after the second injection. The average "free acid" secretion of group D was considerably lower than those of the other 3 groups. Group D animals were very sensitive to methacholine and usually survived only 2 injections.

SPONTANEOUS HEARTBEAT IN HYPOTHERMIC DOGS BELOW 13°C. Frank Gollan. VA Hosp., Nashville, Tenn.

The heart of newborn non-hibernating animals continues to beat at temperatures close to 0°C. If one ascribes this phenomenon to the higher sodium content of the myocardium of the newborn, then one should be able to reproduce the same effect in adult animals by inducing sodium retention. Dogs were pretreated with 10 mg of desoxycorticosterone acetate/day and 10 gm of sodium chloride/day was added to their food for 1 wk. After slow intravenous administration of 30 mg quinidine/kg their body temperature was lowered by elective cooling by means of a pump-oxygenator. After about 1 hr of total body perfusion with refrigerated and oxygenated blood the lowest myocardial temperatures of 5°C were reached. Ventricular or auricular contractions could still be recorded electrocardiographically and the extrapolation of the heart-rate-temperature curve showed that the heart would have stopped beating at 0°C. The heart of control animals without steroid and salt pretreatment stopped beating at about 13°C. On rewarming the blood in the extracorporeal circuit the heart rate increased faster than the myocardial temperature. The greater excitability of the heart of DOCA plus salt pretreated dogs at low temperatures lends support to the hypothesis that the increased sodium content of the heart of the newborn may be the cause of its greater tolerance to cold.

EFFECT OF RENAL TRANSPLANT IN ADRENOCORTICAL HYPERTENSION. A. Gomez,* S. W. Hoobler and P. Blaquier.* Dept. of Internal Medicine, Univ. of Michigan Med. School, Ann Arbor.

A method for transplanting a kidney to the hind limb of a rat is described. Renal blood flow and urine output of the transplanted kidney were calculated by direct measurement; the values thus obtained were then compared with those from a kidney in situ. Comparison of these data allows one to conclude that the function of the transplanted kidney is satisfactory. The inclusion of a normal kidney in the circulation of a normotensive rat does not result in significant variations of the blood pressure of the recipient (6 experiments), but the pressure of rats made hypertensive by uninephrectomy and figure of eight ligation 2 months previously is promptly reduced to normal (15 experiments). The response of adrenocortical hypertensive rats to kidney transplant was then studied. Hypertension was produced by implant of a wax pellet containing 20 mg of DCA and the feeding of 0.85% salt solution in the drinking water. Such metacorticoid hypertensive rats which had undergone this procedure 6 months or more previously failed to exhibit

a blood pressure reduction to kidney transplant (14 experiments). The kidneys of these animals when transplanted to renal hypertensive rats lowered the blood pressure in 5 of 7 experiments. Thus the metacorticoid kidney had not lost the ability to remove or inactivate the hypothetical pressor substance in renal hypertension. Rats whose DCA hypertension was milder and of shorter duration have exhibited variable responses to kidney transplant.

INJECTIONS OF THYROXINE AND OXYGEN CONSUMPTION OF RAT KIDNEY SLICES. Roger L. Greif and Jean Moroney.* Dept. of Physiology, Cornell Univ. Med. College, New York City.

Slices made from kidneys of thyroidectomized rats show an unusual response to in vitro addition of thyroactive materials. If the oxygen consumption (Q_{O_2}) of such tissue is measured manometrically daily at 37°C, and between measurements the flasks are stored at 4°C, thyroxine and l-triiodothyronine decrease the rate of fall in Q_{O_2} (Barker, S. B., Endocrinol. 59:719, 1956). In this investigation one kidney was removed from a previously thyroidectomized rat under ether, then 1 mg of thyroactive material was given intravenously. Ten minutes later the second kidney was removed, after which both kidneys were sliced and studied as outlined above. After 48 hr the Q_{O_2} (wet weight) measurements were as follows: 1) control kidney $1.96 \pm .07$ (S.E.) thyroxine injected $2.35 \pm .05$, $p < .001$ (16 rats); 2) control kidney $2.09 \pm .11$, diiodotyrosine injected $2.24 \pm .08$, $p > .1$ (7 rats); 3) control kidney $1.97 \pm .03$, l-triiodothyronine injected $2.32 \pm .06$, $p < .001$ (10 rats). Injection of labeled thyroxine resulted in I-131 concentrations within kidney slices equivalent to $.03 \pm .004$ μg of thyroxine per mg wet weight. The relationship of these findings to the mechanism of action of thyroid hormones will be discussed.

ISOLATION OF A BROMSULFALEIN (BSP) METABOLITE. G. M. Grodsky, R. Fanska and J. V. Carbone (intr. by Ellen Brown). Dept. of Medicine, Univ. of California School of Medicine, San Francisco.

Despite the widespread clinical use of BSP clearance as a liver function test, there is no proof of the actual liver function(s) involved in the clearance of the dye. Assumptively, BSP is complexed with protein in the blood. This complex is broken in the liver and supposedly free BSP is excreted. We have investigated the nature of the pigmented BSP to determine whether a biochemical function is involved in BSP excretion from the liver. Protein-free acetone extracts containing BSP from normal human bile or urine and from serum of subjects with obstructive jaundice were paper chromatographed in 2 independent solvent systems (dioxane-water and tert-butanol water). Two fractions were obtained; the fastest moving was identical with a BSP standard. The slower second fraction, containing 65 to 75% (in bile or urine) and 90% (in the serum) of the total pigment, represented an altered BSP product. This metabolite was stable to hydrolysis in 2 N HCl at 100° or after incubation with beta glucuronidase and gave a negative Dische reaction. Treatment with water at 120° in a sealed tube for 18 hr resulted in partial conversion of the metabolite to apparent free BSP. After similar treatment with 6 N HCl, the pigmented fraction of the metabolite was chromatographically similar to free BSP treated in the same manner. Metabolized BSP and free BSP had similar spectrographic curves and pK values. It is concluded that BSP is metabolized

in the liver and excreted as a complex or conjugate which does not appear to be a glucuronide or ethereal sulfate.

RECOVERY OF ELECTROENCEPHALOGRAPHIC ACTIVITY WITH AND WITHOUT HEPARIN FOLLOWING CEREBRAL ISCHEMIA. M. Mason Guest and Ted Bond.* Dept. of Physiology, Univ. of Texas Med. Branch, Galveston.

The spontaneous electrical activity (electroencephalogram) from the cerebral cortex of dogs disappeared within 40 sec after complete arrest of circulation to the brain. Electrical activity eventually reappeared following 12 min of circulatory occlusion but did not reappear after 16 min of circulatory occlusion. Circulatory arrest was produced by ligating the vertebral arteries, blocking the spinal arteries with paraffin and inflating a blood pressure cuff which had been placed around the neck. To occlude the spinal arteries, tissue mat in the molten state was injected into the vertebral foramen followed by bone wax in the solid state and under pressure. In animals in which circulatory arrest was maintained for 8 min, essentially normal electrical activity returned within 45 min after releasing the pressure in the cuff. In dogs in which circulatory arrest was maintained for 12 min partial recovery of activity occurred within 120 min. Sixteen min of occlusion resulted in no return of electrical activity within 3 hr. In dogs which were heparinized sufficiently to prevent clotting of Lee-White samples for more than 4 hr and then subjected to circulatory occlusion, the recovery of electrical activity was neither greater than nor sooner than in dogs which were not heparinized but were subjected to the same period of circulatory arrest. Thus these data show no indication that the anticoagulant, heparin, materially assists in recovery of cortical activity following ischemia.

RESTORATION OF DIAPHRAGMATIC FUNCTION FOLLOWING VAGOPHRENIC ANASTOMOSIS. Lloyd Guth* and Karl Frank. Labs. of Neuroanatomical Sciences and Neurophysiology, Natl. Inst. of Neurological Diseases and Blindness, Bethesda, Md.

Unilateral vagophrenic anastomosis or phrenicophrenic anastomosis was performed at the brachial plexus level. Five to 8 months later, motion picture records of diaphragmatic movements, taken through an abdominal incision, showed the initially-paralyzed ipsilateral hemidiaphragm to be contracting normally in 5 of 8 vagophrenic rats and in all 6 phrenicophrenic controls. Transection of the vagus just below the nodose ganglion abolished the restored diaphragmatic contractions in the vagophrenic rats but not in the phrenicophrenic rats. Motor end-plates appeared normal histologically in both groups. In electrophysiological studies of additional vagophrenic rats, inspiratory action potentials were recorded from the "phrenic" nerve, which now contained regenerated vagal fibers. These inspiratory volleys were unaffected by spinal cord transection above the phrenic motoneurons (C1), but were abolished by cutting the vagus nerve rostral to the anastomosis. Inspiratory volleys were recorded from the vagus of unoperated rats proximal to the recurrent laryngeal branch and from the recurrent laryngeal nerve itself. No such volleys were found in the vagus nerve distal to the recurrent laryngeal branch. Therefore, recurrent laryngeal fibers of the vagus are presumed responsible for the observed return of diaphragmatic function after vagophrenic anastomosis; there is no need to postulate reorganization of intracentral neural pathways.

PULMONARY NITROGEN WASHOUT AT DIFFERENT DEGREES OF LUNG INFLATION. Pierre Haab and James E. Cimino (intr. by H. Rahn). Dept. of Physiology, Univ. of Buffalo, Buffalo, N. Y.

Positive pressure breathing has been demonstrated to affect the distribution of ventilation-perfusion ratios in the lung. In order to determine if the distribution of ventilation per se is affected by pressure breathing, the pattern of nitrogen clearance curves has been studied. Continuous positive and negative pressures were applied by means of a pressurized box to normal supine subjects. Varying pressures from -25 to +25 cm of water caused changes in FRC from 1700 to 4800 ml. Concomitantly, anatomical dead space varied in the same direction from 100 to 185 ml. Analysis of the N_2 washout curve allows division of the lung into at least 2 theoretical compartments washing out at different rates. During varied pressures the volumes of both compartments changed. With increasing pressures the slowly ventilating compartment increased to a greater extent than did the volume of the rapidly ventilating one. (Supported by the Air Research and Development Command - Wright Patterson AFB.)

EFFECT OF ELEVATION OF SERUM SODIUM CONCENTRATION UPON LARGE AND SMALL VESSELS OF THE DOG FORELEG. F. J. Haddy, D. Emanuel* and J. Scott.* Depts. of Medicine and Physiology, Northwestern Univ. and VA Research Hosp., Chicago, Ill., and the U. S. Army Med. Research Lab., Fort Knox, Ky.

Ten percent solutions of sodium chloride, sodium bicarbonate, sodium lactate and sodium sulfate have been infused into the brachial arteries of 19 dogs. The rate of blood flow was held constant at an average value of 118 ml/min. Pressures were measured in the brachial artery, a small artery (0.5 mm) in the foot pad, a small vein (0.5 mm) in the subcutaneous tissue of the paw and in the cephalic vein. Infusion rates were graded over the range 0.3 to 2.2 ml/min. Brachial and small arterial pressures decreased as a function of infusion rate with all 4 sodium salts. Venous pressures were unaffected. Average serum sodium concentrations in the cephalic vein of 147, 160 (NaCl 1 ml/min) and 168 mEq/l. (NaCl 2.2 ml/min) were associated with potassium concentrations of 3.5, 3.3 and 3.3 mEq/l., brachial arterial pressures of 134, 126 and 113 mm Hg and small arterial pressures of 73, 58 and 45 mm Hg, respectively. The changes occurred before the concentration of serum sodium changed in the hindleg. The effects of intra-arterially injected norepinephrine (1 γ) and acetylbetamethylcholine (1 γ) upon brachial arterial pressure progressively decreased as the infusion rate of sodium chloride was increased. Infusions of 10% calcium salts increased large and small arterial pressures. These studies indicate that small vessels dilate and are less responsive to vasoactive substances as sodium concentration is locally elevated.

ENDOCRINE IMPLANTS AND BREAST CANCER IN THE MOUSE. Franz Halberg, John J. Bittner* and Harvey L. Cole.* Div. of Cancer Biology, Dept. of Pathology, Univ. of Minnesota, Minneapolis.

D_8 (Dilute Brown, Subline 8) females, with the mammary tumor agent (MTA), were given weekly implants of certain tissues from female D_8 donors, starting at 4-5 wk of age and continuing for 8 or 14 wk. Twelve months later, some breast cancers appeared in the group receiving a total of 24 pituitaries (3/wk), while over one-third of the mice receiving a total of 70 pituitaries (5/wk) had breast cancer; no

cancers were seen at the 12-month check in mice given certain other endocrine implants or muscle. Comparable results were obtained in the C (Bagg Albino) stock, lacking MTA. Thus, in agreement with Mühlbock's findings, pituitary implants shortened cancer age in mice with MTA and induced breast cancer in mice without MTA. Moreover, in C mice, a total of 24 ovarian implants (3/wk) alone resulted in breast cancer, while another series of implantations of ovaries (3/wk), adrenals (3/wk), as well as thyroids and parathyroids, all into the same recipients, was not associated with breast cancer. Likewise, no breast cancer was seen in groups given a total of 24 implants 1) of adrenals (3/wk) alone, 2) of thyroids and parathyroids alone or 3) of muscle only. An ovarian-adrenal-cortical antagonism may characterize carcinogenesis in the breast of C mice.

PROGRESSIVE REGIONAL RENAL ISCHEMIA PRODUCED BY PARABIOSIS IN THE MOUSE. C. E. Hall, O. Hall* and A. H. Nevis.* Carter Physiology Lab., Univ. of Texas Med. Branch, Galveston.

Our earlier investigations showed that parabiosis causes hypertensive cardiovascular disease in about 20% of rats of the Holtzman strain. This includes hypertension, nephrosclerosis, periarteritis nodosa and cardiac lesions. Others have since confirmed this in parabiosed Wistar rats. Recently we have found that a related, but slightly different pattern of response results from parabiosis in mice. Mice of strain 129, said to be genetically homogenous, both dystrophics and normals, have been studied. In most there is produced a syndrome consisting of progressive ischemic infarction of the kidneys, accompanied by cardiac hypertrophy, suggestive of hypertensive disease. The syndrome differs from that observed in rats in the following respects. In rats only 1 member of the pair is ever affected, whereas in mice both may succumb; in the former the smaller arterioles in the kidney tend to be diffusely affected, whereas in the latter there is rather regional involvement of the larger arteries. Hence in the former the left and right kidneys are similarly enlarged and equally involved, whereas in the latter they are usually of dissimilar size and unequally affected. Mesenteric and cardiac vessels are involved in rats but not in mice. Cardiac hypertrophy characterizes the response in either species. (Supported by grants from the Natl. Muscular Dystrophy Research Fndn., Inc. (Liberty, Texas) and the Am. Cancer Soc. Inc.)

EVALUATION OF SPIROMETERS USED IN PULMONARY FUNCTION STUDIES. Lyle H. Hamilton and Ross C. Kory.* Med. Research Service, Wood VA Hosp., and Physiology and Medicine Depts., Marquette Univ. School of Medicine, Milwaukee, Wis.

In a recent comparison of spirometer response curves studied with a mechanical pump, Stead and Wells have indicated that the commonly used Collins spirometers are inaccurate at breathing rates above 80-90/min. They have designed a more accurate instrument with a lightweight plastic bell. In order to assess the significance of their findings on ventilatory measurements, we have made comparisons of the metal and plastic bell spirometers using normal subjects and patients. No differences could be demonstrated between 13.5 l. metal bell and 13.5 l. plastic bell spirometers for 0.5 sec, 1.0 sec and 3.0 sec expiratory capacities, total vital capacity or maximal mid-expiratory flow. The 200-1200 cc flow rate was greater ($P < .01$) for the 13.5 l. metal bell. The maximal ventilatory volume was measured at graded breathing

rates from 10-180/min in normal subjects. At low breathing rates no differences in spirometers were demonstrated. At rates above 90/min the ventilatory volumes recorded with the metal bell spirometer exceeded those with the plastic bell spirometer.

AMMONIUM INTOXICATION. Stanley W. Handford. Physiology Dept., Naval Med. Research Inst., Bethesda, Md.

Reversible ammonium intoxication was induced in unanesthetized, normal dogs by intravenous infusion at varying rates of ammonium sulfate and by rapid injection of ammonium carbonate equivalent to 50 mg nitrogen/kg body weight. A rise in urea nitrogen attends the rise in blood ammonia nitrogen. Pyruvic acid and glucose levels are elevated, but no significant change occurs in blood alpha keto-glutaric acid or plasma glutamine. The duration and severity of ammonium intoxication is shown to be independent of the pH of the dose but dependent upon the amount of nitrogen given and its rate of administration. From the measurements made on blood and plasma constituents there is no evidence to support the thesis that the symptoms of ammonium poisoning may derive from the reductive amination of alpha keto-glutaric acid thus interrupting the tricarboxylic acid cycle necessary to the metabolism of brain. It is pointed out, however, that measurements of blood and plasma constituents do not necessarily reflect the concentration of these substances at any particular moment in the organism as a whole.

OXIDATIVE PHOSPHORYLATION AND ADENOSINETRIPHOSPHATASE ACTIVITY OF LIVER TISSUE OF COLD ACCLIMATIZED RATS. John P. Hannon. Arctic Aeromed. Lab., Ladd AFB, Alaska.

The ability of liver tissue to couple phosphate esterification to the oxidation of succinate and β-hydroxybutyrate was assayed in control and 4-wk cold-acclimatized rats. The results of these experiments showed that cold exposure led to a lowering of the P/O ratio with both substrates. Thus, with succinate oxidation, it was reduced from 1.71 to 1.42 and with β-hydroxybutyrate oxidation from 2.08 to 1.52. With water homogenates a similar degree of activation by either calcium or magnesium ions was observed in tissue from control and cold-acclimatized rats. Simultaneous use of both activating ions resulted in lower activity than either alone. This lowering was significantly greater following cold acclimatization as compared to controls. With isotonic sucrose homogenates the effects of varying tonicity of the assay medium were studied. A progressive lowering of the activity was shown to be associated with increasing tonicity when calcium was the activating ion. An increasing activity, reaching a maximum at isotonicity, followed by a decreasing activity was associated with increasing tonicity levels when magnesium was the activating ion. Tissue from both cold-acclimatized and control animals behaved similarly in these experiments.

EFFECT OF LUNG INFLATION AND HYPOXIA ON PULMONARY BLOOD FLOW, PRESSURE AND VASCULAR RESISTANCE IN THE DOG. M. Harasawa* and S. Rodbard. Univ. of Buffalo Chronic Disease Research Inst., Buffalo, N. Y.

The portions of the cardiac output passing through each lung of 12 thoracotomized, anesthetized dogs were measured with rotameters in each branch of the pulmonary artery. Increases in lung insufflation pressure (pneophore) from 10 to 40 cm water diminished the cardiac output about 20%; pulmonary, mean and diastolic arterial pressures

(electromanometer) increased during the insufflation phase. The calculated vascular resistance increased linearly with insufflation pressure. These effects were dissipated during each succeeding expiration as the air pressure in the lung fell toward atmospheric levels. Breathing of pure oxygen, or 95% oxygen with 5% carbon dioxide, had no effect on these values. Acute hypoxia, induced by nitrogen breathing, produced a progressive rise in blood flow through the lungs for about 90 sec, with a flow increase of 25%. The pulmonary systolic and mean pressures increased, but the diastolic was unchanged. Pulmonary vascular resistance based on diastolic pressures usually declined. In other experiments the air pressure in each lung was controlled separately by means of a Rahn double lumen catheter. As the insufflation pressure in one lung increased, the resistance to flow through it increased linearly. These data demonstrate that an increase in intrapulmonary air pressure raises the pulmonary vascular resistance.

RESPONSES OF CONSCIOUS DOG TO LOCAL HEATING OF ANTERIOR HYPOTHALAMUS (MOTION PICTURE). J. D. Hardy, M. Fusco* and T. Hammel.* Aviation Med. Acceleration Lab., U. S. Naval Air Development Ctr., Johnsville, Pa., and Dept. of Physiology, Univ. of Pennsylvania, Philadelphia.

The film demonstrates the responses of a normal conscious dog to local heating of the thermo-sensitive area of the anterior hypothalamus. The heating is accomplished by applying radio-frequency energy between 2 needle electrodes implanted in the pre-optic and supra-optic region. Electrode location has been confirmed by histologic section. Hypothalamic temperature recorded is that measured by a thermocouple inside the tip of the needle electrode. (We are greatly indebted to Dr. R. B. Squires for his invaluable help in the preparation of this animal.) In response to mild heating of the anterior hypothalamus (39°C at the electrodes) the animal becomes very quiet, lies down, stretches out and appears drowsy. As the heating is increased (41°C) the animal sits up, becomes alert, salivates and begins to pant, continuing to pant as long as the central heating is maintained. At the end of 1 hr of heating, 30 min of which is a period of sustained vigorous panting, the heat is turned off and the dog stops panting. Central temperature is now 2°C below the preheating level of 38°C and the animal begins to shiver vigorously. The shivering is inhibited and the panting again elicited on re-application of heat. This sequence is then repeated. The responses observed are to the local thermal stimulation of the anterior hypothalamus.

ELECTROCORTICOGRAPHIC DIFFERENCES IN D_8 MICE AT TIMES OF DAILY HIGH AND LOW SUSCEPTIBILITY TO AUDIOGENIC CONVULSIONS. Richard N. Harner* and Franz Halberg. Univ. of Minnesota Med. School, Minneapolis, and Cambridge State Hosp., Cambridge, Minn.

Under controlled conditions (light from 06:00 to 18:00, for 1 wk prior to study, see Proc. Soc., 1955, 88:169), D_8 mice approximately 5 wk of age have a higher incidence of convulsions following exposure to noise at 21:00 than at 09:00. Using Nembutal anesthesia (0.06 mg/gm), electrocorticograms with frequency analysis were recorded from 93 such D_8 mice at times of low (09:00) or high (21:00) convulsive susceptibility. An index of energy content of each electrocorticographic tracing was obtained by summing the height of the pips from 2 epochs of frequency

analysis. Percent time abnormal recording, a blind subjective grade of abnormality (0, 1 to 4 plus), and a calculation of mean frequency were also obtained. Mean frequency was decreased at 21:00, as compared to 09:00, from 10.39 cps to 9.99 cps in males ($P < 0.01$) and from 10.23 cps to 9.74 cps in females ($P \sim 0.05$). In males, mean values for energy index, percent time abnormality and subjective grade were all more than 50% greater at 21:00 than at 09:00 ($P \leq 0.01$). In females, these same variables were over 150% greater at 21:00 ($P \leq 0.001$). Clearly, an increase in electrocorticographic abnormality characterizes the time of higher convulsive susceptibility in this model for one clinical type of 24-hr periodic convulsion.

PRODUCTION OF VERY HIGH EXTRACELLULAR POTASSIUM CONCENTRATIONS IN THE INTACT RAT AND ITS EFFECT ON MUSCLE MEMBRANE POTENTIAL. John C. Harvey* and Kenneth L. Zierler. Dept. of Medicine, Johns Hopkins Univ., Baltimore, Md.

It is the purpose of these experiments to measure the relationship between the membrane potential (E_R) of gastrocnemius in the intact rat and $[K^+]_o$ in the muscle extracellular fluid. $[K^+]_o$ was increased by close arterial injection into the femoral artery. In earlier experiments $[K^+]_o$ could be increased only 2- to 3-fold owing to systemic effects. To obtain greatly increased $[K^+]_o$, the venous effluent from the leg was diverted into an extra-corporeal vena cava which could be set to prevent recirculation. Blood volume was maintained by transfusion. Although these experiments should permit establishment of a steady state, none was attained. Therefore no quantitative relation between $[K^+]_o$ and E_R is yet available in this preparation. However, venous plasma $[K^+]$ from muscle increased transiently to 15, 21, 56 and 101 mEq/l. with concomitant decrease in E_R. (Aided by a contract from the Office of Naval Research.)

ENTEROCHROMAFFIN CELLS IN INTACT, TRANQUILIZED AND ADRENALECTOMIZED MICE. Erhard Haus,* Walter Runge* and Franz Halberg. Cambridge State Hosp., Cambridge, and Univ. of Minnesota Med. School, Minneapolis.

Argentaffinity (Masson-Hamperl), argyrophily (Bodian) and the reduction test of Chèvremont-Frédéricq were demonstrated in duodenum of mice of both sexes and several stocks (C, D_8, and B_1). The degree and distribution of granulation were subjectively graded and the proportion of the most abundantly granulated stage (expressed as % of total number of argentaffin cells/100 villi/mouse) was used as endpoint. This endpoint was, on the average, higher in adrenalectomized mice, as compared to sham-operated controls and, in intact mice, it was not significantly changed by 400 μg/20 gm body wt of compound Ro 1-9569 (2-Oxo-3-isobutyl-9, 10-dimethoxy-1, 2, 3, 4, 6, 7-hexahydrobenzo-[a] quinolizine hydrochloride—a new tranquilizer from Hoffmann-LaRoche). In higher doses, however, the compound lowered the endpoint more significantly at 2 hr post-injection than at one-half or 4 hr post-injection. In mice receiving the higher doses of tranquilizer, as compared to saline-injected animals, brain 5-hydroxytryptamine content also was lower. Tranquilizer effects upon the contents of 5-hydroxytryptamine in brain and gut could not be dissociated; as compared to the effect of reserpine, however, the effect of Ro 1-9569 was of shorter duration.

GALACTOSE AND URINARY CALCIUM. F. W. Heggeness (intr. by E. S. Nasset). Dept. of Physiology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

The effect of dietary galactose on urinary calcium excretion was studied in rats. Handler (J. Nutrition 33:221, 1947) reported that rats receiving diets containing 80% galactose showed large urinary losses of this ion. McCay and others (J. Gerontol. 7:161, 1952) found in rats fed a cow's milk diet 11% of the excreted calcium was in the urine. Urinary calcium excretion was compared in pair-fed rats receiving a complete synthetic diet containing either 60% galactose or glucose. None of the animals had diarrhea. A significantly greater urinary calcium loss occurred in the rats receiving the galactose diet; the difference between the 2 groups was of a lesser magnitude than shown in earlier studies. The animals receiving galactose excreted approximately 1 mg of calcium more than control animals. That this effect is probably unrelated to the effect of galactose on calcium absorption is indicated by the finding that the same differences in urinary calcium were noted following feeding of a diet providing a calcium intake of only 0.3 mg/day. Urinary calcium excretion was found to be elevated as soon as galactose was added to the diet and persisted for the 4-wk period of observation. Urinary sodium and potassium also increased but not for several days following feeding galactose diets.

EFFECT OF BLOOD FLOW ON MUSCLE OXYGEN CONSUMPTION IN THE DOG. S. R. Heisey,* J. T. Fales* and K. L. Zierler. Depts. of Environmental Medicine and Medicine, Johns Hopkins Univ., Baltimore, Md.

It is commonly held that oxygen consumption of resting muscle is a biological constant and that, accordingly, when blood flow to resting muscle increases, arteriovenous oxygen difference decreases proportionately. In the isolated, normally-circulated, gastrocnemius-plantaris of the dog this does not appear to be true. "Spontaneous" increases in resting blood flow clearly produced increased oxygen consumption in 11 of 19 dogs. In the remainder in most cases the variance was too great to determine whether or not oxygen consumption increased with flow and in some cases A-V O_2 differences did decrease with increased flow. To test this observation further, blood flow to the leg was changed by changing cardiac output. A-V O_2 difference was either constant or decreased only relatively slightly with increased blood flow, and muscle oxygen consumption rose. (Aided by a contract from the Office of Naval Research and grant A-999 from the PHS.)

SOME FACTORS AFFECTING RENAL CLEARANCE OF POTASSIUM. R. C. Herrin and C. M. Corlett.* Dept. of Physiology, Univ. of Wisconsin Med. School, Madison.

In anesthetized dogs previously given KCl, the K uptake by the left kidney was determined as the (A-V, K difference x C_{PAH}) minus urinary K, during the infusion of KCl. C_K/C_{cr} rose with renal uptake. Initially, small increments of uptake elevated C_K/C_{cr} much more than later ones. In conscious dogs, after KCl infusion, the C_K/C_{cr} could be maintained at about 1.0, when the +K balance for the whole dog had decreased to less than 5 mEq but the $C_{PAH} \times P_K$ had remained at about 1.0 mEq/min for both kidneys. This suggests that the renal excretory mechanism for K after its activation may operate due to K delivered to it by the circulation and somewhat independently of the K content in the renal

cells. In 9 anesthetized dogs, partial clamping of the aorta to reduce femoral pressure to 50-75 mm Hg, always markedly reduced C_K and C_K/C_{cr}. This was also true when C_K/C_{cr} was 1.0 in the intermediate periods. E_{PAH} was not reduced by clamping.

SITE OF REABSORPTION OF SULFATE IN THE NEPHRON OF THE DOG. K. Hierholzer,* R. S. Gurd,* R. H. Kessler and R. F. Pitts. Dept. of Physiology, Cornell Univ. Med. College, New York City.

We have applied the stop flow technique to provide direct evidence as to where solutes are either secreted into or reabsorbed out of the tubular fluid. This study presents data from experiments on dogs which indicate the proximal tubules as the site of reabsorption of sulfate ions. Sodium sulfate was infused to establish plasma concentrations of 7-17 μEq/ml. Under these conditions sulfate concentrations were significantly lower in "proximal urine samples" (i.e. tubular fluid which remained in proximal tubules during the clamping period) than in distal or control urine samples. C sulfate/$C_{creat.}$ ratios reached lowest values of .18 - .29 at the site of maximal p-aminohippurate secretion. While there is no indication that sulfate is either secreted or reabsorbed in distal tubules, the presence of a load of sulfate ions alters distal tubular functions by accentuating the acidification of urine and enhancing the secretion of ammonia.

INHIBITION OF CONCENTRATING OPERATION IN HYPOTHERMIC KIDNEY. Suk Ki Hong and John W. Boylan (intr. by H. Rahn). Dept. of Physiology, Univ. of Buffalo, Buffalo, N. Y.

The effect of hypothermia upon the renal concentrating operation during hydropenia and during constant infusion of 2M urea in isotonic saline was studied in 8 dogs. The PAH, exogenous creatinine and osmolar clearances were determined as well as the renal oxygen consumption. Following 2-4 control periods the body temperature was lowered to approximately 25°C by the use of an ice-water bath. The above measurements were then repeated during this steady state of hypothermia. The PAH and creatinine clearances as well as the renal O_2 consumption were reduced to approximately 1/3 of control, while the urine flow remained either unchanged or slightly increased. Thus a relatively less proportion of the filtered water is reabsorbed. Since osmolar clearance was only slightly lowered during hypothermia, it implies also a reduced tubular reabsorption of the filtered osmotic particles in spite of a decreased glomerular filtration rate. Thus free water clearance (T^cH_2O) was reduced to approximately 1/4 of control and the U/P osmolar ratio approached 1.0 in hypothermia. On the basis of these results which indicate a relatively greater inhibition of water reabsorption than that of salts, it is postulated that the mechanism which controls the balance between H_2O and salt reabsorption is temperature sensitive.

PRODUCTION OF LABELED CARBON DIOXIDE BY AN EXCISED SYMPATHETIC GANGLION. Paul Horowicz* and Martin G. Larrabee. Dept. of Biophysics, Johns Hopkins Univ. Baltimore, Md.

Rate of production of radioactive CO_2 by superior cervical ganglia excised from rats was recorded continuously. Solution containing glucose, randomly labeled with carbon-14, flowed past the tissue and onto filter paper. Gas passing over the paper transported the $C^{14}O_2$ past a Geiger counter. At 36°C the rate of $C^{14}O_2$ production slowly

increased after changing to labeled glucose. After 2 hr the $C^{14}O_2$ production reached a steady state and remained constant for at least 10 hr. The steady state production of $C^{14}O_2$ accounted for about 35% of the glucose consumed. Lactate production, previously measured, accounted for about 30% of the glucose consumed, leaving 35% unaccounted for at rest. The $C^{14}O_2$ production from C-14 glucose accounted for only 45% of the oxygen consumption at rest. Stimulation of the preganglionic nerve (5.0/sec) soon after $C^{14}O_2$ production reached the steady state produced a small increment in $C^{14}O_2$ production. This increment accounted for only 20% of the observed increase in oxygen consumption of ganglia so stimulated. This substantially agrees with previous evidence that glucose oxidation is not the major source of the increased oxygen uptake during activity at 36°. This contrasts with evidence that accelerated glucose oxidation could account for activity oxygen uptake at 23°. (Aided by Grant B 702 from PHS.)

MACROELECTRODE RECORDING FROM SUPRACALLOSAL MESIAL CORTEX OF UNANESTHETIZED CATS. John R. Hughes and John A. Mazurowski.* Meyer Hosp. and Buffalo Med. School, Buffalo, N. Y.

A previous communication (Fed. Proc. 17:75, 1958) outlined the technique for studying the supracallosal mesial cortex of unanesthetized cats. Thin electrode assemblies, used for stimulation or recording, were implanted onto the mesial surface; a bidirectional waveform was used for stimulation. This waveform separates well current thresholds for movement (lower) and after-discharge (higher); unidirectional waveforms of increasing duration bring these thresholds closer together. Studies on movement show two "felunculi": the anterior one, lower in threshold, is mainly contralateral in representation; the posterior one has prominent ipsilateral and bilateral representation. Studies on after-discharge show that the frequency of 18/sec is common, along with 9/sec. The effect of periodic stimulation (for 1-8 days) producing after-discharges is to decrease the amount of the faster frequency (18/sec), increase the amount of the slower frequency (9/sec) and raise the threshold for after-discharge. Full-blown seizures from cingular gyrus stimulation are psychomotor-like in character and feature high amplitude spike and wavelike complexes, not appearing on the lateral cortical surface, but spreading to the hippocampus. The mesial cortex shows photic driving of highest amplitude at 5/sec. The locus showing best driving varies according to the frequency of the stimulus. Sharp responses to sudden auditory stimuli during drowsiness strongly resemble the K complex; the distribution of amplitude of these responses is similar to that of sleep spindles (12/sec).

HISTAMINE METABOLIZING ACTIVITY OF DOG AND RAT STOMACH AND INTESTINE. A. C. Ivy and Yutaka Kobayashi.* Dept. of Clin. Science, Univ. of Illinois College of Medicine, and the Worcester Fndn. for Exper. Biology, Chicago.

The gastric mucosa of the dog and rat was examined for histamine-metabolizing activity using the method of Schayer and Cooper (J. Appl. Physiol. 9:481, 1956) which employs only a microgram of C^{14}-histamine. As a control, for diamine oxidase (DO) (histaminase) the intestine was used. In the dog no evidence of DO was found in cell-free extracts of the pyloric and fundic mucosa though much was present in the intestinal mucosa. But a small amount of histamine destruction not inhibited

by aminoguanidine and semicarbazide occurred when minced fundic and pyloric mucosa was used, the nature of which remains undetermined. The fundic and pyloric mucosa of the rat, however, contained about 10% as much DO activity as the intestine.

TEMPERATURE REGULATION OF NORMOTHERMIC DOGS IMMERSED IN WATER. Frank H. Jacobson (intr. by M. H. F. Friedman). Dept. of Physiology, Jefferson Medical College, Philadelphia, Pa.

The temperature of clipped, unanesthetized dogs immersed to the neck in water regulated at 36.6 ± 0.03°C was measured in the rectum, brain (lateral ventricle), carotid artery or neck muscles and abdomen. The temperature at each point was measured at intervals not longer than 2.5 min. Each of the core temperatures tended to oscillate ±0.05-0.12 about a mean in irregular periods of 5-15 min or to drift continuously, oscillations being superimposed on the drift. The tendency to drift was unrelated to the existing temperature. Rectal temperature might be 0.5° either higher or lower than brain temperature. Arterial, abdominal and neck temperatures were lower in the order of writing. In each dog, the relative levels of the temperatures measured tended to be fixed even after the water bath had been cooled 1° and then rewarmed. Frequently the temperatures changed in opposite directions but only because nearly parallel temperature:time curves were out of phase by several minutes. The core temperature of all dogs increased 0.1-0.4 while the temperature of the bath was being lowered. Thereafter the temperature of some remained elevated while the temperature of others returned to the control level or fell 0.7° below it. The temperature of some dogs increased - that of others decreased - during and after rewarming of the bath.

NEUROTROPHIC EFFECTS ON THE DIAPHRAGM. N. C. Jefferson,* T. Ogawa* and H. Necheles. Dept. of G. I. Research, Medical Res. Inst., Michael Reese Hosp., Chicago, Ill.

This is continuation of work reported at the previous meeting. Section of phrenic nerve leads to disappearance of contraction of diaphragm upon stimulation of its phrenic after 7-9 hr, and progressive atrophy of the diaphragm, complete after 1 year. However, following crush of a phrenic or section and anastomosis, there is little degeneration of the diaphragmatic muscle, although respiratory motion of the diaphragm is absent 10-12 wk and return of contraction of diaphragm upon stimulation of its phrenic nerve is not obtained before 7-8 wk. This trophic effect is also obtained with vagophrenic and intercostal-phrenic anastomoses. With the 2 latter procedures, respiratory functions of the diaphragm did not return in periods of 12 and 3 months, respectively, but stimulation of anastomosed nerves produced contraction of the hemi-diaphragm. (Supported by PHS Grant B-1356.)

VENOUS-ARTERIOLAR RESPONSE IN THE INTESTINAL VASCULAR BED. Paul C. Johnson* and Ewald E. Selkurt. Dept. of Physiology, Indiana Univ. School of Medicine, Indianapolis.

Studies in a number of vascular beds, including the intestine, have shown an increased resistance with elevation of venous pressure. This has been variously attributed in other beds to extrinsic nerve activity, local reflexes or a myogenic response. The purpose of this study was to determine the mechanism of the venous-arteriolar response in the intestine. Employing dogs anesthetized with 30 mg/kg sodium

pentobarbital, a segment of ileum was prepared for measurement of intestinal weight and venous flow. Venous pressure was elevated from 5 to 30 cm H_2O in 5 cm increments for a period of 5 min at each pressure. With intact preparations elevation of venous pressure caused an increase of 50.6% in vascular resistance, accompanied by cumulative increases of interstitial fluid of 7.4 gm/100 gm tissue and blood volume of 4.1 gm/100 gm tissue. After section of all extrinsic nerves this response was not appreciably altered. Intra-arterial infusion of dibenzyline and 4% procaine were likewise ineffective, indicating the response is not dependent upon nerve activity. Tonus changes and increased tissue pressure were also ruled out. With continuous infusion of the smooth muscle relaxant, papaverine hydrochloride, the vascular resistance rose 11.6% as compared with 61.6% in the control preparations. Cyanide and anoxia were more effective, entirely preventing the increase in resistance. It is concluded that a non-nervous mechanism, perhaps a myogenic response, is involved.

LOCALIZATION OF RADIOPHOSPHORUS (P-32) IN RAT OVARY. Bergene Kawin and Glenda Vogt (intr. by Joseph Meites). Biology Operation, Hanford Labs., General Electric Co., Richland, Wash.

The autographic localization of radiophosphorus (P-32) in rat ovary was studied to facilitate evaluation of its potential radiation hazard to gonadal tissue. To accomplish this solutions of inorganic P-32 were injected intraperitoneally into young adult female Sprague-Dawley rats. The rats were killed at periods of time ranging from 1 to 56 days following injection. Autoradiograms of ovaries showed marked concentration of P-32 in the granulosa layer, and in cellular elements lining the follicular cavity or surrounding the ova. Grain density over fluid areas of the follicles was negligible. Little P-32 was observed in atretic and degenerating follicles and in the vascular areas. Radiochemical analyses indicated that P-32 concentration in ovary decreased as a power function with time, while its concentration in bone remained constant throughout the experimental period. The application of these findings to calculations of maximum permissible concentrations (MPC) of P-32 in air or water will be discussed. The valuable assistance and advice of N. L. Dockum, Biological Analysis Operation, and of J. W. Healy, Radiation Protection Operation, is gratefully acknowledged. (Performed under Contract No. W-31-109-Eng-52 between the U. S. Atomic Energy Commission and General Electric Co.)

SITE OF URATE TRANSPORT IN THE NEPHRON OF THE DOG. R. H. Kessler, K. Hierholzer,* R. S. Gurd* and R. F. Pitts. Dept. of Physiology, Cornell Univ. Med. College, New York City.

The localization of renal tubular mechanisms for urate transport was studied by the stop flow technique. Urate was infused at 7.5 mg/min with a resultant $C_{urate}/C_{creatinine}$ ranging from 0.5 to 0.9 in the control periods. Reabsorption of urate during stop flow occurred at the site of maximum PAH secretion, the proximal segment. Probenecid, in a dose sufficient to eliminate proximal PAH secretion, reduced reabsorption of urate but without any clear-cut indication of the site at which this effect occurred. One Dalmatian failed to reabsorb infused urate.

PANCREATIC ISLETS IN FETUSES AND OFFSPRING OF DIABETIC RATS. Jae Nam Kim, Walter Runge, Lemen J. Wells and Arnold

Lazarow (intr. by W. Lane Williams). Dept. of Anatomy, Univ. of Minnesota, Minneapolis.

Diabetes was induced in 25 females by alloxanization or pancreatectomy either before conception or on day 12 of pregnancy. Fetal islets were examined at 21 days and 15 hr (9 control, 15 experimental) and islets at various times after delivery (29 control, 23 experimental). The cytological alterations observed in islets of fetuses of diabetic mothers were: 1) very marked decrease in the number of granulated beta cells and in number of granules per cell, 2) hydropic changes usually present in the centrally-located islet cells and 3) hyperplasia of islets. In preliminary quantitative counts, granulated cells constituted 41.6% in 1 control fetus and 0.17% and 0.16% in 2 experimental fetuses. During the 6 days following delivery, the number of granulated beta cells increased progressively; by day 6, it approximated that of controls. The hydropic change decreased during the 6-day period following delivery. PAS staining, controlled by amylase digestion, indicated that the hydropic change was associated with glycogen deposition. Hyperplasia of islets was most striking at birth. Although the blood sugar of offspring of diabetic mothers was markedly elevated at the time of delivery, it became normal within 24 hr, and it remained normal during the subsequent 6-day neonatal period. Nevertheless, the cytological alterations in the islets persisted for a much longer period. (Aided by PHS Grants A-1244 and A-1659.)

ELIMINATION OF DL-THYROXINE-1-C^{14} IN BILE, URINE AND EXPIRED AIR OF HYPO-, HYPER- AND EUTHYROID RATS. Howard M. Klitgaard and Peter A. Kot.* Physiology Dept., Marquette Univ. School of Medicine, Milwaukee, Wis.

Biliary elimination of C^{14} activity in the control rats amounted to 11.8% of the injected dose within 6 hr. Desiccated thyroid treated animals showed an increased excretion of radioactivity with an increased volume of bile produced. Thyroidectomized and thiouracil-treated rats showed no change from normal in the amount of radioactivity eliminated but both groups eliminated a reduced volume of bile. Urinary excretion of thyroxine activity during the 12-hr period never exceeded 2% of the injected amount regardless of the group studied. Hyperthyroid animals showed increased urinary excretion of radioactivity with increased volume of urine eliminated. The urinary C^{14} activity of the hypometabolic groups was lower than the control animals. The recovery of C^{14} in the expired air was taken to indicate that decarboxylation of the administered thyroxine had occurred. Within 12 hr about 12% of the injected activity appeared as $C^{14}O_2$ in the control group. No alteration in this amount was observed in the hyperthyroid animals. Both hypometabolic groups showed decreased $C^{14}O_2$ production; however, this was only significant in the thiouracil-treated animals. (Supported by PHS Grant A-957.)

BREATH HOLDING AFTER NORMAL BREATHING AND HYPERVENTILATION ON OXYGEN. Francis J. Klocke* and H. Rahn. Dept. of Physiology, Univ. of Buffalo, Buffalo, N. Y.

Seven untrained subjects held their breath at full inspiration after normal breathing of O_2 gas. Breath-holding times ranged from 3 to 8.5 min and "breaking point" alveolar CO_2 tensions from 51 to 91 mm Hg. Under these conditions, the maximum breath-holding time is linearly related to the change in alveolar CO_2 tension. With prior

hyperventilation of O_2 followed by a full inspiration, the periods of maximum voluntary apnea were noticeably extended, total times ranging from 6 to 14.5 min, but the "breaking point" alveolar CO_2 tensions did not exceed those noted above. The measured changes in lung volume during breath holding were almost entirely due to O_2 consumption since the total amount of CO_2 in the lung at the onset of breath holding was essentially the same as at the end. The decreases in lung volume are approximately related to the total breath-holding times, about 13 min being required for a change in lung volume equal to the vital capacity. (Supported by the Erie County Heart Assoc.)

EFFECT OF OUABAIN ON RENAL ELECTROLYTE TRANSPORT IN ANESTHETIZED DOGS. Alan Koch (intr. by J. W. Woodbury). Depts. of Physiology and Biophysics, Univ. of Washington School of Medicine, Seattle.

When renal Na excretion was initially high, the administration of 0.1 mg/kg of ouabain profoundly inhibited Na reabsorption and as much as 30% of the filtered Na appeared in the urine. The nature of the anion excreted depended on the experimental situation. When Na excretion had been elevated initially by the infusion of an NaCl solution, the increment in anion excretion after administration of ouabain was composed almost entirely of Cl, but when an $NaHCO_3$ solution had been infused, the increment was composed almost entirely of HCO_3. The data are consonant with the hypothesis that a) the cardiac glycoside inhibits a renal electrolyte transport system which is directed primarily toward Na, the reabsorption of Cl and HCO_3 taking place as a result of the electrostatic gradient so produced, and that b) the ratio of permeabilities of the tubular epithelium to the 2 anions varies inversely as the ratio of their concentrations in plasma. (Aided by Grants B462, B-823 from the Natl. Inst. for Neurological Diseases and Blindness, and by Grant HTS5204 from the Natl. Heart Inst., PHS.)

NEUROMUSCULAR TRANSMISSION IN A SODIUM-FREE MEDIUM. K. Koketsu and S. Nishi (intr. by L. G. Abood). Research Labs., Dept. of Psychiatry, Univ. of Illinois College of Medicine, Chicago.

The present study was performed to determine whether the neuromuscular transmission could be maintained in sodium-free media. Neuromuscular transmission of frog nerve-sartorious was completely blocked when soaked in a sodium-free 224 mM sucrose solution (containing 2.0 mM KCl and 1.8 mM $CaCl_2$) for 30-40 min. A surprising restoration of neuromuscular transmission occurred in the preparations which were first immersed in sucrose for 60-90 min and then in a sodium-free hydrazine solution (containing 2 mM KCl and 1.8 mM $CaCl_2$). Meanwhile, the resting potential of the muscle fibers maintained a normal value, and muscle action potentials, similar to those observed in normal Ringer, were produced by intracellular direct stimulations. With nerve stimulation the end-plate potentials and local responses were recorded from the end-plate regions. The muscle contractions, however, disappeared shortly after continuous nerve stimulations (1/sec) were applied for 10-20 min, although the electrical activity of the nerve twig innervating the sartorious muscle and the sensitivity of the end-plate membrane to directly applied Ach were sufficiently maintained. These results showed that, in addition to the activity of the motor nerve axon and the muscle fibers, the activity of pre- and post-synaptic membrane was restored in the sodium-free

hydrazine solution. Although a trace of sodium may be retained around the junctional regions, it is not likely that the concentration was sufficient to maintain the transmission. (Supported by PHS Grant B-1650.)

ELECTROCARDIOGRAPHIC AND PATHOLOGIC EFFECTS OF NOREPINEPHRINE ADMINISTRATION DURING EXPERIMENTAL HEMORRHAGIC HYPOTENSION. Ross C. Kory, A. Stephen Close and Joseph M. Lubitz (intr. by James J. Smith). Surgery and Pathology Depts., Wood VA Hosp. and Marquette Univ. School of Medicine, Milwaukee, Wis.

In a previous investigation of the role of norepinephrine in a standardized type of hemorrhagic hypotension, there was a 64% mortality in 41 dogs who received norepinephrine as compared with a 33% mortality in 45 control dogs. Serial electrocardiograms were taken during and after the experiments and the hearts were removed at the time of death. Survivors were killed 4-9 days after experiments. Electrocardiographic abnormalities were more frequent and more severe in the animals given norepinephrine. These consisted of the appearance and deepening of Q-waves, ST and T-wave abnormalities, and widening of QRS. In 22 of 23 hearts from animals treated with norepinephrine, areas of subendocardial hemorrhage were seen, but in only 2 of the 20 control hearts examined were such lesions encountered. Extensive fatty degeneration of the myocardium was noted in 5 of 10 norepinephrine-treated animals who survived and were later killed. No other major microscopic abnormalities were observed in the hearts from either the controls or those animals receiving norepinephrine. Although norepinephrine has been shown to increase both cardiac output and coronary blood flow during hemorrhagic hypotension, the myocardial damage noted in this study suggests that these increases are inadequate to meet the accompanying increase in myocardial oxygen requirement due to increased cardiac work.

CHANGES IN POTASSIUM FLUXES IN SKELETAL MUSCLE EXPOSED TO ACID. R. J. Kossmann* and R. C. Swan. Dept. of Physiology, Cornell Univ. Medical College, New York.

In a very thin skeletal muscle of the frog, changes in K influx and efflux were measured as the pH of the phosphate or bicarbonate buffered medium was varied from 7.5 to 5.5. In phosphate buffered medium or in bicarbonate buffered medium in which pCO_2 is constant, K influx and efflux decrease by only 10% of the control rates at pH 7.5 as the hydrogen ion concentration of the medium increases 100-fold. This is in contrast to the much larger changes in the Na fluxes observed under similar conditions. In bicarbonate buffered medium in which bicarbonate concentration is constant and pCO_2 varies from 10-600 mm Hg, K influx and efflux decrease by approximately one third of the control rates at pH 7.5 for each 10-fold increase in hydrogen ion concentration of the medium. These changes are prompt, reversible and reproducible, and, in the media used, the muscle remains electrically excitable and microscopically intact for several hours. Assuming that CO_2 readily penetrates the fiber membrane but that the bicarbonate ion does not, these results suggest that the K fluxes are functions of intrafiber pH, are relatively insensitive to changes in the pH of the medium and that a linkage between K influx and Na efflux may be less direct than previously supposed.

TARGET ORGAN ACTIVATION BY STRESS. Jenö Kramár, Margaret Simay-Kramár* and Anthony J. Carnazzo.* Dept. of Pediatrics, Creighton Univ. School of Medicine, Omaha, Nebr.

Increased corticosteroid activity, required in stress conditions, has been believed to occur solely by pituitary-adrenocortical activation resulting in increased corticosteroid production. Studies of the relationship between capillary stress response and adrenocortical activation suggest that the organism possesses an additional mechanism to meet the increased demand for corticosteroid activity. This mechanism functions by increasing the sensitivity of the target organs to corticosteroids. The following method was found suitable for the demonstration of sensitivity changes of the capillaries to corticosteroids. An ointment containing 0.5% Δ^1-hydrocortisone was applied on a circumscribed skin area of the flexor surface of the arm in human subjects and of the abdomen of dogs. The vehicle of the test ointment was applied in the same manner on an adjacent control area. Five hours later the resistance of the capillaries was measured in both areas by the negative pressure method. No difference was noted as long as the subjects were leading a routine life and avoiding any extra stressful activity. Following physical or emotional stress the capillary resistance was found to be markedly higher in the cortisone-treated skin area than in the control area. The studies suggest that this capacity of the organism to deal with stressful situations in a way other than by adrenocortical activation, as shown by the specific example of the capillaries, is related to the sympathetic nervous system.

METHOD FOR POLAROGRAPHIC CONTINUOUS IN VIVO RECORDING OF BLOOD OXYGEN TENSION. F. Kreuzer and C. G. Nessler, Jr. (intr. by S. M. Tenney). Dept. of Physiology, Dartmouth Med. School, Hanover, N. H.

A catheter-type PO_2 electrode for continuous recording of blood oxygen tension in vivo by ordinary catheterization has been constructed. The basic principle was similar to that employed by Clark. The electrode system was included into a polyethylene tubing (external diameter 1.5 mm), covered with a "Teflon" membrane 0.001" thick on its proximal end. For application in animals, coating with "Velvasil" prevented any coagulation in the vessel. The current developed was about 1-2 μA for air at 0.6 volts. It was amplified by a General Radio Company Type 1230-A DC amplifier and recorded by a Honeywell 906 Visicorder. The in vitro calibration curves yielded straight lines between 0 and 100% O_2 with a low rest current for helium. The standard deviation was never more than 3% for any reading. The response time was 1.5 sec for 95% amplitude. In dog experiments (in collaboration with T. R. Watson, Jr. and M. L. Heller) such catheters were introduced into the aorta over carotid or femoral artery for periods of more than 2 hr. The animals were ventilated with various oxygen mixtures at constant ventilation. Blood samples withdrawn at equilibrium were analyzed for PO_2 in our in vitro polarograph. The readings were plotted against the inspiratory oxygen mixtures and the PO_2 values and yielded straight lines in both cases.

LOCALIZATION OF ENZYMES IN SUBCELLULAR FRACTIONS OF ANTERIOR PITUITARY. Frank S. LaBella* and J. H. U. Brown. Dept. of Physiology, Emory Univ., Atlanta, Ga.

Fresh anterior pituitaries from beef and pig were separated by

differential centrifugation into subcellular fractions. Nuclei and debris were obtained at 1200 rpm for 15 min, acidophilic granules at 7000 X g for 20 min, mitochondria at 34,000 X g for 15 min, and microsomes at 78,000 X g for 3 hr. Basophilic granules, visible electromicroscopically in sections of intact pituitary gland, were not present in homogenized tissue. The distribution of nitrogen, pentose nucleic acid and phospholipid were very similar to that reported for liver, if the values for the acidophilic granule fraction were included in the data from the mitrochondrial fraction. Beef and pig anterior lobes were quite similar in their intracellular composition as seen in the various fractions. Succinic dehydrogenase was localized in mitochondria, while alkaline phosphatase and adenosine-5-phosphatase were concentrated in the microsomes. A proteinase with pH optimum at 8.2 was exclusively localized in microsomal and supernatant fractions. Acid phosphatase, acid ribonuclease and a proteinase with pH optimum 3.8 were distributed among the subcellular fractions in another pattern, indicating the presence of a particle type distinct from mitochondria and microsomes. The distribution of cytoplasmic PNA paralleled that of alkaline phosphatase and adenosine-5-phosphatase.

RAT GASTRIC SECRETORY RESPONSE TO CONDITIONING. Ardelle Lane. Dept. of Physiology, Northwestern Univ. Dental School, Chicago, Ill.

Five tests were performed on each of 10 rats which had been previously prepared with a gastric fistula and conditioned to eat with the ringing of a bell. Each day for 2 months, the rats were placed in Bollman cages and fed once during the day concomitant with the ringing of a bell. To eliminate association of eating with time or cage, animals were maintained in cages all day and the feeding time was varied. After 2 months, gastric secretory responses were determined. During an experiment, secretion was collected from rats 1-5 until "control" was established. The bell was then rung and rats 6-10 were fed. This status of individual rats was alternated in successive tests. The average volumes of gastric secretion the 2nd and 1st hr before controls and the 1st and 2nd hr after the conditioning stimulus were respectively: 1.4, 1.3, 1.8, and 1.0 cc. The corresponding average HCl outputs in mg were: 3.8, 3.4, 4.8, and 2.2. Analysis of variance permits the same conclusion for both volumes and acid outputs. There was no significant difference between the 1st and 2nd control values. The values of the 1st post-stimulation hr were significantly greater than either control. The 2nd post-stimulation hr values were significantly less than the 2 controls, and the 1st post-stimulation hr. This experience indicates that rat gastric secretion can be conditioned.

EFFECT OF LSD-25 ON CORTICAL EVOKED POTENTIALS IN THE CAT. Thomas W. Langfitt and Louis A. Finney (intr. by A. Earl Walker). Div. of Neurological Surgery, Johns Hopkins Univ., Baltimore, Md.

The effect of LSD-25 on primary visual, auditory and somatic potentials, evoked by physiological stimuli, on the transcallosal evoked potential and on the direct response of the suprasylvian gyrus to electrical stimulation was studied in the cat. Nembutalized and unanesthetized preparations paralyzed by succinylcholine were used. Simultaneous oscillographic and electroencephalographic recordings were obtained. The temperature, electrocardiogram and blood pressure

were recorded. LSD-25 was administered in doses from .025 mg/kg to 4.0 mg/kg via the femoral vein. Except under deep Nembutal anesthesia, the variability in evoked potentials was so great that a significant drug effect was problematical by visual inspection alone. Therefore, the mean amplitudes of a series of evoked potentials obtained at fixed times during a control period were statistically analyzed (analysis of variants) and compared to a series evoked at similar time intervals post-injection in the same animal. Usually changes in amplitude following injection were within the range of changes in amplitude during the control period. However, slight increases in amplitude of visual, auditory and somatic evoked potentials were seen when the drug was given in doses from .05 mg/kg to 2.0 mg/kg. In a similar dose range, great variability in LSD-25 effect on the transcallosal evoked potential and direct response of the suprasylvian gyrus was seen, an increase or decrease in mean amplitude occurring with approximately equal frequency.

GLYCOGEN CONTENT OF THE RAT. L. L. Langley and W. A. Beall.*
Univ. of Alabama Med. Ctr., Birmingham.

We previously reported that, in the dog, no glucose appears in the parotid saliva until the blood glucose level exceeds about 500 mg%. It was also found that the insulin content of the blood markedly influences this threshold. This finding, in combination with the report that epinephrine also alters the threshold, suggested to us the possibility that the deposition of glycogen in the parotid gland may be the determining factor. To investigate this hypothesis we analyzed the glycogen content of the rat parotid gland under varying conditions. In the normal fasting rat the parotid glycogen content averages below 0.01%. As the blood sugar is elevated glycogen is deposited in the glands reaching a maximum of over 0.03% at a blood sugar level of 300 mg%. Higher blood sugar values do not increase the parotid glycogen. If insulin is administered along with blood sugar, the glycogen content of the parotids does not exceed approximately 0.02%, a value which is significantly lower than that obtained in the absence of exogenous insulin. In marked contrast, the administration of epinephrine completely depletes the parotids of their glycogen stores. (Supported by Grant USPH-D-329(C).)

PREDICTIVE VALUE OF THE RELATION OF % RELATIVE BILATERAL LUNG WEIGHT TO BILATERAL OXYGEN UPTAKE, TIDAL VOLUME, FUNCTIONAL RESIDUAL CAPACITY AND STATIC COMPLIANCE IN THE DOG. Michael T. Lategola* and John A. Schilling* (intr. by A. N. Taylor). Physiology and Surgery Depts., Univ. of Oklahoma Med. School, Oklahoma City.

Based on 21 washed and air-dried lungs, Rahn et al. (J. Appl. Physiol. 8:417, 1956) have reported the % relative lobar weights of the dog. According to these data, the right lung constitutes 58.3% and the left lung 41.7% of the total lung weight. In the supine, Nembutalized dog, bilateral measurements of oxygen uptake, tidal volume, functional residual capacity and static compliance at 20 cm H_2O inflation pressure have been tabulated from the control data of several cardiopulmonary studies. These data reveal an amazing degree of agreement of the right:left relative function of these 4 parameters with the % relative right:left lung weight. This relation may be used as a baseline for the measurement of bilateral changes in these 4 parameters when both lungs are present in the animal. On the assumption that the % relative function also exists at the lobar level, one may, under certain specific

conditions, use this relation as a baseline for the measurement of functional changes at the lobar level. (Supported by funds from the School of Aviation Medicine, Randolph Field, AF contract #41-657-105.)

GASTRIC ACID SECRETORY EQUIVALENT OF DIFFERENT FOODS. Marjorie K. Lavers,* Suzanne Saint-Hilaire* and Charles F. Code. Mayo Clinic and Mayo Fndn., Rochester, Minn.

This study was undertaken to determine precisely the relative stimulating value of different foods on the gastric acid. The quantitative estimates were made in 6 dogs with vagally innervated gastric pouches. Foods of equicaloric value, brought to equal volumes by blending with distilled water, were fed to each dog. The responses were standardized by expressing the acid output of each of the pouches to each of the foods, as a percent of the mean response of the particular pouch to repeated feedings of 100 calories of beef. Thus, the mean acid secretory equivalent value of each food (meat = 100) was obtained. More than 20 different foods were tested. The mean secretory equivalent values for some of the foods are as follows: haddock, 214; salmon, 76; chicken, 120; pork, cheese, eggs and milk, 70-80; vegetables, 50-75; potatoes (boiled or French fried), 40-50; butter, 41; white bread, 37; fruits, 15-25. A close correlation has been found between the grams of protein per calorie in each food and the milliequivalents of hydrochloric acid secreted in response to each calorie of the food.

EFFECTS OF BODY POSITION ON THE PULMONARY CAPILLARY BED IN NORMAL SUBJECTS AND PATIENTS WITH PULMONARY CONGESTION. Benjamin M. Lewis, Tai-hon Lin,* William T. McElroy* and L. Carl Sandberg.* Dept. of Medicine, Wayne State Univ. College of Medicine and Detroit Receiving Hosp., Detroit, Mich.

A rebreathing method for measuring the diffusing capacity of the lungs for carbon monoxide ($D_{L_{CO}}$) (Fed. Proc. 11:95, 1958) is well adapted to detecting the changes in $D_{L_{CO}}$ with changes in body position since both the absorption of carbon monoxide and the dilution of helium can be determined at one time, thus taking account of possible changes in residual volume with body position. Using this method, we have found that $D_{L_{CO}}$ increases on changing from the standing to the recumbent position, both while breathing room air and while breathing oxygen. When capillary blood volume (V_c) and true membrane diffusing capacity (D_M) are calculated from these data by the method of Roughton and Forster (J. Appl. Physiol. 11:290, 1957) V_c increases while D_M decreases on changing from the standing to the recumbent position, confirming previous work using the single breath $D_{L_{CO}}$. In 2 subjects with pulmonary congestion due to rheumatic heart disease, no change in $D_{L_{CO}}$ occurred on changing from the standing to the recumbent position.

EFFECT OF 3-BETA-AMINOETHYL-1,2,4-TRIAZOLE ON GASTRIC SECRETION. K. W. Liepins* and A. C. Ivy. Dept. of Clin. Science, Univ. of Illinois, College of Medicine, Chicago.

It has been reported that this triazole stimulates gastric secretion (Ainsworth and Jones, J. Am. Chem. Soc. 75:4915, 1953, and T. M. Lin, in press). The purpose of this study was to make a comparison of the potency by weight of this compound and of histamine. Both compounds

were used as the di-hydrochloride. Two Heidenhain pouch dogs (16 kg) were used. They were selected on the basis of their rather uniform response to histamine. When there was very little or no free acid (pH 4.5) in the basal secretion, the drugs were administered subcutaneously and the secretion was collected for 3 hr after the injection. Ten to 12 tests were made on each dog at each dose level. On injecting the dog with 0.3 mg histamine base the output of HCl in mg was 59 ± 11 and 53 ± 7 (S.D.), respectively. With 0.3 mg of triazole base, the HCl output was 32 ± 9 and 33 ± 7 mg, respectively. With 0.39 mg of triazole base, the HCl output was 42 ± 10 mg and 42 ± 9 mg, respectively. With 0.45 mg triazole base, the HCl output was 68 ± 15 mg, respectively. From the curve of HCl output for triazole it was calculated that 0.42 mg of triazole base would be required to stimulate the production of 56 mg HCl, or 0.3 mg histamine base is equivalent to 0.42 mg of triazole base, at level of production of 56 mg HCl used as a comparative base.

INCREASED RESISTANCE TO EPINEPHRINE SHOCK IN ENDOTOXIN TOLERANT DOGS. Richard C. Lillehei and Lloyd D. MacLean (intr. by J. A. Johnson). Dept. of Surgery, Univ. of Minnesota, Minneapolis.

We have noted that, in the dog, there is a marked similarity between shock induced by the injection of epinephrine and that induced by the injection of endotoxins of gram-negative bacteria. In both, the irreversible state is characterized by a significant loss of plasma volume, hemoconcentration and a rise in plasma hemoglobin. In addition, at autopsy, liver congestion and hemorrhagic necrosis of the bowel also characterize both types of shock. To more clearly define the relationship between these 2 types of shock, dogs were made tolerant to lethal amounts of endotoxin or epinephrine by the daily or every other day injection of increasing amounts of these substances for periods of 8-16 days. Eight dogs made tolerant to endotoxin were then given an intravenous dose of epinephrine, 16-17 μg/kg/min for 120 min, which we had previously found to be lethal for 90% of normal adult dogs. Seven of these dogs survived permanently and did not manifest the characteristic plasma loss, hemoconcentration or rise in plasma hemoglobin to the extent usually seen in lethal epinephrine shock. When killed, the bowels of these survivors were normal. On the other hand, all 5 dogs made tolerant to epinephrine died precipitously when given an intravenous dose of crude E. coli endotoxin, 7.5 mg/kg, previously found to be lethal for 90% of normal adult dogs. Before death from endotoxin shock, these epinephrine-tolerant dogs had large plasma losses measured and at autopsy the characteristic visceral lesions were found.

CHANGES IN LUNG COMPLIANCE AND FUNCTIONAL RESIDUAL CAPACITY WITH POSTURE. Thomas P. K. Lim* and Ulrich C. Luft. Dept. of Physiology, Lovelace Fndn., Albuquerque, N. M.

By means of concomitant recordings of air flow and intraesophageal pressure together with an oxygen open-circuit system, lung compliance (C_L) and functional residual capacity (FRC) were determined in duplicate on erect standing and supine lying positions in 6 healthy adults. The postural change from the standing to the supine did not alter tidal volume appreciably, but it caused an increase in static esophageal pressure difference in all subjects, thereby reducing lung compliance significantly from 0.190 to 0.139 l/cm H_2O. At the same time FRC was also reduced (mean decrease of 33%) so that the specific lung compliance

($C_{SL} = C_L/FRC$) remained the same at 2 body positions. The high correlation between lung compliance and FRC found in this study at 2 postures is evident and it agrees well with that reported by others on normal subjects of different body sizes. The importance of considering the initial volume of the system in assessing elastic properties of the lung will be discussed.

COMPARISON OF PYRIDOXAL AND THYROXINE EFFECTS ON OXYGEN CONSUMPTION OF RAT KIDNEY SLICES. R. H. Lindsay* and S. B. Barker. Dept. of Pharmacology, Univ. of Alabama Med. Ctr., Birmingham.

Rat kidney cortex slices in Krebs' Ringer glucose with either DL-alanine or L-proline consumed oxygen at almost the initial rate after 3 days incubation at 5°C in the presence of L-thyroxine compared to about 10-20% of the initial rate without thyroxine. The addition of pyridoxal or pyridoxal phosphate to the Ringer-alanine-glucose medium resulted in better maintenance of tissue oxygen consumption without thyroxine but had no effect in the presence of thyroxine. When Ringer-proline-glucose was the medium, only a very slight pyridoxal effect was seen. No maintenance effect was obtained with pyrodoxine, pyridoxamine or pyridoxamine phosphate. Preliminary determinations indicate that the level of α-keto acid in the medium following incubation with thyroxine was 45% lower than the concentration found in the controls. Experiments with pyridoxal phosphate in the absence of tyroxine resulted in 25% less α-keto acid than controls without pyridoxal phosphate. The α-keto acid level of the medium with thyroxine was not affected by the addition of pyridoxal phosphate. Thus, thyroxine and pyridoxal appear to produce similar effects on kidney cortex slice metabolism in the presence of Ringer-alanine-glucose. (Supported by grants from the PHS and the American Cancer Soc.)

TRANSPORT OF VITAMIN A ACROSS NORMAL ISOLATED RAT INTESTINE AND INTESTINE SUBJECTED TO "PARTIAL" RESECTION (6-12 WEEKS POSTOPERATIVE). M. R. Loran and T. L. Althausen (intr. by L. L. Bennett). Gastrointestinal Research Lab., Dept. of Medicine, Univ. of California School of Medicine, San Francisco.

Transport of vitamin A across isolated intestine was studied, using the method of Darlington and Quastel (Arch. Biochem. Biophys. 43:194, 1953). The mucosal solution contained vitamin A and tween 80 in Ringer-glucose-bicarbonate. The serosal solution contained tween 80 in Ringer bicarbonate. It was necessary for tween 80 to be present on the serosal side for transport of vitamin A out of the normal intestine, indicating that during transport the vitamin is converted to an insoluble form. Under aerobic conditions, the rate of transport of vitamin A was the same for normal and resected intestine. Under anaerobic conditions, transport was reduced 50% for resected intestine and totally inhibited for control intestine. These results were duplicated under aerobic conditions when DNP (1×10^{-5} M) was added to the mucosal solution. Thus, for the control intestine transport is entirely dependent on DNP-sensitive phosphorylation mechanisms (Berry and McMurray, Canad. J. Biochem. Physiol. 35:799, 1957), which require tween 80 on the serosal side for transport of vitamin A out of the intestine. The DNP-insensitive mechanisms responsible for 50% of the total transport across resected intestine did not require tween 80 as a solubilizing agent on the serosal side. Partial resection resulted in alteration of the mechanisms of vitamin A transport.

CORRELATION BETWEEN MEAL SIZE, PYLORIC SPHINCTER ACTIVITY AND GASTRIC EVACUATION. Hortense Louckes and J. P. Quigley. Dept. of Physiology, Univ. of Tennessee Med. Units, Memphis.

Pyloric sphincter activity of unanesthetized, well-trained dogs was recorded by the Inductograph method (Brody and Quigley: J. Lab. & Clin. Med. 29:3, 1944). Gastric evacuation was determined fluoroscopically. The "test" meal was a mixture of 100 gm canned commercial dog food (Daily); 50 gm corn meal; 100 gm $BaSO_4$ and 450 cc H_2O. Following an 18- to 24-hr fast, the dogs were fed 10, 20 or 30 gm/kg body weight of this "test" meal. The activity of the pyloric sphincter was recorded continuously until the stomach was empty; and the x-ray shadow of the stomach was recorded at 15-min intervals. Variation in the size of the meal had no significant effect on pyloric sphincter tone, frequency of pyloric sphincter contractions, or amplitude of pyloric sphincter contractions. Variation in the size of the meal had no significant effect on the time of onset of evacuation of the meal from the stomach. There was a wide variation both in the time of onset of evacuation and complete evacuation of the stomach. The tendency of larger meals to be evacuated at a faster rate could not be correlated with pyloric sphincter activity. (Supported by a grant from the PHS.)

GRAPHICAL SYSTEM FOR VISUALIZATION OF OVERALL METABOLIC PATTERNS IN TERMS OF ENERGY, GAS EXCHANGE AND FUEL MIXTURE. Lorne MacHattie (intr. by A. C. Burton), Physiology Dept., Univ. of Buffalo, N. Y.

The quantitative relations of heat production, gas exchange and metabolic fuel mixture, though somewhat refractory to verbal description, may be clearly portrayed by graphical means. The correspondence between fuel mixtures and their respective Heat:O_2:CO_2 ratios is most conveniently displayed by a graph of the reciprocal caloric equivalent of O_2 vs. that of CO_2, on which fuel mixtures are found to lie in a straight-line pattern. To each point on this graph there corresponds a set of 6 parameters, of which, given the value of any one, the other 5 may be deduced. These parameters are 1) heat production, 2) O_2 consumption, 3) CO_2 production, 4) energy from carbohydrate, 5) energy from fat, and 6) energy from protein. R.Q. too may be read off. This scheme shows the relations for metabolism involving interconversions as well as catabolism of fuels, partially-anaerobic metabolism, ketolysis or ketogenesis, or the handling of other metabolites. The effects of non-steady states in the exchange of heat and gases can be shown quantitatively.

EXISTENCE AND NATURE OF A CORTICOGENICULATE OPTIC INHIBITORY SYSTEM. Amedeo S. Marrazzi, José M. Rodríguez* and E. Ross Hart.* VA Research Labs. in Neuropsychiatry, Pittsburgh, Pa.

We have previously noted that after lateral geniculate destruction the initial enhancement of geniculocortical responses, induced by intracarotid injection of serotonin, disappears and is reversed. We have interpreted this as the interruption of a negative feedback between visual cortex and lateral geniculate. Additional evidence for this system is obtained by partial decortication in the optic area by locally applied procaine and by local freezing. These procedures immediately result in an increase in the size of the radiation spikes initiated by

stimulation of the optic tract. Furthermore, changes in the amplitude of radiation spikes elicited by direct stimulation of the optic radiations demonstrate that geniculate transynaptic influences affect post-synaptic axonal excitability. Complete masking of both eyes minimized possible retinal participation. The data point to a cortical origin and a geniculate locus for a negative feedback or corticofugal inhibitory circuit which is susceptible to interruption, by the synaptic inhibitory actions of serotonin, LSD-25, and gamma-aminobutyric acid.

EFFECT OF DURATION OF INJECTION ON INDICATOR-DILUTION CURVES. Hiram W. Marshall,* Newton C. Birkhead* and Earl H. Wood. Mayo Fndn. and Mayo Clinic, Rochester, Minn.

The effect of varying durations of injections of dye on various parameters of dilution curves was studied in 8 dogs and 4 normal subjects. T-1824 in a volume of 1-2 ml was injected rapidly in 0.4 (0.3-0.7) sec via a cardiac catheter into the pulmonary artery or superior vena cava and recorded at a systemic artery. This was followed immediately by slow injection of an equal volume of dye averaging 4.2 (3.1-6.4) sec in duration and then by a second rapid injection. Average appearance and build-up times of 5.9 and 4.2 sec were significantly increased with slow injection to 6.6 and 5.9 sec, respectively; disappearance time was not significantly altered. Slow injection was associated with an average decrease in peak concentration of 21%. There was, however, no systematic difference in cardiac output values. Since the mean transit time was uniformly increased with slow injection the central blood volume (Stewart-Hamilton) was increased an average of 14% while by the Newman method no systematic change occurred. These studies confirm the theoretical conclusion that "instantaneous" injection is not a prerequisite for measurement of cardiac output by the sudden-single injection technic. Relatively small changes in contour of the dilution curves associated with this 10-fold difference in duration of injection reduce somewhat requirements for rigid control of this parameter.

FACTORIAL ANALYSIS OF EFFECTS OF ESTRADIOL, TESTOSTERONE AND PROPYLTHIOURACIL ON SECONDARY SEX CHARACTERS. Richard C. Mason (intr. by David F. Opdyke). Dept. of Physiology, Seton Hall College of Medicine and Dentistry, Jersey City, N. J.

A factorial design involving 3 variables was used to demonstrate the influence of low levels of thyroid hormone, produced by giving 0.2% propyl-thiouracil (PTU) in diet, on the response of the secondary sex characters to androgens and estrogens in White Leghorn pullets. A marked depression in the ability of testosterone-propionate (TP) to produce comb growth was observed in the presence of PTU. This finding is in agreement with the results of others. In contrast, no failure in oviduct growth was observed in response to estradiol valerate (EV) in the presence of PTU. Despite the failure of TP to produce normal comb growth in the presence of low levels of thyroid hormone, there was only slight inhibition of the ability of TP to enhance the growth effects of EV on oviducts in the presence of PTU. These data demonstrate the effectiveness of a factorial design in elucidating hormone interactions. Comparative mammalian studies suggest that these interactions may be of practical importance. (Supported by NIH Grant #A-1560.)

INDUCED HYPERTHERMIA; EFFECT UPON SYSTEMIC, PULMONARY AND CORONARY HEMODYNAMICS AND METABOLISM OF THE INTACT DOG. G. M. Maxwell, G. G. Rowe, D. J. Freeman, D. H. White, Jr., L. A. Lucas and C. A. Castillo (intr. by Q. R. Murphy). Cardiovascular Lab., Univ. of Wisconsin, Madison.

Cardiac output (Fick), and coronary blood flow (N_2O Fick) were measured in 9 dogs before and after raising body temperature (average +8°F) by diathermy coil. Respiration rate, minute volume of ventilation, O_2 consumption and CO_2 production all increased significantly. Arterial-mixed venous O_2 difference increased, arterial and mixed venous CO_2 levels decreased. Cardiac output increased 3.2-4.5 l/min, ($P < 0.01$), heart rate increased by 56% ($P < 0.05$); systemic and pulmonary arterial blood pressures were unchanged, but total pulmonary resistance fell by 25%. Left ventricular work increased significantly. Coronary blood flow increased from 102 to 151 cc/100 gm myocardium/min ($P < 0.05$). Coronary sinus O_2 and CO_2 contents fell significantly, cardiac metabolic rates for O_2 and CO_2 increased. Coronary vascular resistance declined. The O_2 consumption of the weighed left heart increased by 95%, but stroke O_2 consumption was unchanged. Index of efficiency (L.V. work/$\bar{C}MRO_2$), and calculated external cardiac efficiency decreased. Lactate and pyruvate in the arterial and coronary sinus blood increased, as did the pH. Induced hyperthermia increased respiration, pulse rate, cardiac output and coronary blood flow. Venous O_2 and CO_2 levels decreased. The cardiac metabolism increased and its efficiency fell.

ULCER FORMATION AND GASTRIC DISTENSIBILITY IN THE MOUSE. W. H. McArthur,* T. Ogawa* and H. Necheles. Dept. of Gastrointestinal Research, Michael Reese Hosp., Chicago, Ill.

Dr. Ogawa has reported a possible difference in gastric tensile strength of pyloric ligated young and old mice and has related early rupture of the stomach in the young and late appearance of ulcer in the old mouse. The early rupture in the former occurred at the pyloric ligature and was due to overdistention. The stomach of the old mice showed greater distensibility and, while at times it contained relatively large amounts of secretion, it never perforated at the pyloric ligature and perforation of ulcers was relatively rare. For these reasons, the maximal distensibility of the stomach of young and old mice was tested. The pylorus was ligated, a plastic tube was introduced through the esophagus and saline solution was injected with a syringe. The pressure in this system was measured with a mercury manometer. The breaking point of the stomach was recorded in ml saline and mm of mercury. (Supported by U. S. Vit. Corp.)

EFFECTS OF PHYSIOLOGICAL ALTERATIONS OF BLOOD VOLUME IN MAN ON HIS CARDIOVASCULAR RESPONSE TO STRESS. John P. Meehan and H. I. Jacobs (intr. by C. Hyman). Physiology Dept., School of Medicine, Univ. of Southern California, Los Angeles.

A series of experiments has been conducted to test the hypothesis stating that blood volume is a determining factor in the response of man's cardiovascular system to stress. A group of subjects were placed on a program of 1 month of bed rest followed by 1 month of arduous exercise. Their cardiovascular responses to standardized exposures to whole body cooling and acceleration were extensively studied at 3 points during the experiment; namely, before the regimen

started, after rest period and again after the exercise period. Their blood volumes were measured by the T-1824 dye dilution technique. The differential activity regimens produced marked changes in total blood volume of approximately 25%. In spite of such large changes in total blood volume there were no observable changes in their peripheral vascular responses to whole body cooling as measured by rectal and skin temperature and metabolic rate measurements. Further, there was no change in their g tolerance as indicated by peripheral light loss measurements. These data indicate that when blood volume is altered by physiological means over a prolonged period, the circulatory system is capable of adequately responding to an acute stress without relation to the absolute blood volume existing at the moment.

VENOUS-ARTERIOLAR REFLEX IN THE SMALL INTESTINE. M. W. Meyer (intr. by M. B. Visscher). Dept. of Physiology, Univ. of Minnesota, Minneapolis.

A venous-arteriolar reflex has been reported by Burton and collaborators (Circ. Research 1:27, 1953) in the extremities of human subjects after the venous bed had been distended. Haddy (Circ. Research 6:659, 1956) described this phenomenon in the renal vessels of the dog. The evidence for arteriolar constriction in the above studies was indirect. In the present study a Leitz Ultropak microscope was used to observe vessels in the small intestine of 7 dogs following laparotomy in order to obtain direct evidence of arteriolar constriction after the portal vein pressure had been mechanically elevated. Records were made with a 35-mm camera. The portal vein pressure was monitored via the splenic vein and recorded on a twin-visco recorder. The systemic arterial pressure was recorded from the carotid artery. The initial diameter of the arterial pressure was recorded from the carotid artery. The initial diameter of the arterioles varied from 80 to 250 micra, the venules or small veins from 50 to 670 micra. The venules were distended from 8 to 78%. The arteriolar radius decreased 10 to 45%. In 6 of the experiments the pressure was elevated for 10 min with an increase ranging from 15-32 mm Hg above the control value. In one experiment it was elevated 4 mm Hg for 3 min. The characteristic response of the systemic pressure was a transient drop followed by a partial return to the control level and usually complete recovery after the portal pressure was decreased. This study has a special interest because in the dog there is an increased portal pressure in endotoxin shock and its reflex consequences may play a role in the total shock reaction.

FACTORS IN REANIMATION OF MICE FROM LESS THAN 1°C. James A. Miller and Faith S. Miller.* Dept. of Anatomy, Emory Univ., Atlanta, Ga.

Hypothermia protects newborn and adult mammals from experimental asphyxia (Miller, '54, '57). By contrast, a simple and very effective method for cooling animals to 0°C with subsequent recovery utilizes partial asphyxiation during the first stage of cooling (Andjus and Smith, '55). To resolve this apparent paradox, mice were cooled by the Goldzveig-Smith method. After 1 hr in sealed vessels the O_2 content was 6%, CO_2 was 11%, deep colonic temperature approximately 15°C. The relative importance of hypoxia, hypercapnia and high humidity was tested by addition of soda lime, silica gel, or both. Hypercapnia proved most beneficial, hypoxia next, and increased humidity

of least value for recovery of postural reflexes, prevention of hind limb weakness and indefinite survival. Tests of the efficacy of air, 100% O_2, 95% O_2 + 5% CO_2, and 90% O_2 + 10% CO_2 for artificial respiration during rewarming demonstrated the superiority of 95% O_2 + 5% CO_2, whether the hypothermia was of short duration (15 min) or of long (30 or 60 min below 5°C). Mice cooled without hypoxia and hypercapnia and injected with "Micropaque" showed generalized severe arterial vasoconstriction. Those cooled in sealed vessels did not show arteriospasm until 2 hr below 5°C, at which time resuscitation was no longer possible.

LATENT HEAT OF FAT AS A SOURCE OF HEAT DURING COOLING. G. W. Molnar and J. C. Rosenbaum, Jr.* Environmental Med. Dept., U. S. Army Med. Research Lab., Ft. Knox, Ky.

The latent heat of fat has not been seriously considered as a source of heat during cooling. Since this heat is about 40 cal/gm, it can conceivably be a factor in protection against cooling. To test this possibility hog subcutaneous fat was placed in a metal cylinder (2.5 cm in diameter, 20 cm in length) and exposed to still air at about 5°C. Cooling at the center proceeded rapidly down to 29.2°C; then stopped for 8-10 min; thereafter it again proceeded rapidly. Beef suet warmed to 40°C cooled continuously; if warmed to 100°C its cooling was interrupted for 8-10 min at 35.3°C. The heat treatment apparently altered the crystalline structure (fat is polymorphic) or released fatty acids (which even in small quantities lower the melting point). Thus whether or not latent heat is a factor as a source of heat in the physiological range of temperature varies with species, saturation, crystalline form, etc. Abdominal surface temperatures of nude human corpses, both obese and lean, exposed to still air at 0°C showed no indication of evolution of latent heat; unfortunately the initial temperature was always about 30°C. Similar cooling curves on living men were affected by vasodilatation and by shivering so that the possible effect of latent heat could not be discerned.

EFFECT OF CO_2 ON VENTRICULAR FUNCTION. R. G. Monroe,* G. French* and J. L. Whittenberger. Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

The effect of both a high and low pCO_2 on ventricular function was investigated in an open-chested preparation by allowing the animal to breathe varying concentrations of CO_2 and evaluating cardiac performance in terms of left ventricular stroke work. Cardiac output exclusive of coronary flow was measured by a flowmeter inserted in the aorta. Left auricular, pulmonary artery and aortic pressure were measured with strain-gauge manometers. Cardiac rate was maintained constant by electrical stimulation of the ventricles after previous ligation of the bundle of His. Alveolar CO_2 was monitored with a Liston-Becker rapid CO_2 analyzer. On allowing the animal to breathe a mixture of 8% CO_2 and air the alveolar pCO_2 rose to approximately 70 mm Hg with a concomitant rise in left auricular pressure. Upon correcting the left auricular pressure to its original level by phlebotomy there was depression of left ventricular stroke work which varied from 9 to 45% of the control value obtained at the same left auricular pressure. In contrast, when the animals were hyperventilated with room air the pCO_2 fell to approximately 10 mm Hg. With a low pCO_2 there was no significant alteration of either left auricular pressure or left ventricular stroke work at a constant heart rate.

CARDIAC DEPRESSANT EFFECT OF ACID AND ITS REVERSAL. Gabriel G. Nahas. Dept. of Cardiorespiratory Diseases, Walter Reed Army Inst. of Research, Washington, D. C.

The cardiac depressant effect of CO_2 on the heart-lung preparation (HLP) and its reversal by the sympathomimetic amines has been reported (Nahas and Cavert, Am. J. Physiol. 190:483, 1957). Acute myocardial failure is also observed when the denervated HLP is rendered acidotic by addition of 3-12 mM of lactic or hydrochloric acid (arterial pH 6.84-7.31). Evidence of this failing state includes increased vena caval pressure, decreased aortic pressure, diminished cardiac output against a constant resistance, bradycardia and acute cardiac dilatation. Reversal of acid induced failure is obtained by raising the blood pH close to its normal value, either by eliminating CO_2 from the HLP (ventilation with 100% O_2) or by addition of base. Reversal of acid induced failure is also produced by the administration of 1-4 mcg/min of epinephrine, norepinephrine, methamphetamine or isoproterenol. The similarity of the production of acidotic heart failure by hypercapnia or by addition of acid indicates a common underlying cause: the increase in H^+ ion concentration.

RELATION OF EVANS BLUE DISAPPEARANCE FROM THE BLOOD AND TRANSPERITONEAL TRANSFER IN CARBONTETRACHLORIDE LIVER DAMAGE. Thomas E. Nelson, Jr. (intr. by D. B. Tyler). Dept. of Pharmacology, Schools of Dentistry and Medicine, Univ. of Puerto Rico, San Juan.

It was shown by C. Hyman and co-workers that it is invalid to draw conclusions about blood vascular permeability from Evans Blue disappearance data alone, that in normal rabbits a significant fraction of the disappearance rate is accounted for by uptake in reticuloendothelial cells (primarily in the liver), and this activity can be stimulated or depressed by various drugs or eradicated by evisceration. However our experiments with rabbits in which the liver was acutely poisoned with CCl_4, as evidenced by jaundice and extremely low blood prothrombin levels, showed a marked increase rather than reduction in the disappearance rate. Histologically the Kupffer cells appear inactivated or destroyed by CCl_4, and the blue appearance of the liver is due to dye in parenchymal cells. Simultaneously with disappearance measurements a method for estimating transperitoneal plasma protein transfer rate yielded values equal to or less than controls. Apparently both types of measurement are largely dependent upon liver function but effected by different mechanisms. Their relationship to hypoprothrombinemia caused by CCl_4 or Dicumarol will be discussed. (Supported by research grants H-2779 and H-3552, Natl. Heart Inst., PHS.)

CARDIAC CONDITIONAL REFLEXES IN THE OPOSSUM. J. E. O. Newton* and W. Horsley Gantt. Pavlovian Lab., Johns Hopkins Univ., Baltimore, Md.

Previous work from this laboratory has established in dogs and humans: a cardiac component of the orienting reflex (OR), of the motor defense reflex, of food reflexes, with differentiation according to nature of the stimulus - excitation, inhibition and intensity. For comparative physiology and for determining universality of cardiac conditioning we are studying other animals (opossum, penguins). In the opossum the unconditional stimulus (US) was faradic shock to tail; the conditional stimuli, two tones, one excitatory, the other inhibitory. Results. Two

opossums showed motor respiratory and cardiac components of conditional reflexes (CRs) and unconditional reflexes (URs), sometimes ORs (motor ORs transient, no definite cardiac or respiratory ORs). UR: motor reflexes to shock to tail range from flexion of tail to generalized motor activity. Respiratory URs occurred consistently: sudden marked inspiration, apnea 10"-15" followed by return to normal respiration. Cardiac acceleration, 20-40 beats/min occurred at first in both animals; in one, after several reinforcements, deceleration occurred. CR: no motor reflexes (after 220 reinforcements). Respiratory reflexes to excitatory and inhibitory tones formed after 70 reinforcements, similar to URs; differentiation after 160 reinforcements. Cardiac CRs to excitatory tone in one animal consisted of acceleration, average 6-12 beats/min, in the other animal of deceleration (84%), average 6 beats/min. Acceleration occurred to inhibitory tone first, differentiation (no acceleration) developing after 50 reinforcements. Conclusions: Opossums form and differentiate cardiac and respiratory CR components; but there was no evidence of motor CRs.

ELECTRORETINOGRAPHIC PHENOMENA OF HEREDITARY VISUAL CELL DEGENERATION IN MICE. Werner K. Noell. Roswell Park Memorial Inst., Buffalo, N. Y.

In all adult mice of the C_3H strain, the electroretinogram was found extinguished when mice were screened for hereditary visual cell abnormalities. The adult retina of this strain lacks all photoreceptor elements; the visual cells are missing except for one row of nuclei. This condition is inherited as a recessive Mendelian character. It develops during the post-natal differentiation of the visual cell to a functional state. No significant abnormalities exist at birth and for about 9-10 days thereafter. At 10 days the ERG makes its first appearance, i.e. at the same time as in control strains. ERG development proceeds for about 2-3 days; then it fails and it disappears between 20 and 28 days. Apparently, the visual cell dies (pyknosis) and deteriorates (lysis) within a few days after it begins to function. At all times during its presence the ERG shows abnormalities (low, slow a-wave, late b-wave, high threshold) which suggest that a defective sensory organelle has been formed as the first manifestation of the inherited cell abnormality. (Supported by PHS Grant B-812.)

RENAL FUNCTION CHANGE WITH LOW TEMPERATURE EXPOSURE. William C. Nungesser (intr. by Benjamin DeBoer). Depts. of Physiology and Pharmacology, Univ. of North Dakota, Grand Forks.

Unanesthetized trained dogs were exposed to low environmental temperatures +8 to -25°C for 1-2 hr. Temperatures and renal function changes were recorded, including glomerular filtration rate, renal plasma flow, urine volume, sodium and chloride excretion and osmolality, osmolar and free water clearances. Chloride excretion consistently increased in the cold. Dogs unlike man did not show a water diuresis in the cold. No significant change in rectal temperatures was seen although marked falls in both back and foot temperatures occurred consistently.

RADIOFREQUENCY IMPEDANCE PULSES OVER CARDIAC AND EXTRA-CARDIAC REGIONS. Jan Nyboer, Rodney Willard,* Cleto Di Giovanni, Jr.,* Thomas Herrmann* and Erwin Finkelstein.* Harper Hosp., Detroit, Mich.

Variations in the volume of blood modulate a radiofrequency signal and produce variations in electrical shunt or parallel resistance in the cardiac and extra-cardiac regions. The mass motion of blood associated with the distributed volume pulse or cardiac emptying is studied by local impedance explorations of the torso using the tetrapolar impedance plethysmograph operating above 100 kilocycles/sec. The electrocardiogram and the electrical impedance characteristics across the shoulders serve simultaneously as respective indices of rhythm and conduction of the heart as well as the central systemic pulse for correlation with the exploratory impedance pulses, pressure pulses, heart sounds, low frequency ballistocardiograms and roentgenfluorokymograms. The forms of the impedance pulses permit identification and timing of atrial and ventricular dynamic events over the heart as compared with events over the aorta, pulmonary artery, lungs, head and extremities by the same method. In general, the impedance method yields graphic information closely comparable to roentgenphotofluorokymograms and densograms of the heart and lungs. The central cardiac area has the largest pulse mass motion and the abdomen the least per given surface area. Studies by this impedance method afford a physiological approach to mechanics of the heart beat without gross bloodletting or complex mechanical encapsulation. The final data may be defined in ohms resistance, percent differences, in amplitudes, time intervals, slopes and gradients.

NORMAL URINARY EXCRETION OF FOLIC AND FOLINIC ACIDS. John S. O'Brien and Douglas W. Terry (intr. by C. M. Wilhelmj). Depts. of Physiology and Medicine, Creighton Univ. School of Medicine, Omaha, Nebr.

Urinary excretion of folic (PGA) and folinic (CF) acids was studied in 32 normal individuals using a bioautographic assay technique. The subjects studied were ostensibly healthy adults on unrestricted diets. Urine samples were collected for 24 hr and aliquots were assayed for PGA with Streptococcus fecalis and for CF for Leuconostoc citrovorum. Activity for S. fecalis was corrected for CF content. CF values were corrected relative to the naturally occurring form. The 24-hr urinary excretion of PGA ranged from 0.00 to 5.58 μg with a mean of 1.16 μg and a standard deviation of $\pm$ 1.29. The 24-hr urinary excretion of CF ranged from 0.19 to 1.6 μg with a mean of 0.57 μg and a standard deviation of $\pm$ 0.37. Urinary excretion of these compounds was studied in some individuals from day to day. The excretion of CF from day to day and from individual to individual remained more constant than PGA excretion. The variability of the excretion of PGA in these subjects is probably a reflection of a variable dietary intake. The constancy of the CF excretion, as opposed to the variable PGA excretion in these subjects, further supports the view that CF is the metabolically active pteroylglutamate compound. Therefore, values for the excretion of CF may be more representative of the status of pteroylglutamate metabolism than PGA excretion values.

EFFECT OF RETICULO-ENDOTHELIAL BLOCKAGE ON CORTISONE AND PITUITARY GROWTH HORMONE(STH) ACTIVITY. R. L. O'Brien,* H. H. McCarthy* and C. M. Wilhelmj. Depts. of Physiology, Pharmacology and Surgery, Creighton Univ. School of Medicine, Omaha, Nebr.

There is some controversy about the effect of RE block on the

eosinopenic response to ACTH and cortisone. In this study capillary resistance (C.R.) has been employed as an indicator of cortisone and STH activity. It has been shown that cortisone increases and STH decreases C.R. Six dogs were standardized with respect to C.R. and were given cortisone (1 mg/kg/d) i.m. for 6-10 days. They were then allowed to return to control levels of C.R. and given STH (1 mg/kg/d) i.m. for 6-10 days. They were then injected with India ink (5 cc with 10 cc saline/2.5 kg body wt.) i.v. and the regimens of cortisone and STH were repeated. Before RE block all 6 dogs showed marked increases of C.R. with cortisone and marked decreases with STH. After being blocked, all 6 dogs demonstrated complete abolition of the STH response. In 4 of them the cortisone response was completely blocked and in the other 2 it was significantly diminished. These results may afford a clue regarding the findings that RE block increases the susceptibility of animals to stress. (Aided by grants from the Am. Heart Assoc. and the Natl. Heart Inst.)

GASTRIC ACIDITY VERSUS DISTENSION IN ULCER FORMATION IN SHAY MICE. T. Ogawa* and H. Necheles. Dept. of Gastrointestinal Research, Michael Reese Hosp., Chicago, Ill.

We have reported here previously that 50% of pylorus ligated mice developed ulcers of the prostomach. Since then, we have studied gastric secretion of the mouse and the controlled production of ulcer by pyloric ligation (+90%). Basal secretion of acid is continuous and is increased only by very large doses of histamine. The optimum period for appearance of ulceration after pyloric ligation was 8 hr; up to 6 hr, acidity was high and thereafter declined and ulcers formed. The highest incidence of ulcers did not coincide with the highest period of acid secretion, but was related to the degree of gastric distension and congestion. Age and ambient temperature play an important role in ulcer formation; very young or old animals are not suitable; in the former group, degree of gastric distension is high and perforation at the pyloric ligature occurs early, apparently due to poor elasticity of the stomach walls, while in old animals, the reverse seems to prevail. We raise the question, whether acidity is the causal factor in ulcer formation in the pylorus ligated mouse, rather than distension and interference with circulation. (Supported by U. S. Vit. Corp.)

RETENTION OF Na^+ AND K^+ BY GLYCERATED MUSCLES. Eleonore A. Ohr (intr. by W. O. Fenn). Dept. of Physiology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Glycerated skeletal muscles of frogs were equilibrated in solutions of NaCl and KCl for 5 hr and then measured for their Na^+ and K^+ content. In one series of experiments the concentrations of Na^+ and K^+ in solution were equal to one another, and were varied from 0.000 to 0.080 mol/l. The amount found in the glycerated muscle was found to increase with increasing concentration and to change with changing ionic strength. The retention of Na^+ was always greater than that of K^+. The Na^+ and K^+ content of glycerated muscles was also measured in solutions containing decreasing amounts of KCl and increasing amounts of NaCl in steps of 25%, e.g. 100% KCl, 0% NaCl; 75% KCl, 25% NaCl; 0% KCl, 100% NaCl. Consequently the ionic strength remained constant with $\mu = 0.160M$ or $\mu = 0.080M$. Calculating the cationic content as mEq/kg wet weight of glycerated muscle ($[Na]_i$ or $[K]_i$) and as mEq/l. solution ($[Na]_o$ or $[K]_o$) the following relationships were found: $[Na]_o + [K]_o = 160$ (or 80);

$[Na]_i = k_1 [Na]_o + 5.5$; $[K]_i = k_2 [K]_o$. At $\mu = 0.160M$, $k_1 = k_2$. At $\mu = 0.080M$, k_1 was slightly greater than k_2. Under the conditions of these experiments glycerated muscle contains 5.5 mEq Na/kg that is not removed by any KCl solution up to 0.160M.

WATER, NEUTRAL FAT AND SOLIDS IN ADIPOSE TISSUE. Andrew A. Pandazi, Jack K. Herrington and Donald Schlueter (intr. by Howard M. Klitgaard). Dept. of Physiology, Marquette Univ. School of Medicine, Milwaukee, Wis.

It is variously stated that adipose tissue contains from 5 to 30% water. Since such tissue can account for 1-40 or more percent of the total body weight, it seemed important to determine with greater accuracy the amount of water with which it is associated. Peri-renal adipose tissue was removed from etherized exsanguinated white male rats who were previously subjected to a 4°C temperature for from 7-21 days. Water was estimated by weight difference after drying in vacuo at 38°C for 24 hr. Neutral fat was removed by ether extraction and solids considered to be the dry defatted residue. The data indicate that in both control and cold exposed animals, adipose tissue devoid of solids contains only neutral fat; however in adipose tissue depleted of neutral fat there are approximately 21% solids and 79% water. Correcting wet weight for neutral fat provides data which indicates a constant amount of water is present in the solids of adipose tissue. That this water is associated with the solids and not the neutral fat is evident by comparing the percent solids with the percent water; thus it appears as though the amount of water in adipose tissue will vary directly with the solids present. (Supported by the Wisconsin Heart Assoc.)

CHLORPROMAZINE AND INTERMITTENT PHOTIC STIMULATION IN THE CAT. E. L. Pautler,* A. C. Norton,* C. L. Taravella* and George Clark. Dept. of Physiology, Univ. of Buffalo, Buffalo, N. Y.

Cats can be trained to discriminate between intermittent photic stimulation of frequencies as high as 65 fps (flashes per second) and a steady light. The prolonged plateau of the learning curves representative of animals attaining this high level of discrimination in conjunction with the subsequent rapid improvement suggests the possibility that at least 2 processes are involved. After complete removal of the striate cortex and some adjacent tissue, the discrimination can be relearned with a rather large saving score. Preliminary results indicate that proper dosage levels of chlorpromazine will disrupt the performance of normal animals discriminating between a frequency of 55 fps and a steady light but will not interfere with the lower frequency of 31 fps. However, this dosage level will disrupt the discriminative performance at both high and low frequencies in the operated animals. Considering that the frequency of 31 fps is well within the photic driving range of the visual cortex and that 55 fps is too high for continuous driving, it is suggested that the striate cortex is specifically functional in normal cats for discriminating at lower frequencies of intermittent photic stimulation but not at higher levels. The discrimination demonstrated by the operated animals is presumably mediated by an alternative mechanism which may have predominantly subcortical loci. This alternative method is blocked by proper dosage levels of chlorpromazine. (Aided by Grant B-868C, Natl. Insts. of Health, PHS.)

CENTRAL EFFECTS OF D-TUBOCURARINE ON CARDIOVASCULAR RESPONSES TO ELECTRICAL STIMULATION OF MEDULLA AND HYPOTHALAMUS. Clarence N. Peiss and John W. Manning.* Dept. of Physiology, Stritch School of Medicine, Chicago, Ill.

In the course of experiments involving electrical stimulation of the medullary vasomotor area, it was observed that responses to such stimulation were markedly depressed or absent in curarized animals. Subsequent investigation of this phenomenon has demonstrated the following points: 1) intravenous doses of d-tubocurarine (300 gamma/kg) which produce moderate depression of the myoneural junction raise the threshold for electrical excitation of the vasomotor area; 2) small intracarotid doses of d-tubocurarine (100 gamma/kg) which have no blocking action at the myoneural junction are nevertheless effective in depressing cardiovascular responses to electrical stimulation of the brain stem; 3) similar results are obtained by microinjection of 20 gamma/kg directly into the vasomotor area; 4) this depression does not involve blockade of sympathetic ganglia; 5) when both myoneural blockade and depression of cardiovascular responses are produced, the latter show a more rapid recovery.

OXYGEN TENSION IN THE VASODILATED SKIN. Raymond Penneys. Robinette Fndn., Univ. of Pennsylvania Hosp., Philadelphia.

Skin oxygen tension in the "moderately" vasodilated fingers was compared with that in the "fully" vasodilated fingers to see whether the large increment in blood flow which occurs with full vasodilatation is accompanied by a comparable increase in oxygen tension. A state of moderate vasodilatation was obtained in normal subjects by allowing them to lie covered with blankets, except for the hands which were left exposed, in a constant temperature room with an air temperature of 20°C. A state of full vasodilatation was produced by the addition of heating pads to the body. The skin temperature of the finger tips at moderate vasodilatation averaged 29.9°C and at full vasodilatation, 31.5°C. On the basis of Montgomery, Naide and Freeman's (Am. Heart J. 21:780, 1941) and Catchpole and Simeone's findings (Surgery 38:936, 1955) this would indicate an increase in blood flow of some 50% in passing from the moderately to the fully vasodilated state. Skin oxygen tension was measured in each of these states with the open-tip polarographic oxygen electrode, inserted in the finger pads. Oxygen tension of the skin (11 experiments on 7 subjects, 3 or 4 fingers per experiment) increased only 5%, in spite of the 50% increase in blood flow, on passing from the "moderately" to the "fully" vasodilated state.

DEVELOPMENT OF TEMPERATURE REGULATION IN THE OPOSSUM. Jack H. Petajan and Peter R. Morrison. Zoology and Physiology Depts., Univ. of Wisconsin, Madison.

At ambient temperatures ranging from 5 to 30°C, equilibrium body temperatures were recorded at ages ranging from 57 to 100 days. The change from poikilothermism, a significant rise of body temperature above the ambient level, occurred earliest at 30°C ambient and 60 days of age, and latest at 5°C ambient at an extrapolated age of 70 days. Under these conditions normal body temperature (35°C) resulted 20 to 30 days later. The initial response was characterized by the slope of the body temperature curve divided by the difference between body and ambient temperatures at standard initial exposure times. This "living conductivity" value plotted against age approaches zero almost linearly

as regulation is achieved. Differences between conductivity of the dead animal, a physical characteristic, and "living conductivities" plotted against age result in parabolic curves with minima falling between 70 and 80 days. Preceding the minimum, dead conductivity decreases more rapidly, following it living conductivity decreases more rapidly. Metabolism values fall about a line from 1 cc O_2/gm/hr at 70 days to 4 cc O_2/gm/hr at 100 days. Departure toward the basal level occurs as a constant body temperature is acquired and regulation becomes effective. Factors such as fur length, postural adaptation and shivering all undergo rapid developmental change or make their appearance as active regulation ensues.

TOXIC EFFECT OF PHYSIOLOGICAL SALINE SOLUTIONS FOR TISSUE CULTURED CELLS. H. J. Phillips and Vera Skank.* Depts. of Physiology and Pharmacology, Creighton Univ. School of Medicine, Omaha, Nebr.

Tissue culture techniques are unique for studying effects of various agents on mammalian cells. One advantage is that cell suspensions can be prepared which are free of proteins or other agents normally found in interstitial fluid. Toxic effects of agents on cells are determined by live-dead counts. Dead cells in suspension stain with 20 mg% Erythrosin B. These cells do not respire nor glycolyze and are digested by dilute solutions of trypsin. Previously we reported that L and HeLa cells suspended for several hours in modified Ringer solutions contained more dead cells than suspensions in tissue culture medium composed of salts, serum and hydrolysates. The following results were obtained while investigating this phenomenon: cell survival in Ringer solution cannot be improved by changing tonicity with sodium chloride. Inulin, sodium glucuronate, fibrinogen, globin, 0.1-2.7% glucose and lactalbumin hydrolysate in Ringer solution do not increase cell survival. Substances protecting cells but not as well as tissue culture medium are yeast hydrolysate, dextran and buffered 5.3% glucose. Gelatin, albumin and 15 CPS methocel protect cells as well as tissue culture medium. These results indicate that certain high molecular weight substances in combination with inorganic ions are necessary for survival of mammalian tissue cultured cells. (Aided by the Natl. Cancer Inst.)

METABOLIC STUDIES WITH PROPIONIC ACID ANALOGS OF THYROXINE. Constance S. Pittman* and S. B. Barker. Dept. of Pharmacology, Univ. of Alabama Med. Ctr., Birmingham.

Tetraiodothyropropionic acid (Tetraprop, Desaminothyroxine) has been evaluated on the basis of its metabolic action in thyroidectomized rats, using whole animal and tissue oxygen consumption measurements. To duplicate the metabolic increase caused by 1 mg/kg L-thyroxine, 6-12 mg of the tetraiodothyropropionic are required. When 3',5'-dimethyl-3,5-diiodothyropropionic was used, the response was about 30% greater than with an equimolar dose of Tetraprop. Tissue metabolism studies have revealed very little metabolic response to 3,3'-diiodo- and 3,3',5-triiodothyropropionic acids, even when a dose level of 20 mg/kg was used. The corresponding 3,3'-diiodo- and 3,3',5'-triiodothyronines were also found inactive. (Supported by grants from the PHS and the Am. Cancer Soc.)

EFFECT OF NIACIN ON CHOLIC ACID OUTPUT IN BILE. C. Ram Prasad* and A. C. Ivy. Dept. of Clin. Science, Univ. of Illinois College of Medicine, Chicago.

Rats with a chronic bile fistula and a polyethylene tube in the distal portion of the common bile duct for the return of bile were maintained on Pablum (Meade Johnson & Co.) and 0.2% aqueous NaCl solution. Two to 3 days after operation the bile secreted during the prior 12 hr was slowly returned through the tube in the distal portion of the bile duct. An aliquot of the bile was withheld for analysis of the concentrations of cholate. When the cholate output became relatively constant, generally 6-7 days post-operatively, Niacin was added at a level of 0.1% and 1.0% by dry weight of the diet for 1 wk. The level of 0.1% caused no significant change in cholic acid or bile volume output, but the level of 1% increased the cholic acid output by an average of 38% in 3 rats.

CARDIAC GLYCOGEN OF RAT IN ACUTE ANOXIA. F. A. Purdy* and D. K. Meyer. Depts. of Physiology and Pharmacology, Univ. of Missouri, Columbia.

Male rats subjected to an atmosphere of nitrogen until convulsions occurred were allowed to recover in air for 15 hr. Hearts were analyzed for free glycogen, β-amylase digest to limit dextrin free glycogen (LDFG), bound glycogen and limit dextrin bound glycogen (LDBG) at 8 stages of anoxia or recovery. The LDBG rose from 54% to 87% during anoxia although the bound glycogen itself fell 90 mg%. In contrast LDFG remained constant at 63%, even though the free glycogen fell from 84 to 21 mg%. During recovery bound glycogen returned to normal by 40 min and stayed there while the LDBG increased steadily throughout the recovery period. Free glycogen climbed to 162 mg% at 1 hr then fell slowly to control levels. The LDFG reached and remained at control values after 1 hr. During anoxia bound glycogen degrades to branching points while free glycogen degrades at both α1-4 and α1-6 linkages. Resynthesis of glycogen proceeds by lengthening the peripheral chains. Bound glycogen, however, reverts to normal chain length and branching by internal conversion but free glycogen degrades its long chains to normal length by splitting off the excess glucose units. (Supported by PHS Grant H-1801 C3.)

VENOUS ADMIXTURE OF PULMONARY CIRCULATION IN THE ANESTHETIZED DOG. H. Rahn, T. N. Finley* and C. Lenfant.* Dept. of Physiology, Univ. of Buffalo, Buffalo, N. Y.

Venous admixture to the oxygenated pulmonary blood stems primarily from 2 sources—the pulmonary artery and the bronchial veins. This contamination must necessarily contribute to the alveolar-arterial oxygen difference which is also effected by the distribution of unequal Va/Q ratios and the diffusion barrier. Pure oxygen breathing essentially eliminates these latter factors making it possible to measure only the venous admixture. The venous admixture was measured with and without pressure breathing. The alveolar oxygen tension was assumed to be equal to that of the oxygenated capillary blood. The arterial and mixed venous blood tensions were measured by the Clark electrode. All tensions were converted to content for calculation of the venous admixture as percent of the cardiac output. Without pressure breathing the venous admixture was 5.5%. With 20 cm of H_2O positive pressure breathing the shunt decreased significantly to 1.4%. However, it is necessary in each case to assume the oxygen content of the bronchial veins was similar to that of mixed venous blood. Hemodynamic observations of the pulmonary artery and vein pressures would indicate no change in the venous admixture from the pulmonary artery suggesting

that selectively the bronchial admixture was blocked by pressure breathing. (Supported in part by the Erie County Heart Assoc. and the Air Research and Development Command - Wright Patterson AFB.)

ASPHYXIA NEONATORUM IN MACACA MULATTA. J. Ranck* and W. F. Windle. Natl. Inst. of Neurological Diseases and Blindness, Field Station of Perinatal Physiology, Univ. of Puerto Rico, San Juan.

Effects of asphyxiation during and after birth were recorded cinematographically in 20 monkeys weighing 360-526 gm. Asphyxia was induced in 1 during "natural" breech delivery, 3 after normal birth (nitrogen), 16 in amnio at 157-164 days gestation (placental detachment at hysterotomy). Comparisons were made with 14 controls: 1 premature (200 gm, 148 days), 4 normal vaginal births, 9 hysterotomies. Eight, asphyxiated 4.5-11.5 min, requiring no resuscitation, exhibited transient functional defects, persisting several weeks to months in 3. Twelve apneic infants, asphyxiated 10-17 min, were resuscitated by oxygen inflation of lungs; respiration could not be established in 1 or maintained in 3 for more than 11 hr; 5 showed severe neurological deficits and were killed at 2-10 days for histology; 2, asphyxiated 16.5-17 min, and the breech (at least 10 min), showed persistent deficits. Sucking was impaired or lost in nearly all resuscitated monkeys. Retinal hemorrhages occurred in 4; impaired motor and sensory functions, exotropia, and/or tremors occurred in survivors. Spasticity, convulsive seizure, laryngospasm, catalepsy, decerebrate state, impaired visual and auditory response, and pronounced lethargy appeared in the most severely affected. Effects were usually maximal on days 2 or 3. Survivors were dull in contrast with controls. Preliminary histological studies revealed severe, extensive, diffuse, bilateral neuronal lysis, most marked in interneuron groups of brain stem and spinal cord.

SYMPATHETIC AUGMENTATION OF VENTRICULAR AND ARTERIAL PRESSURE PULSES. Walter C. Randall and Albert Kelso.* Dept. of Physiology, Stritch School of Medicine, Chicago, Ill.

Electrical excitation of the stellate ganglion in the dog elicits increased pressure in both right and left ventricles which in turn augments both the pulmonary and carotid arterial pressure pulses. The augmented arterial pulses are characterized by a shortened isometric contraction phase, a steeper rise in the systolic ejection phase, and a greater rise in systolic as compared with diastolic pressure. Cardiometer tracings reveal an increase in volume of systolic ejection, a smaller end-systolic volume, and little or no increase in end-diastolic volume. Ventricular augmentation of nervous origin has been induced in preparations in which both preliminary filling and emptying was prevented (isovolumetric ventricle). It is clear therefore, that augmentation in these experiments is related to altered myocardial contractility associated with events at the neuro-effector junction and not to increased diastolic filling.

EVALUATION OF USE OF LEFT CORONARY ARTERY INFLOW AND OXYGEN CONTENT OF THE CORONARY SINUS BLOOD AS A MEASURE OF LEFT VENTRICULAR METABOLISM. C. R. Rayford,* F. B. Lewis* and D. E. Gregg. Walter Reed Army Inst. of Research, Walter Reed Army Med. Ctr., Washington, D. C.

In the open chest dog using special cannulae, total left coronary and total coronary sinus flows and the oxygen saturations of these bloods

were measured continuously by rotameters and densitometers, respectively. Coronary inflow was supplied either by gravity perfusion or from a systemic artery. The findings are: 1) 75 to 85% of left coronary flow is usually recovered in the coronary sinus with occasional higher and lower values during aortic or pulmonary artery constriction, hemorrhage (to zero blood pressure), infusion, heart rate changes ventricular fibrillation, change of coronary perfusion pressure and levophed; 2) the right coronary artery contributes maximally 2 to 3% (1-2 cc) to coronary sinus flow; 3) with any one variable in an experiment coronary sinus flow/left coronary artery flow generally varies by less than 10%; 4) the oxygen uptake of left ventricle on basis of left coronary artery flow X the difference between the arterial and coronary sinus oxygen content agrees with the oxygen uptake based on the respective volume flows and oxygen contents of the left coronary venous drainage fractions (in this instance systemic venous return was made to bypass the right heart and the right coronary artery was clamped). Hence, in the open chest dog a combination of left coronary artery flow and coronary sinus arteriovenous oxygen difference gives a precise value for left ventricle metabolism under these experimental conditions.

COMPARISON BETWEEN SOME VASCULAR ACTIONS OF NORADRENALINE AND OF SEROTONIN IN MAN. W. Redisch, K. de Crinis* and J. M. Steele. New York Univ. Med. Div., Goldwater Memorial Hosp., and New York Univ. College of Medicine, New York City.

Some evidence for similarities between vascular responses to noradrenaline and to serotonin has been reported. In a few animal experiments an increase in cardiac output and arterial pressure was observed after serotonin. Results in man were inconclusive though a diphasic pressure response was usually seen. In 15 experiments in 5 normotensive subjects, both noradrenaline and serotonin regularly increased systolic and diastolic pressure. The response to serotonin was transient and followed by a distinct hypotensive wave. When hypotension was produced by adrenergic blocking agents the hypertensive action of noradrenaline and serotonin was blocked. Ganglionic blocking agents did not prevent hypertensive response to noradrenaline, although the response was somewhat delayed; in contrast, serotonin injected during pentolinium induced hypotension produced a short elevation of systolic and diastolic pressure followed by a marked and sustained drop. Hypotension induced by intravenous reserpine was readily abolished by noradrenaline, but not by serotonin.

EFFECT OF DIETARY OXALATE ON DEVELOPMENT AND PROGRESSION OF SPONTANEOUS MAMMARY CARCINOMA IN C3H MICE. Allen F. Reid, Margaret C. Robbins* and Jack K. Jeanes.* Dept. of Biophysics, Univ. of Texas, Southwestern Med. School, Dallas.

Appearance of spontaneous mammary tumors was mildly accelerated and survival after tumor appearance was markedly shortened in an inbred strain of mice (C3H) when sodium oxalate was added to the drinking water in a concentration of 3.7×10^{-4} molar. The shortening of life after tumor development was more pronounced when oxalate was administered for the period before tumefaction was noted. The dose of oxalate, from 2-3 μmoles/day, was too small to cause any detectable change in growth, bone or organ development or to cause any pathological manifestations other than an increased rate of carcinoma development and progression.

CEREBRAL BLOOD FLOW IN THE RAT FOLLOWING FEEDING AND ADMINISTRATION OF ALCOHOL. Edward J. Reininger* and Leo A. Sapirstein. Dept. of Physiology, Ohio State Univ., Columbus.

The cerebral blood flow fraction of the cardiac output may be measured by the brain's uptake of labeled iodoantipyrine (I^{131}) following a single intravenous injection of this label (Sapirstein and Hanusek, Am. J. Physiol. 193:272, 1958). The cerebral blood flow may be calculated as the product of the cardiac output and the cerebral blood flow fraction. The cerebral blood flow fraction of fed rats was not significantly different from that of fasting controls; however, feeding increases the cardiac output in rats. Therefore, the brain shares proportionately in the postprandial increase in cardiac output (Reininger and Sapirstein, Science 126:1176, 1957). Rats injected with 5 ml of 20% alcohol i.p. exhibit an 85% increase in the cerebral blood flow fraction compared to pentobarbitalized controls. Since cardiac output is unaffected by this amount of alcohol, the increase in cerebral blood flow fraction indicates a corresponding increase in cerebral blood flow. (Supported by the Smith, Kline and French Research Fndn.; portion of work was performed on contract between USAF School of Aviation Medicine, Randolph Field, and Ohio State Univ. Research Fndn.)

PLASMA LOSS AFTER BLOOD INFUSION IN NORMAL AND IN BLED DOGS. J. W. Remington and C. H. Baker.* Dept. of Physiology, Med. College of Georgia, Augusta.

It is well documented that dogs given large transfusions show rapid plasma loss, with hemoconcentration. Hoping to find a critical blood volume level above which this leakage would occur, dogs have been given serial infusions (50-100 cc each) at 30- to 45-min intervals. Each infusion took about 10-20 min. Even with the first, the hematocrit rose, indicating a plasma loss (corroborated by T-1824 determinations) to hold the original blood volume fairly constant. Plasma specific gravity showed but minor change. Since the original blood volumes varied from 45 to 110 cc/kg, and there was no correlation between the amount of plasma "leak" and this volume, there was no "ideal" blood volume below which all given blood would be held in the circulation. Another group of dogs were bled rapidly from an artery to a pressure of 40 mm Hg. After 30 min, they were infused serially in the above manner. Both hematocrit and dye (but not specific gravity) showed a large plasma gain during and just after the bleeding. During the infusions, the plasma volume was held fairly constant, the blood volume increasing by the amount of cells added. When the pre-hemorrhage blood volume was restored, it was held despite further infusions. Hence even in oligemia, plasma leakage occurs. These shifts could not be correlated with changes in arterial or venous pressures. (Supported by grants from the PHS (H-240) and Life Insurance Med. Research Fund.)

COMPARATIVE EFFECTS OF 17-ALPHA-ETHYL-17-HYDROXYNORANDROSTENONE AND TESTOSTERONE PROPIONATE ON COMB RESPONSE AND BODY WEIGHT CHANGES IN COCKERELS FED AN "ATHEROGENIC" DIET. Gerald M. Reynolds,* Harry Y. C. Wong and William L. West.* Depts. of Physiology and Pharmacology, Howard Univ. School of Medicine, Washington, D. C.

The purpose of the present investigation was to study the comparative effects of 17-alpha-ethyl-17-hydroxynorandrostenone (Nilevar)

and testosterone propionate on changes in body weight and comb response of cockerels fed an "atherogenic" diet. After 8 wk on an "atherogenic" diet of 2% cholesterol and 5% cottonseed oil mixed with starter-grower mash, the following results were observed: 1) cockerels fed an "atherogenic" diet only had the smallest comb response even smaller than the untreated controls on plain mash; 2) birds treated with Nilevar and fed an "atherogenic" diet, and the control cockerels untreated on plain mash were not significantly different; 3) birds treated with testosterone propionate and fed an "atherogenic" diet had the highest increment of comb size of all groups observed; 4) the body weight of control birds on plain mash was greater than any of the other groups; 5) the Nilevar treated birds showed less of an increase in body weight than the controls but more than either the testosterone propionate treated cockerels or those fed an "atherogenic" diet. (Supported by grants, #H-2420, Natl. Heart Inst., PHS, Washington Heart and Am. Heart Assocs.)

COMPARISON OF EFFECTS OF GLUCAGON AND INSULIN ON PLASMA UNESTERIFIED FATTY ACIDS. Paul S. Roheim* and John J. Spitzer. Dept. of Physiology, Hahnemann Med. College, Philadelphia, Pa.

The source and uptake of unesterified fatty acids (UFA) has been investigated by measuring arterio-venous differences of various organs. It seemed desirable to use the same technic for the study of hormonal effects on UFA. Glucagon and insulin were selected first because of their marked influence on UFA and the close relationship between the metabolism of glucose and UFA (Dole and Gordon). Normal, postabsorptive dogs were used under Nembutal anesthesia. Glucagon was injected in 0.6-12.0 μ/kg, insulin in 0.15 units/kg doses. Glucagon, while increasing blood sugar, decreased both the arterial and venous level of UFA in the femoral vessels. However, the normally existing negative arterio-venous difference was not abolished. Glucagon did not decrease UFA in animals with very low normal UFA levels, although it was effective on blood sugar and on arterio-venous glucose difference. Insulin, on the other hand, lowered UFA in both the femoral artery and vein even in animals with very low normal UFA levels. The negative arterio-venous difference was frequently decreased or abolished by insulin. Further studies of the difference in the mechanism of action of the two hormones is in progress. (Supported by the Natl. Heart Inst., PHS.)

PRE- AND POSTNATAL GLYCOGEN INFILTRATION IN OFFSPRING OF DIABETIC RATS. Walter Runge, Jae Nam Kim, Lemen J. Wells and Arnold Lazarow (intr. by Louis Tobian). Dept. of Anatomy, Univ. of Minnesota, Minneapolis.

Pancreatic islets from 20 fetuses and 40 newborn rats of normal or alloxan diabetic mothers were studied at various times ranging from 1 day before to 6 days after birth. These were examined for glycogen by the PAS reaction, controlled by amylase digestion. In the normal group, glycogen was sparsely distributed as fine droplets (0.2 micron in diameter) in cells adjacent to capillaries in the center of islets (B-cell area). In offspring of diabetic mothers, before and at birth, glycogen was similarly distributed. However, the amount of glycogen was very much greater, and it formed clumps up to 2.5 micra in diameter. During the subsequent 6-day period, the amount of glycogen decreased

progressively. Nevertheless, on the 6th day it was still greater than that seen in the offspring of normal rats. Although the degree of glycogen infiltration in the B-cell at Caesarian section or at birth could not be directly correlated with the height of the blood-sugar level in diabetic mothers, this infiltration was probably the result of maternal hyperglycemia. "Vacuolization" of the B-cells due to glycogen infiltration persisted a long period after the hyperglycemia had disappeared. (Aided by PHS Grants A-1244 and A-1659.)

EFFECTS OF HYPOTHERMIA IN IRREVERSIBLE HEMORRHAGIC SHOCK. Clem Russ and Wayne Foster (intr. by T. K. Kruse). Dept. of Surgery, Lab. of Exper. Surgery, Univ. of Pittsburgh, Pittsburgh, Pa.

Recent evidence would suggest that hypothermia may prevent irreversible hemorrhagic shock. It would seem that a more rigid definition of shock in relation to this problem is in order. In this laboratory, metabolic, physiologic and survival observations on 10 normothermic animals subjected to irreversible hemorrhagic shock served as controls. Seven animals made hypothermic during the initial period of circulatory decompensation were similarly followed. The therapeutic effects of hypothermia based on prolongation of survival time, elevation of a markedly depressed cardiovascular system and elimination of accumulated acid metabolites is not secured if it is applied during this initial period of decompensation. In a 3rd group, animals were transfused at a time equivalent to that in which hypothermia was used. All animals in this group survived in contrast to the others where there was a 100% mortality. Under the conditions of these experiments, hypothermia would seem to have no beneficial therapeutic effects in experimental irreversible hemorrhagic shock. (Supported by the Donner Fndn.)

INDICATOR-DILUTION METHOD FOR SIMULTANEOUS MEASUREMENT OF PULMONARY AND SYSTEMIC BLOOD FLOW IN THE PRESENCE OF LEFT-TO-RIGHT SHUNTS. James L. Russell,* André David,* David E. Donald* and Earl H. Wood. Mayo Clinic and Mayo Fndn., Rochester, Minn.

Dogs were studied in which ventricular septal defects had been created. Pulmonary and systemic blood flows and left-to-right shunts were determined by Fick and by dilution technics, using curves recorded from the pulmonary and femoral arteries after injection of cardio-green into a distal pulmonary artery. An early deflection on the pulmonary-artery curve represents blood shunted from left to right, which, expressed as a fraction of pulmonary flow (F_{L-R}) and assuming uniform mixing of injected and shunted dye, is equal to the ratio of the forward-triangle portions of the curves recorded simultaneously from the right side of the heart and a systemic artery (SA). These areas are calculated from the equation $A\text{-}BT \cdot C_p/2$, in which BT and C_p are the build-up times and peak deflections of the respective curves. Values for left-to-right shunts calculated thus and pulmonary (Q_p) and systemic (Q_s) blood flows calculated from the equations $Q_p = 47\ I/(C_p \cdot BT)_{SA}$ (Cir. Research 4:400, 1956) and $Q_s = Q_p\,(1 - F_{L-R})$, respectively, show satisfactory agreement with values determined by conventional direct Fick methods. It is noteworthy that the dilution values are measured simultaneously from curves recorded over a period of less than a minute and do not require accessory measurements or constancy of blood oxygen content or respiratory gas exchange.

PRECIPITATION OF PROLONGED CONVULSIONS IN STRESSED RATS AND MICE. Stelios C. Samaras and Nicholas Dietz, Jr.* Pathology and Biochemistry Depts., Creighton Univ. School of Medicine, Omaha, Nebr.

Subcutaneous administration of "injection NaCl, USP" containing 0.5% phenol, after swimming stress, was followed by prolonged convulsions in rats and mice; 13 rats (123-197 gm), 165 mice (17.5-44.5 gm), were utilized in matched groups. Swimming, in individual aquaria, was followed by subcutaneous "injection NaCl, USP" injections; unphenolized saline was injected into controls. Longer swimming was followed by increased tendency for full-blown and longer lasting convulsions after phenolized injection. Trembling, jerking, convulsions, occasional teeth chattering, cries, loss of "righting" ability and clockwise rotation of prone animal develop rapidly in typical case of 0.5 cc injection into 20 gm mouse after 4-hr, 27°C swim. Matched unstressed animals, similarly injected, show slight reaction; matched stressed animals, injected with saline only, show no reaction. Sufficiently large phenol injections precipitate convulsions without stress. Hydrocortisone acetate injections (68-135 mg/kg) before phenol were without observable influence. Autopsies revealed frequent pulmonary and gastric mucosal hemorrhage in stressed animals, whether phenolized or not. In unstressed, phenolized animals, pulmonary hemorrhage was frequent, with conspicuous gastric hyperemia rather than bleeding. All brains appeared normal at autopsy. Phenolic tests of blood, urine, bile, adipose tissues of phenolized mice were positive; their urine gave strong homogentisic acid-like reaction. In conclusion, swimming stress lowers threshold for phenol convulsions, and prolongs them. Further studies, histopathological, biochemical, and electroencephalographic, are under way. (Aided by A.M.A. grant.)

EFFECTS OF NITRATE ON THE VERATRINE RESPONSE OF MUSCLE. Alexander Sandow and Alan A. Rubin.* Dept. of Biology, New York Univ., New York City.

Veratrinic effects in frog sartorii, in either chloride or nitrate Ringer's, have been studied in isotonic mechanical responses, and in externally recorded electrical responses (with local application of veratrinic drug at only one electrode). To distinguish between propagated and unpropagated veratrinic effects in the mechanical experiments, the muscle is treated with a drug and also stimulated either: 1) at only its very lower (1 mm) pelvic end, and the shortening (a twitch or brief tetanus) is then due practically entirely to propagated disturbances; or 2) by full drug exposure and massive stimulation to give the complete veratrinic response, i.e., tetanus or twitch plus contracture. Nitrate reversibly antagonizes the effects of 10^{-6} (w/v) crude veratrine, veratridine or cevadine by curtailing tetanus (sometimes to a mere twitch) and contracture. These effects are the same independent of order of application of nitrate and alkaloid, i.e. unlike eserine antagonism (Sandow and Kiebel, Am. J. Physiol., 169:649, 1952). Comparable electrical changes occur, nitrate reducing periods of repetitive spikes and later depolarization. Other anions yield similar results: i.e., $B_r < NO_3 < I < SCN$. Pure veratrinic and pure nitrate effects involve augmentation of the spike's negative after potential, and nitrate can cause veratrinic responses (Sandow and Stein, Fed. Proc. 15:162, 1956); it is therefore provocative that NO_3 antagonizes veratrinic effects.

EXCHANGEABLE POTASSIUM OF HEART AND KIDNEY. Leo A. Sapirstein. Dept. of Physiology, Ohio State Univ., Columbus.

From a knowledge of the inflow of K^{42} into an organ as a function of time after a single injection of $K^{42}Cl$, and of the total organ content of the isotope as a function of time, it is possible to calculate the venous outflow of the indicator as a function of time. The relationship between the inflow curve of K^{42} and the outflow curve can be used to estimate the size of the exchangeable reservoir of K^{39} in the organ. In the intact rat, the reservoir of K^{39} available for exchange in 1 min in the heart and kidney is identical with the total organ content of K^{39}. This suggests that all of the chemical potassium of these organs is immediately available for exchange with the potassium of the circulating plasma, and that no potassium is "bound" in non-exchangeable or slowly exchanging form. The immediately exchangeable K^{39} content of other organs is only a fraction of their total K^{39}; the limitation on exchange in these organs is believed to be a circulatory one. (Supported by Grant-In-Aid from the Central Ohio Heart Assoc.)

BRAIN GLYCOGEN CONTENT IN CORTISONE-INSULIN TREATED RATS. Joseph Schiller. Psychiatric Service and Research Lab., VA Hosp., New York City.

The effect of insulin on the glycogen content of the brain in rats pretreated for 4 days with various amounts of cortisone was determined. Adult albino female rats were divided into 5 groups of 7-9 rats each. After overnight fasting a standard dose of 6 units crystalline insulin was administered i.v. and the drop in blood sugar compared before and after the injection. The brain was removed when rigidity appeared as a result of the intraperitoneal injection of 200 mg/kg body weight of Na iodoacetate. This followed the second blood collection from the tail vein. In group I (untreated controls) the brain glycogen level averaged 66.5 mg/100 gm of tissue corresponding to a blood sugar level of 86.8 mg%. Group II received insulin alone resulting in a fall of 56% in the blood sugar the brain glycogen averaging 18.9 mg% all animals being sluggish or convulsive. In group III pre-treatment with 0.05 mg daily did not confer protection against hypoglycemic effects. Group IV received 0.1 mg cortisone daily and the insulin injection resulted in a blood sugar fall of 67.2% and a brain glycogen content of 23.9 mg%, 1 rat out of 9 being sluggish. Group V received 0.5 mg of cortisone daily and were best protected: the blood sugar fell by 56.8% of the initial value, the brain glycogen averaged 24.75 mg% with no observable deleterious effect on the nervous system.

A METHOD OF DETECTING SPHINCTERIC PRESSURE PROFILES. Jerry F. Schlegel* and Charles F. Code. Mayo Clinic and Mayo Fndn., Rochester, Minn.

Widely different pressure profiles usually are recorded when different types of pressure-detecting systems are withdrawn in succession through the gastroesophageal sphincter of human beings, and differences are recorded even when systems built to identical specifications are used. Suspicion arose that these differences are not due to changes of tone in the sphincter but to differences in the pressure-recording fidelity of the detecting systems. The ratios of volume (microliters) to pressure (cm H_2O) of 4 naked differential transformer transducers ranged from .044 to .032 (mean .038). When open-tipped tubes were attached the mean ratio rose to .14, and when the differential

transformer transducers were replaced by strain gauges the mean ratio increased to .51. To test the adequacy of such systems an artificial sphincter was constructed, being made similar to the apparatus conventionally used to provide arterial resistance in isolated circulatory systems. This so-called sphincter provides no volume for displacement into pressure detectors, and none of the systems mentioned recorded the pressure in it. Pressures were recorded accurately when a small volume for displacement was provided. This was accomplished by attaching small (0.15 ml) water-filled but not distended balloons to the naked transducers and to the open tips of the tubes. When these units were withdrawn through natural or artificial sphincters, pressures always were recorded.

KINETICS OF SLOW CHANGES IN MEMBRANE POTENTIAL INDUCED BY DIRECT CURRENT POLARIZATION. Gordon M. Schoepfle. Dept. of Physiology, Washington Univ. School of Medicine, St. Louis, Mo.

A direct current pulse applied to an isolated single fiber of the frog sciatic induces a slow drift in membrane potential which can be described by a single exponential term throughout most of its time course. Both magnitude and time parameter are functions of pre-existent membrane potential. With increasing cathodal polarization the magnitude of the drift approaches a limiting value which is dependent only on the duration of the polarizing pulse. No change in resistance is detectable with brief test transient pulses. In fibers sufficiently hyperpolarized to minimize sodium inactivation it is observed that impulses fired off at any time during the course of the slow potential drift are characterized by identical peak values of membrane potential. This indicates that active firing results in a short circuiting of the mechanism responsible for the slow drift. Whereas the data presented favor a change in some emf as responsible for the slow drift, there exists strong evidence that the potassium emf remains constant. This is indicated by observations on the direction of the after potential initiated in a previously hypopolarized fiber at various intervals during the slow drift subsequent to brief but intense hyperpolarization. (Supported by Public Health Research Grant B-173 (C6).)

RECOVERY OF NEUROMUSCULAR TRANSMISSION FOLLOWING WET COLD EXPOSURE AT 2°C. Donald Scott, Jr., Ann Sayen* and Hugh Montgomery. Physiology and Medicine Depts., Univ. of Pennsylvania, Philadelphia.

Impairment of neuromuscular transmission in rabbit hind leg following 4 hr chilling in water at 2°C has been described and the proportionate involvement of nerve and muscle evaluated (Scott, Sayen, Montgomery; Fed. Proc. 17:144, 1958). Differences in the pattern of recovery of motor nerve, muscle and neuromuscular function at intervals between 3 hr and 6 wk have been determined by simultaneous recording of evoked nerve action potential and muscle twitch tension. Primary involvement of the neuromuscular junction previously demonstrated 3 hr after chilling is shown to persist. Later overall neuromuscular impairment involves histologically identifiable myelin degeneration. The relative importance of these 2 factors becomes transposed during the course of recovery. (Supported by contract between Office of Naval Research and Univ. of Pennsylvania.)

BIOELECTRIC STUDIES FOLLOWING PHRENIC ANASTOMOSES. W. Scruggs,* T. Ogawa,* N. C. Jefferson,* J. Toman and H. Necheles. Dept. of Gastrointestinal Research, Michael Reese Hosp., and Div. of Neurology and Psychiatry, Chicago Med. School, Chicago, Ill.

This is a report on results of bioelectric studies mentioned in the paper by Jefferson et al. Following phrenicotomy, fibrillation potentials in the ipsilateral diaphragm may appear in 7 days, but motor units may persist for up to 8 wk. Action potentials disappear in the cut and anastomosed phrenic within hours and may reappear after 5 wk. Seven to 8 wk after anastomosis, stimulation of the phrenic produced a contraction of the diaphragm and fibrillation potentials in the latter were occasionally seen, but motor units prevailed. Similar observations were made following vago-phrenic and intercostal-phrenic anastomoses. (Supported by PHS Grant B-1356.)

EFFECT OF HYPERTONIC SALINE SOLUTION ON THE PULMONARY CIRCULATION. Herbert J. Semler,* John T. Shepherd* and H. J. C. Swan. Mayo Clinic and Mayo Fndn., Rochester, Minn.

A 20% saline solution was injected within 5-10 sec into the pulmonary artery or right atrium of anesthetized intact dogs (dose, 0.5 to 1 ml/kg body weight). Pressures were recorded simultaneously in the pulmonary artery, pulmonary artery wedge, pulmonary vein, left atrium, right atrium and aorta. Eight observations were made on 4 dogs. The response was consistent and included apnea, bradycardia, marked rapid drop in aortic pressure with a simultaneous rapid rise in pulmonary artery pressure. Right atrial pressure rose, but there was little or no change in mean left atrial pressure. These findings are similar to those reported by Eliakim and associates (Cir. Research 6:357, 1958) and are attributed to an extreme transient increase in resistance to flow across the pulmonary bed. Eliakim and associates also found a marked rise in pulmonary venous pressure and, therefore, attributed the pressure changes across the pulmonary bed to a spasm at the pulmonary vein-left atrial junction. In the present experiments, however, while the pressure gradient between the pulmonary artery and the "wedge" was greatly increased, that between the "wedge" and the left atrium did not change. Our data, therefore, support the concept that the major site of the increased vascular resistance was at or more likely proximal to the capillary bed.

EFFECT OF CERTAIN ADSORBENTS ON ABSORPTION OF CHOLESTEROL IN THE RAT. C. S. Narayana Setty (intr. by A. C. Ivy). Dept. of Clin. Science, Univ. of Illinois College of Medicine, Chicago.

Two adsorbents, a resin called "Deacidite," and a plant derivative, "Pectinol 100D," were found to adsorb bile salts in an aqueous solution of dried alcohol extract of ox bile in vitro. It was decided to ascertain if these adsorbents decreased the absorption in vivo, because it has been established that in the rat bile salt is essential for the absorption of cholesterol. Three groups of female rats (Sprague-Dawley strain) were fed for 8 days on 11 gm of a basal diet containing 9% by weight of corn oil and providing a daily intake of 45 mg of cholesterol. The 1st group of rats served as a control. The 2nd and 3rd groups received an addition of 10% of "Deacidite" and "Pectinol," respectively. On the 5th day 0.1 microcurie of cholesterol-4-C^{14} was added to the diet of each group. (All the diet was eaten each day.) The feces were collected from the 5th to the 8th day, dried and extracted with petroleum ether.

No significant difference was found in the radioactivity present in the feces. Therefore, these 2 adsorbents had no effect on the absorption of cholesterol.

RENAL BLOOD FLOW DETERMINED BY AN EXTERNALLY PLACED SCINTILLATION DETECTOR. Gunnar Sevelius and Philip C. Johnson (intr. by R. M. Bird). Radioisotope Service, VA Hosp., and Dept. of Medicine, Univ. of Oklahoma, Oklahoma City.

Huff et al established that cardiac output can be estimated by using a scintillation detector placed over the heart to measure the time activity curve of the passage of radioactive albumin. The technique has been applied to the estimation of individual kidney blood flow by determining the ratio between the radioactivity over each flank during one circulation cycle and over the heart during this same cycle. The values for renal blood flow obtained in 13 healthy males were 730 ± 32 for the right kidney and 732 ± 27 for the left kidney. The mean differences between this technique and PAH and diodrast clearances were 17% and 11%, respectively. Patients with chronic glomerulonephritis, glomerulosclerosis, pyelonephritis and cardiac failure were also tested. The values obtained for kidney blood flow in each subject were more than 2 S. D. below the normal range. Determining the area of the first peak of radioactivity that follows the 2 cardiac peaks provides a general method for determining blood flow in peripheral organs.

SITE OF ACTION OF 5-HYDROXYTRYPTAMINE ON PULMONARY BLOOD VESSELS IN THE DOG. John T. Shepherd,* David E. Donald,* Erland Linder* and H. J. C. Swan. Mayo Clinic and Mayo Fndn., Rochester, Minn.

The effects on the pulmonary circulation of continuous infusion of 5-hydroxytryptamine creatinine sulfate into the right atrium has been studied in the intact dog. The smallest dose of 5-HT that caused a definite increase in pressure in the pulmonary artery was used (approximately 20 $\mu g/kg$ of body weight per min) in order to minimize the effects of this substance on cardiac output, heart rate, systemic blood pressure and respiration. Pressures were recorded simultaneously in the pulmonary artery, pulmonary-artery wedge, left atrium and aorta. Cardiac output was measured by the indicator-dilution technic, using cardio-green. In 9 experiments on 3 dogs, the mean pulmonary-artery pressure increased an average of 86% and the cardiac output 20%; the pulmonary vascular resistance increased in every instance (average 40%). In 9 experiments on 3 other dogs, pulmonary-artery pressure consistently increased, while left atrial and pulmonary-artery wedge pressures remained unchanged. These observations, in addition to confirming the results of Rudolph and Paul (Am. J. Physiol. 189:263, 1957) and of Borst and associates (J. Clin. Invest. 36:669, 1957) and others concerning the pulmonary vasoconstrictor action of 5-HT, demonstrate that the site of action is proximal to the pulmonary capillary bed.

DEPENDENCE OF PLASMA POTASSIUM CONCENTRATION ON BLOOD pH, pCO_2 AND BICARBONATE. D. H. Simmons and M. Avedon.* VA Ctr. and Univ. of California Med. Ctr., Los Angeles.

It is known that serum [K] concentration varies inversely with blood pH. It has also been suggested that metabolic and respiratory acid-base derangements have comparable effects on serum [K] for a given

pH change. The present study is a test of this concept, which implies that pCO_2 and bicarbonate are related to serum [K] only as they influence pH. Experiments were conducted on dogs anesthetized with Nembutal (25 mg/kg). Measurements were made during 30-min periods, 2 before and 3 after starting infusion of HCl or $NaHCO_3$ (0.075-0.15 M) at the rate of 0.3 cc/kg/min. Either arterial pH, pCO_2 or bicarbonate was held constant in 3 separate series by controlling respiration with a variable-stroke pump. In the 1st series (13 experiments), arterial pH was held constant while infusing HCl or $NaHCO_3$ so that pCO_2 and bicarbonate decreased or increased together. Serum [K] dropped 0.05 and 0.44 mEq/l., respectively, with no significant difference between these responses. In the 2nd series (10 expts.), arterial pCO_2 was held constant during the infusions, allowing pH and bicarbonate to change in the same direction. In the 3rd series (13 expts.), bicarbonate was held constant, allowing pH and pCO_2 to change in opposite directions. The changes in plasma [K] per unit change in arterial pH for the 2nd and 3rd series were not statistically significant (-2.83 and -1.67; overall mean -2.18). These 2 sets of data suggest that pH alone determines serum [K] and that comparable changes in serum [K] for a given pH change should be noted in respiratory and acid-base disturbances.

EFFECTS OF STIMULUS STRENGTH AND FREQUENCY ON CONTRACTIONS OF ISOLATED HEART MUSCLE. William Sleator Jr. and Taisija de Gubareff.* Washington Univ. Med. School, St. Louis, Mo.

When the voltage of stimuli driving isolated left atria of guinea pigs is increased to about 10 times threshold, contraction strength increases to approximately twice normal. A similar "voltage effect" in cat heart muscle has been tentatively explained as due to the release in the tissue of epinephrine-like substances by high-voltage stimuli (Whalen, Science 127:468, 1958). The present experiments provide further evidence that the voltage effect in guinea pig atria is due to action of epinephrine-like substances, but that, contrary to Whalen's other suggestion, the frequency dependence of contraction strength (normally a 10-fold increase at 27°C as frequency increases from 0.1 to 2.5 beats/sec) cannot be explained in this way. 1) Agents which blocked epinephrine effects (regitine, ergonovine maleate, dibenamine) abolished (or reduced by 90%) the voltage effect, while changing frequency effects relatively little. 2) High voltage stimulation increased durations of intracellular action potentials by about as much as does 5×10^{-8} gm/ml epinephrine. 3) When atria from guinea pigs pretreated with reserpine (known to remove over 98% of catechol amines from rabbit hearts) were given high voltage stimulation, contraction strength remained within 5% of standard (controls increased 100%), action potentials did not change, and frequency dependence of contractions was indistinguishable from controls.

PHOSPHORYLATIVE MECHANISMS IN THE COLD-ADAPTED RAT. Robert E. Smith and Alan S. Fairhurst.* Dept. of Physiology, Univ. of California School of Medicine, Los Angeles.

Further determinations have been conducted on the oxidative phosphorylation of mitochondria isolated from livers of cold-adapted, adult male rats (Long-Evans strain, maintained at 2°C for 60-80 days). It has been found that the marked lowering of P/O ratios in these

mitochondria, reported earlier with in vitro systems incubated at 37°C, occurs whether alpha-ketoglutarate or beta-hydroxybutyrate is employed as substrate. However, in either case, when the incubation temperature is lowered to 30°C, the P/O of the cold-adapted system is decreased to a value only slightly below that of the normal system. Concurrently the ratio, $Q_{O_2}^N$ of normal/cold mitochondria, is also reduced. ATPase activities, while absolutely higher at 37° than at 30°, remain substantially identical in both normal and cold-adapted mitochondrial systems; hence the observed differences are evidently not ascribable to increased dephosphorylation in vitro. It would appear that an enzyme system associated with oxidative phosphorylation in the cold-adapted mitochondria contains some step which has an energy of activation different from that in the unadapted control. (Aided by PHS Grant C-3635, Natl. Cancer Inst.)

ELECTROMETRIC MEASURE OF CARBON DIOXIDE AND BICARBONATE. Fred M. Snell (intr. by A. Baird Hastings). Dept. of Biological Chemistry, Harvard Med. School, Boston, Mass.

With the use of a membrane permeable to carbon dioxide and impermeable to ions it has been found possible to measure the equilibrium partial pressure of carbon dioxide in a solution or gas phase as an equivalent hydrogen ion activity (cf. Stow, R., et al. Arch. Phys. Med. and Rehab. 33:646, 1957). A glass electrode is moistened with a dilute bicarbonate solution in saturated KCl in which is suspended inert particulate material to serve as a spacer, and a 0.0005 inch thick polyethylene membrane is stretched over the surface. The resulting film of solution is made continuous with a reference electrode, but is otherwise isolated. In accordance with theory the measured EMF or pH is linear with the logarithm of the partial pressure of CO_2 at a given temperature, a pH unit corresponding to a decade change in the partial pressure. The assembled unit may be standardized with a known CO_2 pressure. The sequential measure of the pH and the PCO_2 of a solution allows the calculation of the bicarbonate ion activity or concentration. Apart from the standardization and sample handling, the errors of the method are dependent upon the precision of the electrical measure. Measurements to a precision of ± 0.01 pH unit correspond to an error of $\pm 2.3\%$ in PCO_2 and to $\pm 3.3\%$ in bicarbonate ion concentration.

LENS BIOELECTRIC POTENTIALS. Nick Sperelakis and Albert M. Potts (intr. by Robert M. Berne). Western Reserve Univ., Cleveland, Ohio.

Bioelectric potentials of bovine lenses were studied with Ag:AgCl wick electrodes and conventional microelectrodes. Lens fiber transmembrane potentials were found averaging -23.3 ± 1.2 mv, negative inside. A transcapsular potential (TCP) of -30.2 ± 1.2 mv, negative inside, was also found. Another potential averaging -10.3 mv was observed between the extracellular space and the bathing medium. These 3 potentials were in series, hence the potential difference between the intracellular compartment and the outside of the capsule was -63.8 mv. The DC resistance of the posterior capsule measured 800 ohms/cm^2; the short-circuit current was 36 μA/cm^2. The TCP and resistance were decreased in local areas by mechanical injury, hyperosmotic solutions of univalent electrolytes, K^+, and cathodal current producing an "injury" potential approaching the TCP. Opacity of the fibers beneath the injured capsular area occurred with some of these

treatments but not with others. Hyperosmotic solutions of divalent electrolytes or nonelectrolytes produced more opacity than capsular injury. Cooling, UV, EDTA, IAA and DNP decreased the TCP. Isosmotic KCl abolished the TCP, choline-Cl had no effect, Na_2SO_4 produced a partial decrease and K_2SO_4 produced a slightly positive potential; presumably the K^+ partial conductance is large relative to those for Na^+ or Cl^-. The results will be discussed in terms of a 3-compartment model partitioned by the capsule and fiber membranes across which electrochemical gradients of ions are maintained by active transport.

HARMONIC ANALYSIS OF AORTIC PRESSURE PULSES. Ralph W. Stacy and Robert L. Farrow.* Dept. of Physiology, Ohio State Univ., Columbus.

A total of 343 pulses recorded from 2 points in the abdominal aortas of dogs were subjected to Fourier analysis by a digital computer technique. From these data, apparent phase velocities for each harmonic were calculated. Variation with administration of vasoconstrictors and vasodilators, and mechanical occlusion peripherally were studied. In general, the spectral diagram was similar to those reported before. The physiological manipulations produced great variations in the phase and amplitude of the fundamental, with smaller variations in the higher harmonics. The changes in fundamental are responsible for changes in pulse wave velocity. These studies indicate a need for further elucidation of true wave velocity. (Supported by the Natl. Insts. of Health and the Central Ohio Heart Assoc.)

MEMBRANE POTENTIALS IN VASCULAR SMOOTH MUSCLE. Wm. W. Steinberger,* Donald C. Brodie* and David F. Bohr. Dept. of Physiology, Univ. of Michigan School of Pharmacy and Dept. of Pharmacology, Univ. of California, San Francisco.

Mesenteric artery from the rabbit was mounted in oxygenated Krebs bicarbonate solution at pH 7.4 and 38.5°C. The tissue was placed so that penetrations with glass microelectrodes were made from the outside of the artery. Membrane potentials were monitored through a Grass P-7 pre-amplifier and recorded on a Grass Model 5 polygraph. Large membrane potentials could be obtained only with electrodes of higher resistance than those required in sartorious studies. With resistances of the order of 10 megohms, the maximum potentials were in the 20-40 mv range. With higher resistances, 30-100 megohms, potentials well over 40 mv were measured. In 1 experiment in which the resistance of the electrode was 56 megohms and later, after breaking, 35 megohms the number of potentials that "held" were as follows: 10-19 mv, 1; 20-29, 9; 30-39, 4; 40-49, 9; greater than 50 mv, 6. In the last category 1 potential of 73 mv held for 4 sec and 1 of 71 mv for 36 sec. The maximum potential recorded was 85 mv which held for 2 sec before starting to decay. It appears that membrane potentials of vascular smooth muscle cells correspond to those that have been reported for the intestine and uterus of the guinea pig. (Supported by Grant H-3308, Natl. Heart Inst., PHS.)

USE OF INDICATOR-DILUTION TECHNIQUE FOR STUDY OF PERIPHERAL CIRCULATION. Wm. J. Stekiel,* Robt. A. Grace* and Jas. J. Smith. Dept. of Physiology, Marquette Univ. School of Medicine, Milwaukee, Wis.

Dilution and sampling techniques have in the past been used primarily

for measurement of flow, vascular volume and functional abnormality of the cardiopulmonary circuit. Theoretically, peripheral circulatory beds should be amenable to similar analysis provided accurate indicator-dilution curves can be inscribed by continuous sampling from the venous side. In the present study a dye-dilution method was used to study the circulation of the hind limb of the anesthetized dog. Small amounts (0.25-1.0 mg) of Indocyanine II (Cardio-Green) were injected into the femoral artery and sampling done via polyethylene tubing from the corresponding femoral vein. Dye curves were recorded with a modified Colson densitometer and blood flow was measured directly by means of Shipley-Wilson rotameter. Steady baselines and linear calibration curves indicated that at the peak absorption of this densitometer (805 μ), records are unaffected by venous alterations of oxyhemoglobin saturation. With the amounts of dye used, no recirculation effects were evident. With careful control of injection and withdrawal conditions, successive curves usually, though not invariably, reveal similar patterns and transit times. Selective occlusion experiments suggest that this approach might be useful in comparing flow characteristics of different tissues. Limitations of the method include curve distortion due to 1) respiratory and other changes in flow rate and 2) the low withdrawal rates required for sampling.

ERYTHROPOIETIC FACTOR IN MILK OF "ALTITUDE" GOATS. J. Clifford Stickney, Theadore L. Browne* and Edward J. Van Liere. West Virginia Univ. Med. Ctr., Morgantown.

Four kids were fed the milk from goats exposed 4 hr daily to 22,000 ft; 4 control kids were fed the milk of does kept at ground level. The regimen on "altitude milk" was begun 8-12 hr after birth. Hemoglobin and RBC were determined on peripheral blood, sampled at intervals of 2-7 days. A micro-Wong iron method was used for hemoglobin; RBC counts were made after 1 to 500 dilution. No reticulocytes were seen with Brilliant Cresyl Blue. Average hemoglobin for experimentals and controls decreased together from 12 gm/100 ml at birth to 9.5 at 8 days. A divergence then appeared, with experimental values tending to rise gradually and control values continuing to fall, reaching the lowest and most divergent point at the 30th day. The averages were then 9.92 and 7.61, significantly different at the 2% level. RBC averages tended roughly to reflect the above changes in hemoglobin. Differences between the two groups were significant at the 0.2% level on the 18th and on the 30th days. Actual paired values were: 12.84 and 9.07; 15.58 and 11.96 million/mm^3 for experimentals and controls respectively on the 2 dates. These preliminary experiments suggest that an erythropoietic factor appears in the milk of the goat exposed to simulated altitude. (Supported by a grant from the PHS.)

SKIN BLOOD FLOW VERSUS TEMPERATURE IN MINUTE VOLUMES OF TISSUE. R. W. Stow and J. F. Schieve (intr. by Eric Ogden). College of Medicine, Ohio State Univ., Columbus.

The flow in deep cutaneous tissue within approximately 1 mm of the tip of a 25-gauge needle thermometer has been measured in the lower extremity of humans. The method consists in assessing the rate at which heat is brought to (or taken from) the tissue by the inflowing arterial blood. The temperature of the local arterial supply is estimated by means of a second observation. From these data the flow may be calculated. Measurements have been made over a range of

tissue temperatures of 30-38°C. Flow has been found to vary from 1 - 100 x 10^{-4} grams of blood per gram of tissue per second. Although great variability is observed indicating that many factors other than temperature are important, the temperature coefficient of flow may be assessed. It has been found to be about 0.75°C. A by-product of the study has been the measurement of the temperature of the local arterial supply. It has been found to differ from the local tissue temperature by amounts ranging from -0.5 to +1.0°C.

POTENTIATION OF MECHOLYL OR HISTAMINE-STIMULATED GASTRIC SECRETION BY HYDROCORTISONE IN HEIDENHAIN POUCH DOGS. David C. H. Sun* and Harry Shay. Samuel S. Fels Research Inst., Temple Univ. Med. Ctr., Philadelphia, Pa.

In our studies on the stress effect of insulin hypoglycemia on gastric secretion in patients before and after vagotomy, we found the magnitude of the cephalic humoral (adrenal) phase of gastric secretion to be considerably less pronounced after vagotomy. In order to elucidate the physiologic significance of that difference, the present investigation was conducted to study the combined action of hydrocortisone and mecholyl-stimulated gastric secretion in Heidenhain pouch dogs. Three Heidenhain pouch dogs were used. Each dog served as his own control. Three series of 3 studies each were done in each dog. In 1 series, intermittent mecholyl injections were given; in the 2nd series, hydrocortisone was administered and in the 3rd series, hydrocortisone was given in addition to the intermittent mecholyl injections. The results show a potentiating action between hydrocortisone and mecholyl on gastric secretion, in that the volume, free and total acid concentration and acid output, were significantly greater than the values for the combined responses of these 2 drugs used separately. The significance of this finding will be discussed in its relation to the results on gastric secretion by the stress effect of insulin hypoglycemia before and after vagotomy. In addition, the potentiating effect of hydrocortisone on histamine-stimulated gastric secretion was investigated.

NORMAL ABSORPTION OF CHOLESTEROL OBTAINED IN BILE FISTULA RATS BY ADEQUATE ORAL ADMINISTRATION OF EXTRACT OF OX BILE. R. Suzuki* and A. C. Ivy. Dept. of Clin. Science, Univ. of Illinois College of Medicine, Chicago.

It has been previously reported (Am. J. Physiol. 193:521, 1958) that a continuous flow of bile into the intestine is required for the absorption of cholesterol and that attempts to restore bile to the intestine artificially so as to obtain normal absorption had failed. We now have found an artificial method which works. The following food mixture was prepared: 0.2 microcurie of cholesterol-4-C^{14} was emulsified with 0.5 cc of rat bile, 0.5 cc of water, 0.4 cc oleic acid, and 50 mg cholesterol, 650 mg of ox bile extract (Wilson & Co.) (50% cholates) powder was mixed with 12 to 15 gm of Pablum (Meade Johnson & Co.) and then enough 0.2% NaCl aqueous solution was added to make a thick paste. Then the cholesterol emulsion was added and mixed thoroughly in the paste. The emulsion was washed from the test tube twice with 1 cc of 1 to 1 diluted rat bile. The paste was divided into 24 parts and was fed every hour for 24 hr. The bile and feces were assayed for radioactivity. In 3 rats from 31 to 47% of the radioactivity was found in the bile, 95% of the remainder was found in the feces during a period of 5 days after feeding.

SODIUM FLUXES IN SKELETAL MUSCLE AS A FUNCTION OF HYDROGEN ION CONCENTRATION. R. C. Swan and R. J. Kossmann.* Dept. of Physiology, Cornell Univ. Med. College, New York City.

Sodium fluxes in frog skeletal muscle vary inversely and approximately linearly with the logarithm of the hydrogen ion concentration of the medium as the pH of phosphate or bicarbonate buffered Ringer solution is varied from 7.5 to 5.5. In phosphate buffered medium, or in bicarbonate buffered medium in which pCO_2 is constant and bicarbonate concentration varies from 2-60 mM, both Na influx and Na efflux decrease approximately by 0.25 of the control rates at pH 7.5 for each 10-fold increase in hydrogen ion concentration of the medium. When the pH of the medium is varied from 7.5 to 5.5 by varying pCO_2 and maintaining bicarbonate concentration constant, the Na fluxes again vary as inverse linear functions of the logarithm of hydrogen ion concentration of the medium. However, the relationship is such that both Na efflux and influx decline by approximately 0.40 of the control rates at pH 7.5 (pCO_2 10 mm Hg) per 10-fold increase in hydrogen ion concentration of the medium. Assuming that bicarbonate ions penetrate the fiber membrane relatively slowly, these results are interpreted to indicate that both Na efflux and Na influx are functions of both intrafiber pH and the pH of the interfiber fluid. These prompt, reversible and reproducible changes in Na influx and efflux, as hydrogen ion concentration varies, are apparently equal as shown by measurements of changes in Na influx and efflux in the same muscle. Thus an appreciable fraction of the Na entering the resting fiber is apparently transported by a mechanism which shares some common feature with that for Na extrusion.

EFFECT OF AGING ON THE LATENCY OF SUPERFICIAL REFLEXES IN NORMAL HUMANS. R. D. Teasdall, J. W. Magladery and A. H. Norris.* Div. of Neurological Medicine and the Gerontology Branch, Baltimore City Hosps., Baltimore, Md.

Action potentials accompanying plantar flexor and superficial abdominal reflexes were recorded by electrodes fixed to skin over respective muscle groups and after amplification were photographed on a cathode ray oscilloscope. The latencies of these reflexes could be calculated since the sweeps were triggered by the initial contact of the scratching device to the skin. In 14 individuals, averaging 32 years of age, the average latency of the plantar flexor reflex was 203 msec; whereas in 15 subjects whose average age was 75 the latency was 279 msec. Latencies for abdominal reflexes in 2 comparable groups were 50 msec for the young and 160 msec for the elderly. The increased latencies of these reflexes in older individuals were significant according to the t test. The reaction time for voluntary plantar flexion of the foot in response to a cutaneous stimulus to sole, however, was 170 and 189 msec for young and aged groups, respectively. In elderly persons the lowered excitability of these reflexes, as determined by increased latency, is felt to be due to a deficiency of central excitatory processes which is reflected in effector systems governing reflex activity, rather than those related primarily to simple voluntary motor performance. (Supported by Grant B-367, Natl. Inst. of Neurological Diseases and Blindness.)

EFFECT OF EXERCISE ON CORONARY ARTERIES OF SMALL ANIMALS REVEALED BY THE VINYL ACETATE CORROSION CAST TECHNIQUE. Jay Tepperman and David Pearlman.* Dept. of Pharmacology, State Univ. of New York Upstate Med. Ctr., Syracuse.

Epidemiologic studies of Morris et al. (Lancet 2:1053, 1110, 1953) suggest that the antecedent exercise history of men may influence susceptibility to myocardial infarction. In order to test the hypothesis that the anatomy of the coronary arterial tree may be modified by long-continued exercise, a method was developed for estimating the capacity of the tree by preparing vinyl acetate corrosion casts of rat coronaries (wt. 3-8 mg/pair) and weighing them on a Cahn electromagnetic balance (capacity 10 mg, sensitivity 0.003 mg). In 2 experiments on rats adapted to spontaneous running in conventional activity cages (0.5-1.5 miles/day for 10 wk), the exercised rats showed significant increases in coronary cast weights over those of "sedentary" controls (males $P < 0.01$; females $P < 0.05$). In male exercised rats the cast/heart weight ratio was unchanged; in females it was increased ($P < 0.05$). Rats adapted to swimming 30 min b.d. for 10 wk showed increases both in cast weight ($P < 0.02$) and cast/heart wt. ratio ($P < 0.01$). It is uncertain whether the observed changes are attributable to increases in the internal diameter of the larger vessels, increased arborization of the smaller ones, or to both. The relation between these findings and the epidemiologic studies cited above will be discussed. (Supported by Life Insurance Med. Research Fund.)

CARBON DIOXIDE BALANCE AFTER SUCCESSIVE UNILATERAL OCCLUSION OF PULMONARY ARTERY AND BRONCHUS. Richard A. Theye* and Ward S. Fowler. Mayo Clinic and Mayo Fndn., Rochester, Minn.

In a study of ventilatory requirements during thoracic surgery measurements were made of the oxygen uptake, carbon dioxide output and carbon dioxide tension of arterial and mixed venous blood and expired alveolar gas in anesthetized and paralyzed dogs ventilated with air at a constant rate. Retention of carbon dioxide was not observed when the dogs were in the lateral decubitus position with either closed or open thorax. Small amounts of carbon dioxide were eliminated from the exposed pleura. Occlusion of the left pulmonary artery after left thoracotomy was followed in 1 hr by additional occlusion of the left bronchus, or the order was reversed. A major or minor degree of retention of carbon dioxide was observed after initial occlusion of the artery or the bronchus, respectively. During the 2nd hour (after additional occlusion) the previously retained carbon dioxide was eliminated. Change of body levels of carbon dioxide can be appreciated best by measurement of tension in mixed venous blood. Knowledge of the rate of elimination of carbon dioxide during the initial steady state and thereafter is similarly useful.

CONDUCTION VELOCITY OF MOTOR FIBERS OF THE ULNAR NERVE IN INFANTS AND CHILDREN. Juergen E. Thomas* and Edward H. Lambert. Mayo Clinic and Mayo Fndn., Rochester, Minn.

The conduction velocity of motor fibers of the ulnar nerve in the forearm was measured in 146 subjects, including 6 premature infants, 42 full-term newborn infants and 98 children up to age 14 yr. In premature babies, values as low as 18 m/sec were found. At full-term birth, velocities ranged from 21 to 33 m/sec (mean 28 m/sec), which is

slightly less than half the values obtained in young adults (48 to 72 m/sec; mean 60 m/sec). At the age of 6 months the values for a few infants already approached low adult values and by the age of 1 yr the velocity had risen to a mean of 50 m/sec. At 3 yr almost all values were in the lower part of the adult range, while by 5 yr the values were essentially the same as those obtained in adults. These data are in harmony with the observations of Rexed and others that, in the infant at birth, the diameter of the nerve fibers of ventral roots is roughly one-half that of the adult and that maturation is attained between the ages of 2 and 5 yr. It is of interest that the H-reflex response was readily elicited by stimulation of the ulnar nerve in most newborn infants, but rarely occurred after the age of 1 yr. The conduction velocities in the sensory fibers subserving this reflex were similar to those of the motor fibers. The data obtained have been of value in the study of neuromuscular disorders in children, particularly in the diagnosis of chronic polyneuropathy wherein conduction velocities are low.

EFFECTS OF CORTICAL LESIONS IN INFANT AND ADULT CATS ON ROUGHNESS DISCRIMINATION. Richard F. Thompson and Robert M. Benjamin (intr. by C. N. Woolsey). Lab. of Neurophysiology, Univ. of Wisconsin Med. School, Madison.

Zubeck has reported that bilateral ablation of somatic sensory areas I and II in cat results in total loss of ability to discriminate roughness. This study compares effects of lesions in newborn and adult cats. Experimental conditions were: control 1, 4 normal adult cats; control 2, 4 normal cats, age 6 months; experimental 1, 4 adult cats with total bilateral ablation of somatic I and II 6 months prior to test; experimental 2, 4 cats age 6 months with total bilateral ablation of somatic I and II at 6th postnatal day; experimental 3, 2 cats age 6 months with total bilateral ablation of somatic I and II and all "precentral" motor cortex at 6th postnatal day. All animals were trained to differentiate cardboard and rough sandpaper, which covered interchangeable floorboards of Zubeck's modified Y-maze. If successful, the animals were then given threshold tests on finer grades of sandpaper. All animals in all groups learned the discrimination except those of the adult operate group (experimental 1). Only one of the 4 animals in the adult operate group learned, and the number of trials to criterion (694) was greater than for any other animal. Thus lesions of the infant cortex result in considerably smaller behavioral deficits than do comparable lesions of the adult cortex. In contrast, all animals with lesions showed comparable deficits in placing and hopping reactions.

DIMENSIONAL AND DYNAMIC FEATURES OF MAMMALIAN GASTROCNEMIUS MUSCLE. J. D. Thomson. Dept. of Physiology, State Univ. of Iowa, Iowa City.

Dimensional features and contractile responses of medial and lateral heads of rat gastrocnemii were compared with those of whole gastrocnemii. The lateral head is heavier than the medial head, but there is no significant difference in maximum tetanus tension. The sum of tetanus tensions and the sum of maximum rates of tetanus tension development of the 2 heads are less than the observed values for whole muscle, due to loss of mechanical advantage by being separated. The medial head is a slower muscle than the lateral. Dimensional features, total twitch tension and maximum rates of twitch tension development are additive. Averaged values for both heads for degree

of fusion of repetitive twitches approximated values for whole muscle. Latent periods and contraction times for twitches of individual heads are longer than those of whole muscle, possibly because of smaller tendons of the separate heads. An additive relationship suggests absence of mutual interaction between heads, while an average relationship suggests mutual interaction between heads.

RELAXATION-PRESSURE CURVE IN PULMONARY EMPHYSEMA. Er Yi Ting and Harold A. Lyons (intr. by Frederick Kao). Dept. of Med., State Univ. of New York, Downstate Med. Ctr., Brooklyn.

The relaxation-pressure diagram of Rahn has been employed in the study of patients with obstructive pulmonary disease (as emphysema). This method of study of the mechanics of respiration has previously been used only in normal subjects. After the total lung capacity and its subdivisions were measured, each patient had a measurement of intrapulmonary pressure (P_R, total pressure), and the intraesophageal pressure (P_L). By subtraction of P_L from P_R, P_C (thoracic wall pressure) is obtained. Each measurement was made at a known volume of lung inflation at points of no air flow. The data were then used for the construction of a relaxation-pressure-volume curve. Repeat studies produced reproducible curves. In the patients, a marked alteration of the P_R curve was found. It became concave in shape, and shifted upward and to the left. Analysis finds this change to be due to both P_L and P_C pressure-volume relationships. The characteristic finding appears to be due to a "fixed" thoracic cage and hyperinflation of the lung. A brief comparison with the curves obtained in normal subjects and patients with restrictive lung disease will be made. This method of study gives information concerning the properties of the lung and chest wall, and allows separation of these components as they influence the total pulmonary compliance.

SOME FACTORS WHICH INFLUENCE THE RESONANT FREQUENCY OF LARGE ARTERY SEGMENTS. Alan F. Toronto* and Homer R. Warner. Latter-day Saints Hosp., Salt Lake City, Utah.

In a previous report from this laboratory (Circ. Research 5:79, 1957) a technique involving the use of an analog computer was described by which segments of the aorta and large arteries in man and dogs were shown to transmit certain frequency components of the arterial pressure wave more readily than others. In fact it was shown that 40-50 cm segments between the thoracic aorta and the radial artery, or thoracic aorta and the femoral artery could be closely simulated by a simple series resonant circuit. Measurements of resonant frequency (f_n) have now been made on 44 human subjects ranging in age from 16 to 61. The average f_n of the aorta to radial system was 4.7 cps (range 3.0-6.9). The correlation coefficient with age was 0.62. For the aorta to femoral system in the same subjects f_n averaged 3.0 cps (range 1.9-4.5) and there was no correlation with age. In 41 dogs studied under Nembutal anesthesia the average f_n of the descending aorta segment was 4.2 cps with a range from 3.4 to 5.2. In a given dog f_n varied directly with mean arterial pressure regardless of whether the pressure variation was induced by drug infusion, stimulation of vagus or carotid sinus nerves, or blood volume alteration. In a given subject wide fluctuations in heart rate do not influence measured resonant frequency.

STRENGTH DURATION CURVES IN THE HYPOTHERMIC DOG HEART. J. C. Torres,* E. T. Angelakos* and A. H. Hegnauer. Physiology Dept., Boston Univ. School of Medicine, Boston, Mass.

Strength-duration curves were constructed from threshold measurements obtained with anodal and cathodal stimuli. Stimuli of 0.1, 0.5, 1.0 and 10 msec durations were delivered during diastole via an electrode sutured to the left ventricular epicardium. During continuous cooling, thresholds were measured for each stimulus duration at $37 \pm 2°$, $29 \pm 2°$, $23 \pm 2°$ and $19 \pm 2°$C. The curves for anodal stimulation were consistently higher than those for cathodal. Although rheobases remained relatively constant, the chronaxies increased considerably with cooling. Except at normal temperature there were no significant differences in the chronaxie values due to stimulus polarity. If threshold stimuli are expressed in terms of the energy (coulombs) required to excite, then the impulses of short duration are more effective than rheobasic currents. With cooling, however, the superiority of the short pulses diminishes relative to the longer pulses, as reflected in the elevation of the corresponding portions of curves. This suggests that cold renders myocardial fibers relatively less susceptible to depolarizing currents of short duration.

SALIVARY SECRETION OF I^{131}. Eugene J. Towbin and W. H. Perkins (intr. by E. F. Adolph). Dept. of Medicine, Univ. of Arkansas School of Med. and VA Hosp., Little Rock.

Polyethylene catheters were placed in a parotid and submaxillary vein, the salivary ducts and the femoral artery of anesthetized dogs. One half millicurie of I^{131}, as sodium iodide, was administered intravenously approximately 1 hr before the collection of saliva. Standard counting technique for I^{131} was employed. Salivary secretion was induced by pilocarpine or by unilateral electrical stimulation. Initially it was hoped that the extraction ratio for iodine would be large enough to permit its use as a measure of parotid plasma flow in experiments in which parotid venous blood would not be collected. However, the large variation in extraction ratio, from 25 to 88% in a group of 7 technically satisfactory experiments, precludes the use of "clearance" technique. The first specimen of parotid saliva almost always has a much greater specific activity (higher iodide concentration) than subsequent specimens. In a number of preparations the parotid venous concentration of iodide rose above the arterial level for the first minute or two following stimulation. In experiments employing electrical stimulation, the resting gland contained approximately 10 times as much iodide as the gland immediately after stimulation. This point was demonstrated both by counting tissue specimens and by radioautograph techniques. These results are interpreted to demonstrate that the parotid gland in the dog stores iodide during rest and releases it rapidly upon stimulation.

INTERACTION BETWEEN MAGNESIUM AND OXALOACETATE, ATP AND SUCCINOXIDASE. David B. Tyler. Dept. of Pharmacology, Schools of Dentistry and Medicine, Univ. of Puerto Rico, San Juan.

Magnesium has been shown to form a readily dissociable complex with an enzyme, ATP and oxaloacetate rendering the latter keto acid incapable of inhibiting succinic dehydrogenase; calcium antagonizes the formation of this complex. In an effort to clarify the mechanism of action of magnesium, kinetic measurements were made of the interactions

between magnesium, calcium, the enzyme and the substrates. The experimental data indicate that: more than one metal binding site is probably involved in the reaction; the strength of the interaction between the enzyme and magnesium decreases below pH 7.0; the interaction of magnesium in the above system is modified by the presence of ions other than calcium. (Supported by a grant from the Natl. Science Fndn.)

HEPATIC REGULATION OF ADRENAL CORTICAL FUNCTION. John Urquhart,* F. Eugene Yates and Arthur L. Herbst.* Dept. of Physiology, Harvard Medical School, Boston, Mass.

The rate of hepatic inactivation of circulating adrenal cortical hormones by reduction of Ring A can theoretically influence the rate of ACTH release in unstressed animals by determining the biological half-life of secreted corticosteroids. We studied the effect of changes in hepatic capacity for Ring A reduction on the size of the adrenal glands in rats and golden hamsters. In rats, females have larger adrenals than males (0.027 and 0.012% of body weight), and a parallel sex difference was found in hepatic capacity for steroid Ring A reduction. Slices and homogenates of livers from females reduced Ring A of numerous Δ^4-3-keto steroids at rates more than double those of livers from males. In hamsters, males have larger adrenals than females (0.019 and 0.014% of body weight), and in this species livers of males had greater capacity for inactivation of corticosteroids than did those of females. Furthermore, in both sexes of rats it was possible to increase hepatic capacity for Ring A reduction by treatment with thyroid hormones, and to decrease it by thyroidectomy. Parallel changes in adrenal weights were observed, and the correlation between total hepatic capacity for inactivation of corticosteroids by Ring A reduction and adrenal weights was excellent ($r = 0.97$). These results suggest that the rate of enzymatic reduction of Ring A of adrenal cortical steroids by liver is the primary determinant of the rate of ACTH release, and therefore of adrenal cortical secretion, in unstressed animals.

EXCHANGE OF SODIUM^{24} WITH ETHER-SOLUBLE SODIUM OF KIDNEY. John C. Vanatta, Edward L. Rhodes* and Allen F. Reid. Depts. of Physiology and Biophysics, Univ. of Texas, Southwestern Med. School, Dallas.

Extracts of kidney tissue were made 1 and 3 hr after administration of Na^{24} to a rat. Extract I was made of dried, minced, kidney tissue with anhydrous ether; and Extract II was made of fresh, homogenized, kidney tissue with alcohol, followed by 1:1 alcohol-ether, then anhydrous ether. These extracts were pooled, dried, re-extracted with ether and again dried. Extracts I and II were purified by washing the residue with acetone, dissolving the non-acetone soluble material in petroleum ether, and washing the ether solution once with deionized water and twice with 70% alcohol. The Na^{24} and Na content of the material in 70% alcohol was determined as was that of plasma. The average ratio of the specific activities of extract:plasma in each of the above experiments for Extract I was 0.028 at 1 hr and 0.095 at 3 hr, and for Extract II was 0.66 and 0.71 at the respective times. The first 3 values are averages of determinations on 4 animals; and the last value is the average of 3. Five in vitro control experiments showed an average value of 0.004 as the ratio of specific activity of extract to that of the bath. These data

suggest 2 different ether-soluble substances present in the kidney. (Supported by Grant H-1574 (C4), Natl. Insts. of Health.)

TOLERANCE AND SUDOMOTOR RESPONSE TO HEAT AFTER BODY COOLING. James H. Veghte* and Paul Webb. Aero Med. Lab., Wright-Patterson AFB, Ohio.

The effect of prior body cooling was studied to determine its influence on tolerance to a high level of heat stress. Five subjects were exposed to 3 levels of precooling consisting of 30, 60 and 90 min exposure in a 60°F water bath, prior to entering the heat chamber at 160°F. Results indicated tolerance to heat can be increased significantly by prior body cooling. The longer the body is precooled, the greater the increase in tolerance to an environment of 160°F. The tolerance limit appears to be determined by a narrow range of rectal temperature which, when reached, terminates the exposure due to impending heat stroke. Recruitment of sweating in heat is inhibited by prior body cooling. This inhibition occurs despite high skin temperatures and low rectal temperatures. Analysis of the results indicates that a combination of skin and rectal temperatures (mean body temperature) controls the onset of sudomotor activity. Once sweating is initiated, true or normal sweating follows after a given time interval—in these experiments, 12 min. A person is able to tolerate a heat stress of 160°F for periods as long as 40 min with no or little sweating with no adverse physiological effects, if sufficiently precooled prior to the heat exposure.

ELEMENTARY SERVO-ANALYSIS OF THE CIRCULATION USING AN ANALOG COMPUTER. Homer R. Warner. Latter-day Saints Hosp., Salt Lake City, Utah.

Although much is known regarding the various components of the circulation, an adequate analysis of its performance as an intact closed-loop system has yet to be undertaken. Such an analysis would involve finding equations to describe the relationship of each component to its adjacent components and then solving all these equations simultaneously. In the present study an analog computer is used to obtain simultaneous solutions to 16 integrodifferential equations chosen to represent the relationship among flow, volume, pressure and time in the various system components. The time-course of equation variables from the computer is compared with corresponding physiologic variables previously recorded on a multi-channel magnetic tape loop from a human subject or experimental animal. The theoretical and experimental curves may be made to correspond by varying potentiometers whose settings represent in the computer the coefficients of the equations. Systematic variation of equation coefficients allows thorough analysis of each parameter's role in determining system performance. The solutions predict that return of the circulatory system to a steady state following a transient disturbance such as a valsalva maneuver will be rapid and non-oscillatory except at high flows. It is concluded from these studies that reflex changes in nervous or humoral activity are not essential for satisfactory transient performance of the circulatory system.

PERSISTENCE OF SNIFFING AFTER BILATERAL ABLATION OF OLFACTORY BULBS IN RAT. W. I. Welker (intr. by C. N. Woolsey). Lab. of Neurophysiology, Univ. of Wisconsin Med. School, Madison.

The olfactory bulbs were aspirated bilaterally in 9 21-day-old albino

rats. Beginning 120 days postoperatively, "sniffing" reactions of these animals were compared with those of 9 control animals. Analysis of the behavior sequences was made by means of high-speed cinematography. In normal rats, novel external stimuli (visual, auditory, tactile, olfactory) elicit a characteristic pattern of behavior which consists of the following elements: a) general head and body orientation in the direction of the stimulus; b) burst of polypnea; c) recurrent protraction and retraction of vibrissae; d) repeated ventroflexion of the tip of the nose and nostrils; and e) a rapid succession of head movements and head fixations. Elements b-e occur at a rate of about 6-8/sec in bursts of varying duration (1-5 sec). These 4 behavioral elements may occur independently of one another, but when they occur together, which is more common, they blend at the same rate and in a fixed temporal sequence with respect to one another. Although the successive nostril movements and polypnea implicate the operation of an olfactory mechanism, these behavioral sequences appeared identical in operated and in control animals, indicating that the initiation and patterning of sniffing is not dependent upon olfactory input.

GESTATION PERIOD IN DIABETIC RATS AND BODY WEIGHT IN FETUSES AND NEWBORNS. Lemen J. Wells, Jae Nam Kim, Walter Runge and Arnold Lazarow (intr. by Edward A. Boyden). Dept. of Anatomy, Univ. of Minnesota, Minneapolis.

Of 80 pregnant rats used in this study, 26 were normal, 25 had manifest diabetes and 29 did not develop diabetes after they had been alloxanized or pancreatectomized. Fetuses were removed by Caesarian section at 21 days and 15 hr, i.e. 519 hr after observed mating. Newborns were weighed promptly after witnessed spontaneous delivery. Diabetes, induced by alloxan or pancreatectomy either before conception or on 12th day of gestation, produced 3 related effects. 1) The fetal body weight was reduced 14% at 519 hr: 19 normal litters averaged 5.49 gm; 12 litters from diabetic mothers (alloxan day 12) averaged 4.73 gm. 2) Pregnancy was lengthened from 538 hr (25 control litters) to 563 hr (8 litters, alloxan day 12): since prolongation of gestation gave fetuses extra time for growth in utero, the body weight of spontaneously-delivered newborns from diabetic mothers approximated that of normal newborns which were delivered 25 hr earlier. 3) Increased fetal and/or neonatal mortality occurred. These effects were not due exclusively to hyperglycemia, which was verified in the fetus at 21 days and 15 hr, since all of them also were observed in fetuses and newborns of alloxanized or pancreatomized mothers which did not develop diabetes. (Aided by PHS Grants A-1244 and A-1659.)

MEASUREMENT OF REGIONAL FUNCTION IN THE LUNGS. J. B. West and P. Hugh-Jones (intr. by Julius H. Comroe, Jr.). Postgraduate Med. School of London, London, England.

Preliminary work with 2 new methods of measuring regional lung function is described. In the first method, gas sampled in lobar or segmental bronchi at routine diagnostic bronchoscopy is continuously analyzed by a mass spectrometer which will record the concentrations of 4 gases simultaneously. The distinctive patterns of gas concentrations which follow partial obstruction of lobar bronchi or branches of the pulmonary artery have been elucidated in dogs. The changes can be explained by alterations in the ventilation-perfusion ratio and in the phase of ventilation of an obstructed lobe. In the 2nd method, the

short-lived radioactive isotope, oxygen-15, has been used to study both the intake of oxygen on inspiration, and its clearance by the blood, in small regions of the lung. The isotope is produced on the Medical Research Council cyclotron in the hospital grounds and decays by positron emission. Pairs of counters in coincidence record the radiation from a small volume of lung. Following a single breath of activated air, the counting rate is determined initially by the ventilation of the lung and then, during breath holding, by the rate at which oxygen is removed by the pulmonary blood. Examples of tracings obtained from normal and abnormal subjects are shown.

SYMPATHETIC IMBALANCE AND BLOOD PRESSURE HOMEOSTASIS. C. M. Wilhelmj, R. L. O'Brien* and H. H. McCarthy.* Depts. of Physiology-Pharmacology and Surgery, Creighton Univ. School of Medicine, Omaha, Nebr.

The blood pressure and heart rate of dogs with bilateral paravertebral sympathetic ganglionectomy are not strikingly different from normal dogs, although a few will show occasional periods of marked fluctuations of blood pressure. To date 7 dogs have been studied after either right or left unilateral paravertebral ganglionectomy and 5 have shown very marked daily and hourly fluctuations of both systolic and diastolic pressure when determined on either the sympathectomized or the normal hind limbs. The average blood pressures have been abnormally high. Heart rate has been reasonably constant. The normally enervated pupil has shown hippus and a tendency to be constantly or periodically widely dilated. It appears that unilateral paravertebral ganglionectomy interferes with blood pressure homeostasis more than bilateral. (Aided by the Am. Heart Assoc. and the Natl. Heart Inst.)

INCREASED CARDIAC OUTPUT WITHOUT CHANGES IN CORONARY FLOW OR OXYGEN UTILIZATION: A CRITIQUE OF THE CONCEPT OF THE WORK OF THE HEART. F. Williams and C. Williams (intr. by S. Rodbard). Chronic Disease Res. Inst., Univ. of Buffalo, Buffalo, N. Y.

Numerous studies have attempted to establish relationships between heart "work," oxygen consumption and coronary flow. These have generally been based on the mechanical formula that "work" is the product of cardiac output and blood pressure. The present study demonstrates that marked increases in cardiac output have no significant effects on coronary flow or oxygen utilization. Cardiac output and coronary flow were measured separately (J. Appl. Physiol. 6:311, 1953) in 10 anesthetized, thoracotomized dogs. Blood pressure was determined from the carotid artery. Cardiac oxygen consumption was determined gasometrically in arterial and coronary venous bloods. When a shunt between aorta and pulmonary artery was opened, left ventricular output nearly doubled without effect on arterial pressure; no change was seen in either coronary flow or myocardial oxygen consumption. By contrast, a rise in aortic pressure produced the expected increase in both these measurements. The calculated "work of the heart" did not, therefore, correlate with other parameters of energy utilization. It is evident that the heart operates through different biochemical pathways in accomplishing a pressure load, as against a volume output load. These fundamental differences are under continued examination.

REFLEX FACILITATION BY ANTIDROMIC VOLLEYS. Victor J. Wilson. The Rockefeller Inst., New York City.

Facilitation of monosynaptic reflexes by antidromic volleys in muscle nerves originating from neighboring motoneurons, described by Renshaw (1941), has been studied in spinal cats; it is at its peak with a conditioning test interval of 20-30 msec, can last 50-100 msec, and may increase reflexes by as much as 50%. Facilitation is often preceded by recurrent inhibition. Frequently, however, this facilitation is not preceded by inhibition and therefore it cannot be a rebound effect. The facilitation threshold is about the same as that of recurrent inhibition: both phenomena may be present when the antidromic spike is less than 10% of maximal, and both increase as the size of the antidromic spike increases. Latency of facilitation, measured in cases where the latter is not preceded by inhibition, is longer than that of recurrent inhibition. The extra time, approximately 1 and sometimes more msec, suggests the presence of at least 1 more synaptic delay. The pharmacological properties of the facilitation resemble those of recurrent inhibition. Dihydro-beta-erythroidine partially blocks facilitation; the peak is decreased and occurs earlier, and the duration is shortened. Eserine increases the duration of facilitation and recurrent inhibition and sometimes enhances their magnitude. It is concluded that the facilitation is mediated by the cholinergic motor axon collaterals, and that at least 2 interneurons are located between collateral and motoneuron.

INFLUENCE OF STRESS AND TESTOSTERONE PROPIONATE ON BODY WEIGHT AND SOME ENDOCRINE CHANGES IN PULLETS FED AN "ATHEROGENIC" DIET. Harry Y. C. Wong, Abbie K. Wong* and Smith W. Ames.* Dept. of Physiology, Howard Univ. School of Medicine, and Office of the Surgeon General, USAF, Washington, D. C.

Previous reports from our laboratory have shown that stress (exercise) and the male sex hormone "Oreton," whether used singly or in combination, resulted in weight loss of cockerels or capons on an "atherogenic" diet. The following investigation was undertaken to study whether similar changes in body weights as well as endocrine changes could be observed in pullets on an "atherogenic" diet when subjected to exercise and administration of male sex hormone. After 10 wk of feeding on this regimen of 2% cholesterol and 5% cottonseed oil, the following results were observed: 1) statistically there were no differences in body weights of the pullets fed an "atherogenic" diet or those similarly fed but treated with testosterone propionate when compared to the controls on plain mash. There were no significant differences in the body weights of the groups exercised as compared to the controls whether fed a cholesterol diet or a similar group treated with testosterone propionate; 2) as to the comb sizes, no significant differences were observed in the "atherogenic" fed pullets with the exception of those treated with testosterone propionate which showed a significant increment when compared to any of the other groups, whether fed an "atherogenic" diet or plain mash. (Supported by Grants #H-2420, Natl. Heart Inst., Washington Heart and Am. Heart Assocs.)

GROWTH OF MICE WHILE EXPOSED TO GRAVITIES OF VARIOUS INTENSITIES. Charles C. Wunder. Dept. of Physiology, College of Medicine, State Univ. of Iowa, Iowa City.

This investigation demonstrates that growth can be influenced by the

intensity of a gravitational field. Developing white mice, varying in age from 1-7 wk at the onset of exposure, have been continually centrifuged at 2, 3, 5, 6, 7, 9, and 10 times the earth's gravity for as long as 7 wk. The initial response to increased gravity is a drop in both animal weight and food consumption. The magnitude of this response is almost the same for any of the fields employed. This is followed either by continued loss in weight with eventual death or by adaptation to the new gravitational environment and renewed growth. As would be expected, mice subjected to the more intense fields are less able to adjust to the new environment. Mice which have just been weaned are the least able to exhibit this adaptation.

CHRONIC CONGESTIVE FAILURE IN DOGS WITH TRICUSPID INSUFFICIENCY AND PULMONIC STENOSIS. Nicholas A. Yankopoulos* and James O. Davis. Natl. Heart Inst., Bethesda, Md.

Chronic congestive heart failure was produced by the method of Barger (Am. J. Physiol. 169:384, 1952) except that pulmonic stenosis was achieved with a ligature in order to control the degree of stenosis. All of 9 dogs developed ascites. Ascitic fluid occurred after tricuspid insufficiency alone (1 animal) and following the slight stenosis produced by merely placing the ligature (3 dogs); 5 dogs required tightening of the ligature before ascites formed. Seven dogs were studied for 2-4 months. Ascitic fluid was present throughout the course but the volume of fluid varied greatly among the animals; paracentesis was not performed. On a constant Na intake, daily urinary Na excretion varied from very low excretion to that associated with Na balance; in some animals there were long periods of mild Na retention. The average increase in mean right atrial pressure (RAP) associated with the appearance of ascites was 12 cm water. In contrast, right ventricular systolic and mean pressures were unchanged or increased slightly. Left ventricular end diastolic pressure remained at the control level (measured for 4 months in 2 dogs only). The data show 1) a high incidence of successful preparations probably attributable to use of the technique of controlled progressive pulmonic stenosis, 2) a high RAP associated with the onset of ascites, and 3) marked variability in the renal excretion of Na in the presence of chronic ascites.