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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

CORTICAL CONTROL OF FUSIMOTOR NEURONS. Konrad Akert and Elizabeth M. Mortimer.* Dept. Physiol., Univ. Wisconsin, Madison.

In continuation of work by Granit and Kaada (1952) the relationship between sensorimotor areas of cerebral cortex and spinal motor units was studied in cat and monkey. Records were taken from fine strands of ventral lumbosacral and spinal accessory nerve roots under chloralose-urethane and nembutal anesthesia. Fusimotor fibers were identified on the basis of spike size as well as conditions and patterns of discharge. Bipolar and unipolar stimulation of sensorimotor cortex with single shocks of 0.1 - 2.0 msec. duration had no detectable affect on fusimotor units. Repetitive stimulation, e.g. 60 cycles per second, accelerated or decelerated their discharge. Driving of single units occurred after a delay of from 100 msec. to 2 seconds when the precentral motor system was stimulated. Foci for such activation conformed to the cortical localization pattern found for large fiber units. The small fibers had a lower threshold to cortical stimulation than the large fibers; with intensities at or slightly above that for muscular responses small fiber activation preceded that of the large ones. This difference was further accentuated by transecting the dorsal root of the same and adjacent segments. Under this condition, the alpha units, responded only sporadically and with considerable delay, whereas gamma fibers were still easily excitable. Decrease of fusimotor activity by cortical stimulation was more readily obtained under nembutal anesthesia. Lumbosacral units were decelerated from foci of axial musculature and from postcentral leg area.

STUDY OF CERTAIN ASPECTS OF ACUTE ORAL IRON INTOXICATION. Harold Albert*, C. R. Kemp* and Wayne G. Rohse. Dept. of Physiol., Coll. of Med., State Univ. of Iowa, Iowa City, and Dept. of Biochem., Rockford Memorial Hosp., Rockford, Ill.

It is now clearly evident that the accidental ingestion of overdosages of therapeutic iron preparations may be fatal to children. As little as one gram of ferrous sulfate is now considered to be a potentially fatal dose. The data to be reported in this study indicate that the toxicity of iron may be more closely related to the systemic effects induced by absorbed iron than to localized traumatic effects

of the iron upon gastrointestinal tissues. In experimental animals toxicity and death appear to be directly associated with the serum iron rises during the first few hours subsequent to the oral administration of iron in aqueous solution. Serum iron rises may vary widely when standard dosages of elemental iron per kilogram body weight are administered in the form of different iron preparations. Moreover, serum iron responses may vary widely from animal to animal when a standard toxic dose of a given iron preparation is administered. Since bile and pancreatic juice have been reported to affect the uptake of iron from small dosages, comparisons of serum iron responses in intact dogs with those in which bile and pancreatic juice were excluded from the gut before administration of toxic doses of iron will be reported and discussed.

METABOLISM OF NORMAL AND MALIGNANT TISSUE CULTURE CELL STRAINS. R. V. Andrews,* H. J. Phillips and Vera Skank.* Dept. of Physiol. and Pharm., Creighton Univ. Sch. of Med., Omaha, Nebr.

Some tissue cells adapt or alter to "in vitro" conditions when cultivated for prolonged periods by the tissue culture technique. This adaptation to form cell strains is manifest by a change to a uniform morphology, by a marked increase in the rate of cell proliferation, and by the ease with which trypsinized cultures attach to the glass culture flask. The metabolism of eight normal and six malignant cell strains which had adapted to tissue culture conditions was studied. Respiration was determined by the direct method of Warburg; glycolysis in terms of lactate produced. All cell strains were grown in the same nutrient medium supplemented with 20% horse serum. Cells were harvested for study when most viable, that is, one day after the medium had been changed. The number of live cells per unit volume of solution was determined by staining with 36 mg % Erythrosin B and then counting on a hemocytometer. Since only dead cells take up the dye, live cells appear clear in the counting chamber. Respiration, succinate stimulated respiration, and glycolysis determinations based on live cell count were the same for cell strains derived from normal and malignant tissues. (Aided by Nat'l. Cancer Inst. and Nebr. Heart Assoc.)

TEMPERATURE-TENSION RELATIONSHIP OF MAMMALIAN MUSCLE. Julia T. Apter, (intr. by John S. Gray) Dept. of Physiol., Northwestern Univ. Sch. of Med., Chicago, Ill.

The relation between temperature of environment and tension exerted by muscle in vitro has appeared to be capricious. Some laboratories reported that muscle contracted when warmed; others that a reverse relationship replaced or followed this response. The source of this disparity has never been established. It has simply been assumed that muscle varied from one species or body site or state of stretch to another. We found during tests on intraocular smooth muscle that a long transient response preceeded a reversed steady state response to changes in environmental temperature. It seemed likely, therefore, that the discrepancies in previous studies may have resulted from experimenters' overlooking the time

course of the complete muscle response. The present study attempts to explore this possible error by establishing, first, the time course of the response of muscle to a specific temperature change; second, the temperature-tension relationship at the steady state of response. These tests were performed on mammalian smooth and striated muscle at 5 controlled temperatures from 7° to 40° C. The results revealed that there is a transient change in tension followed by a reversal to a new tension which remains constant. If readings are taken at various places on the transient one could get both positive and negative relationships with temperature. If readings are taken only during the steady response, the temperature-tension relationship is reproducible and similar for all muscles tested.

MARROW CELLULARITY IN RABBIT FOLLOWING BILE DUCT OCCLUSION. James W. Archdeacon and Robert S. Davis.* Dept. of Anatomy and Physiol., Univ. of Kentucky, Lexington.

In the present experiments the bile duct of the rabbit was ligated and, after considerable body weight was lost, femur marrow was examined for evidence of modification of nucleated cellular concentration and erthropoietic activity. The latter was measured, using as an index, the concentration of normoblasts and reticulocytes. Supravital staining technique was employed in cellular differentiation. The average number of nucleated cells obtained for each milligram of femur marrow from twenty-two control rabbits was 67.0×10^4 cells. The value for eighteen bile duct ligated rabbits was 41.5×10^4 cells. ($P < .01$). Further analysis revealed that the nucleated cellular concentration of the male rabbits was most affected by the bile duct ligation. Likewise there seemed to be a more pronounced trend toward decrease in numbers of normoblasts and reticulocytes in the marrow of the bile duct ligated male animal, indicating some repression of erythropoietic activity. The average loss in body weight of the entire treated group was 23%. The average length of time that elapsed from ligation of the duct to sacrifice of the animal was 16 days. Usually younger rabbits resisted weight loss to a greater degree than older rabbits. In all cases at the time of sacrifice the appearance of yellow pigment in body tissues generally indicated a severe degree of jaundice. In some instances the appearance of the yellow pigment was manifested in the bone marrow.

DIAPHRAGM FUNCTION AFTER TEMPORARY ACTIVATION OF CROSSED PHRENIC PATHWAY. Eugene Aserinsky (intr. by M. H. F. Friedman). Dept. of Physiol., Jefferson Med. Coll., Philadelphia, Pa.

Respiratory stress is known to stimulate a dormant crossed phrenic pathway, thereby restoring function to a hemidiaphragm which has been paralyzed by high cervical hemisection of the spinal cord. Experiments have been conducted to determine whether the crossed phrenic activity persists after the respiratory stress has been removed. Seven adult dogs were hemisected on the right side at the C1 or C2 level. After a recovery period, ranging from 5 days to 20 weeks, specially designed bipolar pincer electrodes were implanted in the right and left leaves of the disphragm through an

abdominal incision. The electrical activity of the right hemidiaphragm was insignificant in all cases and there was no sign of spontaneous recovery; the left hemidiaphragm of each dog clearly exhibited bursts of potentials more or less coincident with inspiration. Hexylcaine hydrochloride applied to the left phrenic nerve in the neck abolished or markedly reduced the electrical activity of the left hemidiaphragm and at the same time caused reactivation of the previously paralyzed right hemidiaphragm. As judged from the activity of the left hemidiaphragm, the anesthetic was effective for at least 4 hours. Of four dogs that survived the respiratory stress, one animal's right hemidiaphragm returned to the quiescent state within 24 hours after the crossed phrenic pathway was activated. In the three remaining animals, the crossed activity persisted (the right hemidiaphragm was still active) until the animals were sacrificed at one day, six days and twenty days, respectively. Deep nembutal anesthesia tended to suppress the crossed phrenic activity before affecting the direct pathway. (Aided by a grant from The National Foundation.)

RELATIONSHIP BETWEEN RADIUS AND WALL THICKNESS OF HUMAN THORACIC AORTA AT DIFFERENT AGES AND DIFFERENT PRESSURES. Hermann Bader and Ewald Kapal (intr. by C. R. Park). Physiologisches Institut der Universitat, Munich, Germany.

From pressure-volume diagrams a relationship can be calculated between the radius (r) and the wall thickness (D) of the human thoracic aorta using a simple formula. For this calculation the interior volume and the volume of the wall of the aorta must be known. As shown previously, these calculations show that the ratio r/D at all ages is 5 to 6 with 0 pressure. If there is a higher pressure in the aorta, the ratio changes with age. For example, r/D rises at a pressure of 100 mm Hg from a value of 14 in the second decade of the life to a value of about 18 at the beginning of the fourth decade and then falls from this point to a value of 12 in the sixth decade. When these observations are compared with the values of the volume-elasticity and the volume-elasticity-modul obtained from the same aortas, the results show again that the transformation of the aorta from an extensible tube to a nearly rigid tube begins with about 20 years and reaches its end in the sixth decade of life.

RELATIVE ABILITY OF VARIOUS PORTIONS OF RAT SMALL INTESTINE TO ABSORB GLUCOSE AND SORBOSE. R. David Baker and Gordon W. Searle (intr. by J. D. Thomson). Dept. of Physiol., Coll. of Med., State Univ. of Iowa, Iowa City.

Movements of glucose and sorbose across the wall of rat small intestine were studied under in vitro conditions, using cannulated, inverted sacs (Crane, R. K. and Wilson, T. H., J. Appl. Physiol. 12: 145, 1958). The small intestine was divided into eight segments of nearly equal length, each of which was incubated for 1 hour at 37° C in Krebs-Ringer-bicarbonate gassed with 5% CO_2 in O_2. Mucosal solutions initially contained 16.65μ moles/ml of either glucose or sorbose, and the serosal solutions no sugar. Glucose experiments:

Maximum absorption rate from mucosal solution occurred in the mid-jejunum (mean of 88.9μ moles/segment/hour in 6 animals); however, there were no statistically significant differences among any of the upper four segments. In the lower four segments the absorption rate progressively decreased as the intestine was descended. The terminal ileal segment absorbed glucose at a mean rate of 16.2μ moles/hour. Gassing with N_2 significantly inhibited glucose movements in the upper 6 but not in the lower 2 segments. Poisoning with fluoride (48 mM) depressed glucose absorption in all segments, and completely abolished the gradient in absorptive ability along the intestine. Sorbose experiments: Sorbose was absorbed at about the same rate as was glucose under fluoride inhibition. No consistent gradation in absorptive ability along the intestine was seen. (Supported in part by P.H.S. grant no. A-837.)

EFFECT OF CERTAIN CENTRAL NERVOUS SYSTEM DEPRESSANTS ON CEREBRAL ENERGY METABOLISM. William M. Balfour,* Frederick E. Samson and Nancy Dahl.* Physio. Dept., Univ. of Kansas, Lawrence.

There is evidence that disturbance in cerebral energy flow is an important part of anesthesia. By preventing ATP regeneration and observing its disappearance rate, energy utilization may be studied. Rats injected with sodium iodoacetate (to inhibit glycolysis) were placed in nitrogen (anoxia) for various measured periods of time. One group of rats was frozen in liquid nitrogen immediately after the anoxia and the cerebral ATP determined by firefly luminescence. A second group of rats was observed for survival after the periods of anoxia. The effects of ether, paraldehyde and alcohol were studied. The 50% survival times in nitrogen (ST_{50}) were: control, 10.5 sec; alcohol, 11.5 sec; paraldehyde, 17.0 sec; ether, 23.8 sec. The rate of ATP disappearance was similar in the controls and alcohol rats starting at 1.7μ M/g of brain and falling to approximately 1.0μ M/g in 10 sec. The rate was slowest in the ether group falling from 2.2μ M/g at zero time to 1.3μ M/g at 24 sec (ST_{50}). The paraldehyde group was intermediate, falling from 1.8μ M/g to 1.3μ M/g at 17 sec. (ST_{50}). Thus, ether and paraldehyde decrease utilization of cerebral ATP and increase anoxic survival time of the brain; in the dose used, alcohol has no appreciable effect. It is felt that the effects are the result of decreased functional activity of the brain due to anesthetic action. (Aided by PHS Grant B-1151 and PHS Postdoctoral Fellowship.)

CENTRAL SITE OF PYROGENIC ACTION OF BACTERIAL ENDOTOXIN. Philip Bard and James W. Woods.* The Johns Hopkins Med. Sch., Baltimore, Md.

There is evidence that bacterial endotoxins and endogenous pyrogens produce fever by action on some cerebral mechanism. In this study 10 cats without cerebral removal or with unilateral partial removals of forebrain served as controls in 16 experiments on 8 chronic poikilothermic preparations. Each control animal developed a substantial fever in response to intravenous injection of typhoid vaccine. Seven cats tested in 15 experiments carried out from 30

to 349 days (average, 118 days) after truncation of the brain stem at levels between the upper mesencephalon and the rostral third of the pons invariably failed to show any trace of a febrile response. The same negative result was obtained in a cat 50 days after unilateral decerebration and removal of the contralateral hypothalamus. A hypothalamic cat with full ability to maintain normal core temperature in the face of extreme cold (but with impaired regulation against heat) responded normally to endotoxin and to endogenous pyrogen. After endotoxin all cats developed a transient leucopenia and serum taken from them at its height produced fever in normal cats. Thus chronic mesencephalic and pontile animals respond to endotoxin as do normal cats except that they do not develop fever. It seems likely that the ability to respond to endotoxin (or endogenous pyrogen) with fever depends on the functional integrity of the hypothalamic mechanism which enables an animal to regulate against cold.

AGITATED BEHAVIOR OF RATS AND MICE IN ISOLATION CAGES. T. C. Barnes. Hahnemann Med. Coll., Philadelphia, Pa.

Previous reports (Barnes, Pharmacol. Soc., Fall Meeting, 1958; Fed. Proceed. 18:365, 1959) have described the head twitch in white mice and pugnacious attitude of white rats kept alone in metal containers. Animals were deprived of visual but not auditory and olfactory stimuli from their fellows. Rats were tame at start and could be touched lightly with a blunt glass rod without effect, but after a few days or weeks of solitary confinement they bit the rod savagely. Some attacked a stream of water filling a dish, squealed, showed catatonia or rolled over. Reserpine, 1 - 10 mg/kg was given daily to etherized rats by stomach tube and inhibited agitation in most of the animals, but in others pugnacity persisted in spite of total of 100 mg/kg reserpine (when probably catechol amines were depleted). Reserpinized rats perched on water dish as has been described for LSD. Ptosis, hyena-posture, sedation and death resulted. Isolated mice twitched head when occiput was touched and some gave convulsive movements. Besides expected inhibition by tranquilizers and anticonvulsants, acetazoleamide (Diamox), 800 mg/kg oral, stopped twitch in 37%, convulsions in 50% and sedated 33%, but chlorothiazied (Diuril) had no effect. Isolation stress occurs from fish to man (exceptions sheep and goat). Besides sensory deprivation, social isolation is also a factor (rats and mice were taken from a large community).

HISTOCHEMICAL LOCALIZATION OF PROTHROMBIN IN LIVER PARENCHYMAL CELLS USING FLUORESCENT ANTIBODY. Marion I. Barnhart. Dept. of Physiol. and Pharm., Wayne State Univ. Med. Sch., Detroit, Mich.

The cell type responsible for synthesis of any of the plasma proteins has not previously been identified. In this study the fluorescent antibody technique and other immunochemical procedures were used in an attempt to find out the cellular site for synthesis of protheombin. Purified bovine prothrombin was the antigen used in production of antiprothrombin in rabbits. Beef liver provided the responsibe cells. Antiprothrombin was conjugated either with the

orange dye, lissamine rhodamine B 200 or with the green dye, fluorescein isothiocyanate. Protein denaturation was minimal and there was little loss of antibody titer. Such products exhibit considerable stability when refrigerated or frozen. Either of these labeled antiprothrombins precipitated out on beef liver parenchymal cells containing adequate concentrations of prothrombin. Several procedures were used to establish the specificity of the reaction and showed that these antiprothrombins were species specific. Pretreatment of liver sections with serum containing uncoupled antiprothrombin reduced or abolished the specific staining. Removal of the antiprothrombin from a dye-conjugate by addition of purified prothrombin also decreased or eliminated the specific staining capacity. A patchy distribution of strongly fluorescing liver parenchymal cells was seen. This may mean that only a certain type of parenchymal cell produces prothrombin or that there is asynchrony in the liver's production of prothrombin. (Supported by USPHS Grant H 3447, NIH.)

ELECTRICAL AND MECHANICAL RESPONSE OF ARTERIAL SMOOTH MUSCLE TO ELECTRICAL STIMULI, DRUGS AND ALTERATIONS OF EXTERNAL POTASSIUM CONCENTRATIONS. Lloyd Barr (intr. by F. Sargent II), Dept. of Physiol., Univ. of Michigan, Ann Arbor.

In preliminary experiments, using external wick electrodes in oil and a strain gauge to record action potentials and mechanical activity of dog femoral artery preparations, contractions and complex action potentials were recorded in response to DC stimuli. The action potentials consisted of slow waves upon which spike-like variations were superimposed. The maximum amplitude of these action potentials was 5 mV and the duration of the slow waves varied up to one minute. The duration of the "spike" varied upwards from 25 milliseconds. These observations have been confirmed and extended using helically cut strips of dog femoral arteries in a sucrose gap chamber. Depolarizations of 40 mV have been obtained with Krebs-Henseleit solutions in which all the NaCl and KCl was replaced with K_2SO_4. Epinephrine (10^{-7} w/v) caused prolonged partial depolarization, increased spike activity and much greater mechanical response than electrical stimulation. Epinephrine (10^{-7} w/v) increased the tension development and spike activity in response to electrical stimuli. The action potentials recorded with the sucrose gap technique varied in amplitude up to 20 mV. The smaller magnitudes were probably due to the presence of many resting cells.

CARDIODYNAMIC AND ADRENAL MEDULLARY RESPONSE TO ACUTE CORONARY OCCLUSION. N. Bass and V. V. Glaviano (intr. by R. Greenberg). Dept. of Physiol., Univ. of Illinois, Coll. of Med., Chicago.

Mean blood pressure, heart rate, adrenal blood flow and adrenal epinephrine and norepinephrine secretion were determined in dogs before and after ligation of the anterior descending coronary artery at its origin. Fourteen male mongrel dogs were anesthetized with

chloralose and placed on positive pressure respiration. Blood pressure and bipolar standard limb leads were continuously recorded. Samples of adrenal blood were collected from a cannulated adrenal vein and analyzed for epinephrine and norepinephrine content by a modification of the trihydroxyindole method. Within 2 to 5 minutes following coronary ligation, 9 or 14 dogs had a decrease in blood pressure of 28 to 46 percent from control levels. Subsequently this groups of dogs developed ventricular fibrillation. The 5 dogs which did not develop ventricular fibrillation within this period had a blood pressure decrease of 10 to 27 percent. In all experiments there was a decrease in heart rate and in adrenal blood flow in association with the drop in blood pressure. The epinephrine concentrations of adrenal vein plasma increased from 2 to 5 times above the level present during the control period. In general, the adrenal vein samples did not contain norepinephrine in detectable amounts during either the control or the experimental period. The relationship between epinephrine secretion and ventricular fibrillation will be discussed. (Supported in part by a grant from National Institute of Health, USPHS-3696.)

ELECTRIC ACTIVITY AT THE GASTRODUODENAL JUNCTION. Paul Bass*, Charles F. Code and Edward H. Lambert. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Cyclic electric potential complexes occurring in dogs at rates of 18 per minute in the duodenum and 5 per minute in the antrum have been demonstrated by others. Spike potentials related to contractions also occur in the duodenum. This investigation was undertaken to determine the nature of the electric potentials in the pyloric zone. To obtain satisfactory records, the region was exteriorized by mobilizing the pylorus, bringing it and the adjoining duodenum and antrum out of the abdomen in front of the rectus muscles and covering it with skin. Repeated studies were made on six trained unanesthetized dogs after they had recovered completely from the operation. Electric activity detected by needle electrodes in the wall of the gut was recorded on an 8-channel pen writer. The slow potentials (basic electric rhythm) in the duodenum (18 per minute) between pylorus and bile duct were of lower voltage and more variable in polarity than those in the remainder of the duodenum. The pyloric region usually showed little or no electric activity. Occasionally, potentials (0.2 mv, 0.6 sec) occurred in the pyloric region which were temporally related to the slow potentials of the duodenum. At times, 3-second bursts of potentials (0.4 mv, 0.4 sec) occurred and were sometimes associated with similar bursts from the antrum. In the antrum, these bursts, when they occurred, immediately followed the slow potential. No temporal relationship was noted between the slow potentials of the antrum and those of the duodenum. (Supported in part by research grant No. 2015, USPHS.)

GANGLION BLOCKING DRUG ON LETHALITY FOR MICE OF TOURNIQUET TRAUMA. Lyle V. Beck and Virginia R. Alexander.* Dept. of Physiol. and Pharm., Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

Adult Carworth Farms male mice were subjected to tourniquet trauma by occlusion of circulation to both hind legs for 2 hours. At time of removal of ligatures each mouse was injected intraperitoneally, .01 ml/gm. Control mice were injected with water, test mice with ganglion blocking drug, chlorisondamine dimethochloride, 5 mg/kg. Significantly higher percent survivals were noted for test than for control mice (by Chi Square method, P values for differences between test and control groups were .01 or less at 6, 24, 48, 72 and 120 hours after removal of ligatures; no deaths were recorded beyond 72 hours). These data suggest that further animal experimentation may reveal means whereby one or more ganglion blocking drugs would prove useful in increasing the likelihood of survival of humans involved in accidents wherein tourniquet trauma is a major factor. (Supported in part by NIH Grant RG-3740.)

ESTIMATION OF VENTRICULAR VOLUMES FROM CONTINUOUSLY RECORDED INDICATOR-DILUTION CURVES IN THE DOG. Walter Beck,* Kenneth H. McLean* and H. J. C. Swan. Mayo Clinic and Mayo Foundation, Rochester, Minn.

In the closed-chest dog under nembutal anesthesia, densitometer-catheter systems of rapid dynamic characteristics (time to 90% response, 0.2 to 0.5 sec) were used to record the concentration of dye in the aortic root and pulmonary artery after injection of indicator into the left and right ventricles, respectively. End systolic volumes (ESV) and end diastolic volumes (EDV) were calculated according to Holt (Circulation Res., 4:195). The downslope of the curves closely followed an exponential decline in almost all instances. The values for the ratio ESV/EDV were consistent within each animal (SD - 3-9% for four animals with six to 16 observations on each). However, there was a considerable variability between the animals (ratio ESV/EDV, 0.58 to 0.80, stroke volume, 7.8 to 11.9 cc per 10 kg of bod weight for eight animals). From changes in dye concentration at the aortic root during diastole and by sampling simultaneously at two sites 1 to 2 cm. apart at the aortic root, it appeared that dye-blood mixture ejected during each systole is not homogeneously mixed. Further, cineangiography suggested that the blood entering from the left atrium does not mix completely with the ESV, so that the latter contributes a lesser proportion to the subsequent stroke volume than does the former.

ORIGIN OF ACTION POTENTIAL. R. P. Beliles,* G. E. Price* and Reinhard H. Beutner. College of Osteopathic Med. and Surg., Des Moines, Iowa.

Ion movements are the consequence of electric currents in tissues, not their source of origin. Experiments with biphasic batteries have shown that e.m.f. arise in tissues under conditions which were described before. A new attempt to solve the problem was undertaken as follows. Young male white rats were placed on a

diet containing more than 1.2 of all-saturated fat. No unsaturated fat was present. These animals died within 10 days. Death seemed to be due to cardiac arrest, as shown by electro cardio graph. A control group of rats of the same age received a diet including unsaturated fat. All these rats survived. (Supported by research grants of Natl. Heart Inst. P.H.S., Bethesda, Md. and from the Amer. Heart Assoc., New York.)

EFFECT OF VITAMIN-E DEFICIENCY ON MYOGLOBIN CONCENTRATION OF GUINEA PIG SKELETAL MUSCLE. A. D. Bender* D. D. Schottelius*, and B. A. Schottelius. Dept. of Physiol., Coll. of Med., Iowa City, Iowa.

Thirty-five-day old guinea pigs were maintained 21 and 30 days on a vitamin E-deficient diet. Control animals were supplemented with dl-alpha-tocopherol. An additional 21 day experimental group was supplemented with dl-alpha-tocopherol after the 15th day. Gastrocnemius and masseter muscles were examined for myoglobin concentration, component protein nitrogen, muscle solids and muscle weight as per cent of body weight. Although a previous investigation (Am. J. Physiol., in press) revealed a statistically significant increase in myoglobin concentration after 15 days on the deficient diet, in the present study at 21 and 30 days the concentration was significantly decreased. Vitamin E supplementation from the 15th to the 21st day stabilized the myoglobin concentration at control levels. Creatinuria was not evident in any group; while sparce, mild cytological lesions were present only in the gastrocnemii. In 21 and 30 day deficient gastrocnemii there was a decrease in contractile nitrogen, an unchanged sarcoplasmic nitrogen, and an increased collagen nitrogen. These chantes did not occur in the masseter muscles. The results support the conclusion that an alteration of myoglobin metabolism is one of the earliest occurrences in nutritionally induced muscular dystrophy. (Supported by Muscular Dystrophy Assns. of Americ, Inc.)

RENAL EFFECTS OF THAM IN MAN. L. B. Berman,* T. F. O'Connor,* G. G. Nahas and P. C. Luchsinger.* Dept. of Med., Georgetown Univ. Med. Center, (Georgetown Division, D. C. General Hospital) Washington, D.C.

Six essentially normal adults were infused intravenously with 517 - 997 ml of a solution containing tris-hydroxy-methyl-aminomethane (THAM) 300 millimoles/liter, sodium chloride-30 mm/L, and potassium chloride - 5 mM/L. The infusions lasted 30 - 60 minutes. Blood pH and bicarbonate concentration rose as previously reported in dogs. Endogenous creatinine clearance and serum concentrations of sodium and chloride remained unchanged. Serum potassium rose in 3 subjects by 0.2, 0.5, and 0.8 mM/L. Urinary excretion of sodium, potassium, bicarbonate and chloride increased markedly in all subjects. Chloride excretion during THAM significantly exceeded the combined excretion of sodium and potassium in each case. The pH of the urines rose above 7.0 and approximately 10% of the filtered bicarbonate appeared in the urine, thus indicating an increase in both reabsorption and excretion of bicarbonate. In 3 subjects, the

excretion rates for potassium and for chloride were greater than could be explained by the infusion rate plus the control period excretion rate. Urine flow in the control periods ranged from 6 - 13 ml/min and behaved variably during THAM administration. Recovery of THAM from the urine varied inversely with its infusion rate. The changes reported may be best explained by the presence of an increased bicarbonate load and a non-reabsorbable cation in glomerular filtrate.

MEASUREMENT OF EXERCISE TOLERANCE. C. E. Billings, Jr.*, J. F. Tomashefski, Earl T. Carter and W. F. Ashe.* Ohio Tuberculosis Hosp., Columbus.

In an effort to define a simple, precise measure of cardiovascular response to exercise, a test devised by Balke was studied. The test involves walking at constant speed on a treadmill whose slope is periodically increased while pulse rate is measured accurately each minute. Balke had observed physiologic alterations indicative of impending exhaustion (including a respiratory exchange ratio greater than unity and a marked rise in blood lactic acid level), and had noted that these changes occurred at or near the time the pulse rate reached 180 per minute. He used the time at which this rate was attained as an end point. Our studies indicated that a single temporal measurement was perhaps insufficiently sensitive as an estimate of cardiovascular response to the standardized exercise stress. Another method of scoring test runs was derived which took into account pulse rates at all levels of exercise. This measurement, which involves integration of pulse rate with respect to time, was studied in terms of the effective work done (against gravity) during the period of exercise. A strong positive correlation was found between the described measurement and the work done during each of 130 test runs. This correlation was noted over a wide range of work levels in twenty subjects. Additionally, evidence was obtained which suggests that it may not be necessary to carry subjects to an end point near exhaustion in order to estimate their ability to tolerate exercise of the type described.

INHIBITORY EFFECT OF SEROTONIN (5HTP) ON RETENTION OF CARDIAC AND MOTOR CONDITIONAL REFLEXES: SCHIZOKINESIS. Lee Birk,* Louis Conte,* and W. Horsley Gantt. Pavlovian Lab., Johns Hopkins Univ., Baltimore, Md.

5HTP was injected IV in a previously conditioned dog, 30 mg/kg. Each drug trial was preceded by a saline control on the day prior, and followed on the day subsequent by a control to evaluate residual effects. Differentiation between a food reinforced tone 256 and an unreinforced tone 512 was 100% on control days. On drug injection days the motor CR was completely inhibited; the cardiac CR was present though reduced, with differentiation impaired, between tone 256 plus and 512 minus. Conditional inhibition of respiration to tone 256 also was blocked by the drug. 15 mg/kg also produced the same marked effects on CR retention, without the striking somatic effects seen with 30 mg/kg (ataxia, lacrimation, diarrhea, respiratory distress). In summary, the drug 5HTP, in doses as low as 15 mg/kg.,

blocks completely, though transiently, retention of motor, and respiratory CR's. The cardiac excitatory CR was not abolished though diminished; cardiac differentiation was impaired. The difference in effect on cardiac (preserved) and motor components (inhibited) of the CR (schizokinesis), has been seen with other drugs.

AFFERENT INITIATION OF SHIVERING. Clark M. Blatteis (intr. by Steven M. Horvath). U.S. Army Med. Res. Lab., Fort Knox, Ky.

The stimulus for shivering was investigated in thirty lightly nembutalized dogs by surface cooling of the left rear leg amputated at the hip, excepting the bone, the femoral and sciatic-peroneal nerves and the femoral artery and vein. Shivering was monitored fisually and body temperatures were recorded by thermocouples. The onset of shivering, although variable, was evidently not dependent on shivering afferent impulses returning from the cooled limb because nerve section before or during cooling did not affect its occurrence; whereas it appeared to be dependent on the cooled blood entering the general circulation because occluding the femoral vessels abolished shivering. The locus of action of the cooled blood in initiating shivering remained undetermined. There was no apparent relation of the onset of shivering to rectal, esophageal, surface temperatures, core-to-surface temperature gradients and/or total body heat content. Internal carotid temperatures at the beginning of shivering were variable, although generally 1-2° Clower than control. It was noted that contra-lateral surface temperatures on cooling the amputated limb were maintained at control levels longer when the nerves were sectioned than when they were intact; occluding the vessels had no effect on this response.

INFLUENCE OF pH ON VASCULAR RESPONSE. David F. Bohr and Ruth B. McVaugh.* Dept. of Physiol., Med. Sch., Univ. of Michigan, Ann Arbor.

In an investigation of factors affecting vascular resistance in the isolated, perfused rat hind leg, the pH of the perfusing fluid was found to exercise a consistent influence on vascular responsiveness. A modified Krebs-bicarbonate solution was perfused at constant rate through the amputated leg. In each experiment the normal perfusate (pH 7.2-7.4) was alternated in turn with one approximately 0.5 pH unit lower and another 0.5 pH unit higher. The pH of the perfusate was adjusted by altering the proportion of CO_2 in the aeration mixture or by the addition of HCl. Changes in perfusion pressure in response to standard constrictor stimuli (0.2 γ epinephrine or 0.012 mEq KCl, in 0.008 cc, introduced into the perfusate just prior to its entrance into the leg) were recorded by means of a Sanborn pressure transducer. In general, increased H-ion concentration of the perfusate, by whichever means achieved, enhanced the constrictor response whereas decreased H-ion concentration inhibited the constrictor response. The former was true in eleven of twelve preparations studied, the latter in eight of twelve. In no case was the response inhibited by increased H-ion concentration or potentiated by decreased H-ion concentration. These results are at variance with the generally

accepted concept that, within physiologic limits, an increase in H-ion concentration exercises a vasodilator action. (The authors acknowledge with appreciation the support of the Michigan Heart Assoc.)

INFLUENCE OF PARTIAL HEART-LUNG BYPASS ON THE FAILING HEART. Naci Bor,* Peter F. Salisbury, P. Andre Rieben,* and Cecil E. Cross.* Dept. of Med. Res., St. Joseph Hosp., Burbank, Calif., and Dept. of Physiol., Emory Univ., Atlanta, Ga.

Acute heart failure was produced in open chest dogs by creating mitral insufficiency plus shunting blood from the subclavian artery into the left ventricle. During the resulting cardiac dilatation left atrial and left ventricular diastolic pressures rose. A femoral vein to femoral artery heart-lung bypass (pulmopak^{R}) was installed and its effects on the cardiac and systemic arterial pressures were studied. Bypass of 25 ml/kg reduced the heart size and chanber pressures to normal. Perfusion was continued for four hours with beneficial effects. There was an "optimal flow rate" which reduced the elevated chamber pressures. It was different for each dog. Lower or higher flows had less influence or even aggravated the failure. In severe cardiac failure the arterial blood pressure could be maintained at any desired level by a partial heart-lung bypass until the heart regained forceful contractions and could support again the circulation. The chance for defibrillation of a failing heart was greatly improved by heart-lung bypass.

ORIGIN OF SLOW POTENTIAL VARIATIONS IN THE SMALL INTESTINE OF CAT. Alex Bortoff (intr. by C. L. Prosser). Dept. of Physiol., Univ. of Illinois, Urbana.

Monopolar potentials recorded from the isolated intestine of the cat consist of slow rhythmical potential changes and spike potentials super-imposed on the positive phase of the slow wave. It has been suggested by some investigators that the slow waves originate in the myenteric plexus, while others claim that they are myogenic in origin. That the slow waves are not nervous in origin is indicated by their persistence under the following conditions: (1) when 90% of the extracellular sodium has been replaced by choline, (2) some forty hours after the isolated segment has been kept in aerated Tyrode's solution at room temperature, (3) at temperatures lower than that which blocks post-ganglionic excitation. That the slow waves originate in the longitudinal layer is indicated by the fact that they can be recorded from this layer when it is stripped from the rest of the intestinal segment, but are absent in records obtained from circular muscle. The fact that spikes recorded from the longitudinal layer occur in short bursts during the positive aspect of the slow waves, while those recorded from the circular layer may persist over a much longer period of time, supports the view that the slow waves represent alternate periods of refractoriness and excitability. These phenomena are being further investigated by attempting to correlate the monopolar potentials with those obtained intra-cellularly from the longitudinal muscle layer.

MECHANICAL PROPERTIES OF INTACT THENAR MUSCLES OF PATIENTS WITH MUSCULAR DYSTROPHY. Stella Botelho, Sibyl Beckett* and Eleanor Bendler.* Dept. of Physiol. and Pharm., and Physical Med., Univ. of Pennsylvania, Philadelphia.

The characteristics of single twitches of intact thenar muscles induced by supramaximal stimulation of the ulnar nerve in young patients with muscular dystrophy have been reported previously (Physiologist; 1'9, 1957). From passive tension-length diagrams it was found that the stiffness of thenar muscles is less in 7 male dystrophy patients (mean, 89 Gm/cm) ages 6 to 17 years than in normal male subjects (120 Gm/cm) of the same ages. Since Sandow and Brust have reported an increase in stiffness of muscles excised from genetic dystrophic mice (Am. J. Physiol. 194:557-563, 1958), the assumption that the disease process in human muscular dystrophy is identical to that in genetic mouse dystrophy is untenable. Active tension-length diagrams from the 7 male childhood dystrophy patients are flat, thereby differing from those obtained from 7 normal male children (mean, 20 Gm/cm), 4 dystrophic adult male patients (mean, 249 Gm/cm) and 5 normal adult males (mean, 226 Gm/cm). Data will also be presented which indicate that post-tetanic potentiation of twitch tension is less, both in degree and in duration, in the young male dystrophy patients. (Supported by grants from the Muscular Dystrophy Associations of America, Inc. and the National Institute of Neurological Diseases & Blindness, Public Health Service (B-128.)

SOME EFFECTS OF RESERPINE IN RENOPRIVAL HYPERTENSION. Robert L. Bowe (intr. by R. R. Overman). Clinical Physiol. Lab., Univ. of Tennessee Coll. of Med., Memphis.

Bilaterally nephrectomized dogs, maintained by intermittent peritoneal dialysis, were administered reserpine to determine its effects upon renoprival hypertension. Reserpine (0.001 mg/Kg) was administered intra-muscularly once daily after an initial injection of 0.025 mg/Kg. This administration, begun after control values had been determined, was continued without interruption for eight days after unilateral, and five days after bilateral, nephrectomy. Plasma volume, cardiac output, femoral aterial blood pressure, circulation time and peripheral resistance were determined. Results indicate some increase in cardiac output and plasma volume after unilateral hephrectomy, with a return toward control values after bilateral nephrectomy both during and after cessation of reserpine administration. Peripheral resistance decreased during reserpinization after both unilateral and bilateral nephrectomy, but rose again toward control values upon discontinuance of reserpine. Similarly, circulation time was prolonged during tranquilization, but returned toward control values upon withdrawal of the drug. Most significantly, no renoprival hypertension appeared during reserpinization, however, within four days after withdrawal of reserpine, mean blood pressure rose 80 mm. Hg. above control in some of the bilaterally nephrectomized animals. Renoprival hypertension has previously been shown to occur in sympathectomized dogs, indicating humoral agent(s) as a possible cause. Reserpine has been considered a centrally acting drug, yet here it seems to effect what appears to be non-neurally evoked hypertension. (Supported by grant-in-aid USPHS (H-3488).)

RELAXATION OF ATP-INDUCED TENSION OF GLYCEROL-TREATED MUSCLE FIBERS BY POLYPHOSPHATE. W. J. Bowen and K. Laki.* National Institutes of Health, Bethesda, Md.

Several enzymic factors, all of which increase the concentration of ATP, have been found to relax ATP-induced tension of blycerol-treated muscle fibers. Also, several non-enzymic relaxing factors have been found. These include versene, pyrophosphate and triphosphate. We have found that the polyphosphate, sodium "hexametaphosphate", which is more nearly $(NaPO_3)_{14-20}$, causes up to 85% relaxation of ATP-induced tension of glycerol-treated psoas muscle fibers. The full relaxation in high concentrations requires 1.5 to 3 minutes. Concentrations ranging down to 0.001M cause progressively less relaxation but in 0.001M fibers relax 60% if allowed 13 minutes. $MgCl_2$ reduces both the rate and the extent of relaxation, but low concentrations of ATP enhance it. Cyclic tri- and tetra-metaphosphate $Na_3P_3O_9$ and $Na_4P_4O_{12}$ are much less effective than $(NaPO_3)_{14-20}$. Also, sodium pyrophosphate and adenoisine tetraphosphate are less effective than $(NaPO_3)_{14-20}$. Myosin B has been found to split about 1% of the available $(NaPO_3)_{14-20}$ in 30 minutes.

COMPARISON OF SLOW AND UNIT RESPONSES IN CAT CEREBRAL CORTEX. L. L. Boyarsky, G. Santambrogio* and D. T. Frazier.* Dept. of Anatomy and Physiol., Univ. of Kentucky, Lexington.

Unit and slow primary responses to stimulation of the radial nerve have been compared in the sensori-motor cortex using Hubble type electrodes. As frequency of stimulation is increased, the amplitude of the evoked positive potential falls but the size at a given frequency remains constant. The primary may follow the stimulating frequency up to rates as high as 40/sec but slow potentials usually disappear at frequencies below 20/sec. Unit responses, however, are easily recorded at frequencies at which the primary is absent. In a study of about 50 units, the deep unit responses failed only after surface slow waves had disappeared. Above a critical frequency, failure was intermittent. Intermittent responses have been obtained to frequencies of stimulation as high as 200/sec. Since slow responses appear to be postsynaptic responses which depend upon the firing of units within deeper cortical layers. Slow and unit synapses have also been differentiated pharmacologically. Atropine blocks the synapse of the slow response; that of the unit response is unaffected. It is hypothesized that at least two chemically different synapses are present in the sensory system.

REABSORPTION-REPLACEMENT AND LUMINAL VOLUME DISTENTION IN THE STOP-FLOW TECHNIQUE: EFFECT OF REDUCED RENAL BLOOD PRESSURE. John W. Boylan and Dorothy Antkowiak (intr. by H. Rahn). Dept. of Physiol., Univ. of Buffalo Sch. of Med., Buffalo, N.Y.

Inulin was injected at the 3-minute point of a 7-minute stop-flow period and creatinine, with PAH, was injected one minute before release of the clamp. Inulin appears in samples 4-5 ml prior to new filtrate, signalled by creatinine rise. Inulin appearance coincides with or precedes that of PAH and may approach the chloride minimum.

This indicates the position to which inulin has advanced by "reabsorption-replacement." In bilateral stop-flow studies, arterial pressure of one kidney was reduced acutely until urine formation almost ceased; both ureters were then clamped and the above procedure followed. The arterial clamp was released a few seconds prior to collection. From the kidney with "arterial-ureteral stop-flow" inulin appears within one ml of the creatinine rise. Moreover, on this side the volume of urine arriving before new filtrate is only half the corresponding volume on the control side, an indication of the volume-distention of the collecting tree in conventional ureteral stop-flow. The volumes before and after the chloride minimum on each side demonstrate that most of this distention is proximal to the distal segment. These findings bear upon the interpretation of stop-flow data particularly as it relates to proximal tubular function.

CONTINUOUS AND AUTOMATIC RECORDING OF THE OXYGEN CONSUMPTION, RESPIRATORY MOVEMENTS AND SPONTANEOUS ACTIVITY OF SMALL ANIMALS. Pietro O. Bramante (intr. by A. W. Richardson). Dept. of Physiol., St. Louis Univ. Sch. of Med., St. Louis, Mo.

The accurate study of minute and brief changes in the calorigenic response of the experimental animal generally requires cumbersome instrumentation, continuous attendance and observation of the animal in the metabolic chamber, and a series of manipulations and visual readings which, even if closely spaced, do not permit the graphic construction of a smooth curve of metabolic rate. To overcome some of these difficulties, a relatively simple metabolic apparatus of the closed-circuit type has been developed. This instrument, which is based on the principle of the oil demand valve, has already been used in more than 350 metabolic determinations of the albino rat. By means of electronic transduction, amplification and recording, the apparatus permits the continuous and automatic registration of oxygen consumption, respiratory parameters (rate, depth, rhythm) and muscular activity of three animals at one time, under very precise conditions of temperature ($\pm$ 0.05°C), pressure ($\pm$ 1 mm of water) and gas delivery. With the introduction of a plastic oil valve of improved design, together with novel characteristics of the oxygen circuit and of the respiration chamber, the instrumental error, at calibration, is limited to 0.28 - 0.58 per cent. The technique for the quantitation of the oxygen consumption and of the spontaneous activity exhibited by the animal during the entire metabolic determination is described. (Aided by a grant of the St. Louis Heart Association.)

BILE PANCREATITIS: EFFECT ON BLOOD SUGAR. A. B. Bridgwater,* T. Ogawa* and H. Necheles. Dept. of Gastrointestinal Research, Micheal Reese Hosp., Chicago, Ill.

We have reported (The Physiologist, Vol. I, No. 1, 1957), that bile injection into the pancreatic duct of fasted and non-fasted dogs produced a marked increase in blood sugar within 10-20 minutes, with a return to normal in 1-3 hours. In further experiments, cottonseed oil, sesame oil and 1% bile in coconut oil caused this

same effect. Sterile saline produced no change. Bile was injected into other parts of the body: intramuscularly, subcutaneously, intraperitoneally and into the salivary glands, without any remarkable change in blood sugar. Given in saline intravenously, bile caused a decrease in blood sugar, corroborating the finding of others. However, bile, intravenously, did not decrease blood sugar in 2 depancreatized dogs. The cause of blood sugar increase in bile pancretitis has not been identified. Two dogs with bilateral adrenalectomy showed definite increases in blood sugar after bile injection into the pancreatic duct. When this operation was performed on 7 animals previously injected with cobaltous chloride, the average increase was 13 mg % as opposed to 87 mg % for normal non-fasted and 49.5 mg % for normal fasted animals. These results suggest that glucagon rather than adrenaline may play a role. Cross-transfusion experiments are under way to test this theory. (Supported by U.S.P.H.S. Grant.)

NEW EXPLANATION FOR SIMILARITY OF COMPOSITION OF URINARY SOLUTE IN DIABETES INSIPIDUS AND IN HYDROPENIC DIURESIS. W. A. Brodsky. Dept. of Med., Univ. of Louisville Sch. of Med., Louisville, Ky.

Renal papillae, during production of hypotonic urine, are hypertonic to systemic plasma. If the collecting duct is more permeable to water and consequently to urea in the presence than in the absence of vasopressin, then urinary urea per total solute in diabetes insipidus would be greater than that in hydropenic diuresis. This contradicts data on solute loading in normal and in D.I. dogs. The discrepancy can be resolved by application of the law of diffusion. Appropriate steady state assumptions lead to

$$1) \qquad Q = -DA\frac{dc}{dr} + Vc,$$

where Q is the steady rate of movement of solute from lumen to interstitium across any small finite cylindrical element; D is diffusivity; A is area of collecting duct wall; r radius; c, colute concentration at any radial distance r; and V is trans-tubular bulk flow from osmotic drag--a constant. A limiting solution is 2) $Q = VC_{in}$, where C_{in} is average intra-luminal concentration of diffusible solute, say urea. The limit is reached by reduction of pore area or of trans-tubular gradient. Thus, the average composition of urea-containing fluid reabsorbed from collecting duct is the same as that in the lumen. Even if pore size changes greatly, the similarity of C_{in} and C_{out} (for urea) reduces the integrated solution to equation 2 . Then the osmotic force can vary from zero to infinity without changing C_{in} and consequently without changing the composition of collecting duct solute.

CHANGES IN EXCITABILITY AND ELECTRICAL RESPONSE IN AREAS OF HEART MUSCLE MADE ISCHEMIC BY CORONARY ARTERY LIGATION. Chandler McC. Brooks, Jerome L. Gilbert* Gertrude Lange* and Hector M. Mazzella*. Downstate Medical Center, State Univ. of New York, N.Y. City.

Comparison was made with surrounding tissue and with responses of the same area before creation of localized ischemia by ligation of

the anterior descending branch of the left coronary artery. Excitability increased initially in ischemic areas. Thresholds then rose progressively until complete inexcitability was attained 20 to 30 minutes later. In some dogs greater collateral circulation apparently was present and the ischemic area actually showed increased excitability as indicated by reduction in thresholds. Initially monophasic action potentials showed a progressive shortening but after 5 to 10 minutes they also decreased in amplitude. Duration of refractory periods was proportionately reduced. Plateau phase of the action potential and duration of absolute refractory period were most changed. Conduction and response failed as tissue became electrically inexcitable and much variation and alternation occurred as failure ensued. The greatest tendency toward generation of ectopic beats was manifest within 10-15 minutes after ligation. Fibrailation resulted most readily from stimulation within the ischemic area. It is obvious that during the first 5-10 minutes after coronary ligation an anodal current flow is generated by early repolarization of ischemic cells. This has significance with respect to generation of arrhythmias. (Support from Life Insurance Medical Research Fund.) (Dr. Mazzella is Visiting Professor, Facultad de Medicina, Montevideo, Uruguay.)

INFLUENCE OF pH ON THE RESPONSE OF TRACHEAL MUSCLE TO ADRENALIN. E. B. Brown, Jr., and Aryabala Prasad.* Dept. of Physiol., Univ. of Minnesota, Minneapolis.

In recent years considerable evidence has been accumulated to show that the pressor response to sympathomimetic drugs is altered by variations in blood pH. Decrease in pH reduces the response and increase in pH enhances the response. It was the purpose of this investigation to determine whether or not this influence of pH could be demonstrated on the relaxing effect of adrenalin on bronchial or tracheal muscle. A chain was made by tying together rings cut from the trachea of an anesthetized guinea pig. The chain was suspended in a bath of Chenoweth's solution maintained at 38° C and equilibrated with 95% O_2, 5% CO_2. The pH of the bath was altered by changing the CO_2 tension in the gas mixture, keeping bicarbonate concentration constant, or by changing bicarbonate concentration and keeping CO_2 tension constant. Decreasing the pH reduced or inhibited completely the action of adrenalin on tracheal muscle. Increase in pH produced an augmentation of the response. These findings emphasize the importance of blood pH as a factor in treatment of asthma with adrenalin.

EFFECTS OF THAM DURING CO_2 BREATHING IN MAN: VENTILATION AND CO_2 EXCHANGE. E. S. Brown*, T. E. Bennett,* I. L. Bunnell,* J. O. Elam,* J. L. Evers,* D. G. Greene,* C. D. Janney,* H. J. Lowe,* G. G. Nahas and R. Tarail*. Buffalo General Hosp. and Roswell Park Memorial Inst., Buffalo, N.Y.

Carbon dioxide retention was induced in four human volunteers by administration of carbon dioxide in air. While carbon dioxide breathing was continued, tris hydroxymethylaminomethane (THAM) was given intravenously. (cf. Tarail et al., The Physiologist, this

issue). The increase in ventilation induced by carbon dioxide was greatly reduced or abolished during THAM infusion through decrease in tidal volume. In the same period CO_2 output was reduced by 67 to 123cc/min. Twelve to twenty-four percent of this retained CO_2 appeared in the urine during the infusion. Arterial blood pH increased by 0.08 to 0.18 pH units but arterial CO_2 tension showed little change from levels observed before THAM. Alveolar CO_2 tension showed a transitory decrease of 3 mm Hg as THAM was started but immediately returned to previous levels. When CO_2 breathing was continued after THAM was discontinued, ventilation increased once more, but pH remained elevated, and arterial and alveolar CO_2 tension did not change. O_2 uptake remained essentially constant throughout except during two periods of marked hypoventilation with the highest dose when arterial hypoxemia was observed.

LOCALIZATION OF RENAL TUBULAR REABSORPTION OF AMINO ACIDS. J. L. Brown,* A. E. Samiy* and R. F. Pitts. Dept. of Physiol., Cornell Univ. Med. Coll., New York, N.Y.

Utilizing the "stop flow" technique of Malvin, Sullivan, and Wilde, we have studied the reabsorptive patterns of glycine, d, l-alanine, l-alanine, l-arginine and l-lysine. All of these amino acids show maximal reabsorption coincident with or slightly distal to the site of maximal PAH secretion within the proximal tubule. By employing successive "stop flow" studies on the same kidney, we have also shown that l-lysine and l-ornithine inhibit the proximal reabsorption of l-arginine. Studies of other amino acids are in progress.

EFFECT OF RESERPINE ON URINARY TRYPTAMINE EXCRETION IN MAN. Guenter G. W. Brune* and Harold E. Himwich. State Research Hosp., Galesburg, Ill.

Sjoerdsma et al have reported an increased excretion of urinary tryptamine after administration of monoamine oxidase inhibitors to men. Because reserpine is known to deplete the brain contents of serotonin and noradrenaline as well as to increase the urinary excretion of 5-hydroxyindoleacetic acid, we decided to determine the effect of reserpine on the concentration of tryptamine in the urine. Five schizophrenic patients received reserpine, 2 mg b.i.d., and 24 hour urinary collections were made. Tryptamine was determined by the method of Sjoerdsma et al. As a result of reserpine, urinary tryptamine excretion increased significantly in all patients. Furthermore, this increase was also noted when tryptamine was compared with the daily creatinine output. After cessation of reserpine medication, the tryptamine excretion remained high for several days and then decreased slowly toward normal. These results suggest that tryptamine, like the other biogenic amines mentioned above, is no longer bound to its usual sites in the presence of reserpine.

EFFECT OF CHLOROTHIAZIDE, SULFANILAMIDE, AND ACETAZOLEAMIDE ON CARBONIC ANHYDRASE OF CANINE GASTRIC MUCOSA AND RBC. L. S. Buck,* K. C. Kalkof* and W. S. Rehm, Dept. of Physiol. and Chem., Univ. of Louisville, Louisville, Ky.

The above inhibitors were injected intravenously into anesthetized (amobarbital) dogs. Histamine and methacholine were used to stimulate secretion. The chambered gastric segment preparation or a while stomach preparation was used. After the effect on secretory rate was determined (acetazoleamide markedly inhibited secretion and the other two produced little or no change) the stomach was removed, the secretory mucosa was scraped off and frozen. The red cells were frozen after centrifugation (they were not washed). The frozen tissues were homogenized with a Carver press. A modified Philpot method was used. The control Philpot time for both RBC and mucosa was about 4 seconds for a 1-10 dilution and 28 seconds for a 1-100 dilution. In four experiments with sulfanilamide (1.25 gm/kilo), the times with 1-100 dilutions were about the same as for the water on boiled tissue blanks while with the 1-10 dilutions they were all less than 80% of the time for the blanks. The inhibition was about 95%. However, the calculated ratio for the parietal cells of the rate with this inhibitor present to the uncatalyzed rate was greater than 200. Results similar to the above were obtained with chlorothiazide. With acetazoleamide, there appeared to be complete inhibition with a 1-10 dilution. However, the confidence limits were such that the above ratio could be as high as 20. (Supported by grants from NIH and NSF.)

EFFECTS OF CARBACHOL AND ATROPINE ON DISTRIBUTION OF L-ARGININE-U-C^{14} IN THE MOUSE PANCREAS IN VITRO. Harris Busch, Howard Allen, and Dolores C. Anderson. (intr. by K. R. W. Unna) Dept. of Pharm., Univ. of Illinois Coll. of Med. Chicago.

Previous studies from this laboratory (Busch, Davis and Anderson, Cancer Res. 18, 916, 1958) have indicated the remarkably active uptake of labeled amino acids into intracellular proteins of the pancreas. In addition, the radioactivity was rapidly transferred from microsomes to particles of mitochondrial size and thence to zymogen granules. In the present studies, two types of experiments were carried out to provide a basis for differentiation of the biosynthetic and the secretory activities of the pancreas. In the first, whole mouse pancreases were incubated with 500,000 cpm of L-arginine-U-C^{14} for intervals up to 30 min. Carbachol (5×10^{-7} M) was found to stimulate the incorporation of the labeled amino acids into proteins of the microsomes and zymogen granules. In the second type of experiment, mouse pancreases which had been prelabeled by incubation for 30 min. with radioactive arginine were incubated for intervals up to 60 min. in a medium containing no radioactive amino acids. Carbachol was found to markedly enhance secretion of radioactive proteins into the medium and to induce a corresponding decrease in radioactive proteins of the zymogen granules and the cytoplasmic sap. Atropine (1×10^{-5} M) suppressed the above effects of carbachol. These data suggest a feedback mechanism in the pancreas which suppresses formation of proteins in the absence of protein secretion.

EXCRETION OF MONOVALENT AND DIVALENT PHOSPHATE IN DOGS. G. Carrasquer,* W. N. Scott* and W. A. Brodsky. Dept. of Med., Univ. of Louisville Med Sch., Louisville, Ky.

An influence of plasma pH on excretion of phsophate in dogs was found. Two sets of anesthetized dogs were studied. Set (I): Infusion of monovalent phosphate was given, such that urine flow reached constant rates of 10 ml/min/kidney, and plasma levels of creatinine and phosphate were fixed at 2-4 mM/L. Plasma pH was between 7.10 and 7.25. After 40 minutes, instantaneous injections of NaH_2PO_4 and creatinine (500 uM each) was administered into one renal artery. Set (II): Infusion of divalent phosphate was given such that levels of urine flow and of plasma phosphate and creatinine were similar to those achieved in set (I). Unlike results in set (I), levels of plasma pH were between 7.4 and 7.5. After 40 minutes, instantaneous intra-arterial injection of Na_2HPO_4 and creatinine was given. Data indicate reproducible transient secretion of phosphate under conditions of set (I), but not of set (II). Two conditions appear necessary for demonstration of transient phosphate secretion: a) Plasma phosphate level of 2-4 mM/L(Carrasquer and Brodsky, Fed. Proc. 18:89, 1959); b) Acidotic levels of plasma pH. A tentative hypothesis is that phosphate is reabsorbed mainly as divalent ion and secreted as univalent ion. Not excluded is the possibility that H_2PO_4 ion secretion accounts for titratable acid excreted during phosphate loading. (Supported by grants from the U. S. Army and U.S.P.H.S.)

OBSERVATIONS ON THE BREATH TO BREATH VARIABILITY OF PULMONARY DISTRIBUTION FUNCTION. Earl T. Carter, Robert L. Carter,* Joseph F. Tomashefski, and Fred A. Hitchcock. Dept. of Physiol. and Ohio Tuberculosis Hosp., Ohio State Univ., Columbus.

If one assumes that ideal distribution and mixing of inspired air flowing into the alveolar compartment occurs on a given breath, one can derive a theoretical equation expressing the decrement in alveolar nitrogen concentration following a breath of pure oxygen. Such an equation was derived and contains the tidal volume, functional residual capacity, and dead-space as factors. Variability of these factors can thus be corrected for in an analysis of variability of distribution function. A measure of pulmonary "efficiency" would be the ration of the actually observed decrement in alveolar nitrogen fraction, to the decrement predicted on the basis of the ideal pulmonary mixing equation. This ratio was observed in a series of healthy adults employing a nitrogen meter and a pneumotachograph. FRC was determined by the closed circuit helium method. Marked variability in pulmonary mixing efficiency was observed from breath to breath as indicated by observed values ranging from 0.3 to 1.5 for the ratio of the observed alveolar nitrogen dilution to that predicted on the basis of perfect mixing. It was also observed that the mean ratio over a series of breaths was always less than unity. Implications of the results will be discussed.

CEREBELLAR INFLUENCE ON CORTICOSPINAL NEURONS. K. L. Casey and A. L. Towe (intr. by H. D. Patton) Dept. of Physiol. and Biophysics, Univ. of Washington, Seattle.

Anatomical and electrophysiological studies have shown that cerebellar facilitation and inhibition of cortically induced movements might occur via a cerebello-cortical system; such a system would be implicated if cerebellar stimulation altered corticospinal neuronal activity. Accordingly, the amplitudes of pericruciate cortical and medullary pyramidal responses to contralateral forepaw stimulation were studied following cerebellar conditioning stimulation (o.05 msec square pulses delivered at 312/sec in 60 msec trains via bipolar electrodes to culmen and centralis). The corticofugal discharge was augmented for the first 6 msec following the end of the conditioning train, then depressed between 6 to 400 msec, and finally augmented in amplitude between 400 to 1100 msec. The negative phase of the evoked primary response was not systematically altered by cerebellar stimulation; the positive phase was depressed for 650 msec following the conditioning volley. Cerebellar activation of a system facilitatory to corticospinal neurons may increase the number of such neurons excited by subsequent lemnisco-thalamic discharge. This condition prevails only when the population common to cerebellar and lemniscal input is not blocked by the preceding cerebellar discharge. Whether this blocking is inhibitory or occlusive at a subcortical level cannot be specified from this work. (Supported by Grant B-396 from the National Institute of Neurological Diseases and Blindness.)

IS THE OXYGEN CONSUMPTION OF NEWBORN MAMMALS DEPENDENT ON AMBIENT OXYGEN CONCENTRATION? S. Cassin and A. B. Otis. Dept. of Physiol., Coll. of Med., Univ. of Florida, Gainesville.

Suggestions appearing in the literature indicate that oxygen consumption in the newborn mammal may be supply dependent. An adaptation of this nature would be of considerable value to the fetus and newborn when faced with an acute decrease in environmental oxygen concentration. In an attempt to investigate further the possibility of supply dependency in mice and dogs we subjected the newborn of these species to reduced environmental oxygen concentrations at ambient temperatures of 35° C and 30° C, respectively, and measured their oxygen consumption. With a reduction in the ambient oxygen concentration from 21% to 10% and 5% we found no significant difference in the oxygen uptakes of newborn mice (2.14 ml/Kg/hr in 21% oxygen and 1.92 ml/Kg/hr at 10% and 5%, respectively). In the case of newborn pups, oxygen consumption decreased by sone 47% when they were transferred from room air to 10% oxygen (1.38 L/Kg/hr in 21% to 0.73 L/Kg/hr in 10% oxygen). The above data indicate that supply dependency for oxygen does not exist in the newborn moust at an ambient temperature of 35° C. The newborn hypoxic pup does show this phenomenon at an ambient temperature of 30° C.

SENSITIVITY OF DIFFERENT GANGLIA TO GANGLIONIC BLOCKADE. G. R. Chandrasekhar,* Lester Soyka* and Laszlo Gyermek. Dept. of Pharm., Univ. of Illinois Coll. of Med., Chicago.

For the simultaneous investigation of ganglionic blocking drugs on parasympathetic and sympathetic ganglia, the pelvic nerve-bladder and cervical sympathetic-nictitating membrane preparation of the dog were used. The action of the same drugs was also tested by the mouse pupil method, measuring blockade of the ciliary ganglion. Six different ganglionic blocking agents: hexamethonium, pentolinium, trimethaphane, chlorisondamine, 1,1-diethyl, 2,6-dimethyl piperidinium and mecamylamine were compared with a standard (tetraethylammonium bromide). Both sympathetic and parasympathetic ganglia were blocked to about the same extent by any of the compounds. Relative potencies of the compounds obtained on the mouse pupil test did not parallel their potencies in depressing transmission at the pelvic and superior cervical ganglia of the dog. Longer acting ganglionic blocking agents (pentolinium, chlorisondamine, mecamylamine) were found much more potent in the mouse pupil test than on the dog.

SYNCHRONIZED AND UNSYNCHRONIZED REFLEX DISCHARGE IN INTACT FROG SPINAL CORD. Y. C. Chang (intr. by D. M. Easton). Div. of Physiol., Dept. of Biological Sciences, Florida State Univ. Tallahassee.

Synchronized spinal reflex discharge (5-10 msec latency and about 5 msec duration) was recorded from ventral root of intact, unanaesthetized bullfrog (Rana catesbeiana) during stimulation of the dorsal root of the same or adjacent segment. An unsynchronized discharge, lower in amplitude and lasting about 35 msec, follows the synchronized discharge. The amplitude of synchronized discharge increases with intensity of single 0.1 msec stimuli to reach a maximum that is maintained relatively constant. Maximum response to a particular intensity was not obtained unless 3-6 min was allowed to elapse between shocks. Pairs of maximal stimuli were applied to a dorsal root and the discharge was recorded on the corresponding ventral root. At intervals of 0.5-5 msec, the discharge due to the conditioning volley was enhanced. Separation of the response to the conditioning and testing volley began at C-T intervals of 1-2 msec. At longer intervals, the discharge evoked by the conditioning volley dropped to the control level. The discharge evoked by the testing volley was decreased considerably below the control level, but gradually reappeared to return to the maximum by 3-6 min. The synchronized discharge failed to appear if the cord was slightly injured, in which instance a synaptic potential and an unsynchronized discharge was recorded. (Supported by NIH Research grant B927(C3).)

EXPERIMENTAL STUDIES ON A NEW METHOD OF ANALYSIS OF INDICATOR-DILUTION CURVES. Richard J. Cheesman,* Jose M. Gonzales-Fernandez* and Earl H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Experiments were carried out in an attempt to assess the validity of an integral-equation method for the analysis of indicator-dilution

curves. Injections of indocyanine dye were made into the pulmonary artery and into the aortic root of dogs, dye curves being recorded simultaneously from the femoral artery via a Y-shaped cannula, by two systems having widely different dynamic responses. Following each experiment, the dynamic response of the sampling-detecting-recording systems used was studied. As expected, the amplitude, time components and general contour of the simultaneous curves thus obtained differed markedly. When analyzed by the integral-equation method, recovery of similar "input" curves in every case was possible; this supports the validity of this method. Among other parameters, the mean transit times of the "input" curves thus recovered were nearly identical with each other, but markedly different from those of the recorded curves. A formula was derived for the computation of this "true" mean transit time, which consists of subtracting the "mean transit time" of the sampling-recording system from that of the recorded curve. The values obtained by this independent method correlate satisfactorily with those obtained by direct measurements from the recovered curves. This method may allow measurement of "true" transit times in the central circulation of intact animals or human beings.

GLUCOSE-U-C^{14} INCORPORATION INTO LIPIDS BY ANOXIC RAT LIVER SLICES. Richard Chenoweth,* Norman R. Alpert and Richard J. Winzler.* Dept. of Physiol. and Biochem., Univ. of Illinois, Coll. of Med., Chicago.

Incorporation of activity from glucose-u-C^{14} into lipids and CO_2 by rat liver slices was determined. Tissues incubated in nitrogen were compared with control tissues respiring in room air. The C^{14} incorporation into CO_2 was three times higher in the control than in the anoxic tissues. However, the lipids showed the same incorporation in anoxic as in control tissues. In a preliminary study, anoxia produced a ten-fold decrease in the ATP level. These experiments indicate that fat synthesis proceeds even under anoxic conditions when ATP levels are low. Assuming that the Krebs cycle is inoperative during anoxia, it is postulated that the glycolytic and hexose monophosphate shunt pathways furnish enough TPNH and DPHH to permit a high rate of fat synthesis. (Supported by Grant H2345 USPHS.)

STARVATION ULCER IN THE MOUSE. Th. Chiles,* T. Ogawa* and H. Necheles. Dept. of Gastrointestinal Research, Med. Res. Inst. of Michael Reese Hosp., Chicago, Ill.

In the Shay rat, nearly all ulcers occur in the prostomach, and recently it was reported that in the starving rat ulcers also form in the prostomach. We are reporting here our opposite experience in the starving mouse in which all ulcers occurred in the glandular stomach. These results are different from previously reported work on the pylorus ligated mouse, in which practically all ulcers were found in the prostomach. At that time we attributed the formation of these ulcers to distension and impaired circulation of the stomach. The cause of ulceration in the glandular stomach in the starved mouse remains to be investigated. On the basis of present concepts,

it may be due to acid-pepsin; however, acid values were not particularly high. In the starving mouse, a decided sex difference was found, with a smaller percentage of ulcers in the female than in the male animal. Effects of pregnancy on ulcer formation will be discussed.

ANALYSIS OF DROMIC AND ANTIDROMIC RESPONSES TO DIRECT STIMULATION OF THE CORPUS CALLOSUM IN THE CAT. M. H. Clare, W. M. Landau and G. H. Bishop. Div. of Neurology, Washington Univ. Sch. of Med., St. Louis, Mo.

The cortical response to direct stimulation of the corpus callosum consists of a brief surface-positive spike which originates deep in the cortex, followed by a slower positive-negative wave sequence which derives from structures extending to varying depths of cortex. The spike is assigned to dromic and antidromic axonal and possibly cell body discharge. The wave sequence is assumed to represent predominantly a response propogated upward along apical dendrites. The excitability cycle, strychnine spike driving, and post-tetanic potentiation phenomena are described, and the direct callosal response is compared with that elicited by homatotopic cortical stimulation. The antidromic calloresponse is described in preparations in which dromic fibers had previously been allowed to degenerate. The response is remarkably similar to the normal mixed dromic and antidromic response, and it is concluded that the latter is mediated synaptically via retrograde axonal collaterals. The interpretation of potential reversal in the cortical volume conductor is considered in relation to the probable anatomical substrate of the callosal response.

ELEVATED PANTING LEVELS IN CATS WITH CHRONIC LESIONS IN HEAT SENSITIVE AREA OF ANTERIOR HYPOTHALAMUS. George Clark. Dept. of Physiol., Univ. of Buffalo, Buffalo, N.Y.

The current concept of the results of ablation of the heat sensitive area in the anterior hypothalamus of cats is erroneous. The enoromous deficiency in regulation against heat persists for 1 - 3 months but ultimately considerable recovery occurs and an elevated panting is the only permanent result. This second stage persists at least six months and is presumably permanent. These findings are consistent with the discordant results in the literature which have not been incorporated into current theory. (Supported by Air Research and Development Command, Contract 33(616)5675.)

STUDIES OF PULMONARY FUNCTION IN PARKINSONIAN PATIENTS. John J. Connolly, Jr.,* Harold C. Neu,* Fred W. Schwertley,* Harold A. Ladwig* and Alfred W. Brody. Regional Rehabilitation Center, Creighton Mem. St. Joseph's Hosp., and Chair Cardiovascular Research, Creighton Univ. Med. Sch., Omaha, Nebr.

In a continuation of studies of the effects of various types of neuromuscular disorders on pulmonary function, 23 patients with Parkinson's disease of varying severity were evaluated clinically, including assessment of rigidity, tremor, daily activities; physio-

logically by 20 tests of pulmonary function. Six types of tests were included: (1) lung volumes, capacities; (2) rate, tidal volume, minute ventilation; (3) measurements of maximal ventilation and maximal respiratory pressures; (4) total respiratory resistance and elastance; (5) tests of gas distribution; (6) oxygen saturation (oximetry), end-alveolar P_{CO2}. Extensive decrease in respiratory efficiency, usually only to an extent that reduced reserve, correlated in some tests with impairment of activity. Severity of rigidity and tremor correlated with activity limitation, and with these impairments of respiratory function. Adequate ventilation at rest was shown by normal arterial O_2 saturation and en-tidal P_{CO2}. Mild defects in gas distribution were scattered throughout the group, without correlation to other abnormalities. The complaint of breathlessness was elicited in only a few patients, and without correlation to disability. (Supported in part by Research Grant #H-1951CS, Nat. Ht. Inst., U.S.P.H.S., and by the National Foundation.)

BRAIN CONCENTRATIONS OF BIOGENIC AMINES AND EEG PATTERNS OF RABBIT: INTRACAROTID INJECTIONS OF BIOLOGICAL PRECURSORS. E. Costa,* G. R. Pscheidt,* W. G. Van Meter* and H. E. Himwich. State Research Hosp., Galesburg, Ill.

Serotonin and catecholamine brain concentrations were analyzed in rabbits given 5 Hydroxytryptophan (5HTP) and dihydroxyphenylalanine (DOPA). The following findings will be discussed: 1) Because the vascular distribution of the intracarotidly injected 5 HTP (44 mg) in the brain is not constant the rise of serotonin in the brain structures analyzed was not uniform. However, in 5 out of 8 experiments the increase of brain serotonin was greater in mesencephalon-diencephalon than in telencephalon or hippocampus. The EEG of these 5 animals was characterized by a progressive persistence of a desynchronized alert pattern after an initial enhancement of synchronized activity. In the remaining rabbits with smaller increases in mesencephalon-diencephalon the alert pattern was not enduring. Four other rabbits given 22 mg of 5 HTP evinced neither a conspicuous serotonin increase in mesencephalon-diencephalon nor an enduring desynchronized EEG record. 2) 44 mg of 5 methyltryptophan failed to change the EEG or brain serotonin content. 3) 44 mg of DOPA did not alter appreciably the EEG patterns nor the brain catecholamine contents of normal rabbits.

TIME COURSES OF RESPONSES TO EPINEPHRINE IN FROG AND CAT LIVERS. Albert B. Craig, Jr., and Carl R. Honig.* Dept. of Physiol., Univ. of Rochester Sch. of Med. and Dent., Rochester, N.Y.

This study describes the courses of metabolic and circulatory responses to epinephrine in the liver. The time for attainment of a significant epinephrine concentration in an isolated perfused frog liver was determined with Na^{22} labeled perfusate. Hepatic tissue oxygen tension was measured continuously with bare platinum microcathodes. Within the limits of measurement error, appearance of epinephrine in the liver coincided with a profound fall in pO_2 and the

onset of the potassium loss. Increased glucose production began 2 - 3 minutes later. Hepatic vein catheterization in cats afforded an opportunity to examine these relationships in vivo. Changes in oxygen utilization, if any, were obscured by hemodynamic factors affecting oxygen delivery so that pO_2 initially increased, decreased, or remained unchanged. Nevertheless, in every case potassium loss began simultaneously with the arrival of epinephrine at the liver. Maximum potassium concentration in the hepatic vein was noted one minute from the end of either a short or prolonged intravenous epinephrine administration. Glucose loss did not begin for about one minute and increased while the potassium concentration was decreasing. We conclude that metabolic responses may occur as rapidly as vascular ones. The onset of hyperkalemia and the change in liver oxygen tension occur simultaneously; hyperglycemia begins somewhat later. In intact cats the metabolic responses vary independently of oxygen tension in the liver.

EFFECT OF SINGLE ATRIAL EXTRASYSTOLES ON TRANSMEMBRANE POTENTIALS OF THE ATRIOVENTRICULAR NODE. Paul F. Cranefield and Brian F. Hoffman. Dept. of Physiol., State Univ. of New York, Downstate Med. Center, Brooklyn.

Action potentials recorded from single fibers of the atrioventricular node typically show rather low amplitude and a slow rate of depolarization. Increase of atrial rate or the addition of acetylcholine enhance the degree of slowness of depolarization and often produce notching and slurring of the upstroke. If the atrium is driven at a slow constant rate and single extrasystoles are interpolated at various intervals the nodal action potentials show an unexpected change. The nodal action potential corresponding to a single induced extrasystole often shows a more rapid upstroke and a higher amplitude than does that corresponding to the driven beat. One implication of this observation seems to be that the nodal fibers do not have an unusually high time constant and therefore do not have a high membrane resistance and capacity. It further seems probable that the inactivation which results from the spontaneous depolarization characteristic of nodal fibers is an important factor in producing the slow upstroke and, presumably, the slow conduction velocity. (Supported in part by a grant from the National Heart Institute (USPH Grant 3916).)

EFFECT OF IONIC ENVIRONMENT ON THE ACTIVE INTESTINAL SUGAR TRANSPORT. T. Z. Csaky. Dept. of Pharm., Univ. of North Carolina Sch. of Med., Chapel Hill.

Active sugar transport from the small intestine of the toad has been studied in vitro. A quantitative measure of this transport can be made by using the non-metabolized 3-0-Methylglucose. Active sugar-transport is completely abolished if Na is replaced by Li, Mg, or choline in the Ringer Solution bathing the mucosal surface. The inhibition is reversible by restoring the original Na concentration. Replacement of Na on the serosal side has no effect on the active sugar transport. In anesthetized rats the jejunum in situ was perfused through the lumen with a 500 mgm/liter glucose solution made

isotonic with either Na_2SO_4 or Li_2SO_4. From the perfusate rapid sugar absorption was observed in Na_2SO_4 solution but none in the Li_2SO_4. (Supported by a grant from the PHS.)

EFFECTS OF MICROWAVE IRRADIATION IN DOGS. Roger W. Dahlen,* Gordon W. Searle* and C. J. Imig. Dept. of Physiol., Coll. of Med., State Univ. of Iowa, Iowa City.

The head or abdominal regions of anesthetized dogs were subjected to irradiation with 2450 megacycle, continuous wave electromagnetic energy at field power densities of 0.3 to 0.5 watt/cm^2. Temperature changes at various sites were followed with copper-constantin thermocouples. Clinical chemical tests for liver or brain damage were carried out in vivo. Gross and microscopic examinations of tissue in the path of irradiation were made post mortem. Temperature elevations within the gall bladder, stomach, intestine and cisterna magna were less than expected from prior studies in rabbits and were noted to be inversely related to animal weight. Bromsulfalein retention tests in the abdominal irradiation series and cerebrospinal fluid transaminase tests in the head irradiation series were negative. While damage of a thermal type has been noted in the superficial tissues of the regions irradiated, no histological alteration has been seen in deeper-lying organs with the patterns of irradiation used. (Supported in part by U.S. Air Force Contract No. AF41-(657)113.)

CHANGES IN GASTRIC MUCOSAL REACTION ASSOCIATED WITH ALTITUDE AND DISTENTION. Ivan E. Danhof (intr. by Robert W. Lackey). Dept. of Physiol., Univ. of Illinois, Urbana, and Univ. of Texas Southwestern Med. Sch., Dallas.

Changes in gastric mucosal pH measured by an indwelling glass electrode were determined two hours post-prandially in humans with mild respiratory alkalosis associated with chamber ascents to simulated altitudes of 15,000 feet. Reactions were measured prior to ascent, at 15,000 feet with and without oxygen inhalation and with and without gastric distention by oxygen or nitrogen introduced by a Rehfuss tube. Changes in urinary reaction before and immediately following recompression were determined. Definite increases in mucosal pH from the control values occurred with ascent to altitude with the subject breathing air while the values decreased toward control levels with gaseous distention of the stomach. The mild systemic alkalosis was corroborated by increases from the control values in urinary pH following recompression. Oxygen inhalation upon ascent to altitude diminished the respiratory alkalosis, the alkaline unrinary shift, but not the gastric acid secretion with gastric distention. Experiments in lightly anesthetized dogs in which the altitude conditions were simulated by gas mixture inhalation gave essentially similar results. In the animal experiments the blood pH and P_{CO2} were also determined. It is concluded that gastric acid formation can be induced by gaseous distention of the stomach in spite of a prevailing mild respiratory alkalosis and is not dependent upon the P_{CO2} level for formation.

ARTERIAL BLOOD PRESSURE IN THE DOG HIND LIMB. D. L. Davis* and W. F. Hamilton. Dept. of Physiol., Med. Coll. of Georgia, Augusta.

Pulse pressures and pulse wave velocities of the major arteries of the dog hind leg were studied by recording simultaneously from four sites in the hind leg. Blood pressures were recorded from: the arch of the aorta; the femoral artery in the groin; the femoral artery at the knee level; the dorsalis pedis artery at the ankle level; and the digital artery in the toe. All pressures were recorded with optical membrane manometers adequate in frequency to record true pulse contours. A progressive decrease in diastolic pressure occurred at successively more peripheral levels. This decrease was most abrupt at the digital level. Peak pressures progressively increased to the knee level, and then progressively decreased to the digital level. The pulse pressures at the groin, knee, ankle, and digital levels were higher than that at the aortic arch. Simultaneous pressure peaks occurred at the groin and knee levels. At more distal levels the peak pressures were delayed progressively. Stimulation of the sciatic nerve produced an initial increase in mean and pulse pressures in the digital tracing with increased transmission velocity from the ankle to digital level. Continued stimulation decreased the ankle and digital mean and pulse pressures with a concomitant decrease in transmission velocity. Preliminary experiments indicate that at higher than normal arterial pressures, the area of simultaneity in peak pressures is extended to the ankle level.

ROLE OF ANTERIOR PITUITARY IN CONTROL OF ALDOSTERONE SECRETION IN EXPERIMENTAL SECONDARY HYPERALDOSTERONISM. James O. Davis, Nicholas A. Yankopoulos,* John Holman* and Robert C. Bahn. National Heart Institute, Bethesda, Md. and Mayo Clinic, Rochester, Minn.

The effect of removal of the anterior pituitary on aldosterone secretion in dogs with hyperaldosteronism secondary to caval constriction was reported previously (The Physiologist 1:15, 1958); a 76-97% fall in adrenal vein aldosterone output occurred within 2 hours following hypophysectomy. In the present study, ACTH was administered following hypophysectomy of 2 dogs with caval constriction and aldosterone secretion remained at the high control level. To inhibit secretion of ACTH, large doses of cortisone were administered to 6 dogs with experimental ascites. Aldosterone and corticosterone production was significantly lower than in dogs with chronic ascites without cortisone therapy and in one of the 6 animals aldosterone output was depressed to normal. Subsequent hypophysectomy of 5 of these 6 dogs resulted in a further decline in aldosterone and corticosterone output. Attempts to produce hypersecretion of aldosterone in simple hypophysectomized dogs failed: 1) adrenal vein aldosterone output was significantly lower than normal in 10 simple hypophysectomized dogs during maintenance on a low Na diet; 2) in 2 simple hypophysectomized dogs, acute thoracic caval constriction failed to produce an increase in adrenal vein aldosterone output. In a previous study, this stimulus produced hypersecretion of aldosterone consistently in normal dogs. It is

concluded that the anterior pituitary plays an important role in the increased production of aldosterone in experimental secondary hyperaldosteronism.

ABDOMINAL COMPRESSION REACTION AFTER BILATERAL VAGOTOMY AND CAROTID SINUS DENERVATION. L. D. Davis,* J. K. Turner,* and W. B. Youmans. Dept. of Physiol., Univ. of Wisconsin, Madison.

The abdominal compression reaction (ACR) has been described as a phenomenon which occurs in dogs under conditions which tend to cause inadequate venous return (Physiologist, 1 (No. 4) : 27, 195, Amer. J. Physiol. 196 : 1160, 1959, and Fed. Proc. 18 ; 161, 1959). The methods which were used to cause a decrease in venous return (vasodilatation or hemorrhage) also cause a fall in systemic arterial blood pressure. Therefore, it is necessary to know whether the ACR, like the respiratory stimulation elicited during a sudden fall in blood pressure, is dependent upon sinoaortic pressoreceptors. In experiments on eight dogs anesthetized with sodium pentobarbital (30 mgm/kg) it was found that bilateral vagotomy does not prevent the appearance of the ACR in response to hemorrhage or the injection of nitroglycerin. When, in addition to vagotomy, the carotid sinuses were isolated by means of ligatures and excised the ACR still could be elicited and there was no apparent difference from the reaction as observed in the animals before vagotomy. It may be concluded that the ACR is not dependent upon afferent pathways in the vagus nerves or from sinoaortic pressoreceptors. This lends further support to the hypothesis that the ACR is elicited by a fall in pressure somewhere in the "low pressure" portions of the cardiovascular system (systemic veins, atria or pulmonary circuit).

SHIVERING IN MAN. T. R. A. Davis (intr. by J. R. Blair). U.S. Army Med. Res. Lab., Fort Knox, Ky.

A total of 10 nude subjects were studied. Time of onset of shivering in 14°C air occurred between 3 and 55 minutes of exposure. Skin temperature at time of onset varied from 27.2 to 33.0°C. Rectal temperature at time of onset varied from 37.0 to 37.5°C. Shivering occurred in a cyclical manner with periodicities of 15 to 45 minutes. The correlation between the development of shivering and rectal temperature was -0.005; between shivering and skin temperature it was -0.80. Upon immersion in seawater at 11°C it was found that a significant hyperthermia existed during immersion accompanied by shivering. In the post-immersion period a significant hypothermia existed without demonstrable shivering. The inhibition of shivering by psychical and physical means is demonstrated. Both types of inhibition were of short duration and failed to affect the course of the development of shivering in that the periods of inhibition were soon followed by compensatory increased shivering activity. From these results it may be concluded that (1) Shivering is a highly variable mechanism. (2) It maintains itself in a cyclical manner. (3) Within physiological limits it appears to be dependent upon the difference between the temperature of cold receptors on the skin and central temperature. (4) The regulation of the cyclical character of shivering is not readily discernible in this study.

DETERMINATION OF FORM OF AMPHIBIAN RED BLOOD CELL. John Davison (intr. by H. J. Lipner). Div. of Zoology, Florida State Univ., Tallahassee.

Observations prompted by a mercury drop model of the elliptical red cell (Davison, Exp. 13, 472, 1957) have disclosed the following: the eccentricity of the red cell (a/b, the ratio of the major to minor axes) is dependent on the ratio of the cell area to the average cross-sectional area of tail fin capillaries. Red cells with an eccentricity greater than 1.3 slide through the capillary with one elliptical surface applied to the capillary wall, and with their form determined in accordance with the equation: $(a/b)-1 = K(A_{cell}/A_{cap})$. As red cell area approaches that of the capillary, eccentricity rapidly approaches 1(circular form). Increase in capillary area leads to a rapid decrease in red cell eccentricity supporting the view that red cell form is plastic. Circular red cells and large peripheral capillaries are associated with rapid growth in R. pipiens larvae. During fasting, capillary diameter rapidly decreases and the red cells become elliptical. In a wide variety of amphibians differing widely in red cell size and capillary size, a plot of a/b versus the ratio of cell to capillary area results in a linear relationship as expected from the above equation.

DEPENDENCE OF THE LIPOLYTIC ACTION OF EPINEPHRINE IN VITRO UPON THYROID HORMONE. Albert F. Debons* and Irving L. Schwartz. Medical Res. Center, Brookhaven National Lab., Upton, N.Y.

Epididymal fat pads were removed from normal rats and rats that had been rendered hypothyroid (propylthiouracil, 0.05% in drinking water) and hyperthyroid (triiodothyronine, 0.2μ gm/100 gm body weight subcutaneously daily). The tissues were shaken at 37°C under 95% O_2-5% CO_2 in a Krebs-Ringer bicarbonate buffer (pH 7.4) containing bovine albumin (5%). The release of non-esterified fatty acids (NEFA) from untreated tissues and tissues challenged with l-epinephrine (10μ gm/flask) was measured. The normal response to epinephrine of the epididymal adipose tissue was observed in the euthyroid animals, confirming observations previously reported by others. In the hypothyroid animals, no release of NEFA from the fat pad was observed after epinephrine; in the hyperthyroid animals, the epinephrine-induced release of NEFA was markedly exaggerated. This thyroidal enhancement of epinephrine action on the fat pad was not evident when tissues were removed from euthyroid animals 3 hours after injection of triiodothyronine (50μ gm intraperitoneally) but was maximal in tissues removed from animals that had received four doses of triiodothyronine (50μ gm intraperitoneally) at 3 hour intervals. When triiodothyronine was added in vitro to fat pads from euthyroid rats, the basal release of NEFA was not affected nor was the normal response to epinephrine altered. These studies show that the thyroid hormone is essential for the epinephrine-induced re-

lease of NEFA from adipose tissue. (Supported by the U.S. Atomic Energy Commission.)

POTASSIUM IONS AND ELECTRICAL ACTIVITY OF THE HEART. Walmor Carlos de Mello* and Brian F. Hoffman. Dept. of Physiol., State Univ. of New York, Downstate Med. Center, Brooklyn.

The effect of K^+ on electrical activity of single fibers of rabbit heart has been studied with intracellular microelectrodes. Fibers of the atrioventricular node, atrioventricular ring, sinoatrial node and pacemaker fibers in the crista terminalis are less sensitive to the depolarizing action of K^+ than atrial or ventricular muscle. Depolarization by K^+ is most marked in atrial fibers, less marked in sinoatrial fibers and fibers of the crista terminalis and least in fibers of the atrioventricular node. Spontaneous activity was maintained in fibers of the crista terminalis after 4 hours in Tyrode solution containing 8 times the normal K concentration (21.6 mEq/l) and in atrioventricular nodal fibers after 4 hours in a solution containing 15 times the normal K^+ concentration (40.5 mEq/l). Depolarization caused by excess K^+ was increased in solutions containing 1/2 Ca^{++}; sinoatrial fibers lost spontaneous activity after 30-40 minutes in a low Ca^{++} solution containing 21.6 mEq K^+/l; atrioventricular nodal fiber, however, maintained spontaneous activity for several hours under these conditions. Observed values of resting potential at several extracellular K^+ concentrations have been compared to the potassium equilibrium potential calculated from flame photometric determinations of fiber K^+ and measurements of the inulin space. (Supported in part by a grant from the New York Heart Association).

EARLY EFFECTS OF INSULIN AND TOLBUTAMIDE ON NEOGLUCOGENESIS FROM C^{14}-LABELED LACTATE IN DIABETICS. Roger C. De Meutter and Walton W. Shreeve (intr. by Irving L. Schwartz). Med. Res. Center, Brookhaven National Lab., Upton, N.Y.

Studies were performed in two groups of volunteers: unstable, tolbutamide non-responsive diabetics, and stable, tolbutamide responsive patients. The labeled precursor was given as a single fast intravenous injection (60 to 100 microcuries of 2-C^{14} DL lactate or 3-C^{14} DL lactate). Blood samples were collected at short intervals over a two-hour period. Blood glucose specific activity was determined by isolation of its osazone without addition of carrier glucose. The same patients were studied repeatedly at intervals of 6 to 8 weeks with the same radioactive compound. In the control studies, a rapid and extensive conversion of the lactate C^{14} to glucose was observed. When glucagon-free insulin or sodium tolbutamide (0.1 unit and 40 mg per kilogram of body weight, respectively) were injected intravenously 5 and 15 min prior to the lactate injection, the specific activity as well as the total amount of C^{14} found in glucose was consistently decreased. These experiments demonstrate that in diabetic humans, neoglucogenesis from lactic acid is an active metabolic process. During the period of action of insulin and tolbutamide,

no complete halt of production or outflow of the newly formed glucose occurs. The decreased conversion observed after insulin and tolbutamide injection, however, is suggestive of some early effect on the production or release of glucose by the liver. (Supported by the U. S. Atomic Energy Commission.)

DISTRIBUTION OF CARBONIC ANHYDRASE IN THE GASTRO-INTESTINAL TRACT OF DOGS. Jeanne N. Dial* and F. R. Steggerda. Dept. of Physiol., Univ. of Illinois, Urbana.

The gastro-intestinal tract of the dog was regionally subjected to quantitative chemical analysis for carbonic anhydrase content. A modified method of Philpot and Philpot was employed. The results indicate that carbonic anhydrase concentration on the wet weight basis is significantly different in different areas of the gastro-intestinal tract. The enzyme concentration in the cardiac stomach mucosa was found to be the highest, and the combined mocosal and submucosal layers of the esophagus the lowest. Carbonic anhydrase concentration in such secretory organs and tissues as the submaxillary gland, cardiac stomach mucosa and pancreas is significantly higher than that found in the small intentine. The carbonic anhydrase of the caecum and different parts of the colon is consistently higher than the concentration found in the small intestine. The pancreas has a significantly higher carbonic anhydrase concentration than the gall-bladder. Throughout the stomach and intestine the enzyme concentration in the mucosal layers is higher than in the adjacent submucosal and muscle layers. The mean concentration of carbonic anhydrase is higher in the muscle layers than in the submucosal layers in the small intestine. The reverse is true for the stomach and colon.

CHARACTERISTICS AND PERFORMANCE OF A RECORDING PROTHROMBIN-METER. Homer L. Dorman,* J. G. Bishop, D. R. Redden,* and J. L. Matthews.* Baylor Univ. Coll. of Dent., Dallas, Texas.

A system has been developed which records progressive clot formation by intermittently monitoring the increase in electrical conduction of the sample which occurs as fibrin is formed. Diagnostic plasma yielded prothrombin times of 11.33 seconds$\pm$0.2 seconds. These results were obtained from 72 samples using two separate instruments. These data are more consistent than those obtained with various manual techniques and are somewhat shorter. Prothrombin times were found to be greatly affected by changing the temperature of the mixture. At 40°C the prothrombin time of diagnostic plasma was 9.3 seconds and it decreased to 26.3 seconds at 20°C. No essential difference was detected between measurements of prothrombin times using whole blood and separated plasma from the same subject.

PHASIC AND MEAN ARTERIAL FLOW INTO THE CANINE SEPTAL ARTERY AND ITS VENOUS DRAINAGE. Richard W. Eckstein. Dept. of Med. and Physiol., Western Reserve Univ. Sch. of Med., Cleveland, Ohio.

Measurement of phasic blood flow into coronary arterial orifices probably fails to indicate true intramural flow. During isometric contraction the uncompressed superficial arteries may minimize (buffer) rhe metered backflow and during the rise of aortic pressure they may accentuate the metered systolic inflow. In an effort to minimize these variables and to test this hypothesis, phasic flow into the septal artery was recorded with an orifice meter and an optical differential pressure manometer. The lack of compression on that portion of the septal artery normally subjected only to right ventricular pressure was largely corrected by constriction of the pulmonary artery to elevate right ventricular pressure. The recorded flow patterns show a much greater backflow during isometric contraction than previously measured in major branches of the left coronary artery. During injection forward flow is minimal or absent. Studies on a model in which measurements were made of inflow and outflow through rubber tubing perfused at aortic pressure and compressed by ventricular pressure suggest that flow through deep and strongly compressed vessels may vary considerably from the metered septal arterial inflow. The volume of mean septal flow approximates that measured in other portions of the left ventricle. Measurements of coronary sinus and anterior cardiac venous outflow during septal artery clamping suggest that the septal artery drains through Thebesian veins.

TEMPERATURE REGULATION IN DOGS FOLLOWING REDUCTION OF RESPIRATORY SURFACE. H. E. Ederstrom and J. A. Linfoot.* Dept. of Physiol. and Pharm., Univ. of North Dakota Sch. of Med., Grand Forks.

A series of animals were prepared with permanently implanted tracheal cannulae that could be adjusted so that air entered a side-arm without passing through the upper trachea and buccal cavity. These animals regulated at 40°-43°C air temperature, but with some difficulty. This was indicated by respiratory volumes which were about 25% greater than when the normal air pathway was used. Respiratory water loss, measured by a freezing method, was found to be about 50% lower when the shunt was used. Further difficulty in temperature regulation with the shunt in place was also reflected in the changes in hematocrit, serum refractive index, carbon dioxide combining power, and higher skin and rectal temperatures. Skin fluid loss increased slightly during the 3 hours in the hot room, presumably as a result of softening of sebaceous secretions rather than by active sweat secretion. Some acclimatization to the hot environment occurred in most dogs, resulting in considerable improvement in regulation after about 6 exposures. The effects of removal of one lung on temperature regulation will also be discussed. (Supported by U.S.P.H. Grant RG 3772.)

CONFIGURATION OF INDICATOR-DILUTION CURVES RECORDED FROM THE CENTRAL CIRCULATION OF THE DOG IN RELATION TO DYNAMIC RESPONSE OF THE SAMPLING SYSTEM. Anthony W. T. Edwards,* Richard J. Cheesman* and Earl H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The pulmonary artery was cannulated directly with an 8-cm polyethylene catheter (I.D. 2.7 mm). This was connected by one arm of a Y to a densitometer-galvanometer system with a fast dynamic response. The other arm was connected to a similar densitometer via a 40-cm, no. 6 Lehman catheter. Indocyanine was injected into the right atrium, and blood was drawn at 250 ml/min through the short system (dead space 0.7 ml) and at 20, 50 and 100 ml/min hrough the catheter system (1.15 ml). Dynamic responses of these systems were determined by introducing a square-wave change in concentration of dye at the common inlet. The 90% deflection time of the fast system was less than 0.1 second, and that of the slow system varied from 0.3 second with a flow of 100 ml/min to 2.0 seconds at 20 ml/min. Dye curves recorded by the rapidly responding system were sharply defined, showing clear steps in dye concentration. Curves recorded with sampling through the catheter system, even at rates as high as 100 ml/min showed considerable loss of detail. Simple estimates suing dead space and sampling rate consistently overestimated the delay due to the catheter and hence underestimated appearance and mean transit times measured with the catheter system.

REGENERATION OF CELL STRUCTURE AND RESTORATION OF PROTEOLYTIC ACTIVITY FOLLOWING ETHIONINE FEEDING IN RATS. Leslie E. Edwards and Anne Brehme.* Dept. of Physiol., Medical Coll. of Virginia, Richmond.

Ethionine, although it seems to destroy the cytology of the pancreatic acinar tissue, does not produce a permanent damage to these cells under the conditions imposed in our experiments. These cells are able to regenerate or to re-establish their original cytological appearance. The potential proteolytic activity falls to a low level on ethionine feeding but gradually returns to the normal values after ethionine has been removed from the diet. Rats fed 0.5% ethionine in their diet for a period of three weeks begin to recover immediately from this treatment on changing back to the normal basal diet. The first indication of recovery seen is the rapid weight gain after returning to the basal diet. The general cell structure appears to be completely restored within the first two-week period, whereas the proteolytic activity is not normal until six weeks after changing from the ethionine diet to the normal diet. Proteolytic activity was measured by the method of Kunitz (Journal of General Physiology. 30:291-310, 1946-1947) on the total pancreas of the rat. Rats were sacrificed two weeks, four weeks and six weeks following the ethionine feeding. (Supported by PHS Grant No. A-1390.)

NERVE CONDUCTION AND LIPID METABOLISM CHANGES IN ALLOXANIZED RATS. Sven G. Eliasson, Juanita T. Hamilton,* Ann H. Hughes* and Elizabeth K. Pierce.* Dept. of Internal Med., Univ. of Texas. Southwestern Med. Sch., Dallas.

Diabetes induced by injection of alloxan into rats is associated with a decrease in the incorporation of acetate-1-C^{14} into fatty acids and cholesterol of peripheral nerves in vitro (Hughes and Eliasson). In an attempt to correlate the conduction velocity in nerves with the described metabolic defect, a pair of normal and alloxanized rats weighing 350-450 grams were sacrificed simultaneously. One sciatic nerve from each aninal was used for metabolic studies. The remaining sciatics were mounted in a moist chamber at constant temperature and the conduction velocity on supramaximal stimulation measured. Blood sugar, serum potassium and carbon dioxide combining power were measured. A decrease in maximal conduction velocity from 80-9- m/sec to 50-60 m/sec was observed in nerves from diabetic animals. A decrease was not seen in alloxanized non-diabetic animals, serving as another control. The presence of acidosis or hyperpotassemia did not influence the conduction change. A greater decrease in conduction velocity accompanied a severe depression of acetate incorporation. Although great care must be taken in the interpretation of these observations, a possible explanation of the decrease in conduction velocity could be successive demyelination of large nerve fibers. (Supported in part by a grant from the Multiple Sclerosis Society.)

EFFECT OF MUSCLE RELAXANT AGENT (FLAXEDIL) ON PERIPHERAL BLOOD FLOW. Eugene Evonuk,* Wilbert Greenfield* and Charles J. Imig. Dept. of Physiol., State Univ. of Iowa, Iowa City.

It has been reported that following an anesthetic dose of sodium pentobarbital, peripheral blood flow is initially increased several fold. It gradually returns to the pre-anesthetic level within approximately one to two hours (Imig, C. J., Proc. Soc. Exp. Biol. Med. 82: 9, 1953). The present experiments were concerned with the investigation of the effect of Flaxedil on blood flow through the hind limb of the dog as measured by venous occlusion plethysmography. Blood pressure and heart rate were also measured. Measurements were made beginning at 15 minutes following administration of 5 mg per Kg of body wt. of the drug and at 10-minute intervals for approximately two hours. Additional dosages of Flaxedil were administered when necessary to maintain muscle relaxation. During the period of measurement the blood flow remained essentially unchanged. Blood pressure and heart rate remained at approximately a constant level. These data suggest that Flaxedil (a muscle relaxant) provides for a more constant blood flow than does sodium pentobarbital. This permits a better control for determining the effect of a painless experimental procedure upon peripheral blood flow. (Supported in part by Grant H-2608, USPHS.)

TELEMETERING OF GASTROINTESTINAL PRESSURES IN MAN BY MEANS OF AN INTRALUMINAL CAPSULE ENERGIZED FROM AN EXTERNAL WIRELESS SOURCE. John Farrar and Vladimir Zworykin (intr. by Martin Lipkin). Medical Service, Veterans Admin. Hosp., New York, Dept. of Med., Cornell Univ. Med. Coll., New York and Medical Electronics Center, Rockefeller Inst. New York.

Gastrointestinal motor activity has previously been studied by means of an ingestible, battery-powered, radiotelemetering capsule which responds to intraluminal pressure changes and permits recording of these data without connecting tubes. A modified capsule has been built which is significantly smaller, and is energized from outside the body. It is a rigid, plastic cylinder 0.7 cm in diameter, 2.5 cm in length, and contains a coil, capacitor and transducer consisting of a ferrite armature attached to a diaphragm. After the capsule is ingested, an external coil is placed around the patient. A high-frequency signal is delivered intermittently to the capsule through this external coil. Intraluminal pressure on the capsule diaphragm modulates the frequency at which the capsule circuit "rings" in response to this signal. The modulated signal is picked up by the external coil, rectified, and a pressure curve recorded. The capsule has been employed to study gastrointestinal motility in five subjects. Records of gastric, small intestinal and colonic intraluminal pressures are similar to those observed with the battery-powered capsule. Since the capsule is externally energized, it has an indefinite "life", and may have application in recording other physiological information from remote sites in man and animals.

ELECTROPHYSIOLOGICAL INVESTIGATIONS OF ANTERIOR BRAINSTEM RELATIONS TO VESTIBULAR NUCLEI. Shaul Feldman,* Irving H. Wagman and Morris B. Bender. Dept. of Neurology, Mt. Sinai Hosp., New York City.

In view of the possible influence of higher brainstem structures on vestibular nuclei activity, their relationships were investigated in unanesthetized, immobilized cats. Midline thalamic nuclei, the hypothalamus and the midbrain reticular formation were stimulated and the resultant electrical responses in the vestibular nuclei were studied. Stimulation of the diencephalon did not cause the appearance of evoked activity in the vestibular nuclei. The maximum responses in the latter were obtained upon stimulation of the midbrain in the region of the third nerve nucleus, the median longitudinal fasciculus and the median reticular formation adjacent to these structures and below the central gray. The responses, recorded both monopolarly and bipolarly from the ipsilateral and contralateral vestibular nuclei, consisted of one or two spikes usually followed by a wave of longer duration. The spikes were of less than half a millisecond latency and one to two milliseconds duration. These potentials did not diminish, and even grew during 100 per second stimulation. They were resistant to anoxia and pentobarbital. The slower wave was about 20 milliseconds in duration and on double stimulation showed complete recovery only after 100 milliseconds separation. It was abolished by pentobarbital anesthesia. The present findings suggest

the existence of direct axonal as well as polysynaptic pathways from median midbrain structures to the vestibular nuclei. (Supported in part by USPHS Grant No. B-294.)

EFFECT OF pH AND pCO_2 ON THE PERFORMANCE OF THE HEART. H. Feinberg,* W. Aronow,* A. Tatar* and L. N. Katz. Cardiovascular Dept., Med. Res. Inst., Michael Reese Hosp., Chicago, Ill.

Work on coronary flow (CF) and myocardial oxygen consumption (O_2C) of the dog heart has established that hypercapnia, under various pressure-loads, decreases oxygen extraction (O_2E) and increases CF proportionately to the cardiac effort. The O_2 cost of cardiac effort, as indexed by the product heart rate times blood pressure (HR x BP) was not affected. Hypocapnia, on the other hand, had no effect on O_2E, CR, or the O_2 cost of cardiac effort. In order to differentiate pH from pCO_2 effects, hypercapnia, hypercapnia plus alkali infusion, hypocapnia and hypocapnia plus acid infusion were employed. Each steady-state adjustment of pH and pCO_2 was studied over an increasing pressure-load. Heretofore, a relative constancy of O_2E has been noted despite large changes in cardiac output, HR and BP. Thus, CF appeared the main variant in the adjustment of O_2C to various cardiac loads. By contrast, alteration of pH produced an increased lability of O_2E, most pronounced at acid pH. Thus, an increased pressure-load resulted in a decreased O_2E and an increased CF for a given O_2C -- apparently without regard to the arterial pCO_2. The prediction of O_2C obtained with HR x BP was not altered by the inclusion of pH or pCO_2 as an additional independent variable. Thus, the wide variation in pH and pCO_2 apparently does not significantly affect the O_2 cost of cardiac effort.

ELECTRICAL RESPONSE OF THE EIGHTH CRANIAL NERVE DURING FREE-FALL AND ROTATION EXPERIMENTS. Vincent Fiorica,* Takehiko Semba* and F. R. Steggerda. Dept. of Physiol., Univ. of Illinois, Urbana.

After transection of the cochlear branch of the eighth cranial nerve, chronically indwelling electrodes were inserted unilaterally into the ganglia of Scarpa of cats under Nembutal anaesthesia. At the completion of the operation, while the animals were still under the influence of the anaesthesia, simple tilting and rotation experiments were performed to test the success of the electrode implants. Electrical response of the ganglion to dynamic changes in position were recorded oscillographically. Following a period of operative recovery, the unanesthetized animals were subjected to free-fall and rotational conditions by means of specially constructed apparatus. Electrical activity of the ganglion during these conditions was recorded on magnetic tape. These recordings were subsequently reproduced oscillographically at which time photographs were made of the activity observed. As the animals were rotated in a vertical plane at varying speeds between 8 and 19 rpm, discharges were recorded from the ganglia of the eighth nerve having a magnitude of approximately 150-200 μv and a frequency of about 400-500 cycles. During the condition of free-fall (1.2 seconds), electrical activity of

the same nature was recorded. Electrical responses observed during this condition were of a magnitude of approximately 150μv and a frequency of about 300-400 cycles.

HYPERGLYCEMIC SUBSTANCES ORIGINATING IN THE PANCREATO-DUODENAL AREA. Piero P. Foa, Giorgio Galansino,* Doris Kanameishi,* and Fred G. Berlinger.* Dept. of Physiol. and Pharm., Chicago Med. Sch., Chicago, Ill.

Hypo- or hyperglycemic materials may be released in the pancreato-duodenal area in response to stimulation with different substances. For example, the injection of glucose and other sugars into the pancreato-duodenal artery causes hypoglycemia suggesting insulin release, whereas the intravenous injection of growth hormone causes the appearance of a hyperglycemic material in the pancreato-duodenal blood. The effect of this material is blocked by dihydroergotamine (DHE), suggesting that the active principle may be a catecholamine or serotonin and not glucagon. Serotonin injected intraportally causes hyperglycemia in normal dogs. Deserpidine, which releases catecholamines and serotonin, causes hyperglycemia when injected into the pancreato-duodenal artery, but not when injected into the portal vein, into a branch of the superior mesenteric artery, or elsewhere. The diethanolamine salt of p-tolylmethylcarbinol camphoric acid ester (DTCE), a cholagogue believed to affect blood sugar concentration, also causes hyperglycemia only when injected into the pancreato-duodenal artery. DHE blocks the effect of serotonin and of DTCE, but not that of deserpidine. It is suggested that more than one type of hyperglycemic substance may be produced in the area supplied by the pancreato-duodenal artery: one which, like serotonin or the catecholamines, is blocked by DHE and another which, like glucagon, is unaffected by it. (Aided by grants A-522 and 24-5102 NIAMD, PHS.)

EFFECT OF THIO- COMPOUNDS ON THYROIDAL AND GASTRIC IODIDE TRANSPORT. William C. Foster. Lab. of Physiol. Res., Misericordia Hosp., Philadelphia, Pa.

It has been demonstrated that animals treated with 4-hydroxy-2-thiopyrimidine (1) accumulate iodide in the thyroid gland in normal, or even greater amounts, but that the formation of organic iodine compounds is inhibited. It was proposed that thio- compounds might be used to elucidate the mechanism of active transport of iodide in the thyroid gland and stomach. Adult Wistar-Strain albino rats were treated with the following compounds: 4-hydroxy-2-thiopyrimidine (thiouracil) (1), 4, 6-dihydroxy-2-thiopyrimidine (2), 4-hydroxy-6-methyl-2-thiopyrimidine (3), 4, 6-dimethyl-2-thiopyrimidine (4), 4, 6-diamino-2-thiopyrimidine (5), 5-carboxy-4-hydroxy-2-thiopyrimidine (6), 4, 6-oxy-5-ethyl-5 (1-methyl butyl)-2-thiopyrimidine (7), 4, 6-oxy-5-ethyl-5 (1-methyl butyl)-2-hydroxy pyrimidine (8), 4, 6-dihydroxy pyrimidine (9), 6-hydroxy-2-thiopurine (10), 2, 8-dithio-6-hydroxy-purine, and potassium thiocynate (12). Four-hour I^{131} uptake studies were made and the rdioactivity in the thyroid gland and stomach measured. Compounds (7) and (12) reduced the uptake of I^{131} by 80 and 40 per cent, respectively, in the thyroid

gland, while both compounds enhanced the uptake of I^{131} in the stomach by 100 percent. The results suggest an active transport mechanism is affected by substituted pyrimidine compounds. (Supported by Grant #H-3700, Nat'l. Heart Inst., USPHS.)

DIODRAST (I^{131})BLOOD CLEARANCE AS AN INDEX OF RENAL BLOOD FLOW. H. A. Fozzard and R. Jackson. (intr. by J. P. Gilmore). Naval Medical Field Res. Lab., Camp Lejeune, N.C.

In order to obtain an index of renal blood flow which is more simple and rapid than the standard constant infusion method, this laboratory has studied the blood clearance of a single injection of radioactive (I^{131}) diodrast in dogs. The clearance pattern was first studied, including measurement of extraction per cent, and a method was developed. Briefly, a single injection of diodrast (I^{131}) is given and blood samples are obtained at 10, 15, 20, and 25 minutes. Counts/milliliter/minute are plotted on semilogarithmic paper and an extrapolated value obtained. Utilizing this value a volume of distribution (V_D) was calculated and the clearance calculated in the following manner;

$$C_D \text{ (ml/min)} = 2.303 \frac{V_D}{25 \text{ min.}} \log_{10} \frac{\text{whole blood activity } t_0}{\text{whole blood activity } t_{25}}$$

Forty-three simultaneous measurements of diodrast blood clearances and PAH clearances by the constant infusion method were made in 22 animals, values being obtained before and after hemorrhage to 60 mm Hg. and/or after acute bilateral nephrectomy. The diodrast values were found to be 4.4 ml/kg/min higher than the corresponding PAH values, with a correlation coefficient $r = +0.938$, over a range of flows from 0 to 45 ml/kg/min. The uses of the diodrast method are discussed.

EFFECT OF SO_2 ALONE AND IN COMBINATION WITH SALINE AEROSOL ON PULMONARY FLOW RESISTANCE IN HEALTHY VOLUNTEERS. N. R. Frank,* Mary O. Amdur,* Jay Bartlett* and James L. Whittenberger. Dept. of Physiol., Harvard Sch. of Public Health, Boston, Mass.

SO_2 has been shown to increase pulmonary flow resistance (PRF) in unanesthetized guinea pigs (Amdur, M. O., Am. Ind. Hyg. Assoc. Quarter. 18: 149, 1957); this change becomes greater when the gas is given in combination with saline aerosol. We have compared the effect of SO_2 alone, and when combined with aerosol, on the respiratory mechanics of healthy human subjecrs. The measurements were made using an esophageal catheter and a body plethysmograph. Thirteen subjects (ages: 21 - 57) were exposed 26 times to concentrations of gas ranging from 1 to 20 ppm; the aerosol averaged 7.7 mg./m^3 (range: 5.6 - 12.0 mgm/m^3); each exposure lasted about 10 minutes. During exposure to SO_2 alone, there was no essential change in mean PFR at concentrations of 1 - 2 ppm (-7%; rane: -14 to +2, expressed as $\frac{\text{control - exposure}}{\text{control}} \times 100$).

At 4 - 5 ppm, mean PFR rose 18% (range: -3 to +52%) while over the range of 8 - 20 ppm it rose 49% (range: + 12 to +100%); the average

response to aerosol plus SO_2 in concentrations of 8 - 15 ppm was slightly higher than for the gas alone: 69% (range: +3 to +163%).

ALTERATION OF SPINAL REFLEXES WITH AGE. D. T. Frazier,* G. Santambrogio* and L. L. Boyarsky. Dept. of Anatomy and Physiol., Univ. of Kentucky, Lexington.

Measurements have now been made on forty six Wistar strain rats. These measurements include nerve conduction velocity changes with age and central delay changes with age of the flexor twitch. The principal change occurs in central delay. Animals of six age groups have been studied; 50, 100, 200, 400, 550, and 750 days. Central delay (in sigma) changes from 4.85 at 50 days to 3.52 at 100 days: remains constant at this value for the rats between 100 and 550 days old. In the oldest animals central delay has risen two-fold to 6.38. Thus, during both maturation and ageing there is a rise in latency. Conduction velocities between 30 and 50 meters per second were obtained. No significant changes in velocity with age were observed. Histological analysis of 23 spinal cord in the lumbar region has been completed. The cell counts of the ventral horn show a steady decrease with age. Further data are needed to establish the onset of this change. The amplitude but not the central delay of this reflex may be increased two to ten fold by injection of caffeine. Our method of reflex testing reveals only a small fraction of the reflex pool.

SOME QUANTITATIVE BEHAVIORAL CORRELATES OF PREPYRIFORM ELECTRICAL ACTIVITY. Walter J. Freeman (intr. by Victor E. Hall). Dept. of Physiol., Univ. of California Sch. of Med., Los Angeles.

It is known that bursts of high frequency (18 - 58/sec) electrical activity occur in the basal forebrain in association with excited behavior in man and in cats, and that in cats and in dogs these bursts occur in synchrony with the respiratory cycle. In this study a quantitative correlation was made between the changes in measures of frequency and amplitude of these bursts, and the changes in some concomitant measures of behavior. Recordings were made from 3 - 4 sites in each prepyriform cortex bilaterally of cats with implanted electrodes. It was found that (1) there was no correlation between changes in frequency and changes in behavior; (2) when the amplitude at one part of the prepyriform cortex changed, the amplitude at all parts did so in the same direction at the same time; (3) increases in amplitude occurred following visual, auditory, or tactile stimulation, and the amount and duration of the increases were identical to those following olfactory stimulation; (4) with increasing hunger (duration of deprivation) there was increasing amplitude of electrical activity, but only during anticipation of a response and not during a response (e.g. eating, lapping, or working to get food); (5) at low hunger levels (up to 24 hours of deprivation) the higher the electrical amplitude recorded during work the greater the amount of work done to get food; after longer deprivation there was no longer a correlation. Preliminary observations on fear, rage, sexual activity, play, etc. indicate that the same pattern occurs in these states. However, changes in amplitude do not accompany reflex activity.

ESTIMATION OF DAILY ADRENAL CORTICAL HORMONE SECRETION IN RATS BY MEANS OF A SIMPLE COOLING TEST. Melvin J. Fregly. Dept. of Physiol., Univ. of Florida, Coll. of Med., Gainesville.

The effects of cortisone acetate and thyroxine, administered separately or in combination, on cooling rate (CR) of restrained, adrenalectomized rats subjected to cold air (5°C) have been studied. Normal and bilaterally adrenalectomized rats of Holtzman strain weighing between 200 and 250 gms were used. Thyroxine alone, administered intraperitoneally to adrenalectomized rats, failed to influence CR until 5 μg/day had been given. This dose reduced the rapid CR of adrenalectomized rats but failed to return CR to that of sham-operated rats. Doses higher than 5 μg were poorly tolerated. Cortisone acetate alone, administered intraperitoneally to adrenalectomized rats, reduced cooling rate maximally when 1 mg/day was given although this does level also failed to return CR to that of sham-operated rats. Higher doses of cortisone were less effective. Cooling rate of adrenalectomized rats given the combination of 5.0 ug thyroxine and graded doses of cortisone acetate daily returned to that of sham-operated rats when 2.0 or 2.5 mg cortisone acetate was given; however, CR of rats given 2.5 μg thyroxine and cortisone daily did not return to that of sham-operated rats. In the former group an inverse linear relationship was observed between the logarithm of CR and the dose of cortisone administered. When thyroid secretion rate is 5.0 μg/day, the results suggest that adrenal glands may secrete cortical hormone equivalent to 2.0 to 2.5 mg cortisone acetate/day. Conversely, at different adrenal secretion rates (1.0, 1.5 or 2.0 mg cortisone acetate equivalent/day), secretion rate of thyroxine is estimated to be 5.2 to 6.0 μg/day. Thus, an interrelationship between thyroid and adrenal glands can be demonstrated under these conditions. (Supported by Contract AF 41-(657)-171 with the School of Aviation Medicine, Randolph Air Force Base, Texas.)

EFFECT OF LOAD CHARACTERISTICS ON MYOCARDIAL OXYGEN CONSUMPTION AT CONSTANT DIASTOLIC VOLUMES. Gordon French and R. G. Monroe (intr. by J. L. Whittenberger). Dept. of Physiol., Harvard Sch. of Public Health, Boston, Mass.

The hypothesis that end-diastolic volume determines myocardial oxygen consumption regardless of work load has been tested critically. An isolated perfused canine heart was prepared with the left ventricular cavity isolated from the aorta and left atrium. An arrangement of valves, an enclosed Krogh spirometer and the use of air instead of a blood system permitted load characteristics to be varied from nearly isovolumetric to isobaric. Heart rate was maintained constant. Left ventricular oxygen consumption at any given diastolic volume was several times greater when pressure changes were developed under nearly isovolumetric conditions than when volume decreased in systole without change in intraventricular pressure. When both volume and pressure changed with systole, oxygen consumptions were equally well related to systolic developed pressure or to systolic volume, but not to diastolic pressure or diastolic volume.

DIFFERENTIATION BETWEEN EFFECTS OF HISTAMINE AND SEROTONIN LIBERATION BY HEMORRHAGIC GASTRIC ULCERATIONS IN THE RAT. M. H. F. Friedman, R. Constable* and D. D. Mergenthaler.* Dept. of Physiol., Jefferson Med. Coll., Philadelphia, Pa.

A simple rat procedure is described for determining the relative effectiveness of mast cell disrupting agents (or "histamine liberators") to release serotonin by differentiation of the distinct gastric effects of serotonin from the minimal effects of concomitantly released histamine. Histamine, administered either continuously or in depot form, was ineffective in producing ulcers of the gastric mucosa in the rat. Except in very large doses, histamine was also without effect on acid gastric secretion. On the other hand, serotonin as well as serotonin precusor, 5-hydroxytryptophan, had marked ulcerogenic action on the glandular portion of the rat stomach. Acute hemorrhagic ulcerations were also readily produced in the rat by mast cell disrupting agents such as Compound 48/80. Pretreatment of the rat with atropine reduced the incidence of ulcer formation due to serotonin but not significantly that due to 48/80. Both serotonin and 48/80 had a biphasic effect on gastric secretion, with inhibition predominating over initial excitation.

ESTIMATION OF THYROID SECRETION RATE OF RAINBOW TROUT USING RADIOACTIVE IODINE. P. O. Fromm and J. R. Hoffert (intr. by W. D. Collings). Dept. of Physiol. and Pharm., Michigan State Univ., East Lansing.

Thyroid secretion rates of Salmo gairdnerii were determined using a technique which has been successfully applied to homoiothermic animals. Since the pattern of iodine metabolism and control of the teleostean thyroid is similar to that of higher vertebrates, this method should be satisfactory for the determination of thyroid activity in trout. The mean thyroid secretion rates for yearling trout kept at 13° and 3°C were 0.244 and 0.139 μg.1-thyroxine/-100gm/day respectively. No significant differences in thyroid secretion rate occurred between yearling and two-year-old trout kept at 13°C. The secretion rates of fish at 3°C were significantly lower than both the two-year-old fish ($P = 0.05$) and one-year-old fish ($P = 0.01$) kept at 13°C. Q_{10} values of 2.17, 1.97 and 1.75 for oxygen consumption, opercular rate, and thyroid secretion rate, respectively, were calculated from mean values obtained at 3° and 13°C. It is concluded that the thyroid of trout has little or no influence on the oxidative metabolism at low temperature, and it appears doubtful that the trout thyroid is involved in a temperature compensating mechanism as has been previously postulated.

EFFECT OF REPLACEMENT THERAPY ON IMPAIRMENTS IN GESTATION AND LACTATION FOLLOWING HYPOTHALAMIC LESIONS. C. Gale* and S. M. McCann. Dept. of Physiol., Univ. of Pennsylvania, Philadelphia.

Impairments in gestation and lactation resulting from lesions placed stereotaxically in the median eminence of pregnant rats have been tentatively attributed to a deficiency of anterior pituitary

hormone(s) (Gale Fed. Proc. 18:194 '59). In the present study an attempt was made to abolish the impairments in gestation and lactation by replacement therapy. Progesterone (4 mg/day) plus estradiol benzoate (0.2 μg/day) given on days 8-12 of gestation protected pregnant rats completely against abortion, suggesting that lesions result in a deficiency of ovarian steroids consequent to a deficit of anterior pituitary gonadotrophin(s). Prolactin (60 U/day) given on days 8-12 was ineffective in maintaining gestation, thus indicating that abortion is not caused by a simple deficit of prolactin. The efficacy of estrogen alone in maintaining gestation will be reported. Prolactin (100 U/day) did not improve the impaired lactation of operated rats. Hydrocortisone (1 mg/day) improved lactation to about 50% of normal. Hydrocortisone plus prolactin had the same beneficial effect as hydrocortisone alone. Adrenal weights correlated significantly with lactational performance. Pituitary infarcts were present in rats that aborted and that had impaired lactation, as well as in those that did not abort; however, abundant well vascularized pituitary tissue was present in the majority of rats with impairments. (Supported by PHS Grant A-1236 C2.)

PULMONARY BLOOD FLOW DURING PARTIAL HEART-LUNG BYPASS IN CLOSED-CHEST DOGS. Pierre M. Galletti and Max A. Hopf (intr. by Gerhard A. Brecher). Dept. of Physiol., Emory Univ., Atlanta, Ga.

Since during partial heart-lung bypass blood gas exchange occurs at two places (lung plus heart-lung machine), the ratio of extracorporeal flow to pulmonary flow becomes an important factor for total body tissue perfusion. 15-20 kg dogs were anesthetized with morphine (1 mg/kg) and chloralose (80 mg/kg) ahd heparinized (2 mg/kg). 500-700 ml heterologous donor dog blood was transferred intravenously while a corresponding volume was withdrawn from an artery. The withdrawn blood served to prime the extracorporeal circuit (Pulmopak^{R}). Partial heart-lung bypass (inferior vena cava to vemoral artery) was performed using the gravity venous suction and gravity arterial infusion technique. Extracorporeal flows of 300, 600, and 900 ml/min were achieved stepwise for periods ranging from 20 to 40 minutes. Sampling of expired gas, of central venous and carotid artery blood permitted calculation of pulmonary blood flow. At low extracorporeal flow rates (less than 20% of control cardiac output) the pulmonary blood flow was little affected and consequently the total body perfusion (pulmonary plus extracorporeal flow) increased. When the extracorporeal flow was set to vary from 30 to 70% of the control cardiac output, the pulmonary flow decreased sharply. Therefore, the total body perfusion was decreased.

QUANTITATIVE MEASUREMENT OF BLOOD FLOW IN VARIOUS AREAS OF THE SMALL AND LARGE INTESTINE. William F. Geber (intr. by D. M. MacCanon). Dept. of Physiol. and Pharm., State Univ. of South Dakota Sch. of Med., Vermillion.

The metabolic gradient theory of Alvarez has been advanced as an explanation of the physiologic activity and peristaltic polarity of

the intestine. All previously investigated parameters have indicated a definite gradient did in fact exist. In a study to reevaluate the problem, the quantitative measurement of blood flow through the various areas of the small and large intestine was carried out in fasted dogs. Segments of duodenum, jejunum, ileum, and descending colon were selected. The artery leading to a particular area was cannulated and the blood flow measured by an electromagnetic flowmeter. Average blood flow in the various areas expressed in ml/gm wet tissue/min was found to be as follows: duodenum 1.38, jejunum 0.98, ileum 0.82, and descending colon 0.73. An attempt was made to correlate visible gut activity with alterations in blood flow. Only in the case of the descending colon during defecation was there marked changes in blood flow. All other areas exhibited minimal or no alteration in flow during marked activity in any given area. The relative number of anastomoses in any area and their relation to the blood flow in that area will be discussed. (Supported by South Dakota Heart Association.)

ARTERIOVENOUS FISTULA CHARACTERISTICS OF THE GRAVID UTERUS. V. Glaviano (intr. by R. Ingraham). Dept. of Physiol., Univ. of Illinois Coll. of Med., Chicago.

The cardiodynamic events which follow acute occlusion of the uterine arteries in a pregnant dog have been observed to be similar to those which accompany the occlusion of a peripheral arteriovenous fistula. Twelve female mongrel dogs, pregnant for approximately 45 to 55 days were anesthetized with chloralose. Cardiac output was measured by the direct Fick principle. Central venous and arterial blood pressure were measured with Statham pressure transducers. After bilateral ligation of the ovarian arteries, uterine blood flow was measured by diverting blood from the right common carotid artery to an electromagnetic rotameter. The outflow from the rotameter was in turn diverted to the uterine arteries. With the exception of the cardiac output, all parameters were continuously recorded with a photokymograph. Occlusion of the rotameter inflow for periods of 1 to 2 min was accompanied by an immediate decrease in cardiac output and heart rate, and an increase in blood pressure. The sudden reestablishment of the uterine blood flow caused a decrease in blood pressure and an increase in cardiac output and heart rate. A comparison of the cardiovascular alterations produced by the gravid uterus were made with those accompanying the opening and closing of a peripheral arteriovenous fistula in 6 non-pregnant dogs. Changes in heart rate, blood pressure, cardiac output and venous pressure were similar for the two groups, and only differed in magnitude. This difference in magnitude of responses is probably due to the uterine flow averaging only 8 per cent of the cardiac output. (Supported by a grant from the National Institutes of Health, H-3686.)

INTERMANUAL TRANSFER OF SOMESTHETIC DISCRIMINATIONS IN SPLIT-BRAIN RHESUS MONKEYS. Mitchell Glickstein* and R. W. Sperry. Div. of Biology, California Inst. of Tech., Pasadena

Section of the corpus-callosum has been shown to block interocular transfer of visual learning in chiasma-sectioned cats and

monkeys, and the interpaw transfer in cats of tactual learning, including its motor, pedal-pushing components. By contrast, callosum-sectioned monkeys trained to perform tactual discriminations with one hand may show moderate to good transfer to the untrained hand. Further analysis using 4 monkeys with midline section of corpus-callosum and 5 unoperated controls showed that various components of the learned response did not transfer with equal ease. Motor Transfer: The motor pattern and testing set (reaching out and feeling the two test objects before selecting one or the other) readily transferred in 3 out of 4 experimentals, and 4 of the 5 controls. Sensory Transfer: With reversal training (previously negative stimulus changed to positive upon testing for transfer to the second hand) distinctive sensory knowledge transferred in only 1 out of 3 split-brain animals run to date, compared to strong transfer in both controls tested. Also, with re-reversal (retesting first hand with stimuli reversed to original values), all 3 experimentals tested so far showed no transfer; both normals showed strong transfer. One experimental, tested without reversal, showed immediate high-level but temporary transfer of sensory as well as motor components that survived through only 50 trials.

MATHEMATICAL ANALYSIS FOR THE RECOVERY OF A DYE-DILUTION CURVE DISTORTED BY THE SAMPLING-RECORDING SYSTEM. Jose M. Gonzalez-Fernandez,* Richard J. Cheesman* and Earl H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Recording of dilution curves from the central circulation in intact animals or human beings requires sampling of the indicator-blood mixture via narrow-bore hydraulic systems of considerable length. Prediction of the fidelity of reproduction of such dilution curves necessitates investigation of the dynamic-response characteristics of the recording system and the distorting effect of this response on the contour of the dilution curve in question. A numerical recursive method has been devised to recover this curve, based on the determination of the dynamic response of a given recording system and the dilution curve recorded by this system, as the solution of an integral equation of the convolution type. Different mathematical aspects of the method such as stability of the solutions, effect of random errors, quantizing levels and frequency resolution have been investigated. This numerical method was programmed for the IBM 650 digital computer which then was used for processing the data from dilution curves recorded to test the method.

RHINENCEPHALIC INFLUENCE ON THE THALAMUS. Elsie F. Goodfellow* and William T. Niemer. Dept. of Anatomy, Creighton Univ. Sch. of Med., Omaha, Nebr.

In a series of seventy cats, the spread of ictal after-discharge to the thalamus has been studied following stimulation of various rhinencephalic areas, i.e. the septum, dorsal and ventral portions of the hippocampus and the lateral and basal amygdaloid nuclei. In curarised, locally anesthetized cats, liminal and supraliminal stimulation of these rhinencephalic structures resulted in ictal activity in

all thalamic nuclei. The highest amplitude activity was seen in the caudal region of the nucleus lateralis posterior and in the medial geniculate body and frequently in the anterior thalamic nuclei. Ictal activity of the ventro-lateral group of nuclei was predominantly of low amplitude. In cats anesthetized with Dial (0.3 cc/kg), liminal stimulation of the five rhinencephalic areas limited the spread of ictal activity to certain specific nuclei. These varied according to the area stimulated. However, in all cases liminal stimulation of the five areas evoked ictal activity in the medial geniculate body, nucleus medialis dorsalis and usually in the nucleus lateralis posterior. Liminal stimulation of the ventral hippocampus also resulted in ictal activity in the nucleus ventralis lateralis and nucleus ventralis lateralis posterior. The anterior nuclei were not consistently fired at liminal stimulation. The constant, early involvement of the non-specific and associational nuclei of the thalamus provides evidence for a thalamic integrating mechanism between the rhinencephalon and the associational cortex. (Aided by USPHS Grant B-1046.)

SEROTONIN MODIFICATION OF BLOOD SUGAR AND GLYCOGEN COMPARTMENTS. Paul Gordon and Morris Lipton (intr. by F. J. Haddy). Veterans Admin. Res. Hosp., Chicago, Ill.

Serotonin blood sugar elevation at a single point in time has been observed in rats and rabbits in the presence or absence of the adrenal medulla. We report Serotonin modification of blood sugar and glycogen in three preparations: 1) 24 hour starved normal rats were injected im and sc with 3(s3), and 6(s6) mg per kilogram serotonin, with saline, or with adrenaline. Blood sugars, liver and muscle glycogens were examined at 20', 60', and 140'. At 20' sa blood sugar was 88, A was 152, s3 was 102, s6 was 104 mg %. Liver glycogen at this time was lowered equivalently by A, s6. Muscle glycogen was lowered by A but not by s6, or s3. At 60' sa blood sugar was 64, A was 142, s3 was 145, s6 was 154 mg %. At 140' sa blood sugar was 62, A was 97, s3 was 90, s6 was 162 mg %. 2) Blood sugars of rats with 75% of their liver removed the day preceding averaged 32 mg %. S3 did not increase blood sugar in this preparation. 3) s3 caused the blood sugars of 24 hour starved alloxan diabetic rats to increase from 161 mg% to 309 mg% at 140'. s3 increased the liver glycogen of normal rats by 125% and did not significantly change that of diabetic rats at 140'. Other glycogen findings will illustrate that s3 increases the calculated total body carbohydrate by 12% in the normal and 25% in the diabetic rat at 140'. It is concluded that serotonin produces hepatogenic hyperglycemia while evoking gluconeogenesis.

RESPONSE OF THE ISOLATED AORTA STRIP TO ANGIOTENSIN AND TO EPINEPHRINE. Patricia L. Goulet* and David F. Bohr. Dept. of Physiol., Univ. of Michigan, Ann Arbor.

Helically cut rabbit aorta strips were suspended in Krebs solution at 37°C. A one-quarter maximum isotonic contraction was used in most studies. Such responses to repeated epinephrine stimulations did not diminish in an eight-hour observation period. In contrast, a similar response to angiotensin disappeared in four to

eight hours. This loss of the angiotensin response is not due to tachyphylaxis, since it occurred with time even in the absence of previous exposure to angiotensin. Furthermore, in contrast to this early disappearance of the submaximal contraction, the responses to supramaximal concentrations of angiotensin did not diminish during observation periods as long as twelve hours. This disparity could be due to a gradual failure of some component of the contractile mechanism. By using supramaximal concentrations of angiotensin this component could still be driven to give a maximum response. The effectiveness of the failing component must be a critical determinant of the response to submaximal concentrations of angiotensin. Addition of plasma or extra potassium to the Krebs solution did not prevent this loss of responsiveness. The condition of the failing component has no apparent influence on the response to submaximal concentrations of epinephrine. (Supported by grant H-2578 C2, National Heart Institute PHS.)

GLUTAMIC ACID DECARBOXYLASE IN DEVELOPING BRAIN. Juanita Graves* and Williamina A. Himwich. State Research Hosp., Galesburg, Ill.

Brain tissue anterior to and including the superior colliculi were taken for analysis of glutamic acid decarboxylase activity. The brain was immediately homogenized in ice cold phosphate buffer (0.05 M at pH 5.9) and diluted to give a final concentration of 100 mg fresh weight tissue per ml of buffer. The carbon dioxide produced was measured in a Warburg respirometer at 37.5°C, in an atmosphere of 95% N_2 and 5% CO_2. Total fluid volume was 3.0 ml. The contents of the side arm, 0.5 ml of 0.5 M glutamic acid (pH 7.0-7.4), were tipped in and control readings were taken after a ten minute equilibration period. The carbon dioxide produced in one hour per 100 mg fresh tissue by brains with and without the addition of 200 γ pyridoxal phosphate were compared. Determinations were made on young animals from birth to 28 days and on adult animals. The rat, mouse and rabbit brains showed no change of activity due to pyridoxal phosphate until the animals were older than 14 days. In the case of the guinea pig however an increase of activity with pyridoxal phosphate was noted even in the newborn. The relation of these data to other chemical and neurological events in developing brain will be discussed.

CARDIOVASCULAR EFFECTS OF ADRENALINE AND NORADRENALINE. Zora Jasincuk Griffo* and Fred R. Griffith, Jr., Dept. of Physiol., Buffalo Univ. Sch. of Med., Buffalo, N.Y.

Measurements of heart rate, systemic arterial blood pressure, central venous pressure, as well as plethysmographic data of volume changes in intact and skinned hind limbs, livers, spleens, loops of small intestine, and kidneys show the following upon intravenous infusions of adrenaline and noradrenaline into anesthetized cats: A qualitative difference in pulse frequency upon administration of the catechols, adrenaline causing a more or less extensive tachycardia while noradrenaline elicits a pure bradycardia. Adrenaline effects a rise in systolic arterial blood pressure, while the diastolic may

decline, show no change, or rise, depending on preinfusion blood pressure levels. The varied diastolic response correlates with the occurrence of quantitatively different volume changes in the hind extremities of the respective animals. Noradrenaline invariably causes a strong pressor response of both the systeolic and diastolic blood pressures as well as a quantitatively similar effect on the blood volume of the hind limbs regardless of the resting blood pressure. Plethysmographic records of the various organs tested show a quantitatively similar decrease in blood volume of the liver, spleen, and kidney, an increase followed by a decrease in skinned and intact hind extremities, and an increase in the intestine with both, adrenaline and noradrenaline. Both catechols cause a slight elevation of the central venous pressure.

EFFECT OF BLOOD VISCOSITY ON VENOUS RETURN AND CARDIAC OUTPUT. Arthur C. Guyton and Travis Q. Richardson.* Dept. of Physiol. and Biophysics, Univ. of Mississippi Sch. of Med., Jackson.

In 18 dogs the effect of acutely induced anemia or polycythemia on cardiac output has been studied. An open-chest preparation was used in which it was possible to measure continuously the flow of blood from all the great veins into the heart. Special precautions were taken to insure that the mean circulatory pressure was the same in the controls as in the anemic and polycythemic animals, thus assuring that any recorded changes would not be the result of blood volume increase or decrease rather than viscosity changes. Venous return was plotted against hematocrit, this increasing approximately linearly as the hematocrit fell. At a hematocrit of 60 the cardiac output was 42 ml/min/kgm; at a hematocrit of 20 it was 146 ml/min/kgm. Oxygen availability to the tissues--that is, the total amount of oxygen in each 100 ml of arterial blood times the cardiac output--was plotted against hematocrit. Peak availability occurred at a hematocrit of 41, and this decreased to 50% of normal when the hematocrit had either risen to 65 or fallen to 15. The decrease in venous return and cardiac output corresponded within a few per cent with the increase in blood viscosity as reported by Whittaker and Winton (J. Physiol. 78:339) when using a high-speed viscometer. (Supported by a grant-in-aid from the National Heart Institute.)

CHOLINERGIC STIMULATION AND BLOCKADE ON THE BLADDER OF THE DOG. Laszlo Gyermek (intr. by Arnold V. Wolf). Dept. of Pharm., Univ. of Illinois Coll. of Med., Chicago.

For determining the relative potency and mode of action of some cholinomimetics the pelvic nerve-bladder preparation of the dog was used. The potencies of the compounds investigated, as determined in 4 point assays, related to that of acetylcholine (ACh) are as follows: muscarine: 110, trimethyl-ammonium propanediol acetal: 42, acetyl-beta-methylcholine: 5.5, arecoline 2.5, dimethylphenyl piperazinium iodide: 5, serotonine creatinine sulfate: 20, histamine: 10, Ba Cl_2: 0.1. Atropine does not influence significantly the effects of pelvic nerve stimulation, DMPP, serotonin, histamine and Ba Cl_2; it antagonizes the effects of ACh to some extent. It completely

inhibits the effects of muscarine and acetyl-beta-methylcholine. After atropinization, ganglionic blocking agents decrease while neostigmine increases the responses of nerve stimulation and of ACh. ACh differs from muscarine and muscarinic drugs in having predominantly ganglionic type of action of the bladder. On the basis of these findings it must be assumed that part of the parasympathetic effector sites of the bladder functionally resemble autonomic ganglia. These ganglionic receptors of the bladder seem to play an important role in the effect of the pelvic nerve stimulation, in the action of ACh and also in regulating spontaneous movements of the bladder.

DISTRIBUTION COMPONENT OF THE ALVEOLAR-ARTERIAL OXYGEN PRESSURE DIFFERENCE. Pierre Haab,* Johannes Piiper* and Hermann Rahn. Dept. of Physiol., Univ. of Buffalo, Buffalo, N.Y.

Under normal conditions, the alveolar-arterial oxygen pressure difference (A-a difference) is believed to be due primarily to two causes: venous admixture (shunt component), and variation in ventilation-perfusion ratios (distribution component). In order to assess quantitatively the role played by the latter factor, the difference in oxygen tension between end-tidal air and arterial blood was measured in anesthetized dogs under two conditions: (a) at normal ambient pressure (P_B = 747 mm Hg), breathing air; (b) at low ambient pressure (P_B = 192 mm Hg), breathing 100% O_2. The essential feature of this procedure is that, while the inspired O_2 tension is identical in both conditions, there is no nitrogen in the gas inspired at low ambient pressure. Theoretical analysis indicates that, if all or part of the A-a difference measured under condition (a) is due to a random distribution of ventilation-perfusion ratios, then this difference must be significantly reduced under condition (b). Such a decrease in the A-a difference should provide an index of the magnitude of the distribution component. However, in our experiment, the A-a difference was found to be the same in both conditions. Therefore, our results do not support the hypothesis that a part of the A-a difference is due to a random distribution of ventilation-perfusion ratios. (Supported by the Air Research and Development Command - Wright-Patterson AFB.)

SIMPLIFIED REBREATHING TEST FOR ESTIMATING VENTILATORY FUNCTION. J. H. Hackney* and C. R. Collier. Coll. of Medical Evangelists, Los Angeles, Calif.

A rebreathing technique of estimating the arterial CO_2 tension with the rapid infrared CO_2 analyzer has previously been used to estimate ventilatory function in patients. Because of the steep slope of the whole body dissociation curve, it has seemed likely that a prolonged rebreathing period with analysis of the bag contents would serve as a test of ventilatory function without need for an expensive analyser. A mathematical model was used to visualize the theoretical aspects of this idea. The bag, lungs and tissues were assumed to exchange CO_2 continuously and the resultant three simultaneous differential equations were solved. The bag tension after one minute rebreathing was found to be linearly related to the initial alveolar

tension. The parameters identifying the constants were: alveolar ventilation, equivalent tissue volume, cardiac output, bag volume, equivalent lung volume, metabolic CO_2 production, and initial CO_2 tensions of bag and tissues. Wide variations of the above parameters with the exception of very low alveolar ventilation, produced little change in slope or intercept of this relationship. The bag CO_2 tension after one minute rebreathing of 3L of 8% CO_2 was compared with the arterial CO_2 tension in sixty-six clinical tests (arterial tensions 23-92 mm Hg). The data fell into the area predicted by the model. The linear regression line was:

$$P_{arterial} = 1.3\ P_{bag} = 24.4$$

The standard error of the estimate was 4.5 mm Hg.

COMPARISON OF SMALL AND LARGE VESSEL HEMATOCRITS AT TWO FLOW RATES. Francis Haddy. Sect. of Med., Vet. Admin. Res. Hosp. and Dept. of Physiol. and Med., Northwestern Univ. Med. Sch., Chicago, Ill.

Numerous studies suggest that blood in small vessels has a lower hematocrit value than blood in large vessels. On the other hand, hematocrits of blood expressed from isolated perfused kidneys during interruption of the circulation differ little or not at all from hematocrits of blood supplying the kidney during perfusion (Morgan, D.P., Am. J. Physiol. in press). In none of the above studies was blood actually sampled from small vessels during perfusion. In this study, blood was simultaneously withdrawn from the dog aorta and foreleg brachial artery, small artery, small vein and cephalic vein with the rate of blood flow in the brachial artery held constant at 50 and 150 ml/min. Small vessel blood was obtained through 0.5 mm glass tubes wedged distally as far as possible. Hence, the blood came from distal collaterals. Average hematocrit values in % from 10 experiments with flow at 50 ml/min were aorta 40, brachial artery 40, small artery 40, small vein 40 and cephalic vein 41. Corresponding values with flow at 150 ml/min were 40, 40, 41, 40 and 40 respectively. This study shows that small vessels, as defined by the method of cannulation, and vessels of large caliber provide the same hematocrit and that the small vessel hematocrit is not different at the two studied flow rates.

APPLICATION OF GAS CHROMATOGRAPHY TO RESPIRATORY AND BLOOD GAS DETERMINATIONS. Lyle H. Hamilton, Wood Vet. Admin. Hosp. and Marquette Univ. Sch. of Med., Milwaukee, Wisc.

A technique has been developed for the use of a Model 25 Fisher Gas Partitioner in the determination of air and blood gases. Modifications of the partitioner included adjusting the column composition and length to permit optimum separation of the gases, increasing the sensitivity of the balance control, and using a special 2-channel valve for the introduction of air samples. A method for determining blood gas content has been developed and compared with other techniques of analysis. It utilizes a vacuum extraction procedure and a special valve to introduce the gas sample into the partitioner. The gas

partitioner has been adapted to an Electronics for Medicine recorder, using the electronic integrator channel and incorporating a special reset circuit. It has also been attached to a Model 153 Brown recorder with a Disc integrator attached. A comparison of these two recording systems will be presented.

STUDIES ON BILE ACID TOXICITY IN DOGS. Rupert P. Hammond and Gordon W. Searle (intr. by G. E. Folk, Jr.). Dept. of Physiol., Coll. of Med., State Univ. of Iowa, Iowa City.

The effects of various bile salt preparations given orally or intravenously upon bromsulfalein (BSP) retention and serum transaminase levels have been tested in dogs. Given orally in doses of 4 and 8 gm, dehydrocholic acid was associated with greater BSP retention than cholic acid, while ox bile extract resulted in no significant BSP retention compared to controls. Serum glutamic-oxalacetic transaminase (GO-T) and glutamic-pyruvic transaminase (GP-T) were measured in dogs given 4 to 23 gm of dehydrocholate in 20 per cent solution intravenously over 2 to 11 hours. In dogs which survived such a regimen, GO-T and GP-T rose as long as the infusion was continued and for about 5 minutes afterwards, reaching a peak of 300 to 500 per cent of control levels. From this point GP-T fell to control levels in 6 to 8 hours, but GO-T declined more slowly and reached control levels at 48 to 60 hours after exhibiting a secondary rise to 400 to 600 per cent of control midway in the recovery period. In dogs which did not survive, death was associated with progressively severe convulsions and as much as 20-fold increases in transaminase levels. (Supported in part by PHS Grant No. A-837 and a grant from the AMA.)

TEMPERATURE RESPONSES DURING AND AFTER FORCED EXERCISE IN RATS WITH HYPOTHALAMIC LESIONS. P. Han* and J. R. Brobeck. Dept. of Physiol., Univ. of Pennsylvania, Philadelphia.

Small bilateral electrolytic lesions were made in the rats' hypothalami systematically. Temperature responses during and after forced exercise were measured. Three patterns of response were noticed: 1. Rats with lesions in the preoptic area between anterior commissure and optic chiasma showed a higher T_{out} (temperature at end of exercise), while T_{30} and T_{60} (temperature at 30 and 60 minutes after the end of exercise) also remained above control levels. 2. Rats with lesions in ventral medial nucleus showed hyperphagic behavior and gained more weight. Their T_{out} was also higher than that of the controls but their T_{30} and T_{60} returned to control levels. 3. Rats with lesions in lateral hypothalamus 2 mm from base of the skull at the level of ventral medial nucleus showed response similar to that of the hyperphagic obese rats except that they did not over-eat and did not become obese. These three patterns are reproducible and are not found after lesions in other areas of the hypothalamus. Simultaneous skin temperature measurements indicated that impairment of peripheral vasodilation is one of the causes of these responses. (Supported by Grant G 1744, National Science Foundation.)

METHOD FOR STUDY OF RESPONSES OF AIRWAYS TO PHYSIOLOGICAL STIMULI AND DRUGS. Michiyoshi Harasawa* and Simon Rodbard. Univ. of Buffalo Chronic Disease Res. Inst., Buffalo, N.Y.

Intermittent positive pressure insufflation of the lungs of thoracotomized, curarized dogs was maintained with the Burns valve. During each respiratory cycle, the duration of the insufflation phase with this instrument is determined by the rate of rise of intratracheal air pressure to the selected value at which the valve will close; passive expiration is then triggered. Occlusion of a bronchus shortens the cycle; an increase in available lung volume prolongs it. The respiratory cycle was found to be shortened after administration of serotonin, histamine, or acetylcholine. The cycle was prolonged by aminophylline, TEAC, or vagotomy. The responses increased with the amount given. These results suggest that the drugs used modify the pulmonary air space available for insufflation, presumably by an action on the bronchiolar musculature. Thus, the data suggest that bronchoconstriction results from serotonin, histamine, or acetylcholine, while bronchodilation follows TEAC, aminophylline, or vagotomy. Hypoxia, hypercapnea, tachycardia, occlusions of branches of the pulmonary arteries or veins, and rapid infusion or removal of fluid from the circulation, all had no significant effects on respiratory cycle length. These studies provide a new approach for testing agents or physiological conditions which modify ventilatory lung volume. They suggest that compliance measurements may include a factor representing air entrapment by broncho-constriction.

DISPERSION OF MICROSCOPIC RADIO-OPAQUE PARTICLES IN THE WALLS OF THE STOMACH AND SMALL INTESTINE. R. W. Harrison* and F. R. Steggerda. Dept. of Physiol., Univ. of Illinois, Urbana.

It has previously been reported that when Thorotrast (thorium-dioxide) is injected into the walls of the colon, this organ will remain opaque to x-rays for physiological studies for several years. It was also found that visualization of the stomach and small intestine was not satisfactory. This was thought to be due to the particle size of the Thorotrast and the degree of lymphatic drainage present. Furthermore, because of the radio-activity and carcinogenic potentialities of thorium-dioxide, a study of the value of suspensions of inert Barium Sulphate, of varying particle sizes was undertaken. The material was injected in the region of the Cardiac, Pyloric and Illeo-caecal Sphincters as well as in different regions of the stomach and small intestine. This was done by suspending Barium Sulphate particles in Ringer's solution and then injecting small amounts underneath the serosal layers along the gastro-intestinal tract with a hypodermic syringe using a 26 gauge needle. Routine sterile operative techniques were used. The distribution, location, and duration of the opaque material in the walls of the gastro-intestinal tract was studied by means of x-ray and histological techniques.

24-HOUR SUSCEPTIBILITY RHYTHM TO ETHANOL IN FULLY-FED, STARVED, AND THIRSTED MICE AND THE LIGHTING REGIMEN. Erhard Haus,* Edward M. Hanton* and Franz Halberg. Cambridge State Hosp. and Univ. of Minnesota Med. Sch., Minneapolis.

Under conditions standardized for periodicity analysis (J. Lancet, 73: 20, 1953), C mice kept in light from 06:00 to 19:00, alternating with 12 hours darkness, were given a 25% solution of ethanol in doses of .7 to .8 cc/20 grams body weight; in two experiments, groups of mice were injected intraperitoneally at 4-hour intervals, starting at 08:00 and continuing for 24 hours. Mortality was recorded at 20 minutes, 1-, 4-, 12-, and 24-hours post-injection. Significant and predictable within-day differences in mortality were consistently recorded in these and additional experiments on mice of several stocks and ages. Peak mortality was recorded at 20:00, corresponding in time (in D_8 mice) to peak susceptibility to audiogenic convulsions (Science, 128: 657, 1958); peak susceptibility to ethanol was dissociated in time from peak susceptibility to endotoxin (Fed. Proc., 17: 439, 1958) or ouabain (Fed. Proc., 18: 63, 1959). The temporal placement within the 24-hour period of peak susceptibility was shifted gradually by abrupt inversion of the lighting regimen. Persistence of susceptibility rhythm in mice deprived of either food or water for up to 48 hours showed that these predictable and critical changes in physiologic state of the organism are not direct results of periodic food or water intake.

ELECTROLYTE BINDING IN ARTERY WALL. Verle E. Headings and Paul A. Rondell (intr. by Horace W. Davenport). Dept. of Physiol., Univ. of Michigan, Ann Arbor.

A sodium space greater than total hydration of artery wall has been reported from this laboratory (Fed. Proc. 118: 130, 1959). This observation indicates that part of the sodium of this tissue is non-ionized under physiologic conditions. As both hyaluronic acid and chonodroitin sulfate have been shown capable of binding cation in osmotically inactive form and since mucopolysaccharides are presumed and demonstrated components of arterial tissue, studies of the possibility of in situ cation binding by these compounds have been undertaken. As these substances have a low pK value they would be expected to act as polyanions with metal cations as the counterion at physiological pH and would be expected to bind such cations in inverse relation to the H-ion concentration. Analysis of pure medial fragments after 3 minute exposure to Krebs solutions adjusted with HCl or NaOH to various pH values (range pH 3 to pH 11) indicated an inverse relationship between Na content and H-ion concentration. The implications of this phenonemon in terms of tissue buffer mechanisms will be discussed. Further attempts to release bound sodium have been made by employing enzymatic degredation of mucopolysaccharides. (Supported by a grant from the Michigan Heart Association.)

EXCITATION OF NON-CONDUCTING STRIATED MUSCLE. Gretchen Hebb* and F. J. M. Sichel. Dept. of Physiol. and Biophysics, Univ. of Vermont Coll. of Med., Burlington.

These experiments were done to determine whether the optimal angle for direct current excitation is the same in non-conducting as in conducting striated muscle. If the current target is different and differently oriented in the two cases it might be expected that the optimal angles would also be different. The threshold current strength as a function of the angle between the direction of the external field and the muscle's longitudinal axis was studied in frog sartorius muscles in both conditions. The usual duration of the rectangular shock was 3 msec although durations from 0.03 msec to 30 msec were studied. The muscles were made non-conducting by immersing them in K^+-enriched Ringer's solution (13-17mM/liter) or by use of procaine hydrochloride or of choline chloride Ringer's solution. Stable preparations were obtained with all these which responded for long periods, with complete recovery on returning to normal Ringer's solution. The criterion of conduction was the presence of a propagated action potential. Although the threshold is higher in non-conducting muscle the relation between threshold and the direction of the stimulating current is similar in both cases. It is concluded that the effect of the stimulus in both cases is either on the same structure or on similarly oriented structures. (Supported by a research grant, H-336, from the Natl. Heart Inst., PHS.)

GALACTOSE- AND XYLOSE-INDUCED CATARACTS IN RATS. Franklin W. Heggeness (intr. by W. O. Fenn). Dept. of Physiol. Univ. of Rochester Sch. of Med. and Dent., Rochester, N.Y.

There are known differences in the susceptibility of several strains of laboratory rats to galactose-induced cataract formation. The cataractogenic effect of D-xylose was studied in two strains of white rats, one resistant and the other relatively susceptible to the development of galactose cataracts. When fed a 60% galactose diet the resistant strain develops cataracts in 32 days. Galactose has been shown to depress bile volume flow in the susceptible strain of animals. No change in bile volume flow occurred in the resistant strain following administration of sufficient galactose to reduce flow in the susceptible strain. When this strain of rats was fed a 30% D-xylose or L-arabinose diet no cataractous changes were observed. In the relatively susceptible strain of rats, cataracts develop in 20 days when a 60% galactose diet is fed. Morphologic changes in the lens accompanied by the typical pre-cataractous modifications of electrolyte composition developed during the second week of feeding a 30% xylose diet. Usually lens appearance gradually returned to normal; in 30% of the animals unilateral cataracts developed. When fed a 15% xylose diet cataractous changes were present on the 18th day. Dietary L-arabinose and D-ribose were without effect on lens appearance or composition. The finding that susceptibility to galactose- and xylose-induced cataracts occurs in one but not the other strain suggests that the ultimate mechanism could be the same.

ORGANIZATION OF TACTILE DERMATOMES, C_1 THROUGH L_4, IN CAT. Javad Hekmatpaneh (intr. by W. I. Welker). Dept. Physiol., Univ. Wisconsin, Madison.

Early investigations of dermatomes in animals and man were made by anatomical dissections (Krause; Herringham; Bolk). Sherrington (1893-98) used physiological methods, by isolating single dorsal roots and mapping the skin areas of remaining sensibility as indicated by reflex movements induced by pinching the skin. In 1953 Kuhn published his findings on hindlimbs of cats and monkeys, obtained by recording electrical responses evoked in dorsal root filaments by stimuli applied to the skin. The present study extends Kuhn's work to the thoracic and cervical segments. Twenty-three cats were used. Recordings were made from filaments of all dorsal roots from C_1 through L_4, while afferent impulses were initiated by mechanical displacement of shortened hairs. For each filament, a continuous skin area was defined, consisting of a central area yielding maximal potentials and a fringe area producing weaker discharges. Each dermatome was determined by combining the results for all filaments of the related root. Extensive overlap was found for adjacent roots and filaments. Some dermatomes (C_1, C_2, C_6, T_1, T_2) failed to reach either one or both (dorsal and ventral) midlines. The results allow the sensory unit study of Puletti to be related to the dermatomes. (Aided by grant B-732 (C4), NINDB.)

PULMONARY HEMODYNAMICS DURING PNEUMOTHORAX. Allan Hemingway and Daniel H. Simmons. Dept. of Physiol., Univ. of California at Los Angeles.

Dogs anesthetized with Na pentobarbitol were subjected to pneumothorax of varying degrees, the insufflated pneumothorax air being a ration, usually 1.0, 2.0 or 3.0, of the functional residual capacity. The amount of lung collapse was measured by a closed circuit respiratory apparatus. Pulmonary arterial and venous pressures were measured by right and left heart catheterization and in some experiments right atrial and systemic arterial pressures were measured. In addition, respiratory minute volume tidal volume and oxygen consumption rate were measured. Cardiac output was determined by the direct Fick procedure. As the amount of insufflated pneumothorax air increased to deflate the lung pulmonary arteriol and venous pressure increased, cardiac output decreased and pulmonary vascular resistance increased, all progressively as the lung was collapsed. With a lung collapse of 85-90% caused by insufflatory air equal to 3 times the functional residual capacity pulmonary vascular resistance increased 4 to 8 times the control (no pneumothorax) value.

MEASUREMENT OF LUNG VOLUME. Claire J. Hemingway,* Allan Hemingway and Douglas G. Stuart*. Univ. of California at Los Angeles and San Fernando V. A. Hosp., San Fernando.

The residual volume is the volume of the lungs and airways after a forced expiration. It is approximately one to two liters in normal individuals but may increase to four to six liters in patients with pulmonary disease such as emphysema. The residual volume is

measured by first breathing air, then making a forced expiration and changing to oxygen breathing for a 7 minute period, and then reverting to air breathing. During the 7 minute oxygen breathing period the exhaled gas is collected, its volume measured and analyzed for nitrogen content. The nitrogen washed out of the lung is measured by this procedure and knowing the concentration of nitrogen in the pulmonary air during air breathing the lung volume can be computed. A connection is made for nitrogen eliminated from blood and tissues to pulmonary gas. In a student laboratory experiment, a nitrogen meter of the Lily type is used as a rapid gas analyzer for nitrogen. Expired gas is collected in a 120 liter spirometer. A special 5-way valve with a mouthpiece, two O_2 breathing arms and two air breathing arms is used for rapidly shifting the inspired gas from air to oxygen. A group of 8 students is divided into two teams of 4 students per team. Each member of the team is assigned a duty such as (1) operator of the spirometer, (2) recorder of data and calculator (3) nitrogen analyst and (4) subject whose lung volume is being measured. These duties are rotated. One nitrogen meter is used for the two teams and is set in a position between two cots (or two chairs) for the subjects. A member of the laboratory staff operates the nitrogen meter for the first determinations but students take over this duty later. This experiment illustrates (1) the principles involved in measurement of lung volume (2) the method of denitrogenation of lungs and tissues and (3) changes in lung tension of oxygen during changing from air to O_2 breathing. It has clinical significance and application in emphysema and oxygen therapy.

KINETICS OF CHROMIUM UPTAKE IN THE EHRLICH ASCITES TUMOR CELL. H. G. Hempling. Cornell Univ. Med. Coll., New York, N.Y.

The kinetics of chromium uptake have been studied in the Ehrlich ascites tumor cell, using $NaCr^{51}O_4$. The curve of uptake can be described by two components, an initial fast phase with an average half-time of twenty minutes and a slower component with an average half-time of one hundred fifteen minutes. More than eighty percent of the Cr^{51} remains firmly bound to the cell, since up to 10^4 times as much non-radioactive Cr in the environment does not exchange with the radioactive Cr of the cells. The rate of uptake and total amount both increase with decrease in pH in the range of 6.8 to 8.0. In the temperature range, 1°C to 37°C, total Cr^{51} uptake increases with temperature rise. The data are compatible with the hypothesis that the initial uptake represents the binding of Cr as the anion, in contrast to the passive movement of the anion into the cell, as postulated for the human erythrocyte.

FACTORS IN DESERT HEAT STRESS. Austin Henschel and Harold E. Hanson*. Environmental Protection Res. Div., QM R&E Command, Natick, Mass.

The study was designed to assess the relative roles of solar radiation, clothing and activity in the total heat stress experienced by heat acclimatized men exposed to desert conditions at Yuma, Arizona in July and August. Eight basic combinations of conditions

were used with each of the 16 subjects undergoing each combination four times. A randomized block design with replications was used. Comparisons were made between all 8 combinations of the following conditions: Sun and shade; nude and clothed; work and rest. The physiological variables used to assess the impact of two hours exposure were: total sweat production; evaporated sweat; pulse rate; rectal temperatures. Average environmental conditions during exposure: temperature 102°F, relative humidity 25%, wind 7 mph, solar radiation 886 Cal/m^2/hr. Work consisted of walking at 3 mph; clothing was standard Army desert uniform. On exposure to sun, irrespective of state of dress or level of energy expenditure, sweat production and evaporation were statistically significantly increased; rectal temperature and pulse rate were not changed. Wearing clothing with all combinations of work or exposure to sun decreased sweat production and evaporation with no change in rectal temperature or pulse rate. Work produced an increase in sweat production and evaporation, in rectal temperature and in pulse rate. The shade-clothed-rest combination resulted in the least physiological response and sun-nude-work combination in the greatest physiological response.

METHOD FOR ESTIMATING MUSCLE CONNECTIVE TISSUE ELECTROLYTE COMPOSITION. J. K. Herrington, A. A. Pandazi and D. P. Schleuter (intr. by A. F. Rieck). Dept. of Physiol., Marquette Univ. Sch. of Med., Milwaukee, Wisc.

In order to estimate and correct for the electrolytes which connective tissue contributes to those already present in whole muscle it is necessary to assume that muscle connective tissue has the same composition as tendon and to measure the electrolytes and collagenous nitrogen in whole muscle. The accuracy of this approach depends upon the validity of this assumption. This report is concerned with a way of procuring and determining the composition of muscle connective tissue. Muscle rapidly excised from etherized white rats was immersed in liquid nitrogen and lyophilized to dryness while frozen, thus avoiding diffusion of ions which occurs during conventional drying. The connective tissue was separated by selective sifting after the dry muscle was ground and pulverized. Non-sifted sample and samples which passed and did not pass meshes of 20, 40, 60, 80, 100 and 200 holes per inch were analyzed for Na, K, Mg, total N and NCN. The data were plotted as % CN vs Meq Na, K and Mg per Kg dried defatted sample. A regression equation was determined and the Na, K, and Mg concentrations in pure connective tissue and in muscle minus connective tissue were estimated from these equations. (Supported by Wisconsin Heart Association and U.S. Public Health Grant (1706-C).)

SUPPRESSION OF SWEATING IN A WATER BATH. B. A. Hertig,* M. L. Riedesel* and H. S. Belding. Dept. of Occupational Health, Graduate Sch. of Public Health, Univ. of Pittsburgh, Pittsburgh, Pa.

Observations were made of the sweating behavior of young men immersed to the neck in a well-stirred, controlled temperature

water bath. Sweat rates were determined at half hour intervals by correcting observed weight loss for water ingested and urine passed. Water absorption from the bath was small compared to sweating; in 4-hour control tests (30-33°C) uptake was observed to be 20 to 50 grams. In hot baths sweating declined markedly after reaching a maximum in the first hour. (Example: sweating for successive hours was 650, 420, 180 and 110 g/hr). No correlation of sweating with oral, rectal, or skin surface (bath) temperatures was observed. Whether the bath was hot for the first two hours (sweat glands active) or thermally neutral (sweat glands inactive), sweating during the last two hours in the hot bath was suppressed. Thus, fatigue of sweat glands from prior use was ruled out as a factor in the suppression. Gerking and Robinson (Am. J. Physiol., 147:370, 1946) observed a greater decline in rate of sweating during 6-hour exposures in humid air than in dry. In view of our findings, we suggest that this effect may be attributable to self-soaking with sweat in the humid environments. Apparently penetration of a small amount of water into the skin affects the sweating mechanism in some fundamental way. (Supported in part by NIH Research Grant #4347.)

MECHANISMS OF AUTOREGULATION IN BLOOD AND DEXTRAN PERFUSED KIDNEYS. Lerner B. Hinshaw, (intr. by Maurice B. Visscher). Dept. of Physiol., Univ. of Minnesota Med. Sch., Minneapolis.

Experiments were performed on isolated dog kidneys alternately perfused with blood and dextran. Renal artery pressure, tissue pressure, perfusate flow rate and vascular volume changes were measured as arterial pressures were progressively elevated. Increases in overall vascular resistance (RA/F) occurred in all dextran and blood perfused kidneys throughout the autoregulatory range. Increases in intraorgan vascular resistance (RA-TF/F) were observed in blood perfused kidneys, but were essentially absent in the same kidneys perfused with dextran. Relationships between tissue pressure and ureteral pressure were obtained in additional experiments in which the ureter was continuously clamped. It was found that the slopes of tissue pressure and ureter pressure, plotted against progressive rises in renal artery pressure, became increasingly divergent throughout the autoregulatory range. Results from these experiments suggest that (1) autoregulation of blood flow is brought about primarily by the combined effects of extravascular pressures within and without Bowman's capsule, but (2) an additional fraction of the total increase in resistance may be accounted for on the basis of changes in viscosity in the post-glomerular vascular bed.

MICROELECTRODE STUDIES OF POSSIBLE MECHANISMS OF ATRIOVENTRICULAR DELAY. Brian F. Hoffman and Paul F. Cranefield. Dept. of Physiol., State Univ. of New York, Downstate Medical Center, Brooklyn.

Records of transmembrane potentials of single fibers of the rabbit atrioventricular node show that much of the normal nodal delay occurs over a very short distance at the atrial margin of the node. This delay apparently results from conduction, which may be

decremental, at velocities as low as 0.02 m/sec in cells with low resting potential and slowly rising, small action potentials. Abnormal atrioventricular delay results either from further slowing of the action potential upstroke or from action potentials which arise late from graded depolarizations resembling local responses. Preparations of trabaeculae carnae of rabbit atrium and cat papillary muscles have been studied in solutions containing excess K^+, low Na^+, or both in order to study the type and magnitude of delay which can occur in plain cardiac muscle. Results indicate that no anatomical specialization is necessary for delays similar to that normally observed in the atrioventricular node. In contrast, a delay comparable to the maximum encountered in nodal fibers under abnormal conditions has been reproduced only at the junction of fibers with dissimilar action potentials, as at the junction of Purkinje fibers and ventricular muscle. In the presence of low Ca^{++}, retrograde transmission at the papillary-Purkinje fiber junction shows delays of this sort. (Supported in part by a grant from the American Heart Association.)

ELECTRICAL ACTIVITY OF THE ENTORHINAL CORTEX DURING CONDITIONED BEHAVIOR. J. E. Holmes* and W. R. Adey, Dept. of Anatomy, Sch. of Med., Univ. of California at Los Angeles.

Chronically implanted bipolar electrodes were used to study the entorhinal area of the temporal lobe in ten cats. The animals were trained in a delayed response test which involved walking a narrow bridge to a goal box. A slow 5 to 6 c.p.s. electrical rhythm was found to occur spontaneously in most of the animals and to be consistently associated with the act of walking to the goal box. With extinction of the conditioned response the electrical rhythm also tended to disappear. Electrical stimulation of the cortex at several frequencies did not interfere with behavior as long as seizure discharges were not produced. This 5 to 6 c.p.s. rhythm is similar to that observed by other workers in the hippocampus. The authors believe it is correlated with the attention and motivational aspects of the test situation. Further studies of its relationship to behavior are being undertaken. Simultaneous recordings from the globus pallidus in these animals show a rhythmical spindle-shaped discharge at 50 c.p.s. occurring during the test, seemingly related to the readiness to act.

QUANTITATIVE RELATIONSHIP BETWEEN PAIN DEVELOPMENT AND FATIGUE IN RHYTHMICALLY CONTRACTING ISCHEMIC HUMAN FOREARM. Bruno Horisberger (intr. by Simon Rodbard). Univ. of Buffalo Chronic Disease Res. Inst., Buffalo, N.Y.

When the blood supply to the forearm is arrested and recurrent gripping movements of the hand are carried out, localized pain develops. With further exercise, a sensation of numbness and fatigue demands the cessation of exercise. The periods necessary for the production of pain (T_P) or of fatigue (T_F) both decrease exponentially with increasing frequency of gripping movements. A plot of the reciprocal of the time before development of pain and of fatigue,

against frequency of gripping, results in a slightly sigmoidal curve that can be transformed into a straight line. The slope of this line is a measure of the rate of development of the pain factor and the fatigue factor. Statistical analysis demonstrates that these relations are constant for each individual tested. At frequencies between 20 and 40 per minute the difference between the number of movements necessary to produce fatigue and the number to produce pain becomes maximal, and T_F/T_P reaches its greatest value. Prolonged arrest of blood flow for 4 to 12 minutes prior to exercise does not alter the relation between T_F and T_P, nor does it recognizably expedite the onset of pain or fatigue. The close relation between the times of pain and of endurance in the rhythmically contracting ischemic forearm suggests that both are related to anaerobic metabolism of the working muscle. These results also suggest that the reaction producing pain and fatigue are reversible, even in the absence of oxygen.

INTRALUMINAL SMALL INTESTINAL PRESSURES IN MAN AS RECORDED BY A RADIOTELEMETERING CAPSULE. Lawrence Horowitz and John T. Farrar. (intr. by Henry D. Janowitz). Medical Service, Vet. Admin. Hosp., New York, and the Dept. of Med., Cornell Univ. Med. Coll., New York.

An ingested, pressure-sensitive radiotelemetering capsule has been used to detect and record small intestinal intraluminal pressure in twenty patients. These include: eleven normals, five patients with "functional" gastrointestinal complaints and no organic disease, three patients with ulcerative colitis and one patient with idiopathic steatorrhea. Continuous records of at least three hours duration were obtained in all patients and include both fasting and post-cibal periods. The pressure patterns observed grossly resemble records obtained by means of sensing devices attached to intestinal tubes. However, the so-called type III waves, noted by other investigators, were very infrequent in our normal patients. Approximately periodic occurrence of type III waves, at 2-3 minutes intervals was noted in those patients who had either diarrhea or abdominal discomfort during the study. A sustained increase in pressure with superimposed type I waves was noted to occur in two patients simultaneously with periumbilical pain. Long periods of apparent inactivity of the bowel alternated with periods of active pressure change. Great variation in the frequency and amplitude of wave forms was present during periods of activity. Recordings of several hours duration are therefore required for adequate interpretation.

SYMPATHETIC INFLUENCE ON MUSCLE SPINDLES. Carlton C. Hunt. Dept. of Physiol., Univ. of Utah, Salt Lake City.

Discharge from single afferent fibers from muscle spindles in hind limb muscles of cat were recorded in dorsal root filaments. Sympathetic efferent fibers were activated by tetanic stimulation of peripheral end of sympathetic chain in lumbar region. Motor fibers to the spindle were also isolated for stimulation in ventral root filaments. Upon prolonged sympathetic stimulation, the resting discharge frequency from a spindle receptor gradually increased by

about 25 per cent and shortly thereafter fell to zero. On cessation of sympathetic stimulation the discharge frequency could remain at zero then rather rapidly return to the control level. The duration of sympathetic stimulation required to produce this effect depended upon upon stimulation frequency. Minimal effective frequencies were as low as 2/sec. If sympathetic stimulation was reduced in duration the initial acceleration of frequency could be produced with only slight subsequent depression. During the period of silence following sympathetic stimulation, the receptor was responsive to muscle stretch and to stimulation of fusimotor fibers. The above effects occur in the tenuissimus muscle without circulation and therefore do not appear to be dependent on changes in blood flow.

RELATIONSHIP OF BLOOD pH AND GLYCOGEN STORES TO RECOVERY FROM HYPOTHERMIA. J. Hunter. Defence Res. Med. Lab., Toronto, Canada.

In the technique described by Andjus for the production of hypothermia the increased concentration of respiratory carbon dioxide in blood and respired air during cooling is essential for recovery. It has been demonstrated in the present study that a high cardiac glycogen is associated with recovery of rats from low body temperature associated with respiratory and cardiac arrest. With CO_2 induction an average value for cardiac glycogen is 0.59% at the point of cardiac arrest as compared with 0.19% for cardiac glycogen without CO_2 accumulation. The respiratory acidosis produces a blood pH of 6.7-6.8. The substitution of a metabolic for a respiratory acidosis is equally effective in producing high survival rates in hypothermic rats. A number of ammonium salts have been used with limited success. Intraperitoneal injection of acetazoleamide ("Diamox"), has been used successfully in place of external CO_2 accumulation. Cardiac and respiratory arrest in hypothermia after treatment with "Diamox" is tolerated for one half an hour with almost 100% recovery. For longer periods of hypothermia, recovery rates are higher than obtained with a CO_2 acidosis. The "Diamox" exerts a similar sparing effect on cardiac glycogen. The known pharmacology of "Diamox", the absence of local damage associated with its injection and the simple control of blood pH down to 6.8 by graded dosage seem to offer an ideal approach to controlled physiological studies at low body temperature.

GALVANIC SKIN RESPONSES PRODUCED BY STIMULATION OF LIMBIC CORTEX. Fabian Isamat (intr. by G. H. Wang). Dept. Physiol., Univ. Wisconsin, Madison.

The medial wall of the right cerebral hemisphere of the cat (under chloralose-urethane or Nembutal) was exposed surgically by removing the left hemisphere. The mesial surface was then explored systematically with a monopolar electrical stimulating electrode, the "indifferent" being clipped to the head holder. Twelve successful experiments were performed. Offner's transistorized electroencephalograph was used for recording the electrical potentials induced in the sweat glands of the pads of all four limbs. Responses of about one-third the amplitude of those produced reflexly by sciatic

nerve stimulation were evoked in the contralateral limbs and of slightly less amplitude in the ipsilateral limbs, on stimulation of the anterior limbic and infralimbic areas of the cortex, around and beneath the rostrum of the corpus callosum. Stimulation of other areas of the medial wall yielded no responses or very much smaller ones. The results support the view that the anterior limbic region is a cortical autonomic motor field. (Aided by National Paraplegia Foundation and grant B-1460, NINDB.)

EFFECT OF AMINOGUANIDINE INTRODUCED INTO THE INTESTINE AND GASTRIC POUCHES. A. C. Ivy, H. M. Janecek* and K. W. Liepins.* Dept. of Clinical Science, Univ. of Illinois, Chicago.

This study was designed to ascertain the site of the gastric secretory stimulating action of aminoguanidine (AG) given orally. In two dogs with a large Heidenhain pouch (40% of fundic mucosa) 50 cc of a 0.4% solution of AG as the base (12 mg/kg) in the form of the hydrochloride was introduced into the pouch and held there for 2 hr. Dog B in 11 tests showed no stimulation, whereas Dog L showed a slight stimulation -- appearance of free acid -- in 4 of 11 tests. Two dogs with a vagotomized pouch of the entire stomach were used to determine the effect of the introduction of AG into the intestine or into the pouch on gastric secretion. 50 cc of the solution introduced into the Heidenhain pouches above was introduced into the pouch of the entire stomach. Decided stimulation occurred each time. When 12 mg/kg of AG in 50 cc of saline was introduced into the intestine, the secretion of the pouch of the entire stomach was also stimulated. To determine the role that the pyloric mucosa plays will be ascertained by resecting the pyloric portion of the entire stomach pouches and repeating the tests and comparing the HCl before and after resection.

CHEMICAL PROPERTIES AND OCCURRENCE OF THE OLFACTORY PIGMENT. Richard T. Jackson (intr. by L. M. N. Bach). Loyola Univ. of New Orleans, La.

A yellow-brown pigment colors the olfactory tissue of most vertebrates. The chemical nature of the pigment is imperfectly known, but it has been implicated in a theory of olfactory stimulation. The fat-soluble pigment has been isolated from rabbits, dogs, and opossums. Fractionation of this olfactory pigment discloses the phosphatidic acid and lecithin fractions to contain all the pigment. Comparison of the properties of this pigment with other phospholipids leads the author to believe that the yellow-brown color is due to auto-oxidation products of phospholipid origin such as hydroperoxides, epoxides, and aldehydes. The degree of pigmentation could not be influenced by various nerve transections. Rabbits were subjected to unilateral transection of the cervical sympathetic, the ethmoidal and olfactory nerves. These procedures had no obvious effect on the degree of pigmentation. The degree of pigmentation varies slightly within a species and between species. The author could not distinguish between the epithelia of dog, cat, rabbit, rat, sheep, and calf on the basis of pigmentation. The epithelia of frogs, turtles,

and alligators is a less saturated yellow than the higher vertebrates. There was no difference in pigmentation between albino and pigmented rabbits and rats. The questionable relationship between albinism and anosmia may have another basis. Because the pigment is a mixed, unstable, oxidation product, histochemical localization should only be attempted with caution.

EFFECT OF HYPOXIA ON EXPERIMENTAL VENTRICULAR TACHYCARDIA. Eugene D. Jacobson and William Schiess (intr. by Gordon K. Moe). Dept. of Physiol. and Med., S.U.N.Y., Upstate Medical Center, Syracuse, N.Y.

It has been shown that hypoxia abolishes the "current of injury" of the electrocardiogram of a dog with a recent infarction. This effect of hypoxia has been attributed to a reduction in the oxygen-gradient existing between normal and damaged tissue. Infarction produced by coronary artery ligation (method of Harris) results in a high incidence of ventricular tachycardia in dogs. This study was undertaken to see what effect hypoxia would have on the arrhythmia. For this purpose 15 dogs were subjected to the Harris procedure. After 24 hours the animals were anesthetized and exposed to hypoxia (4 to 16% oxygen) for periods of 15 to 20 minutes. In about half the animals anesthesia caused an increase in the percentage of sinus beats. In these animals a stable ventricular arrhuthmia was re-established by administration of eserine or vagal stimulation. Gas mixtures containing 5 to 10% oxygen were found to increase the percentage of sinus beats occurring during ventricular tachycardia by at least three-fold in 14 of the 15 dogs (room air: mean 6.8% with S.D. of 1.8%; hypoxia mean 48.7% with S.D. of 6.6%; $t = .01$). Hypoxia also consistently elevated blood pressure. No regular effect on overall heart rate or pacemaker rate was noted. Gas mixtures with more than 10% oxygen were ineffective. Mixtures containing less than 5% oxygen were lethal, the most frequent result being ventricular fibrillation.

EFFECT OF INDUCED COLD TORPOR ON BLOOD COAGULATION OF PSEUDEMYS ELEGANS. F. A. Jacques,* X. J. Musacchia and D. H. Bowden.* Dept. of Biol. and Path., St. Louis Univ., St. Louis, Mo.

The effects of induced cold torpor on the blood coagulation of the turtle, Pseudemys elegans (Wied), were studied in 82 control and experimental animals. The clotting time of whole blood was significantly increased in the experimental animals kept at 2°C for periods of 2 to 6 months as compared with the control animals maintained at room temperature. An anticoagulant substance with the metachromatic staining properties of a mucopolysaccharide was extracted from the plasma of animals in both groups. The quantity of this substance was increased three fold in the group kept at low temperature. No correlation was found between the number of mast cells in the intestine and liver and the quantity of the metachromatic staining anticoagulant extracted from the plasma. Indications of seasonal factors, independent of cold exposure, were also noted. The conclusion was reached that the blood coagulation time is

prolonged in turtles exposed to cold and that an anticoagulant substance extracted from the plasma appeared to bear no relationship to the number of mast cells in the intestine and liver.

CAPACITY OF THE CHICKEN'S INTESTINE TO ABSORB CHOLESTEROL. J. M. Janecek,* R. Suzuki,* and A. C. Ivy. Dept. of Clinical Science, Univ. of Illinois, Chicago.

The capacity of the intestine to absorb cholesterol has been studied in man and the rat but not the chicken. Twelve cockerels 14 weeks of age were used. They weighed an average of 2100 gm during the period of the test. They were fed a synthetic diet (25% casein) known to yield good growth in chickens. The diet contained no cholesterol and 3% cottonseed oil which contained 260 mg/100 gm of digitonin precipitable sterol; so 80 gm of the diet contained 6.2 mg of phytosterol of which only 22% or 1.4 mg was absorbed. After preliminary tests it was found that all would eat 80 gm of the diet daily. To this amount cottonseed oil and/or cholesterol could be added. The feces were collected every 12 hours and stored in jars containing 95% alcohol during the last 5 days of each 9-day test period and then analyzed. Twelve test periods were conducted in which the following amounts of cholesterol were ingested daily: 0, 85, 280, 328, 440, 537, 550, 600, 680, 916, 920, and 1145 mg. The endogenous output of digitonin sterol was found to average 24 mg/day. The milligrams of cholesterol absorbed daily increased until 210 mg/day of dietary cholesterol were absorbed. This amount approximately was absorbed when the dietary intake was 916, 920 and 1145 mg/day.

BLOOD PLASMA AND AQUEOUS HUMOR SUGAR LEVELS DURING GLUCOSE AND GALACTOSE TOLERANCE TESTS. Ralph G. Janes, Nadine K. Johnson* and Norman D. Paul.* Dept. of Anatomy, State Univ. of Iowa, Iowa City.

Adult rabbits which were fasted for 15 hours were fed 2 gm of glucose or galactose /kg body weight. In animals fed galactose the galactose was separated from glucose by glucose oxidase. Plasma sugar levels were determined at 0, 1/2, 1, 2, 3 and 5 hours. Aqueous humor sugar levels were determined for one eye at 0 and 3 hours and for the other eye at 1 and 5 hours. The maximum elevation of plasma sugar in the glucose-fed animals was found in one hour, but the aqueous sugar values were lower than those of plasma. At 3 and 5 hours the plasma glucose levels approached their control level but the aqueous sugar levels declined more slowly and were higher than the plasma sugar levels. The maximum elevation of galactose, in the galactose-fed rabbits was found at 2 hours in the plasma and 3 hours in the aqueous. Moreover, the plasma and aqueous galactose levels were quite similar at 3 and 5 hours. There was some galactose present in the aqueous and plasma 5 hours after this material was fed. (Supported by grant B-237 USPHS.)

RESTORATION OF RESPIRATION BY NERVE ANOSTOMOSES. N. C. Jefferson,* T. Ogawa,* C. Syleos* and H. Necheles. Dept. of Gastrointestinal Research, Med. Res. Inst. of Michael Reese Hosp., Chicago, Ill.

We have reported at these meetings the trophic effect of anastomosis of the peripheral end of a phrenic nerve with other nerves. Restoration of diaphragmatic respiration did not occur with vagophrenic anastomosis below the recurrent laryngeal nerve. With anastomosis of intercostal nerves and the long thoracic nerve to the distal phrenic, normal respiratory motion of the diaphragm appeared 5 and 6 months respectively after establishment of the anastomosis. We conclude that auxiliary respiratory nerves are able to relay respiratory impulses from the medullar centers to the diaphragm. This is supported by Guth's work, who obtained restoration of diaphragmatic function following anastomosis of the vagus above the recurrent lanyngeal nerve with the distal phrenic nerve. The pathway of conduction of respiratory impulses via intercostal-phrenic anastomosis was interrupted following section of the spinal cord at C4-5. (Supported by USPHS Grants.)

SEARCH FOR FACTORS AFFECTING GASTRIC SECRETION IN THORACIC DUCT LYMPH. Ivan D. A. Johnston* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

These experiments were designed to determine if lymph carries factors which control gastric secretion. The thoracic duct of dogs was annulated by means of surgical technics. When the dogs had recovered, lymph was collected during stimulation of gastric secretion by a standard meal. In some tests the gastric secretory response to the meal was inhibited by placing fat in the stomach. Lymph taken at night during rest was also examined. The samples were tested on the day of collection by intravenous injection into dogs with vagally innervated and denervated gastric pouches secreting at low rates in response to histamine. About half of the samples inhibited gastric secretion. The rest of the samples produced transient stimulation or showed no effect. Reactions were noted in about a third of the animals which had inhibition. Inhibitory and stimulatory factors were present as often in lymph taken while resting as in post-cibal lymph. Although inhibition was present more frequently in lymph collected after a fatty meal, it was not present in all such samples. Samples of lymph after fatty meals were separated into fat and fat-free portions by high-speed centrifugation at 0° C. The fat fractions usually stimulated gastric secretion slightly while the nonfat fractions carried the inhibitory factor when it was present. The presence of an inhibitory factor in the lymph has not been found to correlate consistently with any physiologic event or sequence. (Supported in part by research grant No. G-6207 NSF.)

COMPARISON OF THE PLASMA PROTEIN BOUND IODINE CONCENTRATION OF MALE AND FEMALE RATS. Sanford L. Jones* and L. Van Middlesworth. Dept. of Physiol., Univ. of Tennessee, Memphis.

Albino male and female rats were fed a "low residue" diet which contained casein, sucrose, corn starch, cotton seed oil and an

adequate vitamin and mineral mixture. The thyroid glands were blocked with 0.03% propylthiouracil which was added daily to the diet (5 mg/16 gm diet). Each day, during 14 days, they were injected with a fixed volume of sodium I^{131} L-thyroxine stock solution (0.35 μc/μg thyroxine). The thyroxine dose was calculated to be 0.6 μg L-thyroxine per 100 gm final body weight for both male and female rats. Within eight days, the total daily excretion of I^{131} was 90% of the daily injected dose of I^{131}. The excretion of urinary and fecal I^{131}, at equilibrium, was the same in male and female rats. The concentration of plasma PBI of four male rats was compared with that of four females. The males had a PBI of 5.2 ± 0.59 μg%, which was significantly greater ($P < 0.01$) than that of the female rats which had a PBI of 3.2 ± 0.78 ug%. Thyroid enlargement was similar in both males and females. The thyroid size of the males was 18.3 ± 2.5 mg per 100 gm body weight and that of the females was 21.2 ± 6.5. Additional PBI determinations were observed in male and female rats maintained daily on 2.5 and 5.0 μg of L-thyroxine. Eight males and eight females were used at each dose level. The plasma PBI of the females was lower than that of the males on all comparable determinations.

REPRODUCIBLE, MAINTAINED GRADIENTS OF CO_2 TENSION BETWEEN URINE AND PLASMA DURING FORMATION OF ACIDIC URINE. J. T. Kaim,* L. L. Cohen* and W. A. Brodsky. Dept. of Med, Univ. of Louisville Med. Sch., Dept. of Chem., Graduate Sch., Univ. of Louisville, Louisville, Ky.

Anesthetized dogs, under conditions of loading with NaH_2PO_4 (plasma P maintained at 3 mM/L), and of inhalation of 15% CO_2, produced urine of pH 5.1 to 6.1, and of CO_2 content 2.5 to 6.5 mM/L. Urine, collected through ureteral catheters, was maintained at flow rates of 1-3 ml/min/kidney by underlying infusion of mannitol. Plasma levels of pH and CO_2 content were 6.8-6.9 and 28-29 mM/L respectively. CO_2 tension of urine was less than that of plasma by 30 to 90 mm. of mercury in 6 successive experiments covering 37 periods of observation. Addition of large amounts of carbonic anhydrase to urine by I.V. injection did not affect magnitude of gradients. If anything, enzyme may have increased the magnitude of CO_2 tension gradients. In all but one case, tonometric determinations of α (CO_2) and of pKa were made on aliquots of urine and plasma. If there are no gradients of pCO_2 in papillary interstitial fluid, the finding of urine $pCO_2 <$ plasma pCO_2 is compatible with distal reabsorption of bicarbonate ion as such. Such a gradient is not compatible with secretion of acid into a tubule with CO_2 - permeable walls, if interstitial fluid pCO_2 in cortex is the same as that in papilla.

RELATION OF LENGTH AND TENSION TO RELAXATION IN TWITCH RESPONSE OF RAT'S TRICEPS SURAE. Donald B. Katz* and Sheppard M. Walker. Dept. of Physiol., Univ. of Louisville Sch. of Med., Louisville, Ky.

Rats, anesthetized with 275 mg of sodium barbital/kg of body weight, were used in a series of length-tension experiments. The

muscle was left in situ and the distal tendon was connected to an isometric lever. At the point of the muscle origin, the femur was fixed by means of a muscle clamp and drill. The muscle was stimulated indirectly through the sciatic nerve, and an isometric twitch response was obtained. The stimulation was applied 30 seconds after each stretch. The contractions were recorded optically. The greatest amount of developed twitch tension occurred at approximately 110% of resting length. At muscle lengths of less than 110%, the muscle relaxed completely during the twitch response. At greater lengths, the muscle failed to relax completely in the same unit of time. For example, at 139 msec after the beginning of twitch response, the muscle at 104.7% resting length was relaxed completely; at 110.4% resting length, it was 98% relaxed; and at 123.7% resting length, it was 36% relaxed. At resting lengths of 104.7%, 110.4%, and 123.7%, the maximum developed tensions were 440, 520, and 160 grams, respectively. (Supported in part by grant H-697(C9) from the Natl. Heart Inst., USPHS, and an American Heart Association grant.)

DEGLUTITION RESPONSES IN THE GASTROESOPHAGEAL SPHINCTER. Maurice L. Kelley, Jr.,* Dwight L. Wilbur, III,* Jerry F. Schlegel* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The pressure changes in the gastroesophageal sphincteric zone of healthy persons during deglutition were detected by means of a balloon-covered differential transformer pressure transducer and two lateral orifice water-filled polyethylene tubes attached to transducers placed extracorporeally. The balloon was 5 by 5 mm and contained 0.06 ml of water. The pressure detecting units were passed into the stomachs of 12 healthy persons and the resting pressures of the sphincteric zones were recorded during the step-wise withdrawal of the units. The withdrawal was then repeated and the persons were asked to swallow at each 0.5 cm "station." The pressures detected by the balloon-transducer were similar in "profile" to those detected by the lateral orifice tubes, but as a rule they were double to eight times greater in magnitude. In the subhiatal segments of the sphincter, relaxation, producing a decline in pressure below the resting sphincteric tone, was the most prominent change with deglutition. The degree of relaxation was greatest at the hiatus. After relaxation, the sphincter contracted and produced a pressure greater than the resting sphincteric pressure. Relaxation became progressively less prominent as the units were withdrawn through the suprahiatal portion of the sphincter, while the contractions became more powerful. The responses to swallowing were detected in the upper portions of the sphincter earlier in the sequence of deglutition than in the inferior segments, which indicated a peristaltic progression of the response in the gastroesophageal sphincter. (Supported in part by research grant No. A-2015 USPHS.)

EFFECTS OF HIGH INTENSITY ULTRASOUND ON THE MECHANICAL RESPONSE OF EXCISED BICEPS MUSCLE OF THE FROG. Elizabeth Kelly,* Francis J. Fry* and William J. Fry. Biophysical Res. Lab., Dept. of Electrical Engineering, Univ. of Illinois, Urbana.

Instrumentation has been designed for the application of high intensity ultrasound (over 100 watts/cm^2) to the excised biceps muscle of the frog. The primary objective of this research is to use the ultrasound as an investigative tool for elucidating some of the primary mechanisms of muscle contraction. Recent investigations have been concerned with the effects produced by variation in the temperature of a portion of muscle (particularly in the range above 20°C) by the sound field. In addition, direct effects of the sound field itself, apart from those induced by temperature, are under investigation. The muscle is stimulated by a series of electrodes inserted completely through the muscle tissue. These electrodes have been specifically designed to eliminate possible artifacts caused by the presence of a high intensity ultrasonic field. Present observations are being made on the effect of the sound on the isometric twitch tension. A thermocouple probe is inserted through the muscle and simultaneous records are made of twitch tension and temperature before, during and immediately following the application of the sound. The characteristics of the sound field are determined with a precision thermocouple designed for accurate determination of sound level and beam configuration.

CHARACTERISTICS OF DIFFUSION COEFFICIENT FOR OXYGEN IN SOLUTION. Albert F. Kelso* and Clarence N. Peiss. Dept. of Physiol., Chicago Coll. of Osteopathy and Loyola Stritch Sch. of Med., Chicago, Ill.

Various biological applications of the diffusion coefficient for oxygen require corrections for variations in temperature and viscosity. In addition these applications assume that the coefficient is independent of concentration. A diffusion chamber has been designed which makes it possible to follow the variation in the oxygen gradient with time during free diffusion. The gradient is established on the basis of multiple determinations of oxygen concentration by polarographic analysis. The characteristics of the diffusion coefficient will be established from analysis of the changes in the gradient with time. A tentative value of 2.36×10^{-5} $cm^2 sec^{-1}$ has been established for the diffusion coefficient in 0.9% saline at 25°C for a space gradient of one milliliter of oxygen per centimeter. The temperature coefficient and influence of viscosity are being investigated and will be reported. In addition the data will be evaluated for the dependence of the diffusion coefficient upon concentration.

EXTRACALLOSAL INTERHEMISPHERIC CONNECTIONS. Thelma T. Kennedy* and L. T. Rutledge. Dept. of Physiol. and Biophysics, Univ. of Washington, Seattle.

The transcallosal response (TCR) is a well-established phenomenon and is a likely basis for much interhemispheric organization. however, the existence of interrelations between cortical and sub-

cortical activity and the difficulty of identifying specific deficits after corpus callosum section has led to a search for possible extracallosal (and extracommissural) links between the cerebral hemispheres. Cats were anesthetized with chloralose and paralyzed, the cerebral cortex exposed and maintained under oil. Single shocks of 0.1 msec duration were delivered via bipolar electrodes to a point on one hemisphere while monopolar recordings were oscillographically made contralaterally. At stimulus intensities which evoke a maximum TCR, a delayed potential follows the TCR. This is generally a triphasic complex with a prominent positive component which peaks at 65-95 msec. The delayed response survives acute or chronic callosal section, is abolished quickly by small doses of barbiturates, is very sensitive to asphyxia, follows stimulus frequencies of only 4/sec or less, and tends to be labile, often waxing and waning. The response can be blocked by peripheral auditory or photic stimulation; however, habituation to a specific stimulus readily occurs. This interhemispheric delayed response is believed to result from subcortical transmission via a multisynaptic system. Similar intrahemispheric responses have been demonstrated also. (Supported by grant 2-B-5082 from the National Institute of Neurological Diseases and Blindness, and Senior Research Fellowship SF-122 from the Public Health Service.)

REDUCTION OF CHLORIDE EXCRETION BY ARTIFICIALLY LOWERING THE CHLORIDE CONCENTRATION OF THE RENAL PAPILLA. Richard H. Kessler. Dept. of Physiol., Cornell Univ. Med. Coll., New York, N.Y.

According to the countercurrent hypothesis urine tonicity depends in large part on the degree of osmotic equilibrium of collecting duct fluid with the hypertonic interstitium of the papilla. Tissue hypertonicity is presumably achieved by extrusion of filtered salt from the ascending limb of Henle's loop into the interstitium. One suggested role of ADH is that of regulating water permeability of collecting duct epithelium. Under conditions of water deprivation ADH would facilitate water movement from collecting duct to the hypertonic papilla with a resultant hypertonic urine. Support for this hypothesis is offered in the experiments to be reported. These studies make use of the observations that ureteral clamping curtails glomerular filtration while renal blood flow continues unimpared. Hence, the filtered load of sodium chloride, from which the papillary store is derived, is reduced. Continued blood flow reduces the existing store of salt within the papilla. The chloride content of papillary tissues obtained from dog kidneys subsequent to several minutes of ureteral clamping were compared to those from the opposite kidney. In saline loaded animals stasis uniformly lowered tissue chloride with the production of urine lower in chloride content and less hypertonic than that of the contralateral side. These alterations in tissue and urinary chloride were minimized following urinary stasis in mannitol loaded animals. During water diuresis urinary stasis did not alter urinary composition.

ELECTRICAL RESPONSES OF THE AUDITORY NERVE TO REPETITIVE ACOUSTIC STIMULI. N. Y. S. Kiang, W. T. Peake and M. H. Goldstein, Jr. (intr. by S. S. Stevens). Research Lab. of Electronics, Mass. Inst. of Tech. and Eaton-Peabody Lab. of Auditory Physiol., Mass. Eye and Ear Infirmary.

Auditory nerve responses in both anesthetized and unanesthetized cats have been studied as a function of the repetition rate of acoustic stimuli. (Sinusoids, clicks, and bursts of noise.) Steady-state responses were recorded from gross electrodes located near the round window of the cochlea and in the eighth nerve. To eliminate background activity and cancel microphonic potentials, an averaging device was used. For moderate stimulus intensities the size of the neural responses decreases as the repetition rate is increased above 10/second. Stimulus-locked activity becomes progressively smaller until it is undetectable, by our methods, at rates near 3000/second. Curves of response amplitude vs. frequency do not show the "staircase" shape reported by Derbyshire and Davis (1935) for tonal stimuli. In cats with denervated cochleas microphonic potentials for repeated clicks are independent of rate, as long as the individual responses do not overlap (for rates up to 700/second). (Supported in part by the U.S. Army (Signal Corps), the U.S. Air Force (Office of Scientific Research, Air Research and Development Command), the U.S. Navy (Office of Naval Research), and research grant B-1344, National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service.)

CARDIOVASCULAR EFFECTS OF AET. David H. Knott (intr. by R. R. Overman). Inst. of Clinical Investigation, Univ. of Tennessee, Memphis.

The cardiovascular effects of the radioprotective compound AET (S-2 aminoethylisothiuronium Br·H Br) were investigated in anesthetized and unanesthetized dogs at various slow intravenous infusion rates. The rates used were 3, 6, and 10 milligrams of AET per kilogram of body weight per minute. Each experiment was terminal, and an inverse relationship was found between the total body concentration of AET causing death and the intravenous infusion rate. There was a marked and consistent rise in systolic, diastolic, and mean blood pressures. Commonly bigeminal and in some cases trigeminal pulse pressure curves were noted. It appeared that AET acted as a peripheral vasoconstrictor. Abnormal electrocardiographic patterns invariably occurred consisting usually of an augmented T-wave, inverted T-wave, and a profound depression of the S-wave. Tachycardia appeared and persisted at every infusion rate. In addition to these variables, cardiac output, circulation time, peripheral resistance, central blood volume and other hemodynamic parameters will be discussed. Studies were made of rapid intra-arterial and intravenous injections of AET to gain insight into the comparative response evoked by rapid administration of protective doses of AET and slow intravenous infusions of this compound.

EFFECT OF OUABAIN ON RENAL POTASSIUM SECRETION. Alan Koch (intr. by J. W. Woodbury). Dept. of Physiol and Biophysics, Univ. of Washington Sch. of Med., Seattle.

Previously reported experiments have indicated that the cardiac glycosides are potent inhibitors of renal Na^+ reabsorption. Because of the known actions of these agents in inhibiting a coupled Na^+-K^+ ion pump and because the renal action of glycosides can be antagonized by elevation of plasma K^+, it has been postulated that a coupled Na^+ - K^+ pump is responsible for renal reabsorption of Na^+ and, secondarily, Cl^-. Such a mechanism would also be expected to be involved in renal K^+ secretion and the present series of experiments shows this to be the case. Experiments were conducted on anesthetized dogs in which the rate of K^+ excretion was initially high. After ouabain, the rate of K^+ excretion fell sharply, despite increases in the rates of both Na^+ and HCO_3^- excretion, and an elevation in plasma K^+. In a representative experiment, K^+ excretion fell from 230 μEq/min to 70 μEq/min within 10 minutes after the administration of 0.13 mgm/kg ouabain. It is concluded that a coupled Na^+-K^+ transport system is responsible both for active Na^+ reabsorption with associated passive Cl^- reabsorption and active K^+ secretion. Tenuous calculations of the transtubular potential based on K^+ concentrations in urine and plasma, suggest that the transtubular potential is reduced by cardiac glycosides. (Aided by support from grant B1752 from the National Institutes of Health and by grant HTS5204 from the National Institutes of Health.)

STEROID HORMONE LIKE ACTION OF BETA GLYCYRRHETINIC ACID. Shirley D. Kraus (intr. by B. B. Blivaiss). Pharm. Dept., Brooklyn Coll. of Pharmacy, Brooklyn, N.Y.

Salt and water retention induced by crude licorice extract has been attributed to glycyrrhizinic acid and its aglycone glycyrrhetinic acid. Glycyrrhetinic acid is a triterpene resembling the stereochemistry of allopregnane and having a double bond at $\Delta 12$ and a ketonic oxygen at C11. It was the aim of this investigation to study an isomer of glycyrrhetinic acid in respect to actions attributed to steroids containing an alpha beta unsaturated ketonic group (testosterone, progesterone, adrenal corticoids) in an effort to elucidate fundamental physiological mechanisms. In a study of the uterotrophic response to exogenous estrogen in immature rats, beta glycyrrhetinic acid was observed to antagonize estrogen at the target organ site. Doses which restricted the uterotrophic response did not antagonize the estrogenic effect on pituitary-trophic hormones, nor influence somatic growth or gonadal size. A comparison of dose response curves of estradiol benzoate with and without glycyrrhetinic acid indicated that a total dose of 6 mg reduced the potency of estradiol benzoate to .53 .05. Beta glycyrrhetinic acid had no estrogenic, androgenic nor anti-androgenic action. However, it depressed granuloma formation in adrenalectomized rats (cotton pellet technique). Beta glycyrrhetinic acid therefore resembles naturally occurring steroids in both estrogen antagonism and anti-inflammatory action. It may prove to be a valuable tool in correlating structural specificity with specificity of steroid action.

RETICULAR FORMATION POTENTIALS CORRELATED WITH EYE MOVEMENTS. H. P. Krieger and F. Proctor. Dept. of Neurology, Mt. Sinai Hosp., N.Y.C., N.Y.

Electrophysiologic relationships between the vestibular complex and that part of the reticular formation lying just below the median longitudinal fasciculus have been demonstrated (Feldman, Wagman and Bender). The present study shows that action potentials recorded from this part of the feline reticular formation can be correlated with eye movements. Correlation was achieved by studying evoked potentials at points in this formation from which eye movements were elicited by electric stimulation. These potentials were evoked by electric stimulation within the brain stem oculomotor system or vestibular complex or by stimulation of the vestibular end organ. The area from which both movements and potentials were elicited was sharply delimited in the dorsoventral and transverse planes. Stimulation of the paramedian region evoked potentials in the nerve to the inferior oblique muscle. Antidromic stimulation of this nerve activated the third nerve nucleus but not the paramedian zone. Single threshold stimuli to the vestibular complex or oculomotor points in the paramedian zone evoked single potentials without concomitant eye movements. Repetitive stimuli of frequencies greater than c. 100/sec elicited eye movements accompanied by potentials equal in frequency and duration to the stimulus. In contrast, during induced nystagmus rhythmic potentials which outlasted the stimulus were observed. Evidence of self-sustained electrical activity was not otherwise noted.

METABOLISM OF LEUKOCYTES IN THE EUTHYROID AND HYPERTHYROID STATE. M. S. Krotkov,* G. S. Kurland* and A. S. Freedberg, Beth Israel Hosp. and the Harvard Med. Sch., Boston, Mass.

Leukocyte oxygen uptake and thyroxine metabolism has been studied in various thyroid states in the human, guinea pig and dog. Polymorphonuclear leukocytes were isolated from the blood of the human and dog using dextran and sequestrene as an anticoagulant, and from peritoneal exudates of the guinea pig. The washed leukocytes were homogenized and incubated with various cofactors and thyroxine labelled with I-131. Oxygen uptake was measured by the direct method of Warburg. The incubated homogenate was chromatographed on paper in various solvents with added carriers; the dried strips were scanned with a GM tube, and the zones of radioactivity were quantitated by planimetry. The oxygen uptake of leukocytes from all three species was increased in the hyperthyroid state. The O_2 uptake of human leukocytes increased from 0.334 ± 0.1 S.D. to 0.444 ± 0.15 S.D. $\mu l\ O_2/10^6$ cells/hour. The human and guinea pig leukocyte has been found to possess a thyroxine deiodinase. Other than iodide, no thyroxine metabolite has been found. Human leukocyte thyroxine deiodinase activity as measured by the iodide formed as a per cent of total radioactivity on the paper strip was increased in hyperthyroidism. The per cent iodide formed by leukocytes from euthyroid females was 19 ± 11 S.D., from euthyroid males 28 ± 11 S.D., from hyperthyroid females 44 ± 15 S.D. While the complete

guinea pig leukocyte homogenate shows no deiodination of thyroxine, a particulate fraction (spun at 8,500 G) has been demonstrated to have the deiodinating activity. (Supported by USPHS A-1843.)

LEAD SELECTION FOR ELECTROCARDIOGRAMS OF BEEF CATTLE. Hugo Krueger and W. C. Van Arsdell III.* Dept. of Dairy and Animal Husbandry, Oregon State Coll., Corvallis.

The choice of planes for studying electrocardiograms depends on experience, anatomical considerations and geometrical configurations. A mid-sagittal or M plane has been placed through the interscapular space, the dorsal lumbosacral border, and the mid region of the sterum. A second or L plane has been placed through the insertions of the right forelimb, left forelimb and left rear limb. A third or S plane has been placed through the dorsal prescapular region, and the right forelimb and the left forelimb insertions. The limb leads were chosen partly on analogy with the important frontal or limb lead plane in man, and partly because experience indicated that the limb leads of cattle, although yielding electrocardiographic complexes difficult to interpret and analyze by themselves, provided valuable information in determining the QRS axis. A semisagittal (SS) plane was envisioned through the prescapular space, the left forelimb and the left hind limb. For many 500-800 pound calves the QRS axis lies in or very near the semisagittal plane and maximum potentials are frequently recorded in leads of the semisagittal plane, and a maximum QRS component is frequently obtained. In the E calves there was a greater variability in leg lead potentials recorded from calf to calf than were found in the scapular lead potentials.

EFFECT OF ACTH AND ALDOSTERONE ON SODIUM AND POTASSIUM OF RAT SALIVARY GLANDS. L. L. Langley and W. A. Beall.* Univ. of Alabama Sch. of Dent., Birmingham.

The infusion of ACTH into a dog actively salivating evokes an increase in the rate of flow from the parotid gland with an augmented sodium concentration and a decreased potassium concentration (Langley, Beall, and Smith, Am. J. Physiol. in press). Others have reported that the chronic administration of the adrenal steroids lowers the sodium and raises the potassium concentration of periodically sampled saliva. It was thought that these opposing results might be explained by the effect of chronic administration of the adrenal steroids on the electrolyte composition of the salivary gland. Accordingly, parotid and submaxillary glands were analyzed in three groups of rats: 1) controls, 2) ACTH (2 units twice daily), and 3) aldosterone (5 μg twice daily). Aldosterone, but not ACTH, was found to influence the sodium concentration. In both the parotid and submaxillary glands the sodium concentration was significantly lowered. ACTH exerted its greatest effect on potassium, especially in the submaxillary gland in which it was significantly elevated. Aldosterone also elevated the potassium concentration in the submaxillary gland, but had much less influence over the parotid. There was no change in the water content. In view of the fact that the composition of the glands of the saliva has been shown to reflect that of the gland

it is concluded that the influence of the chronic administration of adrenal steroids may be explicable on the basis of altered electrolyte composition in the gland. (Supported by NIH Grant D-329(C2).)

EFFECT OF SUCROSE DIET ON CHOLATE EXCRETION IN RATS. Cheng-Chun Lee. The Lilly Research Laboratories, Indianapolis, Ind.

We have reported (Lee and Herrmann, Circulation Research, 7: 354, 1959) that in rats a diet containing 65% sucrose with added cholesterol resulted in hypercholesteremia and increased cholesterol deposition in the liver and aorta. The addition of vitamin D aggravated these conditions. This report summarizes the effect of sucrose plus cholesterol and vitamin D on bile volume, biliary excretion of cholate, cholesterol and total solids, and on tissue cholesterol concentrations. Three groups of 6 female albino rats were fed Purina Laboratory Chow ad libitum for 2, 4, and 6 weeks, and 3 additional groups, a diet containing 65% sucrose, 2% cholesterol and 400 units of vitamin D/gm of diet. The sucrose diet decreased biliary excretion of total cholate, produced hypercholesteremia, and increased total cholesterol deposition in the liver. The bile volume and biliary excretion of total solids were not significantly affected. There was a slight increase in the biliary excretion of total cholesterol in rats fed the sucrose diet for 6 weeks. A modified procedure for cholate analysis in the bile will be discussed.

POST-EXERCISE HYPEREMIA IN THE CALF REGION OF THE LEG FOLLOWING A FATIGUING EXERCISE TO THE PLANTARFLEXORS OF THE FOOT. L. Don Lehmkuhl* and C. J. Imig. Dept. of Physiol., State Univ. of Iowa, Iowa City.

While it has been recognized for some time that an evaluation of resting blood flow provides little information concerning the status of the peripheral vascular bed in diseased states as compared with that of normal subjects, few attempts have been made to determine and express the adequacy of blood flow in quantitative units following a standardized stress, such as exercise. Normal subjects performed a rhythmic exercise which consisted of depressing a weighted foot pedal at the rate of 60 excursions per minute until fatigued. Blood flow was measured by means of venous occlusion plethysmography before and after various intensities of exercises, which resulted in different durations to fatigue. The data show no statistically significant differences in the maximum post-exercise hyperemias among the exercises employed. However, a more definite evaluation of the fatigue end point was evidenced with the more intense exercises. The average maximum blood flow in 50 normal subjects following a rapidly fatiguing exercise (1-5 minutes) was 27 ml/100/min, with recovery within approximately 25 minutes. The post-exercise blood flow in the right and left legs of normal subjects was similar. The pattern of the hyperemia following two successive fatiguing exercises during the same experiment and following two exercises performed on different days were also similar. These studies suggest that a rhythmic exercise of sufficient intensity so as to cause early fatigue may provide a suitable standardized stress for evaluation

of the status of the peripheral circulation. (Supported in part by Grant #H-2608, USPHS.)

I-131 SECRETIN. M. Levinson**, T. Ogawa* and H. Necheles. Dept. of Gastrointestinal Research, Med. Res. Inst. of Michael Reese Hosp., Chicago, Ill.

In our efforts to obtain better diagnostic means for pancreatic disease, we thought that a radioactive secretin compound would localize largely in the pancreas. Secretin Lilly was combined with I-131 by the Abbott Laboratories, using a procedure similar to that for RISA, by which most probably the ring of aromatic aminoacids in the secretin molecule is labeled. The labelled secretin was dialyzed and most of the free iodine removed. The solution contained appr. 5.5 mg secretin and -.9 microcurie I-131 p ml, ph 3 4, radio-chromatogram showed 92.5% iodinated secretin and 7.5% free iodine. Assay showed slightly less pancreatic secretion with the I-131 secretin than with unlabelled secretin. Normal dogs were given I-131 secretin i.v. and the whole animal and exposed or excised organs were scanned. Most activity was in liver, kidney, and urine. The pancreas showed little elevation above background. This finding pointed to a role of the liver in the secretin mechanism and led to work to be reported here by Necheles. (Supported by an Edwin F. Mandel fellowship.)

SOME FUNCTIONAL ASPECTS OF ACOUSTIC RESPONSES IN THE CEREBELLUM OF CAT. C. K. Levy,* J. R. Smythies* and W. P. Koella. Worcester Found. for Exper. Biol., Shrewsbury, Mass.

This study represents an attempt to elucidate some functional aspects of the cerebellar acoustic projection area. Acoustic evoked potentials were recorded from multiple loci on the vermal cortex of cats anesthetized with chloralose. The intensity and rate of acoustic stimuli were varied over a wide range. Under constant stimulus conditions the potentials showed a marked variability in amplitude and configuration at a given locus and between various loci. The response was usually composed of a biphasic main complex, the initial component of which was a positive spike followed by a negative wave usually of lesser amplitude. Often additional spikes were superimposed on both components of the main complex. In most cases an initial small positive deflection preceded the main complex. An increase in stimulation frequency at intermediate stimulus intensities reduced the main complex and late spikes until they disappeared completely at a cut off frequency of about 0.5 p.p.s. Barbiturates reversibly depressed the main complex of the response. Time/area mapping of the responses over the exposed vermal surface revealed a migration of electrical activity from Larsell's lobule VI to lobule VII. Ablation of Lobule VI failed to abolish the response or alter the latency, thus suggesting that the spread of activity was a function of the terminal afferent organization rather than a function of the intracortical connections.

EFFECT OF ORAL AMINOGUANIDINE ON GASTRIC SECRETION. K. W. Liepins (intr. by D. Nelson). Dept. Clinical Science, Univ. of Illinois, Chicago.

It is well established that aminoguanidine (AG) when given intravenously or subcutaneously stimulates gastric secretion in Heidenhain pouch dogs. In this study two Heidenhain pouch dogs, after suitable collection of the control basal secretion, were given orally by stomach tube 12 mg/kg of AG base as the hydrochloride in 50 cc of normal saline solution (pH 6.0). This test was repeated 10 times on each dog and the hourly outputs of HCl were averaged. The basal control output of Dog B was 0.3 mg/hr, and the total output for 4 hours after the AG was 44.3 mg. The basal control output of Dog L was 0.6 mg/hr, and the total output was 31.3 mg. When the hourly outputs of both dogs were combined and averaged, the hourly outputs were as follows: Basal 0.45 mg; after AG 1st hr, 13.5, 15.7, 5.3, 2.2 mg. In 5 tests on each dog, the introduction of 50 cc of "normal saline" (pH 6.0) into the stomach did not stimulate gastric secretion.

EFFECTS OF THAM ON METABOLIC ACIDOSIS INDUCED BY LACTIC ACID INFUSION. J.-C. Ligou* and G. G. Nahas. Walter Reed Army Inst. of Res., Washington, D.C.

The buffering of hypercapnic acidosis by 2-amino-2-hydroxymethyl 1-3 propanediol, (THAM), suggested that this compound would also be effective in acidosis due to accumulation of lactic acid (HLa). Six dogs were paralyzed with succinylcholine and ventilated at constant rate and volume with 100% O_2 throughout the experiments. They were given an intravenous infusion of .15 molar HLa at the rate of 2ml/kg/min for 30 minutes. In the following 30 minutes, 1 ml/kg/min of HLa was administered simultaneously with 0.5 ml/kg/min of a .3 molar solution of THAM. In the first 30 minutes pH fell from 7.40 ± 0.03 to 6.92 ± 0.05, $PaCO_2$ increased from 28 ± to 38 ± 4 mm Hg., and arterial blood lactate from 32 ± 8 to 144 ± mg %, arterial blood pressure from 147 ± 12 to 166 ± 18 mm Hg. Diuresis varied between 1 and 2.5 ml/min. In the second 30 minute period, pH rose from 6.92 to 7.35 ± 0.04, $PaCO_2$ fell to 28 mm Hg and blood lactate fell to 133 mg %. Blood pressure remained at 166 ± 14 mm Hg. Diuresis increased to 3.5-11 ml/min. In three experiments HLa infusion was not buffered by THAM, and all animals died of cardiovascular collapse when pH reached 6.40-6.52. One of them was resuscitated by cardiac massage and rapid infusion of .6 molar of THAM which restored pH to 7.30 in 5 minutes.

EFFECT OF INTRAVENOUS INFUSION OF HYPOTONIC DEXTROSE SOLUTION ON FLUX RATES ACROSS THE CANINE INTESTINAL MUCOSA. James F. Lind*, Charles F. Code and Alan L. Orvis.* Mayo Clinic and Mayo Foundation, Rochester, Minn.

Mongrel dogs with chronic Thiry-Vella loops of duodenum and ileum were used in the study. Under pentobarbital anesthesia, a 2.5 per cent solution of dextrose was infused intravenously, while a constant body temperature was maintained by external application of heat. Tests of absorption were made at designated intervals

before, during and after the infusion. A modified Tyrode's solution containing isotopic water (D_2O) and sodium (Na^{22}) was placed in the gut. Changes in the concentration of isotopic water and sodium were determined with a mass spectrometer and a well-type scintillating counter, respectively. Changes in the osmolality and sodium concentration of arterial plasma and of the test solution were determined by means of a Fiske osmometer and direct-reading flame photometer. The flux rates for sodium and water were calculated according to the method of Visscher. In both the duodenum and ileum the mean rates of insorption and exsorption of water were increased during and after infusion. In the duodenum, the mean net absorption of water was increased despite an adverse osmotic gradient, while in the ileum the net absorption of water was decreased. In the duodenum, the movement of sodium was in accordance with the concentration gradient across the mucosal membrane, insorption and net absorption both being increased. In the ileum, the rate of insorption of sodium was decreased despite the concentration gradient, but the changes in exsorption and net transfer were variable. (Supported in part by research grant No. A-2827, USPHS.)

PULMONARY HEMODYNAMICS DURING POSITIVE PRESSURE BREATHING. L. M. Linde*, D. H. Simmons, J. H. Miller* and E. L. Ellman.* V.A. Center and Univ. of California Med. Center, Los Angeles.

Previous data indicating that positive pressure breathing (PPB) has no direct effect on pulmonary demodynamics was obtained from isolated lungs or incomplete data on intact animals. The present study furnishes additional data on the intact animal. Measurements were made on 8 anesthetized dogs during spontaneous breathing and during PPB (both on O_2) with a Starling pump set at the same respiratory rate and tidal volume. Pulmonary vascular resistance (PVR) was calculated from dye-dilution cardiac outputs (CO) determined in duplicate using indocyanine green, and the pulmonary vascular pressure gradient (PVPG) from artery to vein was measured with cardiac catheters and a differential pressure transducer. Effective distending pressures of the artery and vein were similarly determined against intrapleural pressure. With PPB, mean CO dropped significantly from 97 to 79 ml/min/kg, a response previously reported and presumably due to an increase of 3.4 cm H_2O in intrathoracic pressure and decreased venous return. Mean PVPG also dropped from 11.0 to 8.7 cm H_2O. As a result, there was a minimal decrease in PVR from 117 to 113 units. Absolute pressures in both pulmonary artery and vein rose, but their effective distending pressures did not change significantly (19.8 to 18.1 and 7.6 to 11.6). These data indicate that PPB under these conditions has no significant influence on pulmonary hemodynamics except for the systemic effect of decreased CO, which in turn has relatively little influence on PVR in contrast to the effect of increased CO.

EFFECT OF THYROXIN ON RAT LIVER COPPER CONCENTRATIONS. H. J. Lipner, W. F. Chapman* and Mary Muntz.* Div. of Physiol., Dept. of Biol. Sciences, Florida State Univ. Tallahassee.

The in vitro interaction of thyroxin with copper ions is well established; however, an in vivo relationship has as yet not been reported. We have found that the concentration of copper in rat liver, kidney and heart is inversely related to the oxygen consumption of these tissues. The tissue of intact, athyroid or athyroid-thyroxin treated rats were analyzed for their calcium, magnesium, zinc and copper content. The only mineral whose concentration consistently changed with thyroid status was copper. Completeness of thyroidectomy was checked by I-131 uptake in the neck region and terminally by radioautographs. Oxygen consumption of liver homogenates from hyperthyroid rats was more sensitive to 2,9-dimethyl-1,10-phenanthroline than was that of the liver homogenates of hypothyroid rats. These observations suggest that copper may play an important role in cellular metabolism and that thyroxin exerts its action by affecting the concentration of copper in cells. This investigation was supported by Research Grant A 1904 (R1) from the National Institute of Arthritis and Metabolic Diseases.

OBSERVATIONS OF ALVEOLAR-ARTERIAL GAS COMPOSITION DURING TRANSIENT MECHANICALLY INDUCED HYPERVENTILATION. Joseph Lipsky,* Joseph F. Tomashefski and Earl T. Carter. Cardio-Pulmonary Lab., Ohio Tuberculosis Hosp., Ohio State Univ. Health Center, Columbus.

Following an initial resting state, normal adult humans were subjected to an abrupt increase to a constant level of hyperventilation. An intermittent positive pressure automatic cycling device was utilized for this purpose. Continuous observations of the alveolar P_{CO_2} were made with an infra-red analyzer while frequent end-tidal air samples permitted estimation of the alveolar P_{O_2}. Samples of arterial blood were obtained for analysis of gas tensions, gas contents, and pH at intervals as small as 15 seconds. Ventilation and gas exchange were obtained on a recording spirometer. The asymptotic time functions of the alveolar-arterial gas tensions will be described as well as the arterial pH and gas contents. These data together with the ventilatory data permit calculation of the transient rate of body store CO_2 depletion. In the average experiment total ventilation was increased about 300-400%, the arterial pH approached 7.60, and the arterial-alveolar P_{CO_2} decreased to about 25 mm Hg. Arterial pH and P_{CO_2} reached an asymptote in about 3 minutes. Observations were discontinued after about 12 minutes of hyperventilation.

VENAE CAVAE FLOW IN RELATION TO VARIOUS CARDIAC EVENTS AS STUDIED WITH HIGH SPEED CINEFLUOROGRAPHY AT 260 FRAMES PER SECOND. (MOTION PICTURE). Peter R. Lynch, Barbara L. Carter, and Jose Gimenez, (intr. by M. J. Oppenheimer), Temple Med. Center, Philadelphia, Pa.

Cinefluorographic studies (260 frames per second) of the movements of small lipoidol droplets in the venae cavae of cats were

recorded simultaneously on the same movie film with oscilloscopic tracings of cardiac events. Comparisons of the flow pattern were made between inferior and superior vena cava. Lipoidol droplets in the inferior vena cava flowed 2-3 times faster than in the superior vena cava. Whereas a change in the pattern of flow occurred in the superior vena cava between tachycardia and bradycardia, no appreciable changes were noted in the inferior vena cava.

EFFECTS OF OXYGEN INHALATION ON COLD PRESSOR RESPONSES OF MAN. D. M. MacCanon. Dept. of Physiol. and Pharm., State Univ. of South Dakota Sch. of Med., Vermillion.

Measurements of blood pressure and pulse rate were carried out during 28 experiments on 10 healthy adult male subjects. The subjects, under basal conditions, breathed air or 100 per cent oxygen. Following control measurements the subject's right hand was immersed in cold (4°C) water for one minute. Blood pressures and pulse rates were determined during the last 30 seconds of the cold stimulation, and at one minute intervals after removal of the hand from the cold bath. Values obtained during oxygen inhalation experiments were compared to those secured during similar experiments when air was breathed. Differences between basal values, and changes from basal values resulting from cold pressor responses were subjected to paired analyses. These studies showed that basal diastolic pressures and pulse rates were significantly lower during oxygen inhalation. On the other hand, significantly greater increases in systolic and diastolic pressures and pulse rates attended the cold stimulation when oxygen was breathed. One minute after removal of the cold stimulus, systolic and diastolic pressures remained significantly further from basal levels, during the O_2 experiments, although pulse rates had reached control values. (Supported by Army Contract DA-49-007-MD-1008.)

BODY HEAT BALANCE DURING CALORIGENIC ACTION OF ADRENALINE. Lorne A. MacHattie* and Fred R. Griffith, Jr. Dept. of Physiol., Univ. of Buffalo, Buffalo, N.Y.

Intravenous adrenaline is known to increase the oxygen consumption of intact animals (by a "calorigenic action" whose mechanism is not entirely clear), and also to decrease the effective thermal conductance of peripheral tissues by its vasoconstrictor action. It has been suggested that the latter effect may have some causal relation to the former, since the metabolic response to adrenaline is much reduced in the skinned animal. To study the actual overall thermal effects of intravenous adrenaline infusion, heat output and body temperatures of anesthetized cats were measured, using a low-thermal-inertia gradient calorimeter of original design. At the onset of infusion, while heat production was presumably rising, heat output was found to fall. The resulting heat retention, however, does not appear sufficient to raise the metabolic rate very noticeably by its purely physical effect on metabolic reaction rates. Quantitative interpretation of the results will be discussed. (Supported by PHS Grant G-4242.)

WORK OF THE BIOLOGICAL STAIN COMMISSION. H. P. Mack,* J. P. Longely* and George Clark. Univ. of Maryland, National Institutes of Health and the Univ. of Buffalo.

This exhibit, prepared by a committee of the Biological Stain Commission, brings to the attention of stain users the work of the Stain Commission: the improving of the reliability of commercial stain preparations and the ensuring of their continued reliability. Stains, including the widely used hematoxylins, were extremely erratic in the years following World War I. This need for testing and standardization led to the formation of the Commission in 1923 and in the ensuing years the quality of American dyes has markedly improved. In this exhibit the similar staining qualities of different batches of hematoxylin are demonstrated with photomicrographs. The need for continued testing of dyes is shown by photomicrographs of sections stained with different aniline blues and counterstained with Darrow red, a dye made available through the work of the Commission. There is evident a marked color difference in the aniline blues. In addition other phases of work of the Commission are outlined and tribute is paid to Dr. H. J. Conn, a founder of the organization.

GRAPHIC RECORDING OF THE RATE OF DRAINAGE OF BLOOD FROM THE VEINS OF THE LEGS. I. F. S. Mackay. Dept. of Physiol., Univ. Coll. of the West Indies, Jamaica.

The purpose of this technique was to devise a method to study certain aspects of the aetiology of varicose veins in pregnancy and whether the developing foetus causes a mechanical obstruction of the venous drainage of the lower limbs. Such a technique might be of use in the study of other clinical conditions. The technique to be described is for the graphic recording of the rate of venous drainage from the legs by gravity. The procedure involves the use of a tilting table and a limb plethysmograph. The initial angle of the limb volume change following the completion of the tilting was recorded and from this the venous drainage rate was calculated. The results indicate the freedom with which venous drainage occurs and the lack of resistance that exists to the venous outflow from the lower limbs. The validity of the measurements derived from the technique was examined by causing venous obstruction by a positive Valsalva procedure and by examining the records during and after pregnancy.

EFFECT OF ENDOTOXIN (S. MARCESCENS) UPON THE SYSTEMIC AND CORONARY HEMODYNAMICS AND METABOLISM OF THE INTACT DOG. G. M. Maxwell, G. G. Rowe, C. A. Castillo, C. W. Crumpton, J. E. Clifford and S. Afonso (intr. by O.S. Orth). Cardiovascular Res. Lab., Univ. of Wisconsin, Madison.

Eight dogs were anesthetized with morphine and Dial-methane-Nembutal. Cardiac output (Fick) and coronary blood flow (N_2O Fick) were measured before and after the injection of endotoxin (S.Marcescens, Difco, 1.5 mgm/Kgm) into the right atrium. The following statistically significant (P 0.05 or less) changes were seen. Decrease in oxygen consumption and carbon dioxide production. Increase in R. Q. Increase in arterial - mixed venous O_2 content. Decrease

in mixed venous and arterial CO_2 contents. Cardiac output decreased from 2.6 to 0.9 L/min. Heart rate increased. Stroke volume, mean femoral pressure, left and right ventricular work decreased. Calculated peripheral and pulmonary arterial resistances increased. Coronary blood flow decreased from 100 to 52 cc/100 gm/min. Coronary vascular resistance was unchanged. The coronary sinus oxygen and carbon dioxide contents decreased. Cardiac R. Q. increased. Cardiac metabolic rates for O_2 and CO_2 showed an insignificant decrease. Cardiac efficiency (directly determined) fell from 20% to 6%. Endotoxin then reduces cardiac output, systemic blood pressure, left ventricular work, coronary blood flow, cardiac oxygen consumption and heart efficiency.

ACCOMMODATION IN HEART MUSCLE. Hector Mazzella (intr. by K. Koizumi). Dept. of Physiol., Downstate Med. Center State Univ. of New York and the Facultad de Medicina, Montevideo, Uruguay.

A study was made of the influence of subliminal anodal and cathodal current flow on the excitability of turtle ventricle. The exposed in situ heart, bathed in oxygenated Ringer solution, was driven at a rate of 48 beats per minute (cycle length 1250 msec). Conditioning current (40-50 msec rectangular pulses) of approximately 80% threshold intensity was passed between a Ag-AgCl[2] cardiac and a large indifferent buccal electrode. Testing stimuli (2-3 msec rectangular pulses) were applied through these same electrodes at various intervals before, during and after the conditioning pulses. During diastole accommodation to both anodal and cathodal currents occurred. When these long-duration pulses were applied before full recovery from preceding excitation (during the Q-T interval) no accommodation was observed. Both cathodal and anodal conditioning pulses merely lowered the threshold to testing stimuli. Evidently complete recovery of the membrane must occur before power of accommodation can be demonstrated. This may be of some significance to the study of why the heart is more vulnerable to fibrillation by strong stimuli applied during terminal phases of the repolarization process. (Supported by a grant to C. McC. Brooks from the Life Insurance Medical Research Fund.)

INTRAGASTRIC PRESSURES IN PYLORUS LIGATED MOUSE. Wm. Mc Arthur and A. Michel (intr. by H. Necheles). Dept. of Gastrointestinal Res., Med. Res. Inst., Michael Reese Hosp., Chicago, Ill.

In the pylorus ligated mouse (p.l.m.) the entire stomach is distended and ulcers form in the prostomach. Distension may interfere with circulation and cause ulceration. For this reason, intragastric pressures are determined in the p.l.m. and correlated with number and size of ulcers. The gastric arteries are injected at the end of the experiment, in order to determine circulatory abnormalities in the ulcer area.

LIFE STRESS AND SERUM CHOLESTEROL. Wm. R. McCabe,* James F. Hammarsten* and Stewart Wolf. Dept. of Med., U. of Okla. and Veterans Adm. Hosp., Oklahoma City.

Earlier studies by other workers as well as from our own laboratory have been strongly suggestive that stressful life situations may produce changes in the concentration of serum cholesterol in human subjects independent of diet and exercise. In order to provide more rigorous evidence, three men, all with some indication of coronary artery disease were hospitalized on a metabolic ward and maintained for 4 to 9 months without vigorous exercise and on a rigidly controlled constant diet, the composition of which was self selected. In each instance approximately 40% of the caloric content was derived from fat. In addition to frequent estimation of serum cholesterol long term observation of naturally occurring life stresses was made and short term stress interviews were conducted. During the study the chemical and psychological data were kept scrupulously separate. Despite the uniformity of diet and exercise elevations of serum cholesterol from 10% to 25% were observed which correlated with the separately adjudged stress periods at a better than 5% level of confidence.

STUDIES OF THE RATE OF DEVELOPMENT OF VENTRICULAR TENSION. M. Miyahara (intr. by Simon Rodbard). Univ. of Buffalo Chronic Disease Res. Inst., Buffalo, N.Y.

The interval from electrocardiograph Q to onset of brachial arterial pressure rise in man, measured intra-arterially or by arterial sounds, was prolonged on standing and shortened after exercise or adrenalins. To clarify these dynamics, ventricular, aortic, and femoral pressures and electrocardiogram were recorded with electromanometer in dogs receiving pentobarbital, thoracotomy, and heparin. Left ventricular output was measured by aortic rotameter. The control experiments showed time from Q to initial ventricular pressure rise (QI) averaged 75 milliseconds (ms); time to ejection (QE) averaged 110 ms. At constant diastolic pressures, increased stroke output was followed by a significantly shortened QE; reduced stroke output prolonged QE; QI and pulse wave velocity remained unaffected. At constant stroke volume, an increase in aortic resistance and pressure prolonged IE; a reduced aortic pressure shortened IE. Thus, changes in stroke output or diastolic pressure affect IE primarily, while QI and pulse transmission time are unaffected. These data suggest that (1) changes in time of arrival of the pulse wave (QP time) at selected diastolic pressures indicate effects on the rate of development of ventricular tension (IE), and (2) IE varies with stroke volume. QP at the brachial artery in man may therefore assist in appraising changes in stroke volume and in ventricular tension.

EFFECT OF HYDROCORTISONE ON THE BLOCKADE OF OVULATING HORMONE RELEASE IN THE RAT. W. W. Moore (intr. by E. E. Selkurt). Dept. of Physiol., Indiana Univ., Indianapolis.

The hypophysis of an adult female rat releases ovulating hormone between 1:00 and 4:00 p.m. on the day of proestrus when kept

under controlled conditions (14 hours light, 10 hours of darkness; 77 to 79oF). The release of ovulating hormone can be blocked with dibenamine (30 mg/kg, s.c.), dibenzyline (10 mg/kg, s.c.), atropine (700 mg/kg, s.c.), Nembutal (30 mg/kg, s.c.), epinephrine (80 μgm/kg, s.c.), nor-epinephrine (80 μgm/kg, s.c.), reserpine (1 mg/kg, s.c.), Stelazine (6 mg/kg, s.c.), formaline (10%, 0.2 ml, s.c.), restraint (dorsal decubitus position 1.5 hrs), or ether anesthesia, if the treatment is instituted before 1:00 p.m. Each of the agents induce a marked increase in ACTH output by the adenohypophysis, as judged by the adrenal ascorbic acid depletion test. The blockade of ovulating hormone release may be prevented by pretreatment with hydrocortisone (6 mg/100 gm, i.p.) at 9:00 a.m. on the day of proestrus. The degree to which blockade of ovulating hormone is prevented by hydrocortisone may be correlated with the ability of hydrocortisone to prevent the depletion of adrenal ascorbic acid following the application of one of the stressful agents. The data indicate that in most instances the release of ACTH by the adenohypophysis is accomplished at the expense of ovulating hormone release. (Supported in part by USPHS G-B1296C.)

SYSTOLIC AND DIASTOLIC PRESSURE-VOLUME CHARACTERISTICS OF THE ISOLATED MAMMALIAN LEFT HEART. R. G. Monroe and Gordon French (intr. by J. L. Whittenberger). Dept. of Physiol., Harvard Sch. of Public Health, Boston, Mass.

Pressure-volume curves were obtained in the isolated canine left ventricle by plotting peak systolic and end-diastolic pressures against a range of volumes at which the heart was beating isovolumetrically. The curves were obtained under control conditions, after alteration of rate, and during potassium arrest, digitalization, and infusion of epinephrine. Under these conditions the diastolic pressure-volume curves were found to remain constant and similar to control values. Changes caused by alteration of rate or by drugs invariably affected the systolic pressure-volume curve alone. In addition to isovolumetric studies the isolated heart was allowed to compress air, thereby enabling it to do work without involving the inertial component components of a fluid medium. It was possible to vary the components of "pressure" and "volume" in the work without altering rate or diastolic pressure and volume. At any given diastolic volume the heart was found to be capable of varying amounts of work depending on the volume of the chamber into which it compressed air. At any diastolic volume a pressure-volume work diagram can be constructed which serves to describe the performance of the ventricle at the stated diastolic volume, and appears to be reproducible for the method of loading employed.

HEMATOCRIT OF BLOOD EXPRESSED FROM THE PERFUSED DOG KIDNEY. Donald P. Morgan (intr. by Fred S. Grodins). Dept. of Physiol., Northwestern Univ. Med. Sch., Chicago, Ill.

Right kidneys of 12 nembutalized dogs were perfused with carotid arterial blood while enclosed in a rigid saline-filled box. Once perfusion was established, arterial and venous pressures, blood flow, urine flow, and the hematocrit of arterial and/or venous blood were

measured. The tubes conducting blood to and from the kidney were then clamped simultaneously. T-sidearms between the clamp and the kidney were then opened, and saline was forced into the box to express blood trapped in the kidney at the instant of clamping. Blood expressed via the venous sidearm averaged 5.6 cc in volume, 4.3 cc of which came from within the kidney. The mean hematocrit of the intrarenal blood so obtained was 45.8%, not significantly different from the mean hematocrit of arterial and venous blood samples (47.3%) taken during perfusion. The intrarenal blood obtained by compression represented 11.3% of the perfused kidney volume. The present findings do not confirm estimates of the hematocrit of intrarenal blood made by cell and albumen labelling methods, and suggest that the latter methods may have yielded factitiously low values.

FAILURE OF MIDDLE HYPOTHALAMIC LESIONS TO INHIBIT AMYGDALAR HYPERPHAGIA. P. J. Morgane* and A. J. Kosman. Physiol. Dept., Northwestern Univ. Med. Sch., Chicago, Ill.

Previously we have shown that either open or stereotaxic ablation of the amygdaloid complex in the cat results in hyperphagia and significantly increased rates of weight gain. It seemed possible that the amygdalar effects on food intake were mediated via middle hypothalamic centers thought to influence appetitive behavior in some species. Accordingly, it was decided to determine the location of middle hypothalamic centers possibly influencing food intake and to see whether amygdalar effects were modified following total middle hypothalamic ablation. Nine cats with bilateral stereotaxic lateral hypothalamic lesions failed to show changes in food intake or body weight. In 4 cats with intended ventromedial nuclear lesions, 3 animals showed no appetitive alterations and histological study of the brains revealed that the lesions were outside the ventromedial nuclei in each instance. One cat with perfectly placed bilateral ventromedial lesions showed hyperphagia and increased rate of weight gain, and subsequent lesions (during the statis phase of obesity) produced a further significant increase in food intake and body weight. Three animals with simultaneously placed lateral hypothalamic-ventromedial lesions failed to show any change in the appetitive mechanisms. In 8 additional animals with simultaneously placed lesions in the ventromedial nuclei, lateral hypothalamus, and amygdala, hyperphagia and significantly increased rates of weight gain developed. These findings indicate that the inhibitory effects of the amygdala on food intake operate independently of the middle hypothalamus.

SUMMATION WITHIN THE SOMATOSENSORY SYSTEM. R. W. Morse* and A. L. Towe. Dept. of Physiol. and Biophysics, Univ. of Washington, Seattle.

The initial latency of cortical unit discharge decreases with increasing peripheral stimulus intensity in an approximately logarithmic manner. We propose to account for this latency-intensity relationship by a mechanism depending upon an increase in the number (n) of active presynaptic terminals at each stage of the system as

stimulus intensity (I) increases. We assume that there exists on the cell an excitatory state, ζ, which varies with the amount of presynaptic terminal activity and which will result in a propagated discharge when $\zeta = h$ (where h, as a critical value, is constant except during accommodation or following a propagated discharge). At a given time (t) after a stimulus of intensity i, $\zeta_i = \int_0^t \left(\frac{dn}{dT}\right)_i e^{-k(t-T)} dT$ (where T varies from 0 to t); if we choose $t = t(\zeta_i = h)$, the time when the excitatory state just reaches the critical value, then t will define the initial latency of unit discharge. The family of ζ curves for different values of I intersects h along a series of points which define the latency-intensity function for the initial spike of the unit discharge. Several consequences of this formulation that aid in deciding between it and alternate mechanisms have been tested and found to be consistent with this concept. (Supported by Grant B 396 from the National Institute of Neurological Diseases and Blindness.)

EFFECT OF INDUCED HYPERPYREXIA UPON PULMONARY FUNCTION AND HEMODYNAMICS IN MAN. Kenneth M. Moser, Richard B. Perry, Stephen B. Sulavik and Peter C. Luchsinger (intr. by Estelle R. Ramey). Dept. of Med, Georgetown Univ. Sch. of Med., and the Georgetown Univ. Med. Div., D.C. General Hosp., Washington, D.C.

The purpose of this study was to evaluate the hemodynamic and pulmonary effects of hyperpyrexia induced in man by intravenous administration of a pyrogenic bacterial lipopolysaccharide extract. Conventional techniques of right heart catheterization and pulmonary function testing were employed. Serial evaluation of cardiopulmonary function was carried out in ten subjects at the following times: before intravenous injection of 0.45 microgm of the pyrogen; during the initial temperature rise; at peak temperature; and during the phase of temperature decline. Results: As the temperature rose, a consistent increase in both the cardiac rate and cardiac output was noted. The mean systemic arterial pressure remained at control levels or fell slightly whereas the mean pulmonary arterial pressure remained unchanged or rose slightly. The pulmonary vascular resistance deviated little from control values throughout. The systemic vascular resistance remained at baseline values or decreased. Minute ventilation, oxygen uptake and carbon dioxide output increased in all subjects. The arterial carbon dioxide tension decreased in all cases. All of the changes described tended to be maximal at the peak of the temperature response. Conclusions: While the individual patients varied considerably in their cardiopulmonary response to a given temperature elevation, an increase in the cardiac output and minute ventilation and a decrease in the arterial carbon dioxide tension were consistently observed.

WATER DIURESIS STOP-FLOW ANALYSIS. H. V. Murdaugh, Jr., R. E. Galloway, and E. H. Hayes (intr. by S. B. Barker). Dept. of Med., Univ. of Alabama Med. Center and Vet. Admin. Hosp., Birmingham, Ala.

Stop-flow analyses were performed on 14 dogs during osmotic diuresis and 19 dogs during water diuresis. Water diuresis was

considered accomplished when osmolal U/P was well below 1.0, with collections started after a stable rate of urine flow exceeding 5 ml/min and a specific gravity less than 1.007 had been obtained. The renal dead space during water diuresis was 8-12 ml as compared to 15-24 ml during osmotic diuresis. Creatinine U/P increased more in the proximal nephron samples during water diuresis than during osmotic diuresis. Changes in osmolal U/P were demonstrable during water diuresis with osmolal U/P increasing from 0.3 control to as high as 1.3 in the distal nephron. When PAH was administered by constant infusion correcting PAH concentration to creatinine concentration aided in defining the proximal hephron. Sodium U/P decreased more in proximal nephron samples during water diuresis. The lowest sodium U/P during water diuresis may occur with or proximal to the PAH peak of the proximal nephron as opposed to occurring in the distal nephron during osmotic diuresis. This was not due to replacement filtration with the PAH peak moving to the distal nephron as evidenced by the ability to separate distal nephron changes in osmolal U/P and potassium U/P from proximal changes in PAH and sodium U/P during water diuresis.

EFFECT OF BZT ON RABBIT EEG. Thomas A. Murphy and William G. Van Meter (intr. by H. E. Himwich). State Research Hosp., Galesburg, Ill.

A site of action of BZT (7-(2-(3-phenyl-2-propyl) aminoethyl) theophyllin hydrochloride, Johnson and Johnson, New Brunswick, New Jersey), a CNS stimulant, was sought in experiments in which rabbits were injected with BZT and EEG observations made. The animals were artificually respired and curarized, and electrical leads derived from motor cortex, limbic cortex, and hippocampus. BZT, given intravenously in a series of doses of 5 mg/kg each, produced EEG alerting lasting about 15 minutes after each dose. 4 mg/kg of chlorpromazine prevented or removed BZT alerting, the same phenomenon being repeated with further doses of each. 5 mg/kg of atropine irreversibly blocked BZT alerting. About 20 mg/kg produced seizures in all leads, sometimes appearing first in the hippocampus. In preparations with a pre-collicular brain section, separating the midbrain reticular formation and the diffuse thalamic projection system, BZT alerting was abolished, but not physostigmine alerting. With sections through the posterior colliculus, BZT alerted the EEG which was blocked by chlorpromazine. The electrical seizure patterns caused by high doses of BZT were seen in all leads, including the cortex after precollicular sectioning. The results suggest that BZT acts as a stimulant in the adrenergic portion of the midbrain reticular formation.

EFFECTS OF THAM ON THE VENTILATION OF THE RESTING DOG. Gabriel G. Nahas, and W. L. Lumpkin.* Dept. of Cardiorespiratory Diseases, Walter Reed Army Inst. of Res., Washington, D.C.

Four dogs were trained to breathe through a specially constructed mask with minimal dead space. Five gas mixtures were administered to the animals in the following sequence: air, 5% CO_2 in 21% O_2 and 75% N_2, air, 5% CO_2 in 21% O_2, and air. Each gas mix-

ture was administered for 8 minutes and measurements were made during the last 3 minutes of each period. During the second CO_2 breathing period, a .5 molar infusion of 2-amino-2-hydroxymethyl 1-3 propanediol, or THAM, was administered intravenously in an amount deemed sufficient to buffer the CO_2 contained in the estimated $\dot{V}_A$. During the first period of CO_2 breathing, $\dot{V}_E$ increased from 3.82 ± .46 to 7.6 ± 0.63 L/min; arterial blood pH fell from 7.42 ± 0.03 to 7.37 ± 0.02, and $PaCO_2$, calculated by the Henderson Hasselbalch equation, rose from 33 ± 2 to 37 ± 3 mm Hg. During the second period of CO_2 breathing and of THAM administration, $\dot{V}_E$ was 4.11 ± .38 L/min, within 5% of the control breathing air period, arterial blood pH was 7.43 ± 0.02, and $PaCO_2$ was 38 ± 2. mm Hg. This fall in $\dot{V}_E$ occurred at the expense of tidal volume, ventilation rate being the same during the two CO_2 breathing periods. During THAM administration, ventilation varies according to arterial blood pH changes and independently of $PaCO_2$ changes.

EFFECT OF LIVER ON SECRETIN. H. Necheles, T. Ogawa* and Th. Chiles.* Dept. of Gastrointestinal Res., Med. Res. Inst. of Michael Reese Hosp., Chicago, Ill.

Because I-131 labelled secretin injected i.v. was found in small amounts in the pancreas but in large amounts in the liver, the effect of the liver on secretin stimulation of the pancreas was investigated. In anesthetized dogs, pancreatic secretion was registered and secretin Lilly was injected alternatingly into the portal vein (i.p.) and into a peripheral vein (i.v.). Pancreatic secretion was definitely less with i.p. administration. Liver extract i.v. abolished pancreatic secretion to even large i.v. doses of secretin; boiling of the extract diminished this property considerably. We conclude that the liver plays a role in secretin action and inactivation. The secretin test for pancreatic function in man does not take into account that the secretin liberated normally from the intestinal mucosa passes through the liver first, and that with i.v. injection, more secretin arrives at the pancreas. Thus, a greater effect on pancreatic secretion may be obtained with the same dose of secretin given i.v. than i.p. (Supported by USPHS Grant.)

EFFECTS OF ANOXIA AND ASPHYXIA ON CAT SPINAL MOTONEURONS. P. G. Nelson* and K. Frank. National Institutes of Health, Bethesda, Md.

Depolarization of spinal motoneuron somata during asphyxia has been reported by Kolmodin and Skoglund, Acta physiol. scand. 45: 1, 1959, and others. The present study fails to confirm these findings. Transmembrane potentials were recorded with concentric micropipette-electrodes during several minutes of anoxia by artificial respiration with nitrogen and asphyxia. Both decapitated and nembutalized preparations were used, with and without hexamethonium chloride infusion for stabilization of blood pressure. Both large and small changes in membrane potential--some spontaneously reversible--were seen following 1/2 to 5 minutes of anoxia or asphyxia. Most large and many smaller changes were correlated with transient blood pressure changes. Sometimes membrane potential could be

restored by mechanical adjustment of the micropipette. Sometimes the inner pipette indicated no change in potential but the rise and fall of potential of the outer pipette, 20-40 microns back, correlating with B.P. changes, demonstrated movement was still present. Especially when B.P. was stabilized with hexamethonium, some cells could withstand 4-5 minutes of anoxia or asphyxia with membrane potential changes of no more than 2-5 mV, close to the limit of significance with this technique. Indications of excitability changes were observed with antidromic and spontaneous firing and were frequently correlated with these small potential changes. These small changes may be the result of movement, a direct effect of hypoxia on motoneuron membrane or a change in interneuron background activity.

EFFECT OF NIACIN DEFICIENCY ON THE ABSORPTION OF WATER AND SODIUM FROM THE SMALL BOWEL. Ralph A. Nelson* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The purpose of this study was to determine the effect of niacin deficiency on the movement of water and sodium across the mucosa of the alimentary canal. All tests were done on trained unanesthetized dogs with Thiry-Vella duodenal or ileal loops. Modified Tyrode's solution (25 ml) containing isotopically labeled water and sodium was placed in the intestinal loop for 10 minutes. Rates of movement of the fluid out of the gut (insorption) and into the gut (exsorption) were calculated by Visscher's formula. Net loss by the dog to the solution in the gut (enterosorption) and net gain to the dog from the solution in the gut (absorption) also were determined. Tests were made before, during and after niacin deficiency. A marked decrease in the movement of water and sodium across the mucosa always occurred during niacin deficiency. The decrease was greatest in the insorption rate and net amount transferred. The insorption rates of water and sodium were reduced from a third to a half of the control values. The net amount transferred was reduced severely, and frequently reversed from absorption to enterosorption. Exsorption rates also were reduced, but to a lesser extent than those of insorption. After treatment, exsorption rates returned to control values while insorption rates improved but failed to reach control levels. (Supported in part by research grant No. A-2827, USPHS.)

WHOLE BODY RADIATION PROTECTION USING ENTERIC COATED AET-PAPP COMBINATION IN THE DOG. John R. Newsome (intr. by R. R. Overman). Inst. of Clinical Investigation, Univ. of Tennessee, Memphis.

A study was made on the protective ability of AET-PAPP combinations in enteric coated (SKF) capsules against a lethal dose of whole body X-radiation in dogs. Doses of 100, 125, and 150 mg/Kg AET (S-β-aminoethylisothiuronium), each combined with 3.5 mg/Kg PAPP((R-aminopropiophenone) were given orally to the animals. Each was subjected to a lethal dose of X-radiation of 550 r. Even a dose of 100 mg/Kg AET plus 3.5 mg/Kg PAPP afforded partial protection, as the dogs given this dose survived about 23 days. At the time of death, the animals were anemic but leucocytes and reticu-

locytes were increasing in their peripheral blood. The AET in the enteric coated capsules was found to be relatively non-toxic. The survival and toxicity data will be discussed.

EFFECT OF HOMOLOGOUS MARROW TRANSPLANTATION ON SURVIVAL OF MONKEYS FOLLOWING SUBLETHAL WHOLE BODY X-IRADIATION. Frances E. Newsome* and R. R. Overman. Inst. of Clinical Investigation, Univ. of Tennessee, Memphis.

Homologous bone marrow administered 30 hours after a single wholebody exposure to 550r (approximate $L.D._{10}$) x-irradiation markedly decreased the survival rate in a group of 7 M. mulatta monkeys. Six of the 7 animals died between the 10th and 15th post-irradiation day exhibiting symptoms suggesting that death was caused by radiation. On the other hand, 5 of 6 similar animals subjected to the same dose of whole body x-irradiation but in which bone marrow transplantation was postponed until 48 hours after the insult, survived. The sole fatality occurred on the 23rd post-irradiation day, the peripheral blood picture indicating erythrocyte hyperplasia. Immune responses, peripheral blood studies and bone marrow cell counts of these two groups of animals will be presented and discussed.

SOME EFFECTS OF MINIMAL DAMAGE TO THE LOWER PORTION OF THE PROXIMAL TUBULES OF THE DOG'S KIDNEY. T. F. Nicholson. Dept. of Pathological Chemistry, Univ. of Toronto.

The infusion of 40 to 60 ml of 0.05% dl sodium tartarate through the left kidney in dogs results in histological changes in the last two thirds of the proximal tubules of the infused kidneys which are confined to blurring and disarrangement of the mitochondria. Functionally the creatinine and inulin clearances are not changed by the renal lesion. The PAH clearance and the Tm PAH are reduced on the damaged side. The pH of the urine from the damaged kidney is higher than that from the normal kidney in the same animal, but there is no reduction in the ammonia excretion from the damaged kidney. The excretion of sodium and bicarbonate are increased and that of chloride is decreased by the lesion. Phosphate and potassium excretion are unaffected. These changes resemble closely those found in uncomplicated cases of hyperchloremic acidosis in humans.

METABOLIC ALTERATIONS IN THE INTACT RAT AND EXCISED TISSUES AFTER THYROIDECTOMY. R. R. Nielson,* R. F. Loizzi* and H. M. Klitgaard. Physiol. Dept., Marquette Univ. Sch. of Med., Milwaukee, Wisc.

The oxygen consumption of the intact rat and selected excised tissues were determined for 28 days following the surgical removal of the thyroid gland. The whole animal basal metabolism did not show a significant change following thyroidectomy until after a period of 24 hours. By the third day a reduction to 90% of the normal value was reached followed by a sharp continuous fall to 71% on the 7th day. Thereafter, a gradual decrease was observed until the final value of 63% was attained on the 28th day. A reduction in oxygen

consumption was observed in all tissues after thyroidectomy except for duodenum. Cardiac tissue, which approximates best the whole animal curve, showed a continual decrease to 77% of normal by day 4 and maintained a near plateau decreasing slowly to 70% on day 28. Diaphragm decreased sharply to 71% by day 3 and then less rapidly until reaching the 28 day value of 46%. Skeletal muscle declined rapidly to 64% on day 4 and then decreased almost parallel to diaphragm. Kidney differed from the whole animal pattern by not showing a decrease until day 8, while liver nearly paralleled the whole animal. (Supported by PHS Grant A-957.)

EFFECTS OF CONGENITAL CEREBELLAR DEFICIENCY IN THE CAT. William T. Niemer. Creighton Univ. Med. Sch., Omaha, Nebr.

Five, female, litter mate kittens of a mother-son mating, all showed marked degrees of abnormal motor behavior attributable to cerebellar deficiency. Intention tremor, hypotonia (adductor weakness of hind legs), general incoordinaation, and double alternating dysmetria of head movements manifested themselves and will be shown in a movie. No genetic studies were made since none of the animals survived beyond 8 months. As indicated by motor phenomena before death, marked cerebellar deficiency was revealed at autopsy. Identification and study (in progress) of the remaining intact cerebellar lobules, may be correlated with normal foreleg movement. (Supported by Grant B-1046 USPHS.)

RELATIONSHIP OF CATECHOL AMINE EXCRETION TO RESPONSES TO TEAC IN HYPERTENSIVE SUBJECTS. Arthur Nunn and Colene Walden (intr. by H. M. Hines). Dept. of Physiol., State Univ. of Iowa, Iowa City.

It has been postulated that certain types of clinical essential hypertension may be associated with a hyperactivity of orthosympathetic vasoconstrictor neural mechanisms. In this study a comparison was made of the urinary biologically active catechol amine excretion with the blood pressure responses to an adrenergic blocking agent, TEAC. Urinary collections were made for three days on hospitalized labile hypertensive patients from which all drugs were withheld for several days. At other times the blood pressure responses of the patients were determined after an intravenous injection of 400 mgm TEAC. The urinary excretion of biologically active catechol amines was measured by the blood pressure responses of extracts in anesthetized cats. The active amines were adsorbed on aluminum oxide, centrifuged, eluted with 0.25 N. H_2SO_4. The method afforded excellent recovery of nor-epinephrine added to urine. The blood pressure responses in the cat to urinary catechol amines were standardized against l-nor-epinephrine injection. Statistical analysis of the data showed no correlation existed between the amount of catechol amine excretion and the blood pressure responses of eight patients to TEAC.

RESPIRATORY EFFECTS OF THAM IN MAN. Thomas F. O'Connor,* Gabriel G. Nahas, Leonard B. Berman,* and Peter C. Luchsinger.* Georgetown Univ. Med. Div. of the D.C. General Hosp., Washington, D.C.

Four normal individuals, resting, fasting, and supine were studied before and after 0.3 molar intravenous THAM infusion (5 mEq KCl/L and 30 mEq Nacl/L added) given at a rate of approximately 4 ml/min for periods varying from 30 to 60 minutes. A 30% decrease in minute ventilation was observed during the infusion together with a 33% decrease in carbon dioxide output. The fall in minute ventilation occurred at the expense of tidal volume, the ventilatory rate remaining the same throughout the experiment. The respiratory exchange ratio dropped in every case from normal to values between .49 - .73. In the arterial blood, the pH increased an average of .05. The carbon dioxide tension, calculated by the Henderson-Hasselbalch equation, rose in all four patients and the oxygen saturation fell below 95%.

Thirteen percent of the buffered carbon dioxide was excreted in the urine. The urine pH rose from 5.14 - 6.8 to 6.88 - 7.50. THAM infusion resulted in a partial shift in carbon dioxide excretion from the lungs to the kidneys. This coincided with a decrease in alveolar ventilation out of proportion to carbon dioxide excretion by the lung. During THAM administration, changes in minute ventilation are related to changes in arterial blood pH. No clinical side effects were noted.

LIGATION OF HEPATIC DUCTS. T. Ogawa,* N. C. Jefferson,* C. Syleos* and H. Necheles. Dept. of Gastrointestinal Res., Med. Res. Inst. of Michael Reese Hosp., Chicago, Ill.

We have studied the anatomy of the intrahepatic bile ducts in premature and adult human and canine livers. Our results indicated absence of intrahepatic connections between the major bile ducts and their areas of drainage. Ligation of a single or of 2 hepatic ducts did not lead to formation of anastomotic channels between ducts, and the territory drained by them atrophied. Formation of bile ceases within a few days after ligation of a bile duct. Our corrosion preparations of human fetal liver showed such small bile ducts, that the Longmire operation for agenesis of the extrahepatic biliary system appeared to offer little chance of success. For this reason, exteriorization of part of an obstructed lobe of the liver was done and a few days later, the external hepatic tissue was ablated. In some of the dogs, adequate bile drainage followed. With this technic, bleeding and bile secretion can be controlled; this is not well possible with the Longmire operation. Results of blood chemistries (serum bilirubin, alkaline phosphatase, B.S.P.) in these dogs will be discussed. (Supported by the J. Abeles Fund.)

EFFECT OF HEPARIN ON THE METABOLIC AND LEUKOCYTE RESPONSES TO HYDROCORTISONE INJECTIONS IN RATS. Donald J. Paluszka* and Lyle H. Hamilton. Marquette Univ. Sch. of Med. and Wood Vet. Admin. Hosp, Milwaukee, Wisc.

It has been reported (L. H. Hamilton, Endocrinology, 61:392, 1957) that heparin can block the leukopenic response observed four

hours after the injection of cortisone in rats. In vivo effect of heparin (100 I.U./100 gm body weight) on blood glucose, blood pyruvic acid, leukocyte, and liver alkaline phosphatase responses to hydrocortisone injections (3 mg/100 gm body weight) were studied. Heparin injections produced a marked leukocytosis, while hydrocortisone resulted in a leukopenia. When these two agents were administered simultaneously, the leukocyte count was not statistically different from control counts. Heparin, in the dosage used, did not affect the hydrocortisone-induced hyperglycemia, although it did prevent the blood pyruvic acid increase resulting from hydrocortisone. Liver alkaline phosphatase activity was increased only when both heparin and hydrocortisone were injected.

DEVELOPMENT OF THE EEG IN THE DOG. JoAnn C. Petersen* and Williamina A. Himwich. State Research Hosp., Galesburg, Ill.

The development of the cortical electroencephalogram has been followed in dogs one to sixteen days old. Under light ether anesthesia, a polyethylene cannula was inserted in the trachea. The animals were then immobilized by means of intramuscular intocostrin and placed under artificial respiration. Two holes large enough to permit introduction of silver ball electrodes were drilled in the skull, anterior to the frontal-parietal suture and on either side of the longitudinal suture which divides the frontal bones. The electrodes were placed on the surface of the dura to permit recording directly from the cortex. The electrocardiogram was also followed. By the time the recording was begun the effects of ether were gone, and the animal was essentially unanesthetized. The voltage and frequency of the EEG, low in the newborn, becomes greater as the animal develops. Bursts of ten cycles per second spindles appear in some animals as early as the first day after birth. By the fifth day twelve cycles per second activity, which appears in sequences separated by the alert type of recording, was observed in most animals. Such records suggest alternate sleep and arousal. The effects of injection of substances such as γ-amino-butyric acid and glutamic acid upon the developing EEG also will be discussed.

CHANGE OF TISSUE CULTURE METABOLISM BY CHANGING CULTURE SERUM. H. J. Phillips, R. V. Andrews * and Vera Skank.* Dept. of Physiol. and Pharm., Creighton Univ. Sch. of Med., Omaha, Nebr.

Tissue cultured cells grown in medium containing human serum respire and glycolyze at a greater rate than cells in the same medium containing horse serum. This observation suggested that metabolism of tissue cultures grown in one horse serum might be different from that of cultures grown in another horse serum. Horse serum was collected from three horses. Strain L cells were divided into three subcultures, each of which, were grown at least one month in lactalbumin hydrolysate medium plus 20% horse serum A, B, or C. The day following a medium change subcultures were trypsinized, dispersed, washed in 0.93% saline containing 1.0% methyl cellulose and then run on a Warburg respirometer in balanced saline solution containing 1.0% gelatin. Metabolic values were based on live cell

counts which were determined by differentially staining with Erythrosin B. Respiration and glycolysis of the three subcultures were significantly different. These observations suggest that materials are collected by tissue cells from their environment (medium) which can subsequently influence their metabolism even though the cells are washed and resuspended in saline. In comparing the metabolism of various tissue cells, incorrect interpretation may be made if the cells are grown in different culture medium. (Aided by Natl. Cancer Inst. and Nebr. Heart Assoc.)

CARDIAC RESPONSE TO CYCLIC CHANGES OF LOAD STUDIED IN INTACT ANESTHETIZED DOGS. Heinz P. Pieper. Dept. of Physiol., Ohio State Univ., Columbus.

The arterial system of large closed chest anesthetized dogs was connected by way of one femoral artery to a sinusoidal pump with a volume displacement of approximately 50 cc operated at frequencies varying from .15 to .3 cps. The pressure in the whole arterial system was thereby raised and lowered alternately. Simultaneous phasic recordings of blood pressure and blood flow were both taken in the ascending aorta using a miniaturized catheter tip manometer (E. Wetterer and H. Pieper, Zeitschr. Biol. 105, 49, 1952) and a catheter tip flowmeter (H. P. Pieper, Review of Scientific Instr., 29, 965, 1958). Pulse by pulse, the cardiac output decreased during the phase of rising arterial pressure and increased during the phase of falling arterial pressure. However, at any given pressure level the output was greater if the pressure was falling than if it was rising, giving rise to a typical hysteresis loop when pressure was plotted against flow. Since the mean arterial pressure before and after operation of the pump as well as the heart rate during its operation remain unchanged, it is probable that the slow pressure cycles do not cause regulatory changes in the circulatory system. The output changes described are therefore considered to be a direct response of the heart itself. The relationship of these findings to the applicability of Starling's Law in the intact animal will be discussed.

PSYCHO-PHYSIOLOGICAL RESPONSES TO ANOXIA. Robert S. Pogrund and Ralph Gunter (intr. by F. R. Steggerda). Space Technology Labs and San Fernando State College.

Cats were trained to certain discriminatory patterns, involving both sensory and intellectual function. Preliminary assessment of another untrained group of cats as to their tolerance to repeated exposures, both sudden and gradual, to hypoxia, was evaluated prior to the observations on the trained animals. Duration of exposure was limited by the onset of respiratory and neurological symptoms, primarily manifested by gasping and extensor rigidity. Such alternate exposures and recoveries resulted in increasing tolerances to the hypoxia, until peak levels were reached beyond which decreasing tolerances became evident. The other group of cats trained for higher brain function was observed following one sudden exposure to pure nitrogen. Each cat was then retested to observe any decrement in behavior and, if present, the animal was retrained to a new constancy of post-exposure performance level. This was followed by

repeatedly exposing the animal again to the anoxia, approximately four times a day, until a total exposure time of 70 minutes was reached. Changes in discrimination thresholds were then determined following such repeated exposure by retesting each cat. Electroencephalography was recorded for each cat following the exposure to anoxia so that loss of behavioral function could be correlated with alterations in EEG patterns as a function of time of exposure to the anoxia. Another group of untrained cats were exposed to the anoxia and then trained for discrimination thresholds to determine the effect on their ability to learn new discriminations. A control group consisted of similarly treated animals, but exposed to room air.

EFFECTS OF PITRESSIN ON BLOOD FLOW AND PRESSURE IN THE HIND LIMB OF THE DOG. H. D. Potter and D. C. Sutfin (intr. by R. E. Johnson). Dept. of Physiol., Univ. of Illinois, Urbana.

The effects of small doses of pitressin on femoral arterial blood flow and pressure were investigated using a cannulating-type electromagnetic blood flowmeter and strain gage manometer. Five experiments were conducted on pentobarbitalized dogs. Intra-arterially administered pitressin (0.1 to 5.0 mU in 0.2 ml) resulted in a graded decrease in flow that was not accompanied by a significant increase in pressure. A graded biphasic flow response (increase followed by a decrease) was noted following intravenously administered pitressin (5 to 100 mU in 2 ml). The first phase of the flow response was relatively short in duration as compared to the second phase; neither phase was consistently accompanied by a significant increase in pressure at all doses. The data indicate that exogenous vasopressin causes a relatively large decrease in femoral arterial blood flow at dose levels below those required to produce a significant elevation of the arterial pressure.

CURRENT STUDY IN RELATION TO STIMULATING BRAIN STRUCTURES IN THE CAT. Ervin W. Powell,* Elsie F. Goodfellow*, Gerald T. Schneider* and William T. Niemer. Dept. of Anatomy, Creighton Univ. Sch. of Med., Omaha, Nebr.

A given set of factors of a stimulating parameter results in a constant value of current. A critical uncontrolled variable factor involved in stimulation experiments on the cat brain is the total impedence of the material between electrode tips of both the stimulating pair and/or any recording pair. Thresholds of some rhinencephalic structures in relation to ictal after-discharge in the hypothalamus based on microamperes of current are remarkably different from some based on voltage as read from the stimulator dial. When considering the irritability of structures, voltage, current, and brain impedence should be considered as active components. Such consideration could be given to these factors in the formula $E = IR$ where E = the voltage across the tips of the electrodes, R = the total brain impedence whether remote or local, and I = current threshold in amperes for the particular type of response recorded, whether it be single shock or ictal after-discharge. (Aided by USPHS Grant B-1046.)

BRAIN CONCENTRATIONS OF BIOGENIC AMINES AND EEG PATTERNS OF RABBIT: EFFECT OF MONOAMINEOXIDASE INHIBITORS. G. R. Pscheidt,* E. Costa,* W. G. Van Meter* and H. E. Himwich. State Research Hosp., Galesburg, Ill.

Catecholamine and serotonin brain concentrations were determined after intravenous injections of iproniazid, Catron or SKF trans 385, with the following results: 1) Iproniazid given i.p. to rabbits in daily doses of 25 mg/kg produced an increase of both brain catecholamines and serotonin concentrations in 72 hours. Despite this neurohormonal increase the sleep and wake alternation of normal EEG pattern persisted. 2) Catron (JB 516) given intravenously in two 4 mg/kg doses 17 and 4 hours before sacrifice of the animal also raised brain serotonin without changing brain catecholamine content. These doses of Catron, however, failed to induce a persistent alert EEG pattern. 3) SKF trans 385 given i.v. in a single 2 mg/kg dose produced in 4 hours a continuous alert EEG pattern. Brain serotonin was increased but no change occurred in brain catecholamines. Despite the chemical similarity between amphetamine and SKF trans 385 both EEG and neurochemical findings emphasize their different mechanisms of action.

CUTANEOUS TACTILE UNITS IN CAT. Flavio Puletti (intr. by C. N. Woolsey). Dept. Physiol., Univ. Wisconsin, Madison.

Although physiological studies have been made of single peripheral tactile sensory units (i.e., of a nerve fiber and its associated sensory endings), there is little systematic information on variations in size of units in different regions of skin in any animal. The most elegant data have recently been reported by Lindblom (1958) for skin of lower leg of frog. In the present study single unit discharges have been amplified and recorded with cathode ray oscillograph from 203 fibers brought under observation by dissection of dorsal root filaments in 43 cats. All roots from C_1 through S_2 have been examined. In each case the area of skin supplied by the fiber under study was identified and mapped by manual stimulation with a fine round tipped probe. All units studied were grouped according to root by which they entered the spinal cord and according to the region where the sensory endings were distributed. The areas of skin innervated by single dorsal root fibers were found to range in size from a few mm^2 on hand and foot to more than 300 mm^2 on trunk. On limbs, units increased steadily in size from tip of extremity toward hip and shoulder. In general, areas supplied by single dorsal root fibers were many times smaller than areas firing single cortical neurons (Mountcastle, 1957), suggesting convergence of many peripheral neurons upon single cortical cells. (Supported by National Paraplegia Foundation and grant B-732 (C4), NINDB.)

EFFECTS OF TOPICAL AND SYSTEMIC GABA ON NEONATAL CAT CORTEX. D. P. Purpura and M. W. Carmichael.* Dept. of Neurological Surgery and Pharm., Columbia Univ., Coll. of Physicians & Surgeons, N.Y.C.

Long-duration (40-80 msec) surface-negative responses to local cortical stimulation (SCR) are evoked in 12-15 hr. old unanesthetized-

paralyzed artificially-ventilated kittens. Graded SCR's are compounded of multiple 20 msec responses. Activity cycles reveal no refractoriness beyond 1-2 msec test intervals and only brief periods of depression or facilitation depending on stimulus strength. SCR's are similar during the first 12 day neonatal period. Topical GABA rapidly and reversibly eliminates SCR's but rarely "unmasks" surface-positivity in the latter. Evoked responses are not augmented by ϵ-amino caproic acid or strychnine. Rapid intravenous injections of GABA (50-100 mg/Kg) do not significantly alter SCR's even in the 12 hr. old kitten. Elimination of SCR's with similar amounts of systemic GABA is observed in kittens pre-loaded with 350 mg/Kg GABA over 30-40 min periods with unexposed cortex or in animals in which rapid pre-loading is associated with prolonged exposure of brain. Under these conditions systemic effects of GABA are similar to those observed following topical application, but most prominent on longer-latency SCR components. SCR's eliminated by intravenous GABA are rapidly, but transiently restored by rinsing cortex with Ringer's. Effects of GABA are not reproduced by glutamic acid or other α-amino acids. The data suggest that in neonatal kittens exclusion of blood-borne GABA from cortical synapses is attributable to mechanisms similar to, but more labile than those operating in the mature cat.

SUBENDOCARDIAL HEMORRHAGE PRODUCED BY ELECTRICAL STIMULATION OF THE STELLATE GANGLION. Walter C. Randall, Michael Kaye* and Robert McDonald.* Stritch Sch. of Med. and Grad. Sch. of Loyola Univ., Chicago, Ill.

Prolonged electrical stimulation of the stellate ganglion in the dog elicits a pressor response characterized by a markedly elevated pulse pressure. With low frequency stimulation, the resulting hypertension could be sustained for many hours. With higher frequencies (10/sec or more) cardiac deterioration occurred and post-mortem examination of the heart revealed severe subendocardial hemorrhages. These occurred in nearly all animals stimulated at a frequency of 10 per second but in very few of those stimulated at 1 per second. The lesions appeared along the long axis of the papillary muscles and the trabeculae carnae of the left ventricle, thus forming long and narrow hemorrhagic striations along the septal wall. They rarely appeared in any part of the right ventricle or in the atria. The lesions appeared grossly similar to those induced by intravenous infusions of relatively high concentrations of epinephrine or norepinephrine.

CREATINE PHOSPHOKINASE OF HEART AND SKELETAL MUSCLE. W. O. Read. Dept. of Physiol. and Pharm., State Univ. of South Dakota, Sch. of Med., Vermillion.

The activity of the enzyme, creatine phosphokinase, has been measured in heart and skeletal muscle during foetal development in the rabbit. The enzyme was extracted from pooled foetal tissue by the method of Kuby, Noda and Lardy (J. Biol. Chem. 209: 191, 1954). The activity of the enzyme, measured in glycine buffer (pH 9.0) in the presence of ATP and creatine, was expressed as μM of phosphorus

transferred from ATP to creatine per gram of tissue dry weight in two and one-half minutes at 30°C. The results show that while only a trace of enzyme activity, 0 - 50, is present in 14 day old foetal hearts, it rises to 300 in 21 day old foetal hearts and at birth approximates the adult level, 1226. In skeletal muscle, the appearance of the enzyme is delayed; none is detectable in the two and three week old foetal skeletal tissue. During the last week of foetal development the enzyme activity increases rapidly and at birth reaches a value which is approximately 50 percent of the adult level. The presence of this enzyme, creatine phosphokinase, has been related to the polymerization of actin (Feuer and Wollemann, Acta Physiol. Akad. Sci. Hung. 3:297, 1952; 5: 31, 1954). Viscosity measurements of 3 week old foetal skeletal muscle have been conducted in this laboratory to correlate the three parameters; presence of creatine phosphokinase, polymerization of actin and functional capacity of the muscle. These results will be discussed. (Aided by a grant from the Muscular Dystrophy Associations of America, Inc.)

EXPLANATION FOR CARBONIC ANHYDRASE IN GLANDS PRODUCING ESSENTIALLY NEUTRAL SECRETION. W. S. Rehm. Dept. of Physiol. and Chem., Univ. of Louisville, Louisville, Ky.

Recent work has tentatively convinced writer of the validity of Davenport's original idea for the need of carbonic anhydrase in the gastric mucosa. A summary of some of the arguments follows. 1) Diamox inhibits gastric secretion while sulfanilamide does not. 2) After Diamox, carbonic anhydrase activity is essentially zero while after sulfanilamide considerable activity remains even though percentage decrease is great. 3) Work in respiratory physiology is compatible with complete inhibition of carbonic anhydrase of red cell by Diamox (Federation abstracts 1959). 4) Residual gastric secretory rate in our expirements using Davies and Roughton's calculations is approximately equal to uncatalyzed rate when back reaction neglected. Explanation of effect of Diamox on electrical parameters during secretion on basis of a model in which OH^- ions are formed at cytoplasmic border of outer membrane led to calculations of local pH gradients. Results reveal that even when net intracellular production of H^+ ion and OH^- ions are equal, sizeable pH gradients would exist if sites of production are microns apart. Suggestion is made that in tissues like the ciliary body and choriod plexus, transport mechanisms are involved in which the H^+ and OH^- ions are produced microns apart and that sizeable pH gradients are prevented by presence of carbonic anhydrase. Inhibition of carbonic anhydrase results in localized pH changes which reduce secretory rate. (Supported by grants from NIH and NSF.)

HIPPOCAMPAL EVOKED POTENTIALS. Alvin M. Revzin and Ottilie R. Inman (intr. by W. A. Himwich). State Research Hosp., Galesburg, Ill.

To study hippocampal evoked potentials the pyramidal cat preparation of Morruzzi was used to obviate anesthetic distortions. Bipolar coaxial stimulating and recording electrodes were oriented stereotactically. Stimulating and recording apparatus was conven-

tional. The structures explored were predominantly sub-cortical and included the basal ganglia, thalamus, hypothalamus, amygdala and underlying piriform cortex and septal area. No evoked potentials were obtained in either dorsal or ventral hippocampus by stimulation of the basal ganglia, the specific thalamic relay nuclei or most of the thalamic association nuclei, such as the pulvinar. 200 micro volt, 15-20 ms latency potentials were produced in dorsal hippocampus and, to a lesser extent, the ventral hippocampus, by stimulation of the reticular, intralaminer and midline thalamic nuclei, stria medullaris and habenula. Somewhat larger, and shorter latency, potentials were obtained from stimulation of the hypothalamus, within 0.5 mm of the fornix. Very large (1-5 mV) potentials could be obtained by excitation of the amygdalar complex, the piriform cortex, the septal area, and the fornix. These were most marked in ventral hippocampus. The responsive structures fell rather sharply into two groups. Repetitive stimulation (5 to 20 pps) in amygdala, piriform cortex, septal area or fornix produced marked augmentation of the evoked potentials in the hippocampus. Dramatic post-tetanic potentiation may also be seen here. The other structures studied, capable of producing hippocampal potentials, demonstrated only slight augmentation and no post-tetanic potentiation. This difference in response to repetitive stimulation on the part of two polysynaptic pathways with similar hippocampal terminations is being studied further and results will be reported.

CORRECTION OF MITRAL INSUFFICIENCY BY INPLANTATION OF LEFT AURICLE INTO LEFT VENTRICLE, WITH APPLICATION TO TRICUSPID INSUFFICIENCY. Joseph T. Roberts. Cardiology Sect., Vet. Admin. Hosp., and Univ. of Buffalo Sch. of Med., Buffalo, N.Y.

By invaginating the left auricular appendage so that it can be implanted into the cavity of the left ventricle, the serious hemodynamic defects of experimental mitral insufficiency were quickly corrected. In 20 dogs, acute mitral insufficiency was produced by cutting the chordae tendineae and mitral leaflets with iridectomy scissors introduced through the tip of the left auricle. Within a few heart beats, the left atrium, auricle and pulmonary veins became greatly distended and pulsated with ventricular systole. These defects were corrected at once by invaginating the left auricle into the left ventricle. This was done in the following steps: (1) tying the middle of a heavy (no. 2) silk thread on the end of the left auricular appendage; (2) passing the two ends of this thread on a 2 or 3 inch needle through the wall of the left auricle just proximal to the knot; (3) passing this needle and the threads through the mitral valve orifice, across the cavity of the left ventricle, and out through the anterior lateral apical wall of the left ventricle; (4) tying a hemostatic ligature around the tip of the left auricle to close the hole of entry of the needle and threads; (5) pulling on the two threads so as to invaginate the inverted left auricular appendage so as to implant it through the mitral valvular orifice into the cavity of the left ventricle; (6) placing a knot with the two ends of the thread in the epicardial wall of the ventricle so as to anchor the threads and in-

vaginated left auricle with just the right amount of tensions needed to reduce the regurgitant jet without occluding the orifice entirely. Tolerance for the procedure was excellent. Survival as long as three months (until sacrifice for other purposes) was noted. In one dog, the knot on the tip of the left auricle tore off because too much tension was used. In another dog, death by hemorrhage two days later resulted from omission of the hemostatic ligature on the auricle. The others showed correction of the hemodynamic defects. In five other dogs, similar correction of tricuspid regurgitation followed invagination of the right auricular appendage. These methods are suggested for trial in chronic mitral insufficiency, experimental and clinical.

DELAY OF TRANSMISSION OF THE PULSE WAVE BY THE SPHYGMOMANOMETER CUFF. Simon Rodbard and John W. Kostecki.* Univ. of Buffalo Chronic Disease Res. Inst., Buffalo, N.Y.

Calibrated pulse wave contours were obtained by recording arterial sounds (K) simultaneously with an electrocardiogram, using the Q wave as a reference. The onset of the sound represents the time during the cycle that the rising arterial pressure exceeds the cuff pressure. A plot of QK time against cuff pressures produces an upstroke which is essentially similar to the intra-arterial pulse wave. The present study examined the effect of sphygmomanometer cuffs of various width on the time of occurrence of the sounds. Results were compared with those obtained by intra-arterial puncture. A cuff of 14 cm width consistently delayed onset time of the sounds 0.01 to 0.03 second at diastolic levels, and from 0.01 to 0.06 at systolic values, when compared with a cuff of 8 cm or intra-arterial pressure tracing. The lag was reduced in patients with arms of larger circumference. In patients with aortic stenosis, the lag was as long as 0.10 sec. Systolic and diastolic pressures were lowered 5 to 10 mm Hg by the wider cuff. The delay appears to represent the time required for filling of the collapsed segment of the artery under the cuff. This is dependent on the rate of rise of the arterial pressure, and on the length and diameter of the collapsed vessel. Model experiments utilizing collapsible tubes support this interpretation.

GASTRIC SECRETION IN THE FROG. Lionel W. Rosen,* Ann M. Ambromovage* and M. H. F. Friedman. Dept. of Physiol., Jefferson Med. Coll., Philadelphia, Pa.

This study confirms previous work that in the fasting frog kept at 10°C acid gastric secretion is intermittant and not spontaneous or continuous. Acid secretion was readily elicited in situ by mechanical stimulation of the stomach, such as distension with inert substances or the repeated passage of a gastric tube. This secretory reflex appeared not to be dependent on the integrity of the vagus. It was abolished by destruction of the spinal cord but this may have been secondary to alterations in gastric blood supply rather than interruption of reflex arcs. Using precautions against mechanical stimulation, it was found that pilocarpine excited acid secretion only

very briefly. Epinephrine excited secretion of an alkaline mucus which persisted for as long as the mydriatic effect lasted to be followed by a prolonged phase of acid secretion. Our results also do not support conclusions by Wolvekamp et al but confirm earlier work in this laboratory that histamine is a potent acid secretory stimulant. Evidence for species differences in responsiveness to gastric secretory stimuli was also obtained.

EFFECTS OF ERYTHROPOIETIC STIMULATING FACTOR ON INHERITED ANEMIA IN MICE. Elizabeth S. Russell,* Geoffrey Keighley, Henry Borsook* and Peter Lowy.* Jackson Memorial Lab., Bar Harbor, Maine, and Div. of Biol., California Inst. of Tech., Pasadena.

The plasma of rabbits made anemic by phenylhydrazine contains erythropoietic stimulating material (Blood, 14: 262, 1959) which can be extracted from the plasma and concentrated. When it is injected into normal animals, it causes a polycythemia similar to that caused by lowered air or O_2 pressure. We have injected this erythropoietic material into WW^V mice (Russell et al., Science, 124: 1076, 1956) with hereditary macrocytic anemia. These mice have low numbers of red cells, low hematocrits and increased mean cell volumes. The mice did not respond to doses 10 - 15 times greater than those which produce measurable effects in normal mice. Normal mice, including non-anemic littermates responded in the typical way to similar, or smaller doses, with increases of hematocrit and by a reticulocytosis. Anemic mice, as well as normal mice, did respond to exposure to lowered partial pressures of O_2 with increased erythropoiesis (see also Gruneberg, Genetics, 24: 777, 1939). We could not recover any of the material from the urine of the anemic mice while they were receiving the large doses. (Supported by grants from the Atomic Energy Commission, the American Cancer Society, the National Science Foundation, and the Office of Naval Research.)

PULMONARY GAS EXCHANGE IN OBESITY. Sami I. Said (intr. by J. L. Patterson, Jr.) Dept. of Med., Med. Coll. of Virginia, Richmond.

Respiratory gas exchange was studied in 13 subjects with varying degrees of obesity. Some lowering of arterial P_{O2} was present in all cases, while arterial P_{CO2} was elevated in only three. In subjects with a normal alveolar P_{O2}, an increased A-a oxygen pressure gradient on air breathing represented an increased venous admixture ratio ($\dot{Q}va/\dot{Q}t$) of from 12 to 30%. Physiological dead space was elevated ($V_V/V_T > 30\%$) in 10 of the 12 subjects in whom it was measured. Pulmonary diffusing capacity (D_{O2}) was measured in four subjects and found to be within normal limits. Polycythemia was present in seven subjects. There was no evidence of significant airway obstruction. The explanation for the abnormal ventilation-perfusion relationship remains uncertain. The magnitude of the "shunt" was greater in the cases with high hematocrits. It is possible that the polycythemia contributed to an increased venous admixture by causing variations in alveolar perfusion. This view is supported by the observation that five thin patients with polycythemia

vera showed evidence of an increased $\dot{Q}va/\dot{Q}t$ ratio. In addition, it is possible that the pumping action of the respiratory movements which normally promotes uniformity of perfusion is in some respect faulty in the obese.

FUNDAMENTALS OF PHYSIOLOGY EXHIBITED BY ECCRINE SWEAT GLANDS. F. Sargent, II and R. R. Sonnenschein. Univ. of Illinois, Urbana and Univ. of California, Los Angeles.

Demonstrations will be presented on axone reflex sweating, ischemic hypohidrosis, and the cyclic sweating induced by tetraethylammonium ion. The axone reflex can be used to study neurohumoral physiology. The action of nicotine on the autonomic secretory neuron can be inhibited by the ganglionic blocking agent hexamethonium. The direct effects of muscarinic acetyl-β-methylcholine on the gland can be blocked by atropine. Tetraethylammonium chloride induces cyclical sweating presumably by potentiating the response of the neuroglandular junction to the background tone of secretory neurons. Reflex sweating induced by placing feet and legs in hot water can be depressed by ischemia. The depression does not begin immediately with the onset of arterial occlusion, a fact which demonstrates that sweat formation is an active secretory process and not just the result of ultrafiltration dependent upon hydrostatic pressure. Charts will illustrate experimental evidence that the hypohidrosis is a consequence of depression of the sweat gland, not the secretory nerve. Other charts will be used to compare the rates at which the kidney and the eccrine sweat gland respond to a negative sodium balance.

UNIFIED CONCEPT OF THE DISTRIBUTION OF BLOOD AND GAS IN THE LUNGS. G. A. Saxton, Jr. (intr. by W. V. Whitehorn). Dept. of Preventive Med., Coll. of Med., Univ. of Illinois, Chicago.

By measuring the gas tensions in the inspired air, alveolar and expired gas, and arterial blood, it is now possible to define disturbances in the distribution of blood and gas in terms of four variables. Each of these can be quantitated with reasonable accuracy as follows: 1) Venous admixture, resulting from right-to-left shunting, as calculated from the alveolar-arterial P_{O2} difference. 2) Dead space, or shunting of alveolar gas into inspired air, as calculated from the arterial-expired P_{CO2} difference. 3) Maldistribution of blood, most often due to inadequate perfusion of some areas of the lungs, as calculated from the (A-a) expired alveolar-arterial P_{CO2} difference. 4) Maldistribution of inspired air, when resistance to airflow is greater in some segments than others, may be quantitated in terms of the rate of change of expired alveolar N_2 during a single deep breath of O_2. Furthermore, these disturbances of distribution can be defined in terms of the range of $\dot{V}A/\dot{Q}$ ratios on the Rahn and Fenn O_2 - CO_2 diagram. The range of alveolar P_{CO2} during the latter half of expiration as indicated by infra-red analysis permits one to determine the alveolar P_{O2} and $\dot{V}A/\dot{Q}$ ratios at this time if the patient is in a steady state. Data from patients with a variety of pulmonary diseases will be presented in order to illustrate this approach.

EVIDENCE FOR VENTRICULAR DIASTOLIC SUCTION IN CLOSED CHEST DOGS. Heiner Scheu,* and W. F. Hamilton. Dept. of Physiol. and Pharm., Med. Coll. of Georgia, Augusta.

The question of ventricular filling by "suction" was investigated by recording the transmural ventricular pressure in normally breathing animals who had recovered from surgery. This transmural pressure was recorded as the difference between the thoracic pressure and the intraventricular pressure. The transmural pressure was considered positive whenever the ventricular pressure exceeded the thoracic pressure as is the case during systole. During diastole the difference between these pressures always small (± 10 mm Hg or less). In the normal untramatized animal it is zero or positive (filling by venous pressure). After experimental procedures it may become negative, (filling by an action of the ventricular wall or "suction"). This suction is greater after mitral stenosis or bleeding, conditions which interfere with venous return and diminish the size of the ventricules by x-ray. The force of "suction" is lessened after transfusions which increases the size of the ventricles. Considerations are advanced for believing that the "suction" force originates in elastic recoil of the ventricular wall and that it is not clearly an important factor in the mechanism of cardiac pumping. From the Cardiovascular Research Training Program at the Medical College of Georgia supported by the National Heart Institute (Grant HTS 5044) and by the American Heart Association.

AMYLASE LEVELS OF SERUM AND DIGESTIVE GLANDS FOLLOWING STIMULATION. L. H. Schneyer and C. A. Schneyer*. Dept. of Physiol. and Dent., Univ. of Alabama Med. Center, Birmingham.

Amylase levels of rat submaxillary-sublingual gland, although low in fasted unstimulated animals, rise rapidly and appreciably during stimulation by parasympathomimetic drugs or normal feeding (Am. J. Physiol. 193:1, 1958). The response of this digestive gland to stimulation thus differs from that of pancreas or parotid gland and apparently is not attributable to activation of an immediate amylase precursor, removal of an amylase inhibitor, or binding of serum amylase by tissue elements (Am. J. Physiol. 189:129, 1957). Possible relationship to increases in serum amylase levels during stimulation (Antopol, Schifrin and Tuchman, Proc. Soc. Exp. Biol. & Med. 32: 383, 1934) has, however, required further exploration. Levels of amylase of serum and of submaxillary gland, and, for comparison, liver, have accordingly now been correlated. Amylase in serum of 48-hour fasted animals rises during stimulation by pilocarpine or normal feeding. Liver amylase, although somewhat elevated under these conditions, fails to reach levels in serum of stimulated animals. Submaxillary-sublingual gland amylase levels, however, rise appreciably and may reach values several fold those of serum. An active accumulation of amylase (possibly as a result of new synthesis) which accompanies parasympathomimetic stimulation in vivo is indicated for this digestive gland. (Supported by NIH Grant D-931.)

ACTION OF THYROID HORMONE ON THE RELEASE OF FATTY ACIDS FROM TISSUE STORES. Irving L. Schwartz and Albert F. Debons.* Medical Res. Center, Brookhaven National Lab., Upton, N.Y.

The mechanism by which thyroid hormone elevates the concentration of non-esterified fatty acids (NEFA) in plasma was studied in dogs by comparing the clearance of C^{14}-labeled palmitic acid before and after the administration of l-triiodothyronine (TRITH). Within 5 hours after an intravenous injection of TRITH (1 mg) the rate of disappearance from the plasma of palmitic acid-1-C^{14} was increased although the total concentration of NEFA in the plasma had doubled, extending our previous observations in man (J. Clin. Invest., 38:275, 1959). When a steady concentration of labeled NEFA was maintained by a constant infusion, the administration of TRITH was followed in 5 hours by a significant decrease in specific activity. It is concluded, therefore, that although the thyroid hormone increases the rate of removal of NEFA from the blood, its predominant effect is to enhance the release of fatty acids from tissue stores. (Supported by the U.S. Atomic Energy Commission.)

LOCALIZATION OF THE MOTOR RESPONSE CENTER OF THE STOMACH IN THE MEDULLA OBLONGATA. Takehiko Semba and Hazime Noda (intr. by R. E. Johnson). Dept. of Physiol., Univ. of Hiroshima Sch. of Med., Hiroshima, Japan.

Motor response of the stomach resulting from the stimulation of the dog's medulla oblongata was investigated using monopole electrodes. Motor response of the stomach was obtained during stimulation of the medulla oblongata after bilateral transection of the splanchnic nerves (the vagus nerves were intact). Motor response of the stomach, produced by the stimulation of the medulla oblongata, was obtained after bilateral transection of the vagus nerves to the stomach (the splanchnic nerves were intact). Motor response of the stomach was also obtained following stimulation of the peripheral end of the posterior roots of the thoracic cord, whether the vagus nerves were intact or severed. Similar responses were also obtained after the stomach was perfused in situ. Histological examination of the stimulated parts showed that both areas which produced the vagal and splanchnic motor effects were found in the region of the nucleus alae cinerea. These areas extended into the gray substance of the spinal cord. Thus, it is logical that the motor pathways to the stomach may course via both the vagus and splanchnic nerves with a common origin in the nucleus alae cinerea.

CHOLESTEROL ABSORPTION: EFFECT OF ANTIBACTERIAL AGENTS. C. S. N. Setty (intr. by D. Nelson), Dept. of Clinical Science, Univ. of Illinois, Chicago.

Four groups of rats were fed a basal diet supplemented with 9% corn oil for 15 days. Groups II, III and IV were supplemented with 37.5 mg of cholesterol daily. In addition Group III received 0.2% streptomycin and 1% sulfasuxidine and Group IV received 200 mg of Terramycin and 500 mg of phthalylsulfathiazole daily. These antibacterial agents have been reported to clear the bacterial flora con-

siderably within 24 hours. On the first of the last 4 days of the 15-day test 0.3 μc of cholesterol-4-C^{14} was added to the diet in each group. The feces were collected for 4 days in 95% alcohol, dried and extracted with 95% alcohol for 72 hours. The alcoholic extract was saponified with 10% ethanolic KOH, and the unsaponifiable material (U.M.) was separated. The assay of radioactivity of U.M. shows that there is no significant difference between the four groups. The same is true for the difference between the U.M. and the digitonin precipitable material. These results indicate that it is important to prevent bacterial action after passage of the feces to avoid increasing artificially the difference between the digitonin precipitable and U.M.

PATTERNS OF PHASIC BLOOD FLOW IN THE LEFT CORONARY ARTERY. R. F. Shaw*, C. R. Rayford* and D. E. Gregg. Dept. of Cardio-respiratory Diseases, Walter Reed Army Inst. of Res., Washington, D.C.

Phasic coronary inflow and its possible determinants was studied in 1940 by Gregg, Green and others utilizing an orifice-meter inserted into a coronary artery. The flow patterns were criticized because the small orifice interposed in the coronary stream could possibly alter flow. The present investigation makes use of a modified Kolin-type electromagnetic flowmeter. This instrument fits snugly around the intact artery, does not impede flow and hence should be free of the possible defects of the earlier method. It has been used in eighteen anaesthetized open-chest dogs to study phasic blood flow through the left circumflex coronary artery under control conditions and during infusion, transfusion, hemorrhage, anoxia and drug administration. During these widely varying states, the phasic flow patterns remain basically the same. With isometric contraction, there is a precipitous attenuation of coronary flow--frequently arresting flow and not uncommonly causing backflow. Upon ventricular ejection, flow increases but only rarely to levels attained during diastole. As the aortic pressure pulse falls, flow decreases until protodiastole, at which time there is an abrupt rise in flow. This high level of flow gradually declines during diastole. These patterns and some of their determinants will be presented and discussed in detail. In general, these patterns confirm earlier work with the orifice-meter.

RELATIVE CONTRIBUTION OF CHANGES IN HEART RATE AND STROKE VOLUME TO THE INCREASE IN CARDIAC OUTPUT IN DOGS DURING EXERCISE. John T. Shepherd, Yang Wang* and Robert J. Marshall.* Mayo Clinic and Mayo Foundation, Rochester, Minn.

Six mongrel dogs were trained to run on a horizontal treadmill. Catheters were placed in the pulmonary artery for indicator injections and the aortic root for sampling. Cardiac output was calculated from indicator dilution curves, and heart rate from electrically damped arterial-pressure records. Ten complete studies were made. Standing at rest, cardiac output varied from 2.0 to 4.3 liters per minute, the heart rate from 90 to 158 per minute and the stroke volume from 15.8 to 37.1 ml. At 4 to 6 kilometers per hour (K.P.H.),

the average increase in cardiac output was 56%; in heart rate, 46%; and in stroke volume, 6%. At 8 to 10 K.P.H., corresponding increases were 112%, 90% and 12%; and at 12 to 14 K.P.H., 163%, 137% and 12%. With this last severe exercise the heart rate was 280 to 340 and the saturation of mixed venous blood 25 to 30%. Thus, in the dog changes in stroke volume contribute only about 10% to the increased cardiac output at all grades of exercise. This confirms the recent observations of Rushmer (Am. J. Physiol. 196:745, 1959), using different technics of measurement.

HEPATIC BLOOD FLOW, HEPATIC GLUCOSE OUTPUT AND ELECTROLYTE FLUX IN HEMORRHAGIC SHOCK. William C. Shoemaker (intr. by Ruth Pick). Dept. of Experimental Surgery, Michael Reese Hosp., Chicago, Ill.

A method for simultaneous catheterization of splenic artery and hepatic and portal veins in a simplified one-stage abdominal operation in the dog has been described. Blood samples were obtained from these sites after recovery without anesthesia. Hepatic blood flow (HBF) was measured by a modified bromsulphalein method. Blood glucose, serum potassium and sodium were measured across the lever in a series of dogs subjected to sudden acute hemorrhage and after gradual prolonged hemorrhage. Initial studies on the sudden withdrawal of 1/6 to 1/4 of the calculated blood volume in a series of six unanesthetized dogs confirmed the expected decrease in BP, cardiac output O_2 consumption, pulmonary artery and hepatic vein O_2 content and an increase in peripheral resistence, systemic (Art. B. Vent) and splanchnic (Art-portal) oxygen gradients. With this degree of hemorrhage some decrease in HBF was noted in 3 of 5 animals. In two dogs the HBF was essentially unchanged, despite decreases in BP and cardiac output, suggesting that the HBF may be preferentially preserved with this degree of hemorrhage. With slow but continuous bleeding, frequent measurements of HBF and plasma concentration gradients allow almost continuous evaluation of the status of hepatic flow and metabolism throughout the early and late stages of hemorrhage. In these experiments, four stages were found: 1. initial stage wherein the baseline HBF values were maintained; 2. a period of increased flow, thought to be a compensatory reaction and probably medicated through neural and/or hormonal influences; 3. a prolonged period of progressively decreasing flow culminating in; 4. a final stage of hepatic functional decompensation, with progressively decreasing ability of the liver to clear BSP.

MANOMETRIC ESTIMATION OF HEPARIN-INDUCED LIPOLYTIC ACTIVITY AND SUBSTRATE SPECIFICITY OF THE ENZYME. B. Shore and O.M. Colvin (intr. by A. S. Gilson, Jr.). Dept. of Physiology, Washington Univ. Sch. of Med., St. Louis, Mo.

A manometric method has been devised for quantitatively measuring the lipolytic activity found in blood after heparin injection. CO_2 release from a mixture of blood, suitable lipoprotein or triglyceride, and bicarbonate is measured in the Warburg. Gas release is directly proportional to enzyme concentration, and almost directly proportional to substrate concentration. Furthermore, equimolar

amounts of the fatty acids commonly found in lipoproteins liberate essentially equivalent amounts of CO_2. Gas release from triolein, trilinolein and tripalmitin is in the ratio 2:1:0.7. It is, of course, possible that the low reactivity of the tripalmitin may reflect its solid state and consequent lack of accessibility to enzyme. Data will be presented that argue against this possibility, but do not completely eliminate it. Plasma which was obtained from a subject given heparin, and was freed of all lipoproteins of density less than 1.20 gm/ml, could still hydrolyze pure triglycerides. The fatty acids liberated from human S_f20-400 lipoproteins possess an iodine number higher than that of the fatty acids of the parent triglycerides. (Supported in part by a grant from the American Heart Association.)

PROPRIOCEPTIVE UNITS IN DORSAL ROOTS DRIVEN BY RESPIRATION. Arthur A. Siebens and Flavio Puletti.* Respiratory and Rehabilitation Center and Dept. of Physiol., Univ. of Wisconsin, Madison.

Laminectomies were performed on cats anesthetized with Nembutal. Rootlets of thoracic segments were severed from the cord and the distal stumps were dissected down to strands exhibiting unitary activity. Action potentials were displayed together with respiration on a two-beam oscilloscope. The signal for breathing was produced by a thermistor suspended in the tracheal cannula and incorporated in a bridge circuit. Results: Two types of fibers were found: Those exhibiting activity independent of breathing and those with a periodicity corresponding to a phase of the respiratory cycle. Among the latter, some were active only during inspiration, others only during expiration. More commonly, units were continuously active but discharged more frequently during either inspiration or expiration. Inspiratory units which ceased firing following respiratory arrest with curare began again during intermittent positive pressure ventilation; their discharge frequency increased with tidal volume. When inflation of the chest was maintained constant, the change in frequency of discharge in a given unit was small. Records were unaffected when the skin over the ipsilateral hemithorax was removed. Bursts produced by delicate prodding of localized portions of the denuded thoracic wall were blocked by localized injections of one percent novocain. Conclusion: Normal respiration is attended by extensive afferent neuronal activity originating within the chest wall. Discharges in single units vary in frequency and also in relationship to the respiratory cycle.

LUNG VOLUME AND PULMONARY VASCULAR RESISTANCE. D. H. Simmons, L. M. Linde,* J. H. Miller* and E. L. Ellman.* V.A. Center and U.C.L.A. Med. Center, Los Angeles, Calif.

Evidence suggests that pulmonary vascular resistance (PVR) might increase if lung volume (LV) either increases or decreases from the normal resting level. To study a broad range of LV in the intact animal, 10 anesthetized dogs were ventilated on O_2 with a Starling pump; the pressure gradient between pulmonary artery and vein was measured through cardiac catheters using a differential transducer; and dye-dilution cardiac output (CO) was measured in

duplicate using indocyanine green. PVR was determined at normal, decreased (33%), and increased (75%) functional residual capacity (FRC) by using end-expiratory pressures of 0, -16 and 15 cm H_2). PVR averaged 90.6, 113.5, and 258.7, an increase of 25% and 185% at decreased and increased lung volumes, indicating that PVR is related to LV by a "U-shaped" curve, with minimum resistance near the normal FRC. CO increased 18% with the smaller FRC and decreased 30% with the larger, presumably due to effects on venous return, so that both increases in PVR could not be ascribed to CO changes alone. Nor was it due to decreased transmural pressures of major vessels, since pulmonary artery pressure measured against intrapleural pressure rose from 16.2 to 24.1 and 23.5 cm H_2O at smaller and larger FRC and pulmonary vein pressures changed from 10.4 to 13.6 and 9.0. This suggests that the increased PVR at decreased and increased LV is due to altered geometry of smaller pulmonary vessels which is a function of lung size.

EFFECT OF K+ ION ON POTENTIAL DIFFERENCE, RESISTANCE AND SECRETORY RATE OF IN VITRO FROG'S STOMACH. M. A. Simon,* W. J. Kilgour*, C. Chandler* and W. S. Rehm. Dept. of Physiol. and Chem., Univ. of Louisville, Louisville, Ky.

It has been shown that elevation of K+ ion concentration in the dog's stomach by close arterial injections of KCl solutions results in decrease in PD and resistance. Marked vasoconstriction (blanching of the mucosa) accompanied these effects and prevented an adequate quantitative study. In order to further understand the effects of K + ion on the stomach, the effect of changes of this ion on the nutrient side of the in vitro frog's stomach was studied. A double chamber was used with two pairs of electrodes. Resistance was determined as the change in PD per unit of current at a density of 10 μ amps. cm^{-2}. A bucking voltage was placed in series with the PD electrodes and a recording voltmeter with a sensitivity of 2 mv cm^{-1} was used. In stomachs with and without histamine stimulation (in some without histamine the PD was high and the secretory rate essentially zero,) it was found that reduction of the K+ ion (4 to 1 meq. $liter^{-1}$) resulted in an increase in PD and resistance and an increase in K+ ion (up to 36 meq $liter^{-1}$) resulted in a decrease in PD and resistance. The slope of the PD vs log(K+) was less than 60. Secretion was increased, PD and resistance decreased in going from 1 to 8 meq $liter^{-1}$ confirming oral presentation of Harris and Edelman but not their abstract (Federation 1959) wherein they reported no change in resistance. (Supported by grants from NIH and NSF.)

AUDITORY RESPONSES IN THE VENTRAL TEMPORAL CORTEX OF CAT. Ronald M. Sindberg and Richard F. Thompson (intr. by K. Akert). Dept. Physiol., Univ. Wisconsin, Madison.

Responses of the cortex ventral to AII in cat to auditory stimulation under chloralose were studies. In addition to a previously described insular response region, a response field was mapped in the ventral portion of Ep extending below the ventral tip of the posterior ectosylvian sulcus. The insular response field has latencies to click of 8-10 msec and a maximum amplitude of 300 microvolts. The

ventral Ep region has response latencies of 15-20 msec and maximum amplitude of 1.6 mV. The ventral response field is still present after acute removal of AI and AII. Electrical stimulation of the cochlear nerve indicated that while portions of the insular field responded to both apical and basal turn stimulation, the ventral region was predominanetly apical in representation. Variation of stimulus repetition rate showed that responses of the ventral region were graded, as are responses of AI, in contrast to the all-or-none character of association responses. Responses of the ventral region are thus similar in characteristics to those of the more dorsal Ep field. The latter, however, has representation of the basal turn of the cochlea. This, then, may form an additional auditory area, with the basal turn of the cochlea represented dorsally and the apical portion ventrally on the posterior ectosylvian sulcus. (NIH post-doctoral fellows; aided by grant B-896, NINDB.)

BODY WEIGHT, FLUID LOAD AND DIURETIC DRUGS AND THEIR RELATION TO 5 HOUR URINE VOLUMES IN NORMAL OR FASTED-DEHYDRATED RATS. George M. Sisson, J. D. Haynes, L. M. Lipchuck and J. R. Cummings (intr. by Walter S. Root). Dept. of Pharm. Res., Exptl. Therap. Res., Lederle Laboratories Div., American Cyanamid Co., Pearl River, N.Y.

In setting up a screening procedure for diuretic agents using rats we have studied the relationship of body weight and saline load to 5 hour urine volumes. This was done using acetazolamide, meralluride, theophylline or a placebo. Urine volumes were measured for normal or fasted-dehydrated rats. On the assumption that 5 hour urine volume (E) is related to body weight (W) and fluid load (F) by a heterogonic of the form $E = aF^{b}W^{c}$, we have analyzed our data by multiple regression analysis. In normal rats weight and load exponents (c and b respectively) were +0.70 and +0.39 while in fasted-dehydrated rats they were +0.49 and -0.02 respectively. With acetazolamide the weight and load exponents were +0.89 and +0.07 for normal rats and +0.55 and +0.22 for fasted-dehydrated rats respectively. At 1.2 mg Hg per rat, intramuscularly, meralluride failed to elicit diuresis in normal rats in 5 hours while for fasted-dehydrated rats 5 hour urine volumes were less than for controls. At 3.9 mg Hg per rat weight and load exponents were +0.41 and +0.48 respectively for normal rats and -0.06 and 0.66 respectively for fasted-dehydrated rats. For theophylline load exponent was not studied but weight exponent for normals was +0.19 while that for fasted-dehydrated rats was +0.74.

CENTER OF ARTERIAL PRESSURE REGULATION DURING ROTATION OF NORMAL AND ABNORMAL DOGS. Edward E. Smith* and Arthur C. Guyton. Dept. of Physiol. and Biophysics, Sch. of Med., Univ. of Mississippi, Jackson.

By rotating dogs through 360 degrees about transverse axes passing through various points along the length of their bodies points at which arterial blood pressure remains constant irrespective of position have been located in normal dogs, in dogs with major pressoreceptors abrogated, and in dogs with total spinal anesthesia.

Location of the point of constant blood pressure other than at the mid-portion of the animal signifies the action of presoregulatory mechanisms capable of correcting sudden fluctuations of blood pressure. If regulation is highly effective, this point of constant pressure will lie very near the pressoreceptors. In intact dogs blood pressure was found to remain very nearly constant when they were rotated about a point in the neck 0.119 times chest length above the suprasternal notch. After denervation of the carotid sinuses and aortic pressoreceptors the point shifted into the chest 0.468 times chest length below the suprasternal notch. In animals with total spinal anesthesia the point was located in the abdomen some 1.39 times chest length below the suprasternal notch. These findings indicate that pressoregulatory mechanisms operate to maintain blood pressure within narrow limits at a critical point in the neck, a site no doubt dictated by the necessity of providing adequate cerebral blood flow under all conditions of activity.

EFFECT OF HISTAMINE AND INSULIN-HYPOGLYCEMIA ON GASTRIC CONTENT OF SPIDER MONKEYS (ATELES). G. P. Smith,* F. P. Brooks, R. A. Davis,* and S. S. Rothman.* Dept. of Physiol. Univ. of Pennsylvania, Philadelphia.

Three spider monkeys weighting 3 Kg and equipped with gastric fistulae were studied. Single subcutaneous doses of histamine from 0.03 to 0.27 mg of base/Kg were given and gastric content collected for 1 hour after each dose. Definite increases in conc HCl and volume were obtained after 0.06 mg/Kg and no significant increase was found between 0.13, 0.2, and 0.27 mg/Kg. The mean maximum response for the 3 monkeys was volume 18.1 ± 1.1S.E.ml/hr, conc. HCl 128 ± 4 mEq/hr, output of HCl 2.35 ± 0.22 mEq/hr, Na 19 ± 1, K^+15 ± 2, and Cl^-159 ± 2. Pepsin concentrations measured by both the techniques of Riggs and Stadie and Anson showed an increase over the 1 hour control specimen, greatest in the first hour after histamine (923 vs. 405 x 10^{-4}Hb P.U.). Even after 3 subsequent hourly injections of histamine the conc remained at 540 x 10^{-4}Hb. The response to insulin-hypoglycemia was found to require 2 units/kg intravenously to lower the blood sugar below 40 mg/100 ml (Glucose oxidase method). One animal had convulsions at this dose. Two monkeys responded in the usual fashion with a volume of 16 ml/hr, conc. HCl 122 mEq/1., Na^+25, K^+16 and Cl^- 153. The conc. of pepsin was 833 x 10^{-4}P.U./ml. The 3rd monkey showed a prolonged period of inhibition. During the first hour after insulin the pH was above 3.5. During the 2nd hour the vol. was 7.0 ml and the conc. HCl 49 mEq/1. This was the same monkey previously reported to show lowered gastric acidity during restraint. (Supported by Grant No. RG 5007, National Institutes of Health.)

IS AXONE REFLEX SWEATING A PHYSIOLOGICAL PHENOMENON? R. R. Sonnenschein and J. T. McLaughlin.* Dept. of Physiol., Univ. of California Sch. of Med., Los Angeles.

Since the demonstration by Coon and Rothman (J. Pharmacol. & Exp. Therap. 73:1, 1941) it has been known that the intradermal injection of nicotinic drugs (acetylcholine, nicotine, lobeline) can

produce sweating via an axone reflex; and that the action of these drugs can be blocked by tetraethylammonium and hexamethonium ions (Janowitz and Grossman, Science 109:16, 1949; Duner and Pernow, Acta Physiol. Scand. 25:38, 1952). No evidence has been adduced on the question of whether this phenomenon can and does occur under physiological conditions. If such occurs, it is reasonable to suppose that it may be initiated by endogenous acetylcholine. To test this possibility, potent cholinesterase inhibitors have been administered locally in human subjects: either DDVP, 50% in propylene glycol, applied directly to the skin for 20 to 40 minutes, or a saturated aqueous solution of paraoxon (approximately 0.002%) injected intradermally in a volume of 0.05cc. Sweating occurred which appeared to be localized to the site of administration, and did not have the distribution of an axone reflex. The response was blocked by prior intradermal injection of 1% procaine in most cases, but not by hexamethonium chloride 1:10,000. The results to date suggest that endogenous acetylcholine, under these conditions at least, does not initiate an axone reflex. (Supported by ONR contract Nonr 233(30).)

NON-SYNCYTIAL NATURE OF CARDIAC MUSCLE: MEMBRANE RESISTANCE OF SINGLE CELLS. Nick Sperelakis* and T. Hoshiko. Dept. of Physiol., Western Reserve Univ. Sch. of Med., Cleveland, Ohio.

Previous work has suggested that the myocardium is neither a morphological nor a functional syncytium (Fed. Proc., 18: 279, 1959). During hypertonic perfusion, quiescent cells were often found adjacent to active ones suggesting some cells were electrically isolated from their neighbors. The specific resistance of cardiac and smooth muscle tissues were found to be much more sensitive to interspace ion depletion compared to skeletal muscle. This suggested that the current flow path through the cardiac cells is of high resistance in comparison to the extracellular fluid path. In the present study of frog ventricle, constant current pulses were used to estimate the DC resistance between two microelectrodes: a) when both microelectrodes were extracellular, b) when only one microelectrode was inside a cell, and c) when both microelectrodes were inside neighboring cells. The resistance of one cell was about 12 megohms; this large resistance indicates that the cells are functionally small units, assuming that the membrane specific resistance is about 1000 ohms - cm^2. The resistance between the interiors of two cells was about twice the resistance of one cell indicating that there are no low resistance pathways between cells. Therefore, the myocardium is not a functional syncytium and junctional transmission may occur from cardiac cell to cardiac cell.

CONSTANCY OF OXYGEN UPTAKE BY RESTING DOG SKELETAL MUSCLE WITH DIFFERENT BLOOD FLOWS. W. N. Stainsby, Dept. of Physiol., Coll. of Med., Univ. of Florida, Gainesville.

There are observations in the literature which indicate that oxygen use by resting skeletal muscle may not be constant. For the most part these experiments were performed on pump perfused

mammalian skeletal muscle or isolated frog skeletal muscle. In this study the in situ gastrocnemius-plantaris muscle group of the dog with isolated circulation was used. Some of the preparations were denervated two hours before any data were recorded. By means of a small Starling resistance inserted in the arterial inflow path, the arterial inflow pressure to the muscle group was regulated without altering the animal's systemic blood pressure. Venous outflow was measured by a rotameter. All preparations showed vascular reactivity when the inflow pressure was changed. Arterial and venous blood oxygen contents were determined and oxygen uptake calculated. Reducing the inflow pressure from normal (90-120 mmHg mean pressure) to 15-30 mmHg mean pressure reduced blood flow through the muscle group by approximately 50 percent (25-60 percent). The oxygen uptake by the muscle group was constant over the range of flows studied in both the innervated and acutely denervated preparations.

EFFECT OF METHIMAZOLE ON THE DRY WEIGHT OF THE RAT HEART. J. Clifford Stickney, David W. Northup and Edward J. Van Liere. West Virginia Univ. Med. Ctr., Morgantown.

Sixty male albino rats were divided into two groups: 30 served as controls; 30 were given, as the only source, drinking water containing 0.11 mg/ml methimazole. Both groups were fed Purina Laboratory Chow ad libitum. This procedure was continued for 47 days. The rats were then fasted for 24 hr, weighed, and killed by decapitation following stunning. The heart was removed from each animal, trimmed, washed in isotonic saline, blotted dry, and weighed. It was then dried to constant weight at 105 C to determine the per cent of solids. The heart weight-body weight ratios (wet weight) averaged 2.90 in the controls and 2.72 in the experimentals, the difference, 0.18 is significant at the 0.1% level. The percent solids were 23.02 and 22.80 for the respective groups; the difference, 0.22 is significant at the 4% level. The decline in heart weight-body weight ratios produced by methimazole is thus demonstrated to be genuine and not due to dehydration. On the contrary, there is slightly greater decrease in dry weight than in wet weight, which is in line with the well known tendency of the hypothyroid animal to retain fluids.

DIRECT EXTRACELLULAR STIMULATION OF SINGLE NEURONS. Felix Strumwasser and Suzanne Rosenthal (intr. by M. G. F. Fuortes). Lab. of Neurophysiol., National Institutes of Health, Bethesda, Md.

Extracellularly recorded single neurons in the brain of curarized frogs can be excited by constant current applied through recording micropipettes of $< 0.5u$ tip diameter filled with 5M NaCl. Utilizing this technique, it is possible to detect normally inactive units not fired by available external physiological inputs, to modulate spontaneous activity, to reveal after-effects and to modify the form and size of the recorded action potential. Positive current is required to excite, negative to inhibit; for pulses 100 msec to several seconds long, current magnitude is surprisingly low, (range 0.5 to 10 x 10^{-9}A).

3 x 10^{-9}A is often adequate to excite inactive cells. Strong excitatory currents can cause reversible total inactivation usually preceded by a high frequency burst and abortive spikes. This paper deals primarily with patterns of firing in single neurons when subjected to currents as long as several minutes. During such long polarizations, adaptation of firing rate is rare; instead, it is common to find average spike frequency increasing steadily over the first 1/4 minute when current is applied; in certain units reproducible off-bursts and after-effects are present. We, tentatively, interpret the effects of long term induced firing as modulating or initiating activity in a small network of interconnected neurons of which the directly excited cell is a member. Off and after effects can then be explained in terms of different time courses of decay of excitatory and inhibitory interactions within this network, which must have feedback onto the directly excited cell.

COMPARISON OF VITAL CAPACITY AND MAXIMUM BREATHING CAPACITY OF ATHLETES AND NONATHLETES. Douglas G. Stuart* and W. D. Collings. Dept. of Physiol., Univ. of California, Sch. of Med., Los Angeles and Michigan State Univ., East Lansing.

Twenty athletes and twenty nonathletes were matched in height, weight and age. The vital capacity (VC), maximum breathing capacity (MBC) and MBC/VC measurements of the two groups were compared. The mean VC of the athletes was 5.69 liters BTPS as compared to 5.29 liters BTPS for nonathletes, a statistically significant difference ($P < .05$ with t test). The mean MBC of the athletes was 197 l/min BTPS as compared to 192 l/min BTPS for nonathletes, a difference not statistically different ($P > .5$). When the "capacity ratios" of MBC/VC were computed it was found that 1 liter of vital capacity would support 36.6 liters of MBC for nonathletes and 34.7 liters for athletes, an insignificant difference statistically ($P > .1$). It is suggested that the difference in VC is due to an increased development of respiratory musculature incidental to regular physical training. This increase is not reflected in the MBC since this measurement would appear to be more concerned with the presence or absence of obstructive ventilatory defects that are unaffected by physical training. Similarly, the "capacity ratio" of MBC/VC, used to detect deviations from the normal in either muscular force or air flow resistance, would appear only of value when such deviations are debilative.

EFFECT OF SODIUM DEHYDROCHOLATE ON THE ABSORPTION OF CHOLESTEROL IN THE RAT. R. Suzuki* and A. C. Ivy. Dept. Clinical Science, Univ. of Illinois, Chicago.

It is established that bile salts are obligatory for the absorption of cholesterol in the rat. It has been shown that sodium taurocholate when mixed with cholesterol and the daily ration and fed in aliquots every 2 hr for 12 hrs in a ratio of 325 mg bile salt to 50 mg cholesterol will return the absorption of cholesterol to normal in a chronic bile fistula rat. With sodium taurocholate the absorption of cholesterol ranged from 40 to 50%, with sodium dehydrocholate no or very little absorption has occurred.

EFFECTS OF THAM DURING CO_2 BREATHING IN MAN: METABOLIC AND TOXIC EFFECTS. R. Tarail,* T. E. Bennett,* E. S. Brown,* I. L. Bunnell,* J. O. Elam,* J. L. Evers,* D. G. Greene*, C. D. Janney,* H. J. Lowe* and G. G. Nahas. Buffalo General Hosp. and Roswell Park Inst., Buffalo, N.Y.

0.3 Molar tris hydroxymethylaminomethane (THAM) in 0.03M NaCl and 0.005M KCl was injected intravenously over 30 to 60 minutes into 4 healthy adults (total THAM dose 2.8 to 8.8 mM/kg body weight) during 2.3 or 3.4% CO_2 breathing and water diuresis. Arterial blood serum glucose concentrations fell significantly, without glycosuria, attaining distinctly hypoglycemic levels with the largest dose. Although serum inorganic phosphate tended to fall, potassium did not. High concentrations of THAM in vitro did not lower serum glucose values. Arterial pH (cf. Brown et al. The Physiologist this issue) and CO_2 content rose, serum urea was unchanged; sodium, potassium, calcium, and chloride showed no definite trends. Urine pH and CO_2 content rose strikingly as THAM excretion rose. Sodium, potassium, chloride, and (perhaps) phosphorus excretion rose but urea excretion was steady. 64% of THAM administered was recovered in urine over 2 days and 77% over 3 days. Major side effects (hypotension, hypoxia, hunger, sweating, periodic breathing, weakness, somnolence, diarrhea, intense retching and vomiting; sensations of heat, swelling, and numbness of face) developed in one subject given the largest dose.

ANALYSIS OF WHOLE BLOOD GASES BY GAS CHROMATOGRAPHY. B. W. Taylor and Jean Pressau (intr. by Dr. R. C. Kory). Wood Veterans Admin. Hosp., Milwaukee, Wisc. and Fisher Scientific Co., Pittsburgh, Pa.

A method of analysis for whole blood gases will be described, with special emphasis on a reaction chamber within a gas chromatographic system. Blood handled anaerobically for oxygen and carbon dioxide content, or aerobically for oxygen and carbon dioxide capacity, is charged to the reaction chamber by a special 0.1 ml syringe. The blood gases are flushed into the chromatographic columns by helium carrier gas for separation. The gases are measured by thermal conductivity, and the corresponding peaks drawn on a strip chart recorder are proportional to the quantity of gases in the sample. This method permits a series of 6 to 10 determinations without emptying or cleaning the reaction chamber. It is possible for the above analysis to be performed in approximately 4 to 5 minutes not including calculation of the area under the curve. Data will be presented comparing values obtained by this method with those obtained by the Van Slyke procedure.

BEHAVIORAL ALTERATIONS IN CATS FOLLOWING MAMMILLOTHALAMIC TRACTOTOMY. Garth J. Thomas, Frank J. Fry,* William J. Fry and Burton Slotnick*. Biophysical Res. Lab., Univ. of Illinois, Urbana.

Little is known about the function of the anatomically well defined system connecting the mammilary nuclei of the hypothalamus with the cingulate cortex via the mammilothalamic tracts and synaptic relay in the anterior thalamic nuclei. In this study 19 cats were

trained to criterion in shock-avoidance conditioning in a double-grill box. Sixteen animals sustained stereotaxically placed bilateral lesions aimed at cutting the mammillothalamic tracts. In five cats the lesions were produced by electrocoagulation and in 11 cats the lesions were made by irradiation with focused ultrasound. Three cats underwent control surgery in which no lesions were made. Postoperatively the animals were tested for retention of the avoidance response and then retrained to criterion. After histological study of the brains, a control group comprising the three sham-operated cats and six cats in which the lesions failed to sever the mammillothalamic tracts was compared with an experimental group consisting of 10 cats in which the tracts had been completely severed. Compared with the control group, the experimental group showed severe loss of retention of the avoidance response and took considerably more shock reinforcements to re-reach criterion performance. Differences in terms of both indicators are highly significant ($P < .001$). No postoperative changes in general behavior were observed. The cats continued to show autonomic and behavioral signs of conditioned fear in the testing situation.

AUDITORY RESPONSE FIELDS IN ASSOCIATION AND MOTOR CORTEX OF CAT. Richard F. Thompson and Ronald M. Sindberg (intr. by J. E. Hind). Dept. Physiol., Univ. Wisconsin, Madison.

Cortical response fields to auditory stimulation under chloralose anesthesia were mapped in cat. In addition to previously described auditory cortex, two response foci have been delimited on the middle suprasylvian gyrus, one on the anterior lateral gyrus, and one on the precentral motor cortex. All four foci have very similar response characteristics: 15 msec latency surface positive wave of up to 3 mV amplitude. In addition, a very late response, latency about 100 msec, occurs over the region of visual area II. Electrical stimulation of the apical and basal turns of the cochlear nerve, while producing the same pattern in AI and AII as in cats under pentobarbital, results in a common response field on the middle suprasylvian gyrus. Variation of stimulus repetition rate demonstrated that both the short and long latency responses tended to be all-or-none in character, in contrast to the graded responses of AI. The four short latency foci are very highly correlated with each other in occurrence and amplitude, but are not correlated at all with response amplitude in AI. They are significantly correlated with the late response. All foci are present and normal after chronic ablation of AI, AII, Ep, SII, and insular temporal areas bilaterally. It is concluded that the four 15 msec latency foci represent input to four separate areas of the cortex from a common subcortical system. (NIH Postdoctoral fellows; aided by grant B-896, NINDB.)

RELATIONSHIP OF ACETYLCHOLINE AND EPINEPHRINE TO INTESTINAL TONUS. M. E. Tidball (intr. by W. B. Youmans). Dept. of Physiol., Univ. of Wisconsin Med. Sch., Madison.

Experiments were designed to study the relationships among acetylcholine (Ach), epinephrine and intestinal tonus in isolated seg-

ments of rabbit intestine. A method for expressing tonus in terms proportional to the shortening from the maximal length produced by combined action of atropine and epinephrine, as determined at the end of the experiment, was developed. In the first series of experiments the rabbit intestine was allowed to contract spontaneously without the addition of pharmacologic agents. The Ach concentration of the bath fluid was assayed on guinea pig ileum and the quantity found compared with the tonus of the intestinal strip at the time of assay. In a second series of experiments, the tonus of the rabbit intestine was depressed by epinephrine after a control Ach assay had been made. The Ach concentration of the rabbit bath fluid was determined by assay on guinea pig illeum which had been pretreated with dichlorophenyl-2-isopropylamino-ethanol (DCI) and the amount of Ach compared with the tonus of the rabbit intestine during inhibition by epinephrine. In 43 determinations from 17 experiments, Ach concentration was shown to be proportional to intestinal tonus, whether the intestine was contracting spontaneously or under the depressant influence of epinephrine.

STUDY OF THE EFFECT OF HEART RATE ON CARDIAC OUTPUT IN THE NORMAL MAN AT REST. A. F. Toronto* and H. R. Warner. Latter-day Saints Hosp. and Univ. of Utah, Salt Lake City.

This study is an attempt to quantitate cardiac output as a function of heart rate over a limited range of heart rates in resting man. In six normal subjects a metal-tipped catheter was passed via a peripheral vein into the right atrium in such a way as to maintain firm contact between the tip of the catheter and the lateral wall of th4 atrium. By means of this catheter-electrode and a second electrode on the anterior chest wall, the heart could be driven with a 2 volt--5 millisecond square wave at rates varying from 70 per minute to an upper limit which varied from subject to subject between 130 and 180 per minute. After 2 minutes at each heart rate cardiac output was measured by the dye method. A pulse contour method was used to evaluate the beat-to-beat changes in cardiac output associated with sudden changes in heart rate. The use of the pulse contour method for this purpose seems justified since steady state cardiac outputs calculated from pressure pulses recorded during the dye curves agreed well with the corresponding dye values. An increase in heart rate from 70 to 120 per minute resulted, within one heart cycle, in a sustained increase in cardiac output of 15 to 25 percent of the control value. At higher heart rates cardiac output fell.

POTASSIUM TRANSPORT AND OSMOREGULATION IN LAMB RED CELLS. D. C. Tosteson and R. H. Moulton*. Dept. of Physiol., Washington Univ. Sch. of Med., St. Louis, Mo.

We have recently formulated a theory to account for regulation of cation composition and volume by two genetically different types of sheep red blood cells, one which contains mainly potassium and another which contains mainly sodium as intracellular cation (Tosteson and Hoffman, Proc. of the Biophysical Soc., 1959). We have

studied the cation composition and potassium transport in lamb red cells in order to evaluate further the range of applicibility of this theory. We have confirmed the observation that all lambs have red cells which contain potassium as the main intracellular cation. Serial analyses of the potassium and sodium concentrations in the red cells of 18 lambs at two week intervals after birth revealed that the red cells assumed a cation composition characteristic of the adult phenotype during the first six or eight weeks of life. The magnitudes of potassium influx by active transport (pump) and by passive diffusion (leak) were also estimated in the red cells of some of these lambs at two week intervals after birth by measuring the potassium influx in the presence and absence of strophanthidin, a compound which is known to block the pump. The ratio of potassium influx by pump to potassium influx by leak measured in this manner agreed well with the ratio predicted from the potassium and sodium composition of the lamb red cells and the theory mentioned above. (USPHS Grant No. H-4045.)

ESTIMATION OF THE ANATOMICAL RESPIRATORY DEAD SPACE IN MAN BY SINGLE BREATH ANALYSIS. Pierre Tulou* and Eugene M. Renkin. Vet. Adm. Center, Martinsburg, W. Va. and George Washington Univ., Washington, D.C.

When a tube containing one gas (air) is washed out with another (alveolar gas), the composition at the end of the tube will be exactly half-way between the two gases when a volume of gas equal to the volume of the tube has passed through. This principle has been applied to the estimation of the volume of the respiratory passages in man. The volume of gas expired and the CO_2 concentration were recorded during single expirations, and the volume at which the expired CO_2 was half the alveolar CO_2 was taken as the anatomical dead space. Even when there was no clearly defined alveolar plateau, it made little difference in the calculated volume whether mid-expiratory or end-expiratory CO_2 concentration was taken as "alveolar". The dead space calculated in this way is smaller than the Bohr dead space or that calculated from the same data by the use of Fowler's method. It is considered to represent the volume of the respiratory passages with little or no inclusion of "alveolar" dead space.

VISUAL RADIATIONS IN MAMMALS WITH PURE CONE RETINAE. Prabhakar G. Vaidya* and Ferdinando A. Morin. Dept. of Anatomy, Wayne State Univ., Detroit, Mich.

Lesions of different shape, size and location were made in the cerebral cortex of twenty-two ground squirrels (Citellus tridecemlineatus tridecemlineatus) under aseptic conditions and barbiturate anesthesia. Retrograde cell changes in the lateral geniculate were studied in serial histological sections. Dorsal and ventral parts of lateral geniculate are outlined clearly. The ventral part is unaffected by cortical lesions. The dorsal part does not show evidence of lamination. Preliminary observations show that cell population is uniform in size and shape. Findings indicate that most of the caudal half of the medial and dorsolateral surface of the cerebral

hemisphere receives projections from the lateral geniculate. The dorsal pole of the lateral geniculate projects mainly to the medial cortex and ventral pole to the rostral part of the visual cortex. A study of visual projections with the evoked potential method is now in progress. (Supported by USPHS #B-1201 (C-1).)

EFFECTS OF PENTOBARBITAL ON HYPOTHALAMIC FACILITATION AND INHIBITION OF SPINAL CORD REFLEXES. Irving H. Wagman and Shaul Feldman.* Dept. of Neurology, Mount Sinai Hosp., New York City.

The effects of hypothalamic stimulation on spinal cord reflexes (recorded electrically) were examined in unanesthetized, immobilized cats as well as in the same animals under different levels of pentobarbital anesthesia. In the unanesthetized animal, stimulation of most hypothalamic points potentiated the monosynaptic and depressed the polysynaptic reflexes. A few points, however either did not alter the polysynaptic reflexes or potentiated them. Small doses of pentobarbital diminished these hypothalamic influences on spinal reflexes. These effects were correlated with potentials evoked in the anterior hypothalamus upon dorsal root stimulation. In the unanesthetized animal these evoked potentials had latencies of 20 to 40 milliseconds; they were abolished by small doses of pentobarbital. This stage corresponded with the attenuation of the hypothalamic effects on spinal cord reflexes. Additional amounts of the anesthetic caused the appearance of long latency (60 to 160 milliseconds) hypothalamic potentials following dorsal root stimulation. This stage was correlated either with complete abolition or reversal of the effects of hypothalamic stimulation. The results indicate that different neural mechanisms in the hypothalamus may be distinguished by comparison between the anesthetized and unanesthetized animals. The changes in the evoked potentials in the anterior brainstem obtained upon dorsal root or sciatic stimulation may be helpful in estimating the state of anesthesia and activity of the structure explored. (Supported in part by USPHS Grant No. B-294.)

EFFECTS OF COMBINED DENERVATION AND TENOTOMY ON SKELETAL MUSCLE. Khalil G. Wakim and Lester Clapp.* Mayo Clinic and Mayo Foundation, Rochester, Minn.

In adult albino rats a comparative study was made of the effects of tenotomy, denervation and the combination of both tenotomy plus denervation on the work output, endurance and weight of the skeletal muscles attached to the Achilles tendon. Denervation was achieved by high excision of the sciatic and femoral nerves at the base of the thigh. Tenotomy was effected by excision of the tendo achillis with overlap and suture of the cut end to prevent reinsertion to the os calcis. Four weeks after tenotomy and denervation the work output and weight were determined and compared with the same factors in respect to normal muscles. As compared with the normal controls, the muscle weights, initial and total work output were most severely reduced by combined denervation and tenotomy. Denervation alone caused more reduction in muscle weight and in work output than did tenotomy alone. The average work output of the gastrocnemius

muscle group in gram meters per 100 seconds was 196 for the normal muscles, 108 for the tenotomized, 24 for the denervated and 12 for the denervated and tenotomized. Evidently the combination of tenotomy and denervation of the same muscle group has a practically additive effect on the muscles, causing a very marked reduction in muscle weight and in work output and endurance.

CHANGES IN TWITCH TENSION INDUCED BY QUICK STRETCH AND SUBSEQUENT STRESS RELAXATION IN SKELETAL MUSCLE. Sheppard M. Walker and Antoinette G. Thomas.* Dept. of Physiol., Univ. of Louisville Sch. of Med., Louisville, Ky.

Male rats of the Anheuser-Busch strain, weighing about 400 gm, were anesthetized with 275 mg of sodium barbital/kg. The triceps surae was prepared in situ for indirect stimulation and for mechanical recording of isometric twitch contractions. The muscle was stimulated with two supramaximal shocks/sec. Quick stretch was obtained by release of a steel spring (Am. J. Physiol. 164: 238, 1951). The amount of quick stretch was varied from 2.5 to 12.5% of resting length of the muscle. Twenty to 50% of the tension induced by quick stretch disappears during a one-minute period of stress relaxation immediately following the stretch. A slow stretch to about 110% of equilibrium length is required to attain the optimum length for development of maximum twitch tension. Changes in twitch tension induced by quick stretch are similar to the changes in twitch tension induced by slow stretch, i.e., quick stretch up to optimum length increases twitch tension, and quick stretch beyond optimum length decreases twitch tension. During one minute of stress relaxation the amplitude of twitch tension usually varies directly with the length and inversely with the resting tension of the muscle up to and beyond optimum length. (Supported in part by grant H-697(C9), Natl. Heart Inst., USPHS, and an American Heart Association grant.)

PATHOPHYSIOLOGY OF CANINE CONGESTIVE HEART FAILURE. C. R. Wallace, (intr. by Philip Dow). Dept. of Physiol., Med. Coll. of Georgia, Augusta.

In the 17 dogs studied, congestive failure was caused by valvular disease (7), adult Dirofilaria (heartworms) (7), and congenital defects (3). These dogs exhibited the compensatory physiological mechanisms of tachycardia, cardiac dilatation and hypertrophy, altered distribution of body fluids, and retention of sodium and water. Before treatment, heart rates were as high as 250, with arrhythmias in 50% of the cases. Total heart volumes were as large as 60 cc/kg body weight. Heart weights were as much as 14.4 gm/kg body weight. Blood volumes were increased as much as 50%. In addition to ascitic fluid, 50% had interstitial edema and 33% had pleural effusion. Sodium retention was evidenced by oliguria and low urine sodium. Central venous pressures were variable, with some as high as 30 cm or as low as 8 cm H_2O. Plasma proteins were as low as 4.4 gm %. Plasma electrolytes were mostly within normal limits. Right heart catheterization showed increased pulmonary wedge, pulmonary arterial, and right ventricular pressures. Cardiac outputs were normal or reduced. Therapy with either digitalis or sodium-

absorbing resins tended to return these compensatory conditions to normal. (Supported by the National Heart Institute (grants H-240 and HTS-5044).)

PHYSIOLOGIC EVIDENCE FOR DIRECT CONNECTIONS FROM ANTERIOR HYPOTHALAMUS TO SPINAL AUTONOMIC MOTONEURONS. G. H. Wang. Dept. Physiol., Univ. Wisconsin, Madison.

1.With cats under chloralose (50 mg/kg) and urethane (2 g/kg), single shocks delivered to anterior hypothalamus evoke large galvanic skin responses from all four feet, whereas a shock of equal strength delivered to the central end of a divided cutaneous nerve usually elicits no galvanic skin reflex from the feet or at most a reflex of very small amplitude from the front feet. 2. Tetanic stimulation of the anterior hypothalamus evokes a response 2-80 times higher amplitude than the reflex to tetanic stimulation of a cutaneous sensory nerve. 3. The response to hypothalamic stimulation has a latency 25% shorter than the reflex to stimulation of a cutaneous sensory nerve. 4. This response to hypothalamic stimulation from a hind foot often reaches 80-90% of the response to direct stimulation of the tibial nerve, whereas the reflex evoked by stimulation of a cutaneous nerve equals at most 10% of the response to tibial stimulation. 5. Further administration of pentobarbital sodium abolishes the reflex in 3-4 minutes, but the hypothalamic response is still elicitable for 4-6 minutes after cessation of respiration. These facts strongly suggest that the connections from the anterior hypothalamus to the spinal autonomic motoneurones are direct. (Aided by grant B-1460, NINDB.)

EXAMINATION OF THE "SLOPE VOLUME" METHOD FOR MEASUREMENT OF LUNG BLOOD VOLUME. Yang Wang,* John T. Shepherd and Robert J. Marshall*. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The Stewart-Hamilton method cannot be applied to determine directly the amount of blood in the lungs, mainly because of lack of adequate mixing of indicator with blood in the left atrium. However, sampling at the aortic root after injection of indicator into the pulmonary artery best fulfills the criterion for adequate mixing. The lung plus left-heart blood volume thus calculated agrees well with radio-isotope measurements of this space (Schlant et al., Am. J. Physiol. 196:499, 1959). Newman has suggested that the "slope volume," calculated from the cardiac output and the rate of diminishing concentration of indicator in the disappearance phase of the dilution curve, provides an index of lung-blood volume alone. In the present experiments on 16 dogs, the slope volume correlated well with, but averaged only 30% of, the lung and left-heart blood volume, and was estimated to represent about 45% of actual lung-blood volume. However, occlusion of major pulmonary arteries by a balloon-tipped catheter produced consistent reductions in the lung and left-heart blood volume, but only minor and inconsistent alterations in the slope volume. It is concluded that the slope volume neither gives a measurement of the lung-blood volume nor consistently reflects the direction and magnitude of changes induced therein.

STUDY OF THE RELATIONSHIP BETWEEN HEART RATE AND ARTERIAL PRESSURE. Homer R. Warner. Latter-day Saints Hosp. and Univ. of Utah, Salt Lake City.

Arterial pressure is an important determinant of heart rate by way of presso-receptors such as the carotid sinus (H_S). Heart rate, on the other hand, through its influence on cardiac output affects arterial pressure (G_S). Determination of this system's closed-loop transfer function ($H_S/1\ H_SG_S$) should permit prediction of heart rate changes resulting from any external disturbance whose effect on arterial pressure is known. To obtain (G_S), the heart rate of a dog with a surgically induced complete A-V block was controlled by a stimulator and varied sinusoidally between fixed limits as the dog walked on a treadmill. The sine wave variations in heart rate produced sinusoidal variations of the same frequency in mean arterial pressure. From the relationship of amplitude and phase of the sine wave variations in mean pressure to sine wave frequency an open-loop transfer function (G_S) for this component of the system was obtained. To obtain (H_S), the influence of arterial pressure on heart rate was investigated in an intact dog exercising on a treadmill. Arterial and right atrial pressures, electrocardiogram, and the sinusoidal variations in treadmill speed were recorded on magnetic tape. An analog computer was then used to find a transfer function (H_S) which would predict the time course of heart rate from arterial pressure under these conditions.

BASIC PERSONALITY TRAITS CHARACTERISTIC OF CHRONIC LUNG DISEASE, EMPHYSEMA. Marvin W. Webb* and Alfred H. Lawton. General Research Lab., Veterans Admin. Center, Bay Pines, Florida.

A group of 28 randomly selected laboratory-tested and medically diagnosed emphysematous patients were studied longitudinally by means of amanuensis and a series of 10 depth psychologic tests. The tests were administered on successive days to determine whether such a group manifests personality traits which differ significantly from those of a randomly sampled control group of 51 domiciliary members of like age and circumstances. The study demonstrates by the Chi square technique a statistical difference at the .05 level of confidence in 6 of the 8 primary personality factors tested. It likewise indicates that the members of the experimental group may be identified as belonging in the Szondian paroxysmal and Bohmiam ixoidian classes.

COMPARATIVE STUDY OF PHYSIOLOGY AND MORPHOLOGY OF SOMATIC CEREBRAL CORTEX OF PROCYONIDAE. W. I. Welker. Dept. Physiol., Univ. Wisconsin, Madison.

By means of the evoked potential method, the representation of somatic afferents on the cerebral cortex was studied in Procyon (raccoon), Nasua (coati mundi), and Potos (kinkajou) under Nembutal anesthesia. The raccoon, which exhibits an exaggerated use of forepaws in exploring its environment, manifests the largest cortical hand area. The potentials in this area are evoked almost entirely by light contact with the skin of the ventral surfaces of the forepaw.

The coati mundi, which boasts a large, mobile snout and long, curved digging claws, exhibits an enlarged cortical snout area and a cortical sensory hand area activated primarily by joints in digits, palm, and wrist. The kinkajou, an arboreal carnivore, adept at grasping small objects, has a rather small cortical hand area which is activated by skin and joint stimulation in a pattern similar to that observed in the rhesus monkey. Those sulci which have formed within and around SI in these animals appear to be limiting sulci in that they delimit one physiological subdivision from its neighbor. These data, together with those obtained in similar studies of various other animals, implicate certain developmental factors in the ontogeny and phylogeny of the cerebral cortex. (Aided by grants B-732 and M-2786, NIMH.)

RESPIRATORY AND ACID-BASE VARIATIONS FOLLOWING THE INJECTION OF CARBON DIOXIDE INTO THE SMALL INTESTINE OF ANESTHETIZED DOGS. Alphonse N. Welter (intr. by F. Sargent, II). Dept. of Physiol., Univ. of Illinois, Urbana.

The effects of sub-lethal doses of carbon dioxide (36 cc/kg within one minute) administered into the small intestine upon respiration and acid-base balance have been studied. The carbon dioxide was introduced via a Rehfuss tube tied in the lower duodenum. A ligature was also placed 15 cm proximal to the ileo-cecal junction. The observations made consisted of measuring the disappearance of carbon dioxide from the intestine by indirect oncometry and the effects that the absorbed carbon dioxide has upon acid-base balance and respiratory responses. The values obtained show that the disappearance rate varies among animals (range: 9 min - 20 min). Hematocrit, pH, Volume % CO_2 and Volume % O_2 determinations were made on Femoral Artery, Femoral and Superior Mesenteric Vein blood samples. In all cases, pH values obtained from the Superior Mesenteric Vein decreased significantly following carbon dioxide administration, whereas only slight differences in Femoral Artery and Femoral Vein samples were observed. In all cases, there was evidence of some degree of acidosis. Respiratory gases were analyzed using the Godart Pulmo-Gas Analyzor. Pulmonary ventilation and respiratory frequency were recorded kymographically. Following carbon dioxide administration into the small intestine, pulmonary ventilation and respiratory frequency increased within 3-5 minutes along with marked increases in expiratory carbon dioxide concentration.

SYMPATHOLYTIC AND SYMPATHOMIMETIC EFFECTS ON BLOOD SUGAR AND BLOOD LACTIC ACID IN UNANESTHETIZED NORMOTENSIVE AND RENAL HYPERTENSIVE DOGS. Howard Weisberg* and Fred R. Griffith, Jr. Dept. of Physiol., Univ. of Buffalo, Buffalo, N.Y.

In 10 normotensive and 2 hypertensive unanesthetized dogs, blood glucose (Somogyi-Nelson) and lactic acid (Barker and Summerson) levels were measured before and after intravenous administration of adrenaline, noradrenaline and CCK-179 (Hydergine). Doses of adrenaline elevated blood sugar by 50% and lactic acid by 90%. Equivalent doses of noradrenaline gave virtually no response. Hydergine like-

wise had no effect upon the blood sugar but tended to reduce blood lactic acid. To study the effect of autonomic blocking agents on adrenaline hyperglycemia Hydergine and dibenzyline were given intravenously prior to infusion of adrenaline. Low doses of Hydergine (capable of lowering blood pressure in the hypertensive dogs) did not modify the hyperglycemic effect of adrenaline, observed in our control experiments, in normotensive or hypertensive dogs. Similar results were obtained with dibenzyline. Doses of these blocking agents which are well tolerated by unanesthetized dogs do not modify the adrenaline hyperglycemia. (Supported by PHS Grant.)

AMYGDALOID INFLUENCES ON UNIT ACTIVITY IN HYPOTHALAMUS AND THALAMUS. R. H. Wendt* and W. R. Adey, Dept. of Anatomy and Physiol., Sch. of Med., Univ. of California at Los Angeles, and Veterans Admin. Hosp., Sawtelle, Calif.

In the unanesthetized cat paralyzed with Flaxedil, microelectrode recording of unit activity was employed to determine the distribution of amygdaloid projections to the diencephalon, and their influence on spontaneous activity and activity evoked by physiological or peripheral nerve stimulation. In the hypothalamus, a wide distribution of units responding to stimulation of the baso-lateral and cortico-medial amygdala was found, with concentrations in the premammillary, ventro-medial nucleus and chiasmatic regions. Both facilitation and inhibition of hypothalamic unit discharge were obtained by amygdaloid stimulation, the effect sometimes being frequency dependent. Stimulation of the sciatic nerve or retinal illumination was also effective in facilitating hypothalamic units. Interaction effects produced by simultaneous amygdaloid and peripheral stimulation were observed in units responding to separate amygdaloid and peripheral stimulation. Examples of such effects were amygdaloid inhibition of the unit driving produced by sciatic stimulation and modification of the unit responses to photic stimulation. In the thalamus, amygdaloid stimulation influenced unit discharge in ventralis lateralis, ventralis medialis, centre median and centralis lateralis. Both facilitatory and inhibitory effects were obtained, and a frequent effect observed was periodic bursts of rapid discharge during and after amygdaloid stimulation. Sciatic stimulation produced driving of units in ventralis lateralis and ventralis medialis. Intercurrent amygdaloid stimulation often modified this effect of sciatic stimulation, both facilitation and inhibition of the sciatic driving being observed.

EFFECT OF LONGITUDINAL CONDUCTION OF HEAT ON THE COOLING OF THE FINGER. E. H. Wissler (intr. by G. W. Molnar). Dept. of Chemical Engineering, Univ. of Texas, Austin.

Approximating the extended finger by a honogeneous, right circular cylinder of finite length, formulas were obtained which describe the cooling process in the absence of internal heat generation. It was assumed that heat is lost to the environment from the exposed surfaces at a rate which is proportional to the difference between the temperatures of the surface and the environment. The following conditions were considered at the base of the finger: 1) no heat flow

between the metacarpus and the first phalanx, and 2) heat flow from the metacarpus to the first phalanx in a predetermined manner. Data calculated using the derived equations were compared with experimental data. The computed results were rather insensitive to the value used for the thermal diffusivity, but they were very sensitive to the value used for the heat transfer coefficient at the surface of the finger. The effects at the ends of the finger due to longitudinal conduction are important in the cooling of the finger. During the initial period of cooling (forty minutes in still air) the two end-effects are independent of each other, and in the central portion of the finger heat flows in the radial direction only. By taking advantage of this one can simplify the analysis of more complex systems such as those containing internal heat generation and heat input by blood flow. (Supported by US Army Contract No. DA-49-193-MD-2005.)

ENDOGENOUS EXCRETION OF CHOLESTEROL IN THE DOG. R. Wojciech* and A. C. Ivy. Dept. of Clinical Science, Univ. of Illinois, Chicago.

A synthetic diet containing no sterol and no fat was fed to dogs. The diet contained 30% casein and was fed at a level of 75 calories/kg/day, all being consumed. The feces were collected daily. The diet was fed for 11 days, the feces being discarded the first 4 days and collected for the following 7. The feces were collected immediately and stored in jars containing 95% alcohol to stop bacterial action. The average weight of the dogs during the study was 13.5 kilos. The average amount of endogenous cholesterol (digitonin precipitable) excreted was 74 mg/day. The average caloric intake required for maintenance of the dogs was 1012/day. Thus, the ratio of Total Calories Required to the Endogenous Cholesterol Excreted was 1012 to 74 or 13.5 to 1. This ratio compares closely to that of the chicken; but that of the rat and human is 6 to 1.

EFFECTS OF DIPHENYLHYDANTOIN ON FROG VENTRICULAR ACTION POTENTIAL. J. W. Woodbury and Aya Irisawa.* Dept. of Physiol. and Biophysics, Univ. of Washington Sch. of Med., Seattle.

Diphenylhydantoin (Dilantin) decreases the Na concentration and increases the radiosodium turnover rate in rat brain. These findings suggest that Dilantin increases the rate of active Na transport in brain (D. M. Woodbury, J. Pharm. & Exper. Terap. 115:74). This hypothesis could also explain the effectiveness of Dilantin against cardiac arrythmias; decreased internal Na would prolong the duration of the AP (t_{ap}) by increasing the inward Na current. In isolated, perfused, frog ventricles, Dilantin prolongs t_{ap} (mean, 1.63 times normal). The lengthening is pronounced in 10 minutes and complete in 30. Removal of K from the perfusate increases t_{ap} to 1.9 times normal. Similar effects are obtained with a solution containing twice the normal Ca and 10% of the normal K. Dilantin also prevents or reverses the shortening of t_{ap} of a second AP to the interval since the first AP show that Dilantin prolongs recovery time. All these findings suggest, in addition to any effects on the Na pump, that Dilantin's action on the heart is to slow the rate of inactivation of Na

conductance during the plateau and the rate of slow reactivation immediately following repolarization. (Aided by grant B1752 from the National Institutes of Health and a grant from the Washington State Research Fund.)

SOME FACTORS WHICH INFLUENCE THE EFFECT OF HEART RATE ON CARDIAC OUTPUT. D. M. Worthen,* A. F. Toronto* and H. R. Warner. Latter-day Saints Hosp. and Univ. of Utah, Salt Lake City.

The study is an attempt to elucidate the relationship in dogs between heart rate and cardiac output under various experimental conditions. Heart rate was controlled as the independent variable by surgically inducing a complete A-V block and driving the ventricles electrically. Wires sutured into the right ventricle were brought out between the scapulae and connected to a small stimulator attached to the dog's harness. After right nephrectomy, permanent plastic cannulae were placed in the right renal artery and vein and sutured subcutaneously for later use in pressure and cardiac output studies. Ten to 14 days following surgery, cardiac output was measured by the dye and pulse-contour methods at various heart rates. Calculated cardiac output was independent of heart rate between 60 and 180 per minute in the dog under Nembutal anesthesia. In the resting unanesthetized dog the effect of heart rate on cardiac output was slight and with removal of 10% of the dog's blood volume, cardiac output became independent of heart rate. Similar studies were made with the dog walking on a treadmill at 3 miles per hour. With the dog exercising his cardiac output changed more for a given change in heart rate than it did when he was resting. However, at heart rates between 140 and 250 per minute cardiac output was independent of heart rate both at rest and during exercise.

CARBOHYDRATE METABOLISM AND ELECTROLYTE CONTENT OF THE ISOLATED RABBIT DIAPHRAGM. Ho Lee Young* and I. S. Edelman. Cardiovascular Res. Inst., Univ. of California Sch. of Med., San Francisco.

Skeletal muscle invariably gains sodium and loses potassium when incubated in vitro at 38° C in the presence of oxygen. The effect of variations in glycogen content and in the carbohydrates provided as substrate on this process was studied in isolated segments of the rabbit diaphragm. The first series of experiments revealed that the addition of glucose to the medium did not influence either potassium loss (-0.11 mEq per gm fat-free dry weight) or sodium gain (+0.35 mEq per gm f.f.d.w.) when the animals were fasted for 18 hours. The addition of pyruvate, α-ketoglutarate or fructose diphosphate to the medium did not alter these results materially. In a second series of experiments rabbits were sacrificed after fasting for 1 to 7 days and diaphragm segments were analyzed for glycogen content. Mean glycogen content after 18 hours of fasting was 24 mgm per gm f.f.d.w. and 17 mg./gm f.f.d.w. after 6 days of fasting. Incubation of diaphragms taken from rabbits fasted for 1 to 5 days with and without glucose showed no significant difference in either potassium loss or sodium gain. After 6 days of fasting, however, the addition

of glucose to the medium decreased potassium loss by 20 per cent and sodium gain by 10 per cent.

METABOLISM AND PHYSIOLOGY OF WORK PERFORMANCE IN THE DOG IN THE POST-ABSORPTIVE AND FASTING STATE. D. R. Young (intr. by S. Robinson), Quartermaster Food and Container Inst. for the Armed Forces, Chicago, Ill.

Maximum aerobic work performance with and without water supplementation during work on a treadmill at 3.63 mph and 10 degrees of inclination was studied in 6 dogs a) in the post-absorptive state and b) during three and five days of acute starvation. Measurements were made of respiratory gas exchange and gross energy expenditure, heart rate, body temperature, changes in body weight, blood glucose, lactate, and acetone. Without water supplements, average running time on the treadmill was eight hours. In the post-absorptive state, provision of approximately 1.5 liters of water markedly increased (+80%) running time and the gross energy expenditure. Associated with increased performance through water supplementation there was a diminished degree of work dehydration, improvement in temperature regulation, and a lesser fall in the post-work blood sugar level. Performance (with water provided during running) increased (+74%) after five days of starvation. Associated with improved performance there was an increased mobilization of body tissue for fuel for the working muscles which was marked by an elevation in the post-work blood level of glucose and during starvation a decrease in plasma protein. The average cumulative calorie deficit including the performance trial was 7500 Calories; there was no significant change in the blood level of acetone. Physiologic responses to work and characteristics of maximum running will be presented.