AMERICAN PHYSIOLOGICAL SOCIETY

PROCEEDINGS

FALL MEETING, SEPTEMBER 8-11, 1964

BROWN UNIVERSITY PROVIDENCE, RHODE ISLAND

ABSTRACTS OF PAPERS

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

EFFECT OF SYMPATHETIC STIMULATION ON THE DISTRIBUTION OF BLOOD FLOW IN THE FORELEG OF DOG. Francois M. Abboud and John W. Eckstein. CV Res. Labs., Dept. of Int. Med., Univ. of Iowa, Iowa City, Iowa.

Indirect observations suggested to us that sympathetic stimulation redistributes blood from the paw into proximal parts of the foreleg of dog (Fed. Proc. 23:915,1964). These experiments were done to determine by direct measurements if such redistribution of flow occurs. Six dogs were anesthetized, treated with a neuromuscular blocking drug and ventilated. Blood flow to the foreleg was maintained constant with a pump. Venous outflow from the accessory cephalic vein which drains the paw and also from the brachial vein which drains muscular parts was measured with a drop counter and a rotameter respectively. The nerve trunks were cut high in the foreleg and their distal ends were stimulated during one-minute periods with supramaximal voltage at increasing frequencies (1.5-12 cycles/sec). With each stimulus brachial vein outflow increased and cephalic vein outflow decreased. Promptly after stimulation cephalic vein outflow increased strikingly and brachial vein outflow decreased. During each stimulus pressure increased in the brachial artery, small artery and vein in the muscle and small vein in the paw but decreased abruptly in the small artery in the paw. We conclude that sympathetic stimulation redistributes blood from the paw into proximal segments of the foreleg and constricts predominantly arterial and venous segments.

ISOLATION & QUANTITATIVE ESTIMATION OF PULMONARY SURFACE ACTIVE LIPOPROTEIN & ITS INTERACTION WITH FIBRINOGEN. M. E. Abrams[1] and F. B. Taylor, Jr. (intr. by J. A. Clements) Cardiovascular Res. Inst., Univ. of Cal. Med. Center, San Francisco, Cal.

A lipoprotein has been isolated from homogenates of mammalian lungs by low speed centrifugation in various saline densities. This lipoprotein is highly surface active, by agar electrophoresis is an α globulin, has a molecular weight calculated from surface tension measurements of $2.4\pm0.5\times10^5$ (n=6); it is 40.2±0.6% (n=4) lipid and on thin-layer chromatography it contains only one phospholipid with the R_f of dipalmitoyl lecithin. Instead of filling the trough of a surface balance with extract, we used a method of surface spreading devised by Trurnit which makes it possible to demonstrate that (a) saline extracts of different lung homogenates contain different quantities of surface active material, (b) over 90% of the surface active material of these saline extracts is in the lipoprotein and (c) as little as 50µg of this lipoprotein lowers surface tension to less than 10 dynes/cm on compression of the surface film from 60 to 12 cm^2. Normal rabbit, lamb, and human lungs have been found to contain 2.0 to 11.0 mg lipoprotein/g. lung. In a few histologically proven cases of hyaline membrane disease, no surface active lipoprotein could be demonstrated and saline extracts of these lungs were inactive; the phospholipid content of these lungs was only slightly reduced. Adding equimolar amounts of purified fibrinogen to a saline dispersion of this lipoprotein inhibits its surface activity; the lipoprotein is a powerful inhibitor of clot retraction and fibrinolysis. ([1]Rockefeller Travelling Fellow.) (Aided by USPHS grants HE-06285 and H-5146.)

RUNNING ACTIVITY, FEEDING AND BRAIN TEMPERATURES IN RATS. Robert Abrams and H. T. Hammel. John B. Pierce Foundation Laboratory and the Department of Physiology, Yale University, School of Medicine, New Haven, Connecticut.

8 male and 8 female rats, equipped with stainless steel re-entrant tubes implanted in the brain adjacent to one preoptic area, were placed in cages with accessible activity wheels. Room temperature ranged from 22-26 C, and lights were turned off at 6 PM and on at 6 AM. After two weeks, brain temperatures were recorded continuously for periods up to 48 hrs by means of thermocouples inserted into the tubes. The activities of running, feeding and drinking were recorded simultaneously. About 90% of feeding and drinking activity occurred irregularly during each of 3-9 periods of running activity at night. Active periods at night were associated with brain temperatures 1.0 - 2.5 C higher than inactive periods during the night or day. Moderate restraint with absence of food abolished these temperature variations whereas absence of food alone did not. Brain temperatures from 3:30 - 5:30 PM before the night of estral hyperactivity did not differ significantly from temperatures recorded during these same hours on other days of the estrous cycle. During the night of estrus, marked increases in activity frequently were associated with elevated mean preoptic temperatures (9 PM - 3 AM). In contrast, when a significant reduction in activity occurred after ovariectomy, the mean brain temperature usually was reduced from preoperative, estrus levels. (Supported by U.S.P.H.S. Grant AM-08241).

Electrical Skin Resistance and Eccrine Sweat Gland Activity in the Human. Thomas Adams* and John A. Vaughan.* (Intr. by P. F. Iampietro) Physiology Branch, Civil Aeromed. Res. Inst., Oklahoma City, Okla.

The measurements of electrical skin resistance (ESR) and impedence are generally accepted as indices of peripheral and central nervous system integrity and function, although the physiological mechanisms underlying these responses remain obscure. Rates of evaporative water loss (EWL) and ESR were measured simultaneously from adjacent sites on the palmar skin surface in 15 men under conditions eliciting psychogenic sweating. In all instances a decrease in ESR was accompanied by an increase in EWL after a delay of approximately 1 sec. Correlation coefficients calculated for EWL = f($\log_{10}$ ESR) were as high as -0.964; the same calculation for a change in EWL (ΔEWL) as a function of a change in ESR (ΔESR) was as high as +0.950. Consistently, a stronger correlation existed for EWL = f($\log_{10}$ ESR) than for EWL = f(ESR); conversely, correlation coefficients were higher for ΔEWL = f(ΔESR) than for ΔEWL = f($\log_{10}$ ΔESR). An increase in EWL from a low initial level resulted in a greater decrease in ESR than did the same increase in EWL when initial levels were high (e.g., an EWL elevation from 0.06 to 0.07 mgm/min.$\cdot$cm^2 resulted in a 28k ohm decrease in ESR; an EWL change from 0.15 to 0.16 mgm/min.$\cdot$cm^2 was accompanied by a 4k ohm ESR decrease. These data are interpreted as indicating that palmar sweat gland activity plays an important role in acute changes in ESR and in establishing "basal" ESR levels, possibly by means of corneal hydration or water storage.

MYOCARDIAL HEAT PRODUCTION DURING INDUCED TACHYCARDIA IN INTACT DOGS. S. Afonso,* G. G. Rowe, G. S. O'Brien,* D. H. McKenna,* C. V. Jaramillo,* & C. W. Crumpton. Cardiovas. Res. Lab., U. of Wis., Madison.

It has been demonstrated that at constant external mechanical work O_2 consumption increases proportionately to the heart rate, indicating that the heart works less efficiently at higher rates. However it is not known if this increase of O_2 consumption actually represents loss of energy degraded as heat. Control measurements of metabolic and systemic and coronary hemodynamic parameters and LV heat production (by a previously reported method) were obtained in 10 dogs. Tachycardia was then induced electrically and the same parameters redetermined. Significant increases occurred in coronary blood flow (N_2O method, +33%, $p < 0.01$), cardiac metabolic rate for oxygen (+36%, $p < 0.01$) and LV heat production (+73%, $p < 0.001$). Index of efficiency (LV work $\div$ $CMRO_2$) decreased (-26%, $p < 0.05$). LV work did not change. These results show that the elevated cardiac oxygen consumption at higher rates is accompanied by increased heat production.

EFFECT OF COMPOUND 48/80 ON RELEASE OF A LIPASE FROM THE ISOLATED PERFUSED RAT HEART. E. Aktin*, R. J. Ho*, and H. C. Meng. Department of Physiology, Vanderbilt University School of Medicine, Nashville, Tennessee

Although exogenous heparin has been shown to induce the release of a lipase, information regarding the possible role of the endogenous heparin is scanty. To obtain further insight on this subject, isolated rat heart was perfused with Compound 48/80, a substance known to disrupt mast cells. Perfusate was collected at frequent intervals and assayed for lipolytic activity in terms of FFA liberation using a triglyceride emulsion (Ediol) as a substrate. It was found that Compound 48/80 markedly increased the perfusate lipolytic activity. Histamin or serotonin did not produce this effect. The dose-response curve showed that the minimum effective dose was about 20μg/ml, and the effect was increased with increasing in concentrations up to 40μg/ml beyond which no further increase in lipolytic activity was observed. This effect of Compound 48/80 on lipase release required no added serum in the perfusion medium. Preliminary characterization has shown that this lipase has a pH optimum of 7.8-8.2 and was inhibited by NaCl (1.0 M, 0.6 M), protamine (1 mg/ml), and NaF (0.1 M). The time-response curve of Compound 48/80 was similar to that of heparin; it consisted of a sharp rise and an immediate decline. However, the peak of the lipolytic activity induced by heparin appeared earlier than produced by Compound 48/80.

THE ALTERATION OF LACTIC DEHYDROGENASE ISOZYME PATTERNS OF BROWN FAT IN THE GOLDEN HAMSTER BY COLD EXPOSURE. J. R. Allen* and R. R. J. Chaffee. University of California, Riverside, California.

Fourteen hamsters (Mesocricetus auratus) were divided into two groups; the control group was maintained at 23 ± 2° C while members of the experimental group were kept at 4 ± 1° C for periods of 54, 42, 14 and 9 days. Both groups were given Purina Lab Chow pellets and water ad libitum. After the cold exposure period the animals were decapitated and interscapular brown fat removed. The tissues were homogenized in distilled water 1:20 (w:v) then frozen, thawed and centrifuged at high speed. The resulting supernatants were subject to starch gel electrophoresis in .02M boric acid-sodium hydroxide buffer pH 8.6 for 17 hours at 4.5 volts/cm and 4° C. The gels were stained for lactic dehydrogenase with a p-nitro blue tetrazolium system. Six anodically migrating sites of lactic dehydrogenase activity were derived from the brown fat of the animals maintained at 23° C. Homogenates prepared from the brown fat of the cold-exposed hamsters displayed only very slight staining at the terminal or fast migrating band while bands closer to the origin stained more intensely than those in the corresponding control bands. It appears that cold exposure of the golden hamster results in a shift in emphasis in the electrophoretic banding pattern of the lactic dehydrogenase isozyme system of brown fat.
(Supported by U. S. P. H. S. grant #GM 09110-02, U. S. Army grant #DA-49-193-MD-2558 and U. C. Cancer Research Coordinating Committee Grant.)

SEPTAL INFLUENCE ON BLOOD PRESSURE CONTROLLING MECHANISMS. O.J. Andy, S. Nelson*, D.L. Sparks*, Dept. of Neurosurgery, University Medical Center, Jackson, Mississippi.

The objective of this study was to electrically activate septo-hypothalamic systems to evaluate the probable role of the septum in blood pressure control. In the 15 animals utilized, bipolar Hess electrodes were placed in the septum and nearby structures and in the hypothalamus and motor cortex. Septo-hypothalamic systems were activated by inducing after-discharges by electrical stimulation. Bipolar stimulation and EEG recordings were utilized. Experiments were conducted under local scalp anesthesia with the animal in a hammock. Anectine with controlled respiration was used in 10 experiments. EEG and femoral artery BP recordings were made simultaneously. Electrode placements were histologically verified. Results: Blood pressure elevation most frequently accompanied after-discharges of 20 seconds or longer duration. In some experiments it rose 80 to 90 mm. Hg. Elevation usually occurred during the middle or latter phases of an after-discharge. Blood pressure rise was correlated with altered EEG patterns consisting of a transition from slow to fast after-discharge frequencies propagated to the hypothalamus. There was no propagation to motor cortex. Blood pressure depression or no change occurred with after-discharges which were characterized by slow or an erratic mixture of frequencies. Propagated discharges of very low amplitudes to the hypothalamus were not associated with blood pressure changes. Pulse slowing and irregularity frequently occurred at the termination of a discharge associated with blood pressure elevation. It was similar to that seen following hypothalamic stimulation. Supported in part by NIH Grant # 04754.

EFFECT OF ALTERNATING ACID AND ALKALINE DIGESTIVE SECRETIONS ON THE RATS' GASTROINTESTINAL TRACT

T. Arai*and H. Necheles, assisted by P.Lott,Jr.*
From the Department of Gastroenterology, Medical Research Institute, Michael Reese Hospital, Chicago.

Previously, one of us has shown that exposure of a frog's leg alternately to acid-pepsin and alkali-pancreatic secretion produced rapid digestion of the leg. In this work the question was raised whether duodenal ulcer may be due in part to such alternation between acid and alkaline digestive juices. We are reporting similar experiments with perfusion of rats' stomachs and small intestine with HCl (pH 1.3-1.5), HCl with pepsin, $NaHCO_3$ (pH 7.4-8.3) and $NaHCO_3$ with pancreatin; when two solutions were infused, they were alternated every 15 minutes. After Holtzman strain male and female rats were starved for 48 hours, they were anesthetized with nembutal intraperitoneally and a small tube was introduced either into the upper part of the esophagus or the proximal duodenum. A low perfusion pressure, propelling 0.8 cc of fluid per minute, was employed. The fluid left by way of a tube in the terminal ileum. The main results of these experiments showed that perfusion for an hour's time with acid-pepsin produced diffuse edema and small scattered bleeding points of the entire surface of the small intestine. When acid-pepsin was alternated every 15 minutes with alkali-pancreatin, the digestion was more distinct and was accompanied with hemorrhage and frequent ulceration. The stomach showed marked edema and hemorrhage.

EFFECT OF HEAD MOVEMENT ON GAZE MOVEMENT VELOCITY. A. Atkin (intr. by M.B. Bender). Dept. of Neurology, Mount Sinai Hospital, New York City.

Previous reports state that gaze movement velocity depends only upon initial and final eye positions, relative to the head; effects of head movement have not been examined. In the present study, velocities of saccadic gaze movements of normal human subjects were measured during performance of a vigilance task in which the test field occasionally made a large shift in position. Free head movement was permitted, except during control runs. Eye position was recorded electro-oculographically. Head position was also recorded. Eye and head position signals were summed, after equalization of scale factors, to give a trace representing instantaneous position of the eyes in relation to the surrounding environment. Velocities were obtained by electronic differentiators.

The maximum range of gaze movements was greatly increased when head movement was permitted. Peak head velocity was usually reached at about the time the saccadic gaze movement terminated. It was found that when head movement occurred, instantaneous eye-in-head velocity was reduced, during the saccadic gaze movement, by an amount that approximated the momentary head velocity. As a consequence, the eye-in-environment (summed) velocity tended to remain constant throughout the course of a large saccadic gaze movement, even though its component velocities changed markedly. Furthermore, there was greater invariance of summed velocity than of eye-in-head velocity from movement to movement, even when the accompanying head movements differed.

The observed reduction in saccade eye-in-head velocity appears to be associated with vestibular stimulation, but to be relatively independent both of movement of the visual surroundings (i.e., optokinetic stimulation) and of cervical joint motion. The results imply that the vestibularly-induced compensatory eye movements and the saccadic gaze movements combine additively, at least under some conditions.

Under different experimental conditions, decreases in gaze movement velocity that were much greater than the head movement velocity have been noted, and will be described. (Supported by USPHS Grant # NB 04576.)

EFFECTS OF RESERPINE, SEROTONIN, AND CATECHOL AMINES ON INTESTINAL ABSORPTION OF GLUCOSE, SODIUM, AND POTASSIUM. K. A. Aulsebrook. Dept. of Physiology, Univ. of Ark. Medical Center, Little Rock, Ark.

Reserpine injections of 1.5 mg/kg stimulate absorption of glucose, Na, and K by everted segments of rat small intestine incubated in a Krebs-Ringer bicarbonate buffer. The effects are also produced by the drug in vitro at a concentration of 10 gamma/cc in the mucosal fluid. In vitro serotonin is without effect on absorption at 20 gamma/cc. In vitro epinephrine or nor-epinephrine at 20 gamma/cc produce the same effects as reserpine, and stimulation of ion absorption persists when buffer glucose is replaced by mannitol. Pre-incubation of drug for one hour prior to addition of segments to the medium abolishes effects of epinephrine but not of reserpine. In vitro dopamine or isoproterenol do not stimulate absorption. Phentolamine injection blocks the effects of epinephrine, but not those of reserpine. It is concluded that the effects of reserpine are probably not produced by endogenous serotonin or catecholamines, in spite of the similarity of effects of reserpine, epinephrine, and nor-epinephrine. Supported by NIH grant AM 05025-03.

METIN AND TROPOMYOSIN FROM RABBIT SKELETAL AND BOVINE CARDIAC MUSCLES. Naomi Azuma* and Shizuo Watanabe, Univ. of Calif. Med. Center, San Francisco, Calif.

Skeletal and cardiac metins were prepared by isoelectric precipitation (Proc. Nat'l Acad. Sci. 50:1033, 1963). Both preparations can inhibit superprecipitation (SPPTN) of actomyosin in the presence of 1 mM Mg, 0.5 mM ATP, and 5μM EGTA; in this respect, metin resembles tropomyosin-like protein (Nature 200:1010, 1963). However, in the absence of EGTA, metin preparations activate or inhibit SPPTN depending on KCl concentration. One major (s'_{20}=2.08 S, 0.6 M KCl) and one minor component (s'_{20}=3.625, 0.6 M KCl) can be identified in the ultracentrifuge patterns of both metin preparations. The major component ($s^{o}20,w$=2.5S, 0.21 MKCl), after removing the minor component by amm. sulfate fractionation, shows no metachromatic effect, contains only 0.1 mole tryptophan residue per 10^5 g, has an extinction ratio of 2.04 for 278 mμ/260 mμ, and it is crystallized as tropomyosin prepared by Bailey's method (Biochem. J. 43:271, 1948) also has the properties described above with metin, including the effect on SPPTN. The PCMB-titratable SH content (per 10^5·g) is 2.5 moles in crude metin (skeletal and cardiac), 1.6 moles in crystallized metin (skeletal), and 1.4 moles in tropomyosin (skeletal). When both metin and tropomyosin have all their PCMB-titratable SH groups blocked by NEM, then their ability to inhibit SPPTN is slightly increased. Supported by research grants from the A. H. A. and the N. S. F.

LOSS OF HYPOXIC RESPIRATORY DRIVE AS A CAUSE OF "CHRONIC MOUNTAIN SICKNESS" IN ANDEAN NATIVES. C.R. Bainton,* J.W. Severinghaus and A. Carcelen B.* Cardiov. Res. Inst., Dept. of Anesth., U. of Calif. Med. Ctr., San Francisco, and Univ. Peruana de Sci. Med. y Biol., Lima, Peru.

The respiratory response to alveolar hypoxia and hypercapnia was determined at 4330 M alt. (B.P. 457) in Cerro de Pasco, Peru, for three groups of similar age (mean 35 yr.): 1) 7 newcomers to altitude (4 for one week, others 1, 2 and 9 mo.); 2) 5 normal subjects native to high altitude, and 3) 6 natives with chronic mountain sickness (Hct.> 70%, severe cyanosis, no right heart failure). Results of pulmonary function studies for groups 1, 2 and 3 were: V.C., 2.69, 2.94, 2.55 L/m²; FRC, 2.17, 2.23, 2.23 L/m²; R.V. 0.80, 1.33, 1.47 L/m²; T.V.C. (1 sec.) 79%, 80%, 76%, and maximum expiratory flow rates (from 200 to 1200 ml) 490, 360, 290 L/min. Hct.: 1) 52%, 2) 60%, 3) 75%. On air, Pa_{O_2}: 1) 56, 2) 47, 3) 39 mm Hg, Pa_{CO_2}: 1) 28.2, 2) 32.3, 3) 37.9 mm Hg. At each subject's usual Pa_{CO_2} and at a Pa_{O_2} = 35 mm Hg, $\dot{V}_E$ was 1) 37.5, 2) 15.0, and 3) 8.5 L/min/m². At high $P_{A}O_2$ (200-300 mm Hg), CO_2 response slopes were normal in all subjects: 1) 2.52, 2) 2.94, and 3) 2.16 L/min/m². CSF pH was 7.31 ± .01 for the group with chronic mountain sickness. Ventilation of one subject with Hct. 73% was depressed by low Po_2 and increased with elevated Po_2 (130-250 mm Hg). One American engineer after 9 mo. at high altitude, with Hct. 71%, responded to low Po_2 like those with chronic mountain sickness. Normal natives at high altitude have a normal CO_2 response but diminished respiratory response to hypoxia, particularly in those natives with chronic mountain sickness. The resulting hypoxemia may be responsible for extremely high Hcts. and eventual cardiac failure. (Supported in part by USPHS grants 5T1-GM-63-06, RG-8576, HE-06285 and Career Award 1-K6-HE-19,412.)

NEUROVASCULAR RESPONSES TO PRENATAL HYPOXIA IN RODENTS. Bernard Baird (intr. by M. A. Slusher). Dept. of Anatomy and Brain Research Inst., Center for Health Sciences, Univ. of Calif., Los Angeles, Calif.

Prenatal responses of the fetal heart and thoracic vasculature to controlled maternal hypoxia have been demonstrated in Swiss mice at simulated altitudes (Circulation 22: 720, 1960); in laboratory rats and mice at a high altitude station (Ibid. 28: 686, 1963) and in wild mountain deermice (Fed. Proc. 23 (2): 522, 1964). When dissections of the head and neck disclosed significant vascular abberations in these regions, systematic microdissections of the cranial vasculature were undertaken on two pilot groups of animals, (a) progeny of Swiss mice exposed discontinuously to simulated altitudes (21,500 ft. for 6 hours per day), and (b) offspring of Long-Evans rats subjected to continuous moderate hypoxia at the White Mountain Research Station (12,470 ft.). Criteria for differentiating degrees of variation in the Circle (Polygon) of Willis and in the vertebro-basilar complex were adduced. Three major categories were established: (a) usual patterns, (b) variants, of questionable functional significance, (c) anomalous patterns likely to be functionally significant. No anomalous, 3 variant and 10 usual Circle patterns and no anomalous, 1 variant and 12 usual vertebro-basilar patterns were found among sea-level control animals; by contrast, 4 anomalous, 8 variant and 4 usual Circle and 2 anomalous, 1 variant and 13 usual vertebro-basilar patterns were discovered in the hypoxia-exposed rodents. A tentative hypothesis that maternal hypoxia may increase the lability of patterning of the circulatory supply to the fetal brain is under evaluation in a large series of mammals exposed to intrauterine oxygen deficiencies. (Supported in part by a grant from the United States Public Health Service.)

RECOVERY OF Cr^{51}-LABELED RED CELLS, I^{131}-ALBUMIN AND $Rb^{86}Cl$ IN ISOLATED DOG FORELIMB PERFUSIONS. Carleton H. Baker. Dept. of Physiology, Med. Coll. of Ga., Augusta, Ga.

Forelimbs of mongrel dogs were isolated and perfused by a constant infusion pump. Inflow was measured by a Medicon flowmeter or venous outflow was collected in a graduated cylinder. Perfusion pressure and venous outflow pressure were recorded. The radioactivity of the venous outflow was measured by means of a probe and ratemeter connected to an oscillographic recorder following single intra-arterial injections of Cr^{51}-labeled red cells, I^{131}-albumin and $Rb^{86}Cl$. The integral curve of each time concentration curve was obtained electronically and recorded and compared following alteration of hemodynamics. Blood flow and vascular volumes were also calculated from the time-concentration curves. The recovery of both Cr^{51}-labeled red cells and I^{131}-albumin averaged 100% for normotensive preparations, but averaged about 90% for preparations with high perfusion pressure. The recovery of $Rb^{86}Cl$ always averaged less than the amount injected (84%). When the vascular bed was dilated, the recovery of labeled red cells and albumin averaged 100% but the recovery of $Rb^{86}Cl$ was even further reduced (76%). Following elevation of blood flow in the dilated bed, the labeled red cells and albumin were still 100% recovered, but the recovery of $Rb^{86}Cl$ averaged about 80%. (Supported by USPHS grant HE-04573-05).

EFFECT OF RELEASE OF URETERAL STOP FLOW ON TISSUE CONCENTRATION OF CREATININE, SODIUM, AND UREA. A. Louise Baldwin*, J. E. Ramsey*, and G. Carrasquer. Dept. of Med., Univ. of Louisville, Louisville, Ky.

Stop flow induces an increase of inner medulla concentration of creatinine in oliguria and diuresis, and has been attributed to persistent filtration and intraluminal trapping. The increase in tissue concentration was a function of the Na available for reabsorption from the lumen, being maximal in dogs under NaCl diuresis. Na conc. decreased in both cases, and was attributed to transport from the lumen and washout from the I.S. Urea conc. increased in NaCl diuresis and decreased in oliguria. This variable behavior was attributed to the influence of two opposing factors: intraluminal trapping and washout from I.S. If intraluminal trapping were an important factor, release of the obstruction should result in a decrease in urea conc. Oliguric and NaCl diuresis dogs were nephrectomized. Both ureters were obstructed by connection to a manometer. After 50 minutes, one kidney was removed and the obstruction was released from the other kidney. After 5 min. of urine collection, the second kidney was also removed (released flow kidney). The creatinine conc. in inner medulla in rel. fl. kidney returned to the normal free flow values previously reported. The urea conc. in both oliguric and NaCl diuresis dogs decreased after release of the stop flow. These findings further support the hypothesis that the nephron is poorly permeable to urea. Persistent filtration during stop flow induces accumulation of creatinine and urea in the lumen. Their concentrations fall when fresh filtrate replaces the intraluminal fluid. On the other hand Na (reabsorbed from the lumen and washed out from the I.S. during stop flow) accumulates in the tissue when the normal supply to the nephron is re-established following release of the stop flow. (NIH and AHA support).

Respiratory Pleural Pressure Amplitude in Dogs Studied Without Thoracotomy. N. Banchero*, W. Rutishauser*, A. G. Tsakiris* and E. H. Wood. Mayo Clinic, Mayo Foundation, Rochester, Minn.

Changes in pressure with respirations were measured simultaneously from two to five different sites in the potential right pleural space and the esophagus of eight dogs under morphine-pentobarbital anesthesia using saline-filled catheters and P23D Statham gauges. The dogs were studied in the supine, prone, right and left decubitus positions. The radio-opaque pleural catheters (I.D. and O.D., 0.7 and 1.3 mm., respectively) were inserted percutaneously by an air-tight technic. Catheters were positioned in the thorax so that the tips were at ventral (retrosternal) and dorsal (paravertebral) sites determined by fluoroscopy and biplane x-rays. Maximum dorsal-ventral lung dimension at tricuspid level was 11.8 (10.8-12.7) cm. Ventral, dorsal and esophageal catheter tips were located 7.3 (6.2-8.0) ventral and 3.3 (2.4-4.8) and 2.3 (1.2-2.7) cm. dorsal to mid-chest level, respectively. Respiratory pressure amplitude (ΔP) is defined as the difference between the mean end-expiratory and the minimal inspiratory pressures. Mean ΔP values, irrespective of body positions, were 6.1 (S.E. of Mean ± 0.09) (647 measurements) and 5.2 (± 0.09) cm. H_2O (710 measurements) at ventral and dorsal sites in the thorax, respectively. Ventral ΔP was systematically greater than dorsal ΔP in supine and lateral positions; however, this relation was not always found in the prone position. The ΔP values of pleural pressures in the cephalad portion of the chest were systematically smaller than towards the lung bases, both at dorsal and ventral sites in the thorax. The ratio of pleural to esophageal amplitude was higher in the ventral (Mean 1.25) than in the dorsal (Mean 1.06) portions of the thorax; however, some measurements of dorsal ΔP were smaller than simultaneous esophageal ΔP values. (Supported in part by research grants: AF 33(657)-8899, NIH H-3532 and AHA CI 10.)

FETAL AND NEONATAL CEREBRAL BLOOD FLOW. J. N. Barker. Department of Physiology, Jefferson Medical College, Philadelphia, Pennsylvania.

Rate of blood flow and steepness of the Hb F oxygen dissociation curve are of especial importance for fetal cerebral oxygenation because arterial P_{O_2} approaches the minimal P_{O_2} required for neuronal functions such as those reflected by the electrocorticogram. Minimal estimates of cerebral blood flow for 21-day fetal and neonatal rats were made from timed free outflow ($\dot{Q}$) from the main venous drainage, the torcular sinus. Corrections for CSF contamination were based upon hematocrit and plasma refractive index. Fetal $\dot{Q}$ (mean 1180 µl/g min; maximal 2660 µl/g min) was 100% greater than neonatal $\dot{Q}$ (mean 549 µl/g min; maximal 1350 µl/g-min). Since both flows are minimal estimates, total cerebral flows of both fetuses and neonates are probably higher than in adult rats (510 µl/g min, Sapirstein and Hanusek, 1958). High P_{CO_2} is one factor which contributes to high $\dot{Q}$, and inspired CO_2 (3-5%) may be used to increase fetal and neonatal $\dot{Q}$. Neonates did not achieve maximal flows equal to maximal flows in fetuses, even during 5% CO_2 inhalation. Rabbit flow data are similar. Some data indicate that rabbit fetal and neonatal cerebral O_2 consumption equals or exceeds adult cerebral O_2 consumption, in contrast to lower in vitro rates. It is concluded that a sharp reduction in cerebral blood flow toward adult levels occurs at birth, that fetal and neonatal perfusion is strongly influenced by P_{CO_2}, and that the cerebral flow reduction at birth may be partly but not entirely dependent upon the decrease in P_{CO_2} at birth. (Supported by Fed. Av. FA-3083 and USPHS HD-0495)

CELLULAR LOCALIZATION OF ALBUMIN IN HEPATOCYTES.

Marion I. Barnhart. Wayne State Univ. School of Med., Detroit, Mich.

The fluorescent antibody technique was applied to human, bovine and canine tissues. Antialbumin was prepared in rabbits. Gamma globulin concentrates were complexed with either rhodamine sulfonyl chloride or fluorescein isothiocyanate. Such fluorescent antialbumins were applied to either cell imprints or frozen sections of tissues from the appropriate species. Variable staining of hepatocytes resulted with many cells brightly fluorescent. This cellular fluorescence was established as due to contained albumin on the basis of serum blocking reactions and adsorption procedures. Studies with other fluorescent cell markers such as antiprothrombin and antifibrinogen revealed that hepatocytes contained different amounts of albumin, fibrinogen and prothrombin. In normal individuals the majority of hepatocytes contained relatively large amounts of albumin and only small amounts of fibrinogen. About 15% of these cells also contained a significant quantity of prothrombin. Experimental stimulation of prothrombin or fibrinogen synthesis produced hepatocytes that fluoresced brightly with all of the fluorescent markers. It seems likely that a single hepatocyte can synthesize and store at least 3 important plasma proteins. (Aided by NIH grant HE 04712).

THE EFFECTS OF OSMOLARITY ON PROPAGATION, LONGITUDINAL RESISTANCE AND THE STRUCTURE OF THE NEXUS IN FROG ATRIUM

Lloyd Barr, Winifried Berger* and Maynard Dewey*, I. Physiol. Univ. d. Saarlandes, Homburg/Saar and Depts. Physiol. and Anat. Univ. of Mich., Ann Arbor, Mich.

Using the sucrose gap technique, propagation of frog atrial action potentials past the gap occurred when the gap was shunted by a resistor (Pflug. Arch. 279:192, 1964). Thus, in the region of the gap, current sufficient for excitation flows longitudinally from cell to cell across the intercalated discs. When the sucrose solution in the gap is 3.65% w/v instead of the control 7.3% w/v, propagation occurs at higher shunt resistor values. Conversely, when a 21.9% w/v sucrose solution is used in the gap even an essentially zero shunt resistance will not allow action potentials to jump the gap. At the same time hyperosmotic sucrose in the gap increases the resistance to longitudinal current flow.

Electron micrographs show that in hypotonic solutions the area of disc which is nexus is normal or increased while in hypertonic solutions the nexal portion of the disc separates and a swollen space appears between the cells. Thus, structural changes of the nexus after soaking in these solutions together with the electrical data corroborate the hypothesis that the nexus is a specialized structure allowing current flow between cell interiors (Science 137:670, 1962). (Supported by NIH Grants AM-03819-05 and AM-03449-05.)

Peripheral Blood Elements In Dogs During And After Chronic Ethanol Administration. James D. Beard (intr. by L. H. Hamilton). Marquette Univ. School of Med., Milwaukee, Wis.

Peripheral blood elements were measured in dogs subjected to daily ethanol administration and following the withdrawal of ethanol. Five dogs received a daily dose of 4 g/kg of ethanol (33% v/v) by gastric tube for a period of twelve weeks; then administration of ethanol was discontinued and the animals were allowed to recover. Throughout the experiment all animals were maintained on an adequate diet consisting of liver, beef and Purina Dog Chow. The parameters measured on a weekly basis were: hematocrit, hemoglobin concentration, erythrocyte count, reticulocyte count, red cell mass, leukocyte count and the leukocyte differential. During the first three weeks there was a gradual decrease in hematocrit, hemoglobin concentration, erythrocyte count, reticulocyte count (relative and absolute), and red cell mass, after which the values remained relatively unchanged for the remaining nine weeks. All animals gave evidence of prolonged reduction for peripheral blood elements below control values, e.g., at twelve weeks, hematocrit (22%), hemoglobin concentration (22%), erythrocyte count (20%), red cell mass (20%), reticulocyte count (83%), absolute number of reticulocytes (80%) and leukocyte count (35%). Neither the leukocyte differential count nor the calculated mean corpuscular values were altered. After cessation of ethanol, reticulocytes increased (relative and absolute) and reached a peak in seven days. All of the peripheral blood elements returned to their control values within four weeks after withdrawal of alcohol. These data suggest that alcohol, in the dose employed, suppresses the hematopoietic elements and this effect is promptly relieved when the alcohol is discontinued. (This investigation was supported by U.S.P.H.S. General Research Support Grant No. 1-S01-05434-01.)

INSULIN IMMUNOASSAY USING INSULINASE: SPECIES AND CONCENTRATION EFFECTS. Lyle V. Beck, Daniel S. Zaharko*, Nancy Roberts* and Christine King*. Department of Pharmacology, Combined Degree Program, School of Medicine, Indiana University, Bloomington, Indiana.

In this assay system we have diluted all reactants with 2% albumin in 0.9% NaCl, we have used a fixed amount of Abbott Co. radioiodo-insulin plus varying amounts of unlabeled insulin, and have allowed these to compete for a fixed amount of guinea pig anti-beef insulin serum (AIS), adequate for 50-80% neutralization of the radioiodo-insulin, used alone. Radioiodine of radioiodoinsulin NOT bound by antibody has then been made soluble in dilute trichloracetic acid (TCA) by use of liver insulinase (ultracentrifugally obtained cell sap in isotonic sucrose). Under these conditions, plot of TCA soluble ^{131}I, ordinate, against unlabeled insulin, abscissa, gives an ascending line. The curves obtained from unlabeled beef and pork insulins, competing with beef radioiodoinsulin for AIS, were nearly identical. This relation also held for unlabeled beef and pork insulins, competing with pork radioiodoinsulin for AIS. Hence in this immunoassay system, unlike that described by Yalow and Berson (Nature 1959, 184, 1648), beef and pork unlabeled insulins had nearly identical affinities for the AIS used. In titration of beef radio-iodoinsulin and AIS against each other at 0°C, 90 hour binding period, the amount of AIS, expressed as µl per mµg of radioiodoinsulin, which was required for 50% binding of the radioiodoinsulin, decreased about 4 times with 125 times increase in radioiodoinsulin concentration. This research was supported by PHS Grant AM 05980.

EFFECTS OF DEXTRANS ON THE RHEOLOGICAL PROPERTIES OF HAMSTER BLOOD. Herbert J. Berman, Edward W. Merrill*, and William G. Margetts.* Biological Research Center, Boston University, and Department of Chemical Engineering, MIT.

A series of controlled experiments on pooled hamster blood were made in a special coaxial cylinder (GDM) viscometer capable of measuring very low shear stresses at low and zero shear rates. The rheological characteristics of hamster blood, like that of human blood, were well described, at least empirically, by the Casson equation. The viscosity changes in hamster blood at different shear rates closely paralleled those of human blood, the viscosity in both cases increasing markedly at low shear rates. The viscosity of hamster blood varied with the concentration of fibrinogen, dextran and erythrocytes. A definite yield stress was observed. In the dextran experiments the hematocrit of the different samples of pooled blood was adjusted to 40. Dextrans of 10,000, 40,000, and 80,000 Mw, at a concentration of 27.5 mg of dextran per ml of plasma, had a similar effect on hamster blood. They increased the shear stress at a definite shear rate above that of the control, but left the yield stress essentially unaltered. At a concentration of 27.5 mg/ml of plasma, the 150,000 Mw dextran fraction produced roughly a 36-fold increase in yield stress and the 500,000 Mw fraction, a 90-fold increase above that of the control. Studies with the 80,000 Mw fraction of dextran at concentrations above 27.5 mg/ml showed that the fractional increment in yield stress was approximately linearly proportional to the square of the concentration of dextran. After flow had started but at a low rate of shear, the relative viscosities of dextranated blood to control blood were more or less linearly proportional to the relative viscosities of dextranated saline to plain saline. (Aided by the Department of the Army, OSG., and the National Heart Institute, USPHS.)

THE EFFECT OF THYROPARATHYROID PERFUSION WITH HYPER- AND HYPOCALCEMIC BLOOD ON CALCIUM, PHOSPHORUS AND MAGNESIUM METABOLISM. D. Bernstein*, C. R. Kleeman, S. Ling*, and M. Maxwell. Department of Medicine, Cedars-Sinai Hospitals, Mount Sinai Hospital Division, Los Angeles.

Thyroparathyroidectomy in the dog causes an immediate increase in renal clearance of calcium and an immediate decrease in phosphate clearance. However total serum calcium or free calcium ion concentration (Murexide Method) falls $<$ 1.0 mg% in first 6 hours post-op. Copp, D.H., et al (Endocrinol. 70: 638, 1962) and MacIntyre, I., et al (Lancet 9/7/63, p480) by in vivo perfusion of dog parathyroid glands have suggested the presence of a parathyroid secretion (calcitonin) which lowers serum calcium in the dog. Experiments in this laboratory have investigated the renal clearance of Ca^{++}, $PO_4^{=}$, Mg^{++} and Na^{+}, and the plasma concentrations of these ions after parathyroidectomy (PTX) per se and in vivo perfusion of dog thyroparathyroid glands with hypo- and hypercalcemic blood.

Serum calcium falls at same rate after PTX as after thyroPTX, but $PO_4^{=}$ clearance decreases significantly faster after PTX. Ca^{++} and Mg^{++} clearance rises after both operations. Perfusion of thyroparathyroid glands with hypercalcemic blood causes $>$ 1.0 mg% fall in serum calcium in 2 hours; also causes $PO_4^{=}$ clearance to decrease at faster rate than after thyroPTX and reach minimal levels in 2 hours. Mg^{++} and Ca^{++} clearances increased. Perfusion with hypocalcemic blood caused immediate increase in systemic serum calcium, immediate increase in $PO_4^{=}$ clearance, and an immediate decrease in Ca^{++} and Mg^{++} clearance (when "corrected" for Na^{+} excretion). These studies confirm that hypercalcemic perfusion of thyroparathyroid glands in dogs causes serum and urinary changes suggesting release of material which "antagonizes" osseous and renal effects of parathyroid hormone.

INVESTIGATIONS ON THE BLOOD-BRAIN BARRIER OF FISH. J. J. Bernstein and E. Streicher* Lab. Neuroanat. Sci. and Surg. Neurol. Br., N.I.N.D.B., National Institutes of Health, Bethesda, Maryland.

The blood-brain barrier may be demonstrated in both mammals and fish by the complete or almost complete exclusion of acid dyes (e.g., trypan blue) from the brain. In addition, anions such as iodide, bromide, sulphate, and thiocyanate enter the brain differentially and are therefore maintained at various brain/plasma ratios. In mammals, these ratios, in vivo have always been lower than the brain/plasma ratio for chloride (the sulphate space for brain is approximately 5% and the chloride space for brain is approximately 30%).

The brains of 15 goldfish were examined 4 hours after intraperitoneal injection of 1% trypan blue, bromphenol blue, phenol red, or sodium fluorescein. The various dyes did not enter the brain except at the anterior and posterior choroid plexus.

In addition, sodium thiocyanate (2-8mM/kg) was injected intraperitoneally in 34 goldfish (250 gms) or was introduced into the water of the aquarium (6mM/L). The thiocyanate content of the brain was determined 5, 24, 48, 96, and 144 hours later. The thiocyanate space (brain/plasma ratio) was determined after correcting for protein binding and Donnan effect. The brain/plasma chloride ratio (space) was also determined in 5 normal goldfish. Although the chloride space determined for the goldfish brain (33%) was about the same as that reported for the mammals (30%), the thiocyanate space of the goldfish brain (43%) was larger than that reported for in vivo experiments on mammals (5-17%). This larger thiocyanate space was observed, regardless of dosage, from 24-144 hours after injection.

It may be concluded that there are significant differences between the blood-brain barrier mechanisms of bony fish and mammals.

Adaptation of Resistance and Capacitance Vessels of the Forearm to Leg Exercise in Man. S. Bevegård*, and J. T. Shepherd. Mayo Clinic, Mayo Foundation, Rochester, Minn.

In normal subjects using strain-gauge or water-filled plethysmographs, the reaction of resistance and capacitance vessels has been studied simultaneously in the forearms during supine leg exercise of increasing intensity (up to oxygen consumptions of 2 L./minute). With onset of exercise there was a transient increase in forearm blood flow and a decrease in arterial mean pressure. The amount of blood accumulated at a given venous pressure was reduced indicating an increase in venous tone at a time when there was a decrease of tone in resistance vessels. As exercise continued, the tone of the resistance vessels increased so that blood flow remained close to resting values as the arterial pressure and the venous tone increased progressively with increasing work load. Studies of the oxygen content of the blood from veins draining forearm skin and muscle, respectively indicated that the flow changes were due to active changes in caliber of the muscle vessels. An increase in venous tone graded to the severity of the exercise was also seen in "isolated" venous segments and still occurred at a time when the resistance vessels of the forearm were dilated after local exercise of the forearm muscles. These changes of tone in the resistance and capacitance vessels were abolished after sympathectomy and reduced or abolished by local heating of the forearm. The afferent side of these reflex changes has not been established. They could not be explained by alterations in carotid sinus activity or by changes in the breathing pattern. (Supported in part by research grant: NIH HE 05883.)

A REFINED ANALOG MODEL OF THE LUNG. William B. Blesser (intr. by H. A. Lyons). Polytechnic Institute of Brooklyn and S.U.N.Y., Downstate Medical Center, Brooklyn, N. Y.

A two compartment lung model is often represented by a sample electrical analog consisting of a pair of parallel R.C. branches. Such a model is an overall lumped parameter mode. An analog model of the lung has been developed based upon a definition of basic lung elements. The alveoli are considered purely compliant (comparative) elements, the rigid pulmonary airways are considered purely resistive and the flexible pulmonary airways as a combination of both resistance and compliant effects. From these simple elements a model was developed starting from the alveolus and tracing back up to the glottis. From such a model studies of pressure and flow relationships can be made in various compartments. Studies determining the effects of variation in the system elements are easily made. By gross approximations the model can be reduced to the standard model of a parallel R-C combination. Analog data will be presented.

(Supported by A.F.O.S.R., O.A.S.R. Contract AF-49(638)-1402 and U.S.P.H.S. Grant HE 5485.)

THE INTRAVASCULAR CLEARANCE AND TISSUE DISTRIBUTION OF C^{14} METHYL PALMITATE IN MICE. D. A. Blickens* and N. R. Di Luzio, Dept. of Physiol. and Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

Studies in this laboratory have demonstrated that the intravenous administration of a methyl palmitate emulsion produces a marked impairment in the phagocytic activity of the reticuloendothelial system (RES) and depression of the immune response to particulate antigens. The mechanism of RES depression by methyl palmitate was investigated by measuring the intravascular clearance and tissue distribution of C^{14} labeled methyl palmitate. The intravascular half-times of methyl labeled and fatty acid labeled-methyl palmitate were 18.9 and 16.2 min., respectively. Fatty acid-labeled methyl palmitate manifested a significantly greater liver uptake than methyl-labeled methyl palmitate. The 24 hr. $C^{14}O_2$ recovery was 54% and 85% of the fatty acid labeled and methyl-labeled methyl palmitate, respectively. To determine the mechanism of the intravascular clearance, the removal of C^{14} methyl-labeled methyl palmitate was measured prior to and following the administration of colloidal carbon. The removal rate of methyl palmitate was unaltered following the administration of carbon. The data indicate that methyl palmitate is not removed by a phagocytic process, nor is RE depression induced by the retention of methyl palmitate in RE cells. (Supported in part by USPHS HE-05367, and the Atomic Energy Commission).

GLUCOSE-C^{14} UTILIZATION BY DIFFERENT AREAS OF DEVELOPING CHICK INTESTINE. P. H. Bogner, M. Hill* and M. TaVoularis.* Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

The in vitro tissue accumulation method was adapted for these studies. Intestinal slices from the duodenum, jejunum and ileum of embryos and young chicks between -3 and +10 days of age were incubated with glucose-C^{14} in both the presence and absence of oxygen. A 15 minute incubation period was terminated by addition of 6 N H_2SO_4. Hyamine was then introduced into a center well of the closed flask via a hypodermic needle (inserted through the rubber stopper) in order to trap released $C^{14}O_2$. After an additional hour in the incubated shaker, the flasks were removed and aliquots of the media and hyamine were transferred to a dioxane and toluene phosphor, respectively. Samples were counted in a Packard TriCarb liquid scintillation spectrometer. The quantity of glucose metabolized to CO_2 was greater in oxygen than in nitrogen for all intestinal areas from all aged chicks including the embryos. There was a limited conversion of glucose to CO_2 in a N_2 atmosphere by the embryonic gut which increased substantially by the day of hatching and then levelled off. Similarly, glucose conversion to CO_2 by the embryonic slices in oxygen was low but increased sharply thereafter until 2 days of age. A further slight increase also occurred between 2 and 10 days of age. This enhancement of glucose metabolism to CO_2 between -3 and +2 days of age corresponds exactly in time with the development of an intestinal active transport mechanism for sugars in the chick (Bogner, P. H. and I. A. Haines. Am. J. Physiol., in press). Supported by NIH grant AM 02353.

FACTORS INFLUENCING HUMAN CARDIAC PERFORMANCE AFTER OPEN HEART SURGERY. Clorinda S. S. Bohler*, Robert G. Ellison, and Philip Dow. Departments of Physiology and Thoracic Surgery and Hemodynamic Center, Medical College of Georgia, Augusta.

The beginning of these studies was reported a year ago. Left ventricular performance has been followed in 36 patients during cardiac surgery and for postoperative periods up to 5 days (most cases 12 to 72 hours). Cardiac outputs were measured with Cardiogreen, Gilford densitometer, and Lexington computer. Left atrial pressures and mean arterial pressures were recorded by Statham gauges and either DR8 or Cambridge recorders (always with ECG). Operations included various valve replacements or repairs and correction of congenital defects, and all were done using complete cardiopulmonary bypass. Twenty-two postoperative courses were uncomplicated, 4 were fatal, ten showed evidence of cardiac failure at some time. As we reported earlier, uneventful recoveries continued to be accompanied by favorable rotation of the performance vector. A variety of unfavorable courses were studied, and the vector data paralleled or preceded the clinical signs of cardiac failure. Some hazards, such as overwork, can be specifically identified. Supported by a grant from the Life Insurance Medical Research Fund and grants H-240, H-5432, and He-07266 from the National Institutes of Health.

EFFECT OF THYROID ACTIVITY ON GASTRIC SECRETION IN CHRONIC FISTULA RATS. S.P.Bralow,S.A.Komarov, and H.Shay. Fels Research Inst., Temple Univ.School of Med., Phila., Pa.

Since experimental hypothyroidism produces depression of gastric secretion in young pylorus-ligated rats, further observations of thyroidal influences were made in chronic fistula animals. Initially 0.5 mc. I_{131} administered to adult rats and repeated after 19 weeks. Gastric juice collected at weekly intervals for 31 weeks. Volume of secretion and body weight increased with significant regression on time. Total acidity, pepsin concentration and output decreased, but respective regressions were significant only after second dose. Another 8 groups of rats were followed 16 weeks after varying treatments: 0.5 mc., 1.0 mc. and 1.6 mc. I_{131}, 1.0 mc. I_{131}, 1.0 mc. I_{131} plus 0.15 mg. Cortisone or 50 mcg/kg L-Thyroxine 6 days/week, L-Thyroxine alone and 2 groups of controls. Collections of gastric juice made every 2 weeks and differences of the adjusted means between groups compared. Volume, free and total acid and total chloride outputs were significantly higher for animals given L-Thyroxine alone. Total acidity and output were significantly decreased only in group given I_{131} plus Cortisone. All parameters of secretion decreased significantly in young litter mates given 0.5 mg. I_{131} in comparison to paired control. Between 35.3 to 69.7% of decrease explained by concomitant loss of weight.

METABOLIC RATE AND MUSCULAR ACTIVITY OF THE RAT. P.O.Bramante and G.C. Reis*. Dept. of Physiology, St.Louis Univ.School of Med.,St.Louis, Mo. and Dept. of Biomed.Engineering,Drexel Inst.of Technol.,Philadelphia,Pa.

Rate of O_2 consumption ($\dot{V}$) and spontaneous muscular activity (SMA) of normal albino rats were measured in 106 experiments with apparatus and method previously described (1,2,3). The 'no-activity' metabolic rate per unit weight ($\dot{V}/W$) was best described, as function of age [f(a)], by a high degree polynomial, for the limits of age investigated (36 - 195 days). The metabolic rate as function of activity [f(A)], when expressed as $\dot{V}/W^{\cdot 5}$, confirmed (2) the linear relationship $f(A) = p + qA$. Solving for $\dot{V}$ in $f(a) = \dot{V}/W$ and $f(A) = \dot{V}/W^{\cdot 5}$, the theoretical $\dot{V}$ of a particular animal at any level of activity is described by the equation

$$\dot{V} = \frac{[f(A)]^2}{f(a)} g(A)$$

where g(A) is a correction factor depending on the units of activity.

Analysis by digital computer technique (IBM 1620) of $\dot{V}/W$ at constant levels of activity, in rats of different ages, indicated an essentially parallel behavior at low levels of activity ($A \leq 1.3$ SMA units), but progressively divergent values for age < 60 days, at higher levels of activity, particularly evident in the youngest and most active animals.

(Supported by Research Grant A3367 and Special Fellowship HSP-18,303 of the USPHS). References: 1) JAP, 14:1063,1959. 2) JAP, 16:982,1961. 3) JAP, 18:216,1963.

POTENTIAL DIFFERENCE ACROSS OVARIAN CYST WALL.

Michael O. Breitmeyer*, Susana R. Kruglicoff*, Warren H. Dennis and Milton B. Yatvin*. Department of Physiology and Radiology Research Laboratories, University of Wisconsin, Madison, Wisconsin.

Ovarian cysts can be produced in Long-Evans rats by injections of pregnant mares serum gonadotrophin and their production is enhanced by feeding thiouracil. Such cysts can reach diameters as great as 20 mm. And are filled with a fluid whose ionic and protein composition are similar to serum. In a continuing investigation of the origin of cyst fluid, studies of the electrophysiological characteristics of the cyst wall were undertaken. In the first group of animal studies, the average potential difference determined by microelectrode puncture for animals receiving pregnant mares serum only was 26 millivolts for cysts less than 3 mm in diameter and was 5 millivolts for cysts greater than 4 mm in diameter. For those receiving the goiterigen plus pregnant mares serum the average potential difference was 24 millivolts for those whose diameter was less than 3 mm and 7 millivolts for cysts with diameters greater than 4 mm.

GASTRIC HYPERACIDITY IN THE RAT PRODUCED BY PYLORUS LIGATION. David A. Brodie and Sylvia K. Kundrats.* Merck Institute for Therapeutic Research, West Point, Pa.

A study of titratable gastric acidity in acute fistula rats with and without pylorus ligation confirmed the observation that ligation stimulated gastric acid secretion, since acid values without pylorus ligation were 76.3 mEq./L. as compared to 104.0 mEq./L. with ligation. The site of the tie was found to be important, since ligation at 1.0 and 0.5 cm. above the pylorus, at the pylorus, and 0.5, 1.0 and 2.0 cm. below the pylorus produced acid values of 123.2, 128.9, 126.0, 103.1, 71.9 and 71.7 mEq./L., respectively. The possibility that a stimulant hormone was released from the pylorus was remote, since surgical removal of the pyloric area between ligatures placed 0.5 cm. above and below the pylorus did not significantly lower gastric acidity. Crushing of the pylorus tissue was not essential for stimulating acidity, as non-occluding ties around the pylorus produced the same acidity values as complete ligation. Reduction of gastric acidity to 50% of control values was produced by injection of the following drugs into a tied off area 0.5 cm. above and below the pylorus: cocaine 41.0 mg./kg., atropine 0.2 mg./kg., and mecamylamine 1.2 mg./kg. The results suggested that pylorus blockade stimulated afferent nerve endings which passed through at least one synapse before leaving the pyloric area. The reflex arc appeared to be long rather than local to the stomach, since section of the vagus (by esophagotomy) abolished ligation-induced hypersecretion.

LOOP CURRENT IN RELATION TO NET IONIC TRANSPORT IN THE 'OPEN-CIRCUIT' TURTLE BLADDER. W.A. Brodsky, T.P. Schilb*, and H.R. Wyssbrod*. Univ. of Louisville School of Medicine, Div. of Exp. Med., Louisville, Ky.

Net chloride transport can be related predictably to spontaneous voltage and dc resistance across the isolated turtle bladder. Hemibladder sacs, immersed in oxygenated and nitrogenated Na Ringer's solutions, were filled with NaCl, 0.11 M as mucosal fluid. Paired control tissues of the same bladder, bathed with the same fluids, were mounted in a modified Ussing chamber. Transbladder potential difference (P.D.) and rate of chloride transport from mucosal to serosal fluids (M to S) were measured in sacs, and simultaneously, P.D. and dc resistance across the bladder (R_t) were measured in paired membranes. R_t in ohms, and rate of chloride transfer in coulombs per second were normalized with respect to dry mass of bladder wall. Active transport of both Na^+ and Cl^- ions (M to S) has been shown previously (Fed. Proc. 23:211, 1964). Thus, the assumed equivalent circuit consisted of a sodium pump (E_{Na}) and resistance (r_{Na}) in parallel with a chloride pump (E_{Cl}) and resistance (r_{Cl}); E_{Na} and E_{Cl} oriented to pump the respective ions from M to S. From network laws,

$$1) \quad P.D./R_t = (r_{Cl}/R_t)\, i - E_{Cl}/R_t,$$

where i, the loop current is estimated from net chloride transport. In 4 experiments under O_2, $P.D./R_t$ (O_2) = 1.68 i (O_2). Assuming that $r_{Cl} = r_{Na} = 2\ R_t$ under O_2, E_{Cl} would be 13 mV, S negative; and E_{Na} 133 mV, S positive. In 4 experiments under N_2, $P.D./R_t$ (N_2) = i (N_2) to within 10%. Data from bladders in Choline Ringer's suggest that (E_{Cl}) $\approx$ 0 under N_2, whence $r_{Cl} \approx R_t$, which satisfies the observation that the value of loop current (net ion transport) during anoxia is closely equal to the ratio of spontaneous voltage to resistance. (Supported by USPHS and U.S. Army).

IN VIVO NA^{24} UPTAKE IN BRAIN. G.F. Brooks* and A.R. Koch, Dept. of Physiology and Biophysics, Univ. of Wn., Seattle, Wn.

The exchange of Na^{24} in the heads of dogs was measured continuously while the plasma concentration of Na^{24} was maintained constant. A closed-end nylon catheter was surgically implanted into the brain 1-3 weeks prior to the experiment. At the time of the experiment, a continuous dialysis was instituted to measure the isotope level in plasma. Head counts were made by inserting a Nuclear Chicago DS8 detector with a β-γ sensitive probe, 3 mm in diameter, into the brain catheter. Dialysate and blood counts were made with Nuclear Chicago DS5 detectors with anthracene crystals. The output of each detector was led to a separate count-rate meter. Plasma Na^{24} was maintained constant by coupling the dialysate Na^{24} level to a feedback control system. The contribution of isotope in circulating blood was subtracted from the head count. The resulting curve could be described by a double exponential equation whose components had half-times of about 15 and 350 minutes. The Na^{24} uptake of the entire animal was measured as the amount of isotope pumped into the animal in order to keep the isotope level in plasma constant. This uptake into the entire animal resolved into a single exponential curve with a half-time of about 15 min. Sacrificing the animal and removing the brain indicated the contribution of non-nervous structures to the total head uptake. The ratio of counts of the nervous and non-nervous tissue determined by this ablation agreed with the ratio of compartmental sizes determined from the head curve. The rapid component of the head uptake can be attributed to uptake in the non-nervous tissue and the uptake of Na^{24} by brain tissue can be described by a single exponential process with a half-time of about 6 hours. (Supported by grants NIH 1SO1FR-05432-01 and NB 04653-01.)

EXCITABILITY OF NEURONS IN SIGMOID GYRI.* V.B. Brooks[1] and M. Levitt[2]. Rockefeller Institute, New York.

Responses of 160 cells in lateral sigmoid gyri of 7 cats to somesthetic and kinesthetic stimuli were recorded, employing methods previously described (J. Neurophysiol., 1961, 24, 281 & 322), except that closed-skull preparations with a Davies microdrive and tungsten microelectrodes were used. Extracellular potentials were mostly positive-negative (0.3-2.0mV), and were recorded for 10-180 min. or longer. In many trials cell groups with particular types of input were found during insertion and withdrawal at the same depths $\pm$50 mu. Number of cells, distributions of adequate stimuli, and receptive field types for total discharges (primary plus late) are listed below. 'Labile' signifies change in effective stimuli and/or receptive field. Several 'labile' cells were excited by acoustic as well as somatic stimuli. (see also EEG Clin. Neurophysiol. 1963. Suppl. 24, 13) Most penetrations were postdimple; and 12 of 34 postdimple units tested antidromically could be invaded from the bulbar pyramid.

Cortical area:	Pre-Cruciate				Cruciate to Dimple				Post-Dimple			
Adequate stim:	Hr	To	Pr	Jt	Hr	To	Pr	Jt	Hr	To	Pr	Jt
Fixed local	7	1	0	11	5	6	0	0	65	27	8	1
Fixed wide	5	2	2	0	2	1	0	1	6	3	2	0
Labile	1	1	0	1	0	0	0	0	2	0	0	0
Totals	13	4	2	12	7	7	0	1	73	30	10	1

Abbreviations: Hr: hairbending; To: touch; Pr: pressure; Jt: joint.

*Work supported in part by Grant NB-02618 from N.I.N.D.B., U.S.P.H.S.

Present addresses: 1. Dept. Physiology, New York Medical College, N.Y.
2. Dept. Anatomy, Univ. of Pennsylvania, Phila.

FURTHER OBSERVATIONS ON IN VIVO CO_2 BUFFER CURVES OF BLOOD. E. B. Brown, Jr. and Richard L. Clancy*. University of Kansas Medical Center, Kansas City, Kansas.

In vivo CO_2 buffer curves of blood have a lower slope than in vitro curves when the curves are extended over a wide range of CO_2 tension (up to P_{CO_2} = 200). Over a narrow range of P_{CO_2} increase (10 mm Hg) and with reduced P_{CO_2} (hyperventilation) the slopes are the same. The in vitro buffer curve on blood drawn from an anesthetized dog was established by equilibrating the blood with 5%, 11%, and 30% CO_2 in oxygen. With the animal breathing 100% oxygen, arterial blood and mixed venous blood CO_2 tensions and pH were determined. A rough calculation of the CO_2 tension necessary to raise arterial blood plasma to the same bicarbonate concentration as venous blood plasma was determined, and CO_2 was added to the inhaled mixture to approximate this tension. After ten minutes of breathing this mixture, arterial blood CO_2 tension and pH were again determined. The dog then breathed 30% CO_2 in oxygen for ten minutes and the values were repeated. After breathing 100% oxygen for twenty minutes a new control point was determined, and the dog was then hyperventilated to reduce CO_2 tension to approximately 20 mm Hg. The results demonstrate that the in vivo CO_2 buffer curve of blood (with a very small increment in CO_2 tension above normal and on hyperventilation to a lower CO_2 tension), has essentially the same slope as the in vitro curve. With a very large increase in CO_2 tension the decrease in the in vivo buffer slope was again apparent.

ALDOSTERONE SECRETION AND THE RENIN-ANGIOTENSIN SYSTEM DURING SODIUM DEPLETION. T. C. Brown*, J. O. Davis, P. F. Binnion*, and M. J. Olichney*. Natl. Insts. of Health, Bethesda, Md.

To study the response to Na depletion, 7 dogs were fed a low Na diet and given 2 cc. of mercuhydrin i.m. daily for 4 days. A 3-fold elevation in aldosterone secretion occurred but corticosterone output was augmented only slightly in 2 of 7 dogs. In contrast, hypophysectomized dogs with low corticosterone outputs consistently showed a 3-10 fold increase in corticosterone secretion as well as augmented aldosterone output. These findings show that in the absence of a corticosteroid feedback mechanism corticosterone secretion increased. The peripheral plasma level of renin was 5-fold higher in 4-day Na depleted dogs than in normals whereas renin substrate was unaltered. Plasma electrolyte changes (decreased Na and increased K) were not consistently present until the end of the 4th day of Na depletion and both plasma Na and K were normal at the onset of hyperaldosteronism. In another experiment, the acute response to 2 cc. of mercuhydrin i.m. was studied in 4 normal, unstressed, anesthetized dogs. Over a period of 2 hours there were simultaneous increases in urine flow (from .09 cc/min. to 3.11 cc/min.), urine Na excretion (from 9 μEq/min. to 412 μEq/min.), urine Na concentration (from 30 mEq/L. to 131 mEq/L.), aldosterone secretion rate (from .007 μg/min. to .018 μg/min.) and plasma renin as indicated by angiotensin II formed during incubation (from 7 mμg/cc to 25 mμg/cc). These results demonstrate that coincident with the natriuresis, the plasma renin level and aldosterone secretion rate increased.

MODIFICATION OF EVOKED POTENTIALS OF THE SPINAL CORD BY LONG-TERM STIMULATION. H. Brust-Carmona*, E. L. Gasteiger and H. Levitan*. Dept. of Physical Biology, N.Y. State Veterinary College, Cornell U., Ithaca, N. Y.

It has been shown that the central nervous system controls the sensory input by mechanisms which increase or decrease the electrical response in the afferent pathways. In order to study such processes at the spinal level, stimuli were delivered to the sciatic nerve and various evoked responses were recorded at four sites in the cords of flaxedilized, anesthetic-free decerebrate and spinal cats. In all experiments the blood pressure, rectal temperature, respiration, and spinal electrogram were monitored. Long-term changes of the dorsal cord potential (CDP) at levels T_1 and L_7 or L_6, dorsal root potential (DRP), and ventral root potential (VRP), elicited by a series of 3 shocks (1/sec.) repeated once every 7 or 9 seconds, were recorded over 3 hours. The evoked responses were recorded on a 4-channel tape recorder and averaged (N=30) on a TMC gamma ray spectrometer adapted by F. L. Hiltz. In both spinal and decerebrate preparations, DCP (N_1, N_2, and P waves) and DRP (IV and V waves) decreased in response to stimuli subthreshold for VRP. These potentials increased as much as 50% when the stimuli were maximal for VRP. These changes could not be reversed with transient alteration of the stimulus voltage and frequency. The decrease of the potentials in decerebrate animals was transiently reversed by spinalization. Further attempts to reverse these changes are being made by use of drugs, rest, and long-term alteration of stimulus characteristics. These results suggest the existence of negative and positive feedback which modifies the potentials in relation to the intensity of the stimulus. (Supported by USPH grants # 5K3NB 6877-03, NB 04408-02 and 5T1 GM-223-03 and DASA Contract # DA 49-146-XZ-058.)

CHANGES IN RESPONSES TO A CONSTANT BRAIN STIMULUS. N. A. Buchwald, S. Soltysik*, C. Romero-Sierra* and F. E. Horvath. Dept. Anatomy and BRI, UCLA. (1) Habituation: Low-frequency stimulation of the caudate nucleus in cats decreases the rate of bar-pressing for a food reward or prevents the animal from pressing at all, but does not interfere with consumption of food nor with the orienting responses to visual or auditory stimuli. Often such external stimuli, presented during arrest of bar pressing due to continuous caudate stimulation, are followed by a short burst of bar pressing. With repeated caudate stimulation the threshold current required to stop bar pressing increases markedly; i.e., the response of the animal to the stimulus tends to habituate. Stimulation of the adjacent internal capsule also interferes with the animal's bar pressing but, in addition, produces motor effects (discoordination, tremor). No marked habituation of the suppression of the bar-pressing response occurs with capsular stimulation. Other responses to caudate stimulation also habituate. For example, high-frequency (50 cps, 0.5 msec, 1-5 v) stimulation elicits a cardiac rate acceleration, which gradually diminishes over a period of 15-20 daily experimental sessions. (2) Caudate stimulation as a cue: Animals taught to press a bar for food were presented with caudate stimulation coincident with the withdrawal of the reward. Following a period of training in this situation, in which the caudate stimulus served as a cue of ommission of reward, cats pressed at diminished rates or failed to press at all when the caudate was stimulated at current intensities much too low to produce suppression of pressing in the untrained animal. In contrast, preliminary results show no obvious changes in cortically recorded evoked potentials during repeated caudate stimulation.

Supported by USPHS Grant MH-07097

SOME PHARMACOLOGIC EFFECTS OF VERATRUM EXTRACTS IN THE OVINE AND CAPRINE SPECIES. Wm. B. Buck, R. F. Keeler and Wayne Binns (intro. by R. W. Dougherty). Animal Disease and Parasite Research Division, ARS, USDA, Ames, Iowa and Logan, Utah.

The plant Veratrum californicum produces a cyclopian-type congenital malformation in lambs when ingested by the ewe during the 10th-15th day of gestation. A study was made of the effects of continuous short-term intravenous infusions of a purified teratogenic ethanol extract of this plant in sheep and goats. This extract, containing mostly glycosides and parent alkamines, produced a 3-7 fold elevation in blood glucose levels in both intact and adrenalectomized animals. Concomitant effects on cortical electroencephalographic (EEG) activity included first an increase in magnitude of the waves followed within a few seconds by complete cessation of EEG activity. Artificial respiration with 100% O_2 reversed the effects of the alkaloids on EEG activity and assured recovery of the animals, despite the fact that none of the data indicated the existence of hypoxia or hypercapnia. We postulate that the hyperglycemia was produced by either or both of 2 mechanisms: (1) enhanced glycogenolysis by the alkaloids or (2) inhibition of glucose utilization in tissues. In the latter case, the cessation of EEG activity may have resulted from a reduced supply of phosphorylated energy to the brain. These effects were not observed upon administration of acid hydrolyzed extract, administration of either jervine or veratrosine, which are the two predominant alkaloids in the extract, or administration of another fraction composed mainly of jervine and veratrosine.

POTASSIUM UPTAKE AND SODIUM TRANSPORT AT THE INSIDE SURFACE OF ISOLATED FROG SKIN. O. A. Candia and J. A. Zadunaisky (intr. by G. Carrasquer). Eye Research Laboratory, University of Louisville, Ky.

The relationship between the uptake of K from the inside bathing medium and the net transport of Na, measured as the short-circuit current (S.C.C.) was studied in 20 sq. cm. of abdominal skin of the frog Leptodactylus ocellatus. The inside of the skin was perfused with a solution containing K42 circulated through a closed system including a well scintillation detector. The disappearance of K42 from the perfusate was measured from 30 sec. to 3 hrs after addition of the isotope. Kinetic analysis for a closed two compartment system could be applied to the results since practically no K42 leaked to the outside from the skin. The K content of the skins did not vary throughout the experiment. The cellular compartment was calculated on the basis of the determination of the inulin space. Good correlation values between radioactive and stable K in the medium and the cellular compartment of the skin were found at equilibrium. The amount of K42 that disappeared from the inside medium was such that it must equilibrate with a high K compartment as the intracellular. The $t_{1/2}$ for K42 uptake was of about 1 hr. in 21 experiments and the least square analysis of the slope indicated the existence of only one component. It was found that K influx is nine times smaller than the sodium transport measured as the S.C.C. in sulfate Ringers and six times smaller in chloride Ringers. The absolute magnitude of the K influx does not change in the presence or absence of chloride in the Ringers or changing from open to short-circuit conditions. Addition of Cu(2×10^{-5} M) to the inside medium accelerated the rate of K42 uptake and increased the total K content of the skin. The Na-K link does not seem to be 1 to 1, though a good statistical correlation between the two was found.

EFFECT OF HYPOXIA AND ACIDOSIS ON MEDULLARY SECRETION FROM THE DENERVATED ADRENAL GLAND. R.C. Cantu*, G.G. Nahas, J.W. Correll* and W. M. Manger. College of Physicians and Surgeons, Columbia University, New York, N.Y.

Low PaO_2 (50 mm Hg) without acidosis (pH 7.40, $PaCO_2$ 50) produces a minimal and hypercapnic acidosis (pH 6.88, $PaCO_2$ 122, PaO_2 100) a five-fold elevation in peripheral plasma catecholamines in the intact dog. In 6 dogs, the spinal cord was transected at the eighth cervical segment (C_8). The right lumbo adrenal vein was cannulated and samples periodically taken for catecholamines, pH, pCO_2 and pO_2 measurements. Adrenal blood flow was recorded and adrenal catecholamine output (A.C.O.) calculated. Glucose was measured in arterial blood. In these animals, after mechanical ventilation with 8% O_2 in N_2 for 15 minutes (pO_2 30, pCO_2 20, pH 7.50) there was no significant change in A. C. O., while a 17-fold increase (2.3 to 39.6 mcg/min./kg. body weight) in A. C. O. occurred following ventilation with 10-20% CO_2 in 25% O_2 and N_2 (pO_2 82, pCO_2 124, pH 6.91). Infusion of 0.15 M HCl increased A.C.O. (pO_2 82, pCO_2 50, pH 6.92) to a similar extent. When the acidosis was corrected with tris(hydroxymethyl)aminomethane (THAM), catecholamine secretion fell in all instances. Blood glucose levels paralleled changes in A. C. O. These findings indicate that (ruling out hormonal interaction) a primary direct stimulus of adrenal medullary secretion is an increase in $[H^+]$ concentration.
Supported by Contract DA-49-193MD-2265 and Grant GM-09069-02.

RHYTHMICITY OF THE RAT URINARY BLADDER ELICITED BY AN ELEVATED POTASSIUM ENVIRONMENT. F. G. Carpenter. Dept. of Physiology, Dartmouth Medical School, Hanover, N. H.

An isolated rat urinary bladder maintained in Ringer's, exposed to 10^{-7} to 10^{-8} M acetyl choline, displays prominent rhythmic fluctuations of pressure. Similarly, by increasing the K^+ ion concentration to 15-30 mM, rhythmic contractions amounting to 25 cm of water pressure are produced at regular intervals at a rate of about 1/second at 25° C. These K^+-induced responses are abolished by Ca^{++} deprivation or by 20 mM Mg^{++}, by 10^{-6} atropine, or by anesthetics sufficient to block axonal transmission. They are much less after degenerative section of the motor nerves. Moreover, these rhythmic responses are potentiated by eserine. Contractile responses of the preparation to motor nerve stimulation are also abolished by Ca^{++} deprivation or 20 mM Mg^{++}, by anesthetics or by degenerative section and are potentiated by eserine. However, responses resulting from exogenous ACh or carbamyl choline are not changed. It is concluded that the rhythmicity induced in this smooth muscle by an elevated K^+ environment is mediated through the neural elements and specifically involves the release of ACh from the motor nerves. Accordingly, the smooth muscle fiber itself under these conditions is not active in the absence of endogenous or exogenous chemical mediator.
[Supported by N.S.F. Grant No. G-14350]

A SEARCH FOR NOCICEPTIVE ELEMENTS IN THE THALAMUS OF THE AWAKE SQUIRREL MONKEY. Kenneth L. Casey (intr. by Paul D. MacLean). Natl. Insts. of Health, Bethesda, Md.

The antero-lateral spinal cord has been shown to project to the midline-intralaminar and postero-lateral thalamus (posterior group). The purpose of this study was to test the hypothesis that a neural population, responsive exclusively to noxious stimuli, exists at a thalamic level. Squirrel monkeys, sedated with small doses of pentobarbital (2.5 mg.), were adapted to sit quietly in a restraining chair. By means of a chronic stereotaxic method, microelectrode exploration of the thalamus was carried out. Natural somatic, visual, and auditory stimuli were used. Intensity of somatic stimulation was monitored by a strain gauge; a noxious stimulus was defined as one consistently causing withdrawal of the stimulated part and usually consisted of 500 g of pressure delivered with a pin. The EMG and intracranial pressure served to show whether or not unit firing was associated with movement or with possible alterations in the relative position of the microelectrode. Fifty-six percent (56%) of the 151 midline-intralaminar and 39% of the 148 postero-lateral units responded to somatic as well as to auditory or visual stimulation. No units responded exclusively to noxious stimuli. In both regions, the response of these units varied with the level of wakefulness as estimated by behavioral and physiological criteria. Under pentobarbital sedation, some of these units appeared to be exclusively nociceptive; however, multimodal responsiveness returned as the waking state was regained. In the waking state, unit responses could be altered by interacting effective stimuli. Computer analysis of unit discharges is being performed for further comparison of certain statistical parameters of pre- and post-stimulus activity.

MODULATION OF UNIT CELL ACTIVITY IN THE UNANESTHETIZED CAT CORTEX. R.L.Cechner and D.R.Smith (intr. by D.G.Fleming). Bioengineering Group, Case Inst. Tech., Cleveland, Ohio.

Previous work by author (D.R.S.) indicated that a double Poisson probabilistic model could be used to characterize discharge patterns from spontaneous and electrically stimulated cells in the cortex of encephale isolé cats. Similar experiments are now presented using chronically prepared, immobilized, flaxedilized cats. Statistical tests confirm generally that, under these new conditions, spontaneous activity is still characterized by the double Poisson model and that steady current stimulation causes only one phase of the double parameter model to change. The second phase of activity appears to be invariant during stimulation until the change in total average frequency is greater than two fold. A preliminary attempt was made to estimate the membrane current density necessary to cause a detectable alteration of unit activity. Using experimental electric field plots and field mapping techniques we estimate that a current density of 0.37 pA/μ^2 is sufficient to alter spontaneous activity. Extracellular stimulation was found to create large local depolarizations (1-30 pA/μ^2) and to set up polarization gradients along the surface of the membrane. It appears that exogenous current flow acts mainly on specialized portions of the membrane. Hypoventilation caused complete cessation of unit activity after 30 seconds with recovery within 20 seconds after restoration of normal ventilation.

ELECTRICAL POTENTIAL PROFILES IN FROG SKIN. Marcelino Cereijido* and Peter F. Curran, Biophysical Laboratory, Harvard Med. Sch., Boston.

The influence of ion composition of the bathing solutions on the electrical potential profile in frog skin has been examined using microelectrodes. The skin was supported by a wire mesh placed against the inner side and was penetrated from the outer side with a glass microelectrode filled with 3 M. KCl. The potential difference (p.d.) between the outer solution and the electrode, and the total skin p.d., were observed. As the electrode penetrated the skin, two positive going potential steps were frequently observed, but in some cases, three or more steps were found. In many experiments, the electrode was introduced into the skin so that it was located between the two major steps and left in place while the bathing solutions were changed. Under these conditions, the tip of the microelectrode should be in a basal cell in the epithelium (Whittembury, J. Gen. Physiol., 1964, 47, 795). With the skin bathed in sulfate Ringer's solution, a decrease in Na concentration of the outside solution (Na_2SO_4 replaced by $(choline)_2SO_4$ or K_2SO_4) caused a decrease in total p.d. and a parallel decrease in p.d. across the outer barrier. There was little change in p.d. across the inner barrier. An increase in K concentration of the inside solution (K_2SO_4 replaced by $(choline)_2SO_4$ or Na_2SO_4) caused a marked decrease in total p.d. However, only 40-50% of the p.d. change occurred across the inner barrier. The p.d. between the microelectrode and the outer solution also decreased appreciably. This last observation is not consistent with the model of the skin proposed by Koefoed-Johnsen and Ussing (Acta Physiol. Scand., 1958, 42, 248). The results suggest that the role of K in determining the skin potential is more complex than proposed in the model.

STUDY OF DISTRIBUTION OF VENTILATION AND GAS EXCHANGE FROM SINGLE BREATH GAS ANALYSIS. P. Cerretelli*, R. Sikand*, and L. Farhi. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

During the course of a single breath the composition of the expired gas varies continuously. This study was conducted in order to determine the relative importance of the effect of time and of sequential emptying of elements of different gas composition. The subject inspired 1.5 liters of an oxygen-argon mixture, starting from FRC, and held his breath for a predetermined time. The subsequent maximal expiration was analyzed continuously for O_2, CO_2, A, and N_2 with a mass spectrometer. It is obvious that the inert gas tension in the alveoli may differ as a result of variation in the O_2 and CO_2 exchange with the blood. However, this process should affect all inert gases present in the lung. The ratio of the partial pressures of A to N_2 (A/N_2) will therefore be independent of the perfusion of the various parts of the lung. The A/N_2 in different fractions of the expirate will be an index of the ventilation of the elements contributing to the breath. With no breath holding, A/N_2 decreases throughout the breath, indicating a larger contribution of the better ventilated compartments to the earlier part of the expiration. When the breath is held, A/N_2 decreases in all the fractions of the expirate, becoming more even with long breath holding times. In 20 seconds this mixing process appears to be still incomplete. Analysis of the O_2 and CO_2 data does not allow to state whether all the elements contributing to a breath have the same $\dot{V}_A/\dot{Q}$ or whether their fractional contribution remains unchanged throughout the expiration. The O_2 and CO_2 changes during the course of an expiration can be attributed to time and not to sequential emptying.

(Supported in part by the U.S. Air Force.

SERUM PROTEIN-BINDING OF VITAMIN D. Philip S. Chen, Jr., A. Raymond Terepka* and Kea Lane. Dept. of Radiation Biology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N.Y.

The binding of vitamin D_3-7-H^3 or vitamin D_3-4-C^{14} to serum proteins was studied with a variety of methods. Trichloroacetic acid precipitated the vitamin D quantitatively with the proteins. Failure of serum vitamin D to dialyze or ultrafilter through cellophane cannot be used in itself as evidence for protein binding because of the extreme insolubility of vitamin D in aqueous phases and consequent inability to diffuse through membranes in control experiments where proteins were absent. Vitamin D in serum was very poorly extractable by organic solvents, the following percentages being removed by extraction three times with 4 volumes of solvent: petroleum ether, 0.25%; Iso-octane, 0.9%; chloroform, 0.7%; dichloromethane, 0.9%; ethyl ether, 3.8%; ethyl acetate, 30.4%. The technique of lipoprotein flotation with the preparative ultracentrifuge was used to separate lipoproteins and evaluate their role in serum vitamin D transport. In both dog and human serum about 40% of vitamin D added in vitro was associated with lipoprotein but the specific activity (cpm/mg protein) was 5-6 times greater in lipoprotein than in sedimented protein. Following i.v. administration of vitamin D-C^{14} to a dog, the relative binding was 26% to lipoprotein at 10 min. and 22% at 24 hours. Gradient elution chromatography on Alumina columns was employed to establish identity of the radioactive label with crystalline vitamin D following the various experimental procedures. (Supported by U.S.A.E.C. Contract.)

PULMONARY COMPLIANCE DURING TREADMILL EXERCISE. Shou-Teh Chiang,* Neil Steinbugler,* and Harold A. Lyons. State University of N.Y., Downstate Med. Ctr., Brooklyn, N.Y.

Pulmonary compliance and non-elastic resistance was studied in seven normal subjects during rest and during exercise on a treadmill. Although respiratory frequency, tidal volume, functional residual capacity and cardiac output underwent changes and performed work varied, pulmonary compliance and non-elastic resistance did not significantly change. The results of this study are similar to other studies but in those investigations exercise was performed in the sitting or supine position. Changes were sought when second-wind developed during exercise, and none were observed in the four subjects who developed this phenomena. The mechanics of respiration appears so well ordered that even with pronounced changes occurring during exercise the pressure-volume and non-elastic resistances remain unchanged.

(Supported by U.S.P.H.S. Grant HE 5485.)

COMPARISON OF POTASSIUM CONCENTRATIONS IN HISTAMINE, BETHANECHOL CHLORIDE, AND GASTRIN STIMULATED GASTRIC JUICE. Jolanta Chodakowska* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

This study was undertaken to compare the changes in potassium concentration in canine gastric juice secreted in response to histamine, bethanechol chloride (Urecholine), and gastrin by vagally innervated (Pavlov type) and vagally denervated (Heidenhain type) pouches.

After a single subcutaneous injection of histamine (0.05 mg base per kilogram), potassium concentrations in gastric juice presented a characteristic pattern; a prompt increase in the concentration of the ion was followed by a gradual reduction, often to much less than the initial value. The peak of the potassium concentration preceded that of hydrochloric acid.

After a single injection of Urecholine, a tendency toward a similar pattern was observed in the potassium concentration time-curves; the curves, however, were more irregular. When the drug was given in repeated injections, only small and irregular changes in the concentration of potassium occurred in the majority of experiments.

In contrast to histamine stimulation, after a single subcutaneous injection of gastrin, the onset of acid secretion was slower and the changes in potassium concentration were only moderate and irregular; the potassium concentration time-curves showed no characteristic pattern.

STUDY OF THE ELECTRICAL POTENTIAL IN FROG SKIN AND TOAD BLADDER. T. K. Chowdhury* and F. M. Snell. Department of Biophysics, SUNY at Buffalo, Buffalo, New York.

Specially drawn microelectrodes with large cone angles and tips less than 0.3μ have been used to measure the transmembranal electrical potentials within the frog skin and the toad bladder. The microelectrodes were carefully inserted into successive points within these tissues and at each point the Na^+ concentration of the outside (mucosal) bathing solution and the K^+ concentration of the inside (serosal) bathing solution were varied. The corresponding variations in the transmembranal potential and the microelectrode potential were recorded. The results indicate that neither the whole Na-sensitivity nor the whole K-sensitivity of the total transmembranal potential can be localized to a single cellular boundary or region. Rather, the results suggest that these Na- and K-sensitive regions are multiple and distributed through these tissue membranes.

FUNCTIONAL PROPERTIES OF SmI HINDLIMB CORTEX IN CATS WITH INTACT AND ISOLATED SPINAL SENSORY TRACTS. Janice Christiansen* and Melvin Levitt
Inst. Neurol. Sciences and Dept. Anat., Univ. of Penna., Phila., Pa.[1]

A single unit analysis of mechanoreception in exposed pericruciate cortex of cats under light Pentothal-Flaxedil anesthesia defined the region within 6mm of the longitudinal fissure, between the cruciate sulcus and approximately 2mm of the lateral gyrus, as SmI hindlimb area. A segmental organization of the contralateral hindlimb is evident, with distal representation most medial. Of 477 units studied, 77% were excited with short latency by light mechanical stimuli. These weremodality and place specific, had small contralateral peripheral fields and were located at all depths of the cortex. Modalities represented were: Hair=48%, Touch=5%, Tap=25%, Pressure=18%, and Joint=0%. Incompletely defined tactile units constituted 4%. The essential properties of this cortex are preserved after destruction of either one or both dorsal funiculi or the contralateral dorsolateral funiculus. The same is true when most of the spinal cord was cut except the dorsolateral funiculus. In contrast, contralateral hemisection, dorsal quadrant lesion, or dorsal hemisection abolished unit excitation by all forms of light mechanical stimuli and induced a high voltage EEG with frequent spindling. In these cases, units were excited by strong mechanical stimuli to cutaneous or deep tissues; the foci for peripheral excitation were always on the contralateral hindleg, but total receptive fields ranged from part of the limb to all four limbs. This response was slow adapting with long latency and arterdischarge. Such units were found only in twodepth ranges of SmI hindlimb area: 0-700μ and 1400-2000 μ below the pial surface.

[1]Supported by USPHS Tng. Grants 2T1 NB-5273 & 5T1 GM-281

THYROXINE ABSORPTION, INDEPENDENT OF QUANTITY AVAILABLE. Sung Jang Chung* and L. Van Middlesworth. Department of Physiology, University of Tennessee, Memphis.

In vivo intestinal absorption of thyroxine was studied over a wide range of doses, 0.03, 0.3 and 30 μg thyroxine, labeled with I-131. The thyroxine was injected into 5 cm loops of the duodenum, jejunum and ileum of anesthetized rats. After one hour the loops were excised and the remaining I-131 was measured.

Dose of thyroxine μg	No. of Animals	% Absorbed from lumen (mean ± S.D.)		
		duodenum	jejunum	ileum
0.03	6	22 ± 3.3	28 ± 11	32 ± 17
0.3	7	20 ± 3.2	25 ± 3.3	38 ± 8.9
30	6	18 ± 16	26 ± 8.2	29 ± 5.3
Average		20 ± 9.7	26 ± 8.0	33 ± 11

Previous studies (Endocrinology 74:694, 1964) suggested that plasma albumin, secreted into the intestinal lumen reduced the absorption of thyroxine from the washed intestinal loop. Pancreatin and pronase in vitro digested the thyroxine binding protein of the intestinal lumen. Results of Sephadex gel filtration suggested that the thyroxine binding protein had a molecular weight between 50,000 and 100,000, like plasma albumin. Thyroxine absorption occurs by an unexplained mechanism, independent of the quantity absorbed over a 1000 fold range. The hormone is weakly bound to proteins within the intestinal lumen but the physiological importance of this binding is not understood.
(Supported by USPHS grant (AM-04689-04) and AEC grant (AT-40-1)-1643.)

POTASSIUM MOVEMENT IN CARDIAC MUSCLE DURING CHANGES IN INTRACELLULAR HYDROGEN ION. Richard L. Clancy* and E. B. Brown, Jr. University of Kansas Medical Center, Kansas City, Kansas

The efflux of potassium from skeletal muscle during hypercapnia has been explained by the decrease in ratio of intracellular to extracellular hydrogen ions. In contrast, cardiac muscle takes up potassium during hypercapnia. In vitro studies have shown that cardiac muscle is poorer buffered than skeletal muscle. Studies were made on anesthetized dogs using the DMO method to determine the in vivo CO_2 buffer curve of cardiac tissue and to evaluate the change in intracellular to extracellular hydrogen ion ratio, before and during hypercapnia. Average values from 10 animals are presented.

	Skeletal Muscle		Heart	
	Control	30% CO_2	Control	30% CO_2
pH_i	6.98	6.55	7.01	6.71
pH_e	7.34	6.75	7.34	6.71
$(H)_i/(H)_e$	2.32	1.59	2.17	1.00

These data suggest that cardiac muscle, in vivo, is better buffered against P_{CO_2} increase than is skeletal muscle, and that factors other than changes in $(H)_i/(H)_e$ govern net potassium flux in this tissue.

SIMULTANEOUS PRESSURE AND RADIOGRAPHIC STUDY OF THE DISTAL ESOPHAGUS. B.R. Cohen*, E.M. Aronow* and B.S. Wolf* (intr. by H.D. Janowitz). Mount Sinai Hospital, New York, N.Y.

An assembly of multiple catheters with 6 opaque-marked distal openings 1 cm. apart was positioned in the distal esophagus (DE) and fundus. Continuous pressures were recorded during repeated barium swallows and rapid serial or cine radiography in 17 normal subjects. Characteristic pressure changes corresponded to distinct sequential radiologic configurations. The zone of resting high pressure in the DE could be divided into a distal portion in which resting pressure was greater than fundic pressure and a proximal portion in which pressure was less than fundic pressure but greater than pressure in the tubular esophagus. In contrast to the response in the distal segment, no significant fall in pressure occurred in the proximal portion on swallowing. During barium filling, accompanied by a plateau-type "C" wave, this proximal segment was more distensible than the remainder of esophagus as it became the ampulla of the DE. During contraction, it underwent progressive diminution in overall size as a low-amplitude "D" wave of prolonged duration was recorded. This was in contrast to the "D" wave of peristaltic contraction in the tubular esophagus which was of greater amplitude and shorter duration. Emptying of the entire DE occurred during the height of the "D" wave in the ampulla and coincided with return of the resting elevated sphincteric zone. Characteristic physiologic features are thus demonstrated for the various radiologic segments of the distal esophagus.

O_2-CO_2 INTERACTION AND RESPIRATORY CENTER SENSITIVITY. J.E. Cohn & K. Kearns. Dept. of Medicine, U of K College of Medicine, Lexington, Ky.

Influence of O_2 on respiratory center (RC) CO_2 sensitivity was studied in lightly anesthetized cats. Spinal cord was sectioned in low cervical region, and glossopharyngeal, vagal and phrenic nerves were cut. Electrodes were placed on proximal end of cut phrenic nerve to record discharge patterns, indicating RC efferent impulses. End tidal CO_2 was maintained at control (pre-operative) levels by a respirator. Arterial pressure and rectal temperatures were monitored. Arterial blood gas and pH measurements were made at 37.5°C with electrodes. Control data were collected, consisting of phrenic discharges, end tidal CO_2, and arterial blood values. Ventilation was increased, lowering $PaCO_2$, and phrenic nerve discharges (i.e. RC efferent activity) ceased. Respirator was stopped, and time to initial burst in phrenic nerve determined. At initial burst arterial blood was sampled for gas and pH analyses. The identical protocol was employed using 14% O_2, 70% O_2 and 100% O_2. Ventilation with low O_2 caused shortening of time to initial burst and lower $PaCO_2$ at initial burst than was produced during room air ventilation. High O_2 mixtures produced lengthening of time to initial burst and higher $PaCO_2$ at initial burst than did room air. Conclusion: Respiratory center threshold to CO_2 is related to inspired O_2, suggesting a direct effect of O_2 on the center and O_2-CO_2 interaction.

Supported by U.S.P.H.S. grant No. NB03792.

PHOTOCHEMICAL ACTION SPECTRUM OF THE OXIDASE AEROBIC HYDROXYLASE SYSTEMS OF LIVER MICROSOMES. David Y. Cooper, Ronald W. Estabrook*, Sidney Levin*, and Otto Rosenthal*. Harrison Dept. Surg. Res. and the Johnson Fdn., Univ. of Pennsylvania, Philadelphia, Penna.

The light reversal of the CO-inhibition of the codeine demethylating system of liver microsomes has been measured at 10 different wavelengths of monochromatic light of equal intensity. The resultant photochemical action spectrum conforms with the spectrophotometric difference spectrum of the 450 mu CO-combining pigment of microsomes (P-450). As in the adrenocortical C-21 hydroxylase system previously studied by us, the degree of inhibition of oxidative demethylation of codeine depended on the ratio of CO/O_2 rather than on the CO concentration. This, thus, is the second microsomal mixed function oxidase for which such dependency as well as photochemical action spectrum with a maximum at 450 mu have been demonstrated. Similar maxima for reversal of CO inhibition by light have been observed for hydroxylation of acetanalide and oxidative demethylation of N methyl-4 aminopyrine. These findings support the following conclusions: (a) P-450 is the common oxidase of biological oxygenation reactions; (b) it belongs to the class of hemoproteins such as Warburg's respiration enzyme (cytochrome oxidase) and peroxidase.

(Supported by NIH grants AM-04484, AM-03644 and RG-9956)

STUDIES ON PARENT-F_1 HYBRID PARABIOTIC INTOXICATION
E. A. Cornelius *, E. Yunis * and C. Martinez. Department of Physiology, University of Minnesota, Minneapolis, Minnesota

Experiments were carried out to ascertain the respective roles of anemia and of homologous disease in parent-F_1 hybrid parabiotic intoxication. In this model, a unidirectional immune response (parent vs. hybrid) is obtained. Mice of the A strain and (A x C_{57}Bl/1)F_1 hybrids were placed in celomic parabiosis (group I). In another group (II) of similar parabiotic mice, parabiosis was discontinued 6 and 10 days after union. Homologous disease was produced in a third (III) group of F_1 mice by i.v. injection of parental strain (A) lymphoid cells. These groups were compared from the clinical, hematologic, serologic and pathologic points of view. The survival time of the F_1 partner was much reduced in group I. In groups I and II, the anemia in the hybrid partner due to shunting of blood to the parental strain partner was followed by a reticulocytosis which in turn was followed by a relative reticulocytopenia, despite a persistent anemia. Hybrid partners of all groups showed a leukopenia and a positive antiglobulin reaction. The pathologic features were similar in all groups. While anemia is probably in part responsible for the death of the hybrid in parent-F_1 hybrid parabiotic intoxication, the F_1 partner also suffers the consequences of a graft vs. host reaction (reaction of the parental strain cells against the hybrid).

NEURAL PATHWAYS MEDIATING EFFECTS OF INTRAVASCULAR NOREPINEPHRINE ADMINISTRATION.
James W. Correll *, Robert C. Cantu *, and William M. Manger. College of Physicians & Surgeons, Columbia University, New York, New York.

In the intact dog the intravascular administration of norepinephrine (5 or 10μg/kg) results in an increase in plasma free fatty acids (FFA) and glucose concentrations. In mechanically ventilated animals, under pentobarbital anesthesia, norepinephrine was given before and again one or more hours after transection of the second cervical (C-2) segment of the spinal cord. Serial arterial blood samples were drawn for the estimation of FFA and glucose in the plasma. The right adrenal vein was cannulated and samples periodically taken for catecholamines. The adrenal blood flow was recorded and adrenal catecholamine output (ACO) was calculated. Blood pressure and pulse were monitored and the systolic blood pressure remained in excess of 100 mm HG in all animals. The increase in plasma FFA and glucose concentrations normally observed were reduced after C-2 section. The administration of norepinephrine to 6 intact dogs always resulted in an increase in ACO, at times more than 8 fold (5.7 to 46.7 mμg/min/kg body weight), which continued for at least 30 minutes. After C-2 section the increase in ACO did not occur. It is concluded that intravascular norepinephrine excites central neural structures which stimulate nerves mediated by way of pathways in the spinal cord to the adrenal medulla and possibly to adipose tissue, as well.

Supported by NIH Grant.

RENAL WATER AND SOLUTE REABSORPTION IN ISOTONIC SALINE LOADED RATS. Marshall A. Cortney,* Margaret Mylle,* and Carl W. Gottschalk. Dept. of Medicine, University of North Carolina, Chapel Hill, N.C.

Rats were infused with 0.9% saline at 0.5 ml/min until they had received 10% body wt and then at 0.2 ml/min. Urine flow and C-14 inulin clearances averaged 0.03 and 1.0 ml/min 100g body wt, respectively. Urine osmolality averaged 774 mOs. Proximal tubular fluid was essentially isosmotic with renal venous plasma, which averaged 273 mOs, but both were 10 mOs lower than vena cava plasma, reflecting the high osmolal clearances. H-3 PAH clearances averaged 2.5 ml/min 100g body wt. In these rats GFR, RPF, and urine flow were higher than in nondiuretic rats and approached those found in rats loaded with 5% saline. Proximal TF/P inulin ratios were lower, however, averaging 1.7 at 60% of the tubular length. These ratios were not increased by iv administration of vasopressin at 0.5 mU/min and d-aldosterone at 0.04 ug/min for three hours. Early distal TF/P inulin ratios were also not affected by aldosterone and vasopressin. Thus proximal sodium reabsorption in these animals was quantitatively similar to that in nondiuretic rats, and not increased as in rats loaded with hypertonic saline. This might be a consequence of the failure to raise proximal tubular fluid sodium concentration, or of the absence of some unknown sodium-active hormone. Proximal TF/P (H-3 PAH) : TF/P (C-14 inulin) ratios ranged from 0.7 at 28% to 2.9 at 60% of the tubular length, and averaged 2.2 in the urine samples. Net secretion of PAH was therefore observed only in the proximal tubule. The low early proximal ratios are consistent with either significant plasma-protein binding of these tracer amounts or of net reabsorption from the early part of the tubule.

Cardiovascular Responses to Breath Holding in Air and in Water. Albert B. Craig, Jr., Dept. of Physiology, Univ. of Rochester Sch. Med. and Dentistry, Rochester, N. Y.

Bradycardia is a well known response to breath holding (b-h) when the subject is submerged in water. One of the variables involved in b-h is a change in intrapleural pressure which depends upon the lung volume and the degree of expiratory effort. Heart rate responses to the Valsalva maneuver at various pressures were compared with the subject in air and then in water. In air the increase of the heart rate was directly proportional to the change in intrapleural pressure between 0 and +50 cm H_2O, and was independent of lung volume per se. When the subject was in water, there was a decrease of the heart rate when the intrapleural pressure change was between 0 and +15 cm H_2O. At higher pressures the heart rate increased proportionally to the increased intrapleural pressure. The systolic pressure responses to different increases of intrapleural pressure during apnea were also compared in air and in water. In general the decrease in blood pressure which follows the initial rise at the beginning of the b-h was attenuated when the subject was in water. On the other hand the increase of venous pressure in response to b-h at various developed pressures was more prompt when the subject was in water. It is possible that submersion affects predominately the venous side of the circulation.

THE SPEED OF ACTION OF ATROPINE ON SWEATING. F. N. Craig and E. G. Cummings. U.S. Army Edgewood Arsenal Chemical Research and Development Laboratories, Edgewood Arsenal, Maryland.

The influence of intravenously injected atropine sulfate on sweating was measured in three men by continuous recording of body weight. Most of the skin surface was kept dry by air movement at 1.5 meters per second. The sequence of events was: Completion of injection in 1.1 minutes; cardiac acceleration in 1.3 minutes; and inhibition of sweating in 3.5 minutes. The minimum rate of weight loss occurred at a dose of 0.5 milligrams; larger doses prolonged the inhibition without intensifying it. Heat storage was equal to an average of 92 per cent of the deficit in evaporative heat loss. Although sweating returned to the initial rate within an hour, the normal increase in sweating at elevated body temperatures was prevented for the next hour. Sweating responds to atropine almost as rapidly as the cardiac rate. The degree of inhibition is independent of the initial rate of sweating.

Effect of Heparin-induced Lipase on Removal of C^{14}-Chylomicron Triglyceride by Isolated Perfused Rat Heart. M.F. Crass III* and H.C. Meng, Dept. of Physiol. Vanderbilt Univ. Med. School, Nashville, Tenn.

Isolated hearts from fed rats were perfused for varying periods of time with a Krebs-Henseleit bicarbonate buffer (pH 7.4) containing 5% rat serum and 1-C^{14} oleic acid chylomicrons (1.1 mg triglycerides/ml) in the presence or absence of heparin (5 µg/ml). It was found that the perfused hearts readily removed the chylomicron triglyceride. However, heparin accelerated the removal of the chylomicron triglyceride, and increased the incorporation of radioactivity into tissue lipids. After the separation of heart tissue lipids into neutral lipids and phospholipids by batch elution from silicic acid columns, the neutral lipids were further fractionated by thin-layer chromatography; the distribution of radioactivity in the various lipid fractions was studied. Over 90% of the tissue lipid radioactivity was recovered in the combined triglyceride, free fatty acid and phospholipid fractions, while smaller amounts of activity were found in the tissue di-and monoglycerides, cholesterol, and cholesterol ester fractions up to 45 minutes of perfusion. After 30 minutes of perfusion, more than 50% of the tissue lipid radioactivity was recovered as free fatty acid in the heparinized experiments as compared to less than 20% in the non-heparinized controls. Oxidation of the C^{14}-chylomicron triglyceride appeared to lag during the initial 10-15 minutes of perfusion in both heparinized and non-heparinized experiments; however after 30 minutes the heparinized hearts had produced approximately twice as much $C^{14}O_2$ as had the non-heparin controls. The results indicate (1) that triglyceride fatty acids in the form of washed rat thoracic duct chylomicrons are removed and metabolized as an energy source by the perfused rat heart, and (2) that the heparin-induced lipase facilitates the removal and, perhaps, the cellular metabolism of triglyceride.

EVALUATION OF A NEW PULSATILE FLOW EQUATION BY MODEL EXPERIMENTS. G.J. Cropp* and A.C. Burton. Univ. of West. Ont., London, Canada.

Neither the Fick Method nor constant flow equations using reciprocals of mean concentrations are theoretically sound for the measurement of pulsatile flow when the indicator concentration-time curve is sampled just downstream from the injection site. We developed an equation which makes such measurements possible, and modified it for thermal indicators ($\dot{V} = \dot{V}_i \Delta T_i \{1/\Delta T\} - \dot{V}_i$). We recorded pulsatile temperature-time curves, their reciprocals and mean values for both at several distances from the injection site during constant rate infusion of indicator. Flows were calculated by the constant and our pulsatile flow equation and the results were compared with simultaneously collected flows. We expressed distance from the injection site as a fraction of a pulse wavelength. Increasing this distorted the temperature-time curves so that both equations overestimated flow, the overestimate being most marked, and present even at small increases in distance when flows pulsated maximally (+12% error at 60% wavelength for moderate pulsation; +30% error at 30% wavelength for maximal pulsation). The overestimates almost disappeared at 100% wavelength, returned at 120% and gradually vanished at large distances. When measuring flow at 10-20% wavelength by the pulsatile flow equation accurate results are obtained (Mean % error -1.44, $p > 0.1$). The constant flow equation underestimated flow (Mean % error -5.66, $p < 0.02$). The error increased with amplitude of the temperature-time curve from 5% at amplitudes equal to mean ΔT to 7.7% when it was 1.5 times the mean. Records of the reciprocal of ΔT approximated flow profiles recorded simultaneously by an orifice flow meter. (Supported by the Ont. Heart Foundation).

THE SITE OF INHIBITION BY DIGITALIS OF THE ACTIVE INTESTINAL SUGAR TRANSPORT. T. Z. Csáky and Y. Hara*. Dept. of Pharmacology, Univ. of Kentucky College of Medicine, Lexington, Ky.

The mucosal to serosal flux (Fl_{ms}) of 3-O-methylglucose was studied in the isolated small intestine of the bullfrog (Rana Catesbeiana). When ouabain or thevetin (final concentration 10^{-5}M) was added to the compartment bathing the serosal surface there was a marked decrease of the Fl_{ms}. No change of the Fl_{ms} was observed if the ouabain or thevetin was placed in the compartment in contact with the mucosal surface, even if the concentration of the drugs was increased to 10^{-4}M. Digitoxin (10^{-5}M) inhibited to Fl_{ms} if added to either mucosal or serosal compartments. Digitoxin itself however was found to be rapidly transported across the intestinal wall whereas no transport could be shown for ouabain. It is concluded that the site of the inhibition of the active sugar transport by the cardioactive steroids is the serosal facing membrane. This membrane is probably the site of the sodium pump whereas the sugar pump has been previously localized in the mucosal facing membrane. The various explanations for the relationship between the active intestinal transport of sodium and that of sugar are discussed in the light of the present results. (Supported by grants from the NIH.)

SOME EFFECTS ON TEMPERATURE INSENSITIVE NEURONS IN THE PREOPTIC AREA OF THE DOG. D. Cunningham*, J.A.J. Stolwijk and J. D. Hardy. John B. Pierce Foundation Laboratory, and Department of Physiology, Yale University, School of Medicine, New Haven, Conn.

Microelectrode recordings were obtained from hypothalamic neurons within the preoptic area in dogs maintained under urethane/chloralose anesthesia. Thermodes implanted contralaterally permitted control of hypothalamic temperature within a range of 2°C above or below normal. In this area some of the neurons have been observed to alter their firing rate when the local temperature is changed while many are not affected in their firing rate by temperature. In the present study, the effects of certain agents upon the firing rate of single neurons, as well as upon hypothalamic temperature, have been investigated. Significant short term changes in firing rate were recorded immediately following the intravenous administration of epinephrine and serotonin. Single neuron recordings from this same area have also demonstrated an appreciable increase in firing rate under conditions of induced hypoxia, prior to the abrupt reduction in neuronal firing rate characteristic of the terminal stages of activity. (This investigation was supported by U. S. Public Health Service Research Grant NB 04655).

LETHAL AND DEBILITATING PROPERTIES OF SUBCELLULAR PARTICLES OF A TRANSPLANTABLE RAT TUMOR. J. Dabney, W. Palmer and J. Spath (Intr. by M. J. Keyl). University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

During studies on the induction of immunological tolerance in the King rat to the Murphy-Sturm lymphosarcoma, it was found that a cell free or lyophilized preparation of this tumor will cause the death of over 90% of 2-5 day-old rats when small amounts of the material (5-7 mg dry wt.) is injected intraperitoneally. Death occurs in 1 to 3 days with no gross evidence of tumor growth, but the intestine is discolored and fluid accumulates in the abdominal cavity. Penicillin prevents these early deaths but animals protected by penicillin and animals that survive without penicillin are all severely retarded in growth. However, if tumor material is injected subcutaneously death rarely results but invariably growth is slowed and the animal is in poor health. As with an intraperitoneal injection, a local damaging of tissue occurs and the skin over the area of injection usually sloughs. Penicillin gives no protection against the depressed growth or local tissue damage. Differential centrifugation has shown that the lethal and stunting property of the tumor is associated with mitochondria and microsomes. The supernatant from centrifugation at 35, 000 G for 2 hours or 100,000 G for 1 hour causes no deaths or stunting. A single injection of tumor microsomes and mitochondria (126 mg wet wt.) subcutaneously into 21-23 day-old rats results in retarded growth. This stunting becomes evident after a few days and disappears after 30-40 days. Spontaneous food intake is also reduced. However, preliminary studies show that these tumor-injected rats gain less weight than do normal controls even when the two groups are pair fed. These studies demonstrate that subcellular particles from a transplantable tumor may have lethal or long lasting metabolic effects which are independent of the growth of a new tumor.

MODIFICATION OF RESPIRATORY BEHAVIOR BY HYPNOSIS. Walter J. Daly*, Toner M. Overley* and Joseph C. Ross. Indiana University School of Medicine, Indianapolis, Indiana.

The participation of cerebral factors in the regulation of breathing in man are undoubted, yet there are few quantitative expressions of this relationship. In this study, normal men were hypnotized by a technique essentially that described in the Stanford Hypnotic Susceptibility Scale, Form A. Minute ventilation ($\dot{V}$), end-tidal pCO_2, and ventilatory response to 5% and 7% CO_2 (10 minute exposure) were determined in 6 normal supine subjects awake and then after hypnotic suggestion that all sensations were pleasant. $\dot{V}$ and end-tidal pCO_2 were also measured in 5 normal subjects sitting on a bicycle ergometer at rest and during exercise (1000 ml O_2/min) awake and after hypnotic suggestion that exercise was effortless. Hypnosis decreased mean resting $\dot{V}$ from 9.37±1.33 to 7.24±0.69 L/min ($p=0.025$) and increased end-tidal pCO_2 from 38±2 to 42±3 mm Hg ($p=0.025$). During 5% CO_2 breathing, hypnosis decreased $\dot{V}$ from 22.89±4.07 to 18.33±4.43 L/min ($p=0.01$) and increased end-tidal pCO_2 from 46±2 to 51±4 mm Hg ($p=0.01$). During 7% CO_2 breathing, hypnosis decreased $\dot{V}$ from 51.39±12.27 to 35.67±12.55 L/min ($p=0.05$) and increased end-tidal pCO_2 from 53±2 to 56±3 mm Hg, ($p=0.05$). After hypnotic suggestion that exercise was effortless, $\dot{V}$ during exercise was less, 17.56±1.65 L/min, than during the same exercise awake, 23.08±4.53 L/min ($p=0.05$) and end-tidal pCO_2 was greater, 48±5 mm Hg, than during the same exercise awake, 40±3 mm Hg ($p=0.05$). It is suggested that the normal responsiveness of the respiratory center is set in a background of continuous cerebral influence, that hypnosis affects this relationship and can be used as a tool to study changes in the responsiveness of the respiratory mechanism to conventional stimuli.

THE RELATIONSHIP BETWEEN AMBIENT PRESSURE AND THE TOLERANCE OF MICE TO AIR BLAST[1,2]

Edward G. Damon, Donald R. Richmond, and Clayton S. White (intr. by M. L. Riedesel), Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico.

Mice were exposed to overpressures of "long" duration in the expansion chamber of an air-driven shock tube inside which the initial, pre-blast pressures were varied over six-fold. When the animals were held at the initial pressure for one hour following the blast before being returned to the ambient pressure of the laboratory, tolerance values, expressed as LD_{50}-1-hour gauge pressures, increased four-fold; they were 20.3, 31.0, 44.5, 55.4, and 91.8 psi for initial pressures of 7, 12, 18, 24, and 42 psia, respectively. When animals were returned to ambient level soon after blast exposure, the LD_{50} pressures were lower than the above values for initial pressures greater than ambient and higher for initial pressures lower than ambient. The feasibility of scaling biological blast effects as a function of altitude is discussed and one approach suggested by available empirical data is regarded as a promising but tentative procedure.

[1] Supported by Department of Defense, Contract DA-49-146-XZ-055.

[2] Taken in part from a Ph. D. dissertation to be submitted by Edward G. Damon to the University of New Mexico.

Renal Function in the Fresh-water turtle, Pseudemys scripta, and the Desert Tortoise, Gopherus agassizii. William H. Dantzler* and Bodil Schmidt-Nielsen. Dept. of Zool., Duke Univ., Durham, N. C.

Lower vertebrates cannot make urine hyperosmotic to blood. The urinary system responds to changes in blood osmolality on three levels: 1) glomerular, 2) tubular and 3) bladder or cloaca. The present study shows how these regulations are geared to habitat. Pseudemys is amphibious and, as in the frog, urea is the major nitrogenous waste product. Both glomerular and tubular responses are pronounced in Pseudemys and resemble those of the frog. During water-loading, glomerular filtration rate (GFR) increased. During dehydration or salt-loading, GFR decreased with increasing blood osmolality and ceased when blood osmolality rose 20 mOsm. Tubular response usually preceded glomerular. Osmolar U/P varied from 0.3 in extreme water diuresis to 1.0 during osmotic load or dehydration. Creatinine U/P varied from about 2 to 10. A small dose of pituitary extract gave a predominantly tubular response while a large dose gave a strong glomerular response. Gopherus is terrestrial and has only occasional access to free water. Uric acid is its major nitrogenous waste product. In contrast to Pseudemys, the tubular response was virtually absent while the glomerular response was present but less sensitive. Thus, the distal tubule appears to be insensitive to ADH. Normal GFR was the same as in Pseudemys and increased similarly with water load. It decreased with salt load but ceased only when blood osmolality rose 100 mOsm. For ureteral urine osmolar U/P varied from 0.3 to 0.7 and creatinine U/P from about 2 to 4 regardless of state of hydration. The bladder in Gopherus plays an important role in urine composition. Urine can by-pass the bladder and be excreted hypoosmotic to blood in water diuresis. During dehydration or salt-loading, urine enters the bladder where it becomes isosmotic and uric acid precipitates. (NIH Grant AMO-1956 and Fellowship 5-F2-GM-16, 117-02).

EFFECT OF SEROTONIN, EPINEPHRINE, LEVARTERENOL AND ANGIOTENSIN ON SUPERFICIAL AND DEEP VENOUS OUTFLOW IN THE DOG FORELIMB. Robert Daugherty* and Francis J. Haddy. Univ. of Okla. Med. Center, Okla. City, Okla.

Anatomically, the cephalic vein is predominantly distributed to skin while the brachial vein is mainly distributed to muscle. Outflow from these two veins was measured (graduates) during intra-brachial infusion of epinephrine, levarterenol, and angiotensin (0.05 to 2.0 ug/min) and of serotonin creatinine sulfate (10 to 400 ug/min). All collaterals except those in bone were tied. Outflow from both veins decreased as a function of infusion rate with the former three agents. With epinephrine, the rate of decrease was greater in the cephalic vein. Brachial outflow increased as a function of the infusion rate of serotonin. Cephalic outflow, after a slight increase at 10 ug/min, decreased as a function of serotonin infusion. At the higher infusion rates, cephalic outflow was well below control while brachial outflow was well above control. Occlusion of the cephalic vein raised cephalic venous pressure to 37.3 mm Hg and 66% of its flow appeared in the brachial outflow. Occlusion of the brachial vein raised brachial venous pressure to 51.6 mm Hg and 56% of its flow appeared in the cephalic outflow. Following release of arterial occlusion (1 min), brachial and cephalic outflows transiently rose to 179 and 121% of the control values, respectively. When brachial arterial inflow was set constant with a pump, levarterenol and angiotensin had little effect upon cephalic or brachial outflow. Cephalic outflow decreased slightly and brachial outflow increased slightly as a function of the infusion rate of epinephrine. Cephalic outflow decreased greatly and brachial outflow increased greatly as a function of the infusion rate of serotonin over the range 0 to 40 ug/min. These studies show that at natural flow, intrabrachial infusions of epinephrine, levarterenol and angiotensin decrease both superficial and deep venous outflow while serotonin decreases superficial and increases deep venous outflow.

THE VARIABILITY OF EVOKED RESPONSES

Hallowell Davis and Stanley Zerlin*
Central Institute for the Deaf, St. Louis, Missouri

The amplitude of the slow non-specific evoked response of the human cortex, recorded from vertex to mastoid, varies widely across subjects. The individual responses are usually so small that they cannot be distinguished in the raw EEG record, but one of our subjects produced responses large enough to be measured individually. The variation of amplitude of her individual responses is very wide, the largest being three to four times greater than the smallest within a given series of similar stimuli. The distribution is apparently gaussian. Calculation of the autocorrelation of response amplitudes reveals no tendency to cyclic variation. The standard deviation varies with the mean: therefore the variance is not due primarily to the "noise" of the EEG background on which the responses are superimposed. A smaller average response, whether due to reduction of the intensity of the stimulus or to shorter recovery time between the stimuli, represents a shift of the entire distribution toward smaller amplitudes and not simply a less frequent occurrence of large responses. These conclusions are confirmed by a study in other subjects of the variability of averaged responses to blocks of 16 or 32 similar stimuli. (NINDB Grant B-3856).

DECREASED ALDOSTERONE METABOLISM FOLLOWING ACUTE HEMORRHAGE.

J. O. Davis, M. J. Olichney* and T. C. Brown*. Natl. Insts. of Health, Bethesda, Md.

The rates of metabolism of aldosterone were studied in 7 normal dogs and in 9 dogs subjected to acute blood loss (30 cc/kg); all animals were anesthetized. Following hemorrhage, 20-30 min. were allowed for arterial pressure to return toward normal and to stabilize. H^3-d-aldosterone was injected intravenously and the rate of disappearance of true aldosterone from peripheral plasma was measured during the next 90 min. Two exponential components were present in the disappearance curves and the data were analyzed in terms of a two compartmental system. The biological half-life ($T_{1/2}$) from the slow component of the disappearance curve was 30 min. for the normal dogs; $T_{1/2}$ was prolonged to 55 min. after acute blood loss. The fractional turnover rates of aldosterone were markedly decreased following hemorrhage but the volumes of distribution for both compartments 1 and 2 were not altered appreciably by hemorrhage. The metabolic clearance rate of aldosterone from plasma was decreased from 832 to 453 cc/min by hemorrhage. The hepatic extraction of aldosterone was almost complete (90-100%) in one circulation through the liver for both normal and bled animals. It is concluded that decreased aldosterone metabolism contributes to the hyperaldosteronemia which follows acute blood loss.

EFFECT OF K^+ ON THE POTENTIAL DIFFERENCE OF THE FROG'S STOMACH IN Cl^- AND Cl^- - FREE BATHING SOLUTIONS. T. L. Davis*, J. R. Rutledge*, and W. S. Rehm. University of Louisville, Louisville, Kentucky.

Gastric mucosae were mounted between chambers with either Cl^- or Cl^- - free ($SO_4^=$) bathing solutions. A cation balanced, bicarbonate (25 mM) solution was used on the nutrient side. The control secretory solution contained Na^+ 100 mM, K^+ 4 mM and either Cl^- 104 mM or $SO_4^=$ 52 mM with sucrose making up the osmotic deficit. Experimental solutions with the $[K^+]$ between 10 and 100 mM (K^+ substituted for Na^+) were alternated with control solutions (K^+ 4 mM) on either the nutrient or the secretory side of the mucosa or the $[K^+]$ was increased stepwise from 4 to 100 mM. The PD was measured (positive means the nutrient is positive and vice versa). In Cl^- solutions the PD decreased as the $[K^+]$ on the nutrient side of the mucosa was increased. The slope was slightly greater than one-half that predicted by the Nernst equation, confirming Harris and Edelman (A.J.P. 206:769, 1964). Increasing the $[K^+]$ from 4 to 52 mM on the secretory side in Cl^- solutions gave an average decrease in the PD of 3.1 mv (range 0.5 mv increase to 7.0 mv decrease). This agrees with the findings of Harris and Edelman. However, increasing the K^+ from 52 to 100 mM decreased the PD an average of 8.3 mv (range 5.0 to 12.5 mv), suggesting that the secretory side is more permeable to Na^+ than K^+ under these conditions. In Cl^- - free preparations increasing the $[K^+]$ on the nutrient side gave a slope of -24.6 (SD± 9.6) while increasing the K^+ on the secretory side gave a slope of +24.6 (SD± 6.2). In Cl^- and Cl^- - free solutions, the nutrient membrane is more permeable to K^+ than to Na^+. In Cl^- solutions the secretory membrane is more permeable to Na^+ than to K^+ which in Cl^- - free solutions the secretory membrane is more permeable to K^+ than to Na^+. (NSF and NIH support)

EFFECTS OF PITRESSIN ON MESENTERIC CAPILLARY BLOOD FLOW. J. P. Delaney*, R. L. Goodale*, J. Cheng*, O. H. Wangensteen
University of Minnesota Medical School, Minneapolis, Minnesota

The purpose of this study was to assess the influence of pitressin on tissue blood flow in the esophagus, duodenum, pancreas, gastric antrum and gastric corpus of the dog. Preliminary experiments involving direct venous collection established that the radioisotope distribution method (K^{42} or Rb^{86}) was valid for measurement of blood flow to stomach and duodenum. Thirteen animals received no drug and served as a control group, while five were given intravenous pitressin (.01 pressor u/kg-min x 10 min). A small bolus of K^{42} or Rb^{86} was injected into the vena cava, an arterial isotope dilution curve obtained for calculation of cardiac output, and the dog sacrificed 30 to 35 seconds later. The organs were removed and analyzed for isotope content. Tissue blood flow was calculated by multiplying the fraction of the total isotope contained in each tissue times the cardiac output. A 35% decrease in cardiac output was seen in the pitressin group. Capillary blood flow reductions under the influence of the drug were: Gastric fundus -70%, gastric antrum -50%, pancreas -83%, duodenum -43% and esophagus -65%. Thus, pitressin caused a marked increase in vascular resistance and decrease in capillary perfusion of these organs. The blood flow reduction was of such a magnitude as to account completely for the decrease in portal vein pressure. The drug may be of value in any situation where reduction in gastrointestinal blood flow is desirable.

Supported by USPHS Grant, Hartford Foundation and D. J. Cowling Grant.

HEPATIC GLUTAMIC DEHYDROGENASE ACTIVITY IN FETAL AND POSTNATAL RATS
Louis F. DeWein, M.Sc. and Margaret T. Nishikawara, Ph.D.
Ohio State University, Columbus, Ohio

The activities of many hepatic enzymes show remarkable changes in the transition from the fetal to the postnatal state. Many of the enzymes investigated are concerned with amino acid metabolism. Hepatic glutamic dehydrogenase (GDH) activity in 18 and 20 day fetal rats and 1, 3, 7, 14, 21, and 28 day postnatal rats was investigated. GDH activity was measured in sonicated 900g supernatants by the reduction of NAD at 340 Mm. In fetal rats the hepatic GDH activity was 1/3 or less than that found in normal adult rats. Twenty-four hours after birth this activity had increased to the adult level. Thereafter a slow rise above the adult level occurred. (Supported by USPHS Grant AM-07265-02 from the National Institute of Arthritis and Metabolic Diseases.)

PERIPHERAL VENOUS RESPONSE TO PHENOXYBENZAMINE INFUSION IN THE ISOLATED HINDLIMB OF THE DOG. John N. Diana*, Ronald R. Masden*, and James C. Moore. Dept. of Physiol. and Biophysics, Univ. of Louisville School of Medicine, Louisville, Kentucky.

Following a control period, isolated dog hindlimb preparations were perfused with blood containing phenoxybenzamine (Dibenzylene) in such concentrations that from 0.05 to 0.1 mg/kg/min passed through the leg. Continuous measurements of peripheral venous pressure (digital vein), muscle venous pressure (small vein draining the muscles of the thigh), arterial pressure, and leg weight were made under conditions of constant arterial inflow. Central venous pressure (outflow pressure) was maintained at 7 mm Hg. Venous outflow was measured either continuously with a flowmeter or intermittently by collecting samples every 20 seconds. Phenoxybenzamine infusion resulted in a brief increase in digital peripheral venous pressure associated with decreases in peripheral venous pressure (muscle) and arterial pressure. At the same time, leg weight increased and venous outflow decreased. After this initial pressor response, peripheral venous pressure (muscle), arterial pressure, leg weight and venous outflow remained constant while peripheral venous pressure in the digital vein increased markedly. The secondary rise in digital peripheral venous pressure was eliminated by close arterial injection of diphenhydramine hydrochloride (Benadryl) prior to infusion of phenoxybenzamine. These studies suggest that intra-arterial infusion of phenoxybenzamine causes the release of endogenous histamine from the tissue being drained by the superficial digital vein. (Supported by USPHS Grant HE-07577-02)

DYNAMICS OF STRESS RELAXATION IN SMOOTH MUSCLE. J. C. Dill* and R. W. Stacy. North Carolina State of the University of North Carolina at Raleigh, North Carolina.

Based on a two-state kinetic theory previously derived in an integrated form, a new set of differential equations has been written to describe stress relaxation and stress potential recovery. The new theory permits the prediction of tension behavior of smooth muscle in any sequence of length variations. It also permits easier derivation of significant physical parameters of the muscle. Comparison of theoretically predicted time dependency with experimental behavior has been excellent. Such comparisons have been made with arterial, uterine, and intestinal smooth muscle specimens.

THE INFLUENCE OF RESTRAINT STRESS ON THE DEVELOPMENT OF THE ETHANOL-INDUCED FATTY LIVER AND GASTRIC ULCERATION. N. R. Di Luzio and J. P. Quigley, Dept. Physiol. and Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

Previous studies have amply demonstrated the induction of a fatty liver due to the acute administration of ethanol to normal rats. One postulated hypothesis has been the induction of stressful state via the stimulation of the pituitary-adreno-cortical system by alcohol. In an effort to evaluate this hypothesis, acute ethanol-treated and isocaloric glucose-treated rats were subjected to the stress of restraint by the Hanson and Brodie technique and liver and plasma triglycerides determined 24 hours later. Similarly treated, non-restraint groups served as controls. Ethanol induced a 185% increase in liver triglyceride in the non-restraint group; plasma triglycerides were unaltered. A similar finding was observed in the ethanol-treated restrained rats. Liver and plasma triglycerides were unchanged in either of the glucose-treated groups. Histological evidence, in agreement with Brodie's and Hanson's observations, denoted gastric ulceration in the glucose-treated restrained rats. The administration of ethanol greatly enhanced gastric ulceration in the restrained rats. These studies denote that the addition of a stressful situation during the development of the ethanol-induced fatty liver does not produce an intensification of the hepatic lesion, but does enhance the degree of gastric ulceration. (Supported in part by, USPHS grant AM-08084, and the Licensed Beverage Industries).

RESPONSE OF CAROTID CHEMORECEPTORS TO TRANSIENT PERFUSION OF ACIDIFIED BLOOD. Dario B. Domizi* and John F. Perkins, Jr. Dept. of Physiology, Univ. of Chicago, Chicago, Ill.

Breath-by-breath respiratory minute volume was measured during transient infusion of blood of varying composition into the common carotid arteries of anesthetized dogs, using the technique described by Fitzgerald, et al. for measuring respiratory chemosensitivity of the carotid bodies (The Physiologist, Vol.5, No.3, 1962). Ventilatory responses to infusion of acidified, normocapnic blood were essentially as prompt as those to hypercapnic blood or to cyanide, usually beginning with the first breath after start of the infusion, and becoming maximal within 10-15 seconds. Conversely, alkaline, mildly hypercapnic blood depressed respiration. Thus, acid as such promptly stimulated the carotid chemoreceptors. These findings suggest the possibility of a surface receptor for acid. Hypercapnic, isohydric blood also produced a marked response, suggesting that carbon dioxide had an effect independent of its blood acidifying ability, or acted as an acid at a different site than acidified, normocapnic blood. (Supported by USPHS research grant HE-05516-04.)

TECHNIQUE FOR THE PERFUSION OF ISOLATED RAT SPLEEN. Burton Dornfest* and Sam J. Piliero. New York Med. College, New York.

A technique has been developed for the perfusion of the isolated rat spleen to permit the study of the spleen's role in maintaining peripheral blood cell levels. A peristaltic action-type perfusion pump, with an apparatus designed to circulate a small volume of perfusate, was employed to perfuse leucocyte-intact (8-12,000/mm^3) and leucocyte-depleted (1-400/mm^3) isologous blood through the spleen at a rate of 0.1 to 0.4 ml./min. Polyethylene cannulas were placed in the splenic artery and vein with the spleen isolated using a one hour procedure, during which time the spleen was sustained by the rat's own circulation. Each spleen was perfused for periods of from 2 to 4 hours during which time oxygen utilization was evidenced by a demonstable arterial-venous difference in the coloration of blood in the splenic artery and vein. That each spleen was maintained in physiological condition was also indicated by the utilization of glucose, the ability to respond to various agents such as adrenalin and the examination of histological sections. Leucocytes, predominantly lymphocytes, were discharged from the spleen into leucocyte-depleted but not leucocyte-intact blood perfusates. The number of mature erythrocytes and reticulocytes released by the spleen was not correlated to the initial number of leucocytes in the perfusates.

INFLUENCES OF MECHANICAL DIASTOLIC TIME ON SYSTOLIC FORCE. R. Doughty,* J. Citron,* C. E. Schott,* and G. N. French. Misericordia Hospital, Philadelphia, Pennsylvania.

It is recognized that early extrasystoles may be followed by contractions more forcible than those of the maintained rate, in some direct relation to the degree of prematurity. Also, there is a non-linear direct relation of diastolic interval to force of the succeeding contraction. Blinks has suggested that these and the "Treppe" phenomenon may be understood in terms of two independent influences, one augmentary, the other inhibitory. Studies reported here delineate these occurrences in further detail, using the papillary muscle of the cat, under isometric conditions. Results confirm previously recognized findings, and add the changes seen in more complex stimulus presentation patterns. A hypothesis is suggested which eliminates the role of an "inhibitory" influence.

LEFT VENTRICULAR FUNCTION IN THE NEWBORN LAMB. S. Evans Downing, Thomas H. Gardner*, and Norman S. Talner*. Depts. Path. & Ped. Yale Univ. School of Med., New Haven, Connecticut.

Detailed evaluation of the performance characteristics of the newborn heart have not been made. The present study was initiated with the objective of evaluating in the newborn those aspects of ventricular mechanics which form the basis of the Frank-Starling relation, and which permit a determination of changes in the inotropic state of the heart. Left ventricular function was studied in lambs, 12 hrs. to 5 days old, utilizing a preparation designed to permit control and measurement of systemic arterial pressure (AP), cardiac output, heart rate (HR) and temperature. Continuous measurements of arterial P_{O_2} and pH were made. These data permitted the construction of ventricular function curves relating stroke volume (SV), mean ejection rate, and stroke work and power to left ventricular end-diastolic pressure (LVEDP), at constant AP and HR. In all preparations the Frank-Starling relation was found to be operative. Norepinephrine (NE) infusion, 1-2 ug/kg/min, resulted in a substantial increment of both force and speed parameters, thereby demonstrating the ability of the newborn heart to alter its inotropic state. It is concluded that 1) the output of the left ventricle of the newborn is dependent upon the venous return to that chamber; 2) SV is a direct function of LVEDP and the contractile state of the myocardium; 3) the observation that myocardial contractility is increased as a consequence of NE administration suggests that autonomic control of ventricular function, mediated through the sympathetic nervous system, may be operative in the newborn. (Supported by USPHS grants #HE-7035 and HE-8659.)

Coronary Inflow and Outflow Responses to Coronary Artery Occlusion. Thomas E. Driscol* and Richard W. Eckstein. Western Reserve University, Cleveland, Ohio.

Experiments were designed to characterize and explain the usual rise in coronary inflow following occlusion of a major adjacent artery. It was considered that the rise in inflow might be secondary to 1) flow through collaterals into the ischemic muscle, 2) dilatation of a border zone by diffusable metabolites from the ischemic muscle, or 3) increased oxygen requirement due to a greater work load imposed on the non-ischemic muscle. The left anterior descendens artery was cannulated and perfused from a constant pressure chamber through a Shipley-Wilson rotameter. Polyethylene snare loops were placed about the origins of the left circumflex and right coronary arteries. A clamp on the thoracic aorta was used to maintain blood pressure constant. The great cardiac vein which drained the muscle supplied by the descendens artery was cannulated and its outflow drawn through a Gilford cuvette oximeter calibrated frequently by the Scholander blood oxygen method. Venous flow was measured by timed collections at atmospheric pressure. Circumflex occlusion for 20, 40, and 60 sec. caused 12.2, 14.9, and 18.2% increases in descendens inflow. The inflow rise was gradual and did not return promptly to control value after release of occlusion. Right coronary occlusion (30 sec.) caused no significant change in descendens inflow, outflow, or venous O_2 content. Coronary venous flow increased 20.2% (average) and venous O_2 content decreased (0.9-1.5 vol. %) after 30 sec. circumflex occlusion. Inflow responses to alterations in descendens perfusion pressure were compared to the accompanying venous O_2 change. These findings indicate the increased work load on the non-ischemic muscle of the left ventricle is the most likely explanation for the rise in flow seen after circumflex occlusion.

STUDIES ON THE PHYSIOLOGY OF VASOPRESSIN, (1) ULTRA-SENSITIVE BIOASSAY OF VASOPRESSIN. **Willard M. Duff*, Edward H. Grinnell* and Jeno Kramar. Creighton Medical School, Omaha, Nebraska**

In the wake of recent improvements by Dicker (1953), Thorn (1958) and Heller (1959) of the intravenous vasopressin rat bioassay method originally suggested by Jeffers, Livezey and Austin (1942), the procedure was further refined. A twenty fold increase in sensitivity over pre-existing methods was achieved. White female rats (120-130 gm) previously prepared with ureteral fistula, are anesthesized and rendered diuretic by intragastric 12% ethanol. After cannulation of the tail artery the animal is placed on a balance in a manner allowing direct urine collection from the fistula. A constant fluid equilibrium is maintained by 1% ethanol through an indwelling gastric catheter. When urine flow becomes constant (0.08 to 0.12 cc/minute) a 10 minute pre-injection sample is collected. Regular 2 minute samples are taken after the injection. Using the pre-injection sample as base line, the total per cent change in the chloride concentration is determined. A numerical straight line relationship exists between these changes and the vasopressin dose. Using this method as little as 5 millimicrounits of arginine-8-vasopressin can routinely be measured. Two factors seem to contribute to the high sensitivity of the described procedure: (1) the young age and consequently smaller blood volume of assay animals and (2) the sampling of urine in frequent short intervals. Adaptation of this method for the determination of vasopressin in plasma is in progress.

ERUCTATION, REGURGITATION AND RETICULORUMEN CONTRACTION PATTERNS IN BISON. Harold E. Dziuk (intr. by A. L. Good). College of Veterinary Med., Univ. of Minn., St. Paul

This study was done to obtain information about forestomach motility in bison and to compare the data with those for cattle and deer. Pressure changes in four compartments of the reticulorumen of two young bison with rumen fistulas were simultaneously recorded during eating, ruminating, resting and nitrogen gas insufflation into the rumen. Results indicated that reticulorumen contraction patterns were very similar to those previously reported for domestic cattle. Eructation occurred almost always during contraction of the posterior dorsal blind and dorsal sacs of the rumen. Eructation frequency was nearly the same as that reported previously for cattle and white-tailed deer. Regurgitation always occurred at the time of an extra reticular contraction.

TRYPTOPHAN PYRROLASE ACTIVITY IN ENDOINTOXICATED MICE EXPOSED TO COLD. George N. Eaves* and L. Joe Berry, Bryn Mawr College, Bryn Mawr, Pa.

In a previous report from this laboratory it was demonstrated that the apoenzyme moiety of tryptophan pyrrolase (TP), the inducible enzyme of liver, was depressed following injection of mice with crude endotoxin derived from Salmonella typhimurium (Fed. Proceedings, 23, 2771, 1964). It was the purpose of this study to investigate the induced enzyme response in endointoxicated mice kept in an environment which stimulates TP induction. TP is induced rapidly following exposure of mice to cold alone. In endointoxicated mice exposed to 5°C during the post injection period enzyme induction is delayed but not impaired. At the end of six hours both endointoxicated and control mice have TP activity equivalent to twice the normal value. In a 25°C environment, endotoxin prevents the maximum induction of TP by cortisone; however, in a 5°C environment the cortisone-mediated induction is delayed but not inhibited by endotoxin given concurrently. While the evidence obtained from studies on mice kept at 25°C associates the lethal effects of endotoxin with impaired protein catabolism, it would appear that the toxic manifestations of endotoxin are different in animals stressed by cold. (Supported by Training Grant 2E-148).

FOREARM VENOUS RESPONSES TO STIMULATION OF ADRENERGIC RECEPTORS. John W. Eckstein, Michael G. Wendling,* Francois M. Abboud, C.V. Res. Labs., Univ. of Iowa Coll. of Med., Iowa City, Iowa.

Systemic administration of isoproterenol, a substance which stimulates beta or vasodilator receptors in arteries, causes venoconstriction. These experiments were done to study the direct action of isoproterenol on veins. Venous tone was measured in the left forearm with a plethysmograph and expressed as venous volume existing at a transmural venous pressure of 30 mm Hg (VV_{30}). An increase in VV_{30} indicates venodilatation; a decrease indicates venoconstriction. Blood flow was estimated from the rate of change in forearm volume. Two doses of isoproterenol were infused into the left brachial artery in each of 13 subjects. Flow increased with each infusion but VV_{30} remained unchanged ($P > 0.8$). Infusions were repeated in four subjects after intrabrachial administration of nethalide, a beta receptor blocker, and phentolamine, an alpha blocker. Nethalide blocked the flow response, but neither antagonist altered VV_{30}. In four subjects intrabrachial infusion of isoproterenol, in the presence of forearm venoconstriction induced by systemic administration of norepinephrine, caused increases in flow but no venodilatation. In five subjects intrabrachial infusions of epinephrine decreased VV_{30}. Phentolamine blocked this venoconstriction but nethalide had no effect. Six subjects received isoproterenol, 5.8 µg/min, systemically. This caused venoconstriction which was blocked by intrabrachial administration of phentolamine. We conclude that stimulation of beta receptors in the forearm has no significant effect on venous tone while stimulation of alpha receptors causes venoconstriction. Forearm venous constriction occurring with systemic infusions of isoproterenol must be of reflex origin and mediated through alpha receptors.

A COMPARISON BETWEEN RYANODINE AND DINITROPHENOL ON THE OXYGEN CONSUMPTION IN FROG MUSCLE FOLLOWING THE USE OF HIGH ENERGY PHOSPHATE COMPOUNDS. Leslie E. Edwards and Anne C. Brehme*. Department of Physiology, Medical College of Virginia, Richmond, Virginia.

In metabolic studies both ryanodine and dinitrophenol increase the oxygen consumption of muscle and the question arises do they both stimulate through the same mechanisms. High energy phosphate compounds are involved in the control of oxygen utilization in muscle, therefore it seems important to compare their effects on the oxygen consumption of ryanodine and dinitrophenol-treated muscles. Oxygen consumptions of paired sartorious muscles were measured in the standard Warburg apparatus. The high energy phosphate compounds were allowed to equilibrate overnight with the muscle. Ryanodine and dinitrophenol were added from the sidearm after a control period of one hour. All high energy compounds tried enhance the oxygen consumption of both ryanodine and dinitrophenol-treated muscles. In ryanodine-treated muscles, the maximum rates and the shortest latent periods were obtained after equilibration with creatine phosphate; adenosine diphosphate was next in response and adenosine triphosphate last. In dinitrophenol-treated muscles the maximum rates were obtained after equilibration with adenosine triphosphate. Creatine phosphate gave the next greatest response and adenosine diphosphate the least. These data suggest that ryanodine affects the use of high energy compounds in a different manner than does dinitrophenol. (Supported by NIH Grant AM 06252)

ANALYSIS OF AMYGDALOID SPINDLING[1]. E. Eidelberg[2] and H. M. Neer*. Barrow Neurol. Inst. and Ariz. St. Univ., Phoenix, Ariz.

Amygdaloid spindling is characterized by high-amplitude (up to 2-3 mV), fast (35-50 c/s) waxing and waning discharge recorded from basolateral amygdala, pyriform and pre-pyriform cortex. Similar activity is also recorded from olfactory bulb. Spectral and phase analysis of this activity, by means of analog devices, reveals a large, broad, spectral peak centering at or near 40 c/s. It also indicates close coupling between amygdaloid and pyriform activity in the 40 c/s band, but loose, or no coupling at all, at other frequencies or between the amygdala and the olfactory bulb. There is no consistent relationship between right and left amygdaloid or pyriform spindling. There is no apparent relationship between amygdaloid spindling and thoracic respiration. The effects of some psychoactive agents, which affect rather selectively amygdaloid spindling, will be demonstrated.

1 Supported by USPHS Grant B-3496

2 USPHS Research Career Program Award NB-K3-15, 437

LEARNING IN A SINGLE INSECT GANGLION. E. M. Eisenstein and M. J. Cohen*. Department of Biology, University of Oregon, Eugene, Oregon.

The capacity of the prothoracic ganglion to learn was investigated in 106 adult male cockroaches (Periplaneta americana). The head was removed and the posterior connectives of the prothoracic ganglion were cut. This procedure isolates the prothoracic ganglion from the rest of the CNS, but leaves the sensory and motor nerves to the prothoracic legs intact. A training procedure similar to that employed by Horridge was used. The left prothoracic legs of two animals were connected in series so that when one member of the pair, the "A" animal, extended its leg, a lead attached to its tarsus entered a saline bath to close a circuit and shock both animals. The shock was terminated only when the "A" animal lifted its leg out of contact with the saline. The "A" animal of the pair was thus consistently shocked only when its leg was in an extended position. The other member of the pair, the "B" animal, received shock whenever the "A" animal did, but there was no consistent relationship between its leg position and shock. Following a 45 minute training period, both animals were reconnected for testing so that each could now shock itself independently of the other by extending its own leg. During testing the "A" group held their legs out of the saline for longer periods than the "B" group and therefore took less shocks ($p < 0.05$). Since both groups received the same number of shocks during training, the difference between the "A" and "B" groups during testing indicates that the "A" group learned to make a specific association between leg extension and shock in the training period. The avoidance response could be achieved by a number of different leg positions and appeared to be maintained by proprioceptive feedback. The results indicate that learning can occur in a single insect ganglion that is isolated from the rest of the CNS.

FACTORS AFFECTING THE RESPONSE OF THE SUPERIOR COLLICULUS TO ELECTRICAL STIMULATION OF THE VISUAL PATHWAY. O.T.Ellsworth and S.G. Pickering (intr. by W.J. Freeman) University of California, Berkeley, California.

Modification of wave forms of collicular evoked potentials averaged by the Mnemotron 400A were observed with changes in recording site, stimulus site, stimulus intensity, repetition rate and level of anesthesia. In acute experiments under pentobarbital anesthesia, evoked potentials were recorded from the surface of the exposed superior colliculus (SC) in response to stimulation of optic fibers near the anterior margin of SC. In chronic experiments, stimulating electrodes were placed in the optic nerves immediately distal to the optic chiasm as located in radiographs of the cat's skull. Recording electrodes were passed through SC by means of a new miniature stereotaxic instrument. The instrument attached to a small circular platform permanently attached to the cats calvarium in a known stereotaxic orientation, for electrode penetration during either anesthetized or unrestrained states. In the acute studies, stimulation of fibers entering SC evoked short latency negative-positive diphasic responses in some areas of the collicular surface and concomitant pos.-neg. responses in other areas. In the chronic experiments, stimulation of the contralateral optic nerve evoked longer latency neg.-pos. responses in the superficial layers of SC and pos.-neg. responses in the deeper layers as described by G. H. Bishop and co-workers. In addition, a series of high-frequency deflections preceding the main diphasic response was observed in conscious and lightly anesthetized cats, but was much reduced or absent in deep anesthesia. Both the early, high-frequency activity and the main diphasic response increased in amplitude with increased stimulus intensity, and the former was more sensitive to increased stimulus repetition rate than the latter.

Supported by USPHS Fellowship to O.T.E., and by USPHS Grant MH-06686.

A VENOUS BLOOD OXYGEN RESERVOIR IN THE DIVING ELEPHANT SEAL R. W. Elsner, P. F. Scholander, A. B. Craig, E. G. Dimond*, L. Irving, M. Pilson*, K. Johansen and E. Bradstreet*. Scripps Institution of Oceanography, University of California at San Diego, La Jolla, California.

Four adult elephant seals (Mirounga angustirostris) were captured at Guadalupe Island, Mexico. Body weights ranged from 500 to 850 kg. Diving experiments were performed on shipboard by immersing restrained animals in a canvas pool or in the sea. Profound bradycardia with maintained arterial blood pressure was observed during dives as in other aquatic animals. Blood oxygen capacity averaged 32 volumes per 100 ml. (range 28 to 39). The inferior vena cava of each animal was found to be very large (volume 20 to 25 liters, roughly one-fifth of the blood volume). During dives arterial blood oxygen fell progressively starting from an average value of 30 volumes per 100 ml. Blood from the inferior vena cava, starting from an average value of 27 volumes per 100 ml., decreased at a slower rate. In most instances this resulted in higher oxygen content in the inferior vena cava than in arterial blood during the latter half of the dive. The values for arterial and venous oxygen content at the end of 20 minute dives averaged 4.6 and 6.6 volumes per 100 ml., respectively. One blood volume determination by exsanguination yielded a value of 12 per cent of the body weight. The inferior vena cava of this species can provide a major storage depot of oxygenated blood during dives. (Supported by PHS research grants HE 08323 and GM 10521 and by NSF grant GB 1205.)

SPECIFIC SITE OF GENERATION OF BRAIN WAVES. R. Elul (intr. by W. R. Adey). Dept. of Anatomy and Brain Research Institute, Univ. of California, Los Angeles.

Intracellular recordings from cortical neurons were obtained in unanesthetized cats (midpontine, pretrigeminal preparation). In addition to spike activity, the resting potential was continuously modulated by oscillations of up to 10 mv, similar in time-course and in general appearance to the EEG derived from gross electrodes. Spikes were triggered during the depolarizing phase of the waves; the same depolarization level could often be reached, however, without initiating a spike. The relationships between the two processes seem to be more complex than in other varieties of neurons. No oscillatory activity was detected extracellularly with micropipettes, even when in contact with the neuron membrane (as indicated by the appearance of small positive spikes coincident with increase in electrode impedance). Cells which showed no spike activity, either spontaneously or in response to electrical or chemical stimuli, and which had relatively low membrane resistance - presumably glia - also failed to exhibit oscillatory potentials. It is proposed that: (a) Wave activity is generated by the same cells that are responsible for spikes. (b) The marked difference between intra- and extracellular records indicates that the waves do not arise across the impaled membrane; their intracellular presence implies a voltage gradient and current flow between different regions of the cell. (c) Inasmuch as the membrane across which the slow potentials developed could not be impaled, it is possible that it is situated at the fine, terminal dendritic arborizations. (d) The extracellular gradient of wave activity as measured with the same micropipettes is far smaller than its intracellular counterpart, suggesting a more circuitous extracellular path.

Peripheral Vascular Effects of Angiotensin II and Norepinephrine in the Dog, Cat and Monkey. T. E. Emerson, Jr.*, L. B. Hinshaw and C. M. Brake*. Cardiovascular Sec., Physiol. Branch, Civil Aeromed. Res. Inst. and Dept. of Physiol., Okla. Univ. Med. School, Okla. City, Okla.

The present study was undertaken to investigate the direct effect of angiotensin and norepinephrine on small forelimb veins in the dog, cat and monkey. Both equimolar and equiweight comparisons of the drugs were usually made and in some experiments equiweight infusion tests were completed. Drugs were injected or infused into the brachial artery inflow tubing in pump perfused, constant flow, isolated limbs. Brachial artery pressure (BAP) and small vein pressure (SVP) were measured with pressure transducers and limb weight was monitored continuously. In other experiments the drugs were injected directly into a small vein in dog natural limb flow preparations and SVP measured. On the average, with equimolar injections, angiotensin increased limb BAP and SVP more and caused a greater loss of limb weight in all species. With equiweight doses, angiotensin caused a greater rise of cat limb BAP and SVP and monkey SVP and caused about the same increase of monkey BAP as norepinephrine; limb weight loss was approximately the same in dog and cat limbs, but angiotensin's weight effect was greater in the monkey. The initial SVP elevation produced by angiotensin infusion was equal to that caused by norepinephrine, but the small veins became unresponsive to angiotensin after several minutes of infusion. Norepinephrine increased leg SVP approximately twice as high as angiotensin in the natural flow studies on the average. (Supported by Amer. Heart Grant-in-aid).

LOCALIZATION OF MODALITY SPECIFIC THALAMIC UNITS THAT RESPOND TO STIMULATION OF THE CAT TONGUE. R. Emmers*(Spon.: W. W. Walcott), Department of Physiology, Columbia University, New York City.

Stereotaxically oriented tungsten microelectrodes with a tip diameter of 1-3 microns were used for isolating several dozen thalamic units in cats anesthetized with Nembutal. Each of the units was tested for changes in its firing rate by applying tactual, pressure, thermal, and gustatory stimuli to punctate localities on the animal's tongue. For the stimulation of touch and pressure receptors a thin glass stylus was used. Thermal stimuli were provided by warm (42°C), cool (22°C), and cold (8°C) tap water, and gustatory stimulation was done with a mixture of sodium chloride, hydrochloric acid, quinine hydrochloride, and sucrose solutions. All fluids were applied by utilizing squeeze-drop bottles. - It was found that many units responded to one form of stimulation exclusively. However, those units that were activated by pressure stimuli were also activated when the same locality of the tongue was rapidly cooled to 8°C. A similar dual activation was encountered with some tactile and a few gustatory units. All units responding to tactile or to pressure stimuli were localized within the thalamic region of the lingual nerve projection. Those responding to thermal stimulation were localized medially with respect to the tactile and pressure receptive units, and those that were responsive to gustatory stimulation were confined to the ventromedial nuclear complex entirely. All gustatory units and a majority of the tactile and thermal units were localized ipsilaterally with respect to the site of peripheral stimulation. It appears that contralateral projection should belong mainly to some other lingual modality, possibly pain.
(Supported by grant NB-03266 from NINDB)

CHANGES IN GASTRIC MUCOSAL CELL POPULATION AND GASTRIC JUICE COMPOSITION AFTER FREEZING OF HEIDENHAIN POUCH
J. C. Engle, R. C. Doberneck, A. S. McFee, (Intr. by W. G. Kubicek)
University of Minnesota Medical School, Minneapolis, Minnesota

The 24 hour output of gastric juice by the actively secretory Heidenhain pouch in each of 18 healthy dogs was determined on 20 occasions. The pouches were then frozen for one hour at -20°C inflow and became achlorhydric, remaining so to the present. Six pouches remained achlorhydric on repeated 24 hour collections of juice one to two years after freezing. At that time pre freeze biopsies of pouches and intact stomachs revealed that average cell counts (corrected by the Abercrombie factor) for the stomach were 655 chief, 513 parietal and 171 mucous neck cells per mm. width of mucosa. The pouches contained an average of 171 chief cells (-74%), 130 parietal cells (-75%) and 243 mucous neck cells (+42%). 12 pouches remained achlorhydric up to 30 months after freezing and on more than thirty 24 hr. collections of juice, the volume was reduced by 67%. In 7 pouches, average chloride concentration of the juice declined from 155 mEq/L to 78 mEq/L (-50%) and that of sodium rose from 60 mEq/L to 120 mEq/L (+100%). Average potassium concentration increased from 8 mEq/L to 20 mEq/L (+250%). In 5 pouches, the perchloric acid fraction of the precipitable mucous content of the juice increased from 8.7 to 28 gm (+77%) and the phosphotungstic acid fraction declined by 63%. After gastric freezing long-term changes in the cells of the gastric mucosa appear, therefore, to be associated with pro found changes in composition of gastric juice.
Supported by USPHS Grant, Hartford Foundation and D. J. Cowling Grant

EFFECT OF TEMPERATURE ON THE RECOVERY FROM K^+-CONTRACTURE. David Erlij* and W. G. Van der Kloot. Dept. of Physiology, New York University School of Medicine, New York 16, N. Y.

We have used frog toe muscles (interosseus VII) to study the recovery from 60-80 second exposures to isotonic K_2SO_4 (95 mM). During control and recovery periods the muscles were soaked in Cl-free Ringer's solution. At 20-23°C, propagated action potentials and contractions in response to electrical stimulation were not seen until 40 to 90 seconds after removal of the 95 mM K_2SO_4. At 3-6°C there was no response to electrical stimulation before 600 seconds. Similarly, at 20-23°C, a second K-contracture could be elicited after 40 seconds of recovery in Ringer's solution; while at 3 °C, a second contracture could not be obtained before 450 seconds of recovery in Ringer. Even at 3°C, immediately after the removal of the 95 mM K_2SO_4, a second contracture was produced by 10^{-3} M caffeine. At 20-23°C, the resting potential rose to 70 mV within 60-110 seconds after washing out the K_2SO_4, and rose to 82-87 mV after 140-180 seconds. At 3°C, the resting potential rose to 70 mV in 60-180 seconds and to 82-87 mV within 130-210 seconds after removal of the K_2SO_4. Moreover, at 3°C, a second exposure to 95 mM K_2SO_4 produced the usual depolarization during the interval when no contracture is produced. Apparently at 3°C the mechanisms for both spike generation and for depolarization--contraction coupling remain "inactivated" for almost 400 seconds after the resting potential has returned to its usual level. "Reactivation" has a Q_{10} above 2.5. (Supported by a grant from the USPHS.)

VENTILATORY RESPONSE TO CO_2 AND LOW O_2 FOLLOWING CO_2 EXPOSURE OR BICARBONATE INGESTION. K. Falchuk*, T. W. Lamb*, and S. M. Tenney. Dept. of Physiology, Dartmouth Medical School, Hanover, N. H.

The interaction of hypoxic and hypercapnic stimuli to ventilation was studied in three subjects after, 1) 48 hours exposure to 6% CO_2 in 22% O_2 and balance N_2; 2) ingestion of 50 g. $NaHCO_3$ per day for three days. Control ventilatory response curves to CO_2 with PAO_2 maintained at fixed levels of 150, 60-65, 50-55, and 40-45 mm Hg were obtained before and after the periods of exposure. In both studies the $PACO_2$ and plasma HCO_3 were elevated, but after exposure to CO_2 the plasma pH was still below normal, and after $NaHCO_3$ ingestion the plasma pH was in the alkalotic range. In both studies, when breathing room air, the subjects hypoventilated. After 48 hours of exposure in the high CO_2 environment the $PACO_2$ was 49 mm Hg, but immediately on return to room air it dropped to 44-45 mm Hg, still about 5 mm Hg higher than control. At that time, addition of CO_2 to the inspired air to test ventilatory response resulted in very slight increase of ventilation at all levels of PAO_2 and over a range of $PACO_2$ 45-50 mm Hg. However, above that range of CO_2 the slope of the response curves increased abruptly and ventilatory values approached the control curves. Hypoxic ventilatory drive was diminished at all levels of $PACO_2$. In general, the CO_2 and hypoxic ventilatory response curves during metabolic alkalosis were similar to those observed during respiratory acidosis. [Supported by P.H.S. Grant HE-02888-08]

DETERMINATION OF VENTILATION-PERFUSION RATIO DISTRIBUTION BY INERT GAS ELIMINATION. L. E. Farhi and T. Yokoyama*. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

When an inert gas is eliminated by the lungs, its partial pressure in the alveoli and in the end-capillary blood will be influenced in a predictable manner by the solubility of the gas in blood and the ventilation-perfusion ratio ($\dot{V}_A/\dot{Q}$). Thus knowledge of the partial pressure of a gas of known solubility in the alveolar gas should allow calculation of the $\dot{V}_A/\dot{Q}$. The existence of an arterial-alveolar inert gas pressure difference shows that $\dot{V}_A/\dot{Q}$ is not identical in all alveoli. When this difference is determined simultaneously for two inert gases it becomes possible to describe a two-compartment system which behaves like the lungs under study. The existence of alveoli having a given $\dot{V}_A/\dot{Q}$ ratio can be checked by selection of two appropriate inert gases. Determination of $\dot{V}_A/\dot{Q}$ distribution by inert gas elimination presents the following advantages over the study using the normal respiratory gases: (1) it does not have to take into account the shape of the O_2 and CO_2 dissociation curves; (2) it does not assume that the subject's blood is normal; and (3) by increasing the number of inert gases it is possible to obtain a more refined analysis and to describe a system of n compartments by using n gases.

(Supported in part by the U.S. Air Force)

THE EFFECTS OF VENTILATION WITH DIFFERENT GASES ON THE PRESSURE VOLUME AND SURFACE TENSION PROPERTIES OF THE EXCISED LUNG OF THE DOG. Edmund E. Faridy*, J.W.C. Johnson*, S. Permutt, The Johns Hopkins University, Baltimore, Md.

The effects of ventilation with different gases (room air, O_2, CO_2, N_2,) upon P-V characteristics and lung extract surface tension were studied. In general, prolonged periods of ventilation (1 to 6 hours) decreased the % of air volume remaining at different transpulmonary pressures (30 to 5 cm. H_2O). This effect was most pronounced with room air or 100% N_2 and was of significant but smaller magnitude when 100% O_2 or 100% CO_2 was used. The minimum surface tension observed on compression of the extract (γ_{min}.) was most elevated in lobes ventilated with 100% N_2. If, following ventilation, the lobes were flushed with room air and held at a constant volume for several hours, the effects of ventilation were completely reversed in the lobes which had been ventilated with room air or oxygen but were not reversed in the lobes ventilated with CO_2 or N_2. This suggests that pure N_2 or CO_2 interferes with the metabolism of the alveolar lining cells resulting in a disturbance of their ability to produce surfactant. The changes in P-V measurements and γ_{min}. in lobes ventilated with room air were directly related to tidal volume and duration of ventilation and inversely related to end expiratory pressure. This suggests that the larger the change in the surface area of the alveoli with each inflation, the greater the depletion of surfactant.

INHIBITION OF ENZYMIC ACTIVATION OF BLOOD CLOTTING BY ORGANIC PHOSPHATES (ATP, ADP, AMP). John H. Ferguson and Panayotis G. Iatridis*. Physiology Dept., Univ. of North Carolina, Chapel Hill, N. C.

By quantitation of equivalents (percentage) of prothrombin activated (EPA) in two-stage thrombin-generating test systems, in the presence of Milstone's thrombokinase at controlled ionic strength, relationships of pH and Ca-ion concentration to the enzymic activity are defined. Inhibitory effects of organic phosphates (ATP, ADP, AMP) are analyzed as interference with this enzymic conversion of prothrombin to thrombin, in terms of pH and Ca^{++} concentration. The relatively high phosphate concentrations required (1-8 mM), and the cited relationships, indicate complex non-specific effects unlikely to be encountered in the natural process of blood coagulation or thrombosis. (Supported by USPHS Research Grant HE-01510-11).

GLYCERINATED VASCULAR SMOOTH MUSCLE AS A CONTRACTILE MODEL. R.S. Filo* and D.F. Bohr (intr. by C. Brassfield). Dept. of Physiol., The University of Michigan, Ann Arbor, Michigan.

It has been our aim to study specific aspects of the contractile protein of vascular smooth muscle. A glycerol-extracted preparation of the uncoiled media of hog carotid develops tension of about 100 gm/cm^2 when ATP is added to the bath in which it is mounted. In the presence of 5 mM Mg^{++}, ATP threshold concentration for contraction is approximately 0.1 mM. The amount of tension developed increases with ATP concentration up to 5 mM. At 10-20 mM the relaxing (plasticizing) effect of ATP prevents full contraction. Contraction requires the presence of Mg^{++} and is not supported by Ca^{++}; both divalent cations inhibit relaxation which normally occurs at high ATP concentrations. Optimal tension development occurs when the bathing solution has low ionic strength (e.g., μ = .05). Tension development is depressed when Na^{+} replaces K^{+} as the major component of the bath. The muscle preparation relaxes when the ATP is flushed from the bath and contracts when ATP is again added, thus repeated contraction-relaxation cycles for single fibers have been recorded. In most of the characters described glycerinated vascular smooth muscle is similar to glycerinated skeletal, cardiac, and uterine muscle, but in its ability to undergo repeated contraction and relaxation it is apparently unique. This ability may indicate the presence of a relaxing factor(s) as suggested by Briggs (A.J.P. 204: 739, 1963) for fresh glycerinated uterine muscle. (Supported by a grant from the Life Insurance Medical Research Fund.)

INFLUENCE OF CHLORIDE CONCENTRATION ON CHLORIDE AND SODIUM TRANSPORTS IN FROG SKIN. Jorge Fischbarg and J. A. Zadunaisky (intr. by W. S. Rehm). Eye Research Lab., University of Louisville, Louisville, Ky.

Changes in the chloride concentration of the Ringer solutions bathing both sides of the isolated skin of the southamerican frog Leptodactylus ocellatus were made while the chloride transport shown by these skins or the sodium transport were measured with Cl^{36} and Na^{24} or Na^{22} under short-circuit conditions. The osmolarity of the solutions was kept constant with sulphate and sucrose and the ionic strength of the solutions varied only 5% over the range of Cl concentrations. Chloride concentration was changed stepwise on both sides at the same time to avoid chloride diffusion potentials. The results show that at low chloride concentration, from 1 to 60 mM/l, the chloride transport is small and does not change appreciably over this range. After 60 mM/l there is a sudden increase in the chloride net flux, apparently linear up to 118 mM/l of chloride, the maximum concentration studied. The passive efflux of chloride follows a linear increase with concentration over the whole range studied. A permeability constant of 3.3×10^{-6} cm/sec and a diffusivity constant of 1.3×10^{-7} cm^2/sec was found on the basis of the efflux values. Apparently at low chloride concentrations the influx is independent of chloride concentrations. The sodium transport is affected by chloride concentrations. From 0 to 20 mM/l of chloride the sodium transport decreases, and from 20 mM of chloride to 118 increases with chloride concentration. The observed findings will be discussed in terms of permeability changes at the outside facing barrier of the skin and in terms of intracellular chloride concentrations.

Sodium transport in these frog skins shows Michaelis-Menten kinetics with a Vmax value of 3.03 uEq/h/cm^2 and a Km of 14.1 mM/l.

EFFECT OF SUPERIOR CERVICAL GANGLIONECTOMY ON THE DIURNAL SEROTONIN RHYTHM OF THE RAT PINEAL. Virginia M. Fiske. Dept. of Zool. and Physiol., Wellesley College, Wellesley, Mass.

Kappers (1960) has proposed that the pineal organ of the rat is innervated chiefly, if not completely, by fibers of the autonomic nervous system originating from the superior cervical ganglia. Quay (1963) has shown that the serotonin content of the pineal body varies diurnally in relation to the photoperiod. This study was undertaken to determine what effect, if any, removal of the superior cervical ganglia would have on this circadian rise and fall of serotonin. Fifty-eight male rats were placed under controlled environmental conditions at 22 days of age. Within the next six days 26 of these animals were subjected to bilateral superior cervical ganglionectomy. The rest of the animals served as sham-operated or unoperated controls. Five to six weeks later the animals were sacrificied at the two points in the photoperiod reported by Quay to give maximum and minimum pineal serotonin values. The pineals were removed and the serotonin was extracted and assayed spectrofluorometrically using Quay's modification of Bogdanski's method. It was clear that while the control animals exhibited a diurnal difference in serotonin levels, the mean maximal value being 102 nanograms per gland, the mean minimal value 42 nanograms per gland, the ganglionectomized animals did not. Circadian differences in pineal serotonin content are dependent upon an intact autonomic innervation.

VENTILATORY RESPONSE TO TRANSIENT INFUSIONS INTO THE CAROTID ARTERIES AND VERTEBRAL ARTERIES. Robert S. Fitzgerald, Robert W.B. Penman, (intr. by Richard L. Riley, The Johns Hopkins University, Baltimore, Md.

In an attempt to characterize the action of the central and peripheral chemoreceptors in the control of respiration, small (40-60 ml) and brief (10-30 seconds) infusion of hypercapnic blood were made either into the carotid or the vertebral arteries. In the intact animal carotid artery infusion of normoxic, moderately hypercapnic (Pco_2 = 60 - 90 mm.Hg) or severely hypercapnic (Pco_2 = 250 - 300 mm.Hg) blood produced a marked ventilatory response. The same procedure in carotid-body-denervated (chemodenervated) animals produced either no change or a depression in ventilation. The sensitivity of the medullary centers to changes in arterial Pco_2 was tested in 2 ways: 1) In the intact animal vertebral artery infusions of normoxic hypercapnic blood produced little or no increase in ventilation. If the blood was severely hypercapnic, a depression in ventilation resulted. 2) After chemodenervation and ligation of the vertebral arteries, carotid artery infusion of severely hypercapnic blood produced no increase or a slight depression in ventilation. These results suggest that changes in arterial Pco_2 affect directly only the peripheral chemoreceptors.

RELATION BETWEEN PHOSPHATE METABOLISM AND ACID SECRETION IN BULLFROG GASTRIC MUCOSA. J.G. Forte*, P.H. Adams* and R.E. Davies. Dept. of Physiol., Sch. of Med. and Dept. of Animal Biol., Sch. of Vet. Med., University of Pennsylvania, Philadelphia, Pa.

Gastric mucosae of Rana catesbiana were isolated and tied to one end of plastic tubes with the secretory surfaces facing the lumens of the tubes. Unbuffered saline was placed on the secretory side and the tubes were immersed in HCO_3^-/CO_2 buffered saline. At a prescribed time the tubes were removed from the nutrient solution and rapidly plunged into liquid N_2. The rate of acid secretion (qH^+, $\mu eq/cm^2/hr$) was measured by back-titration of the secretory solution. A portion of the frozen mucosa was weighed, and pulverized and then extracted in 0.25M $HClO_4$ at 37°C. Analyses were carried out on the neutralized extract for ATP, ADP, AMP, Pi and total P. The average [ATP] and [ADP] in 19 oxygenated mucosae was 1.14±0.06(SEM) and 0.20±0.014 μmoles/g wet wt respectively. There was a clear correlation (r=0.81) between the qH^+ and [ATP]. Inhibition of qH^+ by anoxia resulted in a fall in [ATP] with time and an increase in [ADP]. However, anaerobically produced ATP could maintain acid secretion until [ATP] fell to <0.4-0.5 μmole/g. On reoxygenation, acid secretion returned only when the [ATP] was also restored. Inhibition of qH^+ by NaSCN (10 mM) caused an increase in the ratio of [ATP]/[ADP]. In mucosa made anoxic the fall of [ATP] was less in those to which NaSCN had been added. The results indicate that ATP is immediately involved in the process of acid secretion. Calculations of the ratio of H^+ secreted/ATP used gave values of about 2.0. Supported by USPHS grant AM-05707.

ELECTROLYTES IN UNSTIMULATED POUCH SECRETIONS OF GASTRECTOMIZED DOGS IN PROLONGED EXPERIMENTS. William C. Foster, Ward D. O'Sullivan,* Richard D. Sweeney* and Diane L. Pemberton.* Jeanes and Misericordia Hosps., Philadelphia, Pa.

Unstimulated secretions from Heidenhain pouches in dogs, with and without gastrectomy, were analyzed for hydrogen, sodium, potassium and chloride ions in prolonged experiments. The studies were conducted for periods from 6 to 102 days, with a mean period of 42 days. Dogs were maintained on commercial canned food, to which was added a dry high protein supplement. Strained food was fed to maintain the caloric intake when necessary. Hydrogen ions were measured by a sensitive pH meter and other cations by flame photometry. Chlorides were determined by the method of Schales and Schales. The mean daily output of sodium, potassium, hydrogen ions and chloride in the pouch dogs without gastrectomies were 4.36, 0.71, 7.09 and 17.19 and 4.26, 0.23, 0.4 and 5.02 mEq per 24 hour, respectively in the pouch dogs with gastrectomies. The daily volume output was reduced in gastrectomized dogs to one-third. The effect of extended secretory activity in the gastrectomized dogs is demonstrated.

UPTAKE AND RELEASE OF SO_2 BY THE HUMAN NOSE. N.R. Frank, F.E. Speizer*, Dept. of Physiology, Harvard Sch. of Public Health, Boston, Mass.

Seven subjects, breathing quietly, were exposed on 21 occasions to 16 ppm. of SO_2 by nose and for periods lasting 30-45 minutes. Inspiratory and expiratory gas samples were collected for analysis (electroconductivity method) from the following sites: 1-2 cm external to the nose, 1-2 cm beyond the nares, and the oropharynx. Results: less than 2% of the gas entering the nose reached the pharynx. In expiration, about 12% of the gas previously taken up re-entered the airstream. During the first 15 minutes of the post-exposure period, SO_2 was released from the nasal mucosa both in inspiration and expiration. About 3% of the original exposure concentrations re-entered the airstream in inspiration, about 5% in expiration. In a few experiments, SO_2 could still be detected in expired gas 15-30 minutes after exposure had ended. Final net uptake of the SO_2 dosage was about 84%. It is concluded that only traces of the irritant gas (at the dosage studied) reach the tracheo-bronchial tree in inspired air, and that following absorption a significant fraction of the gas remains dissolved at the mucosal surface at least 15-30 minutes.

BLOOD LACTATE AND PYRUVATE DURING PROGRESSIVE HYPERTHERMIA IN CATS AND CHICKENS. H.M. Frankel and F.L. Ferrante*. Department of Physiology and Biochemistry, Rutgers - The State University, New Brunswick, New Jersey.

Changes in blood lactate (L) and pyruvate (P) concentration with increased body temperature (T_r) were followed in adult cats and chickens. Average L and P in 25 normothermic cats, average T_r 36.9°C, was 0.80 and 0.08 mEq/liter, respectively. In 11 normothermic chickens, average T_r 40.8°C L was 2.96 mEq/liter and P was 0.18 mEq/liter. When T_r was raised to 40°C in 12 cats average L was 1.13 mEq/liter and P was 0.14 mEq/liter; at 41°C, L = 1.84 mEq/liter and P = 0.20 mEq/liter. L & P increased with increasing T_r in both chickens and cats. There is evidence that blood Pco_2 is related to L & P levels in both classes of animals. Calculated excess lactate (XL) was + 0.52 mEq/liter, S.E. ± 0.35 for 12 cats with a 4°C increase in T_r (from 37°C to 41°C). At T_r of 42°C and 43°C XL was significantly increased in cats. In 6 chickens a 4°C increase in T_r (from 41°C to 45°C) caused a consistent decrease in XL (-4.00 mEq/liter, S.E. ± 0.76). The high L and P in chickens suggests metabolic acidosis must normally exist in these animals as compared to mammals. The relation between Pco_2 and L and P suggests that respiratory changes found during hyperthermia have acid-base balance and metabolic as well as heat loss effects. (Supported by U.S. Army Med. R. & D. Command Contract #DA 49-193-MD-2423 and U.S. Air Force Contract AF 41 (609) - 1499.)

IONIC DISTRIBUTION ACROSS PIGEON CROPS USED AS PERFUSION MEMBRANES. William L. Frantz, Dept. of Physiology, Michigan State University, East Lansing, Michigan.

This paper is a report of the membrane behavior of the pigeon crop in an Ussing type chamber when oxygenated bird Ringer's, a defined culture medium (Grand Island Biological M-199), and pigeon plasma are used as perfusants. Potentials of 2.0-5.0 mv/cm^2 are maintained for up to 10 hours when the mucosal and serosal surfaces are in contact with initially equivalent amounts of M-199 or plasma, while 12.0 mv/cm^2 potentials which fall to nearly zero in an hour or two are characteristic when bird Ringer's is perfused. These lower potentials correlate with an increasing concentration of organic ions as well as with isosmotic activity. From these and other data of in vitro perfusion we suggest that values reported in the literature for multi-layer membranes are higher than would obtain for in vivo conditions of identical systems. Choline substitution for sodium in the M-199 shows that in part this potential is that of a sodium steady state equilibrium in which the gradient is from serosal to mucosal surface. Because the crop of both the male and the female pigeon is specifically responsive to prolactin in such a way as to begin the hypertrophy of epithelium within a few hours and within a week to begin synthesizing a holocrine secretion rich in protein and lipid and devoid of all but a trace of carbohydrate, the role of charged organic molecules can be observed as a function of potential changes regulated by their utilization by the cells. We plan to report the changes prolactin initiates in the parameters described above following its introduction into the in vitro system and when it is injected intradermally in the usual manner of a bioassay technique.

COMPONENT ANALYSIS OF PREPYRIFORM EVOKED POTENTIAL. Walter J. Freeman Department of Physiology, University of California, Berkeley

Averaged single-shock evoked potentials (AEP) recorded in the prepyriform cortex of cats with in-dwelling electrodes upon stimulation of the lateral olfactory tract were transformed into the frequency domain by use of the Fourier integral. Analysis of the polar plot was carried out in terms of linear combinations of first and second order terms. These results, combined with curve-fitting of AEP in the time-domain, implied that the basic spectrum of the AEP was trimodal. At near-threshold stimulus intensity the dominant peak was near 40/sec, the second peak near 50/sec and the third peak near 20/sec. With increasing stimulus intensity the energy in these modes shifted to the low frequency end of the spectrum, apparently because of an amplitude-dependency of frequency. A proposed explanation is based on the premiss that the cortex is composed of a population of coupled oscillators, in which the coupling coefficient is proportional to input intensity. The dominant 40/sec peak is ascribed to activity in an intracortical feedback loop involving the superficial pyramidal cells and the granule cells. The 20/sec peak is ascribed to a second loop involving the deep pyramidal cells as well. There is no clear intracortical anatomical basis for the third component. Its phase in the time domain indicates that it is a response to secondary excitation. The conclusion is reached that the AEP consists of the sum of a primary response having 2 frequencies, superimposed on an "echo" response at a 3rd frequency, which is owing to antidromic excitation of mitral cells in the olfactory bulb, with recurrent inhibition leading to a brief drop in the level of spontaneous unit activity in the lateral olfactory tract.

Supported by USPHS Grant #MH-06686.

EFFECT OF MINERALOCORTICOIDS ON SPONTANEOUS NaCl INTAKE OF ADRENALECTOMIZED RATS. M. J. Fregly and I. W. Waters*, Dept. of Physiology, Univ. of Florida, Coll. of Med., Gainesville, Florida.

When given choice between water and NaCl solution to drink, adrenalectomized rats choose NaCl solution. Others report that administration of 0.5 to 1.0 mg desoxycorticosterone acetate (DOCA) per day reduced NaCl intake of adrex. rats but increased NaCl intake by intact rats. Our objectives were to re-evaluate the effect of mineralocorticoids on NaCl intake by adrex. rats and to seek an explanation for the difference between NaCl intakes of adrex. and intact rats given similar doses of DOCA. Ten male adrex. rats were used. Daily intakes of water, .15M NaCl solution and food were measured. After a 5-day control period, 5 rats were given d-aldosterone in oil subcutaneously daily for four 5-day periods at dose levels of 0.5, 5, 15 and 50 ug. Control adrex. rats received oil only. Treatments decreased NaCl intake and increased water intake roughly in proportion to logarithm of dose. At the highest dose, treated rats ingested more water than NaCl solution. Administration of DOCA at 50 and 150 ug/day to 5 male adrex. rats in a second experiment produced results similar to those observed for aldosterone. However, administration of either 1.0 or 2.0 mg DOCA/day returned NaCl intake to that of an untreated adrex. rat. Thus, a U-shaped dose-response curve exists between dose of mineralocorticoid administered and intake of NaCl solution. The spontaneous NaCl intake of intact rats places them near the bottom of the dose-response curve. Either adrenalectomy or administration of mineralocorticoid would be expected to increase salt intake. The differences in ingestion of NaCl solution by adrex. and intact rats given similar doses of DOCA may thus be explained by their initial position on the dose-response curve.

(Supported by NIH Grant HE-03503-07)

FACTORS INFLUENCING THE SHAPE OF THE CAROTID PULSE WAVE IN MAN. Edward D. Freis, Peter C. Luchsinger, Robert E. Snell and William C. Heath. VA Hosp. and Georgetown Univ. School of Med., Washington, D.C.

The carotid volume pulse is characterized during systole by two separate maxima. This study attempts to elucidate the factors which influence the contour of the externally recorded carotid "volume" pulse. A special transducer (IRE Trans. BME-10: 173, 1963) with adequate linearity and frequency response was used. The carotid "volume" pulse was recorded simultaneously with blood velocity (spatial pressure gradient technique) and pressure in the ascending aorta. Tracings of the carotid pulse were superimposed on the aortic flow and pressure curves using the time of valve closure as the common point. The first maximum of the carotid pulse coincided with the summit of the aortic velocity while the second occurred at peak aortic pressure. Pressure pulses were recorded at intervals from the ascending aorta to the carotid bifurcation using a Statham catheter tip pressure transducer. As the transducer was moved distally from the ascending aorta the anacrotic limb of the central pulse increased in amplitude and in the carotid formed the first maximum of the carotid contour. Drugs which increase stroke volume and decrease total peripheral resistance, such as isoproterenol and amyl nitrite, markedly increased the amplitude of the first peak of the carotid pulse, whereas drugs which elevate total peripheral resistance, such as angiotensin and methoxamine, decreased the relative amplitude of the first carotid peak. These results suggest that the relative amplitude of the first to the second systolic maximum of the carotid pulse increases with elevation of stroke volume and ejection velocity and decreases with a rise in mean systolic pressure and loss of arterial distensibility.

INTRALUMINAL PRESSURE CHANGES AND CINERADIOGRAPHIC CORRELATIONS IN THE HUMAN SMALL INTESTINE: THE REPRESENTATION OF PROPULSIVE AND NON-PROPULSIVE ACTIVITY. G. Friedman*, J.D. Wave*, L.A. Weingarten*, H.D. Janowitz and B.S. Wolf*. Mount Sinai Hospital, New York, N.Y.

Propulsive activity of the proximal small bowel was studied in ten patients by measuring intraluminal pressure changes at three separate sites simultaneously, during continuous cineradiography. Two types of propulsive activity were noted when recording lumens were placed 7 cm. apart: (1) Tall type I waves (greater than 10 mm. Hg.) occurring in sequence were associated with propulsive movement over short segments. (2) Type III waves occurring in sequence were associated with propulsion over longer segments. Non-propulsive activity was associated with randomly distributed, single monophasic waves usually of low amplitude. Precision timing of cine film and intraluminal pressure changes allows a detailed analysis of a single monophasic wave. The beginning of a contraction, the region of maximum contraction, and the onset of filling of an intestinal segment may be identified on the pressure curves with considerable accuracy.

ACETYLCHOLINE EFFECTS ON VL-FOCAL POTENTIALS EVOKED BY BRACHIUM CONJUNCTIVUM STIMULATION. T.L. Frigyesi* and D.P. Purpura. College of Physicians and Surgeons, Columbia University, New York.

Intracarotid injections of ACh (0.5-20 γ) in locally anesthetized-paralyzed cats produce depression of focal negativity signalling postsynaptic discharges of VL relay elements activated by 1/sec brachium conjunctivum stimulation. Depressant effects are noted within 15 secs after injection and are maximal during the subsequent 5-10 secs. Depression of focal negativity is accompanied by blockade of spontaneous unit discharges in VL and reduction of specific evoked responses in motor cortex. In 30% of the preparations depressant effects are preceded by a facilitatory phase especially with low doses of ACh (0.5-5 γ). Complete recovery of focal negativity occurs 2-3 minutes following single injections. Depressant or facilitatory effects of ACh are not associated with alterations in pre-synaptic components of VL-focal responses or significant blood pressure changes. These effects of ACh contrast sharply with simultaneously observed effects on focal potentials evoked in lateral geniculate body (LGB) by optic tract stimulation. Thus LGB specific responses are consistently facilitated with doses of 2-8 γ ACh and depressed at higher doses as reported by others (David, et al, Int. J. Neuropharmacol. 1963, 2:113). Atropine (0.25-1.0 mg) produces marked depression of both VL and LGB specific evoked responses but more pronounced effects are observed in VL. Unlike effects of ACh, atropine-induced depression is slow in onset and prolonged (20-40 min). High doses of atropine depress pre-synaptic components of focal responses in VL and LGB. These and other data suggest that depressant effects of ACh on VL-focal potentials evoked by cerebellar stimulation are secondary to activation of inhibitory pathways which converge on specific VL relay elements from other sites (Frigyesi and Purpura, Exptl. Neurol. 1964, in press).

COMPARISON OF THE STATIC PRESSURE-VOLUME HYSTERESIS OF THE DEAD SPACE AND LUNG. Herman F. Froeb, Jere Mead, and Edward Berger.* Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

Hysteresis of the tracheobronchial tree has been demonstrated in vitro but not in vivo. If at iso-lung volumes, the volume of the tracheobronchial tree is the same irrespective of the previous lung-volume history, then the hysteresis of the V_D must be that of the lung. If the V_D at iso-lung volume is greater following inflation than following deflation, the V_D hysteresis must be greater than that of the lung. In 3 of 6 normal subjects, there was a significantly greater mean value of V_D of 7-14 ml. at iso-lung volume between 60-80% VC following inspiration to TLC than following expiration to RV. In all other critical experiments, the V_D was the same irrespective of the previous lung volume history. Differences of mean values of these magnitudes were measured by modifying the Fowler technique by using a constant flow device, a cast of each subject's face to support the cheeks, a linearizing circuit for the infra-red CO_2 analyser, and a Stairmond disc for uniform sampling of CO_2. It is concluded that the hysteresis of the tracheobronchial tree in vivo is similiar to or slightly greater than that of the lung. Considering the difference in their structure, the finding of comparable hysteresis is of interest.

OCCURRENCE AND DISTRIBUTION OF TETRODOTOXIN (TARICHATOXIN). Frederick A. Fuhrman and Jane H. Fail*. Stanford University School of Medicine, Palo Alto, California.

Tetrodotoxin, an amino polyhydroxy perhydroquinazoline derivative that is an extremely potent neurotoxin, occurs in the viscera of puffer fish (Tetraodontidae) and has been recently isolated from the eggs and embryos of newts of the genus Taricha. We have looked for evidence of the presence of tetrodotoxin in other amphibia and studied its distribution in the organs of adult Taricha. Tissues were homogenized, acidified and dialyzed against water. The dialysates were concentrated by freeze-drying and the residue assayed by injection into mice. In some instances identification was made by thin-layer chromatography on silica gel. Highest concentrations of tetrodotoxin (per unit weight) were found in Taricha torosa, T. granulosa and T. rivularis. Several species of Triturus or closely related genera were found to contain the toxin in varying smaller amounts. No toxin could be found in the tissues from about 20 species of amphibia from families other than Salamandridae. Tetrodotoxin occurs in the tissues of both sexes of Taricha in this approximate order of decreasing concentration: skin, muscle, blood, testes, liver. The reason for the occurrence of this extremely toxic substance only in the tetraodontoid fishes and the Salamandridae remains unexplained.

STUDIES ON THE MECHANISM OF EXPERIMENTAL SOFT-TISSUE CALCIFICATION. Giulio Gabbiani+ and Beatriz Tuchweber (intr. by Hans Selye) Institut de Medecine et Chirurgie experiméntales, Université de Montréal, Montreal, Canada.

Calcergens are substances (mainly metals) which induce topical calcification when placed in contact with the tissues of normal animals. Among these compounds only lead salts injected i.v. prepare the rat so that subsequent s.c. injection of a histamine liberator (i.e. Polymyxin -B sulfate or PMX) produces topical calcification (Selye et al. J.Pharm. exp.Ther.138,131, 1962). Previous experiments have shown that there is a relationship between the capacity of precipitating phosphate or carbonate from Tyrode solution and the calcifying potency of calcergens (Gabbiani, Experentia, in press). In view of these facts, three experiments were performed on 100 g.rats to investigate further the mechanism of calcium salts precipitation during calcergy. In the first experiment, it was noted that the addition of Na_2HPO_4 to the PMX s.c. induced topical calcification in rats prepared with i.v. injections not only of Pb-acetate but also of other calcergens i.e. Ca-gluconate, $CeCl_3$, $CdCl_2$ and $LaCl_3$. In the second experiment, the oral pretreatment with Na_2HPO_4 permitted the induction of calcification at PMX injection site in rats receiving otherwise ineffective doses of Pb-acetate i.v. The third experiment showed that topical calcification induced by Pb-acetate i.v. and PMX s.c. is inhibited by oral pretreatment with Ca-acetate. In rats treated only with Ca-acetate per os and sacrificed at the time of the Pb-acetate injection, the blood phosphate level was significantly decreased as compared to normal animals. All these results support the view that phosphate is primarily responsible for the initiation of this experimental calcification.

(Supported by the Medical Research Council of Canada.)

+Fellow of the Medical Research Council of Canada.

DIRECT MEASUREMENT OF THERMAL RADIATION ABSORBED BY THE HUMAN BODY. A. P. Gagge and J. D. Hardy. John B. Pierce Foundation Laboratory, New Haven, Connecticut.

A major difficulty in the study of the heat balance of man in his natural environment has been the inability of obtaining direct measurement of the energy absorbed by the body from sources of intense thermal radiation such as the sun. In the past, use of simple geometry, of the estimated areas irradiated and of simplifying assumptions for reflecting power of skin and clothing has been used to calculated body energy absorption. Using a sensitive recording balance, it has been possible to measure the heat absorbed from the incident radiation by the increased evaporative heat loss of a nude or clothed man (regardless of geometry) since in equilibrium the heat loss and gain are equal. In the present experiments, the subject lay on a bed mounted on the balance. The radiation at normal incidence to the bed was essentially uniform for either 2, 4, 6 or 8 lamps. The irradiance was measured with a sensitive radiometer. The area exposed was determined by planimetering the outline of the body while lying on the bed. The energy, spectral quality, and duration of exposure were varied independently. From this arrangement the emissivity of white human skin for a 2500°K source was measured as 69%; and for a 1900°K source, 81%. For a sitting man with two radiators on each side, the surface area irradiated was determined to be 33% of the DuBois area. Using the body as its own radiometric indicator, both the environmental and physiological factors can be evaluated to complete the heat balance equation in complex situations.

O_2 AND CO_2 TENSIONS IN FISH. W. F. Garey* and H. Rahn. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

By implanting catheters in the opercular cavity of the carp and eel it is possible to sample and analyze the CO_2 and O_2 tensions of water leaving the gills of the free-swimming fish. In water saturated with air the CO_2 tensions varied approximately between 1 and 3 mm Hg, while the O_2 tensions ranged between 50 and 75. These values are in the range of those predicted for an exchange ratio of .7 at a water temperature of 15°C. (The Physiologist 6: 259, 1963.) The gas tensions in the venous blood and tissues of fish were estimated from the analyses of equilibrated gas pockets in the abdominal cavity. These attain steady values in about 1 - 2 days after injection. Since the O_2 dissociation curve of carp blood is displaced far to the left compared with that of the trout, it was predicted that lower O_2 tensions would be found in the gas pocket of the carp. In this fish the CO_2 and O_2 tensions averaged 4 - 9 and 4 - 12, respectively. The rainbow trout had similar CO_2 values, but their O_2 tansions averaged 30 - 40 mm Hg.

(Supported in part by Office of Naval Research Contract Nonr 969(03))

BIOELECTRIC PROPERTIES AND PERMEABILITY OF THE ISOLATED AMPHIBIAN LUNG. John T. Gatzy (intr. by R.E. Gosselin), Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, New Hampshire.

When mounted between identical Ringer solutions, the isolated lungs of the bullfrog (Rana Catesbeiana) and toad (Bufo marinus) exhibited spontaneous transmural potentials of 20 and 6 mV respectively, with the serosal side positive. The resistance of both tissues was about 700 ohm cm^2. When Ringer solution containing $HgCl_2$ (10^{-4} M) was added to the mucosal (luminal) side, the potential and resistance declined rapidly after a latency of 1-4 min. The same concentration of Hg^{++} added to the serosal surface caused a gradual fall after a delay of 20 min. These results suggest that the alveolar epithelial layer was the site of the potential. Permeability coefficients for the transfer of Na^{24} and K^{42} in either direction across the short-circuited bullfrog lung were 5×10^{-7} and 8×10^{-7} cm sec^{-1}, respectively. Under the same conditions, the flux constant for carrier-free radioiodide averaged 42×10^{-7} cm sec^{-1} in the direction of serosa to mucosa and 13×10^{-7} in the opposite direction. If chloride transport shows the same asymmetry, it would be adequate to account for the short-circuit current. (This investigation was supported in part by PHS Research Grant GM 11598 and by Amer. Cancer Soc. Institutional Grant).

EFFECTS OF SHORT TERM TREATMENT WITH TESTOSTERONE PROPIONATE ON THE CONCENTRATIONS OF BLOOD AND PITUITARY FSH (FOLLICLE STIMULATING HORMONE) AND LH (LUTEINIZING HORMONE) IN THE ORCHIDECTOMIZED RAT. V. L. Gay*, V. M. Bay*, and E. M. Bogdanove. Dept. of Anatomy and Physiology and Combined Degree in Medicine. Indiana University, Bloomington, Indiana.

Orchidectomized rats were injected subcutaneously once, or daily for one week, with testosterone propionate (1500 µg/day). Controls were injected with the vehicle only (sesame oil, 0.1 ml/injection). The rats given a single injection were killed 3 days later whereas the others were killed on the day following the seventh injection. At autopsy, blood and anterior pituitary glands were collected. Blood was mixed with heparin and the cells removed by centrifugation at 2±1°C. Plasma was collected and frozen until it was to be used for bioassay. Anterior lobes were frozen in 0.85% NaCl and subsequently homogenized and diluted for use in the Parlow and Steelman-Pohley assays for LH and FSH, respectively. These treatments did not greatly alter pituitary LH or serum FSH concentrations. However, serum LH concentration was greatly reduced by either 3 or 7 days of testosterone treatment while pituitary FSH concentration was increased (to nearly two-fold by the end of one week). These findings suggest that androgens influence the secretion of the specific folliculotrophins, FSH and LH, differentially.

VASCULAR AGING AND REACTIVE HYPEREMIA IN THE DOG. William F. Geber and James M. Schwinghamer* Dept. of Physiology & Pharmacology, School of Medicine, University of South Dakota, Vermillion, South Dakota.

The objective of the study was to determine if there was a correlation between the pattern of reactive hyperemia and the age of an animal. A group of ten pups was compared with a group of fifteen old dogs of established age. Measurement of femoral blood flow was carried out with an electromagnetic flowmeter and blood pressure by strain gage. Occlusion of the femoral artery for periods ranging from 3 seconds to 3 minutes resulted in the usual increase in blood flow following release of the occlusion. The pattern of the reactive hyperemia response in the pups was very consistent, whereas the pattern in the old dogs indicated somewhat more variation. Typically the pup response indicated marked vessel elasticity whereas the old dog indicated loss of vessel elasticity. Several old dogs gave responses typical of much younger animals. The old dog response pattern could be partially modified by various compounds to revert to a younger pattern of reactive hyperemia. The measurement of the pattern of reactive hyperemia may be utilized to determine the physiologic age of the vasculature.

BEHAVIOR AND REGENERATION OF MAST CELLS IN CULTURE; GRANULE FORMATION AND RELEASE. TIME-LAPSE MOTION PICTURE. R. S. Geiger, C. Adachi, and W. G. Stone (intr. by J.E.P. Toman). Chicago Medical School, Chicago, Illinois.

Tissue obtained from a mastocytoma maintained in mice was grown in vitro. In order to obtain indefinite cultivation and differentiation it was necessary to supplement the medium with homologous serum. Using time-lapse photomicrography at the rate of 4 per min., mast cells were seen to proliferate by amitosis, "budding". Granule-formation was associated with changes in the nucleolus and other nuclear areas and a direct transfer of macromolecular substances to the cytoplasm. Granules were released by contraction of the cell as a whole. Concomitant studies showed the granules to stain vitally with neutral red, metachromatically with toluidine blue and to incorporate ^{35}S. Incorporation of ^{35}S into granules occurred only within the cell. Addition of adrenalin, 0.005 γ/ml., increased cell proliferation, granule formation and release. A vitally staining Janus Green B material, fibre like in character, was extruded along with the granules. Like the increased vitally staining Janus Green B material in the nucleus, this material does not retain the stain in fixed preparations. (Supported by grants from USPHS MH 07907 and Scottish Rite Comm. on Research in Schizophrenia.)

GASTRIC MOTILITY IN THE DOG: DISTINCTIVE ACTION OF THE CARDIA. T. Geisel*, T. Arai*, N.C. Jefferson, and H. Necheles.
From the Department of Gastroenterology, Medical Research Institute, Michael Reese Hospital, Chicago.

Gastric motility in anesthetized and unanesthetized dogs was studied with a multi-lumen tube passed through the esophagus into the stomach. The tips of the tubes were located at 5-cm intervals, and motility was recorded simultaneously on six channels. The tubes were kept open by a very slow infusion of water, and pressures were recorded through Statham pressure transducers on a type "R" Dynograph. In acute experiments, nembutal, ether or fluoromar were used as anesthetic. The vagi were cut in the neck, and their central ends stimulated. In most dogs this led to distinct contractions of the cardia, with few or none in other parts of the stomach. The unanesthetized dogs had esophageal fistulas of the Komarov type and tubing could be introduced into the stomach without disturbance of the animal. In tests with drugs such as serotonin, epinephrine, reserpine, pitressin, brain-extracts, etc., the response of the cardia was frequently opposite to that of the rest of the stomach. The majority of experiments reported in the literature were performed with one or multiple balloons and it is questionable whether those methods were able to record distinct action of the cardia.

Supported by U.S.P.H. Grants AM-06078-01-02. The Department is supported in part by the Michael Reese Research Found.

USE OF CO_2-INDUCED RESPIRATORY TRANSIENTS IN ANALYSIS OF RESPIRATORY CONTROL MECHANISMS. R. Gelfand,* C.J. Lambertsen and J. Downes*.
University of Pennsylvania, Philadelphia, Penna.

The time course of respiratory change caused by rapid alterations in blood P_{CO_2} or pH ought to reflect the time course of change of stimulus level at respiratory control sites. It may be possible to determine the characteristics of anatomically distinct sites by analysis of CO_2-induced respiratory transients. For this purpose, a rapid fall in arterial P_{CO_2} and pH is intentionally produced in normal unanesthetized man by abrupt removal of 6% CO_2 from inspired air after an equilibration interval. End-tidal P_{O_2} is held "constant", and V_t, f and $\dot{V}$ are automatically recorded for each individual breath. Experiments thus far, involving repeated measurements in a single individual, indicate the presence of three distinct functions of respiratory change. It appears that these functions can be adequately described as exponentials. An early component, starting about 6 seconds after the fall in end-tidal P_{CO_2}, accounting for about 15% of the CO_2 stimulation and having a time constant of about 8 seconds, may be due to peripheral chemoreceptors. A second component has a time constant close to 12 seconds and accounts for about 50% of the CO_2 stimulus. The third component has a time constant of about 120 seconds and accounts for the remaining approximately 35% of the CO_2 stimulus. The onsets of the latter two components both lag the onset of the first one by about 10 seconds and appear due to pH-P_{CO_2} sensitive sites in the CNS. The more rapid component may represent a site where P_{CO_2} changes closely parallel those in circulating blood. The slower component may reflect a damping influence by relatively avascular CNS tissue masses upon the rates of P_{CO_2} change at chemically sensitive neurons.

ACTIONS OF HIPPOCAMPUS ON SUBCORTICAL NEURONES IN THE SQUIRREL MONKEY. J. A. Gergen (intro. by C. D. Hendley), Bowman Gray School of Medicine, Winston-Salem, N. C.

The effects of hippocampal stimulation on single unit activities in the septum, hypothalamus, thalamus and caudate nucleus of the squirrel monkey (Saimiri sciureus) have been studied following isolation of units with etched steel microelectrodes in the cerveau isole preparation. Analysis is carried out by plotting post-stimulus time histograms following electrical stimuli delivered at frequencies of 0.25-10/sec to the posterior ventral hippocampal formation and fornix. Effects on firing patterns induced by hippocampal seizures have also been analyzed. Of 56 units studied in the ipsilateral septum, seven are driven at latencies of 10-15 msec, 15 are recruited at latencies of 10-80 msec followed by a period of depressed firing, and 16 demonstrate only a period of depressed firing lasting up to 400 msec. For 11 units in the mammillary bodies, eight show recruitment at latencies of 20 msec followed by a period of depressed firing and two show only depressed firing. For 34 units in other hypothalamic areas, four show recruitment followed by depression and four show only depression for varying time intervals while four appear to be recruited. Of 16 caudate units, six show only questionable depression. Units unaffected by hippocampal stimulation itself may be profoundly affected by hippocampal seizures; response patterns are variable but effects may persist for 40 secs following cessation of seizure activity. Results indicate that quantitative analysis of extent and nature of hippocampal actions on subcortical neurones is feasible. (Supported by grant B-3992 from USPHS.)

THE EFFECT OF BREATHING 15%, 21%, AND 100% OXYGEN ON THE SHIVERING RESPONSE OF NUDE HUMAN SUBJECTS AT 10°C. F. Girling, Defence Research Medical Laboratories, Toronto, Canada.

Six volunteer subjects wearing swim trunks only, were exposed to an ambient temperature of 10°C for 90 minutes or less, depending on the time to development of continuous, generalized shivering. Each subject was exposed three times, each time breathing a gas mixture of different oxygen content. Minute ventilation and per cent oxygen in the expired air were measured continuously. An observer recorded all movements of the subject noting the incidence of shivering and the onset of severe and continuous generalized shivering. When breathing 15% oxygen, the times to onset and to severe shivering were less than those observed when 21% oxygen was breathed. In the sense that shivering occurs earlier, the breathing of 15% oxygen enhances shivering. When 100% oxygen was breathed, the times to onset and to continuous shivering were increased, that is, shivering occurred later than when breathing 21% oxygen. Once severe continuous shivering was established oxygen consumption was the same with all three breathing mixtures. It has been shown that an increased partial pressure of oxygen in the tissue changes the threshold of temperature sensation. It is suggested that such an increase resulting from an increased concentration of oxygen in the breathing mixture lowers the temperature threshold of peripheral receptors, delaying the onset of shivering.

DISTRIBUTION AND GRADIENT OF LACTATE BETWEEN BLOOD AND HEART MUSCLE. V.V. Glaviano, A. Appel* and J. Doersching* Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Illinois.

The concept that blood lactate is in equilibrium with myocardial concentrations of this substrate could not be demonstrated in this laboratory. In 10 of 30 anesthetized dogs, one of the variables affecting this concept was the distribution of lactate in the myocardium. Levels in the right atrium (2.41 mM/kgH_2O) and left atrium (2.52 mM/kgH_2O) were markedly different from those found from base to apex of right ventricle (4.46 to 5.25 mM/kgH_2O) or left ventricle (3.37 to 4.24 mM/kgH_2O). In 10 of the remaining 20 dogs, increasing the arterial concentration of lactate to 80mg% by infusions did not alter significantly the myocardial content of lactate, although levels of this substrate in arterial and coronary sinus blood were increased by 5 to 8 times the control concentration. In another group of 10 experiments, samples of left ventricular muscle were made anoxic by graded ischemia. A linear relationship was found to exist between the duration of anoxia and the resulting lactate concentration. These data enabled us to calculate by linear regression analysis the "in vivo" concentration of lactate in the left ventricle. The results show this substrate to be present in higher concentration in heart muscle than in arterial blood, indicating the existence of an active transport system, rather than a system involving simple diffusion. (Supported by grant nos. ONR 3502 01 and HE 08682-01 from NIH.)

EFFECTS OF HEART RATE ON CARDIAC DIMENSIONS IN UNANESTHETIZED MAN: STUDIES DURING ELECTRICAL PACING. Gerald Glick*, John F. Williams, Jr.*, Donald C. Harrison*, Andrew G. Morrow*, and Eugene Braunwald. Natl. Heart Institute, Bethesda, Md.

In many investigations of cardiovascular function, interventions are employed which change heart rate. Since knowledge of ventricular size is of fundamental importance in elucidating problems in cardiac dynamics, a study was undertaken to define the effects of alterations in heart rate per se on cardiac dimensions in intact, conscious man. At corrective cardiac surgery, radiopaque markers were sutured to the surfaces of one or both ventricles in 9 patients. At postoperative cardiac catheterization, cineradiograms were exposed at 30 frames/sec. and the distances between the markers were subsequently measured. Heart rate was altered in 4 patients with a radio-frequency pacemaker which stimulated the left ventricle, and in 5 patients with a bipolar electrode catheter in the right atrium. As heart rate was increased (Av. 73 to 127/min.) RV end-diastolic and end-systolic dimensions decreased significantly in 4 patients and remained unchanged in 1. The decline in RV end-diastolic size averaged 7.2% while the decrease in RV end-systolic size averaged 4.9%. LV end-diastolic length diminished in every patient, falling by an average value of 6.0%. LV end-systolic length did not change in the 3 patients in whom the ventricle was stimulated, but decreased by 9.4% and 4.0% in the 2 patients in whom the atrium was stimulated. Stroke excursion usually decreased as heart rate was elevated, since end-diastolic length decreased more than end-systolic length. When pacing was suddenly discontinued, the ventricle returned to its control size within 2 cardiac cycles. In interpreting the influence of drugs and interventions on the human heart, it is thus necessary to consider that tachycardia per se may reduce ventricular end-diastolic volume by as much as 50% of the control stroke volume.

NON-SPECIFICITY OF THE DIVALENT CATION CAPABLE OF RESTORING NORMAL INTESTINAL PERMEABILITY AFTER CHELATION DEPLETION.
A.M. Goldner*, M.M. Cassidy* and C.S. Tidball. Physiology Department, The George Washington University, School of Medicine, Washington, D. C.

It is now established that removal of divalent cations from the mucosa of the small intestine markedly increases the passive aqueous permeability of this epithelial membrane. The present report deals with the differing abilities of alkaline earth ions to reinstate normal permeability after divalent cation depletion by sodium ethylenediaminetetraacetate. Acute experiments were performed on male albino rats in vivo. The intestine was divided into three segments containing equal numbers of vascular arcades. Control and experimental segments were randomized. The absorption of phenolsulfonphthalein was used as an index of aqueous permeability. All solutions placed in the intestinal lumen were at pH 7.0 and 300 mOsm/l. Permeability restoration was possible with all of the ions tested at concentrations below 50 mEq/l. Well defined peaks of restorative ability for each alkaline earth were positioned along the concentration axis in their periodic order: $Be^{++} < Mg^{++} < Ca^{++} < Sr^{++} < Ba^{++}$. This biological specificity pattern suggests a diffusion barrier concept in terms of charge fluctuation interactions based on London-van der Waals forces. The normal interactions are believed to involve Mg^{++} or Ca^{++} and to be located within the junctional complex between epithelial cells.

(Supported by U.S.P.H. Grant 5-T1-HE 5358-05 and NSF Grant GB 1949)

EFFECT OF HISTAMINE ON JEJUNAL SECRETION AND MOTILITY.
Dale P.J. Goldsmith and E.S. Nasset, University of Rochester, Department of Physiology, Rochester, New York.

Dogs were provided with jejunal Thiry-Vella fistulas and injected intravenously every 30 min for 3 hr with 0.9% NaCl or histamine. Motility was measured by means of miniature balloons inserted into the fistulas and connected to pressure transducers and a Grass recorder. Area under the recorder tracing was taken as a measure of motility. Rate of secretion and intensity of motility during the 15 min immediately following injection of histamine were similar to values observed in saline experiments. Secretion and motility 15-30 min after injection of histamine were usually reduced below normal. Total secretion and motility during the 3-hr histamine experiments were never elevated above corresponding values from saline runs. An absolute increase in secretion was obtained by injecting histamine every 15 min for 1 hr. These results suggest that histamine has both depressant and stimulative effects on secretion of succus entericus from a Thiry-Vella fistula and that it has depressant effects on jejunal motility. There was no consistent correlation between secretion and motility. In one set of histamine experiments, average motility during the period 15-30 min after injection of histamine was depressed, while secretion was normal. In another set of experiments, total secretion during the 3 hr of a histamine experiment was decreased while total motility was unchanged.

TRANSPORT OF p-AMINOHIPPURATE (PAH) BY RAT KIDNEY SLICES IN THE PRESENCE OF SODIUM AZIDE. Leon Goldstein and Matthew S. Loewenstein.* Harvard Medical School, Boston, Mass.

The kinetics of PAH entry into rat kidney slices incubated in the presence and absence of sodium azide (37mM) at 30°C and in cold (0°C) were investigated. The slice/medium (S/M) ratios after one minute incubation in medium containing 0.74mM PAH were 0.54 ± 0.03 (mean ± S.E.) in the absence of azide, 0.30 ± 0.02 in the presence of azide and 0.18 ± 0.02 in cold. The S/M ratio at equilibrium in cold was 0.30, a value approximating that of the extracellular space. The S/M ratio at equilibrium in azide was approximately 0.65. Lack of active transport of PAH in the presence of azide was evidenced by the failure of 2,4-dinitrophenol (.1mM), sodium iodacetate (3mM) or lowering the PAH concentration in the medium to significantly alter the S/M ratios. Addition of probenecid to the incubation medium at a concentration equimolar with that of PAH markely inhibited the uptake of PAH in the presence of azide. These results indicate that the entry of PAH into azide poisoned kidney cells is carrier mediated. Slices obtained from the kidneys of female rats transported PAH at two-thirds the rate of those obtained from male rats both in the absence and presence of sodium azide. Supported by U.S.P.H.S. grant AM-06511.

GASTRIC MUCOSAL TEMPERATURE DEPRESSION NECESSARY TO PRODUCE PROLONGED ACHLORHYDRIA. R. L. Goodale, Jr., J. P. Delaney, F. A. Largiader, (Intr. by H. L. Taylor)
University of Minnesota Medical School, Minneapolis, Minnesota

This study proposes to define what minimal mucosal temperature depressions and durations are necessary to provoke achlorhydria to secretory stimulants in the isolated canine gastric pouch and intact stomach. Persistent achlorhydria after gastric freezing undoubtedly depends on a time-temperature relation. Of 31 isolated pouches frozen at -20°C inflow for 1 hr. 12 to 30 mos. ago, 28 such pouches are still achlorhydric. These temps. and times exceed the minimal requirement for prolonged achlorhydria. In another group of 17 dogs, thermocouples were sewn into the mucosal layer of the pouch. In 9 cases, a mucosal depression of -4° to -5°C for 20 min. with temp. kept under 0°for a total of 40 min. provoked achlorhydria to meat stimulus for 9. 5 wks. In 3 dogs, lowering the temp. to -6° to -8°, while shortening the subzero period to 20 min., produced only 4. 6 wks. of achlorhydria. However, extending the duration under 0° to 40 min., the lowest temp. at -6° to -8°, slightly increased the duration of achlorhydria in 5 dogs to 11. 5 wks. The tolerance of the intact stomach to freezing is less than the sterile and drained pouch with no function to perform. Mucosal temp. of -4° to -5° for 25 min. and kept under 0° for 45 min. provokes histamine-fast achlorhydria for 1 wk. After refreeze, 2 wks. of achlorhydria are produced. Whether mucosal temp. depression necessary to produce protracted achlorhydria in intact stomachs can be achieved remains to be determined. (Sup. by USPHS Grant, Hartford Foundation & D. J. Cowling Grant)

CONSUMPTION OF ETHANOL BY THE ISOLATED PERFUSED RAT LIVER. E.R. Gordon (intr. by H. Frankel). Center of Alcohol Studies, Rutgers - The State University, New Brunswick, New Jersey.

Investigation of the consumption of ethanol by the isolated perfused rat liver revealed a dependence of consumption on the aeration of the blood. When blood is aerated with a mixture of 95% O_2 and 5% CO_2, extremely high rates of ethanol consumption are observed; when aerated with 18% O_2, 5% CO_2 and 77% N_2 a much lower rate of consumption occurs. Examination of the consumption curves when the initial dose of ethanol is 200 mg./100 ml. indicated that two quite different mechanisms are involved since the consumption of ethanol in the presence of 95% O_2 falls off exponentially with a $t_{\frac{1}{2}}$ of the order of 35 minutes; whereas consumption for the lower oxygen aeration is constant, typically 25 mg./100 ml./hr./10 g. of liver. The formation of acetone in the system aerated with 18% O_2 remains within normal levels. In the system aerated with 95% O_2 the acetone increased at least 5 fold. Pyruvic, lactic and glucose concentrations in the perfusate were also measured. These data indicate the possibility that a high oxygen concentration in the perfusate removes the rate limiting step in the consumption of ethanol by the liver.

CALCIUM, STRONTIUM AND PHOSPHATE ACCUMULATION IN RAT BRAIN MITOCHONDRIA DURING NEONATAL MATURATION. R.J. Grabske*, T.C. Fuller*, and F.E. Samson. Univ. of Kansas, Lawrence, Kansas.

There is abundant evidence in the literature that mitochondria isolated from several types of tissues actively accumulate divalent cations. The question was raised: Is there any change in the capacity of the mitochondrial population of brain to accumulate these ions during neonatal maturation? Brain homogenates from rats 1, 5, 10 and 21 days old were studied. Sucrose gradient centrifugation of brain homogenates show corresponding distributions of radioactive Ca^{++}, Sr^{++}, inorganic phosphate, (P_i) and succinic dehydrogenase, indicating that the accumulation of these ions is specific to the mitochondria in brain. Trace quantities of Ca^{++} and Sr^{++} are rapidly and completely removed from the homogenization medium by the mitochondria. P_i is taken up coincidently with the cations. The calcium binding activity per unit weight of brain increases by a factor of 2.2 during the first 21 days of maturation. Filtration on filters with various known pore sizes (Millipore) of isolated mitochondria, labeled with Ca^{45}, from various aged rats indicates that there is no major change in the mitochondrial size with neonatal maturation. It is concluded that brain mitochondria actively accumulate divalent cations as do the mitochondria of other tissues and that the increase in energy flow, characteristic of neonatal cerebral maturation, coincides with an increase in the number of mitochondria. (Aided by U.S.P.H.S. Grant 03070.)

THE RELATION BETWEEN HYDROGEN AND POTASSIUM ION GRADIENTS IN SKELETAL MUSCLE. J. J. Grantham* and P. R. Schloerb. Univ. of Kan. Med. Ctr., Kansas City, Kan.

The relation between the intra-extracellular hydrogen ion gradient (H_i^+/H_e^+) and the potassium gradient (K_i^+/K_e^+) in dog skeletal muscle was studied during metabolic alkalosis induced by either gastric juice loss or K depletion and $NaHCO_3$ loading. Intracellular pH was calculated from the distribution of C-14 labeled 5,5-dimethyl-2,4-oxazolidinedione (DMO), tritiated water and chloride-36. No change in H_i^+, K_i^+, or Na_i^+ was found in the alkalosis produced by gastric juice loss. Intracellular acidosis was detected in the K-depleted, $NaHCO_3$-loaded animals. Calculated intracellular HCO_3^- was increased in gastric alkalosis and decreased in K depletion alkalosis. Development of intracellular acidosis appeared to be related both to increased CO_2 tension and to alterations in tissue buffering due to K depletion. Irrespective of the method for inducing alkalosis, the relation $H_i^+/H_e^+ \cong K_i^+/K_e^+$ was found to be highly predictive. Selective changes in individual components of this relationship produced proportional changes in the gradients. It is concluded that a type of Donnan equilibrium modulates the transcellular distribution of potassium and hydrogen ions.

Supported by Research Grant HE 02363 from the National Heart Institute, NIH.

EXCHANGE OF CALCIUM BETWEEN BLOOD, BRAIN AND CSF. Graziani, L.*, Escriva, A.*, and Katzman, R. Albert Einstein Col. of Med., N.Y., N.Y.

In acute experiments Ca exchange between CSF and brain, and CSF and blood was determined in anesthetized cats. By continuous perfusion of the ventricular-cisternal system with synthetic CSF containing tracer amounts of Ca^{45}, the efflux coefficient of this system was determined. This value averaged .026 ml of CSF per minute cleared of Ca and remained constant with the perfusate calcium of 0 to 2.5 mM, indicating passive diffusion of calcium isotope from this system. Regional studies of the brain following these perfusion experiments indicate that the area of brain containing the most activity is immediately adjacent to the CSF pathway with no detectable activity beyond a 5 mm distance from these surfaces. The activity of the total brain averaged 4.97% of the total isotope in the perfusate. Since the rate of perfusion was .19 ml/min the efflux coefficient from ventricular-cisternal system to brain is .0094 ml/min. Hence Ca diffuses from CSF both into brain and into serum. When the Ca^{45} was given to cats systemically the influx coefficient of isotope into the ventricular-cisternal system averaged .018 ml of serum/min effectively cleared of Ca^{45}. In these experiments the specific activity of the CSF calcium becomes equal to the specific activity of the serum during perfusion. Since at this time the radio-activity of brain Ca is very low the chief source of the CSF Ca is the serum. Thus the influx of Ca is from serum, its efflux to both serum and brain. By altering the pH of the synthetic CSF the formation of CSF, as determined from inulin dilution of the perfusate, diminishes or ceases. However, the concentration of isotope entering the CSF from the systemic source does not change in relation to the change in CSF formation, suggesting that Ca entry is independent of CSF formation. (NIH B-1450)

PSYCHOLOGICAL ASPECTS OF FAMILIAL DYSAUTONOMIA. Helen Greenberg*and S.Bernard Wortis.N.Y.U.Medical Center,N.Y.

A psychological test battery was administered to a dysautonomic group ranging in age from 6 years to 22 years of age. Intellectual functioning, visual-motor performance and projective drawings were evaluated and scored by standard procedures. We found that the dysautonomic sample had average intelligence, as measured by the Wechsler Intelligence Scales, though there was a significant difference between verbal and performance abilities. A specific pattern of scores emerged in this sample that is different from any reported in the literature. The dysautonomic sample was significantly higher ($p < .01$) in abstract thinking and significantly lower ($p < .01$) in a perceptual motor task than the mean of their subtest scores. The appearance of both a higher 'Similarities' and a lower 'Object Assembly' was significant at $p < .02$ on a test of significance. Bender-Gestalt reproductions were markedly immature and similar to the reproductions drawn by patients with known organic pathology. Figure drawings, scored objectively, were immature and displayed gross distortions in body image. Mental ages obtained on this test were significantly lower ($p < .01$) than chronological age and intellectual functioning. We found that the dysautonomic sample was not mentally retarded, but had specific difficulties in perceptual motor tasks, especially those dealing with body image.

EFFECT OF VAGAL ACTIVITY AND ACETYLCHOLINE ON REPOLARIZATION AND OXYGEN UPTAKE OF THE HYPERKALEMIC MAMMALIAN VENTRICLE. Kalman Greenspan, Charles Wunsch* and Charles Fisch*. Krannert Heart Research Institute, Indianapolis, Indiana.

The effects of vagal stimulation and acetylcholine on repolarization and oxygen uptake of the normokalemic and hyperkalemic mammalian ventricle were investigated. In the in-vivo dog with normal plasma potassium levels, stimulation of the vagus altered the amplitude and configuration of the T waves. During potassium chloride infusion the T waves became upright and increased in amplitude. As the plasma potassium levels increased, the amplitude of the heightened T waves were further enhanced with vagal stimulation. These results demonstrated that vagal activity does affect ventricular repolarization and the effect is exaggerated as the plasma potassium level is progressively elevated. It therefore seemed important to determine whether acetylcholine could affect other physiological properties of the mammalian ventricle. We chose to study the effect of acetylcholine upon the resting oxygen consumption of the quiescent hyperkalemic rat papillary muscle. It was found that the perfusion of Tyrode's solution containing four times normal potassium increased the resting oxygen uptake. However, the potassium enhanced oxygen uptake was consistently reduced by the addition of acetylcholine to the perfusion fluid. Whether the relationship between potassium and acetylcholine is a synergistic one, as it is on ventricular repolarization, or antagonistic, as on oxygen consumption, depends on a number of factors; one of which may be the concentration levels of these agents. (Supported by Krannert Fund, and in part by USPH Grant H-6308 and Training Grant 5363.)

STUDIES ON THE PHYSIOLOGY OF VASOPRESSIN. (2) EFFECTS OF VASOPRESSIN ON RENAL CREATININE EXCRETION SUGGESTING AN EXTRA-TUBULAR RESPONSE. Edward H. Grinnell*, Willard M. Duff* and Jeno Kramar. Creighton Medical School, Omaha, Nebraska.

Regulation of plasma osmotic pressure by a specific action on the renal tubules without changes in glomerular filtration rate is considered to be the characteristic feature of vasopressin. The concept that ADH is devoid of glomerular activity seems to be so well established that some investigators feel any AD effect which is accompanied by a marked decrease in glomerular filtration rate, as indicated by a concomitant deficit in creatinine excretion, should be considered as being due to a vasoactive plasma substance rather than to vasopressin. Using creatinine excretion as an indicator of glomerular activity after injection of physiological doses of arginine-8-vasopressin we have consistently observed a biphasic change in the creatinine excretory rate (decrease followed by increase). These changes, as a rule, can be seen only when urine samples are collected in frequent brief (2-3 minute) intervals. These observations were made on rats hydrated and anesthesized with ethanol. Preliminary studies on trained unanesthesized dogs are in agreement with the observations on alcoholized rats. Clearance studies in progress will ultimately test the correctness of our assumption that renal vascular effects of vasopressin do have physiological importance.

ADRENERGIC ACTION OF NICOTINE ON ISOLATED VASCULAR SMOOTH MUSCLE. M. Gross* and D.F. Bohr. Dept. of Physiol., The University of Michigan, Ann Arbor, Michigan.

Nicotine in concentrations above 0.01 mM causes contraction of isolated helical strips of rabbit aorta. This contraction is blocked by dibenamine (10^{-6}), and does not appear in strips taken from reserpinized rabbits (5 mg/kg 24 hours prior to experiment). Nicotine (0.5 mM) causes relaxation of isolated helical strips of dog coronary arterioles (400-500 μ), as do norepinephrine (10^{-9}) and epinephrine (10^{-9}). Both nicotine and catecholamine relaxation are blocked by nethalide (10^{-6}). In the presence of nicotine (0.01 mM) epinephrine contractions of aortic strips show no depressed fast component, as might be expected if nicotine loosened bound calcium (Nayler: A.J.P. 205: 890, 1963). Nicotine in concentrations subthreshold to that required for contraction (0.001 - 0.005 mM) does not hasten the loss of epinephrine contraction in calcium-free physiological salt solution. Both lines of evidence indicate that the mechanism of action of nicotine on vascular smooth muscle does not involve calcium mobilization. We conclude that the vascular effects of nicotine on isolated aortic and coronary smooth muscle are mediated entirely through the release of norepinephrine. (Michael Gross is a Trainee, Cardiovascular Research Training Program, HTS-5465, National Institutes of Health).

EFFECT OF SUCKLING UPON PITUITARY GROWTH HORMONE (STH) CONCENTRATION IN THE LACTATING RAT. Clark E. Grosvenor. Dept. of Physiology and Biophysics, University of Tennessee, Memphis, Tennessee.

Injections of STH markedly improved lactation in rats deprived of spinal cord connections between the mammary gland and the CNS. (Fed. Proc. 23:205, 1964) These data suggested that in the rat, STH may be normally released in response to the nursing stimulus. To test this idea, anterior pituitary (AP) glands were obtained on postpartum day 14 from a) lactating rats 10 hrs. after being separated from their litters (Pre-nursed) and b) from lactating rats separated from their litters for 10 hrs. then reunited and nursed for 30 minutes (Post-nursed). All rats were killed with ether. STH content of the pooled AP's was determined using the hypophysectomized immature rat tibia test. Six hypox rats were used for each dose level. 0.5 mg and 2 mg wet wt. AP/rat/day were the dose levels of the unknown: 12.5 ug or 50.0 ug bovine STH/rat/day were the doses of the reference standard. 2 mg/day of prenursed AP contained STH in amounts which exceeded the linear portion of the dose-response curve of the assay. Hence, the potency of each unknown was calculated also in terms of the response to the lower dose only.

Group	Assay design	λ	ug STH/mg AP
Prenursed AP	2+2	.374	176.8
(10 rats)	2+1	.224	186.2
Postnursed AP	2+2	.257	35.2
(10 rats)	2+1	.224	48.2

The marked decrease in concentration of STH in the postnursed AP in comparison with that in the prenursed AP suggests that considerable discharge of STH occurs in response to nursing in the lactating rat.
Supported by grant A-3637 and a Research Career Development Award from the USPHS.

DECREASE OF THE SODIUM PUMP ACTIVITY IN THE FROG SKIN IN A STEADY MAGNETIC FIELD. T. Gualtierotti* (intr. by E. Anderson). NASA, Ames Res. Ctr., Moffett Field, Calif.

Previous work showed (1963) that the sodium transport in the frog skin (Rana esculenta) (Koefoed-Johnson & Ussing, 1958) was decreased up to 30 per cent in a D.C. magnetic field of 700-1000 Gauss. Na 24 was used. To describe the course of the phenomenon in relation with the strength of the field, the effect of a magnetic field up to 10K Gauss has been investigated on frog skin polarization potential: At first, a sudden decrease, in absolute value, of skin polarization is observed, followed by a further progressive change in the same direction. The rate of this change seems to be proportional to the starting level of the skin potential. The threshold for the phenomenon is variable in the different animals and in different parts of the skin of the same animal. In bullfrogs it varied from 800 Gauss to 8K Gauss with the most common value at 5K Gauss. The decrease in the skin polarization seems to be due to partial inhibition of the active sodium transport as it disappears by blocking the sodium pump with asphyxiation, cyanide or ouabain. This effect is reversible within a certain intensity of the magnetic field, above which a permanent alteration is produced.

Functional Significance of Fibrinolysis in the Microcirculation. M. Mason Guest and Ted P. Bond, Department of Physiology, University of Texas Medical Branch, Galveston.

Cinephotography of the microcirculation in the mesentaries of dogs at high speeds (3200 frames per second) has been carried out to determine the locales of clot formation. When thrombin or thromboplastin are introduced into the circulation, either by infusion or by topical application, clots form in the small arteries but no evidence of clot formation is found in capillaries. Arterial vessels with diameters in the 50 to 100 μ range and venules of even larger diameter appear to be freely permeable to thrombin and to urokinase, an activator of profibrinolysin (plasminogen). Capillary endothelium and the intima of veins contain an activator of profibrinolysin. Apparently sufficient activation of the proenzyme occurs within the capillary bed to prevent the formation of clots. These observations will be demonstrated through the projection of some of the film which has been produced.

TIME COURSE AND GLUCOSE DEPENDENCE OF WATER ABSORPTION BY DOG INTESTINAL MUCOSA IN VITRO. A. A. Hakim *, A. C. Nolan *, and N. Lifson, Division of Urology and Dept. of Physiol., Univ. of Minn., Minneapolis; Dept. of Urology, Ancker Hospital, St. Paul, Minnesota

Membranes of dog small intestinal mucosa were mounted in an apparatus permitting continuous observation of water movement. With glucose in the bathing fluids (Krebs bicarbonate Ringer), the rate of water absorption (J_w) was practically constant for at least 1 hr. (means 213 $\mu l/cm^2$ for jejunum, 122 for ileum). Without glucose, J_w during the initial 10 min. was reduced by 50% in jejunum, and progressively decreased so that mean J_w for an hr was reduced by 80%. In ileum, the effects were similar but differences between glucose and non-glucose fluids were not as large. After 1 hr in the latter, the membranes showed marked deterioration by microscopic examination of both fresh and fixed specimens, particularly shredding of the surface of villi. The effects of a variety of substrates were tested, including lactate, pyruvate, succinate, fumarate, malate, and citrate. With the possible exception of fumarate and malate with ileum, none altered J_w in glucose-free media; and, to the extent studied, none maintained structural integrity. Glucose added after 30 min to glucose-free media or to media containing other substrates did not affect the subsequent course of water absorption. It is not clear to what extent stimulation of water absorption by glucose is due to an action on a specific water absorbing mechanism or to maintainance of membrane structure. Supported by Grant AM 06700 from the N. I. H.

Effect of augmented NaCl ingestion on hypertensenogenic response to aldosterone in rats. C. E. Hall and O. Hall*. Carter Physiology Laboratory, University of Texas Medical Branch, Galveston.

There are reports indicating that aldosterone given to rats (a) depresses blood pressure, (b) has no effect on it, or (c) causes hypertension unaffected by salt intake and without vascular lesions. This experiment was undertaken to determine whether the response to aldosterone was appreciably affected by augmentation of salt ingestion achieved by adding sucrose to a 1% NaCl drinking solution as described elsewhere. Forty young female rats of the Josamar strain were unilaterally nephrectomized. Twenty each received 0.25 mg of d-aldosterone acetate in sesame oil by subcutaneous injection twice daily, and twenty received only oil. Ten of each group drank 1% NaCl solution and ten drank 5% sucrose-1% NaCl solution. Either the presence of sucrose or the injection of aldosterone doubled the intake of 1% NaCl, but no further increase was noted when both were given. No rats on salt alone became hypertensive. Doubling the intake with sucrose caused hypertension in half the group, doubling it with aldosterone caused all rats to develop hypertension, whether on saline or sucrose-saline. Although sucrose augmented the hypertensenogenic effect of NaCl among otherwise untreated rats it failed to augment hypertension in aldosterone-treated animals, and actually appeared to protect these animals somewhat. Steroid-treated rats on NaCl often developed edema and ascites, not seen in those on sucrose-saline; furthermore the former had larger kidneys and more severe vascular lesions than the latter at comparable levels of hypertension. With aldosterone, vascular lesions were severe and widespread, being in no wise different from those which would have been expected in rats with desoxycorticosterone hypertension of comparable duration and severity. Sucrose-saline alone did not appear to cause significant lesions in this brief period even in hypertensive rats. Supported by PHS Grant RG-04833.

Sucrose appetite of rats and its exploitation in the rapid induction of salt hypertension. O. Hall* and C. E. Hall. The Carter Physiology Laboratory, University of Texas Medical Branch, Galveston.

Young female rats of two strains originally derived from Sprague-Dawley animals were found to have different levels of preference for sucrose solutions. Groups of unilaterally nephrectomized animals were given either water, 5% sucrose solution, 1% NaCl solution or a 5% sucrose 1% NaCl solution to drink. Both strains preferred sucrose solution to water, but addition of the sugar to saline increased its consumption by 50% in one strain and by about 100% in the strain with the greater preference for sucrose. Neither hypertension nor vascular lesions occurred when either water or sucrose solution was consumed. When 1% NaCl was ingested there was a slow onset of hypertension in some animals of both strains, but one had a greater sensitivity. When 5% sucrose 1% NaCl solution was consumed there was a rapid evolution of hypertension in a higher percentage of both strains and the difference in sensitivity apparent when only saline was consumed was no longer evident. This is attributed to the fact that the naturally more resistant strain had a greater sucrose appetite and therefore consumed more salt when the mixed solution was offered. The observed differences in the incidence and severity of hypertension among the several groups were supported by heart weights and abundance of vascular lesions. It is clear that rat strains display differences in sensitivity to the induction of salt hypertension and in their predilection for sweet solutions. Exploitation of sugar appetite enhanced the development of hypertension in both strains and eradicated the apparent difference in susceptibility. Supported by NIH Grant HE-04327.

FROG SKIN EXTRACELLULAR SPACE AND SODIUM DISTRIBUTION. P.L. Hall* and A.C. Brown. Dept. of Physiology and Biophysics, Univ. of Wash. Sch. of Med., Seattle, Wash.

The role of various tissue layers of frog skin in active transport of Na^+ was investigated by measuring the Na^+ distribution profile and intracellular concentration within the skin. The abdominal skin from pithed Rana pipiens was removed and soaked in a modified Ringer's solution ($[Na^+]$ = 100 mM) containing glucose, Na^{24}, inulin-C^{14}, and HTO. The skin was then rapidly frozen and sectioned (5-10μ) parallel to its face. Every third section was placed on a slide for identifiifaction of the cell types in that tissue layer. The other sections were counted for concentrations of the three radioactive isotopes in a liquid scintillation counter. The H^3 counts indicated total "space" of the section; the C^{14} counts indicated the extracellular space; and the Na^{24} counts enabled calculation of the Na concentration. From the outside of the skin inward, the fraction of extracellular space first decreased steadily, reaching 15-30% of the total space in the germinative epithelium, and then rose again to 80-100% as the inside surface was approached. The Na concentration began at about 40 mM, dropped steadily to about 30 mM in the germinative epithelium, and then rose progressively to 100-120 mM at the inside surface. The calculated intracellular Na in the germinative epithelium was no greater than 50 mM. From this it was concluded that (1) Na concentration distribution is consistent with active transport occurring in germinative epithelium; (2) all epithelial cells retained some ability to extrude Na^+; and (3) Na^+ moves against its concentration gradient in the sub-epithelial tissue. (Supported by PHS grant GM-08240.)

OBSERVATIONS ON SINUS ARRHYTHMIA IN THE DOG: Hamlin, R.L.*, Smith, C.R., and Smetzer, D.L.*, Department of Veterinary Physiology, The Ohio State Univ., Columbus, Ohio (43210).

During inspiration and immediately before, dogs anesthetized with morphine-chloralose exhibit increases in heart rate, systemic arterial pressure, dp/dt of left ventricular pressure during periods of isovolumic contraction and relaxation, and splitting of the second heart sound. Opposite changes occur during expiration; except that dp/dt remains elevated for the initial two systoles following onset of expiration when heart rate is slowest. Identical fluctuations persist following respiratory paralysis with succinyl choline, except for splitting of the second heart sound. All fluctuations--except the latter--may be attributed solely to irradiations from the respiratory centers such that during inspiration sympathetic tone rises and/or parasympathetic tone falls; while during expiration, the opposite is true. Increases in dp/dt during inspiration may not be explained by a Starling effect, since LVEDP decreases. dp/dt remains elevated during the cardiac slowing after onset of expiration due to a Starling effect, demonstrated by an elevation of LVEDP. Splitting of the second heart sound during or immediately after inspiration results from abbreviation of left ventricular ejection and/or the act of inspiration, but not from prolongation of right ventricular ejection.

VARIATION IN VENOUS OUTFLOW FROM MESENTERIC VEINS DRAINING CANINE SMALL INTESTINE IN SITU. S. Hantsoo* and H. S. Louckes, Dept. of Physiology, The George Washington University School of Medicine, Washington, D. C.

Intestinal blood flow was studied in acutely anesthetized, heparinized, fed or fasted mongrel dogs. The mesenteric vein draining one arcade was cannulated in situ and the outflow drained into 9.0 ml low pressure, air activated, self-bailing flowmeter (Metro Scientific Co.). The blood from the flowmeter was returned to the dog via the jugular vein. Observations made at the upper, mid and lower small intestine showed a rhythmic variation in flow, with a cycle length of 1 1/2 to 3 hours. This rhythmic variation appeared to be more pronounced when the flow exceeded 5 ml/min. The flow was increased transiently following i.v. nembutal or by clamping the intestine (mesenteric vessels excluded from clamp) within 2 arcades of the cannulated vein. No consistent variation in flow was attributable to the postprandial state. In 12 animals studied, the range of minimal flow rates was 1.1-5.1 ml/min; maximum flow rates ranged from 3.4-18.0 ml/min.

(Supported by a Grant NSF GB 1949)

DIETARY AMINO ACID PATTERN AND DIET SELECTION. A. E. Harper, Q. R. Rogers,* P. Leung* and K. C. Pant.* MIT, Cambridge, Mass.

Rats offered a choice between a diet containing 6 or 8% of casein supplemented with methionine (balanced diet) and a protein-free diet rejected the protein-free diet. Rats offered a choice between an imbalanced diet (balanced diet with a mixture of amino acids lacking threonine or tryptophan added) and a protein-free diet rejected the imbalanced diet which will support growth. When the amino acid imbalance was corrected by adding the missing amino acid (corrected diet), rats showed a preference for the corrected diet over the protein-free diet. Rats offered a choice between a protein-free diet and a diet containing enough leucine to create an amino acid antagonism involving isoleucine and valine ate the protein-free diet almost exclusively. Even when the antagonism was alleviated by supplementing the high leucine diet with isoleucine and valine, rats showed a decided preference for the protein-free diet. When rats were offered a choice between the high leucine diet and the same diet supplemented with isoleucine and valine, they ate primarily the nutritionally superior diet containing additional isoleucine and valine. These experiments provide examples of clear food preferences by the rat; examples in which the rat selects primarily a diet on which it cannot survive over one that will support growth. They also provide examples of clear preferences for diets that are nutritionally superior. The preferences appear to be learned responses. The rat apparently rejects an imbalanced diet because consumption of it is associated with some physiological disturbance which does not occur when a protein-free diet is ingested and selects a balanced or corrected diet over the protein-free diet because of some sense of well-being which is lacking when the protein-free diet is ingested. Rejection of the imbalanced diet is thought to be associated with changes in body fluid amino acid patterns.

URINARY CONCENTRATING ABILITY IN A STRAIN OF RATS WITH HEREDITARY HYPOTHALAMIC DIABETES INSIPIDUS. Avery R. Harrington* and Heinz Valtin, Department of Physiology, Dartmouth Medical School, Hanover, N. H.

Diabetes insipidus in this strain of rats appears to be inherited as an autosomal recessive trait. In respect to water intake, urine flow, and urine osmolality, heterozygotes occupy a position which is intermediate between normal animals and rats with D.I. Two 24-hour urine collection periods were done on 12 rats in each category. Mean urine osmolality was 2187 mOsm/kg in normals, 1376 in heterozygotes, and 133 in rats with D.I. The response of D.I. rats to exogenous vasopressin was tested by injecting 1.0 unit of Pitressin tannate in oil (Parke, Davis & Co.) subcutaneously, daily for 28 days. Twenty-four hour urine collections were obtained at weekly intervals during the period that injections were given. Mean urine osmolality in 4 D.I. rats rose progressively from 860 mOsm/kg after 2 injections, to 2172 mOsm/kg after 28 days of injections. In normal rats given equal amounts of Pitressin tannate in oil, urine osmolality rose to 2584 mOsm/kg after the first injection and rose no further even after 28 days of injections. Thus, the fluid balance of D.I. rats treated with exogenous vasopressin at first resembled that of heterozygotes and, with time, approximated that of normals. The data are compatible with the hypothesis that the concentrating defect in heterozygotes and in D.I. rats during the early period of vasopressin therapy, resides at the renal level, being due either to interference by oxytocin or an analogue of vasopressin or to anatomical changes. [Supported by U.S.P.H.S. Grants HE-06181 and AM 08469, and by the American Cancer Society.]

CIRCULATORY AND HUMORAL RESPONSES TO FEAR AND ANGER W. S. Harris *, C. D. Schoenfeld *, P. H. Gwynne *, A. M. Weissler *, J. V. Warren. Ohio State University Hospital, Columbus, Ohio.

In order to investigate the circulatory and humoral responses to emotion, cardiac catheterization and serial blood chemical studies were performed during 20 episodes of intense fear and anger induced by hypnosis in nine subjects. Three subjects were studied immediately before and during beta adrenergic blockade by intravenous nethalide. Fear resulted in mean changes of heart rate + 37 beats/min. (+55%), cardiac index + 1.05L./min./M^2 (+29%), stroke volume -13 ml. (-12%), arterial mean pressure + 10mm. Hg and peripheral resistance -19%. Anger produced similar hemodynamic responses. Respirations doubled and two-thirds of the subjects developed respiratory alkalosis. Plasma hydrocortisone doubled and, in two of three subjects, plasma nonesterified fatty acids also doubled. In three subjects repeat studies several weeks apart produced virtually identical results. Beta adrenergic blockade diminished the cardioaccelerator response to fear by two-thirds but did not change the responses of cardiac output, arterial pressure, or blood chemistries. The results indicate that the hemodynamic responses to fear and anger are identical, are constant for a given individual and are mediated, in part, by nonadrenergic mechanisms.

DIFFERENCE IN DEEP BODY TEMPERATURE BETWEEN MOTHER AND FETUS IN RABBITS. Frederick M. Hart* and J. Job Faber. Department of Physical Medicine and Rehabilitation, University of Washington, Seattle, Washington.

Fetal and maternal deep body temperatures were compared in New Zealand White rabbits of about four weeks gestation. A thermocouple junction inserted into the maternal aorta a few days before the experiment provided a continuous measurement of maternal deep body temperature during the experiment. Immediately after the animal and fetusses had been sacrificed by an overdose of warmed sodium pentobarbital, thermisters in 19 gauge needles were thrust into the fetusses through the intact abdominal wall of the mother and fetal temperatures were recorded to an accuracy of 0.1°C. Needle positions were verified at autopsy. Fetal deep body temperatures were higher than maternal by a few tenths of one degree centigrade.

On the assumptions that in the fetal rabbit about one-half of the cardiac output flows through the placenta, and that a rabbit placenta is a countercurrent exchanger, it could be calculated that fetal arterial temperature is approximately the average of maternal and fetal deep body temperatures. Published measurements of the umbilical A-V oxygen difference suggest that about one-half of the fetal metabolic heat is lost via its placental circulation. If the fetal oxygen dissociation curve varies with temperature as does the adult curve, oxygen is made available to the tissues at an increased tension. In this respect, a higher fetal temperature appears to be advantageous to the fetus.

REDISTRIBUTION OF RENAL BLOOD FLOW DURING ACETYL CHOLINE INFUSION. R. B. Harvey. Univ. Minn., Mpls.

Acetyl Choline (ACh) infused intraarterially is a potent vasodilator in several vascular beds including the kidney. In nembutalized dogs the left renal vein and ureter were cannulated. Blood flow was directly measured. Creatinine, and Para Amino hippurate, extractions (Ecr, Epah) were continuously measured by pumping blood from an artery and the renal vein through separate autoanalyzer systems. The accuracy of these systems was checked by drawing blood samples every 10 min. and analyzing for Cr, and PAH by conventional methods. ACh was infused at 0.25 mg/min. in isotonic saline through a 30-gauge needle into the renal artery. Control periods (saline infusion) were run before and after a 20-min. period of ACh infusion. Comparison of ACh infusion with control periods (C) revealed: 1, ACh increased RBF to 1.8 C; 2, ACh decreased Epah to 0.8 C; 3, decreased Ecr to 0.6 C; 4, increased GFR to 1.2 C; 5, increased Tpah to 1.5 C (arterial plasma PAH concentration remained constant at 2 mg % or less); 6, increased urine flow with decreased U/P CR, PAH, and osmolarity. The large fall in Epah indicates that the removal of PAH from plasma did not increase as much as the plasma flow increased. The failure of Tpah to keep pace with RPF might be attributed to a bypass or to reduced efficiency of extraction during ACh infusion.

Supported by PHS Grant #HE-07002

BODY COMPOSITION AND FOOD CONSUMPTION AS MODIFIED BY FEEDING PATTERNS. F. W. Heggeness, University of Rochester, Rochester, New York

Weanling rats were allowed to eat a nutritionally adequate diet to satiety three days, alternating with three days during which food was restricted to that required for weight maintenance. Control rats were fed the same diet ad libitum continuously. In experimental animals, total food intake was reduced, utilization increased, and body content of fat and protein transiently modified. Throughout the time of observation (8 mos.), experimental animals, during three-day period of unrestricted feeding, increased food consumption to 300% of that permitted during restricted periods. Amount was distributed approximately equally throughout the three days of ad libitum intake; no gastrointestinal hypertrophy developed. Total calories ingested were approximately 15% less than that of control group. Despite this lower total intake, experimental animals gained weight and accumulated solids at the same rate as controls. At 60 and 120 days, experimental animals contained significantly more fat but less protein than controls; these differences in body composition disappeared by 180 days. At all ages, food intake of experimental animals was significantly less than that of controls, suggesting that a modification of feeding pattern that does not interfere with growth modifies metabolism or activity.
(NIH Research Career Development Awardee K3-HD-14,904. Work supported, in part, by NIH H.D. 00009-01.)

EFFECTS OF EARLY EXPERIENCE ON THE BLOOD PRESSURE RESPONSE TO THE SOCIAL ENVIRONMENT. J.P. Henry, P. Stephens* and J. P.Meehan, Dept. Physiol., USC Sch. of Med. Los Angeles, Calif.

A previous abstract reported persistent hypertension in the Mercury orbital flight chimpanzee Enos. The condition was attributed to factors of restraint and training of an immature animal. (Meehan, Fineg and Mosely, Fed.Proc. 23: 515, 1964). In related studies of the effects of the social environment on the arterial pressure of a quickly maturing mammal normally raised and weaned CBA mice have been crowded eight to a 25 sq.in. box in place of the 55 sq. ins. usually alloted to six. (Henry & Stephens, Fed.Proc. 23:515, 1964). During 8 months of crowding the blood pressure has progressively risen, the average of the last six months being 158 mHg. To evaluate the effects of early experience, pregnant mice were confined to the 25 sq.in. enclosures. At 3 months the resultant crowded litters were thinned to two boxes, one containing 8 males and one 8 females. Pressures at this time and for four subsequent months have remained a normal 125-130 mHg. In a contrasting experience mice prematurely weaned at 2 weeks were maintained in isolation in boxes providing 100 sq.ins. per mouse up to age 3 months. They remained normotensive during isolation but on crowding eight (5 males, 3 females) to 25 sq.ins. the pressure immediately rose to a mean of 162 mHg. These pressures have been sustained for 6 weeks. The peaceable behavior and sleek physical appearance of the animals crowded from birth contrasts with the fighting and scarring of the crowded male "isolates." (Supported by a grant from NASA office of Space Sciences).

EXPERIMENTAL CYBERNETIC ANALYSIS OF DELAYED FEEDBACK OF BREATH-PRESSURE CONTROL. John Henry*, Richard Junas* and Karl U. Smith. Univ. of Wis. Madison, Wisconsin.

This research introduces experimental physiological cybernetic methods in investigation of delayed feedback of breath-pressure control. Seven subjects were used in a task requiring alignment of a cursor with a zero line indicating constant breath pressure. The analog signals from a breath-pressure transducer were converted to digital form and this digital signal then programed for delay by a general purpose laboratory computer. The programed digital signal was then deconverted to analog form and transduced as a delayed output visual feedback display to the subject. Accuracy of the breath regulation decreased as an inverse function of delay magnitude. This function, however, varied significantly with the delay magnitude on which the subject was trained over a period of twenty-five trials. Both the frequency pattern and the velocity characteristics of the movement varied markedly with delay magnitude, indicating that the dynamic feedback factors in cybernetic regulation, as contrasted to information time sampling, are primarily responsible for the governing of intraoral breath-pressure movements and possibly other aspects of respiration.

The experiment illustrates the way in which experimental cybernetic perturbation theory and related concepts of design of a laboratory closed-loop computer system are applied to systematic analysis of the feedback regulation of respiratory mechanisms.

FACTORS IN ACCLIMATIZATION TO WET HEAT. B.A. Hertig, H.S. Belding, K.K. Kraning* and H. Nagata*. Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Penna.

Benefits of acclimatization accruing from improvement in internal heat transfer (i.e., circulatory efficiency, as opposed to benefits of increased sweating and/or reduction of skin temperature) are unknown. In the present study, three young unacclimatized men pedaled an ergometer (metabolism at 2 met) two hours daily for 12 days, while immersed to the neck in warm water. With skin temperature fixed at 37.1°C by the bath, rectal temperature was forced to a level initially 1.2°C higher than skin, later only 1.0° higher. Equilibrium pulse rates later decreased slightly (about 6 beats/min), and later exposures were regarded by the volunteers as slightly less tiring. These changes are small in relation to the dramatic overall improvements associated with acclimatization to work in dry heat. On the other hand, sweating in the bath increased markedly (initially 600 g/hr, finally 1130 g/hr). On subsequent exposures to dry heat (50°C DB, walking at 5.6 km/hr) the subjects demonstrated that an advanced state of acclimatization had already been achieved; thus, exposure to wet heat can effectively acclimatize for dry. The data are consistent with the view that increased responsiveness of the sweating mechanism (Belding and Hatch: Fed. Proc. 22:881, 1963) rather than increased cutaneous conductance accounts for most of the improvement of acclimatization to heat. The observed reduction in core temperature is suggestive of subtle changes in internal heat transfer efficiency, and deserves further study. (Supported by Contract DA49-193-MD-2580, U.S. Army Medical Research and Development Command.)

THE EFFECT OF SHORT PERIODS OF AIR BREATHING ON OXYGEN TOXICITY IN MICE. Edwin Hiatt, Ronald Wright,* Judith Alden,* Harold Weiss. Ohio State University, Columbus, Ohio.

There is evidence in the literature that animals tolerate exposure to toxic concentrations of oxygen better if the exposure is interrupted by periods of air breathing. Our experiments were designed to determine the minimal proportion of time in air necessary to permit mice to survive exposure to one atmosphere of oxygen for prolonged periods. In a preliminary experiment all mice survived at least 17 days of exposure to one atmosphere of oxygen when they breathed air continuously for at least 8 hrs in each 24 hrs whereas with uninterrupted exposure to oxygen the median time to death was 5 days. In a second experiment 5 groups of 8 mice each were allowed 0, 2, 4, 8, and 24 hrs respectively of continuous air breathing in each day with the remainder of the day in 1 atmosphere of oxygen. The time to death of half the animals in the first 3 groups was 5, 8 and 10 days while the members of last two groups all survived the 27 day period of the experiment. Histological studies of the lungs indicated some reversal of the typical toxic effects of oxygen after periods of air exposure. In a third experiment four groups of 8 mice each were exposed to the following regimens: #1 -continuously in oxygen; #2 -48 hrs in oxygen alternating with 24 hrs in air, #3 -24 hrs in oxygen alternating with 24 hrs in air and #4 -continuously in air. Half of the animals in group 1 died within 6 days but the other groups survived the 16 day experiment. Decrease in weight and water consumption provide indices of oxygen toxicity. Animals which survived the intermittent exposures to oxygen did not show an increased survival time when exposed subsequently to one atmosphere of oxygen continuously. (This work was supported by NASA Grant NsG-295-62.)

DYNAMIC SURFACE POTENTIAL OF PULMONARY SURFACTANT AND ITS ACTIVE AND INACTIVE PHOSPHOLIPID FRACTIONS. T. R. Hill* and T. N. Finley, Dept. of Anesthesiol., Univ. of Wn. Sch. of Med., Seattle, Wn.

Pulmonary surfactant obtained by saline lavage in vivo in dogs was recently divided into its various phospholipid components and surface activity of these determined (T.N.Finley et al.Fed.Proc.23:2,1964). The most active fraction was lecithin whose fatty acid side chains were about 80% saturated. The least active fraction was a mixture of phosphatidyl serine (P.S.) and phosphatidyl inositol (P.I.) whose fatty acids were about 50% saturated. The surface tension (γ) versus area plots of all three showed hysteresis. By means of an air-ionizing electrode we measured dynamic surface potential (ΔV) of monolayers of these three substances spread on saline in a Teflon trough whose surface area was alternately compressed and expanded in 8 min. cycles. Simultaneously we measured γ by means of a modified Wilhelmy film balance. The measurements were made in nitrogen and room air and recorded on an X-Y plotter. Data obtained from the plots are as follows:

	V mv		dynes/cm		slope: mv/(dyne/cm)		
% area	20%	100%	20%	100%	20%	100%	Hysteresis
Surfactant, Lecithin	400	250	10	40	3	10	yes
P.S. + P.I.	350	255	17	27	11	11	no

Hysteresis and change in slope may be related to the molecular characteristics responsible for ΔV and γ. ΔV (a function of the vertical dipole moment and molecular concentration per unit area) is a resultant of the charge separation mainly present in the phosphytidyl group and γ may be influenced mainly by the saturation of the fatty acid side chains. (Supported in part by USPHS Grant #HE-075502).

Role of the Liver in Endotoxin Shock. L. B. Hinshaw, D. A. Reins*, M. M. Jordan* and F. D. Masucci*, Cardiovascular Section, Physiology Branch, Civil Aeromedical Research Institute and Department of Physiology, University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

The purpose of this study was to determine the vascular response of the liver to lethal injections of endotoxin. Experiments were carried out on the isolated perfused dog liver and hepatic artery and vein strips. In twenty-four experiments vessel strips attached to a force transducer were placed in a continuously oxygenated blood-filled reservoir. The liver was transferred to a heart-lung or dog-pump apparatus in twenty-seven experiments, continuously weighed and perfused at constant flow via both arterial and venous inflow vessels. Marked increases in hepatic arterial and portal venous pressures, resistances and organ weight were observed within one minute after endotoxin injection. The greatest increase in pressure was observed to occur in the hepatic arterial segment. These responses were duplicated by histamine and 48/80, but not by catecholamines, acetylcholine or 5-hydroxytryptamine; they were not blocked by phentolamine. A leg bioassay preparation, placed immediately downstream from the liver, ordinarily responded by vasodilatation and a steady gain in leg weight was observed following endotoxin administration to the liver. Isolated vessel strips, though readily responsive to small injections of epinephrine and histamine, constricted to endotoxin in about thirty per cent of the trials. Evidence points to the intrahepatic venous system as the primary site of response to endotoxin with a subsequent active vasomotor change in the hepatic arterial segment (USPHS grant no. A-6313).

DETERMINANTS OF CARDIAC MINUTE OXYGEN CONSUMPTION. L.J. Hirsch*, R. Antic* and L.N. Katz. Cardio. Inst., Michael Reese Hosp. & Med. Cntr., Chicago, Ill.

A series of 19 experiments with a right heart bypass preparation, with controlled cardiac output, was used to compare myocardial oxygen consumption (O_2C) per stroke with that per minute. The O_2C/stroke remained constant without relation to heart rate (HR), over a wide range (88-186/min.), but correlated well with aortic pressures (AP). These observations show that in these experiments, AP determined O_2C/stroke. O_2C/min., however, increased with HR, thus, O_2C/stroke sets O_2C/min. Therefore, HR contributes to O_2C/min. simply to the extent of summating the energy expended by single beats. Coronary blood flow (CBF) showed the same relationships as O_2C but with wider variation. The relation of left ventricular peak pressure (LVPP) to O_2C when AP is kept constant was observed in the isovolumic preparation (with a balloon in the left ventricle set at a known volume); HR being controlled by external pacing. O_2C/stroke again followed the changes in LVPP to a remarkable degree and O_2C/min. also followed HR. Thus, O_2C/min. is not only determined by HR, but by factors which set O_2C/stroke. The most important factor controlling the latter is AP or more accurately LVPP, serving as an index of ventricular wall tension created.

STIMULATION OF GASTRIC ACID AND PEPSIN SECRETION BY 2-DEOXYGLUCOSE IN THE DOG. B. I. Hirschowitz, and G. Sachs*. Division of Gastroenterology, Department of Medicine, University of Alabama Medical Center, Birmingham, Alabama.

2-Deoxy-D-glucose (2-DG) presumably acts by preventing glucose utilization by the cells. 2-DG in doses of 25, 50, 100 and 200 mg/kg was injected intravenously at the rate of 7 mg/kg/minute into fasting trained conscious dogs each equipped with a Komarov esophagostomy and a gastric cannula. Gastric secretion of acid and pepsin started 15-18 minutes after the start of the infusion and continued for as long as 5+ hours. A linear dose response curve was obtained, with 25 mg producing no secretion and 200 mg/kg resulting in almost 200 times as much pepsin and more than 2.5 times as much acid secretion as a maximal dose of histamine given subcutaneously. When 200 mg/kg 2-DG was injected I.V. during a continuous maximal histamine infusion, there was no change in volume, acid or electrolyte secretion, but a significant increase in pepsin output occurred. This effect was depressed by ± 50%, but not eliminated, by the simultaneous injection of 0.08 mg/kg atropine sulfate. It is thus concluded that 2-DG stimulates gastric secretion, probably by vagal excitation dependent upon the induction of glucocytopenia in the vagal centers.

REVERSAL OF CONTRACTILE RESPONSES TO CHEMICAL MEDIATORS IN SMOOTH MUSCLE. Leif Horn (intr. by V. B. Brooks). Department of Physiology, New York Medical College, New York.

Reversal of the contractile responses of smooth muscle can be accomplished *in vivo* and *in vitro* by means influencing the metabolic state of the muscle. Muscle strips from rat stomach in Ringer's solution at 37°C increase isometric tension in response to 10^{-6}M acetylcholine. The preparations, normally relaxing to epinephrine, can be made to contract in response to the catcholamine when preincubated with acetylcholine. This effect does not appear in preparations that were treated with 10^{-6}M chlorpromazine. Bradykinin, 10^{-7}M, which normally elicits a contraction of the muscle, relaxes preparations pretreated with acetylcholine and 10^{-3}M cyanide. Inhibition of terminal oxidation with cyanide alone does not reverse the contractile responses to the mediators used. These data do not fit the conventional view that epinephrine merely potentiates acetylcholine action in experiments such as these. Instead one may consider the reversed muscle responses in terms of acetylcholine-induced metabolic changes affecting the redox state of the muscle.

This work was carried out at New York University Medical Center, supported by U. S. Public Health Special Fellowship HF10678 and grants from John A. Hartford Foundation, Inc., and American Heart Association, Inc.

ACID BASE BALANCE BETWEEN CSF AND ARTERIAL BLOOD IN PATIENTS WITH A RESPIRATORY DISORDER. Chin-Tang Huang,* and Harold A. Lyons. State University of New York, Downstate Medical Center, Brooklyn, N. Y.

Using paired arterial and cerebrospinal fluid (CSF), pH, PCO_2 and HCO_3 levels, relationships were examined for 53 patients with a respiratory disorder. CSF was obtained by lumbar collection and each ventilatory state existed for days. The abnormal ventilatory states were associated with hypocarbia (17 pts.), and hypercarbia (13 pts.); and normocarbic (23 pts.). The data were separately analyzed for each, except the severe hypercarbic state ($PaCO_2 >$ 65 mmHg) was determined as a third group and compared to that of normals. With abnormal arterial carbon dioxide tensions and pH, large changes of HCO_3^- in blood was accompanied by small changes in CSF. Spinal fluid pH was maintained within the normal range ($7.343 \pm .035$). However, for the grossly hypercarbic state CSF pH was lowered with large changes in HCO_3^-. In this last state the CSF-arterial gradient for PCO_2 and pH is similar to the normal but at a very different level for each. The data suggest that whatever mechanism is acting that the cerebrospinal fluid pH is maintained fairly constant within certain limits of change but beyond these limits the CSF pH can no longer be held constant.

(Supported by U.S.P.H.S. Grant NB 01594.)

RESPONSES OF MONKEY GENICULATE CELLS TO MONOCHROMATIC AND WHITE SPOTS OF LIGHT. D.H.Hubel & T.N.Wiesel, Dept.Pharm.Harvard Med.School, Boston.

In a series of 12 anesthetized Rhesus monkeys we have examined the receptive fields of 223 geniculate cells in the light adapted state. In each of the four dorsal layers three main classes can be distinguished. With white light a cell of the first type resembled cat geniculate cells in having receptive fields with on-center and off-surround, or the reverse. With monochromatic light the receptive fields of these cells had two antagonistic components, an excitatory and an inhibitory, which were different not only in spatial distribution but also in spectral sensitivity. The spectral peaks of the two antagonistic components were found in the following combinations: long wavelength on-center(peak about 580mu) & middle off-surround(peak about 540mu); long off-center & middle on-periphery; middle on-center & long off-surround; middle off-center & long on-surround; short on-center (peak about 450) & middle off-surround. The second type of cell resembled the first in having two antagonistic components with different spectral sensitivities: they differed in that the spatial distributions of the two components were identical; there was no center-periphery arrangement. Peripheral suppression did not occur at any wavelength, and the interaction between the two overlapping systems did not depend on spot size. Four subtypes were found: short on/middle off, short off/middle on, middle on/long off, and middle off/long on. The peak sensitivities (450,540,580 mu) of the excitatory and inhibitory systems in color-opponent geniculate cells are consistent with the peak absorption spectra recently described for three types of cones in the Rhesus monkey. Cells of a third type were similar to on-center or off-center cat retinal ganglion cells and geniculate cells: the center and surround of their receptive fields had identical spectral sensitivity. Some had on-centers, others off-centers.

CHANGES IN BLOOD CIRCULATION IN SKELETAL MUSCLE UNDERGOING ATROPHY. O. Hudlická, P. Hník and B. Štulcová (intr. by E. M. Renkin). Institute of Physiology, Czechoslovak Academy of Sciences, Prague.

Muscles of rats were tenotomized, and their vascular volumes measured with Cr^{51}-labelled erythrocytes 7 days later. Paired unoperated muscles served as controls. Absolute vascular volume in different muscles increased in proportion to the loss of weight due to atrophy. Blood flow was measured in m. gastrocnemius of cats at various times after tenotomy. Total flow exceeded that of the control muscle in proportion to the developing atrophy. CO_2 and lactate output (measured by A-V difference and blood flow) of the atrophic muscle increased, and afferent output measured by integration of activity from the sectioned whole nerve increased. These observations suggest that metabolic changes in the atrophic muscle might increase blood flow by stimulating afferent nerve fibers. If section of dorsal roots in rats was performed 3 days before tenotomy, the increase in vascular volume was diminished or absent. In the perfused cat gastrocnemius, increasing or decreasing blood flow produced an increase or decrease, respectively, in integrated afferent nerve activity. The mechanism linking changes of afferent nerve activity and changes in blood flow is under investigation.

EVOKED MYOGRAPHY AS AN INDEX FOR DIFFERENT STAGES OF CONSCIOUSNESS. J. Huertas* (intr. by D. Feller). NASA, Ames Res. Ctr., Moffett Field, Calif.

Up to now the physiologists have studied the monosynaptic reflexes of the spinal cord by a technique which involves the surgical exposure of the posterior roots to stimulate and the anterior roots to record. Consequently, the studies of monosynaptic reflexes have been performed in the anesthetized animal. On the other hand, evoked myography (Hoffman's H Reflex) has the same characteristics of the classical monosynaptic reflexes, and differs only in site of stimulation (a mixed nerve) and the site for recording (a muscle). This fact affords the opportunity for the first time to study such reflexes in the unanesthetized, intact animal. The experiments reported here have been carried out in the Monkey, Macaca mulatta. The site from which best and constant results for stimulus and recording are obtained is described; using a technique which compares the results of stimulation at two different places, the parameters for motor conduction, sensory conduction, synaptic delay, neuromuscular transmission, and muscle fiber action potentials are determined. Using the parameters mentioned above it is demonstrated that the evoked electromyogram has a direct quantitative relationship to the different stages of consciousness.

ANTI-SURFACE FACTOR ACTIVITY of ATPase. Panayotis G. Iatridis* and John H. Ferguson. Physiology Dept., Univ. of North Carolina, Chapel Hill, N. C.

ATPase, even at 10 µg/ml, and pH 7.0, shows a significant inhibitory effect on SF (surface factor or activation product). AMP, ADP and ATP, in low concentrations (less than 1 mM), show no inhibition. Large amounts (10 mM) of AMP, ADP and ATP inhibit the SF activity, but this effect, probably, is because of the pH change (pH 4.3-4.6) since similar pH changes of the SF solution show approximately the same inhibitory effect. ATPase does not change the pH levels of the SF solution, and therefore its inhibitory effect is not a pH matter. ATPase shows no inhibition of thrombin, tissue thromboplastin, thrombokinase, trypsin, stypven, factor IX, VIII, X or V. This specific anti-SF effect of ATPase may be significant since platelets are a source of ATPase (thrombosthenine). Thus the close relationship between platelets and Hageman factor becomes very important for the in vivo clotting mechanism since Hageman factor is first activated on the surface of platelets and is then inhibited by the thrombosthenine (ATPase of platelets). (Supported by N.I.H. Research Grant HE-01510-11).

MUSCLE RECEPTOR DISCHARGES DURING NEAR-SINUSOIDAL STRETCH. Ishikawa, K.*, Ott, K.*, Stuart, D. G.*, and Eldred, E. UCLA and VA Hospital, Long Beach

The firing patterns of primary and secondary muscle spindle and tendon organ afferents from the medial head of the de-efferented gastrocnemius muscle were monitored in 25 deeply anesthetized cats during repetitive near-sinusoidal stretch of the achilles tendon. At increasing rates of stretch the three receptors were contrasted in terms of discharge volume, rate and phase relation to the rate and extent of muscle lengthening. At slow (1-2 cps) stretch rates the peak discharge of all three receptors occurred near peak lengthening (static response); at faster rates (5 to 10 cps) near peak velocity of lengthening (kinetic response). The change in discharge phase from static to kinetic was gradual from 1 to 10 cps with little change from 10 to 20 cps. Primary muscle spindle afferents had a greater volume, rate and earlier phase of discharge than either secondary spindle or tendon organ afferents. (Supported by N.I.H. Grants B-1143 and NB 05199-01).

EFFECT OF LACTIC ACID ON FFA AND GLUCOSE METABOLISM IN DOGS. B. Issekutz, Jr., H. Miller, P. Paul* and K. Rodahl. Div. of Research, Lankenau Hosp., Philadelphia, Pa.

Palmitate-1-C^{14} or glucose-C^{14} (U) were infused i. v. for 3-1/2 to 5 hours at a constant rate into unanesthetized dogs with indwelling arterial and venous catheters. O_2 uptake and CO_2 output were measured. Specific activity of CO_2 and of plasma FFA or plasma glucose were determined. Infusions (40-min) of Na-L(+) lactate greatly decreased the participation of plasma FFA in the expired CO_2 in normal as well as in diabetic animals. During lactate infusion the oxidation of glucose was also consistently depressed but to a lesser degree than that of FFA. In the post-infusion phase, glucose oxidation rose markedly. Lactate infusion caused a striking decrease in the turnover rate of plasma FFA, but tended to increase the turnover rate of plasma glucose. From the elevated sugar uptake accompanied by a decreased glucose oxidation, it could be calculated that approximately 35% more glucose entered pathways other than the citric acid cycle. This mechanism may lead to accumulation of α-glycerophosphate and might explain the FFA lowering effect of lactate. Na-D(-) lactate infused in comparable concentrations had no similar effects. (Supported by NIH grant HE-07687-02.)

REGULATION OF PLASMA LACTIC DEHYDROGINASES IN CHRONIC RESPIRATORY ACIDOSIS. M. J. Jacey* and K. E. Schaefer, U.S.N. Medical Research Laboratory, U.S.N. Submarine Base, Groton, Connecticut

The lactic dehydrogenase (LDH) distribution of guinea pig (GP) plasma was studied by means of disc electrophoresis. The normal GP plasma showed the presence of the heart-type enzyme, H_4, as the major form. During the uncompensated phase of respiratory acidosis (1 day in 15% CO_2 + 21% O_2) an increase in the hybrid enzyme forms containing muscle-type subunits, M, was seen along with a diminishment of the H_4 form. Compensation of the respiratory acidosis (3 days exposure) brought about a return to a pattern resembling that of the normal GP plasma. Pyruvic acid levels in the blood significantly increased during the uncompensated phase of respiratory acidosis and returned to control values during the compensated phase of the acidosis. Susceptibility of H subunits to inhibition by relatively low concentrations of pyruvate is well known. Since no evidence of hypoxia was obtained during chronic exposure to 15% CO_2, the transient shift toward the M subunit forms could not have been caused by a lowered O_2 tension.

ENERGY BALANCE AND PALATABILITY: THE EFFECT OF FOOD DEPRIVATION ON THE INTAKE OF POSITIVELY AND NEGATIVELY FLAVORED SOLUTIONS. H. L. Jacobs and K. N. Sharma.* Depts. of Psychol. and Physiol., Univ. of Illinois, Urbana.

Previous work in this laboratory has shown that calories are primary modulators of food intake under ad libitum feeding conditions (Fed. Proc., 1961, 20:207), but that energy deficits increased the animals dependence upon flavor (The Physiol., 1963, 6:209). In the present studies, satiated or food-deprived rats were given one-hour intake tests with various solutions. After baselines were obtained, all solutions were diluted with increasing amounts of quinine. Food deprivation increased the relative intake of flavored solutions (saccharine, glucose, unsweetened corn syrup solids). The addition of quinine gradually decreased the intake of all solutions in satiated animals. Food deprivation sharply increased the amount of quinine necessary to suppress solution intake in all cases. Glucose intake showed the greatest resistance to quinine addition. Control observation showed that the avoidance threshold for quinine itself did not change, i.e. deprivation did not make the animals less discriminating, but caused them to accept the still unpalatable quinine additive to maximize intake of the increasingly palatable solution base. Conclusion: Food deprivation increases the relative palatability of positively flavored substances as measured by relative intake and resistance to quinine addition. Specificity of this effect is still an open question.

(Supported by grant M5754, USPHS, and by a grant-in-aid from the Corn Products Institute of Nutrition.)

EFFECTS OF CALCIUM DEPLETION ON POTENTIAL DIFFERENCE, RESISTANCE AND ACID SECRETION OF FROG'S GASTRIC MUCOSA. A. Jacobson*, M. Schwartz*, and W. S. Rehm. Dept. of Physiol. and Biophysics, and Dept. of Engineering Physics, University of Louisville, Louisville, Kentucky.

Mucosae were mounted between chambers with Cl^- Ringers on the nutrient side and a Ca^{++}- free solution on the secretory side. The potential difference, resistance (ΔPD/applied current) and H^+ rate (pH stat method) were measured. Depletion of Ca^{++} in the nutrient solution by repeated washings with Ca^{++}- free nutrient solution led first to a small decrease in PD (ave 8% SD± 8, $P < 0.01$), an increase in resistance (ave 36% SD± 14, $P < 0.01$), and a decrease in the H^+ rate (ave 38% SD± 9, $P < 0.01$). These effects were followed by a second phase in which the secretory rate decreased to zero and the PD and resistance to extremely low values (in some mucosae EDTA was used to produce the second phase). The addition of Ca^{++} to either the secretory or nutrient side or the replacement of the nutrient side with fresh Cl^- Ringers restored the PD and resistance to near normal values and the secretory rate partially or wholly depending on the length of the experiment. Forte, J. G. and Nauss, A. H. (Am. J. Physiol. 205:631, 1963) reported the second phase of Ca^{++} depletion and interpreted the depletion as influencing the binding material between the cells, i.e. the intercellular cement. They suggested that the lack of Ca^{++} left unchanged the rate of acid secretion and that the decrease in measured H^+ rate might be due to the diffusion of bicarbonate between the cells into the luminal fluid. An analysis of the present findings of an initial increase in resistance indicates that the H^+ and/or Cl^- pump are affected by Ca^{++} depletion. With Cl^- - free solution ($SO_4^=$) Ca^{++} depletion also resulted in the first phase for relatively high secreting mucosae and the second phase in all cases. This work indicates that Ca^{++} depletion inhibits the H^+ mechanism. (NSF and NIH support).

Physiological Properties of the Post-Auricular Response (Sonomotor) in Man. J. L. Jacobson*, D. T. Cody*, E.H. Lambert, R. G. Bickford, Mayo Foundation, Rochester, Minnesota.

The post-auricular response (Kiang) to binural click stimulation has been recorded by surface electrodes in 55 normal subjects and 20 patients with several types of audio-vestibular lesion. The response has been averaged by a four channel Mnemotron C.A.T. computer system with simultaneous C.R. oscillograph recording of the raw data. The response can be driven to rates of 100 responses per second and shows no evidence of fatigue or habituation. It is regarded as myogenic in origin (arising from the complex of small muscles related to the pinna) on the basis of the following evidence: (1) The amplitude of the response can be markedly enhanced or abolished in suitable subjects by contraction and relaxation of the ear muscles; (2) Local anesthetic block of the post-auricular branch of the 7th nerve will abolish the response unilaterally.

The distribution of the response on the head surface has been mapped using 150 sampling electrodes. The response amplitude and distribution can be greatly modified by changing head position and lateral movement of the eyes. The relationship of the surface recorded unaveraged and averaged potential to that which can be sampled by a concentric needle electrode inserted into the post-auricular muscle has been studied at a motor unit level. Activation of units related to the sound stimulus varies considerably in a time sequence. When unit activity is sampled from an optimal region of the muscle, a close match between the average from the surface and unit recordings can be obtained. In some instances both increased firing of units followed by a relative decrease in firing can be demonstrated. Supported by USPH Grant NB 03225.

EXPLORATION OF THE HUMAN THALAMUS WITH MICROELECTRODES. H. Jasper and G. Bertrand. Montreal Neurological Institute, McGill University, Montreal, Canada.

A technique has been perfected for exploration of the human thalamus and basal ganglia with a tungsten microelectrode controlled by a micrometer mounted on a stereotaxic instrument. Anatomical controls are provided by X-ray ventriculograms with corrections according to the results of electrical stimulation of the internal capsule. Unitary cell discharges 0.8-1.0 msec. in duration can be distinguished from axon spikes (0.3-0.4 msec. duration) by distinctively different sounds in the loudspeaker as well as by marked difference in amplitude. Receptive fields for single units in the basal nuclear complex correspond closely to those found in the monkey except for the presence of proprioceptive receptors in a region at the junction of n.VL with n.VPL. In the latter zone are found cells which fire in bursts synchronous with the tremor movements in patients with Parkinsonism. Somatic I units are highly specific in modality and somatotropic localization to the contralateral side of the body. "Non specific" units behaving as novelty detectors are found in the n. Centrum Medianum. Specific somatic cells respond with remarkable constancy to repeated tactile stimulation in spite of deliberate changes in attention of the conscious patient, though attention may decrease the background spontaneous discharge.

EPINEPHRINE AND GLYCOGENOLYSIS IN THE ISOLATED PERFUSED DOG HEART. L.A. Jedeikin* and N.M. Buckley. Albert Einstein Coll. of Med. N.Y.

The question of whether epinephrine has a direct action on glycogen breakdown in the mammalian heart has been re-examined in the isolated dog heart under carefully controlled physiological conditions. The coronary arteries of the Langendorff preparation were perfused at controllable pressure by means of a closed circuit with 500 ml of defibrinated whole blood from the experimental animal. In order to avoid glycogenolysis due to inadequate glucose or oxygen concentration, 100 mg% of glucose was added, and the arterial blood was completely saturated with oxygen by passage through a Pulmo-Pak oxygenator. Control experiments were carried out for 90 minutes during which time contractile force, heart rate and coronary flow were measured. Epicardial samples of uniform thickness were removed for glycogen analysis at frequent intervals and arterial and venous blood samples were taken for glucose and oxygen analyses. The epinephrine experiments were carried out similarly, except that early in these experiments, a single dose of epinephrine (0.15 mg/500 ml blood) was added to the perfusion reservoir. This dose caused a marked increase in both contractile force and heart rate. Tissue and blood samples were taken before, during and after the obvious physiological response to epinephrine. It was found that epinephrine tended to increase glucose and oxygen uptake. In about half the experiments, epicardial glycogen decreased after epinephrine addition. In the other epinephrine experiments, glycogen level was well maintained as in the control experiments. The differences appeared to depend on whether the animals were fasted or fed, whether hypoxia had occurred, and the time of administration of epinephrine.

Supported by grants from NIH (HE-05624), Am. Heart Assoc. (62 G 98)

BRAIN FACTOR INFLUENCING STOMACH MOTILITY. N.C. Jefferson T. Arai*, T. Geisel*, and H. Necheles.
From the Department of Gastroenterology, Medical Research Institute, Michael Reese Hospital, Chicago.

Previously, we have reported that complete vagotomy in the dog is hardly possible, and that there is a considerable cholinergic outflow from both thoracic and lumbar regions of the spinal cord in this animal. In other observations we found that, if both vagus nerves are cut in the neck and their central ends are stimulated, contractions of the stomach occur. This was observed also in decapitated animals in which only the carotid artery and jugular veins were preserved. In subsequent work with cross-perfusion, including hypophysectomized dogs and chronically vagotomized dogs, our findings confirmed that a certain factor from the brain affects gastric motility. Intravenous injections of liver extracts from normal dogs did not evoke a response whereas brain extracts injected under similar conditions caused gastric contractions. Central stimulation of femoral and sciatic somatic nerves, as well as facial, lingual and trigeminal cranial nerves were all negative. Contractions of the stomach when present were not entirely abolished by cholinergic or serotonin depressants. Sympathetic depressants were entirely negative. A preparation of rat stomachs in Sollman solution contracted following innoculation of the bath with blood collected from a dog during central vagus stimulation.

Supported by U.S.P.H. Grants AM 06078-01-02. The Department is supported in part by the Michael Reese Research Found.

DETERMINATION OF CAPILLARY FILTRATION COEFFICIENT WITH AID OF A CAPILLARY MODEL. P. C. Johnson, Dept. of Physiol., Ind. Univ. Med. Center, Indianapolis, Indiana.

Most experimental studies of capillary filtration and absorption measure net water movement across the entire capillary bed. The data obtained may be analyzed by use of the equation $\dot{V} = k_c A (\overline{P_c} - \pi_p + \pi_{if})$, where $\dot{V}$ is the filtration rate, k_c is the filtration coefficient, A is the capillary surface area, $\overline{P_c}$ is the mean capillary hydrostatic pressure, π_p is the plasma colloid osmotic pressure and π_{if} is the interstitial fluid colloid osmotic pressure. It is usually assumed that π_p does not change in the capillary. However, elevation of $\overline{P_c}$ in the dog intestine may increase π_p by as much as 80% of the change in $\overline{P_c}$. Obviously, accurate calculation of k_c requires an accurate estimate of mean π_p in the capillary. The present studies are an attempt to develop a computer model of a single capillary which could be used in determining $\overline{\pi_p}$. The model is based on an expanded and modified form of the equation given above. The expanded equation describes $\dot{V}$ across any region of the capillary, taking into consideration the changes in π_p and $\overline{P_c}$ which occur en route through the capillary. The equation was programmed on an analog computer and integrated over the length of the capillary. The coefficients were varied to give values for net filtration which agree with our experimental data on the dog intestine. A value for $\overline{\pi_p}$ was thus obtained. Using estimates for A obtained from other studies, and assuming π_{if} to be constant, the above equation could be solved for k_c. Initial calculations based on the model indicate that the relative filtration constant (k') is about 5×10^{-12} cm, which compares well with the average value of 5.1×10^{-12} obtained by Landis in studies on single capillaries of the frog mesentery. (Supported by PHS Grants HE 05200 and AM 06221. Facilities provided in part by PHS Grant HE 6308).

VENOUS PRESSURE AND ARTERIAL BLOOD FLOW IN SKELETAL MUSCLE. Richard D. Jones (intr. by R. M. Berne), St. Luke's Hospital and Western Reserve Univ. School of Med., Cleveland, Ohio.

In isolated, perfused skeletal muscle of the dog a sustained elevation of venous pressure produced a transient (15-30 sec) increase in vascular resistance whereas a sustained reduction of venous pressure transiently decreased vascular resistance. These responses preceded autoregulation of blood flow and were consistently observed during perfusion at constant arterial pressure or constant blood flow. The changes in resistance during the transient cannot be explained on the basis of passive distention or recoil of the elastic vessels since the response is opposite to that predicted on a passive basis. Simultaneous arterial and venous blood flow measurements show that the response is not produced by capacitance effects and the presence of the response in chronically denervated muscle indicates that the response is not reflex in nature. Reduction of venous pressure during constant flow perfusion produces a transient decrease in resistance such that perfusion pressure decreases two or three times more than the imposed venous pressure decrease, suggesting that distention of the venous vessels may possibly interfere with arterial inflow. A model based on this hypothesis was constructed of plastic and thin rubber sheeting. Pressure flow studies with the model indicate that distention of the "vein" increases resistance in the adjacent "artery". Reduction of "Vein" pressure induces a reduction of resistance in the "artery". Histological examination of skeletal muscle vessels fixed at controlled arterial and venous pressures suggests that the arterial-venous relationship observed in the model may play a role in the regulation of skeletal muscle blood flow.

REPRODUCIBILITY AND ERROR OF A CARDIOPULMONARY DYE DILUTION METHOD. R. Jortner*, E. McNally*, A. Ellis* and H. Weisberg. Cardiovascular Institute, Michael Reese Hospital and Medical Center, Chicago, Ill.

In the course of our pulmonary hemodynamic studies we sought an index of "pulmonary blood volume". The product, cardiac output (CO) x mean transit time across the pulmonary bed (MTT) as determined by dilution methods, seemed acceptable. As a first step we sought to define the purely methodologic error of our technique. Slug injection of indocyanine green into the pulmonary artery and withdrawal from the aortic root were made. CO and MTT were obtained by a method of arithmetic and analytic integration and reintegration of curves corrected by exponential extrapolation. In anesthetized dogs, 2 or 3 clusters, each consisting of 4 curves shot at 6 minute intervals, were obtained each 54 minutes. The dog was artificially ventilated, and during each cluster was given succinylcholine in order to minimize flow changes due to erratic intrathoracic pressure variations. Apnea was induced during the actual injection-sampling interval to improve curve "smoothness". Heart rate, mean aortic, mean pulmonary and left ventricular end-diastolic pressures were monitored during each cluster. Absence of significant variations in these parameters was assumed to indicate that central hemodynamics were virtually constant. In clusters where this was true, CO x MTT varied within a range of 10% of the mean value for the cluster.

METABOLIC RESPONSES TO ARTIFICIAL HYPERTHERMIA IN MAN. R. J. T. Joy, W. R. Beisel*, R. F. Goldman. USA Res. Inst. of Env. Med., Natick, Mass. and USA Med. Unit, Ft. Detrick, Md.

Quantification of metabolic responses to hyperthermia was required as a baseline for similar studies in experimental febrile infections. 8 normal male volunteers were studied on a liquid diet by balance technique for 21 days. After 13 control days, a 24 hr. hyperthermia was induced to simulate early fever in tularemia. A heat chamber was continuously adjusted to increase T_r by 0.1°C/hr. for 18 hrs. and then maintain T_r at 39.5°C for 6 hrs. Sweat output varied from 250-400ml/hr; adjusted water intake maintained body weight and urine output(400 ml/hr). Hgb. and Hct. remained stable. An acutely negative Na balance during hyperthermia was due chiefly to sweat loss. Thereafter, renal Na retention caused a strongly positive Na balance lasting 4 days. Negative balances of N, K, Mg and Ca on the day of hyperthermia were from combined losses in sweat, urine and blood sampling. The negative balances of N, K and Mg persisted an additional day due to continued large urinary losses. An exaggerated fall during hyperthermia in serum P_i and virtual absence of total P in urine and sweat could be explained by respiratory alkalosis. Urinary adrenocorticoid metabolites(17-OHCS, 17-KS, Pregnanetriol)were increased by hyperthermia; all but the latter were normal the next day. When compared to the metabolic response to experimental tularemia (Clin. Res. 12, 36, 1964), these data suggest that hyperthermia per se could account for many of the metabolic alterations observed in acute infection.

Pancreatic Secretion of Total N After Feeding. Jin Soon Ju* and E.S. Nasset. University of Rochester, Department of Physiology, Rochester, New York.

Dogs were provided with Thomas duodenal cannulae to permit collection of pancreatic juice without contamination with gut contents. After feeding 100 g of lean beef, the pancreas secreted 75, 76 and 76 mg total N in the 1st, 2nd and 3rd hours respectively. After feeding an isonitrogenous amount of zein (28 g) the response was 52, 51 and 33 mg N. The pancreas in these dogs (14 kg) probably averaged 48 g in weight and contained approximately 1.5 g of N. The total output of N by the pancreas in 3 hours after feeding lean beef was 227 mg or about 15% of the total contained in the gland at rest. This rate was well maintained over the 3-hour period. The response to feeding zein was roughly 2/3 of that obtained from feeding lean beef. These results show that the pancreas makes an important contribution to the mass of endogenous protein that is mixed with the ingested protein during digestion in the small intestine. This mixture also contains additional proteins from other digestive glands and sloughed mucosal cells. Enzymatic degradation of this mixture of proteins produces an assortment of amino acids available for absorption which is quite different from that derivable solely from ingested protein.

INTERSPIKE-INTERVAL ANALYSIS OF PACEMAKER NEURONS IN APLYSIA. Douglas Junge. (intr. by Jose P. Segundo). Brain Research Institute and Depts. of Physiology and Anatomy, U.C.L.A. Los Angeles, Calif.

"Pacemaker" neurons, in the absence of synaptic input, display a stereotyped spontaneous drift of membrane potential, which leads to a production of very evenly spaced spikes. Our purpose was to describe the spike discharge patterns and relate them to subthreshold events (pacemaker potentials, excitability changes). Intraneuronal recordings were obtained from visceral ganglia of Aplysia californica. Interspike-interval histograms were nearly normal, with slight positive skewness, and means from 0.2 to 5.0 sec. The ratio "standard deviation / mean" was 0.01 to 0.1, larger values corresponding to larger means. Pacemaker potentials could usually be fitted by an exponential curve or by a straight line; occasionally they were more complex. Firing thresholds decreased throughout each interval. A computer simulation was made (Perkel, D.H., Rand Report RM 4132-NIH), assuming an exponential pacemaker potential and superimposed normally distributed fluctuations of membrane potential and/or spike excitability. This simple model predicts the natural features of many pacemaker interval distributions, e.g. shape of interval histograms, variation of standard deviation with mean interval, etc. The invariance of the pacemaker potentials in many cases suggests that the interval fluctuation is determined more frequently by variations in threshold.

EFFECT OF ASCORBIC ACID ON SERUM AND CARDIAC MUSCLE REDUCING CAPACITY DURING STRESS. John Kabal* and Estelle R. Ramey. Georgetown University School of Med., Washington, D.C.

Serum and cardiac muscle reducing capacity (R.C.) was measured at intervals in intact fed rats by an oxido-reduction titration before and after the application of a hind limb tourniquet. 300 mg/Kg L-ascorbic acid was administered s.c. to control and tourniquet stressed animals. The untreated control R.C. was 7.6 mEq O/L for serum and 23.5 mEq O/L for heart muscle. 30 min. after the ascorbic acid injection serum R.C. levels reached a peak value of 28.6 and then steadily declined to 9.5 mEq O/L by 4 hrs. The cardiac muscle R.C., however, was elevated to 47.0 at ½ hr. and remained at this high level for 4 hrs. Following tourniquet application, serum and muscle R.C. rose to 16.9 and 35.4 mEq O/L. The addition of ascorbic acid at this point doubled the R.C. of serum but had no effect on the R.C. of cardiac muscle. It is suggested that severe stress leads to markedly increased ascorbic acid turnover in cardiac muscle.

NERVOUS CONTROL OF WING MOVEMENT IN LEPIDOPTERANS. Ann E. Kammer (intr. by D. M. Wilson). Zoology Dept., Univ. California, Berkeley.

For an analysis of the central nervous control of locomotion, flying insects are suitable subjects, primarily because of the relatively small number of units involved. Previous workers have shown that the flight of locusts is relatively constant and that the motor output pattern is generated centrally. In contrast to the rather constant wingbeat parameters of locust flight, large-winged lepidopterans such as saturniid moths produce wingstrokes of more widely variable amplitude and frequency. Forewing movement in a vertical plane was photographed on moving film, and at the same time extracellular muscle potentials were recorded by means of fine, insulated wires inserted into the thoracic flight muscles. Records were analyzed in order to correlate the mechanical parameters of the wingbeat with the timing and number of muscle impulses. At any given frequency of wingbeat, increasing angular movement of the wing is correlated with an increase in the number of muscle potentials per motor unit. Frequency of wingbeat and number of motor neuron impulses are not highly correlated as they are in locusts. This relationship reflects the relative independence of wingbeat frequency and amplitude in lepidopterans. Thus although the central mechanisms which generate the motor pattern are probably similar in both groups, that of the lepidopterans has an additional parameter which is independently variable over a wide range. Awareness of this additional variable places a new restraint on models of the possible interactions among central neurons which produce the coordinated output.

(Supported by NIH grant NB 3927 and NSF grant GB 2116)

THE EFFECTS OF ZYMOSAN AND GLUCAN ON THE CANINE RES, CIRCULATING PLASMA VOLUME, AND VASCULAR RESPONSES TO EXOGENOUS CATECHOLAMINES. J. P. Kampine*, E. F. Banaszak* and J. J. Smith. Marquette University School of Medicine, Milwaukee, Wisconsin.

During the past several years an accumulation of evidence from various sources has indicated that the reticuloendothelial system (RES) may play an important role in those homeostatic adjustments involved in response to severe circulatory stress. Preliminary experiments indicated that colloidal carbon gel (40 mg/kg) provided a reliable test agent for evaluating phagocytic aspects of the canine RES. Zymosan and glucan (Standard Brands, Inc.) 30 mg/kg in three divided doses elicited a proliferation of the canine RES as has been previously reported for smaller mammals. This stimulation was characterized by an enhanced phagocytic capacity, an increase in liver, spleen and lung weights and histologic evidence of proliferative changes in RE elements of liver, spleen and lung. The RES response to zymosan as measured by repeated testing of phagocytosis with the carbon clearance technique was found to be biphasic in nature during a six-week period. Stimulation of the RES with zymosan and glucan in these unanesthetized dogs was not associated with alterations in vascular responses to graded doses of epinephrine or norepinephrine and caused no significant alterations in plasma volume as measured by the RISA technique.

Neural Model of a Quasi Conditioning Phenomenon in Aplysia Depilans. E. R. Kandel and L. Tauc*, Harv. Med. Sch. and CNRS.

In the whole animal, the discharge of the abdominal ganglion giant cell axon can be readily recorded in the right connective (Hughes and Tauc, 1962). In this preparation a stimulus to the left connective, subthreshold for giant cell discharge, increased in efficacy for several minutes and triggered action potentials after a few pairing trials with a suprathreshold natural stimulus. This phenomenon was not specific to pairing and had the electrophysiological characteristics of behavioral alpha conditioning (sensitization). The paradigm was further simplified and applied to the isolated abdominal ganglion using intracellular recordings from the giant cell and electrical instead of natural stimuli. A subthreshold (test) EPSP produced by a stimulus to the left connective was facilitated (100 to 800 percent) for up to 40 minutes after 3 - 9 pairing trials with a train of suprathreshold (priming) stimuli to the siphon nerve. The magnitude of the facilitation was a function of the efficacy of the priming stimulus and any nerve to the ganglion could serve as test or as priming input. The priming stimulus did not produce a conductance change in the postjunctional cell and the facilitation could be demonstrated in the presence of an inhibitory blockade (curare) and with a presumably monosynaptic test EPSP indicating a possible presynaptic mechanism for the facilitation. The finding that EPSPs can be facilitated, for over one half hour, with an input patterning schema derived from a behavioral conditioning paradigm suggests that the concomitant changes in the efficacy of synaptic transmission may underly certain simple forms of short term information storage in the intact animal.

REGIONAL VENTILATION AND PERFUSION OF THE LUNG IN LATERAL DECUBITUS IN MAN. K. Kaneko*, A. Dawson*, and J. Milic-Emili. Joint Cardio-Respiratory Service, Royal Victoria Hospital, McGill University, Montreal, Canada.

Regional subdivisions of lung volume were measured in 5 normal subjects in the right or left lateral decubitus using the Xenon 133 technique (Ball et al. J. Clin. Invest. 41: 519; 1962). All results were expressed as percent of regional lung volume at full inspiration (TLC_r). In the most dependent regions of the lungs, regional Residual Volume (RV_r) and regional Functional Residual Capacity (FRC_r) were 20% and 35% of TLC_r, respectively. Both increased approximately linearly from the dependent to the upper regions of the lungs, where RV_r and FRC_r amounted to 30% and 60% of TLC_r respectively. Regional ERV was smaller and regional IC was larger in the dependent lung. These findings correlated with chest X-ray films taken in lateral decubitus, which showed that when lung volume was varied from RV to FRC the upper lung expanded more than the dependent lung, whereas from FRC to TLC the opposite was true.

At rest, both the ventilation and perfusion per unit volume increased approximately linearly from the lowest to the uppermost regions of the lungs. Values for ventilation and perfusion per unit volume obtained in the uppermost regions of the lungs were respectively 26% and 19% of the values obtained in the most dependent regions.

(Supported by grants from The John A. Hartford Foundation Inc. and The Medical Research Council of Canada.)

SITE OF EFFECT OF HYPOXIA AND HYPERCAPNEA ON PERIPHERAL PULMONARY VASCULATURE. Mikio Kato* and Norman C. Staub. Cardiovas. Res. Inst. and Dept. of Physiol., Univ. of Calif. Sch. of Med., San Francisco

Staub (Fed. Proc. 22:453, 1963) reported unilateral alveolar hypoxia in cat constricted the small pulmonary arteries (PA) at the terminal bronchiole (TB) level. In 17 open thorax cats we used a dual tracheal cannula and pressure-regulated respirator, and ventilated the right lower lobe (RLL) separately from the rest of the lung. While the main lung breathed 100% O_2, the lobe breathed 100% O_2, 100% N_2, 10% CO_2 in N_2 or 10% CO_2 in air. In the N_2 and CO_2-N_2 experiments we determined the fractional blood flow through the lobe by the shunt equation. In each experiment the RLL and LLL were rapidly frozen at end inspiration with liquid propane and in fixed sections the internal diameters of terminal bronchioles and associated pulmonary arteries were measured. In 4 controls the PA/TB ratios between RLL and LLL averaged the same. In 4 of 5 N_2 experiments the PA/TB ratios were lower in the RLL and the shunt flow was less than half expected on lung weight alone. In the 4 N_2-CO_2 lobes the PA/TB ratios were even less than with N_2 alone and the shunt flow was less than 20% of expected in 3 of these. In one completed analysis of the CO_2-air lobe there was no difference between RLL and LLL. The results confirm the site of hypoxic constriction in the small PA and show that with added CO_2, as in respiratory unit hypoventilation, the hypoxic constriction is markedly potentiated. (Supported in part by USPHS grant HE-06285.)

PHYSIOLOGICAL BASIS FOR DIRECT ELECTRICAL STIMULATION IN THERAPY OF PARALYZED HOLLOW VISCERA. Francis Katona and Anna Dobos. (intr. by M. Jack Frumin) Mt. Sinai Hosp., N.Y.C., Neurosurg. Inst. and Post Graduate Med. School, Budapest.

Local electrical stimulation has been used since 1956 for treatment of motility disturbances of the G.I. or G.U. tract in over 500 patients. Intraluminal (G.I.) and intravesical (G.U.) stimulation produced either (a) relaxation in spastic viscera, i.e, cardiospasm, pylorospasm, urinary sphincter spasm or biliary dyskinesia or (b) contraction of relaxed viscera, i.e., paralytic ileus, cord bladder and serious chronic obstipation. ATP and neostigmine applied topically potentiate these effects in man, dogs, cats and rats, while atropine, curare and succinycholine applied topically or by infiltration produced inhibition. Cardiospasm, paralytic ileus and paralysis of the urinary bladder were produced experimentally in dogs and cats by spinal cord section and/or local vegetative denervation. The resulting states of muscle tonus were again reversed by local electrical stimulation. The locomotor smooth muscle of invertebrates (antozoae, holothuriae, annelidae) respond similarly to electrical stimulation and to drugs. These experiments can be explained on the basis of stimulation of intramural ganglia and offer a rationale for the treatment and rehabilitation of paralyzed viscera. Some of these results will be demonstrated in a filmstrip.

TISSUE TEMPERATURES DURING AROUSAL OF HIBERNATING GROUND SQUIRRELS. Kyllikki Kauppinen*, R. W. Bullard and R. E. Smith, Univ. Calif., White Mt. Res. Sta. Physiology, Los Angeles, and Anatomy and Physiology, Indiana Univ., Bloomington.

Hypothalamic and epithalamic temperatures were compared with those of thoracic and visceral organs during successive arousals from hibernation. Temperatures were measured in golden mantled and 13-lined ground squirrels (Citellus lateralis and C. tridecemlineatus) with thermocouples and a suitable recording apparatus. Arousals were induced by handling the animals at environmental temperature of hibernation (+6°C) and in some cases subjecting them further to -8°C. In C. lateralis the temperatures obtained from various organs were referred to those concurrently in the hypothalamus during the respective arousals. The observed temperatures of the heart were consistently higher than those of the hypothalamus, while those of epithalamic, rectal and subcutaneous sites were respectively lower. Depending upon the previous history of arousals, the interscapular brown fat displayed temperatures both higher and lower than those of hypothalamus. During the first experimental arousals the brown fat temperatures were higher than those of any of the other organs that were examined, whereas during the third set of induced arousals the brown fat showed temperatures considerably lower than did the heart and even lower than observed in hypothalamus. The phase of rapid rise of rectal temperature coincided with hypothalamic temperature of +25°C and approximately with the point of terminal decrease in the rate of warming of the interscapular brown fat. This research was supported in part by a Grant from the National Aeronautics and Space Administration, Washington, D. C.

D.C. POTENTIAL CHANGES DURING PARADOXICAL SLEEP IN THE RABBIT. Hiroshi Kawamura* and Charles H. Sawyer. Dept. of Anatomy, UCLA

A study has been made of D.C. potential changes in the brain during various states of sleep and wakefulness in the unrestrained unanesthetized rabbit with chronically implanted EEG and D.C. cortical and subcortical electrodes. In preliminary acute experiments it was found that, with the occipital bone as the reference electrode, the direction of the D.C. potential change induced by stimulation of the midbrain reticular formation was the same in cortical and subcortical active electrodes. With frontal and occipital bones as reference points the cortical D.C. potential changes were similar to one another, but arousal stimuli readily elicited positive D.C. shifts with the frontal reference electrode. In the chronic rabbit with an occipital reference electrode cortical and hypothalamic D.C. potentials shifted strongly to the positive side during slow wave sleep and after injection of pentobarbital; from these conditions stimulation of the reticular formation induced a marked negative shift. During the alert state the same stimulation tended to elicit a positive shift. During paradoxical sleep, which was always entered via slow wave sleep, both cortical and subcortical D.C. electrodes showed negative shifts similar to those seen during an arousal reaction. Grooming and eating elicited strong positive shifts in both cortical and hypothalamic D.C. electrodes.

Supported by grants from the National Institutes of Health (NB 01162) and the Ford Foundation.

SQUARE WAVE ANALYSIS OF THE FROG GASTRIC MUCOSA. D. C. Keesee*, S. G. Spangler*, and W. S. Rehm. University of Louisville, Louisville, Ky.

The purpose of this work is to help clarify certain problems concerning the impedance of the frog gastric mucosa. Mucosae were mounted between chambers and bathed with the usual Cl^- solutions. Two pairs of electrodes were used, one for sending current, and the other for measuring the PD. Square waves of current of from 5 to 10 $\mu a\ cm^{-2}$ were sent across the mucosa and the PD response was measured with a dual beam cathode ray oscilloscope (Tektronix 502-A). The one beam recorded the PD across the mucosa and the second beam recorded the PD across a standard resistor in series with the mucosa. A test circuit was used which consisted of a resistance R_S in series with a RC parallel combination, thus approximating the equivalent circuit of the mucosa. A plot of the log $(R_TI - PD)$ vs t yielded a straight line for the test circuit (R_T represents the total resistance, I the current and t the time). Analysis of the data showed that the calculated values were within 1 per cent of those in the test circuit. For the mucosa the relationship between log $(R_TI - PD)$ and t could be represented by two exponentials and therefore two RC parallel combinations in series. The RC combination with the longer time constant had a capacitance of about 10 $\mu f\ cm^{-2}$ (confirming Teorell and Wersall., Acta Physiol. Scand. 10: 243, 1945), while the capacitance of the combination with the shorter time constant was about 1 $\mu f\ cm^{-2}$ and R_S was about 25 ohm cm^2. R_S remained constant under a wide variety of conditions (confirming Teorell and Wersall) including stimulation with histamine, anoxia and inhibition of H^+ secretion by thiocyanate. The changes in the total resistance under these various conditions are due to changes in the parallel resistance R_P. The total resistance as determined in the past in this laboratory by sending direct current across the mucosa and determining the ΔPD after about 1 second is an accurate method for measuring R_T.

THE LOW RESPONSE OF MICE WITH A HEREDITARY ANEMIA TO DOSES OF ERYTHROPOIETIN. Geoffrey Keighley, Elizabeth S. Russell* and Peter H. Lowy*. Div. of Biology, Calif. Inst. of Technology, Pasadena, and Jackson Laboratory, Bar Harbor, Maine.

WW^V mice have a lifelong hereditary macrocytic anemia with a hematocrit of about 35%. Nonanemic littermates have normal blood values, with hematocrit of about 45%. Both kinds of mice respond promptly to exposure to lowered air or O_2 pressure with increased erythropoiesis. The nonanemic mice respond to standard injections of erythropoietin with substantial increases of reticulocytes and hematocrit, but no similar increases were found in anemic mice, even with doses 10 to 15 times greater. By a more sensitive assay, the uptake of Fe^{59} into the red cells of animals with erythropoiesis depressed by prior exposure to hypoxia, it is found that anemic mice do respond to erythropoietin, but the effective dose is 150-200 times greater than in normal littermates, and the maximum response is limited. When both kinds of mice are exposed to long periods of hypoxia (30 days or more) the final hematocrit reached by the anemic mice is lower than that reached by the normal mice.

PATHOLOGICAL THIRST SELECTIVELY DISSOCIATED FROM A RENAL CONCENTRATING DEFICIT. Allen D. Keller. US Army Medical Research Laboratory, Fort Knox, Ky.

Pathological thirst (primary polydipsia) has been selectively and predictably dissociated from a renal concentrating deficit or osmotic diuresis by hypothalamic and prechiasmal ablations. Overdrinking was usually not obviously spontaneous but was elicitable regularly by an external heat load and by hydropenia. When spontaneous, overdrinking was mild in form but was greatly intensified by heat and hydropenia. Salt loading caused overdrinking in some animals, not in others. The spontaneous and heat elicited polydipsias, with resultant water diureses, simulated precisely the diabetes insipidus syndrome (simulated d.i.). Normal renal concentrating ability was verified by urine specific gravities of 1.060 and by mannitol flow load curves during hydropenia. Simulated d.i. preparations eliminated a water load normally; actually slightly more quickly and completely than unoperated dogs. The enhanced thirst was not caused by a deficit in the oxytocic principle since overdrinking occurred in the absence of reduced renal clearances. Pathological thirst therefore exists as a neurological entity quite independent of a primary polyuria and "functional" or "neurotic" causes.

EFFECT OF DRUGS ON LEFT VENTRICLE FUNCTION. H. Kines* and J. P. Holt. Heart Research Laboratory, University of Louisville School of Medicine, Louisville, Kentucky.

In earlier studies on the contracted left ventricle of a variety of mammals, a pattern of function described by the linear equation: $F/A = e\ R_m\ R_{om} - e$, was shown to exist for the thick-walled elastic sphere equivalent to the left ventricle. F/A is stress, e is elasticity constant, R_m is the radius of the chamber containing the internal volume plus one-half the wall volume, and R_{om} is this radius when the chamber is distended with zero pressure. Preliminary studies on the effect of continuously administered l-norepinephrine and halothane on this relationship have been carried out in a series of intact anesthetized dogs subjected to plethora and hemorrhage. Ventricular end-diastolic, EDV, end-systolic, ESV, and stroke volumes were determined by an indicator dilution technique described earlier. Although the effect was variable, large doses of norepinephrine generally increased the arterial pressure and ventricular wall thickness associated with a particular ESV, and decreased R_{om} and the ratio: ESV/EDV. It shifted the stress-length line toward the stress axis. Halothane had the opposite effects. Neither drug caused a consistent change in e. It is suggested that different states of contractility of a particular ventricle can be described quantitatively by the above stress-length equation, each state being characterized by a particular set of values of e and R_{om}. (Supported by USPHS Grant #2075 and the Kentucky, Louisville and Jefferson County Heart Assns.)

PULMONARY PRESSURE, VOLUMES, FILTRATIONS, AND RESISTANCE OF INTRA- AND EXTRA-LOBAR VASCULAR COMPARTMENTS. S. Kira* and S. Rodbard. City of Hope Medical Center, Duarte, California.

In 17 dog lung lobes, hydrostatic and osmotic gradients and surface forces were obviated by filling the vascular bed, and the air and pleural spaces with saline. Statics: At any constant airway minus pleural pressure, an increase of vascular pressure above pleural pressure produced a linear displacement of extra-lobar fluid. Intra-lobar volume was unaffected until vascular pressure equalled airway pressure; a fluid volume of nearly 10% of the empty lung weight was then displaced from the airway as vascular pressure was raised another 4 cm H_2O; continuing vascular pressure rise had no further effect. Changes in transpulmonary pressure and lobe volume had no effect on intra-lobar vascular volume. Thus, extra-lobar vessels are linearly distensible while intra-lobar vessels are collapsible and relatively nondistensible. Filtrations: Filtration from vascular bed to pleural space was correlated with the direction and magnitude of the venous to pleural pressure gradient; this filtration was relatively independent of arterial pressure. Filtration into the airway began only after vascular pressure exceeded airway pressure by about 10 cm H_2O. Rate of filtration into the pleural space was several times greater than into the airway. Dynamics: Vascular resistance decreased sharply as arterial pressure increased above airway pressure and reached a minimum where intra-lobar volume reached its maximum. These results with the lung are remarkably similar with our earlier data obtained on soft walled collapsible vessels. Implications of these data for pulmonary anatomy and dynamics will be discussed.

Urea Synthesis by Rat Kidney. Leonard I. Kleinman* and Edward P. Radford, Jr. Department of Physiology, Harvard School of Public Health, Boston, Massachusetts.

Previous experiments (L.I.Kleinman and E.P.Radford,Jr. Fed.Proc. 22: 335,1963) have shown that when rats were given a 58% protein diet with 10% urea and 2% NaCl added, in about 20% of clearance periods the amount of urea excreted exceeded the amount filtered. In these instances we believe the only possible explanations are active urea transport or urea synthesis in the kidney. To investigate the latter possibility, indwelling aortic, jugular vein and bladder catheters were placed in rats to allow sampling of blood and urine while the animals were in an unanethetized, undisturbed state. At least six days after the catheters were inserted, urea C-14 was infused through the venous catheter at a steady rate of 1.3 μc/hr after a priming dose of 0.5 μc. Urine was collected during repeated periods when blood C-14 concentration was steady, and the specific activity of urea in blood and urine was compared. In 8 out of 20 rats the specific activity of blood was higher than urine by 30 to 50%. These observations support urea production by the kidneys as an explanation of urea/inulin clearance ratios greater than one, but active transport has not been ruled out. The role of diet, sex and strain of rats on renal urea production is under investigation.

CHEMICAL COMPOSITION OF ISOLATED HOG THYROGLOBULIN. Howard M. Klitgaard and S. Kaneko-Mohammed*. Department of Physiology, Marquette University School of Medicine, Milwaukee, Wisconsin.

Hog thyroglobulin was isolated using a modified procedure of Shulman and Armenia (J. Biol. Chem. 238:2723, 1963). The purified thyroglobulin obtained by stepwise elution column chromatograph was analyzed for its amino acid composition. The thyroglobulin was eluted from DEAE-cellulose with 0.2M Na-phosphate buffer, pH 5.6 and was found to constitute 28% of the crude thyroid extract placed on the column. Upon rechromatographing this material, 75% was recovered as pure thyroglobulin. When analyzed in a Beckman model E ultra centrifuge it appeared as a single peak ($S_{25,w}$ 19.99) contaminated by less than one per cent of faster sedimenting components. Beckman Spinco amino acid analyzer was used to determine the amino acid composition of the purified thyroglobulin. 83% of the material by weight was accounted for by its amino acid content. Our method of preparing thyroglobulin has been modified to study the chemical composition and synthesis of rat thyroglobulin. (Supported by USPHS Grant AM 01706-07.)

STUDIES ON THE MECHANISM OF THE INCREASE OF MYOCARDIAL OXYGEN UPTAKE PRODUCED BY CATECHOLAMINES. F. J. Klocke*, G. A. Kaiser*, J. Ross, Jr., and E. Braunwald. Natl. Heart Institute, Bethesda, Md.

This study was undertaken to define the relative roles of direct stimulation of oxidative metabolism and of augmented contractile activity in the increase of myocardial oxygen uptake produced by catecholamines. Arterial O_2 content was maintained constant and coronary venous P_{O_2} was monitored continuously in 15 isolated canine hearts perfused at constant rates with whole blood. Coronary venous O_2 contents were obtained from individually determined O_2 dissociation curves and myocardial O_2 uptake ($M\dot{V}_{O_2}$) was calculated from the A-V O_2 difference and coronary flow. The effects on $M\dot{V}_{O_2}$ of graded intracoronary injections of norepinephrine (5 dogs), epinephrine (5 dogs), and isoproterenol (5 dogs) were first determined with the hearts beating, but performing no external work. These injections were then repeated after any augmentation of contractile activity by the catecholamines had been prevented with potassium arrest. In 5 arrested hearts, 0.1, 0.3, 1.0, 3.0 μg of isoproterenol produced increases of $M\dot{V}_{O_2}$ averaging 0%, 5%, 8%, and 15% of control values. When the same hearts were beating and isoproterenol augmented their contractile activity, these doses produced much larger increases in $M\dot{V}_{O_2}$, averaging 18%, 55%, 140%, and 191%. The results with epinephrine and norepinephrine were qualitatively similar. Thus, while oxidative metabolism in the non-beating heart can be increased by large doses of catecholamines, the increase of $M\dot{V}_{O_2}$ in the beating heart results predominantly from the augmented contractile activity produced by the amines.

THE VAGOTOMY EFFECT OF GASTRIC FREEZING. Arthur P. Klotz (introduced by E. B. Brown, Jr.). University of Kansas Medical Center, Kansas City, Kansas.

Although vagal blockade of terminal gastric fibers has been suspected in human gastric "freezing" satisfactory animal experiments supporting this have not been reported. Probably this is in part due to the type of animal preparation used, the timing of the experiment, and artifactual changes in the mucosa that always occur when the gastric wall is actually frozen. The experiments herein reported demonstrate that with currently advocated techniques actual freezing of the human stomach and dog's stomach ordinarily does not occur, and that temporary changes in neural physiology cause the secretory alterations that have been observed. The animal preparation is the sham fed dog. Sham feeding results in a vagal flow of gastric juice which is markedly diminished the day after freezing and which gradually recovers from day to day. The stomach, however, responds immediately to histamine commensurate with the vagotomy effect.

CARDIAC RESPONSES AND CATECHOLAMINES FOLLOWING CERVICO-THORACIC SYMPATHECTOMY, M.A. Klouda, Stritch School of Medicine and the Graduate School, Loyola University, Chicago, Illinois.

Predominantly chronotropic or inotropic alterations in cardiac response induced by stimulation of the right or left sympathetic cardiac nerves have been amply demonstrated. The present study was undertaken to determine whether specific patterns of distribution of fibers could account for these variations. Tissue catecholamine levels presumably indicate sympathetic fiber density, and the following values were obtained for the dog (μg per gram of tissue):

		Rt. Atr.	Lt. Atr.	Rt. Vent.	Lt. Vent. Apex	Lt. Vent. Base	Sept.
Control	(8)	1.46	1.13	0.78	0.64	0.62	0.67
Rt. Symp-x	(14)	0.64	0.93	0.48	0.46	0.50	0.47
Lt. Symp-x	(17)	0.88	0.82	0.42	0.34	0.34	0.37

Right cervico-thoracic sympathectomy resulted in a greater reduction in catecholamine content of the right atrium and right ventricle while left cervico-thoracic sympathectomy reduced the catecholamine content of both ventricles with lesser changes in the atria. Hemodynamic responses to stellate stimulation were studied in the unilaterally sympathectomized animal and compared with the response in the control animal. Left sympathectomy resulted in a deficit in left ventricular function with a lesser effect on the right ventricle. Atrial function was relatively unaffected. Right sympathectomy nearly abolished the increase in heart rate following stellate stimulation. There was also some deficit in the inotropic response. It is concluded that the right sympathetic cardiac nerves innervate mainly (but not exclusively) the right side of the heart while the left nerves innervate the entire heart and especially the ventricles. (Supported by grant no. HE 08682-01 from NIH.)

PARAMETRIC EFFECT OF "EXTRACELLULAR VOLUME" ON RENAL NA+ REABSORPTION, A.R. Koch, Dept. of Physiol. and Biophysics, Univ. of Wn., Seattle, Wn.

Renal Na^+ reabsorption in anesthetized dogs was determined with conventional clearance techniques. In experiments in which the plasma values of $[Na^+]$, $[K^+]$, and $[Cl^-]$ were held constant and filtration rate ($\dot{V}_g$) was varied by graded renal arterial constriction, a single functional relationship between filtered load of Na^+ and $\dot{V}_g$ could not be obtained unless isotonic NaCl solution was infused at rates equal to urine flow. When the infusion balanced urinary excretion, a single relation was obtained which was fixed for at least 6 hours. Under these conditions, the percent reabsorption (F_{Na}) was constant through a four-fold change in $\dot{V}_g$. When extracellular volume was varied by infusion of additional saline, the greater the increment in extracellular volume, the lower was the F_{Na}. Because it was independent of $\dot{V}_g$, F_{Na} could be used to measure this parametric effect. Isotonic expansion of the extracellular fluid could reduce F_{Na} to 0.7. Three possible causes of this parametric effect can be tentatively excluded. First, the constancy of F_{Na} as V_g was varied by renal arterial constriction argues against an effect depending on blood pressure sensed in the kidney. Second, the infusion of large volumes of saline into one renal artery modified transport in both kidneys identically. Hence a local dilution of any constituent of plasma does not appear to be involved. Third, experiments were conducted in which the extracellular volume was varied periodically in a triangular wave. When F_{Na} was plotted as a function of extracellular volume, the resulting curves showed either closed-loop characteristics or were slightly open, the path moving counterclockwise. These results are incompatible with the parametric effect depending on the release or destruction of any hormone which persists in the body for as long as 10 minutes. (Supported by grant PHS HE-04469.)

LOCAL PROTEIN BIOSYNTHESIS AND RNA IN MAMMALIAN AXONS.
E. Koenig. Dept. Physiol., State Univ. New York at Buffalo, Buffalo, N. Y.

Axotomy of the XII cranial nerve of the cat about 3 cm from the cell bodies, following irreversible inactivation of 80 - 90% of the acetylcholinesterase (AChE) by diisopropylfluorophosphate (DFP) produces a marked local increase in the specific activity of the enzyme over a period of 24 hours. The increase is restricted to the distal 3 mm segment of the central, regenerating nerve stump and ranges from 6 - 10 times greater than either the adjacent central segment or the equidistant segment of the intact, contralateral nerve. Intracramial injections of puromycin, an inhibitor of protein biosynthesis, appears to suppress slightly the net, local increase of AChE, as well as that of the enzyme regeneration after DFP elsewhere. Preliminary ultramicro analyses of isolated, myelin-free axons taken from the XI cranial nerve root of the cat indicate that a substance is present in pure axonal material which is suggestive of RNA, on the basis of its specific absorption ratio of 265:280 mμ. The evidence indicates that axons are capable of local protein synthesis despite the absence of demonstrable Nissl substance and its ultrastructural counterpart of ribosomes from the axoplasm. Since it has been demonstrated that AChE is lost from the neuronal cytoplasm following axotomy and remains absent during the outgrowth period, its presence and active synthesis in the axon during regeneration suggests the likelihood of the existence of a stable messenger RNA which is always present in the axon.
(Supported in part by PHS Grant NB 04656, from the N.I.N.D.B.)

ELECTRICAL ACTIVITY RECORDED FROM THE PITUITARY STALK OF THE CAT.
Kiyomi Koizumi and Tomoe Ishikawa*. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

There has been no direct electrophysiological evidence in mammalian preparations to indicate that the pituitary stalk contains nerve fibers which conduct impulses following the stimulation of supraoptic nucleus. We have attempted to record action potentials from the pituitary stalk by inserting a fine steel microelectrode into that structure of a cat anesthetized with chloralose. It was possible, in the hemispherectomized preparations used, to visualize the stalk and make correct placement of the electrodes. Stimuli were then applied in the supraoptic nucleus region by a bipolar electrode. Nerve action potentials were recorded during the control or resting state. During repetitive stimulation of the hypothalamus these fiber discharges were definitely augmented. In a few instances, responses clearly evoked by excitation of the supraoptic nucleus were recorded from the stalk. Electrode placements in each instance were checked histologically.
(This work was supported by a grant from the USPHS (NB-00847(09)).

THE NASAL RESISTANCE OF NEWBORN INFANTS. G.P. Kong* and G. Polgar. Department of Otolaryngology, University of British Columbia, School of Medicine, Vancouver and Department of Physiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

The airflow resistance of the nasal airways was measured in 5 newborn infants. First esophageal pressure and airflow were recorded simultaneously when the infants breathed quietly through the nose. Then similar recordings were made while the babies breathed through a plastic oral airway. The total non elastic lung resistance at equal lung volumes for both conditions and the difference between the two values was calculated. After a correction for the resistance of the oral airway (2.7 cm H_2O/L/sec, at flow rates 3.5 to 9 L/min) an average value of 13 cm H_2O/L/sec was obtained for the nasal resistance. This was 27% of the average total non elastic lung resistance. In one infant the nasal resistance, measured by posterior rhinometry, was 13.4 cm H_2O/L/sec.

Considerable variations of the nasal resistance, comparable with data on adults, were observed. The resistance of the nasal passage relative to the lower airway appears to be less in newborns than in adults. This is an advantage to the former who is obligated to breathe through the nose.

STUDIES ON THE PHYSIOLOGY OF VASOPRESSIN, (3) OBSERVATION OF PARADOXICAL URINARY RESPONSES TO SUBLIMINAL VASOPRESSIN DOSES. Jenö Kramár, Willard M. Duff*, and Edward H. Grinnell*. Creighton Medical School, Omaha, Nebraska.

An increase in urinary flow has been described to occasionally occur preceding or following the typical antidiuretic effect of vasopressin; however, this is not regarded as a characteristic or regular feature of vasopressin action. In the course of a systematic study of the dose-effect relationship of vasopressin in the rat rendered anesthetic and diuretic by ethanol, it was observed that the type of vasopressin action upon the kidney is a function of the dose of the hormone i.e., its blood concentration resulting from the injection. As a rule, intravenous injection of 5-20 millimicrounits arginine-8-vasopressin produces antidiuresis, increased urinary chloride concentration and increased actual chloride output as well as a biphasic change in the creatinine excretion (decrease followed by increase). Conversely, 1 millimicrounit causes, in the majority of animals, marked diuresis, decreased chloride concentration and a decrease or no change in the chloride output together with a monophasic change (only increase) in the creatinine excretion. The physiologic and pathologic significance of this finding is the subject of studies in progress.

THE GAS EXCHANGE RATIO OF ANIMALS EXPOSED TO OXYGEN AT ATMOSPHERIC PRESSURES. George H. Kydd. U.S. Naval Air Development Center, Johnsville, Pa.

The question of whether breathing 100% oxygen at atmospheric pressure brings about changes in the respired gases is left unresolved because of somewhat conflicting reports in the literature. It seemed that more light could be thrown on the subject if it were possible to measure both the oxygen absorbed and the CO_2 produced by animals throughout an exposure. Presented here are the results of experimental runs in which such measurements were made on rats and rabbits. The animals were exposed in an environmental system during runs which were ended when there was a death or to 100 hours, whichever occurred first. Oxygen flow into, and CO_2 removed from the chamber were measured by flowmeters and from gas analyses. Control runs were carried out in which measurements were made on animals breathing air. The gas exchange ratio was estimated from summations of the minute-to-minute gas flow rates. The plotted ratios showed two periods when there was variation from the normal: (1) in the few hours following changeover to oxygen breathing when the ratio was depressed and (2) at around 40 hours exposure the ratio began to fall and continued throughout the remainder of the run. Although the effects of high oxygen tensions on cells are not well understood, these effects give rise to other changes in the function and form of organs and tissues with which we are familiar. Of these there are the changes recurring in the pulmonary circulatory system as described by Bennet (J. Exp. Med. 59: 181, 1934). It is suggested that the depressed exchange ratio results from these degenerative changes.

EFFECT OF INSULIN ON HEPATIC K MOVEMENTS AS INFLUENCED BY HYPOTHERMIA, BARBITURATE AND DIBENZYLINE. Luc E. Lambotte[0] and William C. Shoemaker, Hektoen Institute, Cook County Hospital, Chicago, Ill. Arterial, portal and hepatic plasma K were measured in 33 chronic experiments in dogs whose hepatic vessels were catheterized 3 to 8 days previously. In the thiopental anesthetized dog, the control hepatic-portal concentration difference was + 66 $\pm$ 40 (SE) μEq/l. This gradient was reversed 2 min after insulin injection and the greatest change was reached 10 min after injection when the gradient was -675 $\pm$ 200 (SE) μEq/l. The control hepatic K output of 43 $\pm$ 26 μEq/min was changed to an uptake of 173 $\pm$ 36 μEq/min during the first 20 min after the injection. A comparable effect was obtained when the conscious animal was pretreated with the blocking agent, phenoxybenzamine HCl (dibenzyline), 1 mg/kg, but in conscious dogs insulin produced only a slight uptake of K by the liver. Six animals were cooled to 28^0C, the arterial K decreased from 2.85 $\pm$ .15 mEq/l to 2.20 $\pm$ 0.22 mEq/l. When stable low temperatures and K levels were obtained, the injection of insulin produced a new drop in plasma K to 1.30 $\pm$ .14 mEq/l and the liver took up K in comparable magnitude to that which occurred at 37^0. The injection of insulin did not decrease the hepatic glucose output of both fasting anesthetized and unanesthetized animals; the K uptake occurred despite a net release of glucose by the liver. In 4 animals the injection of anti-insulin serum produced a net hepatic K output of 133 $\pm$ 23 μEq/min after injection as compared to 17 $\pm$ 11 μEq/min during the control period. In conclusion, insulin produced an hepatic uptake of K. This effect was greater when epinephrine was blocked by dibenzyline and barbiturate, and it occurred relatively independent of glucose metabolism.

KINETICS OF O_2 EXCHANGE WITH HYPOCHROMIC MICROCYTIC ERYTHROCYTES. W. H. Lawson, Jr. (Intro. by L. W. Eichna). U.S. Army Research Institute of Environmental Medicine, Natick, Massachusetts

We have induced chronic iron deficiency anemia in dogs, and have measured the in vitro rates of red blood cell oxygenation and deoxygenation in a stopped flow rapid reaction apparatus as previously described (Fed. Proc. 1962). As there was no significant difference in oxygenation rate constants, k_o', measured at 37 or 22°, they were done at 22° pH 7.4 to avoid hemolysis. Deoxygenation rate constants, k_c, were measured at 37° pH 7.4. Mean values for rate constants, deoxygenation, half time, mean corpuscular volume (MCV), and mean corpuscular hemoglobin concentration (MCHC) are given for 7 experiments in 3 dogs.

MCV (u^3)	MCHC (%)	k_o' (mM^{-1} sec^{-1})	k_c (sec^{-1})	t 1/2 (sec)
59	35	114	19.5	.036
51	31	126	26.4	.026
34	27	217	55	.013

The values for k_o' at a given MCV are greater than those reported for various mammalian species by Holland and Forster (Fed. Proc. 1962). The deoxygenation rates were used in a modification of the Krogh-Erlang equation to calculate the critical venous PO_2 for resting skeletal muscle, the lowest PO_2 at which O_2 consumption can be maintained constant. Other data used were 1) hgb of 4 grm. %, 2) pH 7.85, 3) capillary density of 70/mm^2 tissue, 4) tissue O_2 consumption of 10^{-4} ml/ml tissue, and 5) tissue diffusion coefficient of 2.4×10^{-4} cm^2/sec./mm. The result for normochromic normocytic anemia with alkalosis is a critical venous PO_2 of 29 mm which is decreased to 25 mm in hypochromic microcytic anemia because of the increased rate of red cell deoxygenation.

OVARIAN RESPONSIVITY TO EXOGENOUS LH OVER A 24-HOUR PERIOD. Irene E. Lawton* and Neena B. Schwartz. Univ. Ill. Coll.Med., Chicago, Ill.

It is well established that a daily facilitation for release of the ovulatory surge of LH occurs between 2PM and 4PM in the cyclic rat. Although much of the influence of "time of day" on the pituitary-ovarian axis undoubtedly is exerted at a hypothalamic-pituitary level, there may also be ovarian circadian rhythms which participate in the regulation of the timing of events in the rat estrous cycle. In the present study the possibility of a 24-hr periodicity in ovarian responsivity to LH was investigated. PMS-plus HCG-primed immature rats were injected with saline, 0.4μg LH, or 1.6μg LH at 10AM, 2PM, 6PM, 10PM, 2AM, 6AM, and 10AM; ovaries were removed 3 1/2hr later for ovarian ascorbic acid (OAA) concentration measurements. The experiment was performed twice, using 2 groups of recipients kept under controlled lighting conditions (lights on 5AM - 7 PM). In both experiments, OAA levels fell markedly between 2PM and 6PM in the saline-treated "controls", not returning to original levels until after midnight, suggesting the possibility of an endogenous LH release after 2 PM. An alternative hypothesis is that the OAA itself shows a spontaneous time-related drop after 2PM, independent of any hypophyseal secretion. OAA levels (uncorrected for saline values) in the LH-treated rats also showed a significant variation with time of day. The % OAA depletion (from saline values) following 0.4μg LH was proportional to OAA levels in the saline-treated rats, and varied significantly with time. The % OAA depletion (from saline) induced by 1.6μg LH did not show any consistent significant alteration with time, and was independent of the saline-induced levels. These results suggest that OAA responsivity, at least to the higher dose of LH, is essentially the same throughout the 24-hr light-dark period. (Supported by grant HD-00440, NIH.)

THALAMICALLY-INDUCED CHANGES IN PYRAMIDAL TRACT CELL ACTIVITY.
F.E. LeBlanc* and J.P. Cordeau, Laboratoire des Sciences Neurologiques, Département de Physiologie, Université de Montréal.

Using curarized, locally-anaesthetized cats, electrodes were placed in the nucleus ventralis lateralis thalami (VL) and in the bulbar pyramid, and the pericruciate cortex was explored with microelectrodes. Pyramidal tract (PT) cells were identified by antidromic responses to pyramidal stimulation. Post-stimulus histograms were used to study the probability of PT cell discharge following VL stimulation. Single shocks to VL were followed by short-latency (1-3msec) responses, followed by a prolonged period of inhibition extending to at least 150msec, and subsequently by a late excitation (200-250msec). This was at times followed by a second period of delayed excitation (400-500msec). The early response increased gradually as the stimulation frequency was increased and reached a maximum at a frequency of 4-6cps. Trains of stimuli at 5 cps were often followed by a few spontaneous bursts of PT cell activity at intervals of 200 msec and this oscillating afterdischarge was prolonged when VL stimuli were short-duration bursts. From this it is concluded that the preferential oscillating frequency of this thalamocortical system is 4-6cps under these conditions. These results and other observations from this laboratory on central unit firing in experimental tremor (Lamarre and Cordeau, Fed. Proc. 1963, 22:456), together with the neurosurgical experience that VL destruction abolishes Parkinsonian tremor support the hypothesis of a central pacemaker circuit, with VL as a component, at the origin of tremor. The time course of the inhibition as outlined by conditioning and test shock technique, its marked prolongation by tetanic stimulation, and our observations that it is resistant to strychnine and prolonged by pentobarbital might indicate that this inhibition is of the presynaptic variety. (Aided by the Medical Research Council of Canada .

ALDOSTERONE ACTION IN THE COUNTERCURRENT MULTIPLIER OF THE DOG NEPHRON.
S.J. LeBrie and D.M. Landwehr*. Dept. Physiol., Tulane Univ. School of Med., New Orleans, La.

Only about 2% of total Na reabsorption is controlled by aldosterone. This suggests a specific and limited site of action. Since the reabsorption of Na in the ascending limb of Henle's loop is a prerequisite for urinary concentration, an action of aldosterone here would be expected to increase urinary osmolality (Uosm). In a previous report (Physiologist 6:220, 1963), we concluded that chronic administration of aldosterone in adrenalectomized animals affects urinary concentration via an action on plasma Na and does not delineate a specific site of hormone action. In the present experiments an acute effect of aldosterone has been demonstrated in normal hydropenic dogs receiving exogenous ADH. An increase in Uosm occurred within 1 1/2 to 2 hours after administration of 200 μg of d-aldosterone. The maximal osmolality increase occurred between 2-3 hours and ranged between 250-350 mOsm/kg H_2O (4 dogs). Three dogs showed decreased Na excretion which could be correlated with rising Uosm. The fourth dog was reabsorbing 99.7% of filtered Na before aldosterone administration. Since urinary osmotic pressure increased with no change in Na reabsorption this may indicate a shift in locus from a more distal to a more proximal (loop) area. An action of aldosterone in the distal tubule could conceivably increase Uosm by decreasing the volume of fluid delivered to the collecting ducts (Cosm) and consequently reducing $T^c_{H_2O}$ thereby decreasing medullary interstitial dilution and concentrating the urine. Since Uosm increased in all experiments without a decrease in $T^c_{H_2O}$, this obviously did not occur. It is concluded that Na reabsorption in Henle's loop is in part controlled by aldosterone. Supported by U.S.P.H.S. Grant AM05050-02.

FAST FIBER ACTIVITY IN RABBIT OPTIC NERVE. R. J. Lederman* and W. K. Noell. Dept. Physiol., State Univ. New York at Buffalo, Buffalo, N. Y.

Optic tract compound potentials were recorded in response to electrical stimulation of the visual pathway at or near the eye, lateral geniculate, and superior colliculus. The electrical stimulus was paired at varying intervals with a preceding light flash and the pattern of light-induced activity determined by the changes in the response to electrical stimulation resulting from impulse collision or refractoriness. Predominance of "killed-end" effects in recordings from within the optic tract made them unsuitable for analysis; recordings from the surface of the nerve or tract, however, showed typical triphasic action potentials (main phase negative) and revealed three major fiber groups conducting at rates of 30-35, 15-25, and 5-10 meters/sec. In response to brief xenon light flashes virtually all of the fast fibers fired simultaneously after a rather consistent latency of about 50 msec, whereas activity of the slower fibers was evident after 15 msec and followed the typical form of the optic tract response to photic stimulation, with no more than 50% of these fibers active at any one time. With long light flashes a similar pattern occurred: fast fiber activity followed "on" after 50 - 70 msec but upon cessation of light they fired after only 30 msec. Flicker (xenon flashes) was followed with little change in fundamental delay, even when this period exceeded the stimulus interval. Evidence will be presented indicating that the fast-conducting optic nerve fibers branch into midbrain and thalamus and that fast and slow fibers converge upon the same post-synaptic elements.
(Supported by USPHS Grant NB-02710-04)

ON THE CONCENTRATION OF GLUCOSE AND ELECTROLYTES OF THE ABSORBED[1] AND ENTEROSORBED[1] FLUIDS ACROSS INTESTINAL MUCOSA. J. S. Lee, Department of Physiology, U. of Minnesota, Minneapolis, Minnesota

When cat or rat intestine was perfused with Ringer + T-1824 + 0.2% glucose through its vascular system, fluid flowed out of the villous tip and intervillous space into the lumen. This fluid contained no glucose, but contained a higher conc. of electolytes than in the perfusate: K increased by 260%; Ca, 20% and Cl, 10%. In an in vitro rat intestine preparation with both mucosal and serosal sides bathed in bicarbonate Ringer containing 0.5% glucose, absorbed fluid was obtained from the main lymphatic duct. This fluid contained glucose in the concentration range of 0.5 to 0.9%, with the conc. inversely related to the electrolyte conc. and lymph flow. The transported fluid was isoosmotic regardless whether net flow was toward the lumen or blood. Based on these data and other evidence, it is concluded that the final solute conc. of absorbed fluid or enterosorbed fluid is most probably not the same as the initially insorbed or exsorbed fluid because of possible exchange diffusion due to: (1) simultaneous bidirectional fluid flow, (2) unequal bidirectional permeability of mucosa to solutes (for glucose, from mucosa to serosa only) and (3) maintenance of isoosmolarity. Therefore, solute conc. ratio between mucosal and serosal bathing fluids as well as lymph does not represent transport gradient. For definition of these terms[1] see Code (Perceptive in Biol. & Med. 3:560, 1960). Supported by USPHS grant AM 05073

THE ISOLATION AND CHEMICAL CHARACTERISTICS OF RENOMEDULLARY DEPRESSOR SUBSTANCE. James B. Lee*, Bertil H. Takman*, and Benjamin G. Covino. Dept. of Medicine, St. Vincent Hospital, Worcester, Mass.

Extracts of renal medulla result in a fall in blood pressure by direct peripheral arteriolar dilatation with a 35% decrease in total peripheral resistance and a compensatory increase in cardiac output and heart rate (Covino, B.G. and Lee, J.B. Clin. Res. 12: 179, 1964). The present studies were undertaken to isolate and characterize renomedullary depressor substance. Depressor activity, present in the supernate of 80% ethanol homogenates of crude rabbit medulla, was chromatographed on DEAE-cellulose by gradient elution. Depressor activity partitioned into chloroform, benzene, and ethyl acetate from acidified but not alkalinized DEAE eluate. Thin layer chromatography of the active fraction revealed a single iodine-staining spot with a greater mobility than crystalline prostaglandin E-1 (PGE-1). Infra-red analysis (KBr pellet) showed absorption spectra consistent with carbonyl and hydroxyl groupings. Changes in U-V spectrum on treatment with alkali and acid indicated that the formed derivative contains the same chromophore as corresponding prostaglandin E derivatives. The present studies suggest that renomedullary depressor substance is an acidic lipid closely related to the prostaglandin E series of compounds. Important differences in its mechanism of vasodepression and thin layer mobilities suggest that it is not PGE-1,2 or 3 but may represent an unknown derivative.

FURTHER EVIDENCE FOR CALCIUM COUPLING OF THE ELECTRICAL AND MECHANICAL EVENTS OF THE PERFUSED, SPONTANEOUSLY BEATING HEART. Y. C. P. Lee and M. B. Visscher, Dept. of Physiology, Univ. of Minnesota, Minneapolis, Minnesota

Cardiac contraction can be reversibly abolished by reducing or chelating the extracellular Ca (Physiologist, Aug. 1962). This report will present more evidence that Ca activity, although it is influenced by extracellular K, may be directly linked to the contractile system. When perfused rabbit hearts were changed to Ca-free solns. containing 1-5 mM/L of K, spontaneous contraction disappeared in spite of the presence of electrical activity. If K and Ca were absent, both mechanical and electrical activity disappeared. Hearts changed to a K-free soln. showed mechanical contraction in the presence of very low Ca. In 0.045, 0.09, 0.2, and 0.4 mM/L of Ca, the heart showed a temporary decrease of contractile force, followed by normal or even stronger contractions. The degree of decrease of contractility was inversely, and the length of time the heart would contract directly proportional to Ca conc. If, in these low Ca solns. K was raised to 1.5, 2.5, 8.1, or 16 mM/L, respectively, the mechanical contraction was inhibited but the electrical activity remained. However, with further increase of Ca, mechanical contraction was restored. The effect of Ca directly on the mechanical contraction was further indicated by the development of contracture during recovery from Ca-lack arrest with a sudden increase of Ca, or by perfusion with high Ca soln. containing no K in the absence of prior arrest.

ELECTROTONUS IN CULTURED CHICK HEART CELLS MEASURED INTRACELLULARLY. D. Lehmkuhl* and N. Sperelakis. Western Reserve Univ., Cleveland, O.

Electrophysiological properties of cultured heart cells are similar to those of intact heart cells. Ventricles from 6-8 day chick embryos were cultured 4-14 days following trypsin-dispersion. Isolated single cells reassembled into various monolayer communities: strands, nets, rosettes, and sheets. A bridge circuit was used to pass current through microelectrode #1 while simultaneously recording membrane potential. Electrotonic spread of current was measured by electrode #2 which was impaled at various distances from the site of current injection by microscopic observation. Most cells were fired by transmission of excitation from neighbors. In driven cells, polarizing currents were without effect upon frequency. The voltage/current relationship for electrode #1 was linear and had a mean slope of about 13 MΩ; e.g., 2 nanoamperes hyperpolarized the cell by 26 mv. The relationship for electrode #2 was also linear and in some cases at short distances had a slope as large as that for #1, i.e., the degree of electrotonic interaction was nearly 100%. However, in other impalements at short distances, interaction was nearly zero. In sparce cultures containing large cells (strands), substantial interaction occurred at distances up to 400 μ. Criteria which helped to determine when both electrodes impaled the same cell included: a) a typically sharp diminution of the resting potential recorded by the first electrode to a common intermediate level upon insertion of the second electrode and b) simultaneous and congruous subthreshold changes in membrane potential. Thus, the degree of electrotonic spread was not dependent upon inter-electrode distance per se, but appeared to depend on whether both electrodes impaled the same cell. (Supported by Public Health Service (H-5087) and Cleveland Area Heart Society.)

FLOW AND VOLUME EVENTS NEAR RESIDUAL VOLUME DURING FORCED EXPIRATORY VITAL CAPACITY MANEUVERS. David E. Leith* and Jere Mead (introduced by Lewis Dexter). Harvard School of Public Health, Boston, Mass.

The record of volume in time during a forced expiratory vital capacity maneuver (FEVC) in young subjects changes slope suddenly near residual volume (RV) and becomes irregular, while that of older subjects is smooth for as long as the effort can be maintained. This suggests that the latter remain on their maximum flow-volume ($\dot{V}/V$) curves, while the former depart from them. Five healthy subjects over 40 years of age and five under 35 did FEVC's into a spirometer while seated within a chamber sealed about their necks. They were instructed to maintain their expiratory efforts as long as possible. Most younger subjects reached zero $\dot{V}$ within 4 seconds, while most older ones were still expiring after 10 seconds. As $\dot{V}$ neared or reached zero, the pressure in the chamber was abruptly raised to 40 cm. water. Little response was seen in the older group, but $\dot{V}$ rose sharply to the extrapolated maximum $\dot{V}/V$ curve in the younger subjects. We conclude that in young subjects with high lung recoil pressures, the minimal air volume is smaller than the volume at which maximum expiratory muscle force is balanced by total recoil forces; this balance then determines RV. In contrast, loss of lung recoil forces in older subjects results in larger minimal air volumes. These subjects then approach closer to the minimal air volume, where maximum expiratory $\dot{V}$ is so low that breath holding ability limits the duration of the maneuver and thus the volume expired.

VARIATIONS OF THE VA/Q DISTRIBUTION IN HUMAN LUNG. C. Lenfant, (Intr. by C. J. Martin), Firland Sanatorium and University of Washington Medical School, Seattle, Washington.

Previous experiments have shown that there are units in the lung with an undeterminable VA/Q. All these units have significant blood flow but their ventilation is minimal or nonexistent. Also, they cause the A-aD_{O_2} and A-aD_{N_2} to be large when breathing a high F_{IO_2} gas mixture. If the VA/Q distribution, including such lung units, was not changing, A-aD_{O_2}, A-aD_{CO_2}, and A-aD_{N_2}, would remain constant after steady state had been reached from the onset of high O_2 breathing. Actual measurements of A-aD in O_2, CO_2, and N_2, in ten subjects having minimal pulmonary tuberculosis (6), or with diffuse obstructive syndrome (4), showed constancy of A-aD_{CO_2} and variations of A-aD_{O_2} and A-aD_{N_2} between successive samplings at 15 minute intervals during a 75 minute period of elevated O_2 breathing. Since A-aD_{CO_2} did not vary, the units responsible for the observed variations must have been units with a low or undeterminable VA/Q whose number and absolute VA/Q changed within the duration of the experiment. Using a model and by comparing the simultaneous variations of A-aD_{O_2} and A-aD_{N_2} the approximate VA/Q of those units was determined. It was found to be lower than .01. It was also determined that some lung units reached complete collapse and that their dependent blood was less than 1%. Supported by grants NIH HE.08465 - HE.01892.

OXYGEN CONSUMPTION OF ISOTONICALLY WORKING HEART MUSCLE. Eugene A. Lentini and William V. Guyton°. Univ. of Oregon Medical School, Portland, Oregon and the Medical College of Virginia, Richmond, Va.

The oxygen consumption (QO_2) of isotonically contracting trabeculae carneae from the rat's left ventricle was measured concomitantly with the amount of shortening and the integrated biological work. The latter was calculated from the magnitude and duration of shortening. This is a tension time index. Muscles were maintained under a total resting tension of either 0.88 or 1.03 gm. The QO_2 was measured by direct Warburg manometry employing a modified flask and a sensitive manometric reading system. The shortening was measured and oscillographically recorded through the use of a calibrated electronic micrometer positioned outside the flask. It was found that the biological work had a significantly high correlation with the physical work. The QO_2 was significantly correlated with the amount of shortening only in those preparations under a resting tension of 1.03 gm. The relationship between the oxygen consumption and the biological work was influenced by the resting tension. The resting tension apparently influenced the muscle's efficiency through the work factor. The calculated heat production of the trabecular muscles was found to approach the caloric equivalent of the QO_2. The apparent conclusion is that heart muscle has a limited Fenn effect and a small but significant portion of the total energy is converted to physical work. Also, the nature of the relation existing between the QO_2 and work is influenced by the resting tension. (Supported by USPH Research Grant HE 04562).

HISTAMINE-LIBERATING ACTIVITY OF DOG SERUM PROTEIN FRACTIONS AFTER CHROMATOGRAPHY ON DEAE CELLULOSE. M. Levy and J.Q. Bliss (intr. by B. Delisle Burns). Dept. of Physiology, McGill University, Montreal, Canada.

Dialyzed dog serum protein fractions prepared by chromatography on DEAE cellulose produce an increase in local capillary permeability with distinct wheal formation when injected intracutaneously into the donor animal. This response does not occur after injection of whole autologous serum of after injection of serum fractions prepared by cation-exchange chromatography on carboxymethylcellulose, but it does occur after injection of fractions prepared by chromatography on DEAE Sephadex A-50. The whealing response to protein fractions appears to be mediated by a release of endogenous histamine, for the responses are diminished or absent (a) after the test animal is given 2 mg./kg. of the antihistamine mepyramine, and (b) in areas of skin depleted of their endogenous histamine by pretreatment locally with the histamine liberator compound 48/80. The addition of whole serum or plasma to serum fractions inhibits their ability to release histamine. It is suggested that subtle changes in the protein molecule occur during chromatography in the presence of the diethylaminoethyl grouping which convert the molecule into a histamine liberator but which cannot be detected by physicochemical means.

Supported by the Medical Research Council of Canada.

THE MINIMAL LATENCY OF INHIBITION IN RABBIT RETINA. M. D. Licker* and W. K. Noell. Dept. Physiol., State Univ. New York at Buffalo, Buffalo, N.Y.

Experiments were designed to measure the earliest appearance of light induced inhibition at the ganglion cell level in relation to the earliest manifestation of excitation. In order to overcome individual element differences, the discharges of groups of ganglion cells were led off by 50 - 100 μ electrodes placed at the surface of the retina in an open-eye preparation (urethane anesthesia). Impulses were tape-recorded or immediately analyzed; they were converted into brief pulses, counted repetitively over 1 msec or longer periods, and/or added by the 400 addresses of a Mnemotron computer. As in Granit's studies, a strong light (xenon flash of maximal intensity) was superimposed upon the various bursts of firing following the "off" of a weaker light of variable duration. Marked inhibition always preceded the firing in response to the xenon flash. Firing had its earliest onset between 16 and 22 msec compared to the minimal latency of 13 msec when the flash was not preceded by the light. In contrast, inhibition was clearly evident after a latency of only 10 msec; under favorable conditions the onset of inhibition could be traced to no later than 8 msec. This earliest inhibition started midway during a-wave development whereas excitation never preceded b-wave rise. Inhibition was strongest when b-wave appearance was delayed and a-wave broadened. Assuming that most of the latency of retinal excitation is contributed by the visual cells, the results suggest that early visual cell reactions oppose the mechanisms which lead to excitation of the retinal network.
(Supported by USPHS Grant 5 TI GM 341-04)

AN ELECTROPHYSIOLOGICAL STUDY OF AV CONDUCTION IN EMBRYONIC CHICK HEARTS. M. Lieberman and A. Paes de Carvalho*. State University of New York, Downstate Medical Center, Brooklyn, New York.

Both intracellular and surface electrodes were employed in the study of embryonic AV transmission. It has been previously reported (Fed. Proc. 23 (2): 249) that action potentials recorded from cells of the embryonic AV ring were similar in configuration to those of the adult rabbit AV nodal cells. The spread of excitation along the AV ring was compared in embryos of 7-8 days and 14-19 days. In both, delay of impulse propagation could be localized to a very narrow band of tissue along the entire extent of the AV ring. The conduction velocity of this tissue was between .003-.005 M/sec. Histological sections of the AV ring were noticeably similar in structure to AV nodal tissue. That the AV ring is capable of behaving in a manner similar to the adult AV node was shown by studies in which increasing the rate of stimulation produced an increase in the PR interval with subsequent AV block. Simultaneous intracellular recording localized the block to cells of the AV ring. Both normal and retrograde stimulation revealed the spread of conduction across the AV ring to be of a decremental nature. The tissue was blocked more readily under retrograde drive when stimulated at higher frequencies. Addition of acetylcholine to spontaneously beating hearts resulted in a decreased heart rate (and eventual arrest) with no apparent effect on PR interval. The same procedure in driven hearts caused AV block. Norepinephrine produced an increased rate in spontaneously beating hearts, along with a decrease in PR interval. The foregoing evidence is offered in support of the idea that the embryonic AV ring is the functional counterpart of the adult AV node. (Supported in part by grants from USPHS NHI (HE-5148(04)) and Life Insurance Med. Res. Fund (G61-26)).

MECHANISM OF PAIN. I. ROLE OF INJURY & INFLAMMATION. R.K.S. Lim, MSRL, Miles Laboratories, Inc., Elkhart, Indiana

The regularity with which pain may be evoked by 2-4 micrograms of the peptides bradykinin, kallidin, subst. P, injected intra-arterially into the skin or other organs throughout the body, indicates that cutaneous and visceral receptors for pain are primarily chemosensitive, and that nociception involves the accidental stimulation of stem axons as well as terminals of chemo- and other (thermo-, mechano-) receptors in skin. This explains the multimodal adequacy of nociceptive stimulation. The sensation of pain is thus a complex somesthetic image, contributed to by all the receptors stimulated, and modulated by psychic influences. The possibility of blocking bradykinin-evoked pain by peripheral analgesics like aspirin, emphasizes the fact that the receptors mediating pain are chemosensitive. Since bradykinin is readily destroyed by kininase in plasma and lymph, the receptors on which it acts may be assumed to be near the capillaries. The paravascular sensory nerves which end as free branching terminals in the connective tissue space of capillary areas are obviously the chemoreceptors concerned. The visceral chemoreceptors usually evoke little response to nociception, probably because of their limited distribution. It is postulated that if injury results in the disintegration of fixed and circulating cells, liberating lysosomal proteases to act on plasma (or tissue) globulin and form peptides like bradykinin, inflammation will follow. The peptides are not only capable of stimulating the chemoreceptors evoking pain and aching, but may sensitize them, reducing their threshold to other stimuli and causing local tenderness. The function of the chemoreceptors for pain is thus to signal the chemical consequences of nociception (or ischemia), and not the incidence of injury itself, although it serves this purpose as well through inevitable involvement of stem axons and terminals, causing supramaximal stimulation.

INHIBITION OF Δ^1 -PYRROLINE-2-CARBOXYLIC ACID REDUCTION TO PROLINE BY THYROXINE. Raymond H. Lindsay (intr. by R. W. Hanson). Radioisotope Service, V.A.H., and Depts. of Pharmacology and Medicine, University of Alabama Medical Center, Birmingham, Alabama.

When slices of rat kidney cortex were incubated continuously at 37°C with DL-proline-^{14}C, Δ^1 -pyrroline-2-carboxylic acid (Δ^1 -P-2-CA) accumulated to a considerably greater extent in the presence of thyroxine than in its absence; yet more proline remained in the incubation medium in the absence of thyroxine. Equivalent amounts of proline plus Δ^1 -P-2-CA were present in both thyroxine and control flasks. The accumulation of Δ^1 -P-2-CA with the accompanying decrease in proline concentration was evident after one hour and occurred with as little as 0.5 μg thyroxine/ml (6.5×10^{-7}M). Metabolism of D- and L-proline proceeds principally by two different pathways. L-Proline is converted to Δ^1 -P-5-CA by proline oxidase and subsequently to glutamic acid. D-Proline is converted by D-amino acid oxidase to Δ^1 -P-2-CA which, catalyzed by a reductase, forms L-proline. Incubation of kidney slices with Δ^1 -P-2-CA demonstrated a T_4 depression of Δ^1 -P-2-CA utilization, proline formation and oxygen consumption. Assays of Δ^1 -P-2-CA reductase in 105,000 x g supernatant fractions from rat kidney cortex showed that this enzyme was very sensitive to thyroxine and was inhibited completely by 0.33 μg/ml (4.3×10^{-7}M), 60-75% by 0.033 μg/ml (4.3×10^{-8}M) and 20% by 0.0033 μg/ml (4.3×10^{-9}M) of the hormone. The accumulation of Δ^1 -P-2-CA and lower proline concentration noted after kidney slice incubation with DL-proline - but not L-proline - in the presence of T_4 can be explained by an inhibition of Δ^1 -P-2-CA reductase.

Cardiovascular Consequences of Acute Adrenalectomy
Edward M. Lintz and Allan M. Lefer (intr. by G. Sayers) Dept. of Physiology, Western Reserve Univ., School of Medicine, Cleveland, Ohio

Although the long-term cardiovascular effects of bilateral adrenalectomy are well known, relatively little information is available concerning the cardiovascular status during the first four hours after adrenalectomy. Pentobarbital anesthetized dogs develop a cardiovascular collapse within 30 minutes after bilateral adrenalectomy. Left ventricular contractile force (LVCF), mean arterial blood pressure (MABP) and femoral blood flow (FBF) fall to about 40% of control values. Heart rate (HR) and central venous pressure (CVP) increase about 25%. Infusion of large doses of aldosterone (up to 2 mg.) or cortisol (up to 200 mg.) after development of the cardiovascular collapse had no detectable effect on any variable studied. Infusion of cortisol (1 mg/min) starting 30 min prior to adrenalectomy and continuing throughout the surgical procedures completely protected against cardiovascular collapse in 4 of 4 dogs. Pretreatment with hexamethonium (5 mg/Kg) 30 min. prior to abdominal laparotomy, prevented the occurence of cardiovascular collapse in 7 of 7 such treated dogs. Hexamethonium itself lowered HR, LVCF and MABP. FBF was only slightly lowered. Pretreatment with phenoxybenzamine protected against cardiovascular collapse in 2 of 3 such treated dogs. Administration of phenoxybenzamine after development of the collapse, had no ameliorative action. (Supported by a grant from the Cleveland Area Heart Society.)

K AND Cl MOVEMENTS IN ISOLATED INTERCOSTAL MUSCLE FROM NORMAL AND MYOTONIC GOATS. R. J. Lipicky* and S. H. Bryant. Department of Pharmacology, College of Medicine, University of Cincinnati.

The intracellular concentrations of Na, K and Cl; and efflux of K^{42} and Cl^{36} (washout following a 200 minute load, at 38°C) were studied in unstimulated muscle bundles, in normal goat ringer. No differences (P greater than 0.05) were demonstrable between normal and myotonic muscles with respect to Na or Cl concentrations, water content or extracellular volume (estimated by mannitol). K concentrations were 20 mEq per liter of fiber water greater in myotonic than in normal muscle. At 38°C myotonic muscle had a time constant of efflux of K^{42} shorter than normal muscles (198 ± 5 and 232 ± 5 minutes respectively), whereas, at 25° myotonic muscles had a slightly longer time constant of efflux than did normal (433 ± 18 and 382 ± 14 minutes, respectively). This is consistent with a slower passive K flux in myotonic muscle which at 38°C is masked by a metabolically linked K movement. At 25°C Cl^{36} washout curves showed equivalent fast and slow components. However, an intermediate exponential component (time constant 10 minutes) appeared in myotonic but not in normal muscle washout curves. This intermediate component is interpreted to reflect a slower moving fraction of Cl in myotonic muscles. Collectively these data offer a possible basis for the previously reported high membrane-resistance in myotonic muscle (Fed. Proc. 21:312, 1962). (Supported by USPHS Grant NB-03178-04; NFND; and USPHS Postdoctoral 5-F2-GM-18, 729-02).

THE VASCULAR PATTERN IN THE HAMSTER CHEEK POUCH: A QUANTITATIVE APPROACH. A. Litton*, H. J. Berman and G. McCormick*. Biol. Res. Ctr., Boston Univ., and Peter Bent Brigham Hosp., Boston, Mass.

The microvasculature has been quantitated in the distal third of the cheek pouch of the living anesthetized hamster, Mesocricetus auratus. Camera lucida drawings and photographs were made of the general and detailed distribution of the vessels. Diameters and lengths of vessels were measured with a calibrated ocular micrometer. Cross-sectional areas, blood volume, and endothelial surface area were calculated for the different types of blood vessels. Magnification varied from 40X to 1200X. Anastomosing arterial arcades maintained an even pressure distribution to the terminal arterioles. No arterial venous anastomoses were noted. The capillaries formed a continuous basketlike network. The small veins formed finer systems of anastomoses than the arterial arcades. Measurements of total cross-sectional areas of the different types of blood vessels in 10 hamsters disclosed a linear relationship from the arterial arcades to capillaries. An approximate three-fold increase was observed from the small artery originating from the arcade to the terminal arteriole, and a similar increase from the terminal arteriole to the capillary bed. A further increase in total cross-sectional area of 20% and 33% occurred in the first and second order of postcapillary venules, respectively. The cross-sectional area then decreased in the third order of collecting vessels to95% of that in the capillary bed. The mean diameter and range of the first and second order venous vessels were 10μ (8-12μ) and 26μ (10-33μ), respectively. Approximately 75% of the blood was in the collecting vessels and only 3-10% in the capillary net. The endothelial surface area decreased from capillary through the first two orders of postcapillary venous vessels in the ratio of 6:4.7:1. (Aided by the Dept. of the Army, OSG., and the Nat'l Heart Institute, PHS.)

RELATIONSHIP OF THE ABSORPTION OF TRIOLEIN AND OLEIC ACID TO INHIBITION OF GASTRIC SECRETION. James F. Long* and Frank P. Brooks, Dept. of Physiol., School of Med., Univ. of Pennsylvania, Philadelphia, Penna.

The absorption of C^{14} labeled triolein and oleic acid was measured together with the inhibition of gastric secretion following a 100 gm meat meal in 4 dogs with vagally innervated gastric pouches and duodenal fistulae. In each experiment 26 ml of lipid were infused through the duodenal fistula at .76 ml/min starting 5 min before feeding. Peripheral blood was sampled at 1, 2, 3, 4, and 6 hrs after feeding and radioactivity in the plasma lipid determined. The vol of the gastric pouch secretion was measured every 30 min for 6 hrs. Acid and pepsin conc were determined on the 30 min samples by titration to pH 7 and the Hb substrate method, respectively. Feeding alone and with paraffin oil infusions served as control experiments. Paraffin oil had no effect. With triolein infusion the inhibition of gastric secretion lasted for 1.5-2 hrs followed by a secretory response which in the 6 hr experimental period equalled the acid and pepsin outputs of the control experiments in 3 of the 4 dogs. With oleic acid infusion the inhibition lasted for over 3 hrs followed by a response; the outputs of acid and pepsin, however, were significantly less than controls over the 6 hr period. Plasma radioactivity reached a peak with triolein at 3 hrs at 3.3% of administered radioactivity. With oleic acid the plasma radioactivity reached a plateau at 3 hrs and remained at 0.6% of administered dose for the duration of the experiment. One dog given triolein was killed 3 hrs after feeding and had 2.5% of administered radioactivity in the small bowel, and a second dog given oleic acid, killed at 3 hrs, had 24.5%. These results show that oleic acid is absorbed more slowly than triolein and that oleic acid inhibits gastric secretion for a longer period than does triolein. (Supported by a grant from Merck, Sharp, and Dohme.)

DETERMINANTS OF CIRCULATORY DRIVING PRESSURE IN ISOLATED LUNG. Raul Lopez-Muniz*, Newman L. Stephens*, and Baruch Bromberger-Barnea, The Johns Hopkins University, Baltimore, Md.

Previous work from this laboratory (Permutt et al) has shown that the driving pressure at any given horizontal layer of lung is given either by P_a-P_{alv} (pulmonary artery-alveolar pressure) or P_a - P_v (pulmonary artery - pulmonary venous pressure) whichever downstream pressure is larger. In the present study, isolated dog lungs were perfused with blood at constant flow. P_a and P_v were recorded with reference to the lowest part of the lung. P_{alv} could be maintained at any desired level. With P_v lower than P_{alv}, increases in P_{alv} caused linear increases in P_a with a slope of approximately 1 (.92 mean). At constant P_{alv}, when flow was stopped, P_a fell to P_{alv} when P_v was less than P_{alv} and fell to P_v when P_v was larger than P_{alv}. This pressure difference in P_a between the flow and stop-flow state is the driving pressure at the lowest level of the lung. When P_v was lower than P_{alv}, changes in P_v did not affect this driving pressure. However, when $P_v \geq P_{alv}$, the magnitude of the driving pressure at the bottom of the lung decreased progressively as P_v was raised. It is believed that the progressive reduction in driving pressure at the bottom of the lung is due primarily to a reduction in blood flow at the bottom of the lung resulting from a larger proportion of the constant total flow going to the upper areas of the lung.

PROJECTION OF DORSAL ROOTS TO CEREBRAL CORTEX OF SQUIRREL MONKEY (SmI, SmII, MsI, MsII AND PENFIELD'S SUPPLEMENTARY SENSORY AREA)
Carlo Ambrogi Lorenzini and Allen J. Blomquist, Dept. of Surgery, Medical School, University of Wisconsin, Madison, Wisconsin. (intr. by C. N. Woolsey)

In this study electrical stimulation of dorsal roots and of the Vth nerve was used to analyze the cortical afferent regions of the squirrel monkey under nembutal anesthesia. Surface positive potentials were recorded from contralateral and ipsilateral regions of SmI, MsI and SmII and the contralateral regions of MsII and Penfield's supplementary sensory area. The SmI and MsI areas extended from the cingulate sulcus on the medial wall to the Sylvian fissure laterally. In both areas the face subdivision was split into two parts by a large hand area. The SmII regions for the leg and the arm and face, respectively, extended over a part of the insular cortex and the upper bank of the Sylvian fissure. Under conditions of light nembutal anesthesia responses were evoked in two areas of the medial wall of the contralateral hemisphere. One of these is the supplementary motor area (MsII) lying just anterior to the MsI region. In this supplementary motor area (MsII) a face subdivision was found on the dorsal surface of the hemisphere. The second area of response lay just posterior to the SmI region and appears to be the supplementary sensory area of Pennfield. No face subdivision was defined for this area. The results support Woolsey's contention that there are several distinguishable, somatotopically organized cortical areas, each of which appears to be concerned with both sensory and motor functions. This investigation was supported by training grant 5TI NB 5326-04 NINDB and by grant B-2061 (C-2) NIH.

MECHANISM OF SYSTEMIC HYPOTENSION PRODUCED BY POLYBASIC POLYMERS.
Lyons, G. W.*, Nicoloff, D. M.*, Chevalier, P. A.* and Fox, I. J. University of Minnesota, Minneapolis, Minn.

Pulmonary artery (P. A.) injection of Polybrene*, a polybasic polymer, produces immediate red blood cell aggregation with pulmonary microembolization followed in 30 seconds by systemic hypotension (30% of control). In 4 mongrel dogs, following P. A. injection of Polybrene (5 mg/kg) a systematic increase (mean:11.1 range:6.7-16.6 μg/gm) in lung tissue histamine contents over control values (mean:29.1 range:8.6-66.5 μg/gm) was found at 30 minutes while successive blood samples taken simultaneously from the right and left ventricles over a 10 minute period, showed no change in plasma histamine contents. An immediately preceding injection of diamine oxidase (histaminase) (40 mg/kg) prevented (4 dogs) or markedly decreased (2 dogs) the expected systemic hypotension following Polybrene injection. Lung tissue histamine contents 30 minutes after successive injections of diamine oxidase and Polybrene approximated control values (mean increase 2.6 μg/gm: range 0.7 to 9.6 μg/gm). Prior injection of heat-inactivated diamine oxidase in 3 dogs failed to inhibit the systemic hypotension of Polybrene. To determine whether the lungs and/or contained white blood cells were involved in the systemic hypotension, 4 dogs were placed on total cardiopulmonary bypass and their lungs removed. Polybrene injection into the arterial inflow catheter in these animals produced a typical systemic hypotensive response indicating that the lung is not the site of release of the vasodepressor substance. (*Hexadimethrine bromide, Abbott)

SOME ASPECTS OF AN EXPERIMENTAL ANALYSIS OF THE VASCULAR PULSATIONS IN THE NECK. Ian F.S.Mackay. R.L.Walker* Jose Berrios* and R.M.Friedman*.Dept. of Physiology. University of Puerto Rico.

The records of the vascular pulsations were made through small spherical balloons, connected to Statham pressure transducers. The ballons were inflated with air to approximately seven cms. water. The earlier observations were confirmed. (The Physiologist 3.1963) (J.Physiol. 106,113:1947.) This communication is mainly concerned with an examination of the 'h' (d'') wave.

(a) The 'h' wave is dependent on the duration of the diastolic period. In heart rates faster than sixty it is usually absent. The timing of it's peak is constant in relation to the peak of the previous 'c' wave.

(b) It is possible to produce or amplify this wave with an experimentally induced bradycardia.

(c) In a slow beating heart a sudden increase in venous return may increase the amplitude of the 'h' wave.

(d) Raising the legs to increase the volume of blood in the central venous reservoir can augment the 'h' wave without changes in the heart rate.

(e) Single short centripetal pulsations in the venous system produced by the sudden application of pressure cuffs to the limbs can augment the 'h' wave.

IT IS CONCLUDED.THAT THE 'h' WAVE :-

1. Is of venous origin.
2. Influenced by the length of cardiac diastole.
3. Amplified by an increase in "venous return"

Supported by P.H.S. Grant No HE 07722.

GASTRIC BLOOD FLOW RESPONSE TO LOCAL HYPOTHERMIA

A. J. Madsen, J. King, Departments of Surgery and Physiology, University of Minnesota, Minneapolis, Minnesota

Gastric blood flow (GBF) was measured in mongrel dogs (15-25 Kg) under pentobarbital anesthesia by an electromagnetic flowmeter on the splenic artery after splenectomy and ligation of right gastric and gastroepiploric arteries and veins at the pylorus. Perfusion of a gastric balloon (volume 500-700cc) produced local hypothermia while heating pads maintained rectal temperature above 35°C. Cardiac output, calculated from pulse contours, remained stable during the experiments. Following onset of gastric hypothermia (+10° to -10°C) an increase in GBF of 100% (40 to 140%) above control values (3.3 to 4.0cc/Kg/min) was found in over 100 dogs. Peak increase in GBF occurs at 3-5 min. returning to control levels at 20-40 min. thereafter falling 65% below control. Perfusion at 27°C caused initial increase in GBF to 75% above control in four dogs while GBF was unchanged in 4 other dogs when perfusion temperatures of 37° and 47°C were used. Severe depression of gastric secretory capacity at temperatures below +30°C has been noted previously indicating a reciprocal relationship between gastric secretion and blood flow. Diamine oxidase I.V. (0.5 to 1.0 gm) did not later the response of GBF to hypothermia. However, the gastric mast cell population, showed a definite decrease from 3-4+ in 10 controls to 1-2+ after hypothermia in 14 dogs, which may explain the progressive decrease in the peak response of GBF to repeated hypothermia with interval rewarming noted in 4 dogs. Supported by USPHS grant AM 05689.

Decrease in Cardiac Activity by Carotid Sinus Baroceptor Reflex. J.W. Manning & Percy Lindgren, Dept. of Pharmacology, Karolinska Institutet, Stockholm 60, Sweden.

Electrical stimulation of the sinus nerve or excitation of the carotid baroceptors by increasing the intrasinus pressure significantly decreased the right ventricular contractile force, heart rate, and blood pressure in 19 anaesthetized cats. The decrease in force and rate, but not blood pressure, were abolished by stellate ganglionectomy and by 3-6 mg/kg of dichlorisoproterenol (DCI). The decrease in cardiac contractile force and rate was not secondary to the hypotension for they were still obtained when aortic pressure was kept constant. The reduction in contractile force and heart rate are the results of an inhibition of sympathetic control of the heart. The data indicates that 40 % of contractile force measured in the anaesthetized vagotomized preparation is dependent upon tonic sympathetic impulses. In the denervated heart, the force and rate were increased to predenervation levels by stimulating the isolated right stellate ganglion at a frequency of 1/sec. Seventy-five per cent of the maximum response in force and rate were obtained at stimulus frequencies of 3/sec. The sinus baroceptor reflex exercises its major effects on the heart and blood vessels within a relatively limited range of 40 mm Hg on eather side of normal blood pressure for the cat.

CARDIAC OUTPUT ESTIMATED BY A CONSTANT INFUSION CONDUCTIVITY METHOD Robert Maronde*, Wallace Frasher, Chester Hyman, Sidney Sobin. Univ. of Southern California and Loma Linda Univ. Schools of Medicine.

Five percent NaCl solution was infused at a constant rate at the right atrial-inferior caval junction while changes in the electrical conductivity of main pulmonary artery (M.P.A.) blood were recorded in 17 anesthetized dogs. Concentration plateaus of the infused NaCl occurred within 3 to 5 sec. and lasted 12 to 20 sec. The level of the plateau varied with respiration but at rates of less than 12/min. inter-respiratory stability usually was present. Using this stable plateau and the mean changes associated with respiration, the output in 49 determinations averaged .11 L/Kg./Min. During intermittent positive pressure breathing (I.P.P.B.) brief but substantial decreases in output related to inspiration were recorded. In 3 open-chest animals decreases in flow associated with I.P.P.B. were measured in the M.P.A. by electromagnetic flowmeter and compared to the conductivity method. The minimum and mean flows correlated within $\pm$ 10%. In sequential observations in the same animal the decrease in flow with I.P.P.B. appeared in the flowmeter record before that in the conductivity record by 0.4 to 1.5 sec., measured from peak inspiration. This may represent the time required for the transient caused by the changed ratio of infused NaCl to blood to appear at the catheter tip.

EVOLUTION OF SINGLE SLUG TO CONSTANT INFUSION INDICATOR DILUTION CURVES. Robert J. Marshall. West Virginia Univ. School of Med., Morgantown, W. Va.

In 7 anesthetized dogs a constant amount of cardiogreen dye was introduced to the right side of the heart via a syringe driven by compressed air either: (A) as a single slug; (B) in aliquots, each preset to occupy a certain time interval (10 to 200 m.sec.) and triggered either by the ECG or manually at constant time intervals (e.g. 1 sec.); or (C) as a constant infusion, using a variable orifice outflow restrictor. The timing, pattern, magnitude and duration of the injections were recorded by a potentiometer linked to the syringe piston, and dilution curves were obtained from the aortic root by a densitometer with a rectilinear calibration between 0 and 25 mg./L. When necessary, corrections were made for the small deflections caused by the dye diluent itself (Sinclair et al., J. Appl. Physiol. 1961:16,669). As the total duration of the fractionated injection (B) or the infusion (C) was gradually increased, the build-up time was disproportionately prolonged, the peak concentration reduced and the CL/CR ratio decreased. Calculation of cardiac output and of mean transit time was unaffected as long as the onset of recirculation could reasonably be defined. With further increases in the total duration there was a gradual evolution to the classical pattern of slow infusion curves, with a plateau or near-plateau prior to the onset of recirculation. (B) and (C) curves were identical, provided that the corresponding total injection times and infusion times were also identical. As was anticipated, they closely resembled curves derived by appropriate mathematical integration of immediately preceding or succeeding curves that resulted from single slug injection. (Supported by NIH grant HE 07758-02).

PRESSURE AND VOLUME STUDIES ON LUNG LOBES IN MAN WITH OBSTRUCTIVE AIRWAY DISEASE. C.J.Martin, Koh Ishikawa* and A.C.Young. Firland Sanatorium and Univ. of Wash. School of Med., Seattle, Washington.

A blocked lobe of the lung may be used as a pressure capsule to measure pressure differences existing within the chest as well as variations in lobar compliance. Following the placement of a Carlens catheter, lobar blocking catheters were introduced and pressure sampled from the isolated lobe. Volumes were measured from unblocked lobes and lungs. In normal subjects less than 40 yrs. of age, the upper lobe compliance was .037 l ± .009 and lower lobe .0401± .004. No difference between right and left lobes was found. The differences between upper and lower lobes were not significant. Subjects beyond 49 yrs., with or without mild obstructive airway disease, had an upper lobe compliance of .050 l ± .011 and a lower lobe compliance of .043 l ± .010. Upper lobe was significantly more compliant than lower lobe. Upper lobe compliance in these subjects was significantly greater than that in normal subjects. Subjects with moderate to severe airway obstruction had an upper lobe compliance of .062 ± .011 and a lower lobe of .048 l ± .007. Again upper lobe compliance is significantly greater than lower lobe compliance and greater than that in normal subjects. Lower lobe compliance is also significantly greater than that seen in normal subjects. The pressure differences between lobes and between lobe and esophagus seen in normal subjects were absent in the cases with obstructive airway disease. Obstructive airway disease results in increased compliance of the lobes, particularly that in upper lobe. The increase in compliance prevents the development of intrathoracic pressure differences at all lung volumes tested.

TRANSCUTANEOUS MONITORING OF SUPERFICIAL VEINS BY REFLECTED INFRARED ENERGY. H.J. Marx*, and R.F. Rushmer, Dept. of Physiology and Biophysics, Univ. of Washington, Seattle, Washington.

Visualization of superficial veins by the eye can be improved by using a red filter. Infrared sensitive film provides better definition. Visualization depends upon the differential transmittance and reflectance of radiant energy by the blood column in the vein and by the surrounding tissues. Skin and subcutaneous tissue are reported to transmit radiation best at a wavelength around 1-1.2 microns while reduced hemoglobin is most opaque at somewhat shorter wavelengths. A study was initiated to determine the optimal wavelength range for recording changes in dimensions of superficial veins by reflected radiant energy using selective filtering and detectors with different spectral sensitivities including Kodak infrared film (types IR135 and 1-Z), an image converter tube (RCA 1P-25 Snooperscope type) and a lead sulfide detector incorporated in a specially constructed electromechanical scanning device. The most useful wavelengths for these purposes appear to be in the very near infrared portion of the spectrum. Changes in width of superficial veins which were barely visible to the human eye could be detected with the scanning device. Initial evaluation of infrared sensitive vidicons, currently under development, show promise of usefullness as detectors for a monitoring system. (Supported by NIH Grants #1-F2-HE21, 316-01 & HE-07293).

EFFECT OF PHENOXYBENZAMINE (DIBENZYLINE) ON HEMODYNAMICS AND SURVIVAL IN ENDOTOXIN SHOCK. Frederick D. Masucci* and Lerner B. Hinshaw. Physiology Branch, Civil Aeromed. Research Inst., Okla. City, Okla.

Other investigations have demonstrated hemodynamic alterations and improved survival using the adrenergic blocking drug phenoxybenzamine as a therapeutic agent in shock. The effect of phenoxybenzamine on survival and vascular changes associated with endotoxin shock were studied in the dog. In a dog-perfused isolated foreleg, injection of endotoxin into the dog produced foreleg arterial vasoconstriction which was abolished by 1-hour, but not 24-hour pretreatment with phenoxybenzamine. Results show that 1-hour pretreatment with phenoxybenzamine decreased blood levels of humoral vasopressors after endotoxin. The systemic arterial response to endotoxin, however, was unaltered by either 1-hour or 24-hour pretreatment. Pretreatment with different dosages, times of administration, and dilutions of phenoxybenzamine, demonstrated no marked increase in the survival of 41 dogs given endotoxin. Post-treatment of 30 dogs with phenoxybenzamine and plasma administered at different times after endotoxin also did not improve survival. Central venous pressure was measured in 5 dogs post-treated with phenoxybenzamine and plasma. Although central venous pressure did not change, there were no survivors.

Cholesterol Flux into Rat Aorta with an Atherogenic Diet. I. Matsuda and N. Kalant (intr. by J.L. Brandt). Jewish Gen. Hosp. and McGill University, Montreal.

A high fat diet produces earlier and more extensive lipid deposition in the vascular intima in alloxan diabetic rats than in controls. To determine whether this is the result of higher plasma cholesterol concentrations obtaining in the diabetic or of a specific increase in flux rate of cholesterol between plasma and intima, the influx rate of free and total cholesterol into the aorta was determined in normal and diabetic rats fed a high fat diet for 2-15 weeks. There was a linear increase in influx rate with increase in plasma cholesterol concentration. For a given plasma concentration, the influx rate at first increased with time, then decreased, in association with a decreasing rate of net cholesterol accumulation in the aorta. There was a linear increase in aortic cholesterol concentration with increasing influx rate. This influx-dependent increase in aortic cholesterol was initially small, but became more marked with time. It is concluded that increasing plasma cholesterol causes increased flux into aorta; this leads to increased efflux and also to net aortic cholesterol accumulation which subsequently limits the further entry of cholesterol from plasma. Thus in the rat, aortic cholesterol deposition is essentially self-limited. The results were the same for free and total cholesterol. There were no apparent differences between control and diabetic rats, so that the increased susceptibility of diabetic rats to an atherogenic diet is not the result of a specific increase in cholesterol flux rates into the aortic intima.

Variability in Short-Circuited Frog Skin to Acetycholine

R.D. McAfee
Veterans Administration Hospital
New Orleans, Louisiana

Investigation of ion transport using isolated short-circuited membranes is widespread. Our study of sodium ion transport and bioelectric current in isolated short-circuited frog skin impresses us with the variability these skins show in response to transport modifying agents. In order to deal with this variability confidently, we built a multi-channel device which automatically short-circuits and records the short-circuit current of 16 skins in rapid sequence. We find that we are confident only of data from many experiments for a true picture of the action of transport modifying substances. For example, acetycholine frequently fails to stimulate short-circuit current significantly but will often produce over 100% stimulation. Various degrees of stimulation are distributed between these extremes. Other substances which stimulate transport show wide variations in effect on skins which are run on the same day and which appear to be alike with respect to short-circuit current and stability. The automatic device is described and data on the variability encountered is presented. The factor of variability may be important in the formulation of theories of ion transport.

SPIROLACTONE AND SWEAT ELECTROLYTES. T. P. McConahay*, S. Robinson and R. W. Piwonka*. Anatomy-Physiology Dept., Indiana University. Bloomington, Indiana.

Men worked (MR 190 Cal/m^2/hr) in the heat (50 C d.b.; 26 C w.b.) three hours/day for 12 to 15 days. Hourly sweat rates during the heat exposures were calculated from net weight losses, and sweat from forearm and hand was collected for analysis. Total urine output was collected each day. Subjects RP and PM were maintained on daily diets containing 158 and 234 mEq of Na respectively for several days, with sweat samples being collected during work in the heat on the last 4 days of this control period. Sudden decreases in the Na content of the diet (to 57 mEq/day for subject RP, and 62 mEq/day for PM) produced Na deficits of 125 and 225 mEq respectively after two days. Sweat Na concentration, urinary Na output, and urinary Na:K ratio all decreased. After two days on the low Na intake, spirolactone (Aldactone-A) was administered; 125 mg/day to subject RP for 3 days, and 200 mg/day to PM for 2 days. The spirolactone did not alter the continued decline of the Na concentration or the Na:K ratio in the sweat of the Na depleted men. On the other hand, the drug produced naturesis and increased the urinary Na:K ratio despite the salt deficient condition of the men. Since spirolactone is known to inhibit the Na retaining function of aldosterone in the kidney, these data indicate that aldosterone is probably not responsible for the slow Na conserving response of the sweat glands in salt deficiency. (Supported by U.S. Army Medical Research & Development Command, Contract DA-49-193-MD-2449.)

VASOMOTOR AND SUDOMOTOR RESPONSES TO RAPID CHANGES IN AMBIENT TEMPERATURE. R.D. McCook, R.D. Wurster* and W.C. Randall, Stritch School of Medicine and the Graduate School, Loyola University, Chicago.

Nude, male subjects were exposed to slowly rising ambient temperatures while sweating was recorded from eight areas, cutaneous volume pulses from six areas and temperatures from twelve cutaneous areas. Tympanic membrane and mean skin temperatures were continuously recorded. After sweating and vasodilatation had become well established, the copper screen bed on which the subject reclined was rapidly moved from the hot chamber into another chamber 30 to 40°C lower. All recordings were continuous throughout the transition period. Depending somewhat upon initial ambient temperature, and with some individual subject variation, sweating was progressively recruited first from the lower extremity and lastly upon the head and upper extremity. In some skin regions, vasodilatation preceded sweating, while in others it followed. The onset of neither sweating nor vasodilatation could be accurately correlated with tympanic membrane temperature since the latter was observed to be either increasing, unchanged, or even falling during recruitment. When the subject was rapidly moved from the hot environment to the cool, sweating promptly stopped on all areas, and profound vasoconstriction appeared on the palm. Vascular responses on non-palmar areas however, were markedly different and there was generally no immediate change in volume pulse amplitude. Tympanic membrane temperature during the same period continued to rise for one to three minutes, and thus appeared unrelated to either vasomotor or sudomotor control under these circumstances. (Supported by grant no. HE 08682-01 from NIH.)

FREQUENCY SPECTRUM CHANGES OF KOROTKOV SOUNDS WITH MUFFLING. Ernest P. McCutcheon*, Curt A. Wiederhielm, and Donald W. Baker*. Dept. of Physiology and Biophysics. Univ. of Wash. Sch. of Med., Seattle, Wn.

Although the Korotkov sounds provide the basis for sphygmomanometry, the changes in the character of these sounds have not been fully described. This investigation was designed to provide a more quantitative description of the changes in the Korotkov sounds occurring with muffling at the diastolic pressure level. Such an analysis is needed as a first step in determining the relation between Korotkov sounds and the diastolic pressure. A standard clinical cuff was placed around the upper arm and the bell of a Littman stethoscope was taped lightly in the antecubital fosa of healthy young adult males reclining in a soundproofed room. The bell was connected by 10 cm of Tygon tubing to a capacitance microphone. Cuff pressure was steadily lowered at a rate of 2-3 mm Hg per heart beat from above systolic to below diastolic arterial pressure; the Korotkov sounds were continuously recorded with an oscilloscope and a 35 mm. Grass camera operating at 100 mm/sec film speed. Muffling of the sounds observed by the auscultatory method occurred at levels similar to those observed with the microphone system Sounds recorded before, during, and after muffling were reproduced by a function generator and evaluated by an electronic spectrum analyzer. At cuff pressures above those which produce muffling, the sounds contain distinct harmonic amplitudes between 50 and 90 cycles/sec. In this range, the amplitude of the frequency spectrum was reduced in the first muffled sound and markedly diminished in subsequent sounds. There were no consistent differences in the sound spectrums between 1 and 50 cycles per sec. Muffling of the Korotkov sounds were concluded to result from attenuation of sound frequencies between 50 and 90 cycles per sec. (Supported by NIH Grant #HTS-5147).

THE SHAPE OF THE TRAVELING PRESSURE PULSE. D. A. McDonald* and E. O. Attinger. Research Institute, Presbyterian Hospital, Philadelphia. The change of form of the arterial pressure wave has been recorded by a Statham SF-1 catheter-tip manometer at successive points 5cm apart throughout the systemic tree from the common carotid to the superficial femoral arteries. Simultaneous recordings were also made with Statham P23 guages from a distal carotid branch, the origin of the left subclavian, the saphenous and distal posterior tibial arteries. All channels were subjected to Fourier analysis 'on line' in a LINC computer. Sampling was triggered by the QRS complex of the ECG which acted as zero reference for the phase of 6-12 harmonics at each position. Heart rate and wave pressure were maintained relatively constant with morphia-pentobarbital anesthesia. In 4 dogs pulse freguency averaged 2.7 to 3.8cps. The amplitude of the 1st harmonic in all increased steadily along the aorta so that at the bifurcation it was double that in the arch; passing up the carotid it also increased, the minimum usually lying in the innominate artery. The increase in the femoral bed was less steep. The second harmonic had a minimum value in the mid-thoracic region and thereafter increased more rapidly than the fundamental. The higher harmonics showed spaced maxima and minima but were all eventually higher in the iliac artery than close to the heart. These findings and the phase velocity patterns are interpreted in terms of reflection of waves and progressive increase in arterial 'stiffness' (as shown by increase in pulse wave velocity).

BRAIN STIMULATION AND PLASMA 17-OH CORTICOSTEROID CONTROL. P. R. McHugh and G. P. Smith (intr. by F. Strumwasser). Walter Reed Army Inst. of Research, Washington, D. C.

In alert, chair-confined Macaca mulatta, an increase in plasma 17-OH-CS concentration regularly follows electrical stimulation[a] to the baso-lateral amygdala with current adequate to evoke afterdischarges (AD). In 13 experiments with 8 macaques the production of amygdaloid AD every 5 minutes for an hour increased 17-OH-CS 17-36 μg % (mean 28 μg % SD ± 6 μg %). On six occasions with 4 monkeys, 15 minutes before stimulation 1000 μg of cortisol (solucortef) was injected I.V. This increased plasma 17-OH-CS (30 μg % mean elevation 15 min. after injection). Subsequent amygdaloid stimulation did not increase plasma 17-OH-CS further. The 17-OH-CS elevation produced by a 1000 μg injection of cortisol plus an hour of amygdaloid stimulation was 10-38 μg % (mean 25 μg %, SD ± 10) and thus did not differ from the elevation produced by an hour of amygdaloid stimulation alone. In contrast 17-OH-CS elevation produced by a 1000 μg cortisol injection plus an hour of hypothalamic stimulation[b] in 4 monkeys (42-54 μg %, mean 46) did substantially exceed that produced by hypothalamic stimulation alone (17-25 μg %, mean 21). Conclusion: a negative feedback mechanism sensitive to plasma 17-OH-CS changes must be interposed between the amygdala and the neurosecretory cells of the hypothalamus. This mechanism appears to function much as predicted by the "variable set point hypothesis" (Yates and Urquhart, Physiol. Rev. 42:359, 1962).

(a) Biphasic rectangular pulses 1.0-3.0 msecs, 25 pp/sec, 5-25 V, 0.3-1.5 ma, 5 sec trains every 5 minutes.
(b) Biphasic rectangular pulses 1.0 msec, 10 pp/sec, 20 V, 1.0-1.5 ma, 30 sec trains every 5 minutes.

(Supported by NINDB Special Traineeship BT-676.)

PARA-AMINO HIPPURIC ACID CLEARANCES IN THE YOUNG CHIMPANZEE UNDERGOING PSYCHOLOGIC STRESS. J.P.Meehan, J.P.Henry, and J. Fineg*. Department of Physiology, School of Med., University of Southern Calif., Los Angeles, Calif.

Restraint and psychomotor training have been shown to produce sustained elevation of arterial blood pressure in the young chimpanzee (Meehan, Mosely, Fineg, Fed. Proc. 23: 515, 1964). Twenty PAH clearances were done on two chimpanzee subjects during the course of such training. Arterial pressure was continuously recorded during the clearance determinations. Arterial pressures ranged from 135/70 to 280/150 for various clearance periods. Using PAH clearances and hematocrits to calculate renal blood flow, the average for all observations was 560 ml/min for a 25 kg chimpanzee. Calculated renal blood flows tended to be higher for the lower blood pressures. The highest value obtained was 960 ml/min at an arterial pressure of 135/70 and the lowest 290 ml/min at a pressure of 180/120 mm Hg. The cardiac rate showed a similar relationship to renal blood flow. These observations are consistent with those made on the young hypertensive human being with a labile blood pressure.

EFFECTS OF ESTROUS CYCLE AND PROGESTERONE ON UTERINE ELECTRICAL ACTIVITY. Carlton E. Melton, Jr. and Julian T. Saldivar, Jr.*
Civil Aeromedical Research Institute, Oklahoma City, Oklahoma.

Forty-eight cycling albino rats (250 gm ± 10%) were used in this study. Estrous cycle stages were identified by vaginal histology. All uteri from 15 proestrus rats responded to shocks with action potentials (av. vel. = 4.23 cm/sec). Uteri from 10 of 11 rats in estrus responded to shocks with conducted action potentials (av. vel. = 4.65 cm/sec). Eight uteri from 12 metestrus rats likewise responded with conduction velocities averaging 3.31 cm/sec while only 3 uteri from 10 diestrus rats responded to shocks with an average conduction velocity of 3.53 cm/sec. Proestrus and estrus uteri showed grouping of spontaneous spikes separated by silent periods which gave rise to relatively clean contraction records; evoked impulses were easily elicited during the silent periods. In metestrus, low-level spikes appeared between bursts of high spikes. Diestrus electrical activity was continuous and contraction records were irregular. Continuous spontaneous activity rendered the tissue unresponsive to shocks. Spontaneous action potentials did not travel at velocities significantly different from evoked responses in the same stages of the cycle. Uteri from animals in estrus induced by gonadotropin injection showed spontaneous activity and shock responsiveness characteristic of normal estrus. Ovariectomy caused diestrus-type spontaneous activity to appear in 24 hr. Ovariectomized animals pretreated with estradiol and progesterone were not different from estradiol-saline treated controls with regard to spontaneous activity and responsiveness to shocks. Progesterone doses that produced surgical anesthesia (12.5 mg/day i.m. for 5 days plus 25 mg just prior to sacrifice) did not inhibit uterine activity. Functional changes shown by the myometrium during the estrous cycle can probably be accounted for entirely by decreased ovarian estrogen secretion.

THE EFFECTS OF PARATHYROID EXTRACT ON THE STOMACH. René Menguy and Y. F. Masters*. Dept. of Surgery, Univ. of Ky. Med. Ctr., Lexington, Ky.

It has been shown that parathyroid extract (PTE) is without effect on gastric secretion of acid. The purpose of this study was to find out whether or not PTE alters gastric production of mucus. The possibility of such an action is suggested by the well-known effects of PTE on glycoprotein metabolism elsewhere in the body. Rats (120), weighing from 130 to 150 gm., were divided into four groups and were treated as follows: Group I: Controls. Group II: Twice daily injections of 1 ml. of (Lilly) PTE. Group III: Twice daily injections of 5 mg. of cortisone acetate. Group IV: Both of these drugs in the doses indicated. The rats were sacrificed 72 hours after the first injection and the stomachs were removed. Gastric mucosal content of mucus was measured by P.A.S. and Alcian Blue staining of histologic sections and by biochemical analysis of hexosamine and sialic acid concentration in freeze dried gastric mucosal scrapings. By comparison with untreated controls, PTE caused a huge increase in gastric mucosal content of mucus. The average changes in concentrations of hexosamine and sialic acid in gastric mucosa were +50% and +224% respectively. These effects of PTE were partially blocked by the concomitant administration of cortisone. The data suggest that the alimentary tract and particularly the mucus producing cells may be an important "target organ" for parathyroid hormone activity.

SMART RATS AND "STUPID" FERRETS VS BEHAVIORAL RELATIVITY, WALTER R. MILES, Naval Medical Research Laboratory, Box 100, U.S.N.Submarine Base, Groton, Connecticut 06342.

Rats rate high in maze-space learning. Like the Biblical ox and ass they quickly learn and know their way to the corn crib. If we attempt to secure comparative maze learning data on Old World ferrets, traditionally bred and used to eliminate rats, we find their learning ability score so low as to rate them stupid. For this comparative study we used four alley mazes, three of them variations of the linear type, one was of T-type. Three month old ferrets, both of English and Fitch varieties, were secured from a breeding farm. They were kept in a room adjoining our rat colony and their diet was bread and milk. Only on reaching the foodbox in a maze were they rewarded with a small cube of uncooked fresh beef. In all four mazes the rats worked well, kept on moving until the food was reached. In each maze it was always in the same place. The ferrets were much more active, swifter in their movements, explored more widely and were more repetitious, retracing their steps often. In terms of developing through experience ("the law of effect") a short and simplified path to the food, the rats won over their 22 competitors. In terms of the usual criteria defining success in maze learning the critical ratios for the score differences exceeded a value of 3 in favor of the rats. To operate well in the role of a carnivore requires inherited traits and the development of activity patterns that differ from those of the ox, the ass, or the ubiquitous rat. Learning theory should not exclude predators and the "unclean."

EFFECT OF NICOTINIC ACID ON THE CARBOHYDRATE METABOLISM IN DOGS. H. Miller, B. Issekutz, Jr., P. Paul* and K. Rodahl. Div. of Research, Lankenau Hosp., Philadelphia, Pa.

Nicotinic acid is known to lower not only the cholesterol but also the FFA level of the plasma. The data concerning the effect on blood sugar are conflicting. C^{14}-glucose (U) was infused (iv) at a constant rate, into unanesthetized dogs (some treated with tranquillizers), with indwelling arterial and venous catheters, for 4 hours. O_2 uptake, CO_2 output, specific activity of CO_2, and plasma sugar were measured. The rate of release and rate of removal of glucose as well as the percent participation of plasma glucose in the respiratory CO_2 were calculated according to the method of Steele et al (Am. J.Physiol. 196, 221, 1959). Infusions of nicotinic acid (for 40-min) lowered the plasma FFA. While no change occurred in the plasma glucose concentration, the rate of release and the rate of removal were increased. A larger percent of CO_2 was derived from plasma glucose. There was a significant correlation ($P < .001$) between the RQ and percent CO_2 derived from glucose. Nicotinamide infusions had no similar effect on either of the above parameters. It was concluded that nicotinic acid tends to shift the metabolism from fat towards carbohydrate. (Supported by NIH grant HE-07687-02.)

THE EFFECT OF LUNG VOLUME ON PULMONARY CAPILLARY VOLUME AND MEMBRANE DIFFUSING CAPACITY AT REST AND DURING EXERCISE. J.M. Miller* and R.L. Johnson, Jr. Cardiopulmonary Lab., Dept. Med., U. Tex. Southwestern Med. Sch., Dallas, Texas.

Diffusing capacity increases as pulmonary blood flow increases but it is not known how this relationship is affected by the degree of lung inflation. To investigate this problem we measured pulmonary capillary blood volume (V_C) and membrane diffusing capacity (D_M) during breath holding by Roughton and Forster's method. Pulmonary blood flow ($\dot{Q}_C$) was measured simultaneously using the acetylene method. Measurements were made at total lung capacity (TLC) and at functional residual capacity (FRC) both at rest and during exercise in 6 subjects. Mean results:

	TLC		FRC	
	Rest	Exercise	Rest	Exercise
D_M (ml/min x mm Hg)	80	86	52	58
V_C (ml)	84	168	98	178
$\dot{Q}_C$ (L/min)	5.9	18.7	6.6	19.1

Pulmonary capillary blood volume therefore increases with pulmonary blood flow but is unaffected by changes in lung volume. Membrane diffusing capacity on the other hand is affected more by changes in lung volume than by changes in blood flow. Furthermore, the results indicate that a subject's membrane diffusing capacity at his operational lung volume, both at rest and exercise, is appreciably lower than that measured at TLC by the single breath technique.

INHIBITION OF GASTRIC SECRETION DURING ELECTRICAL STIMULATION OF THE VENTROMEDIAL HYPOTHALAMUS. Allen Misher* and Frank P. Brooks. Dept. of Physiol., School of Med., Univ. of Penna., Phila., Penna.

Platinum bipolar stimulating electrodes were implanted unilaterally into the hypothalamus of 17 rats previously fitted with chronic gastric cannulae. Interdigestive and insulin-induced gastric secretion was collected with and without periods of electrical stimulation. The stimuli consisted of 0.2 msec pulses delivered 100 cps at 200 μ amps intensity for the duration of the experiment. Volume, total acid concentration and pepsin concentration were measured in four hour collection samples. In five animals the electrode tips resided in the ventromedial (VM) nucleus as determined initially by an appropriate response in feeding behavior and later by histological verification. These animals exhibited a significant decrease in volume and output of both acid and pepsin when the gastric content was collected during electrical stimulation and compared to a control study. The twelve animals in which the electrode tips lay outside of the VM nucleus were studied similarly and there was no significant difference in gastric content between periods of stimulation and control periods. The most likely inference which can be drawn from these observations, when considered with previous ablation and recording studies, is that the VM nucleus probably exerts an inhibitory influence on gastric secretion during the interdigestive phase. (Supported by Smith, Kline and French Laboratories.)

RESPIRATORY RESPONSE AND CSF pH DURING DISTURBANCES IN BLOOD ACID-BASE BALANCE IN AWAKE DOGS WITH DENERVATED AORTIC AND CAROTID BODIES.
R.A. Mitchell, C.R. Bainton*, J.W. Severinghaus, and G. Edelist*
Cardiovascular Research Institute and Department of Anesthesia.
University of California Medical Center, San Francisco.

Three to five days of ammonium chloride acidosis before denervation in three awake dogs with permanent tracheostomies reduced the average arterial pH from 7.42 to 7.32, stimulated ventilation, reduced arterial P_{CO_2} from 37.0 to 32.6 mm Hg, reduced plasma and CSF (HCO_3^-) from 23.5 to 16.5 and 23.6 to 21.8 mEq/L, respectively. CSF pH remained normal (7.35). Following denervation of the aortic and carotid chemoreceptors, control arterial pH was 7.39; $PaCO_2$ was 40.4 mm Hg. Arterial and CSF HCO_3^- were 24.9 and 24.7 mEq/L respectively. Ammonium chloride acidosis and Na_2CO_3 alkalosis in the pH range from 7.3 to 7.5 did not alter $\dot{V}_E$, $PaCO_2$, or CSF pH, P_{CO_2} or HCO_3^-. As blood pH fell below 7.30, ventilation increased and $PaCO_2$ and CSF HCO_3^- decreased. At an average pH 7.25 (3 - 5 days of acidosis) $PaCO_2$ was 33.8. CSF pH fell from 7.35 to 7.33 and HCO_3^- from 24.7 to 21.3 mEq/L. In metabolic acidosis and alkalosis maintained for three days in two dogs, the electrical potential between CSF and blood returned to about +4 mv, the normal value. At arterial pH of about 7.31 (capillary pH 7.28), CSF pH 7.35, and +4 mv in CSF, H^+ is in electrochemical equilibrium. Our observations fit with the concept of an active transport regulation of CSF H^+ capable of maintaining CSF H^+ higher but not lower than capillary H^+. In the pH range from 7.3 - 7.5 changes in ventilation are mediated by the peripheral chemoreceptors alone. Below pH_a of 7.31 H^+ moves down an electrochemical gradient, into CSF, stimulating the medullary respiratory chemoreceptors. (Supported in part by USPHS grants GM 05881, 5T1-GM-63-06, and Career Awards, 1-K3-HE-19,411 and 1-K6-HE-19,412.)

Fiber-Optic Densitometry on Blood. G. A. Mook*, P. Osypka*, R. E. Sturm*, and E. H. Wood. Mayo Clinic, Mayo Foundation, Rochester, Minn.

Due to high dynamic response capability, measurement of light reflection of blood by fiber optics seems the method of choice for O_2 saturation and dye dilution curves from intracardiac and other intrathoracic sites. However, compensation for non-specific effects especially those due to variable flow at the catheter tip must be attained. By inserting a fiber-optic catheter inside another wider one so its tip is just a few mm. from the tip of the outside catheter through which blood is sampled at a constant rate, flow effects are reduced without serious decrement in dynamic response. Studies were made with a fiber-optic catheter (O.D. 1.3 mm.) containing two channels of about 60 fibers each; one for illumination, the other for measurement of reflected light, at two wavelengths using a dichroic mirror, filters and two RCA-7102 photomultipliers. The outer black teflon catheter (I.D. 1.8 mm.) used for sampling gave no reflection from its inner surface. In the range of 8 to 20 gm./100 ml., the fiber-optic light reflection increased almost linearly with hemoglobin concentration in contrast to findings of almost no change in this range obtained with conventional reflection oximeters. Fiber-optic reflection spectra of oxygenated and reduced ox blood, using a Beckman DU spectrophotometer as light source, show an isosbestic region between 840 and 880 mμ whereas transmission spectra of the same blood, measured with a second fiber-optic catheter for illumination, show an isosbestic point at about 790 mμ. The relationship between oxygen saturation and log ratio of reflection at 640 and 880 mμ is linear. The ratio of reflection at 900 and 800 mμ (half-band widths: 15 mμ) is linear with indocyanine green dye concentration to 20 mg./L. Ratios are not constant at different flow rates even when a single photomultiplier with a beam splitting and chopper device is used. (Supported in part by research grants: NIH H-3532 and NIH H-4664.)

POST-SYNAPTIC MEMBRANE POTENTIAL DISTRIBUTIONS AS A REPRESENTATION OF INPUT STATE. G.P. Moore, J.P. Segundo, and D.H. Perkel*. Communications Biophysics Laboratory, MIT; Dept. of Anatomy, UCLA; and The RAND Corporation, Santa Monica, Calif.

The statistical distribution of the membrane potential in a neuron with stationary input has been computed under a variety of conditions using (1) data from intracellular microelectrode recordings from Aplysia neurons, and (2) data obtained from computer-simulated models of Aplysia neurons. The distribution of post-synaptic membrane potentials can be shown to depend on (1) the waveform of each contributing synaptic potential as a function of membrane potential, (2) the statistical properties of the discharge of each pre-synaptic cell, (3) interaction phenomena between synaptic potentials. These factors determine the potential distribution which can then be regarded as a stochastic representation of the state of input to the cell. Furthermore, to any given subthreshold potential distribution there corresponds a statistical distribution of firing times of the post-synaptic cell. A change in the activity of any synaptic source modifies the distribution in a characteristic way and thereby changes the statistical distribution of post-synaptic discharge. Using this property, a simple mechanism can be postulated by which the CNS could "sample" the state, or distribution of potential, in a group of neurons.

Supported in part by grants from NSF (G16526 and G21497),NIH (MH04737-04, FR-00142-01, NH-0518-3, GM-09608-03) and NASA (NsG-496).

VASCULAR CLEARANCE AND ORGAN DISTRIBUTION OF SHEEP RED CELLS IN MICE WITH ALTERED RETICULO-ENDOTHELIAL (RE) FUNCTION. S. H. Morrow* and N. R. Di Luzio, Dept. of Physiol. and Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

Previous studies from this laboratory have demonstrated that the intravenous administration of glucan induces a hyperfunctional state of the RES. Conversely, the administration of a methyl palmitate emulsion produces a profound decrease in phagocytic activity. Associated with alterations in phagocytosis were parallel alterations in immune response to particulate antigens. In an effort to evaluate the mechanism of altered antibody response in RE stimulated and RE depressed mice, the vascular clearance and organ distribution of Cr^{51}-labelled sheep erythrocytes were studied in control, RE hypofunctional, and RE hyperfunctional mice. The vascular clearance of the particulate antigen was profoundly enhanced in RE stimulated mice and markedly reduced in RE depressed mice. The increased vascular clearance was associated with enhanced liver uptake. In RE depressed mice, both liver and spleen uptake were markedly reduced, while in both instances lung removal was unaltered. These studies demonstrate that alterations in antibody formation previously observed are associated with changes in vascular clearance and tissue distribution of the antigen due to altered RE activity. (Supported in part by the Atomic Energy Commission).

COMPARISON OF INTRA-AORTIC AND CONSERVATIVELY OBTAINED BLOOD PRESSURE IN MAN DURING REST AND EXERCISE. Francis J. Nagle*, John Naughton*, and Bruno Balke, CARI and O. U. Med. School, Oklahoma City, Oklahoma.

Most investigators agree that increasing levels of exercise cause a progressive rise in blood pressure. Arguments have been voiced against the usefulness of indirectly measured blood pressures as indicators of hemodynamic response to physical exercise. Tabakin and coworkers have reported most recently that direct recordings from the radial artery did not show significant changes of systolic pressures during graded work on the treadmill. Attempts were made, therefore, to measure during rest and bicycle exercise simultaneously blood pressures by the usual auscultatory method of the brachial artery and directly through an arterial catheter, its tip placed in the ascending aorta. In control experiments the indirectly measured systolic pressures averaged--at energy expenditures of 1, 5, 8.5 and 12 times the basal metabolic rate -- 115, 162, 206 and 219 mm Hg, respectively. In the catheterization experiment the values were: 124, 163, 207 and 230 mm Hg, respectively. In the latter experiment the directly recorded aortic pressures fluctuated considerably from beat to beat mainly in accord with the breathing rhythm, averaging 130, 161, 208 and 223 mm Hg at the four different levels of energy expenditure. The diastolic pressures determined by auscultation were between 80 to 90 mm Hg whereby in this particular subject during more severe work the diastolic sound remained almost unbrokenly loud toward the zero mercury reading. The directly measured values of diastolic pressure were in the range of 80-100 mm Hg. In another subject the indirect diastolic measurements were consistently slightly higher than the directly recorded values while systolic pressures were nearly identical. The latter showed definitely changes in magnitude correlated with changes in metabolic rates.

MEDIATION OF ADRENAL MEDULLARY SECRETION IN RESPONSE TO HYPOTENSION AFTER SPINAL CORD SECTION. G.G. Nahas, R.C. Cantu*, W.M. Manger and J.W. Correll*. College of Physicians and Surgeons, Columbia University, New York, N.Y.

In the intact animal hemorrhagic hypotension will produce an immediate marked increase in peripheral plasma catecholamine levels frequently followed by a secondary rise as acidosis develops. Dogs with spinal cord transection at C_8 were mechanically ventilated at constant volume and bled rapidly (2 to 5 min.) until mean blood pressure reached 50 mm Hg where it was maintained during the experimental period. The right lumbo adrenal vein was cannulated and samples periodically taken for catecholamines, pH and pCO_2 measurements. Adrenal blood flow was recorded and adrenal catecholamine output (A.C.O.) was calculated. Glucose was measured in arterial blood. Immediately following the acute hemorrhages (pH 7.48, pCO_2 30) no increase in A.C.O. occurred, thirty minutes or more after hemorrhage (pH 7.20, pCO_2 38) catecholamines had increased six-fold. When acidosis was corrected with tris(hydroxymethyl)aminomethane (THAM) (hypotension still prevailing), A.C.O. decreased to control levels. Blood glucose levels paralleled changes in A.C.O. These findings indicate that the initial rise in A.C.O., in response to hypotension is mediated through central nervous pathways, whereas the further rise might be due to concurrent acidosis stimulating directly the adrenal medulla.

Supported by Contract DA-49-193MD-2265 and Grant GM-09069-02.

THE MEASUREMENT OF THE APPARENT PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE (DL_{CO}) AT HYPERBARIC PRESSURES. Jean R. Nairn*, G.G. Power*, R.W. Hyde*, R.E. Forster, C.J. Lambertsen and J. Dickson*, Dept. of Physiol., Grad. School of Med.; Dept. of Pharm., Schools of Med.; Univ. of Penn., Phila., Pa.

DL_{CO} has been measured by the breathholding technique within a range of mean intracapillary oxygen tensions (P_{O_2}) from 120 to 3,000 mm Hg in a hyperbaric chamber operating up to 4.8 atmospheres pressure. Preliminary results in 3 normal male subjects show that: A) DL_{CO} decreased from a mean of 35.3 ± 5.5 ml CO/(min x mm Hg) at 120 mm P_{O_2} to a mean of 7.9 ± 0.5 ml CO/(min x mm Hg) at a mean P_{O_2} of 2,200 ± 135 mm Hg. B) $1/DL_{CO}$ increased approximately in a linear relation with mean intracapillary P_{O_2} at the time of breathholding in all subjects up to a P_{O_2} of 3,000 mm Hg. C) The P_{O_2} in the alveoli for the 5 to 10 mins. prior to the breathholding procedure is defined as the "conditioning level of P_{O_2}". We found that this "conditioning level" of P_{O_2} could be varied over a range of 150 to 2,200 mm Hg in 2 subjects without influencing the value of DL_{CO} during the breathholding procedure. D) At a mean intracapillary P_{O_2} of approximately 150 mm Hg DL_{CO} was apparently uninfluenced by the partial pressure of nitrogen varying between 600 and 2,400 mm Hg. These findings agree with previous studies which had been done within a range of oxygen tensions of 100 to 600 mm Hg and show that high "conditioning levels" of oxygen for 5 to 10 minutes have no effect on the diffusing capacity of the lung.

EFFECT OF CO_2 AND HISTAMINE ON GASTRIC HEMODYNAMICS. A. Naitove (intr. by F. V. McCann). Dept. of Physiology, Dartmouth Medical School, Hanover, N. H.

Available evidence suggests that the gastric vascular bed is dilated by high CO_2. It has also been shown that this effect and the hemodynamically similar response to cholinergic stimulation are additive. In this study we wished to determine the influence of hypercapnia on the gastric vascular response to histamine. In anesthetized dogs, a constant volume, flow technique was employed to perfuse the vascular bed of the stomach through the left gastric artery. The infusion of histamine (.01-.1 ug/ml/min) into the gastric arterial inflow caused a prompt fall in vascular resistance, the magnitude of the response being positively related to the dose utilized. 7.5% CO_2 in the inspired air also induced a decrease in vascular resistance. And finally when submaximal doses of histamine and CO_2 were studied in combination the resistance decrease was greater than with either alone. There was, however, no evidence that changes in CO_2 tensions in any way directly modified the hemodynamic response to histamine. The combination of histamine and hypercapnic responses seemed to be a matter of simple summation of the effects of the two stimuli. [Supported by P.H.S. Grant No. AM-05045-03 GM]

MECHANISM OF THE RBF RESPONSE TO URETERAL PRESSURE ELEVATION. F. D. Nash* and E. E. Selkurt, Dept. of Physiology and Heart Research Center, Indiana Univ. Medical Center, Indianapolis, Indiana.

In 47 experiments in variably hydrated dogs, elevation of ureteral pressure (UP) produced significant increase in RBF ($p<.001$). Extension of previous work (Nash, F. D., and Selkurt, E. E., Physiologist 6:244, 1963) compares the hemodynamic transient responses to elevation and release of UP with those to partial (autoregulatory) and complete occlusion of the renal artery. Both pulsatile flow amplitude and mean RBF increase as UP rises. The phasic transients in RBF following the release of ureteral occlusion are qualitatively similar to those following release of arterial occlusion; an initial overshoot, a fall below control (with reduction in pulsatile amplitude), and a secondary hyperemia. The RBF transients with sudden elevation of UP resemble those which follow sudden partial reduction in renal artery perfusion pressure (autoregulation). These findings suggest that: (1) the RBF responses to reduction in perfusion pressure and elevation of UP are due to the same mechanism, (2) the responses are related to changes in the arteriolar transmural pressure gradient, and (3) the mechanism is an intrinsic property of the arteriolar smooth muscle in responses to alterations in the transmural pressure gradient and/or to changes in tension within the vessel wall.

DIPOLE MOMENT OF IN-VIVO AND ISOLATED PERFUSED RABBIT HEARTS. C.V. Nelson, W.C. Waggoner* and P.R. Gastonguay.* Maine Medical Center, Portland, Maine

Absolute magnitude and direction of resultant vector for an isolated perfused heart immersed in a spherical container are found from 3 sets of bipolar voltages (Science 133: 1831, 1961). Limb and chest ECGs were taken on 12 rabbits; hearts from the same animals were then perfused at the sphere center. For isolated hearts, average peak values of P, QRS and T were 72, 355, and 128 μA-cm. Average mean frontal plane angles for in vivo and sphere experiments were: P, 67° and -33°; QRS, 51° and 57°; and T, 73° and -137°. The direction of ventricular repolarization for the isolated heart was opposite that of the heart in vivo. For the P vector, there was about a 100° shift in electrical axis. The average ratio of peak frontal-plane voltage-vector in vivo to peak frontal-plane dipole moment was twice as great for atrial depolarization than for ventricular depolarization or repolarization. It is postulated that, under in vivo conditions, there is a more rapid spread of excitation along the endocardial layers because of the relatively low resistivity of the intracardiac blood. This results in a significant dipole component perpendicular to the atrial wall, as well as tangential spread in myocardium and septum. Supported by grants from N.I.H. and Maine Heart Association. W. Waggoner is now in Colgate-Palmolive Co., Research Division.

INTERACTION BETWEEN SPINAL MOTONEURONS IN THE CAT.
Phillip G. Nelson, NIH, Bethesda, Md.

Synchronous antidromic activation of spinal motoneurons produces a brief predominantly negative extracellular field in the ventral horn. This antidromically evoked field potential may be as large as 8 mv and have all-or-none components as large as 4 mv. Excitability of single motoneurons to intracellularly applied currents and to synaptic activation has been measured. An increase of up to 30% in excitability, lasting 1-2 msec, may accompany the field negativity produced by the firing of nearby motoneurons. This excitatory effect is frequently followed by the recurrent, presumably synaptic, inhibition described by Renshaw. The early onset of the excitatory effect and its brief duration differentiate it from the recurrent facilitation described by Renshaw, and Wilson. Electrical coupling between motoneurons may explain the excitability changes that were observed. Synaptic effects from ventral root stimulation similar to those occurring in frog spinal cord (Kubota and Brookhart) could also explain the results. However, in the present experiments the earliest excitability changes precede any antidromic EPSPs.

The effect of reducing plasma sodium concentration on sodium and glucose sorption relationships as well as water and potassium transport in the canine jejunum. R. Nelson and R. Beargie*, Geo. H. Scott Res. Lab., Fairview Park Hospital, Cleveland, Ohio.
Extracorporeal perfusion of the small intestine was performed in 10 dogs. Blood was pumped from a disc type oxygenator into the abdominal aorta. Femoral arteries and veins, renal arteries and veins, abdominal aorta proximal to the celiac artery and the celiac artery were tied off. Venous drainage was obtained from the right ventricle after occlusion of the pulmonary artery. Blood for the perfusion was collected from donor dogs and red cells allowed to settle overnight. Most of the plasma was removed and the red cells divided into equal volumes. To one set of cells an equal volume of Tyrode's solution was added and to the other set of cells an equal volume of mannitol solution was added. The latter solution was similar to the Tyrode solution except that mannitol replaced most of the NaCl. The sodium concentration was 144 mEq./l. in the Tyrode solution and 108 mEq./l. in the mannitol solution. The glucose concentration of plasma was greater than that of gut contents. A segment of jejunum was isolated for sorption tests. For gut transport studies Tyrode solution with added Na22 and glucose was instilled into the segment and removed after 10 minutes during each perfusion. Blood flow and aortic pressure were similar for the perfusions. No significant change was noted in net water, sodium or potassium sorption or sodium insorption (movement from gut to blood) when results from each perfusion were compared. A statistically significant decrease occurred, however, in net glucose transport and sodium exsorption (movement from blood to gut) when plasma sodium concentration was low. A significant correlation was also found between the quantities of glucose absorbed and the amount of sodium exsorbed regardless of the level of plasma sodium. Approximately 107 micromoles of glucose were absorbed per mEq. of sodium exsorbed.

Supported by N.I.H. Grant #AM 06446-03.

RESPONSES OF PULSED RABBIT AORTIC STRIPS TO COMBINED ACTION OF NOREPINEPHRINE AND SEROTONIN OR LSD. T.E. Nelson, Jr., C.V. Manion*, R.W. Whitehead, and L.B. Peck*, Dept. of Pharmacology, Univ. of Colo. Med. Ctr., Denver, Colo.

Using helical cut aortic strips subjected to continuous pulsed tension as previously described, Manion, et. al. Fed. Proc. 23, 121, 1964, the effects of 5-hydroxytryptamine (Serotonin), d-lysergic acid diethylamide (LSD 25-Sandoz), and norepinephrine were observed singly and in combination. Aortic strips, six from each aorta, were cut approximately 3 mm. wide by 2 cm. long, (unstretched) and suspended between special clips in individual 10 ml. baths containing Kreb's Ringer bicarbonate (pH 7.3-7.4) maintained at 37.5°C and aerated with 95% O_2 + 5% CO_2. The lever arms were balanced for 4 gms. static tension and pulsed 150 times/min. electromagnetically with a momentary tension increase of 3.3 ± 0.1 gms. Using this technique the responses or aortic strips to norepinephrine and epinephrine are completely different in character, being rapid in both onset and recovery, than responses to serotonin, tyramine or LSD 25 which show prolonged contraction. Contraction responses to serotonin are generally more rapid in onset than responses to LSD 25. When norepinephrine is added to a bath which already contains serotonin or LSD (strips partially contracted) the individual responses to norepinephrine are potentiated. These observations may be interpreted as further evidence for the specificity of epinephrine and serotonin receptors in smooth muscle as demonstrated by Furchgott 1954. (Supported by a U.C.M.C. General Research Fund Grant to T.E.N.)

QUALITATIVE CHARACTERISTICS OF FLOW IN THE MINUTE BLOOD VESSELS OF BONE IN LIVING BATS. Paul A. Nicoll, Dept. of Physiology and Heart Research Center. Indiana University Medical Center, Indianapolis, Ind.

Metacarpals and phalanges in bats are thin and bare of muscle over much of their surface. The same is true of the calvaria which in the pipistrilla is also transparent. Exposure by reflection of the overlying skin under local anesthesia allows microscopic observation by transmitted or reflected light at magnifications up to 300 times or more. Vessels of the periostium, intra-osseous matrix, medullary cavity and sub-osseous sites may all be studied in suitable living individuals. Medullary vascular flow is uncomplicated in these metacarpals and phalanges and appears comparable to haversian blood flow in larger bones. The arterial supply enters at one end, either central or distal, and proceeds the full length of the cavity. Numerous branches feed a sub-osseous capillary plexus that drains frequently into venules, these converge to form venous drainage at both ends of the bone. No connections between medullary and periosteal minute vessels are seen. The arterioles or venules do not show active vasomotion. Nutrient needs of the osteocytes must be supplied by the canalicules probably from both outer and inner surfaces. With the calvaria, when no intra-osseous vessel exist, the blood supply is comparable to that of the osseous tissue in the long bones. The sub-osseous meningeal plexus drain through numerous orifices into the diploic sinuses. Where intra-osseous vessels exist their arterial source is largely, if not exclusively, arteriolar branches of the meningeal vessels and again drainage is by the diploic sinuses. Here also the metabolic needs of the osteocytes is by way of fairly extensive canalicular paths. Spread of vital dye injected into the subcalvaular space suggests a bulk movement of fluid in the canaliculi.

HYPOXIA AND PULMONARY EDEMA. Demetre M. Nicoloff*, and M. B. Visscher, University of Minnesota Medical School, Minneapolis, Minnesota

It has been suggested that increased capillary permeability is the reason for pulmonary edema during hypoxia. Isolated dog lungs were placed on a torsion bar balance and perfused with blood by a sigma-motor pump. Pulmonary artery pressure, lung weight and respiratory pressure were continuously monitored. The lungs were ventilated with air plus 5% CO_2 and the pulmonary artery pressure raised by increasing flow to the point of edema formation. Flow and pressure were then decreased and the lungs ventilated with 95% N_2 + 5% CO_2 or 0.5% CO, 94.5% N_2 and 5% CO_2 for periods of 5 to 30 minutes. When the O_2 saturation fell to between 30 and 8% or the O_2 content fell to less than 5 volumes%, the flow and pressure were again increased to the point of edema formation. Edema formation occurred at various pressures in the different lungs (P. A. pressure range 22 to 38 mm. Hg.). However, edema occurred at essentially the same pressure regardless of the gas mixture used or the O_2 saturation of the blood. Hypoxia, therefore, did not promote edema formation. The addition of either 2 mM/L sodium iodoacetate or 2 mM/L of DNP alone did not increase the susceptibility to edema formation. However, if both were added or if either alone were added to hypoxia the lung showed increased susceptibility to edema formation. The rate was more rapid and occurred at lower pressures. Pulmonary edema that occurs in intact animals is most likely related to left heart failure. (Supported by USPHS grant #HE-03212).

CONDITIONED AVOIDANCE RESPONSES TRANSFERRED TO BASAL FOREBRAIN. Harold C. Nielson (intr. by Carmine D. Clemente). VA Hosp., Sepulveda, Calif., and Dept. of Anatomy, Univ. of Calif., Los Angeles, Calif.

Tests were made for the generalization or transfer of a conditioned avoidance response (CR) established to electrical stimulation of the reticular activating system (RAS), hippocampus, or reticular nucleus of the thalamus, to a basal forebrain region (BF) which, when stimulated, produces the EEG and behavioral characteristics of sleep. There was immediate stimulus generalization to BF from the RAS and hippocampus. Cats gave avoidance CRs to their first BF stimulation and 8-9 CRs in the first 10 trials. Throughout these trials, spaced 35 seconds apart, the cats became progressively more drowsy and finally slept through an additional 15 trials. In an attempt to keep the cats awake, the intensity of the unconditioned stimulus (US), a foot shock, was increased to normally intolerable limits, but this failed. These cats fell asleep making avoidance CRs! There was rapid transfer of the CR from the reticular nucleus of the thalamus to BF although not as dramatic as from RAS and hippocampus. These cats also lost alertness after 10 trials and fell asleep. The relationship between BF CS intensity and percentage of CRs was established. 30 to 40% CRs are obtained with CS intensity of .02-.03 mA, between .04-.06 mA the cats are drowsy, as though wanting and expecting sleep, but making 75-80% CRs. From .07-.08 mA the animals are kept awake only by an abnormally intense US. Above .1 mA even extremely high US intensities will not awaken the animal. Once the relationship between CS intensity of BF stimulation was established, positive transfer tests were conducted from BF to other structures. (Supported by grant MH-07037 from the U. S. Public Health Service.)

ION DISTRIBUTION PATTERNS, MEMBRANES AND ENZYMES. Leslie F. Nims and Regina Butera.* Biology Dept., Brookhaven Natl. Lab., Upton, L.I., N.Y.

A material transfer system in which the energy necessary to maintain a non-equilibrium stationary state is supplied by the urease catalyzed hydrolysis of urea occurring in one of the phases is being studied. Those ionic species to which the system is closed move from one phase, through a cellophane membrane, into the other phase, against both their concentration and electrochemical potential gradients when the system contains equal concentrations of such ions in each of the phases initially, and after the system is brought to "life" by the addition of urease to one of the phases. To maintain a particular non-equilibrium stationary state the system must be fed with a urea solution at a constant rate. The system shows some ion selectivity and the ion selectivity ratio in a stationary state is a function of the rate of hydrolysis of urea or the flow of one of the participants in the chemical reaction through the cellophane membrane. Potassium ion accumulates in the phase containing urease to a greater extent than either sodium or lithium ions while chloride concentration is decreased.--
Research carried out at Brookhaven National Laboratory under the auspices of the U. S. Atomic Energy Commission.

ANALYSIS OF TRANSIENT CARDIAC RESPONSES TO "ONSET" & "END" OF EXERCISE
I. Ninomiya*, C. Taquini* and M. F. Wilson. Dept. of Physiol. & Biophy., Univ. of Kentucky, Lexington, Kentucky.

The adaptation to treadmill exercise in the instrumented dog was analyzed in terms of the timing, magnitude and patterns of cardiac responses to the trial sequence within an experiment, the experiment day and the intensity of exercise. In 85 trials of 14 experiments, the incidence of an overshoot reaction at the onset of exercise occurred in 19% with heart rate, 9% cardiac output, 4% peak ascending aortic flow, and 1% with stroke volume. At the first trial it was observed in 57%, 46%, 21% and 7% respectively. At the end of exercise there was no overshoot below the initial resting level. The mean response time of 85 trials, defined as the interval from the onset of exercise level to 63.2% of its final value during exercise, was 7.9 sec. with heart rate, 8.4 sec. with cardiac output, 9.2 sec. with peakflow and 5.9 sec. with stroke volume. However, at the first trial it was shortest, e.g., 3.7, 4.7, 5.8 and 4.7 seconds respectively. The response time increased in relation to the trial sequence but not to the experiment day. The mean recovery time, defined as the interval from the end of exercise value to 36.8% above the initial resting level was 10.4 sec. with heart rate, 11.0 sec. with cardiac output, 15.9 sec. with peakflow and 12.0 sec. with stroke volume. The increase in load intensity, i.e., treadmill speeds from 1.0 to 5.0 mph, had a negligible effect on the response and recovery times, but a significant and nearly linear effect on the magnitude of the cardiac responses. These data suggest that the transient period of response is a function of trial sequence and the magnitude of response is a function of load intensity.
(Aided by grant HE-06136-03 from the NIH)

The effect of adrenal steroids on glucose kinetics in dogs. R. Ninomiya*, N. Forbath* and G. Hetenyi Jr., Dept. of Physiology, University of Toronto.
The rates of endogenous glucose production, utilization, the amount of rapidly intermixing glucose ("pool") and the apparent distribution space of glucose has been measured in non anaesthetized trained dogs by the method of successive tracer injections. The infusion of hydrocortisone caused a reduction in both the rates of production and utilization of glucose. Daily injections of 4 mg/kg methylprednisolone for one week increased the rate of glucose production by +37%, the glucose mass by +25% and the glucose space by +18% above the pre-injection level. Continuing the daily injections for a second week the rate of production was raised by +83%, the glucose pool and space by +36% and 30% respectively. The blood glucose level was raised only slightly. Both before and after one week of methylprednisolone treatment the i.v. infusion of glucose suppressed the endogenous glucose production to the same extent. Preliminary experiments indicate that the simultaneous injection of large doses of protamine zinc insulin may counteract the effects of methylprednisolone. (Supported by the J.P.Bickell Foundation and the M.R.C. of Canada).

A COMPARISON OF ISOMETRIC AND AUXOTONIC CONTRACTIONS IN THE TURTLE HEART. L. J. O'Brien and J. W. Remington. Medical College of Georgia, Augusta, Georgia.

Contractility of ventricular muscle has been defined in terms of either total isometric tension or the velocity of shortening of a purely isotonic contraction. There have been few attempts to record both isometric and isotonic contractions from the same heart and under the same conditions of EDP. In the normally ejecting ventricle, neither measure is directly available. There is a current tendency to use the maximal rate of pressure rise during isovolumic contraction as an index to contractility. This infers an undemonstrated direct relation between this slope and the total tension which would follow if ejection were prevented. For an initial survey, the time course of pressure change during isometric and during auxotonic contractions of a turtle heart have been compared. A fluid filled tube was tied into the outflow tract. Ejection could be prevented by turning a stopcock in this outflow line. EDP was set by atrial filling from a side reservoir. Isometric and auxotonic contractions, at the same EDP, could be alternated. Total contraction times, and the slopes of the pressure change under the two conditions will be compared. (Supported by USPHS Grant HE-04573)

Effect of Vagal Stimulation on Atrial Transport Studied in Dogs Without Thoracotomy. T. P. B. O'Donovan*, J. C. P. Williams* and E. H. Wood. Mayo Clinic, Mayo Foundation, Rochester, Minn.

Pressures and indicator-dilution curves were recorded via catheters introduced percutaneously to the atria, ventricles and aorta of dogs under morphine-pentobarbital anesthesia. Coupled electronic pacemakers attached to a transseptal needle and a right ventricular electrode catheter allowed atria and ventricles to be driven at selected rates and temporal sequences. The vagi were divided in the neck and the distal ends connected to a Grass stimulator. In the control state the heart was without vagal tone and the spontaneous sinus rate averaged 140 (90-185) beats/min. Heart rate was kept constant by pacing about 15 beats/min. above this rate while recordings were made both with effective (PR interval 0.05-0.14 sec.) and "ineffective" (PR interval -0.003 sec.) atrial contraction during the control state and during graded levels of bilateral vagal stimulation. Vagal tone was assessed by the spontaneous sinus rate on cessation of pacing. Circulatory degradation following sudden switches to "ineffective" atrial contraction decreased progressively as vagal stimulation increased. During severe vagal stimulation (sinus rate below 60/min.) ineffective atrial contraction caused an immediate fall in aortic systolic pressures of 4-7% (control 14-33) and in cardiac output of 4.5-14% (control 8.5-32) and a rise in mean left atrial pressure of 0.5-2.5 (control 1.5-6.5) and in right atrial pressure of 0.0-0.5 (control 0.5-5.0) cm. H_2O. The left atrial "a" wave in ineffective atrial contraction rose less, 2.5-10 cm. H_2O above the mean (control 9.5-14). Similar results were obtained in two dogs studied two days after bilateral stellate ganglionectomy. These findings support the view that the atrial contribution to ventricular performance is decreased by vagal activity. (Supported in part by research grants NIH H-3532, AHA CI 10 and BNZ.)

AN ORTHODROMIC RETINAL RESPONSE TO STIMULATION OF CENTRAL VISUAL PATHWAYS IN THE PRIMATE. Thomas E. Ogden. Div. of Neurol. and Dept. of Physiol., Univ. of Utah School of Med., Salt Lake City, Utah.

Intraretinal potentials evoked by stimulation of central visual pathways in Saimiri, rhesus and Cebus monkeys under light nembutal anesthesia were recorded with glass microelectrodes (40-60 megohms). Stimulation of the optic tract or lateral geniculate evoked a compound action potential in optic nerve showing fast (30-40 M/sec) and slow (10-15 M/sec) fiber groups. Their velocities within the retina were 2-4 M/sec and 0.5-1 M/sec. The slow fiber group was identified with the papillomacular bundle and was prominent within the central areal retina contralateral to stimulation. In addition to this antidromic compound action potential of the optic fiber layer, recordings from the area of retina between optic disc and fovea showed a graded monophasic positive wave (P-wave) which followed the slow fiber potential after a delay of 2 msec. The maximum amplitude of the P-wave was identified with the inner plexiform layer and adjacent part of ganglion cell layer by marking with the recording electrode. The P-wave interacts with light evoked retinal activity in a complex manner and may be associated with cone function since it is absent in the periphery of the primate retina and in the cat. It is hypothesized that the P-wave represents a hyperpolarizing postsynaptic response of ganglion cell dendrites evoked by activation of efferent fibers to the retina and mediated by an interneuron (amacrine cell). (Supported by PHS grant NB-04135)

AMINO ACIDS IN THE HUMAN GUT. William W. Olmsted*, E.S. Nasset, and Maurice L. Kelley, Jr.* University of Rochester School of Medicine & Dentistry.

Previous work in this laboratory demonstrated that a significant proportion of amino acids, present in the lumen of dog and rat gut after feeding, is derived from digestion of endogenous protein. The experiments to be reported were done with 5 normal human male subjects. Approximately isonitrogenous quantities of lean beef, gelatin, whole egg and whole milk were the test meals. Each meal was eaten 3 times and no subject ingested the same meal twice. Samples were withdrawn from distal duodenum or proximal jejunum at 1.0, 1.5, and 2.0 hours after feeding. The amino acid mixture present in the lumen yielded molar ratios quite different from those to be expected from hydrolysis of the ingested proteins. It is evident that in man, as in dog and rat, the admixture of endogenous protein with the exogenous protein is sufficient to mask the distinctive amino acid composition of ingested protein.

INFLUENCE OF ARSENATE ON PHOSPHATE TRANSPORT IN THE HUMAN ERYTHROCYTE. Akira Omachi, James D. Pritchard* and Bertil E. Glader*. Univ. of Illinois Coll. of Med., Chicago, Ill.

The study of phosphate (P_i) transport across the cell membrane is complicated by the fact that P_i also participates in metabolism. We have noted earlier (Fed. Proc. 23: 114, 1964) that increasing medium P_i increases P^{32} release from previously labeled red cells. This was explained as being due to the entry of cold P_i and its competition with cell P^{32} in esterification processes, making more P^{32} available for release. When esterification was inhibited by iodoacetate (IAA), P^{32} release increased especially at the lower medium P_i levels so that the isotope release appeared to be independent of medium P_i, and therefore of cell P_i. This result supports the view that the membrane transport process is passive. In the present study, human red cells stored in ACD were separated, washed, and labeled with P^{32} by incubating erythrocytes suspended in Tris-buffered Ringer-Locke's medium for 1 hour at 37° C. The labeled cells were washed and resuspended in non-radioactive medium for the study of P^{32} release. Variation of external arsenate (As) from 1 to 15 mM produced a change that resembled closely the result obtained by varying external P_i rather than the change observed with IAA. This may be attributed to the fact that As inhibition of glycolysis is due to competition with P_i in forming 1,3-diphosphoglycerate rather than to inactivation of an enzyme. P^{32} uptake by IAA-poisoned was not inhibited by AS or P_i which suggests that P_i transport is not mediated by a carrier which is easily saturable. These results imply that arsenate inhibition of phosphate transport in the human erythrocyte, when it is observed, is probably due more to inhibition of a metabolic reaction rather than of a transport process.
(Supported by a grant from NIH.)

THE MECHANISM OF MANNITOL-INDUCED RENAL HYPEREMIA. K. Önen* and L.B.Berman. Univ. of Louisville School of Med., Louisville, Kentucky.

Previous data (Proc. Soc. Exp. Biol. and Med. 1963) have suggested that the renal hyperemia induced by mannitol is a local, intra-renal effect. In the present experiments, 20% mannitol was infused into 12 anesthetized dogs at a rate of 6-10 ml./min. for 15 minutes. Left renal blood flow was measured by direct collection and increased an average of 31% by the end of the infusion. Arterial pressure was unchanged. Neither 5% mannitol, nor whole blood had any similar effect. In an additional 10 dogs, left renal blood flow was measured before and after 15 minutes of total left ureteral occlusion. The range of change was -22% to +25% with an insignificant mean change of +8%. In 8 dogs, mannitol hyperemia was induced as above and the mannitol infusion was continued through 15 minutes of total ureteral occlusion. No decrease in renal blood flow was observed compared to the pre-occlusion values. Finally, 4 dogs were infused with angiotensin 0.2-0.6 μg./kg./min. for 10 minutes with a mean decrease in renal blood flow of 34%. This effect was entirely abolished by infusing mannitol simultaneously with the angiotensin. The elevation of arterial pressure by angiotensin was not affected by the mannitol. The data suggest that marked elevation in renal interstitial pressure does not affect renal blood flow, nor does such elevation reverse the increased blood flow produced by mannitol. The exclusion of tissue pressure as a significant factor, and the results of the mannitol and angiotensin experiments suggest that mannitol may directly impair the contractility of the afferent arteriole.

COMPENSATION FOR INERTIA BY MUSCLE. Lloyd D. Partridge. Dept. of Physiology and Biophysics, Univ. of Tennessee, Memphis.

How the nervous system provides compensation for the effects of inertia in motor activity has long been a question. With the identification of the γ fiber system came the recognition of the possibility of a servo type control. To test this hypothesis, dynamic characteristics of parts of the system should be determined. Dynamic tests of muscle response have been accomplished by replacement of the normal neural pulse signals with computor generated pulse rate modulated stimuli to the motor nerve of circulated cat triceps surae muscles. The muscle moved an inertial load simulating a limb. Acceleration, velocity and position of the load were determined while the muscle was subject to a series of cyclic frequencies of variation of stimulus pulse rate. A large inertial reduction of response amplitude with frequency increase was assumed in advance but not found in the experiment. Similarly, inertia was expected to cause a $\frac{1}{2}$ cycle lag in the position response but for most cyclic frequencies tested the total lag was considerably less than this. Since these tests covered most of the physiological range of movement frequencies and employed pulse rate ranges corresponding to those found in electromyographic studies, it appears probable that in normal motor function the muscle itself contributes a major effect to the compensation for the effects of inertia. The presence of such characteristics in muscle reduces the requirement for nervous system compensatory function but reemphasizes the importance of muscle effects in motor control analysis.

Supported by USPHS NB-04462.

SIMULTANEOUS DETERMINATIONS OF THE CORONARY AND PERIPHERAL VASCULAR BED RESPONSES TO VASOACTIVE AGENTS IN INTACT DOGS] L. T. Paul* and H. P. Pieper. Physiology Dept., The Ohio State University, Columbus, Ohio.

The arterial pressure of intact anesthetized dogs was oscillated (cycle period 4 seconds) by means of a sinusoidal piston pump attached by catheter to the abdominal aorta. The following parameters were simultaneously recorded during these induced pressure oscillations: pulsatile coronary arterial flow by means of a catheter-tip flowmeter; aortic pressure and right atrial pressure by means of catheter-tip manometers. From the pulse-by-pulse values of these recordings a plot of the pressure-flow relationship for the coronary system was obtained. From the same recording of the aortic pressure the peripheral run-off rate was calculated using the pressure-slope method (Wetterer and Pieper, Z. Biol. 106: 23, 1953; Pieper and Leverett, J. Appl. Physiol. 19: 353, 1964) and a plot of total peripheral run-off rate versus arterial pressure was established. These pressure-flow relationships describe the coronary system and the total arterial system for the same set of cardiovascular conditions. Alterations in these relationships produced by infusion of certain vasoactive agents were then compared. The elasticity coefficient of the total arterial reservoir was also calculated (by means of the pressure-slope method) for each induced set of cardiovascular conditions. Supported in part by grants from the American Heart Association and the Wayne County (Ohio) Heart Association.

RECRUITING RESPONSES AND CONDITIONED REFLEXES PRODUCED BY STIMULATION OF CENTRUM MEDIANUM. J. Pecci-Saavedra* and R. W. Doty, Center for Brain Research, University of Rochester, Rochester, New York.

Thalamic stimuli which elicit recruiting responses (RRs) can also be used as conditional stimuli (CS) to elicit conditioned reflexes (CRs). Experiments by Andyan et al. (Fed. Proc. T.S. 23, T264, 1964) indicated that CRs in cats to such CS were performed only after cessation of the CS and concurrent RRs. They thus suggested that RRs are inhibitory in nature and probably preclude CR performance. To check this possibility 4 squirrel monkeys were first trained to press a lever (the CR) to avoid a shock to the tail upon presentation of clicks as CS. After 90-150 trials they could make at least 7 CRs in 10 successive trials. Bipolar electrodes were then implanted bilaterally in nucleus centrum medianum (CM) while monitoring potentials evoked at 8 neocortical loci by stimulation of the CM site. Training was resumed with bilateral stimulation of CM, 0.5-msec., 0.2 to 0.6-mA pulses, 6-8/sec, serving as CS. The EEG was continuously monitored and the CS found to evoke 300-800 μV RRs in central and frontal cortices. An additional 40-60 trials were required to regain previous levels of CR performance, but the CRs were indistinguishable from those elicited by the auditory CS. If it is assumed that frontal and motor cortical regions are participating in the formation and performance of the CRs, it is apparent that the supposed inhibitory nature of the RR is entirely insufficient to impair the monkey's behavior in these experiments. Some diminution in the amplitude of the RR during CRs and increase during extinction were observed. These changes appeared to be associated with shifts in the relative alertness of the animal.

(Supported by USPHS Grants NB 5395 and NB 03606)

PANCREATIC METABOLISM OF ZINC-65 DURING STIMULATION VS. THE RESTING STATE. Jerome C. Pekas. Agr. Expt. Station of the Univ. of Tenn., Knoxville, Tenn.

The conscious pig secretes intravenously administered Zn^{65} in pancreatic juice in a manner markedly different from that of the alkali metals Na^{22}, K^{42}, or Cs^{137} which are in near perfect equilibrium with blood plasma during the postdosing period. In contrast Zn^{65} is difficult to detect in the pancreatic secretion during the first hour, then it gradually makes its appearance, and thereafter the concentration of Zn^{65} varies in rhythmic fashion similar to the variations of the protein concentration of the juice (unpublished). These results suggested that Zn^{65} secretion was protein associated and that this association was related to protein synthesis. To test this under controlled conditions, two anesthetized (pentobarbital sodium) pigs were stimulated at 30 min intervals by alternate intravenous injections of acetylcholine (200 μg/kg) and pancreozymin (2 units/kg). Pancreatic juice was collected in consecutive 10 min fractions for 5 hr, thus two resting fractions were obtained between stimulations. Constant infusion of secretin (0.04 units/kg/min) maintained a good and stable pancreatic secretion rate. The results demonstrate that Zn^{65} is only slightly responsive to stimulation during the first hour. Thereafter the Zn^{65} secreted in response to each stimulation increased exponentially, but always returned to a constant resting level. The quantity of protein secreted in response to each stimulation was nearly the same; thus the apparent specific activity (Zn^{65}/protein unit) increased exponentially with time. These results demonstrate a high degree of association between protein secretion and zinc secretion by the pancreas of the pig.

SYSTOLIC BLOOD PRESSURE CHANGES DURING TWO BEAT SINUS ARRHYTHMIA. J. Perez-Cruet*, J.E.O. Newton and W.H. Gantt. Pavlovian Lab., The Johns Hopkins University School of Medicine, Baltimore, Md.

Two beat sinus arrhythmia is a special type of arrhythmia in which, after a long pause, the sinoauricular node initiates two successive beats, followed by another long pause. This type of arrhythmia resembles cases of premature contractions (coupling). We have observed this type of arrhythmia in about 80% of our dogs. It usually occurs sporadically and in many instances is associated with a fast respiratory rate. In seven unanesthetized dogs, direct systolic blood pressures were measured during two beat sinus arrhythmia. During the second beat the systolic pressure was increased 4 to 10 mm Hg from the pressure level of the first beat except in one dog in which the systolic pressure always decreased during the second beat. The incidence of systolic blood pressure increase on the second beat is greater in central pressures (90 to 100% of occurrences) than in peripheral pressures (43 to 80%). Three mechanisms are responsible for the increase in blood pressure during the second beat: 1) changes in cardiac output, 2) peripheral resistance, and 3) cardiac rate. Respiratory rate is not necessarily responsible for these changes (Perez-Cruet, et. al., Fed. Proc. 20, 1961, p.89). During the second beat the stroke volume is usually decreased as well as the amplitude of peripheral optical plethysmography. The mechanism for the consistent decrease in systolic pressure in the second beat during two beat sinus arrhythmia in one dog is not known and is under investigation. In summary, the study showed that usually in two beat sinus arrhythmia the systolic blood pressure increases slightly during the second beat.

(Supported by NHI grant HE-06945-03 and NASA grant NsG 520)

COMPARISON OF RENAL RESPONSE TO RIGHT AND LEFT VAGOTOMY DURING WATER DIURESIS. Joseph H. Perlmutt. Dept. of Physiol., U.N.C. School of Med., Chapel Hill, N. C.

Bilateral cervical vagotomy during mild water diuresis promotes a prolonged ADH-type of antidiuresis (Fed. Proc. 22: 385, 1963). The relative contribution of each vagus nerve to the response was determined from renal function studies on two groups of dogs subjected either to right or to left vagotomy during mild water diuresis; subsequent to the observations on unilateral vagotomy, the contralateral vagus was sectioned. After section of either nerve, urine flow declined, then rose, and declined again, while changes in urine osmolality were of the reverse order. The peak urine flow following the initial decline after right vagotomy exceeded control values and flow subsequently declined to near control values; in the left vagotomized group the peak flow did not exceed control values and flow subsequently declined to the previous low values. Osmolal clearances remained essentially constant in the two groups, so that changes in urine flow were accompanied by equal changes in free-water clearances. During early drastic changes in urine flow, GFR and RPF fluctuated; however, when urine flow remained at the new level, then GFR and RPF were not significantly different from control values. Subsequent left vagotomy in the right vagotomized group promoted further reduction in urine flow, whereas right vagotomy in the other group had no significant effect. The data indicate that left vagotomy promoted a greater overall effect on urine flow depression than did right vagotomy, and suggest the possibilities either of a larger number or of a greater degree of activity of "ADH inhibitory" fibers in the left than in the right vagus. (Supported by NIH Grant HE-02457-08 and IRSG.)

ABLATION OF THE VASCULAR RESPONSE TO HISTAMINE BY DIAMINE OXIDASE (HISTAMINASE) INFUSION. E. T. Peter*, A. J. Madsen*, and O. H. Wangensteen (intr. by: L. Tobian) Dept. of Surgery, Univ. of Minnesota Med. School, Minneapolis, Minn.

The gastric secretory effects of histamine are well known. Recently it has been shown in this laboratory that infusion of histamine at the rate of 1 μgm/kg/min will result in a 16.7% increase in left gastric artery flow (2 μgm/kg/min results in a 50% increase). It has further been shown that diamine oxidase (D. O.) will block the secretory effects of histamine.

In the present study the vascular responses to histamine in the gastric and mesenteric arteries have been observed during histamine infusion given before and after diamine oxidase infusion. The increase in gastric blood flow and the decrease in intestinal flow observed during the control period were abolished by diamine oxidase infusion which enzymatically inactivated the histamine. It is interesting that both the gastric secretory and vascular responses to histamine are abolished by D. O. whereas these responses are unaffected by the usual antihistaminic drugs.

(Supported by USPHS, Hartford Foundation and D. J. Cowling Grants)

EFFECT OF TRYPSIN ON OXYGEN UPTAKE OF KIDNEY MITOCHONDRIA. H.J.Phillips and Vera Skank. Creighton Univ. School of Med., Omaha, Nebraska.

Trypsin concentrates (N.B.C. 1:300, etc.) have been found to increase respiration of tissue slices. It was not known whether or not the intact cell membrane was necessary for trypsin concentrates to increase oxygen uptake but subseqyent work indicated that oxygen uptake of mitochondria was also increased with trypsin concentrates. Mitochondria from rat kidney were prepared in 0.25 M sucrose, crystalline trypsin (Calbiochem) was used in a final concentration of 50 mg %, oxygen uptake was determined by the direct method of Warburg, and values expressed in terms of the protein content of the preparation. The effect of trypsin on mitochondria is pH dependent; oxygen uptake was highest between pH 7.0-7.2. Amylase and lipase which are found in impure trypsin concentrates does not cause an increase in oxygen uptake. Chymotrypsin has an effect similar to that of trypsin. When mitochondria were treated with trypsin there was an increase in free amino acids in the suspension. These observations suggested the possibility that protein was being hydrolyzed to amino acids which, in turn, was acting as substrate to increase oxygen uptake. Fifteen amino acids were tried on mitochondrial preparations without added trypsin and in each case oxygen uptake was increased. Tests which were made with D and L amino acids and inhibitors suggest that amino acid oxidases are partially responsible for increased oxygen uptake. Trypsin apparently does not change the rate of oxygen uptake simply by alteration of the mitochondria. If mitochondria are incubated in a refrigerator with trypsin and then resuspended in sucrose they do not show an increased oxygen uptake. The supernatant fluid does not take up oxygen but mitochondria plus supernatant shows a significant increase in oxygen uptake over controls.
Supported by N.I.H. Grant GM 10118

POTASSIUM ABSORPTION IN THE ILEUM. Sidney F. Phillips* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The effect of changes in the concentration of potassium on its insorption and exsorption was tested using Thiry-Vella fistulae of the terminal ileum in four healthy, unanesthetized trained dogs. Twenty-five milliliter samples of Tyrode's solution, modified to contain varying concentrations of potassium and kept isotonic by altering the sodium content, were instilled into the loops for 30-minute periods. Isotopically labeled sodium, potassium, and water were added to the test solutions to determine their bidirectional fluxes. When the mean concentration of potassium was less than 4 mEq. per liter, it was enterosorbed. At concentrations greater than 6 mEq. per liter, potassium was absorbed. Its insorption and absorption were directly related to the mean concentration; the exsorption of potassium, however, was independent of the contents, the quantity exsorbed being practically the same in all of the tests.

The net movement of water, whether it was absorbed or enterosorbed, was related to the sum of the net movement of sodium and potassium. The slope of regression line gave a mean cation concentration of 149 mEq. per liter in the net fluid moved.

Measurement of the electric potential difference across the ileal mucosa ranged from 1 to 8 mv., with the lumen negative to the blood. Application of Ussing's calculation indicated passive movement of potassium.

During all of the tests, the concentration of potassium in the contents always changed toward a value slightly higher than that of the blood. (Supported in part by NIH Grant AM-02827.)

STUDIES ON THE INTRARENAL DISTRIBUTION OF BLOOD FLOW. L.A. Pilkington*, R. Binder, J. de Haas*, and R.F. Pitts. Cornell University Medical College, New York, N.Y.

The extraction ratio of para-aminohippurate is always less than unity in both dog and man. Reubi has proposed that, at low plasma concentrations of PAH, extractions below unity result from an admixture of two intrarenal plasma flows: 1) the clearing or cortical flow, from which PAH has been completely extracted and 2) the non-clearing or medullary flow, from which no PAH has been extracted. As a corollary of this, the clearance of PAH would be a measure of cortical flow, and total renal plasma flow minus C_{PAH}, a measure of medullary flow. Experiments were performed on anesthetized dogs to test the validity of this argument as a means of approximating distribution of renal plasma flow. PAH concentrations in arterial plasma, urine, and arterial and renal venous whole blood were used to determine C_{PAH} and TRBF by the Wolf modification of the Fick method. TRPF was determined by TRBF x (1-Hct) and the % extraction of PAH as $C_{PAH}/TRPF$ x 100. Plasma concentrations of PAH were raised until Tm levels were reached. No change in the % extraction of PAH was noted when the load to Tm ratios were 0 - 1.0. Increased plasma concentrations of sodium acetate did not change the % extracted. Decreasing the renal plasma flow to the kidney by inflation of a balloon catheter in the aorta resulted in no change in % extraction. Mannitol diuresis increased TRPF, but decreased the % of PAH extraction by the kidney. These results are consonant with the view that the method of Reubi can be used to indicate qualitatively changes in distribution of blood between cortex and medulla. Aided by research grants from the National Heart Institute, National Institutes of Health (HE 00814) and the Life Insurance Medical Research Fund.

ACCLIMATIZATION OF ATHLETES TO WORK IN EXTREME HEAT STRESS. R. W. Piwonka* and Sid Robinson. Anatomy-Physiology Dept., Indiana University, Bloomington, Indiana.

In a study conducted in April, 1963, five highly trained distance runners appeared to be well acclimatized to work (M.R., 240 Cal/m^2/hr) in the heat (40 C d.b., 23.5 C w.b.) even though none of them had been exposed to heat since the preceding summer. Four of the same men continued their training program the following winter, and during April, 1964 an attempt was made to acclimatize them further by five daily performances of the same work in a more intense heat stress (50 C d.b., 26 C w.b.). Conditions of the experiments were the same as before except for the increased heat stress. At the ends of their first exposures to the 50 C environment their heart rates averaged 160, rectal temperatures 39.7 C, mean skin temperatures 36.0 C, and they experienced severe fatigue and discomfort. Corresponding values at the ends of their original exposures to the 40 C were: heart rate 118, rectal temperature 38.2 C, and mean skin temperature 36.2 C. At the end of their fifth exposure in the 50 C environment heart rates averaged 133, rectal temperatures 38.9C, and mean skin temperatures 37.5 C. Three of the subjects then performed the experiment in the milder environment (40 C). It was found that the five exposures to 50 C had brought about no significant improvement in their performance in the less extreme heat. The intensive training program of the runners completely conditioned them for work in moderate heat, and it apparently improved their capacities for acclimatization to a severe heat stress. (Supported by U.S. Army Medical Research & Development Command, Contract DA-49-193-MD-2449.)

INHIBITION OF OVULATION BY ACTINOMYCIN D. William R. Pool* and Harry J. Lipner. Florida State Univ., Tallahassee, Florida.

The initiation of ovulation in the rabbit is dependent on the release of LH. The changes in the ovary triggered by LH are as yet unknown. Except for enlargement of the estrous stage follicles the first noticeable changes are seen approximately 8 hours after the stimulus. One approach to the analysis of ovulation is to consider it as an example of a stimulus-response reaction. The response is presently believed to be due to synthesis of enzymes. In view of this hypothesis, the use of a protein synthesis inhibitor, Actinomycin D (AMD) was introduced to facilitate the analysis of ovulation. Female rabbits were anesthetized one hour after coitus and bilateral laparotomies were performed. The ovaries were exteriorized and placed on a plexiglass rod. In each ovary mature follicles were selected at random and injected with 1 ul volumes of either AMD solution or saline. Each ovary contained both control and experimental follicles. If the saline injected follicles did not ovulate, data from the entire ovary were discarded. Eighty-five per cent of the saline injected follicles ovulated. Concentrations of 10^{-3} ug/ul AMD or greater caused ovulation while lower concentrations caused only partial inhibition. Injections of 10^{-3} ug/ul AMD given up to three hours after coitus caused complete inhibition of ovulation but injections of the inhibitor given later caused only partial inhibition. From these results we infer that LH initiates the synthesis of a protein (possibly a proteolytic enzyme) which then causes ovulation. Sufficient mRNA is produced within 3 hours after coitus to cause enough protein synthesis for ovulation to occur, since 10^{-3} ug/ul AMD was completely inhibitory only if given within 3 hours after coitus. Supported in part by NIH predoctoral fellowship 1 FL GM-21, 186-01 and in part by PHS grant AM-1904.

RESPONSE OF LUMBAR MOTONEURONS TO NATURAL VESTIBULAR STIMULATION. R. E. Poppele (intr. by C. A. Terzuolo). Department of Physiology, University of Minnesota, Minneapolis, Minnesota

Unilateral labyrinthectomy in the decerebrate cat induces a postural asymmetry in the anterior limbs and releases vestibular reflexes in response to rotation of the head about the antero-posterior axis in the anterior and posterior limbs. Changes in impulse activity in α- and γ-motoneurons were recorded from the ventral root or by monitoring spindle afferent activity while measuring muscle tension. A device was used which reproducibly rotated the head through a choice of angles at constant velocities. The analysis was limited to the gastrocnemius and soleus muscles. Tonic and phasic changes in firing rate of spindle afferents were similar in both muscles. The phasic responses were velocity-dependent while the tonic were dependent on the direction and degree of rotation. Tension changes were often unrelated to the monitored proprioceptive inputs. Moreover, they were little altered after sectioning the homolateral dorsal roots. The above results indicate a large independence between α-motoneuron activity and the afferent activity resulting from the presence of the γ-loop, at least under the stated experimental conditions. This is in spite of the large effects of both phasic and tonic vestibular inputs, upon the γ-motoneurons. (Supported by NIH grant B 2567).

DIFFUSING CAPACITY AND CAPILLARY BLOOD FLOW DURING ACCELERATION. G.G. Power, R.W. Hyde, R. Sever, F. Hoppin, Jr. and Jean Nairn (intr. by R.E. Forster). Dept. of Physiol., Grad. School Med., Univ. of Pa., Phila., Pa. and Naval Air Development Center, Johnsville, Pa.

Arterial oxygen saturation decreases when a subject is accelerated in a centrifuge simulating a missile launching or reentry. We studied possible causes of this impaired oxygenation by measuring simultaneously the pulmonary diffusing capacity, D_{Lco}, by the single-breath technique and the capillary blood flow, $\dot{Q}_c$, by the acetylene method. Four subjects were studied during $+G_x$ (eyeballs in) acceleration of 8G for one minute. Average D_L decreased from an initial control level of 33.6 to 21.5 ml/(min x mm Hg), a decrease of 36%. Among the possibilities for this decrease in measured D_L during acceleration are: (1) reduction in the capillary blood volume available for gas exchange; (2) decrease in membrane diffusing capacity; (3) development of uneven D_L/alveolar volume ratios; and (4) fall in the pulmonary capillary hematocrit. Average $\dot{Q}_c$ decreased 39% from an initial control value of 12.8 to 7.8 L/min during acceleration. One possible explanation for this finding is an actual decrease in the pulmonary capillary blood flow. However, because others using dye dilution techniques have reported that total blood flow is maintained, a more likely explanation of our measured decrease in $\dot{Q}_c$ is uneven distribution of blood flow and alveolar gas. If this is the case, at least 39% of total blood flow passed through poorly ventilated or nonventilated alveoli during acceleration in these experiments. Both D_L and $\dot{Q}_c$ had returned approximately to prerun control levels within 6 minutes after deceleration. In summary, the findings can be explained by blood flow and capillary volume being maintained or increased in dependent, collapsed alveoli while ventilation is directed to more superior alveoli.

AMMONIA PRODUCTION IN ISOLATED RENAL TUBULES OF DOGS. Harry G. Preuss* and Robert F. Pitts. Cornell University Medical College, New York, N.Y.

The production of ammonia from various amino acids by isolated renal tubules of dogs was studied. Tubules prepared by the method of Burg and Orloff were suspended in a phosphate buffered medium; and after an appropriate preincubation period, an amino acid was added to the suspension. At a fixed time interval, samples of the suspension were removed for ammonia determinations. Ammonia was quantified by a modification of the method of Archibald which allowed a control and sample specimen to be run simultaneously. The initial rate of formation of ammonia from glutamine was very rapid. After thirty minutes, the rate slowed. The initial fast rate could be eliminated by preincubation with glutamic acid. In balance studies on ammonia formation from glutamine, more ammonia was produced than could be accounted for by deamidation alone, indicating that the amino as well as the amide nitrogen is utilized. However, with glutamic acid as substrate, formation of ammonia in this preparation was poor. Since filtered glutamic acid at normal plasma levels is totally reabsorbed by the kidney in vivo, it was felt that glutamic acid could enter the tubules. Glutaminase and glutamic dehydrogenase are mitochondrial enzymes. Further studies showed that glutamic acid penetrated mitochondria poorly while glutamine entered readily. 4-(Iodoacetamido)-Salicylic acid, a glutamic dehydrogenase inhibitor, suppressed ammonia formation from glutamine as well as alanine, glycine and glutamic acid. Supported by research grants from the National Heart Institute, National Institutes of Health (HE 00814) and the Life Insurance Medical Research Fund.

SITE OF MAXIMAL EXPIRATORY FLOW LIMITATION IN CATS. N.B. Pride*, P.D. Graf* and J.A. Nadel. Cardiovasc. Res. Inst., Univ. of Calif. Med.Center, San Francisco, Calif.

In 11 anesthetized and tracheotomized cats, we inflated the lungs to a transpulmonary pressure (P_{TP}) of 10 cm H_2O; then we suddenly exposed the trachea to a large tank at a variable subatmospheric pressure and we measured expiratory airflow ($\dot{V}_E$). From these records we constructed isovolume P_{TP}-$\dot{V}_E$ curves. Maximal $\dot{V}_E$ was usually achieved at a P_{TP} of less than 30 cmH_2O; with further increases in P_{TP}, $\dot{V}$ did not change significantly. We measured lateral bronchial pressure during these expirations with a catheter in the bronchial lumen; when the catheter was introduced 1.5 cm beyond the carina (into lobar or segmental bronchi) a point was reached where the difference between lateral bronchial and pleural pressures did not decrease below 0 cm H_2O, even at a P_{TP} of 60-70 cm H_2O (equal pressure point of Mead et al. Fed. Proc. 23:155, 1964). Therefore, in these experiments, at a high P_{TP} most of the resistive pressure drop was between segmental bronchi and trachea. Electrical stimulation of the peripheral ends of both cut cervical vagosympathetic nerves increased resistance to airflow and decreased maximal $\dot{V}_E$; there was either no change or a decrease in the P_{TP} required to achieve maximum $\dot{V}_E$. During vagal stimulation the equal pressure point was nearer the alveolus than in the control state in 8 of 11 cats. These results suggest that in the control state the area of maximal flow limitation was in the lobar or segmental bronchi and that increased bronchomotor tone modified the position of the flow limiting segment. (Supported in part by USPHS grant HE-06285.)

THE EFFECT OF THE CARDIAC SYMPATHETIC NERVES ON THE CONTRACTION SEQUENCE OF THE VENTRICULAR INFLOW AND OUTFLOW TRACTS. D.V. Priola*, C.E. Osadjan* and W.C. Randall, Loyola University, Chicago.

A previous report demonstrated that the inflow and outflow tracts of the left ventricle function as independent chambers during systole (Fed. Proc. 23: 463, 1964). Anatomical studies indicate that the two tracts become separated during contraction by the apposition of the anterior and posterior papillary muscles and by the dependent leaflets of the mitral valve. In early systole, the pressure elevation appears in the inflow tract 4 - 22 msec before it can be detected in the outflow tract. The inflow and outflow tracts of both the right and left ventricles of the canine heart were cannulated and measurements made from the beginning of the R wave of the ECG to the point of initial systolic pressure elevation in each of the four tracts. In the control state, the first to show pressure elevation was the left ventricular inflow tract (LV_I) followed a few msec later by pressure rise in the left ventricular outflow tract (LV_O). About 20 msec after the pressure elevation in LV_O, the first pressure rise was detected in the right ventricular inflow tract (RV_I) followed about 20 msec later by the initial pressure rise in the right ventricular outflow tract (RV_O). In both ventricles, therefore, the pressure elevation in the inflow tract preceded that in the corresponding outflow tract by 4 - 25 msec with the sequence being LV_I-LV_O-RV_I-RV_O. Stimulation of the cardiac sympathetic nerves resulted in a decrease of the interval from the R wave of the ECG to the initial pressure rise in all tracts. This may be interpreted to indicate a general increase in velocity of impulse conduction throughout both ventricles. However, the excitation intervals of the outflow tracts decreased more than the corresponding intervals for the inflow tracts and all tracts contracted more synchronously. (Supported by grant no. HE 08682-01 from NIH.)

AUTOPROTHROMBIN C FORMATION WITH CATHEPSIN B AND LIPID PROCOAGULANTS. Geraldine M. Purcell* and Marion I. Barnhart. Wayne State Univ. School of Med., Detroit, Mich.

Cathepsin, the proteolytic enzyme group in cells, may be released to the circulation by normal or pathologic destruction of cells. The effect of such cellular enzymes on blood coagulation becomes an important consideration. In this study the activation of prothrombin by cathepsin B was examined. Previous work described the limited hydrolysis of prothrombin to prothrombin-R (Am. J. Physiol. 198: 899, 1960). Thrombin did not appear during this activation at pH 7.9 with cathepsin B. Conditions have now been found for the more complete activation of prothrombin with cathepsin B and added lipids. Accelerator globulin was a necessary requirement in this system. About 90% of the theoretically possible autoprothrombin C appeared with cathepsin B in the presence of cephalin and platelet factor 3 at pH 7.9. Only 20% of the theoretical thrombin evolved during the reaction. In contrast, cathepsin C under similar conditions produced full yields of both autoprothrombin C and thrombin. Clearly cathepsins can promote thrombus formation which may or may not be of physiologic advantage. (Aided by NIH grant HE 03447).

EVOKED INTERHEMISPHERIC RESPONSES. S.J. Putnam* J.W. Manning and D. Megirian. Departments of Anatomy and Physiology, Emory University, Atlanta, Ga.

In the opossum Didelphis virginiana, bipolar electrical stimulation of the neocortical surface of one cerebral hemisphere evoked an interhemispheric early response (IER) recorded monopolarly from the homotopic point on the opposite neocortical surface. Homotopical recordings demonstrated that the slow wave evoked potential was biphasic (positive-negative), had a latency of 4 - 10 msec. and was present over the entire neocortical surface. Transection of the anterior commissure in the sagittal plane abolishes the IER. In addition to the IER an interhemispheric delayed response (IDR) was evoked also. Homotopical recordings demonstrated that this slow wave evoked potential was triphasic (negative-positive-negative) and had a latency of 40 - 50 msec. In the visual cortex the IDR was small and sometimes absent. Compared with the IER, the IDR was labile and the level of general anesthesia critical. Two and one-half minutes after the onset of asphyxia the IDR was abolished, whereas the IER was only beginning to decrease in amplitude. Small doses of pentobarbital abolished the IDR in two minutes but the IER was only slightly affected. Heterotopical recordings of the IDR unmasked completely its triphasic character and showed more diffuse neocortical representation than did the IER. (Supported by grants 5TI NB 5255 and 2B 5323 of the National Institute of Neurological Diseases and Blindness).

INCORPATION OF LABELED INORGANIC PHOSPHATE INTO THE NUCLEOTIDES OF DOG KIDNEY CORTEX. A. Quintanilla* and R.H. Kessler. Cornell University Medical College, New York, N.Y.

We have studied the incorporation of inorganic phosphate labeled with P^{32} into the adenosine compounds of dog kidney cortex. The labeled phosphate was injected into the aorta above the origin of the renal arteries and the kidneys removed at times ranging from 3 seconds to 30 minutes. The kidneys were frozen in liquid nitrogen within 1 second of removal from the animal, the cortex separated and homogenized in perchloric acid. AMP, ADP and ATP were separated by column chromatography and quantitated by ultraviolet spectrophotometry. Adenine/phosphate ratios were within 10% of the predicted values. The specific activities of the nucleotides were calculated and expressed as functions of the specific activity of the tissue extract. Our results showed, 1) the specific activity of ADP was 2/3 of that of ATP regardless of time, 2) the specific activity of AMP was low and increased slowly with time, 3) the specific activity of ATP relative to that of the extract, increased exponentially with time. By graphic analysis this function had a half-time of 21 seconds. Those results are consistent with the following conclusions. The rates of synthesis of ADP and ATP are rapid in the dog kidney cortex. The estimated turnover of these compounds is more rapid in the kidney cortex than in other tissues studied to date. The effects of in vitro inhibitors of oxidative metabolism in the above preparation are in progress and will be reported.

FOREARM METABOLISM IN STARVATION. David Rabinowitz* and Kenneth L. Zierler. Johns Hopkins Hosp. and Univ., Baltimore, Md.

Certain metabolic events occurring in forearm muscle and adipose tissue in 4 normal males were examined and compared 12 hours and again 66 hours after their last meal. Results were: (1) Despite a fall of 30% in arterial glucose concentration, glucose uptake by forearm remained unchanged. (2) Although there was no temporal trend in oxygen consumption, muscle lactate production doubled, becoming sufficient to account for all glucose taken up. (3) Free fatty acid (FFA) uptake by forearm muscle was increased sufficiently to account for all forearm oxygen consumption, FFA output from adipose tissue was also increased. (4) Plasma insulin levels fell almost to zero. Conclusions: (1) During prolonged food-free intervals, glucose uptake by muscle reaches its nadir early, and further glucose sparing is achieved by increasing recycling of lactate to the liver. Under these conditions, lactate production by total body muscle potentially can be the source of about one-third of basal hepatic glucose output. (2) Although plasma growth hormone (GH) concentration rises with starvation the metabolic pattern in starvation cannot be explained simply on this basis: effects of GH infusion to normals resemble starvation only with respect to FFA metabolism.

(Supported by MDAA, Inc., NIAMD (AM 00750, AM 05524, 2A-5232) and AHA.)

HIPPOCAMPAL EEG RHYTHMS AND THE ORIENTING REFLEX. M. Radulovački* and W. R. Adey. Dept. of Anatomy and Brain Research Institute, Univ. of California, Los Angeles.

Five cats with implanted electrodes in dorsal hippocampus were initially trained in a T-maze discrimination with a situational tone and with food reward on a visual cue. After this training was completed, the approach trials (40 daily) were randomly interspersed with equal numbers of trials in which approach was prevented, but reinforcing tone and visual cues were provided (orienting trials). Approach performance was characterized by 6 to 7 c/sec hippocampal theta trains, producing highly rhythmic computed averages. Orienting trials produced typical searching behavior, and crouching behind closed doors. Averages of hippocampal activity in these trials were smaller in amplitude, less regular and about 1.5 c/sec slower in dominant frequencies. Behavioral orienting reactions declined over 10-15 training days. A single dose of LSD-25 (70 µg/Kg) produced a sharp disinhibition of the orienting reflexes. Hippocampal theta wave trains during approach were markedly augmented for 3 to 10 days. Averages of orienting trials also showed increased amplitude and regularity, but at slower rates than in approach trials. Increased orienting behavior and concomitant hippocampal rhythm patterns persisted for as long as 20 days after LSD. Single doses of a psychotomimetic cyclohexamine (Cl-400) induced similar disinhibition of orienting reflexes, following an initial period of acute disorientation. Hippocampal electrical patterns were modified as with LSD, but persisted only for 3 to 5 days. It is concluded that hippocampal participation in orienting reflexes induces consistently different EEG patterns from those seen in discriminative behavior, and that these differences are exemplified by hallucinogenic and psychotomimetic agents which enhance orientation for extended periods after a single dose.

Blood and Urinary Levels of NSC 62512, Acetophenone, 2-dimethylamino-3', 4'-dihydroxy-, hydrochloride N. Rakieten, M.L. Rakieten* and M.V. Nadkarni*, South Shore Analytical & Research Lab., Islip, N.Y. & CCNSC Bethesda, Md.

Blood and urinary levels of NSC 62512 were determined as "Blood Sugar" following rapid I.V. dosages of 200 & 300 mg/kg to rats, 400 mg/kg I.V. rapidly to dogs and 400 & 800 mg/kg I.V. by slow infusion (S.I. 2-8 hrs.) to Rhesus monkeys. Rats: the "Blood Sugar" of rats treated with the drug were significantly higher than controls, 160±8 vs. 100±4.2 mg% ($P < .01$); liver glycogen was not significantly different ($P > 0.5$) 3.3±.56 g% vs. 3.98±.65 g%. The reducing fraction of the compound is not present in the blood 60 min. after 200 & 300 mg/kg. 100% excretion occurred at 6 hrs. In beagles 30 min. after 400 mg/kg I.V. the "Blood Sugars" were 280 & 300 mg% with normal valuesat 4 hrs.; at 2 hrs. 63% was recovered in the urine. In monkeys 800 mg/kg. (1.25 & 1.12 g/kg. I.V. S.I. for 6 hrs.) the "Blood Sugars" were at 2 hrs. 328 & 370 mg%, 4 hrs. 232 & 266 mg% and 6 hrs. 208 mg%, with 46.8% excreted at 6 hrs. Excretion following 400 & 800 mg/kg. I.V. (S.I. 4 hrs.) was: 4 hrs. 30-98% (17% 2 hrs.), 24 hrs. 50.2 & 59.8%; 800 mg/kg. I.V. (S.I. for 6 hrs.) 4 hrs. 30-98% (24 hrs. 60% single study). Compound NSC 62512 apparently is excreted rapidly in the three species of animals studied. No histopathology was noted in the islets of Langerhans in the rat, dog or monkey.

Done under USPHS Contract No. SA-43-ph-2389, CCNSC

MODE OF ACTION OF DIETARY FAT IN FACILITATING INTESTINAL ABSORPTION OF CHOLESTEROL. Alfred J. Rampone. Dept. of Physiology, Univ. of Oregon Med. School, Portland, Oregon.

Six-day balance studies in rats confirmed previous findings that the intestinal absorption of cholesterol is enhanced in the presence of certain dietary fats. The present study tests the hypothesis that the mode of action of fat is non-specific and related to its effects on gastrointestinal transit rate. Rats, surgically prepared with colostomies, were trained to eat their ground basal diet in one hour each day. They were then fed either a control diet consisting of the basal diet with added cholesterol (with traces of cholesterol -C^{14}) and polyethylene glycol or a series of test diets containing, in addition, known amounts of safflower seed oil or hydrogenated vegetable oil. From the time of feeding fecal pellets were collected at timed intervals and analyzed for C^{14} activity (alcohol-acetone soluble) and polyethylene glycol. The excretion rate of the non-absorbable polyethylene glycol served as a measure of transit rate. The C^{14} excretion rate expressed as a function of polyethylene glycol excretion rate was linear in all cases. One minus the slope constant of the line so obtained gave a measure of the percentage of dietary cholesterol absorbed. Compared to control values cholesterol absorption was increased when it was fed with the safflower seed oil test diet only, and this was always associated with a decrease in gastrointestinal transit rate. That the decrease in transit rate was the cause of the enhanced cholesterol absorption was suggested by additional experiments showing that the injection of atropine reduced transit rate and increased cholesterol absorption from control diets without added fat. (Supported by USPHS Research Grant AM-1389).

ANAEROBIC METABOLISM IN DOG KIDNEY IN VITRO. Howard M. Randall, Jr.* and Julius J. Cohen. Dept. of Physiology, University of Rochester, Rochester, N. Y.

Previous studies by Hunter (J.B.C. 177:361; 181:67,1949) showed that homogenates of kidney cortex and of liver form ATP anaerobically via a nonglycolytic, substrate-level oxidative phosphorylation. The sum of one such reaction is: α-ketoglutarate + oxaloacetate + ADP $\rightleftharpoons$ malate + succinate + CO_2 + ATP. Washed homogenates and slices prepared from renal cortex and medulla were incubated anaerobically with 10mM α-ketoglutarate and 30-40mM oxaloacetate. Rates of CO_2 production (manometric) were determined. Values of 10.1±1.1 (M±SE) μmoles CO_2/100 mg dry wt·hr were found for cortex homogenates in contrast to 1.1±0.3 for medulla. Similar differences were observed for slices. Cortical slices produced 16.7±1.0 μmoles of CO_2/100 mg dry wt·hr and medulla produced 1.1±1.1. These regional differences were substantiated by chemical balance studies based upon the equation above. Studies were done to determine the basis for these differences: activities of α-ketoglutaric dehydrogenase and succinic dehydrogenase were found to be similar in both cortex and medulla. However, medullary malic dehydrogenase activity was approximately 1/30 of cortical activity. Thus the smaller rate of this energy yielding reaction in medulla may be due, in part, to a low activity of malic dehydrogenase there. These observations point out a potential importance of the cortex in anaerobic CO_2 production, consistent with the high R.Q. of the kidney in vivo. Supported by U.S.P.H.S. A03602 and Life Insurance Medical Research Fund.

STUDIES OF HEMOGLOBIN RECONSTITUTED FROM α^A POLYPEPTIDE CHAINS AND HEMOGLOBIN H (β_4^A). Helen M. Ranney, Robin W. Briehl and Alan S. Jacobs (intr. by E.R. Jaffé). Dept's. of Medicine and Physiology, Albert Einstein College of Medicine, Bronx 61, New York.

An electrophoretic component found in solutions of normal human hemoglobin which had been allowed to stand at pH 4.7 or 11.1 for prolonged periods before neutralization has been characterized by peptide maps and by sedimentation equilibrium as α^A polypeptide chains. These α^A chains are largely monomeric and will combine with hemoglobin H at neutral pH to yield a tetramer, designated reconstituted A. Our studies have indicated that both subunits, α^A or β_4^A lack low oxygen affinity, evidence of heme-heme interaction, or Bohr effect; reconstitution of hemoglobin from the subunits restores at least partially all three of these parameters of hemoglobin function. These studies provide further evidence that the oxygenation function of normal hemoglobin is related to the presence of unlike polypeptide chains in the tetramer.

EFFECT OF SUBCLAVIAN ARTERY OCCLUSION ON CEREBRAL VENOUS AND VERTEBRAL ARTERY FLOWS. C. E. Rapela, C. B. Bush*, T. D. Franklin*, J. F. Toole and H. D. Green. Bowman Gray Sch. Med., Winston-Salem, N. C.

Cerebral outflow (CBF) from sagittal and straight sinuses (after occlusion of lateral sinuses) and right vertebral artery flow (RVF) were measured with e.m. meters; lateral pressures in both carotid arteries (CC) and iliac artery (systemic pressure-SP) were recorded. Clamping right subclavian between origin of right carotid and vertebral reversed RVF. Reversed RVF was decreased by clamping left vertebral (LV) and restored to slight forward flow by clamping CC and LV. With this procedure distal CC pressure fell and SP rose; distal CC pressure increased towards control level with the rise of SP. CBF remained unchanged with above procedures. CBF was reduced by clamping CC only when catheters were passed in both vertebral arteries as far cranially as possible (15-17 cm). Under this condition distal CC pressure did not rise with the increase in SP. Conclusion: Clamping larger arteries supplying the Circle of Willis fails to decrease CBF due to numerous collateral communications of the arterial system plus autoregulation of the cerebral arterioles. Disposition of vertebrals in relation to subclavian and carotid arteries allows reversal of vertebral flow when one subclavian is clamped between the vertebral and carotid; however, this reversal is not accompanied by decreased CBF (supratentorial structures) such as has been postulated in dogs under conditions equivalent to those in the "stealing" syndrome in patients with subclavian stenosis. Supported by N.I.H. HE-00487 and LIMRF.

Use of Dichromatic Earpiece Densitometry for Determination of Cardiac Output. J. H. Reed, Jr.* and E. H. Wood. Mayo Clinic, Mayo Foundation Rochester, Minnesota.

In situations which forbid direct arterial sampling such as space flight, estimation of cardiac output by ear densitometer may be justifiable. Compensation for changes in blood content and saturation recommend dichromatic densitometry (IRE Trans. BME 9:133, 1962). Simultaneous dilution curves by injection of 5 mg. indocyanine green into the superior vena cava of 5 healthy subjects at rest and exercise were recorded by a dichromatic ear densitometer, a conventional ear oximeter and a cuvette coupled to the radial artery. Simultaneous single and double scale operation was used (Medical Physics 3:163, 1960). Calibration of earpieces assumed linearity for extrapolation of the deflection at 90 seconds after injection on the basis of dye concentration estimated from hematocrits and spectrophotometry of plasma from simultaneous blood samples both from the radial artery and an upper arm vein. About 30% of monochromatic ear oximeter curves were unsatisfactory due to variations in blood content of the ear usually associated with respiration; these artifacts were absent in dichromatic earpiece curves. Using the cuvette as reference, cardiac output values gave no systematic variation when calibrated from arterial blood. The standard deviations of differences by ear oximeter was ±7.3 and by dichromatic ear densitometer was ±8.6%. When calibrated by venous blood, there was a systematic underestimation of 15% and standard deviations from cuvette were ±13.2 and ±11.2%, respectively. With exercise, oxygen consumption increased an average of 654 ml./min. (452-793) from resting values with concurrent rise in cardiac output of 5.3 (3.9-7.2) by cuvette and 5.7 (5.0-6.8) L./min. by dichromatic earpiece. It is concluded that dichromatic earpiece densitometry may be useful in situations where more reliable methods are impossible.(Research grants NsG-327, AF33(657)8899)

MICRORADIOGRAPHY OF THE PULMONARY ARTERIOLES, VENULES AND CAPILLARIES OF THE RABBIT. John T. Reeves, James E. Leathers* and Mervyn B. Quigley.* Departments of Medicine and Anatomy, College of Medicine, Department of Anatomy, College of Dentistry, Lexington, Kentucky.

Pulmonary vessels of excised rabbit lungs were injected with a suspension of barium sulfate in gelatin. Slices 50-100 μ thick were radiographed at 5 kv and 2 ma using high resolution spectroscopic plates. When these plates were viewed through a microscope, pulmonary arterioles, venules and capillaries were identified. Arterioles show relatively regular branching at right angles. The capillary bed fills from short (10-20 μ long), thin (10-15 μ in diameter) feeder vessels arising at right angles from arterioles. The alveolar capillary network freely communicates with networks of adjacent alveoli. Venous capillaries join in bulbous confluences which then join venules at acute angles. The capillary network between an arteriole and venule appears to span at least two alveoli. Pulmonary gas transport can be better understood with clear demonstrations of the microanatomy.

EFFECT OF 2, 4-DINITROPHENOL ON THE POTENTIAL DIFFERENCE, RESISTANCE AND H^+ RATE OF THE FROG GASTRIC MUCOSA. W. S. Rehm and Marian E. LeFevre*, University of Louisville, Louisville, Kentucky.

Gastric mucosae were mounted between chambers, some with Cl^- bathing solutions and some with Cl^- - free bathing solutions. The effect of 2, 4-dinitrophenol (DNP) was determined on the potential difference (PD), resistance and H^+ secretory rate. In Cl^- experiments, the H^+ rate was depressed to low levels without a marked decrease in the PD, and the PD did not vary linearly with the H^+ rate. Neither ATP (6mM) nor voltage-clamping (nutrient +100 millivolts) restored H^+ secretion. In the absence of DNP, ATP produced a decrease in the H^+ rate and PD, and an increase in resistance (effects were reversible). The PD is inverted in Cl^- - free solutions (nutrient is negative), and under these conditions the DNP produced a decrease in the H^+ rate which varied linearly with the decrease in the absolute magnitude of the PD. An analysis of this latter finding on the basis of the separate site theory of gastric HCl formation, revealed that during inhibition of H^+ secretion only the electrogenic H^+ mechanism is affected; the parameters of the return circuit within the mucosa are not changed. On the basis of the reasonable assumption that in Cl^- - free solutions, the resistance of the nutrient surface of the tubular cells is negligible, the slope of the PD vs I_H plot is equal to the resistance of the return circuit within the mucosa, and the resistance of the H^+ mechanism under these conditions can be calculated. In five experiments the resistance of the H^+ mechanism ranged from 571 to 1350 ohm cm^2. The emf (minus a constant factor) of the H^+ mechanism was also calculated, and it ranged from 33 to 56 mv. The H^+ inhibition by DNP in Cl^- - free preparations is due to a decrease in emf and/or an increase in the resistance of the H^+ mechanism. (NSF and NIH support)

CARDIOVASCULAR AND METABOLIC EFFECTS OF BRADYKININ IN THE UNANESTHETIZED DOG. Edward J. Reininger and Stanley Sinclair (intr. by E. Rosenberg). Dept. of Physiology, McGill University, Montreal, Canada.

The effects of infusing synthetic bradykinin at 0.8 µg/min/Kg (SBR 640, Sandoz Ltd.) were recorded in 6 trained unanesthetized dogs. Measurements were taken before and during the last portion of the infusion period which lasted 10 minutes. Infusions, measurements of blood pressure, collections of expired gas samples and successive dye dilution cardiac output measurements were effected without physical contact between the animal and the experimenter. The cardiovascular effects of bradykinin were: cardiac output increased 81%; heart rate increased 61%; stroke volume increased 12%; mean blood pressure remained unchanged; and peripheral resistance decreased 43%. The metabolic and respiratory effects were: breathing rate increased 16%; minute volume increased 21%; RQ increased 9%; O_2 consumption increased 19%; and heat production increased 21%. Control experiments were done in the same manner, in which saline containing a "placebo" (the bradykinin vehicle) was infused without significant effects. The decrease in peripheral resistance caused by bradykinin's vasodilating action is considered a major factor responsible for the augmentation in cardiac output.

Supported by a grant from the Quebec Heart Foundation.

Acute Effects of the Insecticide Endrin on Renal Function and Hemodynamics in Intact and Adrenalectomized Dogs. D. A. Reins* and L. B. Hinshaw. Physiol. Branch, Civil Aeromed. Res. Inst., Okla. City, Oklahoma.

These studies were designed to evaluate the separate effects of sympathetic neural control and adrenal discharge on changes in renal function and hemodynamics in acute endrin poisoning. Effects of chemical and surgical denervation of the renal pedicle and adrenergic blocking agents were studied in five intact and six adrenalectomized dogs. Systemic hypertension and bradycardia in response to endrin were not affected by adrenalectomy. Renal blood flow, glomerular filtration rate, and filtration fraction were relatively constant in adrenalectomized dogs but significantly decreased in intact animals. Effects of the adrenergic blocking drug phentolamine were less marked in the adrenalectomized animals. Data indicate that autoregulation, neural control, and circulating catecholamines are all factors in post-endrin renal vascular changes but the most consistent and dominant influence was circulating catecholamines.

THE EFFECTS OF ALDOSTERONE, DESOXYCORTICOSTERONE AND SODIUM DEFICIENCY ON BLOOD PRESSURE RESPONSES TO ANGIOTENSIN IN THE RAT. Bard C. Robert* and Gabor Kaley, Dept. of Pathology, New York University School of Medicine, N.Y.

Recent work suggests that pressor responses to angiotensin are decreased in man, sheep, dog, and rabbit in different experimental states associated with increased amounts of circulating aldosterone. Studies were carried out to ascertain similar responses in the rat. In addition, the sensitivity to angiotensin of rats treated with desoxycorticosterone acetate (DOCA) was compared to that of suitable controls. Treatment of rats with d—aldosterone in doses of 100 μg/kg subcutaneously, daily for 3 days or 20 μg/kg for four to seven weeks did not result in significant changes in blood pressure responses to individual injections or infusions of various doses of angiotensin. Similarly, sodium deficiency could not be correlated with changes in angiotensin responsiveness. In contrast, rats treated chronically with DOCA were found to have maximal pressor responses to angiotensin which significantly exceeded those of normal animals. The above data provide no evidence that aldosterone plays an active role in regulating vascular responsiveness to angiotensin in the rat (Supported by USPHS Grant HE-08191-02).

RENAL HANDLING OF WATER AND SOLUTES BY THE GECKO (Hemidactylus), THE HORNED TOAD (Phrynosoma cornutum) AND THE GALAPAGOS LIZARD (Tropidurus) IN RELATION TO NEPHRON ULTRASTRUCUTRE. John S. Roberts* and Bodil Schmidt-Nielsen. Dept. of Zool., Duke Univ., Durham, N. C.

In an effort to determine the significance of infolded cell membranes seen in many epithelia, we compared renal handling of water and solutes and nephron ultrastructure in the tropical gecko and its desert counterparts, the horned toad and Tropidurus. Renal adaptations to a land habitat in the form of low GFR, uric acid secretion and cloacal water reabsorption occur in each animal but the gecko is adapted to a more available water supply. Its urine stays hyposmotic to blood (osmolar U/P=0.65-0.8) regardless of P_{osm}, whereas urine of the desert lizards remains isosmotic. The gecko's GFR is normally two times higher and its inulin U/P=3.85, compared with 2.3 for the other species. In each species GFR rises during water loading but in the hydrated gecko a fractional decrease in filtrate reabsorption, presumably effected in the proximal tubule, leads to disproportionately high urine flows. Osmotic work involved in diluting urine in the gecko's distal tubule is performed by cells with contraluminal cytoplasmic extensions containing mitochondria. No extensions occur in distal cells of horned toad or Tropidurus, nor does the small mitochondrial population contact the plasma membrane. Up to 80% of the glomerular filtrate may be reabsorbed by the gecko's proximal tubule cells, whose thin lateral and basal extensions and abundant mitochondria contrast with the smooth surfaces and the sparse, randomly oriented mitochondria seen in the less active proximal cells of the desert species. The results have led to the hypothesis that infolded epithelial cell membranes in contact with mitochondria represent a morphological entity whose degree of development determines the solute reabsorptive capacity of the cell.
*Fellowships: NDEA, PHS. Research supported in part by NIH grants.

CORRECTION OF EXPERIMENTAL MITRAL AND TRICUSPID INSUFFICIENCY BY INVAGINATION OF THE AURICLE INTO THE VENTRICLE. Joseph T. Roberts. Cardiology Section, Veterans Administration Hospital and State University of New York at Buffalo, Buffalo, N. Y.

Mitral or tricuspid insufficiency is one of the most damaging of cardiac lesions, poorly controlled by any present methods except occasionally by being replaced with a prosthetic valve. The serious hemodynamic defects of experimental mitral insufficiency have been corrected by invaginating the auricle into the cavity of the ventricle. Mitral insufficiency was produced by cutting the valve leaflets or chordae tendineae with iridectomy scissors introduced through the auricle. After only a few heart beats, the left atrium, auricle and pulmonary veins became greatly dilated and pulsating. Usually if not relieved promptly death occurred soon after such injury. The distention of the pulmonary veins with regurgitation of blood from the left ventricle was corrected at once after invagination of the left ventricle into the cavity of the left ventricle. This was performed in the following steps: (1) tying the middle of a heavy (No.2) thread on the tip of the left auricular appendage; (2) passing the two ends of the thread on a large needle through the wall of the left auricle near 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 and implant it through the mitral valve orifice into the cavity of the left ventricle where it is anchored with a knot on the ventricle's wall. Similar benefit occurred with inverting the right auricle into the right ventricle to relieve tricuspid insufficiency. Dogs were used.

A HYDRODYNAMIC BASIS FOR "EXERCISE HYPEREMIA" IN A PASSIVE MODEL OF THE PERIPHERAL CIRCULATION. S. Rodbard. City of Hope Medical Center, Duarte, California

The complex blood flow patterns in exercising muscle have been attributed to active neurohumoral mechanisms. We have demonstrated similar flow patterns in a model of a capillary enclosed in an "endomysial capsule". An arterial pressure head produced flow through an "artery" which could be constricted by a screw clamp. The stream passed through either a soft-walled Penrose "capillary" or as "transudate" through a "permeable" rubber connection to the extravascular compartment. A permeable downstream connection permitted return of transudate to the capillary. The combined flow then entered a venous reservoir. "Permeabilities" were adjusted by screw clamps on the rubber connections. When downstream permeability was minimal, the system was at basal flow. In this condition the system exhibited autoregulation, and post occlusive and exercise hyperemias. The assumption was made that muscular contraction compressed the extravascular space and the capillary, reducing flow and expelling some "interstitial fluid" via the downstream connection. With "relaxation" and decompression, an immediate overshoot in flow occurred. The rate of return to basal flow was a direct function of upstream permeability. Flow increased to a plateau during a series of contractions, following which flow increased further, and then returned to resting values. The increase in flow was a function of the fall in intracapsular pressure which in turn was a function of "load". The response increased with arteriolar pressure; it was unaffected by moderate changes in venous pressure. The results suggest that the blood flow response to exercise may be a physical property of a system consisting of soft-walled permeable capillaries enclosed in endomysial capsules.

INTESTINAL AND SERUM ALKALINE PHOSPHATASE LEVELS IN THE RAT FOLLOWING IONIZING IRRATIATION. Leonard M. Rosenfeld* and M.H.F. Friedman, Dept. of Physiology, Jefferson Medical College.

Experiments were conducted on a cross-bred closed colony strain of Wistar rats. Radiations used were gamma rays from a Co^{60} source. With $LD_{50/30}$ dose of whole body irradiation of 725r, the intestinal weight was decreased by 30 per cent by the third day: This was due almost entirely to loss in mucosal layer integrity. Activity levels of intestinal alkaline phosphatase paralleled weight levels during the first post-irradiation week but in some respects the alterations from control levels were more extensive. Concurrent with the decrease in intestinal levels there was often increase in serum levels of intestinal alkaline phosphatase. Alterations in magnesium levels were found in both intestinal mucosa and serum, but these could not be correlated with changes in phosphatase activity. Several procedures were found which decreased the magnitude of post-irradiation changes in intestinal and serum alkaline phosphatase activity and magnesium concentrations.

AUGMENTATION OF VENTRICULAR PERFORMANCE AND OXYGEN CONSUMPTION BY REPETITIVE APPLICATION OF PAIRED ELECTRICAL STIMULI. John Ross, Jr., Edmund H. Sonnenblick, Gerard A. Kaiser*, Peter L. Frommer*, and Eugene Braunwald. Cardiology Branch, Natl. Heart Inst., Bethesda, Md.

As shown by Chardack, when a depolarizing stimulus is delivered to the ventricle immediately following its refractory period, little or no extrasystolic contraction occurs and repetitive application of paired stimuli to subsequent beats then permits control of heart rate. The present study examines the sustained augmentation of ventricular performance which accompanies paired stimulation and its effects on myocardial oxygen consumption ($M\dot{V}O_2$). In 27 experiments in 13 dogs in which mean aortic pressure (MAP) and stroke volumes (SV) were held constant by right heart bypass, a change from single to paired stimulation at identical contraction rates markedly increased left ventricular (LV) contractility, as evidenced by a fall of end-diastolic pressure (EDP), shortening of ejection time (Av.= -20%), increase of dp/dt (Av.=+145%), and elevation of aortic flow velocity (electromagnetic flowmeter) (Av.= +43%). In 16 experiments the SV of the LV was varied during single and paired stimulation. The curves relating LVEDP to stroke work, SV, and stroke power demonstrated improvement of LV performance during paired stimulation. Identical results were obtained after administration of reserpine or Nethalide. In 8 experiments $M\dot{V}O_2$ was determined during single and paired stimulation, SV, MAP, and heart rate being held constant. Paired stimulation always increased $M\dot{V}O_2$, (Av.= +35%). Despite this rise in $M\dot{V}O_2$, a reduction in the area under the systolic portion of the arterial pressure pulse (TTI) always accompanied the increased LV contraction velocity. These studies indicate that repetitive application of paired electrical stimuli induces a powerful and sustained positive inotropic influence on the mammalian ventricle, which is accompanied by a dissociation between MVO2 and the TTI.

EFFECT OF THE REPLACEMENT OF LITHIUM FOR SODIUM ON SECRETION IN THE IN VITRO PANCREAS. Stephen S. Rothman*, John G. Forte*, and Frank P. Brooks. Dept. of Physiol., Sch. of Med., Univ. of Penna., Phila., Pa.

Using the technique described by Rothman (Fed. Proc. 23: 439, 1964) the effects of sodium impoverishment on pancreatic electrolyte secretion were studied in vitro by replacing 118 mM of NaCl in a HCO_3^-/CO_2 buffered bathing solution with LiCl two hours after mounting. When flow ceased the normal buffered solution was returned to the chamber. The replacement of sodium by lithium in the bathing solution rapidly produced a profound depression and eventual cessation of sodium, potassium, bicarbonate, and chloride secretion. Lithium at this concentration cannot replace sodium in the NaCl and $NaHCO_3$ secreting mechanism of the pancreas. Recovery of secretory output occurred when the lithium containing medium was removed. These data suggest that sodium moves transcellularly in the production of both NaCl and $NaHCO_3$. As in the kidney, lithium cannot replace sodium in the movement of bicarbonate. In control studies no potential difference was detected between the bathing media and the collecting duct. This finding need not apply to cellular sites of secretion since intratubular resistance may be very high in relation to transtubular resistance. (Supported by USPHS Grant ST1-DE1-07 and a Pennsylvania Plan Fellowship.)

Alteration of Hepatic Clearance of Indocyanine Green During Exercise and Thermal Stress. L.B. Rowell, J.R. Blackmon, R.H. Martin, J.A. Mazzarella, R.A. Bruce (intr. by E.J. Masoro) Dept. Med. (Cardiology) U. of Wash., Sch. Med., Seattle.

During exercise in upright man, hepatic clearance of indocyanine green (ICG) and estimated hepatic blood flow (EHBF) are inversely proportional to percentage of maximal O_2 intake (max VO_2) ($r = -0.89$, Rowell, et al, JCI, Aug., 1964). Effects of competitive thermal and exercise stresses upon redistribution of EHBF have been studied in 9 men during work (requiring from 45 to 91% of max VO_2) at 110°F, 30-50% relative humidity (RH) and compared with results at 78°, 34-50% RH. Neither submaximal nor max $\dot{V}O_2$ were altered in most subjects, but heart rates were faster, work duration shorter and hepatic clearance of ICG more prolonged during work in the heat. Rectal temperatures were higher at rest and increased slightly more during work at 110°. Only at the highest submaximal work loads at 110° was blood lactic acid concentration raised above 78° control values. An exceptional individual showed no greater prolongation of hepatic ICG clearance and higher rectal temperatures and blood lactates during work in the heat. Dehydration and hypovolemia were minimized by salt and water intake. Although greater tachycardia and greater reduction in hepatic clearance of ICG suggested circulatory collapse, the obvious reduction in total work capacity was not accounted for by the variables studied. (Supported by Wash. State Heart Assn. and USPHS Grant HE-00908-14.)

CEREBRAL ISCHEMIA ON MOTOR AND CARDIAC CONDITIONAL REFLEXES. Fred Royer, James Reus and W. H. Gantt. VA Hosp., Perry Point, Md. and Pavlovian Lab., Baltimore.

Clinical cases of occlusion of both carotid arteries show little or no cerebral symptoms unless there is also blocking of the Circle of Willis or cerebral arteries (Wiener and Berry). Previous experimental reports of cerebral ischemia produced by compression of vessels indicated impairment of motor conditional reflexes (Gantt and H. Kabat, Andreyev, Angyan et al.). The work reported here differs from the latter in that the reduction of blood supply was only temporary and that we included the cardiac conditional reflexes not reported in the other experiments. Our work reported here shows that partial temporary reduction of the cerebral blood supply through the total occlusion of both externalized common carotids had no effect on the motor conditional reflexes. The effect on the cardiac conditional reflexes was not parallel to that of the motor. In general, the cardiac positive conditional reflex (CS+) was increased with carotid compression, and the effect on the cardiac inhibitory conditional reflex (CR-) was elevated in one dog and unaffected in the other. Our experiments show that there is 1) a difference in sensitivity to occlusion of the carotids of the motor cr and of the cardiac cr and that 2) the vertebral cerebral blood supply of the dog is sufficient for motor performance measured by the crs. On the other hand the cardiac crs may be somewhat impaired through blocking of the carotids.

EFFECT OF PROLONGED HYPOTHERMIA INDUCED BY THE EXTRACORPOREAL METHOD ON THE HEART IN DOGS. Clem Russ and John Lee*. Dept. of Physiology, Albert Einstein Medical Center, Philadelphia, Penna.

Many of the hazards of immersion hypothermia are apparently circumvented by "core cooling" in which the kidney, heart, brain and liver are cooled first. Consequently, "core cooling" of short duration appears to have an advantage over immersion hypothermia since it overcomes a considerable delay in central temperature changes encountered during peripheral cooling. The present study was undertaken to determine the effect of prolonged hypothermia, induced by "core cooling" on myocardial metabolism and function. Results indicate a relatively profound reduction of cardiodynamics with moderate depression in myocardial metabolism.

Pleural Pressures in Dogs in Supine and Prone Body Positions Studied without Thoracotomy. W. Rutishauser*, N. Banchero*, A. G. Tsakiris*, and E. H. Wood. Mayo Clinic, Mayo Foundation, Rochester, Minn.

Intrapleural pressures were measured simultaneously by saline-filled catheters from 2 to 5 different sites in the potential right pleural space of 9 anesthetized (morphine-pentobarbital) dogs while the animals were supported in the supine and prone positions by means of molded half-body casts. Radio-opaque teflon catheters (I.D. and O.D., 0.7 and 1.3 mm., respectively) inserted percutaneously while connected to P23D Statham gauges were used. Intrapleural tips of the catheters were placed approximately at heart level in the cephalad-caudad dimension at ventral (retrosternal) and dorsal (paravertebral) sites in the thorax and care taken to avoid contact between catheters within the chest. The site of each catheter tip was measured from biplane x-rays taken in each position. The average vertical distance between the dorsal and ventral catheter tips was 10.6 (S.E. of Mean = $\pm$0.3) cm. In the supine position, mean end-expiratory pressure at the superior (ventral) catheter tip was -11.9 ($\pm$0.7) cm. H_2O as compared to -5.0 ($\pm$0.5) cm. H_2O at the dependent (dorsal) site giving an average gradient of 0.64 ($\pm$0.04) cm. H_2O/cm. vertical distance. The respective values in the prone position were: -9.0 ($\pm$0.6) cm. H_2O superior (dorsal)site; +0.7 ($\pm$0.5) cm. H_2O dependent (ventral) site; gradient: 0.91 ($\pm$0.05) cm. H_2O/cm. vertical distance. When two pairs of catheters were manipulated to contiguous dorsal and ventral positions, closely similar pressures were obtained and the vertical pressure gradient was followed during step-wise withdrawal of one of each pair towards mid-chest level. The slightly positive value for retrosternal pleural pressure and the greater dorsal-ventral gradient, when in the prone position, may be due to the weight of the heart. (Supported in part by research grants: NIH H-3532, AHA CI 10, AF 33(657)-8899 and NASA NsG-327.)

EFFECT OF REMOVAL OF POTASSIUM FROM Cl^-- FREE BATHING SOLUTIONS ON THE FROG'S STOMACH. J. R. Rutledge*, T. L. Davis*, D. C. Keesee*, F. J. Bajandas*, and W. S. Rehm. University of Louisville, Louisville, Ky.

Gastric mucosae were mounted between chambers with $SO_4^=$ Ringer solution (4 mM K^+) on the nutrient side and a $SO_4^=$ solution (no K^+) on the secretory side (sulfate replacing chloride). The PD, resistance and H^+ rate were measured, the latter with a pH stat method. With 4 K^+ in the nutrient solution the average values for the PD, resistance and H^+ rate were -18 mv (SD± 3.7) (minus means nutrient negative), 488 ohm cm^2 (SD± 114) and 0.8 μEq $H^+ hr^{-1} cm^{-2}$ (SD± 0.24). With the removal of K^+ from the nutrient solution the H^+ secretion decreased to zero and the PD and resistance increased to average steady state values of +5.1 mv (SD± 3.9) and 903 ohm cm^2 (SD± 404). The magnitude of this PD was significantly different from zero ($P < 0.02$) and decreased to about zero with anoxia. With readmission of O_2 the PD rapidly increased to an average of +8.8 mv (SD± 5.9) and then decreased to approximately the level before anoxia. The resistance did not increase significantly with anoxia ($P > 0.3$). The inhibition of H^+ secretion was not reversed by sending current from the nutrient to secretory sides. Control and experimental mucosae were analysed for Na^+ and K^+. The average control Na^+ and K^+ were 88.1 mEq/kg tissue H_2O (SD± 13.9) and 0.218 μEq/mgm dry wt., (SD± .032). When H^+ secretion stopped the average values were Na^+ 95.1 (SD± 6.8) and K^+ 0.202 (SD± .022). These findings are further evidence that the H^+ transport mechanism is electrogenic and are compatible with the concept that the K^+ in the tissue is compartmentilized with little free K^+ in the cytoplasm and that the free K^+ in the cytoplasm decreases to zero when the K^+ is removed from the bathing solutions. (NSF and NIH support)

LEFT VENTRICULAR EJECTION: EFFECTS OF SPONTANEOUS CHANGES IN SITE OF VENTRICULAR PACEMAKER. H.D. Ruttenberg*, L.J. Zornes*, N.W. Watson*, and R.L. Van Citters*. (Intro. by O.A. Smith Jr.) Dept. of Physiology & Biophysics, Univ. of Wash. Sch. of Med., Seattle, Washington.

Transducers were implanted for measurement of flow velocity (F) and pressure in the ascending aorta and left ventricle diameter in dogs with permanent complete A-V block. In addition, a pacemaker electrode was installed on the anterolateral aspect of the left ventricular (LV) wall. After a post-surgical period of 2-8 weeks, prolonged continuous tape recordings were made of the aforementioned variables and ECG in the unanesthetized dogs. Although a dominant idioventricular pacemaker (I.P.) was established in each animal, spontaneous alternations in the site of ventricular activation frequently occurred under resting conditions. Significant hemodynamic adaptions took place with each change in pacemaker site. In instances in which ventricular rate varied less than 2/min. the aortic pressure remained constant, dP/dt decreased by as much as 33%. At the same time, dF/dt (acceleration) diminished as much as 25% while peak aortic flow velocity, stroke volume, stroke power and cardiac output decreased only 8-12%. When the site of I.P. returned to the original focus, the values of these hemodynamic variables returned to the previous levels. Similar changes in cardiovascular parameters occurred when the original ventricular focus was shifted by an external pacemaker operated at or near the same rate. The site of ventricular pacemaker is thus an important determinant of ventricular performance and especially of the force of ventricular ejection.

(Supported by AHA Grant #60-G-98 and PHS Grant #HE-08433).

EFFECT OF 2-DEOXY GLUCOSE ON ATP CONTENT OF FROG GASTRIC MUCOSA. G. Sachs*, and B. I. Hirschowitz. Division of Gastroenterology, Dept. of Medicine, University of Ala. Med. Center, Birmingham, Ala.

In view of the suggestion that 2-deoxy-D-glucose (2-DG) acts by reduction of ATP levels, and our findings that 2-DG inhibits acid secretion and chloride transport in the in vitro gastric mucosa within 5 minutes at 10^{-2} M, ATP levels were estimated in control and 2-DG treated frog mucosae. Stripped mucosal sections were incubated for 30 minutes in frog Ringer's solution, gassed with 95% O_2 and 5% CO_2, with or without 2×10^{-2} M 2-DG. The membrane was removed, homogenized in 0.25 M sucrose, 0.1 M Tris at pH 7.4, the protein precipitated by rapid heating and the filtrate rapidly chilled to 0° C. Duplicate aliquots were assayed in a Beckman DU spectrophotometer for ATP using the luciferin-luciferase assay system. Control standard curves were run with each experiment. Protein was assayed by the Lowry method. In 5 experiments control values were $1.5 \pm 0.3 \times 10^{-5}$ μM/mg protein and with 2-DG $1.8 \pm 0.4 \times 10^{-5}$ μM/mg protein. These results do not confirm that 2-DG acts by lowering of ATP levels, and also argues against the suggestion that H^+ secretion is directly dependent on mucosal ATP concentration.

THE SITE OF PULMONARY VASOMOTOR ACTIVITY DURING HYPOXIA OR SEROTONIN ADMINISTRATION. Marvin A. Sackner*, Donald H. Will*, and Arthur B. DuBois, Dept. Physiol., Grad. Sch. Med., Univ. of Pa., Phila., Pa.

The object of this study was to separate pulmonary arterial and arteriolar constriction from constriction elsewhere in the pulmonary circulation, i.e. the capillaries and veins. Measurements included pulmonary arterial (P_{PA}) and left atrial (P_{LA}) pressures, pulmonary arterial transit time for ether (pulmonary artery to capillaries) and indicator dilution estimations of pulmonary vascular transit time (PA to LA) and pulmonary blood flow ($\dot{Q}_P$). Pulmonary arterial blood volume (V_{PA}) and pulmonary capillary plus venous blood volume($V_C + P_V$) were calculated from the product of transit time and $\dot{Q}_P$. Dogs were given 7 to 11% O_2 in N_2 to breathe or infused with serotonin 82 to 500 γ/min. In 8 dogs, hypoxia produced a 56% increase in pulmonary vascular resistance (R_P); $\dot{Q}_P$ and P_{LA} were unchanged, P_{PA} rose 12.1 mm Hg ($p<.001$), V_{PA} fell from 30 to 23 ml ($p<.001$) and $V_C + P_V$ rose from 88 to 104 ml ($p<.005$). We concluded that there had been active constriction of the whole pulmonary arterial tree since constriction of the arterioles alone could not account for the volume change. Further, dilatation of the capillary plus venous side occurred. In 4 dogs, hypoxia produce a 17% decrease in R_P; $\dot{Q}_P$ rose from 1.79 to 3.30 l/min ($p<.025$), P_{PA} rose 10.4 mm Hg ($p<.01$) and V_{PA} rose from 29 to 42 ml ($p<.02$). These results suggested that vasodilatation of the pulmonary arterial tree occurred in conjunction with increased blood flow. Serotonin administered to 5 dogs produced an 82% increase of R_P, no change in $\dot{Q}_P$ and P_{LA} and a rise of 17.5 mm Hg in P_{PA} ($p<.005$). Active pulmonary arterial constriction was demonstrated by the finding of a fall in V_{PA} from 31 to 22 ml ($p<.001$). Our study indicates that significant vasomotor activity is present throughout the pulmonary arterial tree.

EFFECTS OF "GLYCEMIC STATES" ON THE TOXICITY OF COMPOUND 48/80. P.J. Sacra* and V.W. Adamkiewicz. Department of Physiology, Université de Montréal, Canada.

The toxic action of histamine liberator 48/80 depends on the "glycemic state" of rats. In normoglycemic rats (glycemia = 100 - 120mg.%) the LD50 of 48/80 is 4.5 (3.9 - 5.2) mg./kg., and the survival time 57 ± 1.7 min. In hyperglycemic rats pretreated with 60 mmol./kg. glucose orally (glycemia = 170 - 190 mg. %) LD50 is decreased 1.3 - 2.0 times, and survival time is prolonged by 30 ± 2.1 min. In hypoglycemic rats pretreated with 20 units insulin - Zn/kg. s.c. (Glycemia = 60 - 80 mg. %) an opposite effect is produced: LD_{50} increases 3.1 - 5.0 times, and survival time decreases by 34 ± 1.6 min. In the three groups of rats plasma histamine levels at 15 min. after 4.5mg./kg. of 48/80 (which is the LD50 of normoglycemic rats) are similar: 1.37 - 1.58 microg./ml. But mast cell disruption is inhibited 25% in glucose treated rats. "Hyperglycemic state" inhibits, "hypoglycemic state" potentiates the toxicity of 48/80 in rats. (Grants: A-184 U.S. Department of Health, Education and Welfare; MA-640 Medical Research Council of Canada.)

LUTEINIZING HORMONE CONTENT OF THE PITUITARY GLAND FOLLOWING INJECTION OF BRAIN LIPIDS. J. A. Santolucito, North Carolina State of the University of North Carolina at Raleigh.

We have previously reported that chloroform:methanol lipid-extracts of hypothalamic tissue chronically injected into pregnant rats resulted in increased embryo mortality. Subsequently, it has been determined that this effect is obtained with extracts from the anterior hypothalamus but not from the posterior hypothalamus or cerebral cortex. In addition, anterior hypothalamic lipids delayed the age at vaginal opening when injected into immature female rats. These results suggested the possibility that active substances are present in the anterior hypothalamus which interfere with the synthesis or release of pituitary gonadotrophins. Consequently, ovarian ascorbic acid assays for LH were made of pituitaries from 28-day old female rats sacrificed 96 hrs following a single SubQ. injection of 30 mg of brain lipids. Pituitaries from animals treated with anterior hypothalamic lipids contained LH equivalent to 6.4 ug standard (NIH-LH-S-1 ovine) preparation/mg dry weight while those from animals treated with sesame oil, medulla, cerebral cortex, and posterior hypothalamus contained LH equivalent to 4.8, 4.2, 4.1, and 3.8 ug standard/mg dry weight respectively. There were no differences between the weights of reproductive tracts, adrenals or body weights from animals treated with the various lipids. It seems probable that the increased content of pituitary LH in animals treated with anterior hypothalamic lipids results from a decreased gland output. Whether or not the effect is general, affecting all three gonadotrophins, remains to be seen. (Supported by USPH Grant AM-03790).

LEUKOCYTOTIC EFFECT OF HEPARIN AND HEPARINOIDS. S. Sasaki (intro. by L.B. Jaques) Dept. of Physiology & Pharmacology, Univ. of Saskatchewan, Saskatoon, Canada.

Leukocytosis was produced in rats on administration of various heparinoids with different molecular size, shape and degree of esterification. Dextran sulfate and heparin caused approximately the same degree of leukocytosis in rats after subcutaneous or intraperitoneal injections, with maximal effect 3 hours after injection. There is a linear relation between log (dose) and the degree of leukocytosis, up to a limiting value, which depends on the molecular weight of the heparinoid. The degree of leukocytosis was proportional to the sulfur content, for a series of compounds prepared from the same dextran. The leukocytotic effect of heparinoid was completely neutralized by the amount of protamine which combines with heparinoid in vitro. Dextran and sucrose had no leukocytotic effect. It is concluded that the leukocytosis is chiefly caused by the presence of sulfate groups in the heparinoid. In rats, injection of heparinoid caused no change in red cell count and platelet count. Hydrocortisone has a leukopenic effect. When hydrocortisone and heparinoid were injected at the same time, antagonism was observed between the two, as reported by Paluska and Hamilton (Am. J. Physiol. 204, 1103, 1963). DNA was determined in tissues of injected rats. As there was an increase in DNA content of lung and spleen, it is unlikely that the leukocytosis was caused by the mobilization of leukocytes stored in these organs.

EFFECT OF ENVIRONMENTAL AND DRUG INDUCED CHANGES IN BODY TEMPERATURE ON POSITIVELY ACCELERATED MICE. C. L. Scheckel and P. Dahlen (intr. by W. B. Schallek). Hoffmann-La Roche Inc., Nutley, N. J.

Groups of male, CF-1 mice were individually placed in the tubes of a refrigerated centrifuge, with heads toward the axis of rotation, and exposed to a constant environmental temperature (ET) for 15 min. following which they were rotated at a fixed rpm for 56 sec. ET (2 to 23°C) and rpm (200 to 2000) were varied from test to test. All drug treated mice were tested at 600 rpm at an ET of 23°C (95xG). At 23°C all nondrugged mice survived rotation at 200 rpm while only 2.7% survived after 600 rpm. Decreasing ET to 2°C increased survival to 83% in mice rotated at 600 rpm, and 28% survived rotation at 2000 rpm at this temperature. Exposure of nondrugged mice to an ET of 2°C for 15 min. decreased body temperature (measured rectally) approximately 7°C. Injection of chlorpromazine (5.0 mg/kg, i.p.) 45 min. before rotation decreased body temperature 3 to 6°C below normal and increased survival 69% (range: 50-83%) in mice rotated at 600 rpm in a 23°C environment. Chlorpromazine-induced hypothermia, therefore, prevented death due to acceleration to about the same extent as the environmentally induced hypothermia. LSD (0.1 mg/kg, i.m.) injected 15 min. before rotation increased body temperature slightly (0.5 to 1°C) and did not increase survival rates at 600 rpm and 23°C. When mice were treated with both chlorpromazine (injected 45 min. before rotation) and LSD (15 min. before rotation) the typical hypothermic effect of chlorpromazine did not occur, and the lethal effects of acceleration were not significantly prevented. The results suggest that death due to positive acceleration may be prevented when body temperature is reduced by either environmental or pharmacologic means.

THE EFFECT OF CONTINUOUS POSTEXTRASYSTOLIC POTENTIATION ON THE ACUTELY FAILED DOG HEART: B.J. Scherlag*, B.K. Yeh* and P.F. Cranefield, Dept. of Pharmacology, College of P&S., New York, N.Y.

The purpose of this study was to investigate the possible applications of postextrasystolic potentiation of cardiac contraction to practical physiologic situations. Dogs (12-20 kg) were anesthetized with sodium pentobarbital. The right external jugular and left carotid artery were cannulated and intraventricular pressures recorded via Statham Pressure Transducers. In some experiments the chest was opened by a mid-sternal incision. An acrylic plaque electrode was sutured onto the epicardial surface of the left ventricle for driving and for introducing electrical extrasystoles. The sinus node was crushed and the ventricles driven at rates between 60-120 per minute. There was no appreciable difference in the degree of potentiation in this frequency range. In other experiments, with no thoracotomy, driving leads were inserted into the left ventricle through the left lateral thoracic wall. The following results were obtained: 1. Postextrasystolic potentiation of contraction was maintained continuously for three or more hours with little or no decrease in peak developed ventricular pressures. 2. Those animals whose hearts were acutely failed by pulmonary artery constriction and/or administration of pronethalol (5 mg/kg) showed a much greater degree of potentiation of developed pressures and rate of rise of ventricular pressure than during control runs; In addition, marked improvement of systolic and end-diastolic pressures was evident. Indeed, circulatory collapse was prevented by the continuous application of electrical extrasystoles which showed practically no mechanical counterpart in the pressure recordings.

(Supported by a grant from the American Heart Association).

PRESSURES IN THE GASTROESOPHAGEAL SPHINCTER DURING DEEP INSPIRATION AND EXPIRATION: Jerry F. Schlegel and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Patients are requested to hold their breath at the end of maximal inspiration or expiration during roentgenologic examination of the esophagus to prevent radiopaque material from passing through the hiatal region. A study was done in healthy human beings to determine whether increased pressure within the hiatal region is associated with the temporary obstruction. Tiny pressure detectors were withdrawn through the gastroesophageal junction while the subjects breathed normally and while the breath was held at the end of maximal inspiration and expiration. At the end of deep inspiration, mean pressures as measured by water-filled open-tip detectors were significantly less than during normal breathing; at the end of forced expiration, they were not different. Using 5 by 5 mm.-balloons as detectors, mean pressures at the end of maximal inspiration and expiration were not significantly different from those encountered during quiet breathing. Pressures were significantly greater, however, with the breath held at the end of deep expiration than at the end of deep inspiration. The length of the zone of elevated pressure was shortened when the breath was held in the maximal positions. The study indicates that the obstruction to the passage of radiopaque material at the hiatus during deep inspiration or expiration is not due to an increase in the resting pressures in the gastroesophageal sphincter. (Supported in part by NIH Grant A-2015.)

THE OXYGEN DEBT IN AEROBIC WORK. E. G. Schneider*, S. Robinson, and J. Newton*. Anatomy-Physiology Dept., Indiana University, Bloomington, Indiana.

The effect of varying the duration of aerobic work on the amount of the oxygen debt was determined in two trained distance runners and one untrained subject. For each experiment the subject's oxygen consumption was determined at frequent intervals during work followed by 15 to 30 minutes of recovery. In the experiments the subjects worked at rates of 5.6 km/hr up a 9% grade, 10.3 km/hr on the level, and 14.5 km/hr on the level. Runs of 14, 8, and 3 minutes and the recoveries following them were performed in this order on the same afternoon with body temperature being essentially the same during the recoveries. The 25-minute runs were all done on separate days. In a typical trained subject working at 5.6 km/hr up a 9% grade oxygen debts of 1.3, 1.4, 1.3, and 1.3 liters were found following 3, 8, 14, and 25 minutes of work, respectively. Corresponding oxygen debts following the work experiments at 10.3 km/hr were 1.6, 1.6, 1.8, and 1.9 liters. Working at 14.5 km/hr the oxygen debts averaged 2.5 liters with a range of 2.0 - 2.7 liters. The lactate levels in venous blood of this subject during recovery were unchanged from the basal value in the 5.6 km/hr and 10.3 km/hr work rates. In the 14.5 km/hr work rate the blood lactate rose an average of 7 mg% above the basal blood lactate value. The data show that the oxygen debt reached and maintained an essentially constant value by 3 minutes of aerobic work. (Supported by National Aeronautic and Space Administration Grant NSG-408.)

THE EFFECTS OF HYPOTHERMIA ON THE DISAPPEARANCE OF ETHANOL FROM ARTERIAL BLOOD. E. Schönbaum*, D. C. MacGregor*, G. Hetenyi, Jr. and W. G. Bigelow*. Depts. of Pharmacology, Surgery and Physiology, Univ. of Toronto.

Normothermic and hypothermic dogs were given ethanol (E) intravenously and rates of accumulation and disappearance of E from arterial blood were studied. All dogs received thiopental, curare, N_2O + O_2, and artificial ventilation. Results: (a) The apparent rate of elimination of E from arterial blood in normo-and hypothermic dogs was similar. (b) Extrapolation of concentration versus time curves after equilibration showed reduction in apparent total available body water space in hypothermic dogs. (c) Equilibration took twice as long as in hypo- as in normothermic dogs. (d) A four-fold increase of tidal volume did not affect disappearance of E in a normothermic dog. (e) The disappearance rate of E in hypothermic dogs was decreased by hexamethonium or a small dose of epinephrine but normalized by a pressor dose of epinephrine. It is suggested that altered rate of disappearance of E from arterial blood in hypothermia results mainly from changes in circulation rather than in hepatic metabolism of E. (Supported in part by grants from the Ontario Heart Foundation, the McLean Foundation and the Defence Research Board of Canada, Grant No. 9325-10).

SOME IN VITRO STUDIES ON THYROTROPIN. M. L. D. Schönbaum†, E. A. Sellers and E. Schönbaum.* Dept. of Pharmacology, Univ. of Toronto.

The in vitro method of Kirkham for assay of thyrotropin (TSH) was found to be sensitive to TSH levels of 1-500μU. The assay is based on effects of TSH on metabolism of I^{131} by cubes of thyroid tissue taken from guinea pigs treated with propylthiouracil. Uptake of I^{131} during a 40 hour incubation at 25±3°C is followed by a KCNS-initiated release of labelled material. The release is inversely proportional to the TSH-like activity. The biological half-life of TSH in this system, the effects of tissue concentration and the effects of Sephadex-G-25 filtration of USP-TSH and plasma or serum on I^{131} release were studied. USP-TSH dissolved in tissue culture medium with either equine or human serum showed increased potency in the Kirkham assay. A temporary increase occurred after 5-10 hours' incubation both in presence and absence of thyroid tissue. On passage through a Sephadex-G-25 column, USP-TSH dissolved in the medium showed potentiation However, Sephadex filtration of TSH added to plasma from normal humans and from patients with thyroid disorders yielded lower and extremely variable recoveries. Increasing the tissue concentration from 5 mg to 20 mg increased both uptake and release of I^{131} at TSH concentrations of 7 and 112μU. (Supported by Grants Nos. MT 1537 and MA 1619 from the Medical Research Council of Canada.)

ANTI-CURARE ACTIVITY OF 5-HYDROXY TRYPTAMINE, 5-METHOXY TRYPTAMINE AND TRYPTAMINE. Robert T. Schopp and Elaine M. Rife*. Department of Physiology, University of Colorado School of Medicine, Denver, Colorado.

It has previously been indicated (The Physiologist 6(3):269,1963) that close intra-arterial injection of 5-hydroxy tryptamine induces anti-curare responses in the indirectly stimulated dog peroneal-tibialis anticus nerve-muscle preparation. This study concerns the activity of 5-methoxy tryptamine and tryptamine compared to 5-hydroxy tryptamine in regard to anti-curare action. All three of these agents cause an immediate increase in the magnitude of contractions following intra-arterial administration in the partially curarized, indirectly stimulated dog nerve-muscle preparation. The approximate anti-curare response threshold for 5-hydroxy tryptamine is 0.00012 μM/Kg while the approximate threshold for both 5-methoxy tryptamine and tryptamine is 0.0024 μM/Kg. As the dose level is increased the degree of anti-curare activity is potentiated. When the dose level is further augmented a slight depression of muscle contractions is observed preceding the anti-curare response. The threshold for this initial depression is approximately 0.12 μM/Kg for 5-hydroxy tryptamine and 5-methoxy tryptamine and 0.24 μM/Kg for tryptamine. At much higher dose levels the action on muscle contractions may be primarily inhibitory with little or no anti-curare activity. The order of increasing effectiveness of these chemicals in causing anti-curare responses is: tryptamine, 5-methoxy tryptamine and 5-hydroxy tryptamine.

(Supported by a contract with the Office of Naval Research, Nonr-3535.

USE OF A MODIFIED THUNBERG BAROSPIRATOR TO MEASURE AIRWAY RESISTANCE. Jules R. Schwaber* and Jere Mead (intr. by J. L. Whittenberger). Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

Thunberg demonstrated that the lungs can be ventilated without accompanying tissue motion by cyclic changes in gas pressure alone. In a modified Emerson Equalizing Pressure Chamber, pressure applied to the airway opening at the mouth is transmitted to the thoraco-abdominal body surface across a variable linear resistance imposed at the neck. This resistance can be adjusted so that the pressure drop from mouth to body surface is equal to that from mouth to alveolus, i.e., the pressure driving gas flow in the airways. Under such circumstances, alveolar pressure is equal to body surface pressure and in a relaxed or paralyzed subject the lungs are immobile. Since the pressure difference between the body surface and mouth, which is readily measured, equals the pressure difference between the alveoli and mouth during immobilization, airway resistance may be obtained by relating it to the associated gas flow. Supine normal human subjects were exposed to pressure variations of $\pm$ 80 to 120 cm. water at 12 to 20 cpm. Satisfactory relaxation was obtained in 25% of non-paralyzed subjects; their thoracic excursions as monitored by a sensitive strain gauge pneumograph corresponded to a change in lung volume of less than 20 ml. Lung volume during immobilization (FRC) was calculated from Boyle's law; the results on separate occasions for any subject agreed within 11%. Values for airway resistance were reproducible for each subject within a range of 30%. Airway resistance at low flows (less than 0.25 LPS) was similar to that reported in supine normal subjects but a substantial non-linear component at higher flows suggested that the upper airway was somewhat narrower during immobilization than during spontaneous breathing.

ABSORPTION OF INULIN BY THE RENAL TUBULE OF NECTURUS. Walter N. Scott,* David L. Maude,* Isam Shehadeh* and A. K. Solomon. Biophysical Laboratory, Harvard Med. Sch., Boston.

Photographic studies of the time course of water absorption from the proximal tubule revealed much greater water absorption than previously found by the stopped-flow microperfusion technique, which utilizes C^{14}-labelled inulin as a reference substance. Investigation of the causes for this discrepancy in 5 experiments showed that only 30% of the perfused inulin could be recovered from the tubule at the end of the 20 minute perfusion period. Furthermore, appreciable amounts of C^{14} could be detected in the blood of the animal. In four double-perfusion experiments it was found that less than 0.003% of the inulin could pass from the renal-portal system into the tubular lumen and be collected in the urine, though an average of 24% of the perfused inulin could pass in the opposite direction from the tubular lumen to the blood stream. These experiments indicated that the inulin did not contain polymers small enough to diffuse through the membrane into the tubule in a simple passive manner and confirmed the existence of a process by which inulin could be absorbed from the tubule. In six stopped-flow microperfusion experiments using I^{131}-labelled human serum albumin as a reference substance, 53% of the albumin was recovered from the tubular lumen. Appreciable amounts of non-dialyzable I^{131} were recovered in the serum. C^{14}-labelled sucrose and C^{14}-labelled inulin were used to demonstrate a similar process in the distal tubule of Necturus. These studies show that inulin is absorbed by the tubule and cannot therefore be used as a reference substance for the measurement of water absorption or of glomerular filtration rate in this species.

EFFECTS OF PULSED SHORT WAVES ON DECUBITUS ULCERS. W. A. Selle, Biophysics and Nuclear Medicine, UCLA Medical Center, Los Angeles, California.

The biological effects of pulsed short waves are being widely studied and their therapeutic value assessed. The effectiveness of pulsed electromagnetic waves of low average power (400-4 settings and 15 watts output of the Theramatic, manufactured by the Dynapower Systems, Corp., Los Angeles) which produce little or no local increase in temperature, is still questionable; specific biological changes have not been demonstrated with such non-thermal energies, although pearl chain formation has. With higher energies (600-6 settings and 39 watts output) the author has previously reported increased peripheral blood flow and a lowering of certain serum enzymes. Because of these observed changes, pulsed short waves by the Theramatic were used on geriatic patients at Long Beach General Hospital having decubitus ulcers, known to be influenced by a variety of physiological and pathological factors, such as nutritive condition, degree of hydration, natural resistance, anabolism, hemoglobin level, local infection and nursing care (including positioning of the body and personal hygiene). Three groups of 60 patients receiving similar nursing and medical care were divided into approximately equal numbers of treated and control members. The former received pulsed short waves to the liver for 10 minutes and to each ulcerative lesion for a similar period. A beneficial influence on ulcer healing was demonstrated in a majority of treated patients although many of the control patients also improved under conditions of the study. Approximately 55% of the controls and 80% of the treated showed improvement.

COMPUTER SIMULATION OF THE VECTORCARDIOGRAM. R. H. Selvester,* R. Kalaba,* C. R. Collier, R. Bellman,* and H. Kagiwada.* Rancho Los Amigos Hospital, Downey, and Rand Corporation, Santa Monica, Calif.

The ventricular depolarization portion of the vectorcardiogram (VCG) has been simulated by use of analog and digital techniques. The ventricular myocardium was divided into 20 segments. The current field contribution from each segment was represented by a dipole vector fixed in space but with a time varying moment. The origin of each was placed at the centroid of each myocardial segment and directed approximately perpendicular to the epicardial surface. The magnitude was assigned a time of onset, duration, amplitude and wave form based on the pattern of sequence of depolarization of Scher. This system was assumed to be in a homogeneous medium. With a cube system of electrode placement on a phantom thorax in an infinite medium, the contribution of each segment was calculated, obtaining VCG loops that were remarkably similar to a normal cube system VCG. Right and left ventricular hypertrophy, and focal and large myocardial infarcts were simulated by appropriate changes in the model. The results were in good agreement with the corresponding clinical conditions. When the dipoles were assigned a common location, VCG's closely resembling those of corrected lead systems were observed. The effect of a spherical boundary of the conducting medium was a result intermediate between the two. Further experiments with more realistic models are in progress.

EFFECTS OF TEMPERATURE ON BLOOD AND PLASMA VOLUMES IN THE TURTLE. Robert E. Semple. Dept. of Physiology, Queen's University, Kingston, Canada.

Each of 25 map turtles (G. geographica) was kept at a constant temperature for at least 2 days. Plasma volume was then measured using T-1824 or I-131 or both; in 7 animals red cell volumes were also measured using Cr-51-tagged cells. Cloacal temperatures were altered by 10 or 15°C and 1 to 2 days later the measurements were repeated. With 6 turtles these changes were then reversed and volumes measured a third time at the temperature of the first experiment. Increases in temperature were invariably accompanied by significant increases in plasma volume, the reverse occurred with a decrease in temperature. Temperature changes from 5° to 20°C (or 20 to 5°C) brought about significant plasma volume changes which ranged in magnitude from 23 to 58% of the volume at 5°C. Cr-51 experiments indicated that cell volumes were not altered. Other results showed that plasma volume remained minimal up to about 10°C (ca 7.0 ml/kg) and increased with temperature to become significantly greater at 20°C (ca 10.2 ml/kg). Further temperature increments were generally ineffective. Heart rates averaged 4/min below 10°C and increased rapidly to average 21/min at a temperature of 20°C. It is concluded that in the cold a portion of the vascular bed is closed; between 10 and 20°C an increasing heart rate and a concomitant increasing blood pressure forces more and more of the bed to open until a maximum is reached at ca 20°C. (Supported by the Ontario Research Foundation).

EVAPORATIVE WEIGHT LOSS, DIASTOLIC PRESSURE, AND BLOOD OSMOLARITY DURING DEHYDRATION. Leo C. Senay, Jr. and Margaret Christensen*. St. Louis Univ., St. Louis, Mo.

Six resting subjects were exposed to 43°C D.B., 28°C W.B. for 12 hrs. with and without rehydration. During rehydration experiments, subjects had an average evaporative loss of 0.5% of original b.w./hr. Average rate during dehydration was 0.46% b.w./hr. Several subjects had similar sweat rates in control and dehydration experiments. However, maintenance of sweat rates did not prevent body temperatures from rising at rates equal to or greater than in subjects exhibiting lower dehydration sweat rates. Conventional methods of plotting weight loss as % of initial body weight show little change in evaporative rates during rehydration or dehydration trials. However, rates of dehydration increase progressively when each observational period is treated as a separate dehydration experiment. Both systolic and diastolic pressures rise during dehydration; with diastolic increase being approximately twice systolic. Comparison of initial and final diastolic readings gave values of $P < 0.1$ and > 0.05. When compared with pressures obtained at similar times during rehydration, increases in diastolic pressure were related to % body weight loss according to the "least squares" equation $\Delta D = 3.5\ \Delta W - 8.43$; correlation coefficient, $r = 0.74$. Apparently increases in diastolic pressure are due to several causes with decreased blood volume probably playing a minor role. Blood osmolarity determined during progressive dehydration is related to body weight loss according to the "least squares" equation $\Delta P = 0.94\ \Delta W + 0.62$, indicating that the rate of water loss from the vascular compartment is no greater than from other fluid compartments in the body. Supported by PHS Grants HE-07075-01 and HE-4939-04.

ENHANCED PROTECTION USING GLOBULIN PROTEINS IN THE TREATMENT OF TOURNIQUET SHOCK WITH PLASMA EXPANDERS. Kenneth D. Serkes* and Stanley Lang. Jewish Hosp. and Washington U. Sch. of Med., St. Louis, Mo.

Commercial reconstituted lyophilized aged human plasma (RLAP) was previously shown to be the most effective therapeutic infusion after an otherwise lethal tourniquet trauma in the rat when compared with normal saline, dextran-in-saline and dextran in glucose-in-water. It was then shown that this high degree of protection was true only of aged but not of recently collected human plasma, and that three months of aging was required for maximum therapeutic benefit.

Comparisons were then conducted between RLAP and clinically used plasma expanders such as Albumisol and Plasmanate, which again strongly favored RLAP in the treatment of the tourniquet trauma, even though the degree of plasma volume expansion provided was the same when measured 4 hours after tourniquet release.

These studies suggested that the superior protection achieved with RLAP was due to the non-albumin protein of the RLAP which was in some way different from the non-albumin protein of Plasmanate and not present in the Albumisol. In subsequent experiments Cohn fractionation of the control plasma was carried out and a single Cohn fraction identified which when added to Albumisol made it equal in therapeutic benefit to the control RLAP.

Electrophoretic studies were performed. (Supported by Dept. of Defense Contract DA 49-007-MD-799.)

EFFECT OF MAGNESIUM DEFICIENCY ON RENAL EXCRETION OF PHOSPHATE L. L. Shanbour*, P. E. Donat*, B. J. Matter*, and H. E. Ginn. V. A. Hosp. and Univ. of Okla. Med. Ctr., Okla. City, Okla.

The effect of acute magnesium deficiency on urinary phosphate excretion was studied. Dogs were rendered magnesium deficient by hemodialysis with a Kiil hemodialyzer. A magnesium absent but otherwise physiological dialysis bath solution was used. Following 9 to 13 hours of dialysis, the plasma magnesium concentration dropped from 1.73±.06 to 0.92±.18 mEq per L. Other plasma electrolyte concentrations, including calcium remained within normal range throughout the experiment. Thereafter, urinary phosphate excretion was measured during the infusion of neutral buffered phosphate at a rate of 30 mM per minute. Phosphate excretion was 28-45 per cent of the filtered load ($U_P V \div C_{I_n} \times P_P$). 10 mM of magnesium chloride was then infused intravenously over a 40 minute period. Plasma magnesium concentration increased to 2-3.2 mEq per liter. Urinary phosphate excretion promptly decreased to 1-6 per cent of filtered load within 60 minutes after starting the magnesium infusion. It is concluded that acute magnesium deficiency results in augmented urinary phosphate excretion. These experiments confirm data obtained from rats and from human subjects that demonstrated augmented urinary phosphate excretion during magnesium deficiency.

EFFECT OF PRIOR EXTERNAL CAROTID ARTERY OCCLUSION ON CAROTID SINUS REFLEX RESPONSES IN THE CAT. N. N. Share*, G. J. S. Abraham* and S. C. Wang. Columbia University, College of P & S, New York, N. Y.

Intrasinual and systemic arterial pressure changes resulting from occlusion of the common carotid arteries in vagotomized cats were recorded and compared with those in which the external carotid arteries were previously clamped. Prior occlusion of the external carotid arteries significantly reduced both the initial fall in intrasinual pressure as well as the reflex pressor response. During common carotid artery occlusion, the intrasinual pressure generally falls to a level below the threshold for baroreceptor activation (about 70 mm Hg, Koch, 1931; Landgren, 1952). This also occurs, although less often, when the external carotid arteries are previously clamped. Carotid body chemoreceptors were functionally eliminated by injecting 0.5 N acetic acid into both sinus regions (Gernandt, 1946). Following this procedure, pressor responses were reduced despite a greater fall in intrasinual pressure after common carotid artery occlusion. Prior occlusion of the external carotid arteries then generally reduced the reflex pressor response to a lesser degree than before treatment. Additionally, the carotid occlusion responses were found to be similar under both chloralose and pentobarbital anesthesia, and were unaltered by positive pressure respiration. It is concluded that in vagotomized cats, the magnitude of the reflex pressor response is dependent on both the degree of baroreceptor deactivation and chemoreceptor activation. Furthermore, there is no apparent difference between chloralose and pentobarbital anesthesia, or positive pressure and spontaneous respiration, on the carotid occlusion response. The results will be further discussed in terms of differences between the cat and the dog. (Supported by USPHS grants 2T1NB5173 and NB00031).

THE EFFECT OF SIGNIFICANCE OF THE CLICK UPON THE EVOKED RESPONSE IN SLEEP AND WAKEFULNESS. Guy C. Sheatz* (Introduced by Felix Strumwasser) WRAIR, Wash., D.C.

The effects of sleep and wakefulness on the ER (evoked response) were studied when the psychological significance of the clicks was, 1) novel, 2) habituated, 3) conditioned, 4) extinguished. ERs were extracted from the spontaneous EEG by the Mnemotron computer Cat 400A. In the early stages of 1 and 3, sleep can only be induced by prior deprivation. Chronic implantation techniques were used to extensively sample cortical and subcortical areas. The typical effect of sleep was to increase the amplitude and complexity of the ER. Some areas did not change and others decreased, the cortex being the chief source of these variables. The sleep ER is similar to the novel ER but both are smaller than the conditioned ER. The effect of habituation and extinction are to reduce the ER but the associated stage of sleep ER is essentially similar in 1, 2, 3 and 4. In the earlier stages of extinction EEG sleep may occur in bursts in the 5 second interclick period and these bursts of sleep waves are triggered by the clicks. The ER is grossly reduced in paradoxical sleep in most areas of the brain regardless of the significance attached to the click at that time.

ABSORPTION OF INULIN BY THE RENAL TUBULE OF THE RAT. Isam Shehadeh,* David L. Maude,* Walter N. Scott* and A. K. Solomon (intr. by E. Page). Biophysical Laboratory, Harvard Med. Sch., Boston.

Since experiments in this laboratory have indicated that appreciable amounts of inulin are absorbed from the proximal tubule in Necturus kidney, the behavior of C^{14}-labelled inulin in single tubules of rat kidney was studied in 4 animals. Using micropuncture techniques, a measured volume of physiological saline (140 mM NaCl), containing 156 μc/ml C^{14}-labelled inulin was perfused through a single tubule blocked, proximal to the injection site, by a column of colored mineral oil. All of the sample was allowed to perfuse the tubule over a period of 20 minutes. At the end of this period both renal pedicles were ligated for an additional 30 minutes to allow for equilibration of the absorbed inulin in the extracellular fluid. Blood was then withdrawn from the aorta and half ml aliquots were counted for C^{14}-inulin. Since the results of White and Rolf (Am. J. Physiol. 188: 151, 1957) have shown that the inulin space is 18.8% at 30 minutes and remains essentially unchanged for the next 2 1/2 hours, this figure was used to calculate that an average of 23% (range 20-27%) of the perfused C^{14}-inulin is recovered in the blood. These studies indicate that in the rat, as in the Necturus, a mechanism exists to absorb inulin from the tubule. Thus it appears that this substance is not satisfactory as a quantitative measure of water absorption or of glomerular filtration rate in this mammalian species.

Effect of Local Exercise of Forearm Muscles on Forearm Capacitance Vessels. J. T. Shepherd and S. Bevegård*. Mayo Clinic, Mayo Foundation Rochester, Minn.

Using strain-gauge plethysmographs, normal subjects were studied to determine whether the dilatation of the resistance vessels in the forearm with local exercise is accompanied by changes in the capacitance vessels. With the forearm elevated above heart level, on inflation of the venous occlusion cuff, the venous pressure did not rise linearly and the pressure in two forearm veins occasionally rose at different rates. Therefore, it was unsatisfactory to use the ratio between the initial slopes of the increases in forearm volume and in venous pressure as an index of venous reaction. When the rate of venous filling was controlled to constant values in spite of the changes in arterial inflow with exercise, the slope of the venous pressure rise was unchanged by the exercise. The amount of blood that could be accumulated in the forearm at a given congesting pressure was similar before and after exercise and the relationship between venous pressure and forearm volume obtained by step-wise deflation of the cuff was unchanged by the exercise. The pressure in "isolated" forearm venous segments was the same before and immediately after exercise of that forearm. Thus no active changes in venous tone could be detected in the post-exercise period. Changing the rate of filling of the forearm veins by including or excluding the hand circulation had no effect on the total amount of blood accumulated at a given venous pressure but with high venous filling rates more of the total increase in forearm volume occurred after venous pressure had reached a constant level. Thus the intrinsic properties of the veins may oppose their distension at high filling rates as in intervals between muscular contractions. (Supported in part by research grant NIH HE-05883.)

DYE RECIRCULATION IN THE ANESTHETIZED DOG. C. W. Sheppard, Philip C. Merker*, and Michael B. Uffer*. Univ. of Tennessee Medical Units, Memphis, Tenn.

In a series of nembutalized dogs, a pressure transducer was placed in the left femoral artery. Through the right external jugular a double-lumen catheter was placed, with the central orifice in the right ventricle, through which T-1824-dyed plasma was rapidly injected. Serial right atrial samples were rapidly obtained through the side lumen and simultaneous arterial samples through a catheter in the left carotid artery. Collecting tubes mounted on a rotating disk were shifted automatically by a signal obtained from the QRS complex of the animal's EKG, through a scaling unit. Thus, beginning with the injection, approximately 3/4 cc samples or less were collected during every 2 heart beats or occasionally every 4. Dye concentrations in the arterial and venous samples were determined spectrophotometrically. From these values, smooth curves were outlined which described arterial first-circulated and recirculated dye. By the mathematical operation of convolution over the dispersion function for the central circulation, the venous recirculated dye curve could be converted to the arterial recirculation curve. Subtraction of this curve from the original arterial curve yielded the approximate arterial first-circulation curve. Curves thus obtained were not unlike those previously observed in canine heart-lung preparations. The overall curves for arterial and venous circulation and recirculation obtained in the animals, resembled those obtained from a mathematical model previously discussed (Sheppard, Minn. Med. 37, 93, 1954).
(Work supported by NIH Research Grant HE-3665 and Marion Laboratories, Inc.)

IN VIVO STUDIES OF THE HAIR FOLLICLE OF THE MOUSE EAR. A.F. Silver and H. B. Chase (intr. by P. F. Fenton). Brown University, Providence, Rhode Island.

Hair follicles in the ears of anesthetized mice were observed and photographed using a light microscope. The follicles are typically resting, but may be activated by plucking, which causes increased local blood flow. Single follicles were followed throughout complete hair cycles. No marked local circulatory changes were noted after the initial hyperemia following plucking.

EVALUATION OF THE LEFT VENTRICLE AS AN IMPULSE GENERATOR. J. A. Siman, D. Watkins, and R. F. Rushmer, Dept. of Physiology and Biophysics, Univ. of Wash. Sch. of Med., Seattle, Washington.

During the initial phase of systole the contracting left ventricle rapidly accelerates blood out of the aorta to reach a high peak flow velocity. The rate at which the ventricle imparts momentum to blood flowing out of the chamber is increased by catechol-sympathomimetic amines and diminished by certain abnormal conditions (i.e. coronary occlusion or severe arterial hypotension). These observations suggest that left ventricular performance may be evaluated by analyzing the initial phase of ventricular systole in terms of the peak outflow rate and peak acceleration of blood in the aorta, by the rate of movement of ventricular walls or by initial upslope of the carotid pressure wave. Aortic flow velocity and changes in left ventricular diameter were measured in intact, unanesthetized dogs with a pulsed ultrasonic flowmeter and sonocardiometer respectively. Carotid pressure was measured with a P23AA Statham strain gauge. An increase in the ventricular impulse was effected by the administration of catechol-sympathomimetic amines l-epinephrine, l-norepinephrine (1 μg/kg body weight/minute), and isopropyl norepinephrine (0.5 μg/kg per minute), and a decrease by sodium pentobarbital (30 mg/kg). The upslope of the aortic flow, carotid pressure pulse and systolic downslope of the left ventricular diameter all become consistently steeper under the influence of the catechol-sympathomimetic amines. Sodium pentobarbital produced a consistent reduction in the corresponding slopes of the recorded variables.

(Supported by NIH Grant #HTS-5147).

EFFECT OF ACID-BASE CHANGES ON RENAL HEMODYNAMICS. Daniel H. Simmons. Mt. Sinai Hospital and Univ. of Calif. Med. Center, Los Angeles.

Fifty-three experiments were conducted on dogs anesthetized with sodium pentobarbital, with ventilation appropriately regulated with a respiration pump. The following were measured during an initial control period with normal acid-base status, during a period of altered acid-base status, and during a second control period: (1) Arterial anaerobic blood pH (Sanz micro-electrode); (2) arterial pCO_2 (interpolation technique); (3) renal blood flow (gated sine wave electromagnetic flowmeter, placed on left renal artery through a flank incision; (4) arterial pressure (pressure transducer). Renal vascular resistance was calculated from flow and pressure. When respiratory acidosis and alkalosis were induced by changing ventilation (20 experiments; $\triangle$ pH = -.22 and +.19), flow varied inversely with changes in pH (+5.7 and -10.2%) and resistance varied directly (-16.6 and +17.5%). During metabolic acidosis and alkalosis induced by infusion of HCl or $NaHCO_3$, ($\triangle$ pH = -.20 and +.19) there were no consistent changes in either flow or resistance (20 experiments). In 10 additional experiments in which respiratory acidosis and alkalosis were induced and pH was returned to normal by appropriate infusion of $NaHCO_3$ or HCl, changes in flow (-14.3 and +19.9%) and resistance (-21.2 and +21.1%) were comparable to those with respiratory disturbances alone. These data suggest that renal resistance is pCO_2-dependent but not pH-dependent, increased CO_2 tension causing vasodilation, and vice versa. Data from these experiments and from 3 additional studies following renal denervation indicate the preparation is an innervated one, that the vascular response is active, and that it is most likely a local effect of CO_2 tension.

THE ADRENERGIC NERVOUS SYSTEM AND THE SPECIALIZED CONDUCTING FIBERS: D.H. Singer* and B.F. Hoffman, Dept. of Pharmacol.,Coll. P&S.,N.Y.,N.Y.

To evaluate direct effects of adrenergic activity on the cardiac conduction system and excitability, reserpine and α and β blocking agents were given to intact dogs with electrodes implanted on the atria and ventricles and over the His bundle. Reserpine caused sinus slowing and arrhythmia, decreased ventricular automaticity and some impairment of conduction through the A-V node. Pronethalol caused qualitatively similar changes. However, even at lowest doses it also depressed atrial excitability and conductivity and prolonged atrial refractoriness. A-V conduction was depressed both proximal and distal to the His bundle. At doses of 10-25 mg/kg intraventricular (IV) conduction slowed and became aberrant. At 25-30 mg/kg depression of automaticity sometimes was so great that arrest ensued and excitability so depressed that driving was difficult. The enhancement of sinus and ventricular automaticity and of AV conduction caused by epinephrine and norepinephrine (5-20γ/kg) became progressively diminished with increasing amounts of pronethalol. Pronethalol accentuated the changes due to reserpine and also depressed atrial excitability, prolonged atrial refractoriness and slowed atrial and IV conduction. The former effects were variably reversed by catechol amines; the latter were unchanged. Phentolamine had no significant effects. Of the properties of the conduction system studied, only automaticity and A-V transmission were both enhanced by catecholamines and depressed by their reserpine induced depletion, suggesting adrenergic mediation. The differential effects of the α and β blocking agents further suggest β receptor mediation. Other changes induced by pronethalol indicate a direct depressant effect. (Supported in part by grants from the John Polachek Foundation and USPHS, H-08508).

EFFECT OF NEOMYCIN SULFATE ON THE ABSORPTION OF XYLOSE AND GLUCOSE IN RATS M.D.Small, V.Folen*, G.Abrahms*, F.Bledsoe*, T.Norris*, and H.Sprinz*. Georgetown University Department of Medicine and Georgetown Division, D.C. General Hospital and Walter Reed Army Institute of Research.

Numerous demonstrations that antibiotic supplementations improve the growth rate in animals resulted in the wide spread application of such diets in animal husbandry. More critical studies indicated that certain of the antibiotics produced a positive growth response, while others, particularly in the swine, such as polymyxin and neomycin seem to supress growth. Neomycin was noted to enhance hypercholesterolemia in animals on a high cholesterol cholate diet and conversely to produce a malabsorptive state in patients treated with high doses. Neomycin sulfate at dosage levels of 250 mg/Kg and 2 gm/Kg was administered intragastrically to Fisher strain rats for 21 days. Pair fed controls received normal saline intragastrically. Rats were then fasted for 24 hours and studied by our modification of the Cori technique or the Cori technique to assess the effects of neomycin on glucose and xylose absorption. The test period was one hour. At the termination of this period the animals were sacrificed, the entire intestine removed and intestinal segments were taken from all animals for histologic examination. Results: Neomycin at 250 mg/Kg produced no alteration in absorption. Neomycin sulfate at 2 gm/Kg produced a significant impairment of absorption of xylose and glucose. There were no consistent histologic alterations noted, though in one experiment a spectrum of histologic changes varying from normal to significantly reduced villus to crypt length ratio was noted. Conclusion: Neomycin at a dose of 2 gm/Kg for 21 days produced a significant reduction in the absorption of xylose and glucose. There were no evidences of an association between this malabsorption and histologic changes.

NEUROLOGICAL ASPECTS OF FAMILIAL DYSAUTONOMIA. Alfred A. Smith and Joseph Dancis (intr.by S.Bernard Wortis) New York University Medical Center,New York.

Familial dysautonomia is a rare,inherited disease,involving autonomic, sensory and neuromuscular systems and appears to be restricted to Jewish children. An exaggerated hypertensive response to infused norepinephrine has been observed in these patients. No vagal reflex occurs during induced hypertension suggesting a cholinergic insufficiency. Supersensitive responses were obtained to infused methacholine supporting the idea of a parasympathetic denervation, clinically evidenced by alacrima and swallowing difficulties. During the infusion, deep tendon reflexes returned temporarily as did pain perception and the flare response to intradermal histamine. Taste perception did not improve with methacholine infusion possibly because of the absence of taste buds, subsequently revealed by tongue biopsy; fungiform papillae are also missing. Failure of adrenergic reflexes, and subnormal responses to high CO_2 and low O_2 tensions indicate deficiencies of other sensory systems. The neurological deficits in dysautonomia thus include a diffuse parasympathetic insufficiency with concomitant supersensitivity and peripheral sensory defects probably localized to the receptor area.

VENOUS RETURN GRADIENTS DURING ANOXIA IN NORMAL AND AREFLEX DOGS. Elvin E. Smith* and Jack W. Crowell. Dept. of Physiology and Biophysics, University Medical Center, Jackson, Miss.

Venous return and, therefore, cardiac output have been shown to be proportional to the gradient for venous return (GVR) or mean circulatory pressure (MCP) minus right atrial pressure (RAP). In the present experiments GVR, arterial pressure, and cardiac output were recorded while the dogs breathed 9 per cent oxygen in nitrogen. After 5 minutes exposure to this hypoxic gas mixture arterial pressure had increased 15 per cent above control values. MCP increased 26.8 per cent while RAP decreased 25 per cent, resulting in a net increase of 27.6 per cent in GVR. This increase in GVR was sufficient to cause a 45 per cent increase in cardiac output. After the normal response to hypoxia had been recorded, the dog's reflexes were blocked by total spinal anesthesia. Arterial pressure was maintained at control levels with an infusion of Levophed and the dogs were artificially respired. The dogs were then placed on the hypoxic gas mixture. Arterial pressure decreased 43 per cent, MCP declined 32 per cent, and RAP fell 11 per cent; the result was a net decrease of 25.9 per cent in GVR. However, cardiac output showed no change. These results show that in the normal animal the vasodilator effect of hypoxia on the circulation is offset, in part, by sympathetic influences. Thus, an increase in cardiac output occurs. In the areflex animal no such influence was noted, thus, hypoxia *per se* did not result in an increased cardiac output.

GASTRIC SECRETORY RESPONSE TO AMYGDALOID AND HYPOTHALAMIC STIMULATION IN CONSCIOUS MACACA MULATTA. G. P. Smith and P. R. McHugh (intr. by F. Strumwasser). Walter Reed Army Inst. of Research, Washington, D.C.

Conscious Macaca mulatta, prepared with chronically implanted electrodes in the amygdala and hypothalamus, and with chronic duodenal and gastric cannulae, were placed in primate chairs and maintained within individual booths continuously. In 7 experiments on 4 monkeys, stimulation of the basal-lateral amygdala for one hour(1) produced amygdaloid after-discharges, a 15-35 γ/100 ml. increase of plasma 17OH-CS and a decrease of basal gastric acid and pepsin secretion. In 10 experiments on 7 monkeys, stimulation(2) of anterior, tuberal or posterior hypothalamic loci for one hour produced the same pattern of increased plasma 17OH-CS and decreased gastric acid and pepsin secretion. No delayed increases of plasma 17OH-CS nor of gastric acid secretion were observed in the four hours following the amygdaloid and hypothalamic stimulation periods. These experiments do not support the hypothesized "adrenal phase" of increased gastric acid secretion (Porter, et al., Surgery 33:875, 1953).

(1) 15-25V, 0.5-1.5 ma., 1.0 msec., 25-40 pp/sec., 5 second trains every 5 minutes.
(2) 15-25V, 0.5-1.5 ma., 1.0 msec., 10 pp/sec., and 30 second trains every 5 minutes.

EFFECT OF HYPOTHALAMIC AND PRE-FRONTAL CORTICAL LESIONS ON CONDITIONED CARDIOVASCULAR RESPONSES. O.A. Smith, Jr. and M.A. Nathan*. Regional Primate Research Center and Dept. of Physiology and Biophysics, Univ. of Wash., Seattle, Wash.

Ten Macaca nemestrina monkeys were trained on one of two procedures: (1)classical conditioning with two lights presented independently for 60 sec., one light always followed by peripheral shock and the other never followed by shock, or (2)instrumental conditioning in which a bar pressing response brought a food reward, and at random intervals a light was presented for 60 sec., which was always followed by shock. After initial training, ultrasonic flow transducers were chronically implanted on the terminal aorta. Further training was then carried out until large increases in flow velocity and heart rate were elicited by the light that was followed by shock. In a subsequent procedure, areas of the diencephalon were electrically stimulated. Those areas from which cardiovascular responses could be elicited were bilaterally destroyed. In some monkeys the conditioned response was temporarily lost, and when these monkeys also sustained prefrontal ablations the response was permanently lost. This effect may be due to destruction of autonomic outflow, decrease of emotional responsiveness or interference with memory or learning ability. (Supported by PHS grants HE-04741 and HE-06691.)

SELF-INDUCED DEPRESSION OF THE MYOTATIC REFLEX IN FLEXOR MUSCLES. Robert E. Smith (intr. by L. D. Carlson). Univ. of Kentucky, Lexington, Ky.

Previous studies of the myotatic reflex have generally been restricted to extensor muscles, the classical "pluck" reflex constituting the only comparable reflex response in flexors. Tibialis anticus and extensor digitorum longus of decerebrate cats were subjected both to "plucks" of the classical form and to repeated sinusoidal, triangular and square wave stretches. Muscle length, velocity, reflex tension and electromyogram (EMG) were recorded. "Pluck" reflexes of the classical type were obtained up to 31 hours after decerebration, and reflex contractions were similarly obtained in response to square, sinusoidal and triangular stretches. Response magnitude was found to be strongly dependent upon the velocity of muscle stretch, square wave stretches eliciting much greater responses than did sinusoidal or triangular stretches. However, when the muscle was subjected to a series of stretches rather than a single pull, the first response of the series was of significantly greater magnitude than were subsequent responses. Similarly, the EMG showed a massive discharge in response to the first pull, but greatly reduced discharges in response to subsequent stretches. This self-induced depression of the flexor myotatic reflex was found to be strongly influenced by the size of preceeding stretches, by their duration, by the time elapsed since the previous stretch and by the resting level of tension during this interim. Asayama (Quart. J. Exper. Physiol. 9: 265, 1915) noted a decrement in repeated "pluck" reflexes and attributed the decrease to fatigue in the afferent portion of the reflex arc. Presynaptic inhibition appears, however, to be a more satisfactory explanation for the reflex depression observed in the present study.

ROLE OF CATECHOLAMINE IN PLASMA NUTRIENT RESPONSE TO DNP. J.F. Snarr* and Allen Lein. Dept. of Physiology, Northwestern University Medical School, Chicago, Illinois.

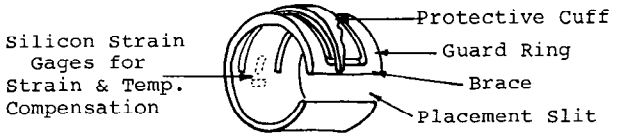
The dinitrophenol (5 mg/kg, I.V.) induced increase in metabolic rate in the fasted, morphinized-barbitalized dog is accompanied by an immediate increase in plasma concentration of glucose, which overshoots before settling to a steady but elevated level, and by a delayed increase in plasma NEFA, which rises continuously for at least three hours. The fact that the plasma pool of these nutrients is increased rather than depleted suggests the operation of a regulating system capable of sensing the increased metabolism and evoking the release of stored glucose and NEFA. Since catecholamine (CA) administration is known to release stored glucose and NEFA, its possible participation in the response was studied by depletion with reserpine (.1 mg/kg, I.P. on two preceeding days). The pre-DNP levels of glucose and NEFA were higher in reserpinized dogs than in undepleted animals; the rate of oxygen consumption did not differ. The changes in metabolic rate and plasma glucose following DNP administration were essentially the same for control and depleted animals. NEFA level, after an initial drop, rose at a rate similar to that of controls. Thus, although in depleted animals the mean NEFA deviation over the first two hours following DNP was significantly below that of controls ($p<.05$), the contribution of CA to the NEFA response appears to be small. However, the elevated pre-DNP level of glucose and NEFA in depleted animals suggests a direct effect of reserpine other than on CA depletion. The reported effect of reserpine on the pituitary-adrenal system may explain this finding and may in addition tend to mask the effect of CA depletion.

NON-IONIC DIFFUSION IN RAT PROXIMAL TUBULE AS A FUNCTION OF LIPOID SOLUBILITY. H. Sonnenberg, K. Baumann, and H. Oelert (intr. by Sidney Solomon). Physiol. Inst. Berlin.

In order to investigate pH-dependent reabsorption of weak organic acids in the rat kidney, segments of single proximal convolutions were perfused in vivo by means of a microperfusion pump with a constant flow rate in the range of normal intratubular flow. Perfusates were buffered to either pH 5 or pH 8 and contained the substance under investigation (PAH, uric acid, phenobarbituric acid, sulfonamides). Reabsorption was determined as a function of perfused length; in addition, in vitro distribution between the respective buffers and lipoid solvents with differing dielectric constants was measured. Backdiffusion of the organic acids was found to be related to pH of perfusate, pK of the acid, and to lipoid solubility. The ratio of calculated transtubular permeabilities at pH 5 and 8 corresponds to the solubility ratio in a lipoid solvent with dielectric constant of approximately 3. The results indicate that non-ionic backdiffusion of organic acids across a lipid phase of tubular epithelium does occur, and that the magnitude of this backdiffusion may be predicted from in vitro solubility measurements in the appropriate solvent.

TRANSMURAL GAGE FOR DETERMINING THE PRESSURE IN BLOOD VESSELS. Merrill P. Spencer, M.D., Virginia Mason Research Center, Seattle, Wash.; Marcos Intaglietta*, Ph.D., California Institute of Technology, Pasadena, Calif.; David L. Johnson*, Virginia Mason Research Center, Seattle, Wash.

A transmural pressure gage of the slit cuff type which surrounds the blood vessel fixing the wall tension, and which senses pressure through radial dilations in the order of 0.2% was developed and tested. Constructed of stainless steel with semiconductor strain gages for obtaining the signal and temperature compensation, the gage virtually prevents movement of the vessel wall so that nonlinearities of the wall can be neglected. Unstable and spurious effects from tissue distortion and drag on the edges of the sensing element are eliminated by a shield and guard rings fixed to the gage. Since this device senses pressure differences between the blood and the surrounding tissues, it finds applications in studies where the ambient pressure changes widely and where problems associated with a catheter system must be eliminated.



METABOLIC ALTERATION OF SELECTED AMINO ACIDS AND THEIR ANALOGUES DURING STUDIES OF INTESTINAL TRANSPORT. Richard P. Spencer, Kenneth R. Brody*, Section of Nuclear Medicine, Department of Radiology, Yale University School of Medicine, New Haven, Connecticut.

Entry of metabolites into cells is usually considered in terms of passive events (no expenditure of cellular energy) or active transport (energy requisite, movement against an electrochemical potential gradient). Still a third type of entry is possible, which combines features of both of the previous processes - this is entry with metabolic alteration of the molecule. There is now considerable evidence that such alteration occurs during the transport of several amino acids and their analogues both in vivo and in vitro. One consequence of this is that the chemical nature of the transported moiety must be rigidly established (by a technique such as paper chromatography). Amino acid esters are apparently split during in vivo absorption, but we have found no appreciable hydrolysis of glycine methyl ester during in vitro studies utilizing the small gut of the rat, hamster, and chinchilla. Amino acid amides are, however, likely cleaved, and we have definitive evidence for this in the case of L-tryptophan amide. Amino acid oxidase activity of the small gut is minimal, but transaminase activity occurs and has been known to involve glutamic and aspartic acids (Neame, Wiseman, 1957) during studies of in vitro transport. There is not an active N-deacylase system in the hamster small gut, but N-chloroacetyl derivatives may be split (Cohen, Huang, 1964). Hydrogenation of unsaturated linkages in amino acids is not a general event during transport, but the enzyme system for converting Δ^1-pyrroline-5-carboxylic acid to proline is present in the small intestine of both rat and hamster.

Supported by Grants AM 7958 and GM 11690 from U.S.P.H.S.

ANALYSIS OF POLYSYNAPTIC REFLEX RESPONSE DECREMENT IN THE ACUTE SPINAL CAT. W. A. Spencer, R. F. Thompson and D. R. Neilson,° Univ. of Oregon Medical School, Portland, Oregon.

The Prosser and Hunter paradigm (1936) has been adapted to the acute spinal cat using single stimuli rather than brief stimulus trains. Under these conditions the occurrence of response decrement (habituation) to low frequency cutaneous stimuli and the abolition of the decrement (dishabituation) by an extra-stimulus has been confirmed. Several features of dishabituation suggest that this phenomenon represents a transient facilitation of the reduced test response rather than an abolition of the process responsible for the decrement. The essential features of the Prosser-Hunter phenomenon may be seen in ventral root recordings after de-efferentation by distal ventral root transection. Records of activity in dissected ventral and lateral columns indicate that these systems show only a small decrement to cutaneous afferent volleys repeated at 1 second intervals and show no restoration when a strong extra-stimulus is presented. During the decrement of the flexor reflex response produced by cutaneous afferent volleys delivered at 1 second intervals, interposed flexor monosynaptic reflexes showed no decrement. Electrotonic and intracellular recordings of motoneuron polysynaptic PSPs generated by repeated cutaneous volleys show decrement, and also increase in amplitude following a strong extra-stimulus. Response decrement is present after I.V. Strychnine and Picrotoxin administration. A "polysynaptic low frequency depression" hypothesis to explain these data will be discussed. (Supported by USPHS Research Grants NB-03494 and B-2161)

AUTOMATION OF COMPUTATION OF RESPIRATORY MECHANICAL PARAMETERS. R. W. Stacy, R. M. Peters,* W. M. Stauffer,* and J. C. Dill.* North Carolina State and University of North Carolina, Raleigh and Chapel Hill, North Carolina.

Computer methods have made possible several computations not previously feasible because of time limitations. Computer methods have developed along two lines: (1) an analog computer technique providing on-line recording of work, resistance, and other selectable parameters, and (2) a digital computer technique utilizing analog to digital conversion in the LINC computer. A major advantage has resulted from the use of a moving average technique to eliminate stochastic variations from input signals. Statistical studies of large numbers of breaths have provided information on the variance of respiratory mechanical data. By processing statistically significant numbers of breaths, patient data is more meaningful and has greater diagnostic significance.

ELECTROPHYSIOLOGICAL PROPERTIES OF CORTICAL MOTONEURONS DURING IONTOPHORETIC APPLICATION OF CHEMICAL SUBSTANCES. C. Stefanis* (intr. by G. C. Salmoiraghi). NIMH, NIH, Bethesda, Maryland.

In a previous study (C. Stefanis and H. Jasper to be published in J. Neurophysiol. 1964) the electrophysiological properties and the effects of orthodromic, antidromic and direct activation of cat's cortical motoneurons have been studied with intracellular recordings. Further investigation was carried out, using microelectrophoretic application of ACh, NE, 5-HT, GABA, Glutamate, local anesthetics and other substances in order to obtain additional information on: (I) the safety factor for antidromic invasion of Betz cells; (II) the effects of endogenous amines on the temporal patterns of recurrent and thalamocortical synaptic activity; (III) the effects of brain rhythms on the firing patterns of cortical neurons under various functional states; and (IV) the effects of iontophoretically applied substances on the flow of extracellular current produced by the spike discharge of pyramidal cells. The results showed that: (I) a large number of Betz cells were invaded antidromically only after the administration of excitatory substances; (II) ACh enhanced facilitation and GABA enhanced recurrent inhibition; (III) the spindle rhythm acts as a gating device facilitating firing of quiscent cells and transforming the chemically induced tonic firing of the same cells to a phasic one; and (IV) certain amino acids and GABA particularly distort the extracellular spike potentials to the extent of inverting their polarity. Associated increase in amplitude and duration of the inverted spikes were analysed in terms of redistribution of current and possible membrane resistance changes.

CARDIOVASCULAR RESPONSES TO TILTING. H.F. Stegall* and R.F. Rushmer, Dept. of Physiol. and Biophysics, U. of Wn. Sch. of Med., Seattle, Wn.

Although the transition from horizontal to erect position diminishes stroke volume, systemic arterial pressure is maintained through tachycardia, vasoconstriction, or both. These reactions were elicited by tilting healthy subjects rapidly from horizontal positions to 60° head-up while continuous measurements were being made of tilt angle, heart rate, arterial and venous pressures, forearm and calf circumference (by mercury-in-Silastic strain gage), and instantaneous brachial and femoral artery flow rates (by transcutaneous Doppler flowmeter). On tilting, heart rate rose by about one-third within 30 sec. When the subject was tilted back to horizontal the rate continued at the elevated level for a few beats and then dropped precipitously to slightly less than the pre-tilt level. In the upright position, flow in brachial and femoral arteries was reduced by one-third to one-half within 15 sec but returned to original levels promptly when the horizontal position was reestablished. When the forearm was supported at shoulder level, forearm venous pressure and circumference declined. However, venous pressure-volume relationships in the forearm were only slightly affected by tilting. Calf circumference increased markedly with muscles relaxed and promptly diminished during muscle contraction. The transmural pressure of vessels in the neck was altered with an airtight chamber placed around the neck of horizontal subjects. The mean systemic arterial pressure was shifted by an amount somewhat less than the pressure change within the chamber. However, the peripheral resistance in the forearm remained relatively constant. This observation suggests that the compensatory vasoconstriction observed in the extremities on tilting was not caused by variations in transmural pressure across the carotid sinus pressoreceptors. (Supported by NIH Grant #HE-07293).

SODIUM DISTRIBUTION IN FROG STOMACH MUSCLE. E.W. Stephenson. Dept. of Physiology, The George Washington University School of Medicine, Washington, D.C.

Frog stomach muscle, like other vertebrate smooth muscles studied, is known to contain much more total Na and less K in vitro than skeletal muscle. However, the present work indicates a partition of total Na such that intracellular ionic Na and K concentrations are not appreciably different in these two tissues. Na and K content, Na^{22} uptake, and sucrose-C^{14} space were determined in rings of muscle cut from the stomach of Rana pipiens. Freshly dissected rings contain only slightly more total Na and less K than frog sartorius. Rings immersed in oxygenated, HCO_3-buffered Ringer's solution stabilize at a much higher Na and lower K content. Most of the cation shift on immersion is attributed to an effective increase in extracellular space due to changes in severely damaged cells at the cut borders. The sucrose-C^{14} space in vitro is about 1/3 tissue weight or 40% tissue water, so that much of the total Na is extracellular. The rest of the Na does not exchange homogeneously. Na^{22} uptake measurements indicate two distinct components: a rapidly exchanging quantity including but slightly exceeding the extracellular Na, and a smaller portion which exchanges extremely slowly. When total Na is markedly increased and K decreased by the cardiac glycoside ouabain (10^{-4}M), the rapidly exchanging component increases in parallel. The unchanging slow component is considered to be bound. Therefore the normal concentration of exchangeable Na in the cell water of frog stomach muscle is maintained at less than 10 mEq/l.

(Supported by USPHS Grants T1 HE 5358 and B-3622.)

CORTICAL, LIMBIC AND VISCERAL CONNECTIONS OF THE BASAL FOREBRAIN AREA IN THE CAT. M. B. Sterman,* M. H. Chase,* T. Knauss* and C. D. Clemente. Sepulveda VA Hosp. and Depts. of Anatomy and Physiology, Univ. of Calif., Los Angeles, Calif.

Evoked potential experiments were performed in the brains of acute cat preparations under local anesthesia. Explorative stimulation of the dorsal, lateral, and basal aspects of the cerebral cortex revealed a basal-lateral region, including the coronal, anterior ectosylvian, anterior sylvian, and proreus gyri, which induced an evoked response in the basal forebrain - pre-optic area (25 msec latency) and dorsal hippocampus. Stimulation of the basal forebrain area in turn produces a bi-phasic response of similar latency at these cortical loci, in addition to evoked potentials in the amygdala, hippocampus and medial thalamic nuclei. It was of interest to note that although stimulation of the central end of the cut cervical vagus nerve did not appear to influence basal forebrain activity directly, we did observe, as have others, that potentials are evoked in these same cortical regions by vagal afferent stimulation. It was also observed that sustained stimulation of the central end of the vagus at frequencies from 10 to 50 pps produces a generalized EEG activation, whereas stimulation at higher frequencies is increasingly effective in the induction of marked cortical synchronization. This synchronogenic influence is similar in nature to the EEG changes induced by basal forebrain stimulation. These facts suggest a complex interaction between ascending visceral, descending forebrain, and limbic system functions. (Supported by a grant from the U. S. Public Health Service.)

HORMONAL ENVIRONMENT AND CHANGES IN MUSCLE ACTION POTENTIALS (in situ.) Fleur L. Strand, Hans Stoboy* and Gunter Friedebold*. New York University and The Free University, Berlin, Germany.

A.P.s were recorded from both gastrocnemii during 10 minute stimulation of the sciatic nerves (1 c/s). Statistical comparison was made of the latent period, amplitude and duration of A.P.s of stressed (24 hour at 4°C) and non-stressed intact and adrenalectomized rats. The latent period lengthens in all groups, but most markedly in intact rats, stressed or not. All groups show a slow decline in A.P. amplitude during stimulation but the initial height is greatest in the adx. rats, both stressed and non-stressed. The striking increase in the duration of individual A.P.s during stimulation is seen only in the non-stressed rats and is accompanied by marked polyphasia. The stressed rats show very little increase in A.P. duration and the initial values are considerably less than in the non-stressed groups. While it is generally considered that changes in ionic balance resulting from adrenalectomy are responsible for alterations in the A.P., the variability in the different parameters in the 4 groups indicates that they are affected differently by the hormonal environment. It is possible that adrenal hormones may be important for some parameters (amplitude) and not for others (duration). Similarly, while there is an increased secretion of ACTH in adx. and stressed animals, ACTH may be involved either directly or indirectly in electrical changes. ACTH apparently affects A.P. amplitude directly, latent period indirectly via adrenal cortical hormones, a not surprising finding as these measurements represent very different phenomena.

LATERAL TRANSMISSION OF TENSION FROM MYOFIBRIL TO SARCOLEMMA IN STRIATED MUSCLE. Sibyl F. Street* and Robert W. Ramsey. Medical College of Virginia, Richmond, Va.

Frog and rabbit muscle fibers can develop at least a third of maximum tetanic tension after stretch to 170% of rest length although, except at the fiber ends, most of the sarcomeres exceed Huxley's critical length of 3.6 u. This result would be consistent with the sliding model if the tension is transmitted by way of the sarcolemma. Eight bundles (2 to 6 fibers) and one single muscle fiber from the semitendonosus muscle of the frog were isolated and extreme care taken that all possible connective tissue was removed at one end, exposing microtendons. Maximum tetanic tension was determined from the records of a partial length-tension diagram. The fibers were then injured at the clean end by pressure with a glass rod. An injury clot formed and retracted leaving an empty sarcolemma sheath connecting the uninjured portion of the fiber and the tendon. Such fibers remain excitable for several hours if the injured region is small. After injury these preparations developed maximum tetanic tensions of from 30 to 100% (1) of the original tension before injury. These experiments could not be repeated on rabbit fibers because of technical difficulties. Although the length-tension developed diagram of the rabbit fibers (red foreleg muscle) is very similar to that of the frog, the fibers are very much more extensible. Conclusion: Tension developed by myofibrils can be largely transmitted to tendon by sarcolemma. (Supported by USPHS Grant HE - 06389-03)

EFFECTS OF TEST-INTERVAL ON H REFLEXES IN NORMAL AND SPINAL MAN. Stuart, D. G.*, Ishikawa, K.*, Bors, E.* and Porter, R. W., VA Hospital, Long Beach and UCLA.

The peak-to-peak amplitudes of 25 consecutive H reflexes, evoked by repetitive single shock percutaneous stimulation of the medial popliteal nerve and recorded with surface electrodes over the soleus muscle in normal and spinal (T_1 to T_7) man, have been averaged with a Computer of Average Transients (Mnemetron 400 B) at stimulus rates from 1 shock/10 seconds to 10 shocks/second. In spinal patients and one hyperreactive intact subject the amplitude of the reflex was not reduced until stimulus rates of 5 shocks/second or greater were used, i.e., test-intervals within the recovery time of the reflex as determined with the double shock technique. In these cases a reduction of H reflex amplitude could be elicited at much longer test-intervals if the stimulus intensity was increased to evoke a direct muscle response (M wave) in addition to the H wave. In normally reactive intact subjects stimulus rates of 1 shock/2.5 seconds or slower were necessary to elicit the maximum H reflex, i.e., test-intervals over 10 times longer than the recovery time of the reflex. Neurophysiological mechanisms underlying these results and implications with respect to stabilizing H reflex recording in man will be discussed.

EFFECT OF ACID-BASE ALTERATIONS ON SURFACE ACTIVITY OF LUNG EXTRACTS. Alton I. Sutnick and Louis A. Soloff (intr. by Bert R. Boone). Temple University Medical Center, Philadelphia, Pennsylvania.

Addition of KOH has been shown to increase the surface tension of distilled water. We have confirmed this with measurements on the surface film balance, and studied the effect of various KOH concentrations on extracts of human lung tissue. KOH extracts of 11 lungs had an average minimal surface tension of 22.6 dynes/cm. in contrast to 6.1 dynes/cm. in saline extracts. KCl extracts, even in saturated solutions, were normal, implying that K^+ ion was not responsible for increases in surface tension. The pH of 5 KOH extracts averaged 8.5, while that of saline extracts averaged 6.4. Acidification of these with 0.1N HCl to pH of 3.3 produced no reduction in minimal surface tension. Five lungs were extracted with NaOH, and pH was increased in an additional 7 saline extracts by adding 10% NaOH solution. Nine of these showed a rise in minimal surface tension, and in 2 we demonstrated a progressive change as pH increased. The other 3 specimens did not rise to abnormally high surface tensions, but the contour of the tension-area curve changed maredly, resulting in a much more gradual slope and narrower hysteresis loop. One of these 3 returned to a normal curve on acidification. Similar abnormalities were produced by lowering pH with 0.1N HCl. Minimal surface tension was consistently raised with addition of K_2CO_3 and $NaHCO_3$ as well. In one of these specimens, neutralization with 0.1N HCl restored normal surface activity. This study has demonstrated that alteration in pH of the subphase in either direction may result in abnormalities in surface activity of lung extracts, independent of which specific anions or cations are used. This is occasionally reversible by neutralization. (Supported in part by NIH Grant HE 08595-01 and Heart Assn. S.E. Penna.).

RELATION BETWEEN BLOOD FLOW AND BLOOD CONTENT OF THE FOREARM DURING LOCAL HEATING AND COOLING. P. J. Swanson* and E. Brown. Cardiovascular Research Institute and Department of Medicine, University of California School of Medicine, San Francisco, California.

Most students of the capacity function of the human limb circulation have measured either the pressure:volume relations of isolated cutaneous veins or the quantity of blood collected in limb segments during venous congestion. We decided to look at the changes in limb volume occurring when blood flow was adjusted experimentally and venous outflow was not restricted. Subjects lay with both arms at heart level in plethysmographs whose water pressure was either just below or considerably above natural venous pressure. Blood flow was measured on one side, volume changes on the other, while plethysmograph temperatures were adjusted symmetrically from 34°C up to 39°C or down to 24°C and back. With warming, volume rose 1.5 to 2 ml/100 ml tissue as flow rose from its resting level to about 8 ml/100 ml/min. At higher flows (maximum 16), volume rose no further. With cooling, volume decreased 2 to 2.5 ml/100 ml as flow fell to about 1 ml/100 ml/min. Flow and volume reversed together as temperature was returned to 34°C. Results were the same at high and low plethysmograph pressures, suggesting that the vessels chiefly involved were probably upstream to the large veins. The total change of capacity (4 ml/100 ml tissue) associated with the range of blood flows between 1 and 8 ml/100 ml/min is about equal to the volume that can be collected in the forearm when transmural venous pressure is raised from zero to 30 mm Hg, as found by ourselves and others. (Supported by USPHS Grant HE-06285.)

METABOLISM AND DISTRIBUTION OF I^{125}-FIBRINOGEN IN HEALTHY MEN. Y. Takeda (intr. by E. B. Reeve). Dept. of Med., Univ. of Colo. School of Med., Denver, Colo.

Using I^{125} labeled fibrinogen, studies were made of the metabolism and distribution of fibrinogen in 12 healthy male volunteers, 16 to 54 years in age. Fibrinogen, averaging 96% clottability, was prepared from the subject's own plasma to avoid transmitting the hepatitis virus, by repeated salt-fractionation with 1/4 saturated ammonium sulfate, and labeled with I^{125} in a ratio of 0.5 or less atoms iodine per molecule of fibrinogen. The I^{125}-fibrinogen was then sterilized by filtration. After I.V. injection of 5 to 15 uc of I^{125}-fibrinogen, blood samples and 24 hour urine collections were obtained over 7 to 9 days. The plasma and urine samples were assayed for radioactivity in a well-scintillation counter with spectrometer attachment. Graphical analysis of the data of a given subject showed that the entire plasma radioactivity curve was closely described by a two exponential equation, $x = C_1e^{-at} + C_2e^{-bt}$. Mathematical analysis of the data gave the following results: The average value for the plasma volume was 35.6 ml/kg; for the plasma fibrinogen concentration, 360 mg per 100 ml; for the intravascular fibrinogen, 127 mg/kg; for the extravascular fibrinogen, 19.1 mg/kg; for the slower half-life of I^{125}-fibrinogen, 3.2 days; for the transcapillary transfer rate of fibrinogen, 85.3 mg/kg/day; and for the catabolic rate of fibrinogen, 31.8 mg/kg/day. Indirect evidence suggests that these values are close to true values.
(Supported by U.S.P.H.S. Grant HE-02262).

COMPARATIVE EFFECTIVENESS OF CENTRAL AND PERIPHERAL VAGUS STIMULATION ON GASTRIC SECRETIONS. Martin F. Tansy*, Robert Mackowiak*, and M.H.F. Friedman, Dept. of Physiology, Jefferson Medical College.

Effects of either peripheral or central vagal stimulation on gastric secretion depend on strength, duration, frequency, and mode of application of the stimulus. Stimulation of the peripheral end of the vagus elicits an alkaline fluid with low voltage - low frequency stimuli, and an acid secretion with stimuli of high voltage and frequency. In bilaterally vagectomized dogs, stimulation of the central vagus produces profuse secretion of thick gastric mucus when stimulus characteristics are those which also evoke "sympathetic" cardiovascular responses. This mucus secretion is not blocked by atropine but is blocked by dibenamine and sympathectomy. No combination of stimuli characteristics, however, was found which elicit acid secretion when applied to the central vagus. Evidence for humoral participation (from central serotonin - norepinephrine depots?) and for species differences between cats and dogs have been found.

EFFECT ON THE CALCULATED PERMEABILITY COEFFICIENT OF THE PULMONARY MEMBRANE CAUSED BY VARYING THE BLOOD FLOW IN AN ISOLATED DOG'S LUNG. Aubrey E. Taylor* and Arthur C. Guyton, Dept. of Physiology, Univ. of Miss. Med. Center, Jackson, Miss.

A previous investigation in which a dog's lower left lobe was filled with Tyrode's solution and perfused with a dextran-Tyrode's solution yielded an average permeability coefficient for Na^{24} of $7.5 \pm 2.1 \cdot 10^{-7}$ cm/sec. This permeability coefficient was calculated by making two assumptions which needed experimental verification: 1. that the circulating vascular fluid was in equilibrium with the extravascular space; 2. that the alveoli were well filled with Tyrode's solution by utilizing a vacuum degassing procedure. This present work was designed to test the validity of these two assumptions. In 11 experiments the alveoli of the lobe were filled with Tyrode's solution after degassing by applying vacuum to the bronchus. Then the lobe's circulation was perfused with a 5 per cent dextran-Tyrode's solution. The flow was varied between the limits of 3.5 and 13 cc/min/gm lung tissue, and the average permeability coefficient obtained using this procedure was $7.3 \pm 1.8 \cdot 10^{-7}$ cm/sec, and the value of this did not change with changes in blood flow. In 6 lobes the lungs were degassed by the O_2 technique, and the flow was varied between 5.8 to 8.9 cc/min/gm lung tissue. A permeability coefficient of $7.5 \pm 1.9 \cdot 10^{-7}$ cm/sec was obtained using this degassing procedure. Thus, the two assumptions were verified by experimental techniques, and in the case of Na^{24} the system was not detectably flow-limited since the calculated permeability coefficients did not change significantly when flow or degassing procedures were altered.

INHIBITION OF CLOT LYSIS BY A SURFACE ACTIVE LIPOPROTEIN FROM LUNG AND INHIBITION OF ITS SURFACE ACTIVITY BY FIBRINOGEN. F. B. Taylor, Jr. and M. E. Abrams[1] (intr. by J. Botts). Cardiovascular Res. Inst., Univ. of Cal. Med. Center, San Francisco, Cal.

Pathogenesis of the membrane in pulmonary hyaline membrane disease has been attributed in part to a lack of fibrinolytic activity. Mixing of a surface active lipoprotein extracted from lung (SAL) with plasma exudate may account for lack of fibrinolytic activity, because 4×10^{-9} moles (2×10^{-6}M) of SAL inhibits clot retraction and clot lysis (>24 hours) of blood diluted 1:10 in phosphate buffer (after Fearnley). Since platelets are required for clot lysis (Bickford and Taylor) and since SAL did not inhibit plasmin hydrolysis of fibrinogen, or streptokinase activation of plasminogen, we assume that inhibition of clot lysis may occur at an earlier stage of the activation process involving platelets or platelet products. Equimolar proportions of SAL and fibrinogen have a minimum surface tension (area=60 to 12 cm^2) 10 dynes/cm higher than the same quantity of SAL by itself. The surface tension for fibrinogen alone was 40 dynes/cm. Albumin, gamma globulin, and plasminogen did not affect SAL surface activity. Fibrinogen which was periodated or hydrolyzed with plasmin still inhibited SAL surface activity. Fibrinogen did not inhibit the surface activity of dipalmitoyl lecithin. When SAL and fibrinogen are dispersed in 4M urea, the inhibitory effect of fibrinogen on the surface activity of SAL is markedly reduced. Lung lipoprotein whose surface tension was above 25 dynes/cm did not inhibit clot lysis. ([1]Rockefeller Travelling Fellow.)(Supported by USPHS grants H-5146 and HE-06285.)

PERSISTENCE OF REGULAR ESTROUS CYCLES IN HAMSTERS UNDER CONSTANT ENVIRONMENTAL CONDITIONS. J. L. Taylor, Jr., (intro. by N.R.Alpert). Univ. of Illinois College of Medicine, Chicago, Illinois

As reported by Greenwald (J.Endocrinol. 28: 123-4, 1963) estrous cyclicity continues for long periods in hamsters under continuous illumination. Females, 8 to 10 weeks old, were maintained for 10-11, 4-day cycles in an acoustically and thermally constant environment of 13 hrs. light and 11 hrs. darkness. Stages of the vaginal estrous cycle were determined at regular times daily by means of visual, tactile and microscopic examination of digitally expressed vaginal secretions deposited on microscope slides. Groups were then maintained in either continuous light or darkness. Smearing is continued once each day, each clock hour appearing randomly once every 24 days to avoid timing cues. All animals exhibiting regular cycles during the control period have retained the same 4-day period in either light or darkness. Three of five animals in darkness and eight of ten animals in light continue cycling after 8 cycles. Estimates of vaginal state near the time of estrus can be made $\pm$ 4 hours. No evidence of free running shifts in timing are apparent as yet. It is suggested that neither light or darkness, or cyclic illumination, nor manual examination are necessary stimuli for persistence of regular 4-day estrous cyclicity in the hamster.

Aided by grants from USPHS and NSF

BEHAVIORAL RESPONSE OF THE FIDDLER CRAB (UCA PUGILATOR) TO LIGHT AND IONIZING RADIATION. Robert C. Terwilliger * and Charles K. Levy. Biology Department, Boston University, Boston, Mass.

Evidence has been presented by a number of investigators that animals can perceive ionizing radiation. There also exists several reports indicating that perception of x-rays may be mediated via the photoreceptor mechanism. In this investigation the response of Fiddler Crab to x-rays and light under both dark and red illuminated conditions was studied. Intact Fiddler Crabs exhibited a characteristic "off" response to both light and x-rays which consisted of a transient cessation of locomotor activity. Responses were recorded electronically by means of a strain gauge and also by direct observation. All animals (100%) responded abruptly to the cessation of light. In the case of x-ray this "off" response was found to be dose-rate dependent. At 240r/min, 70% of the animals showed an "off" response but at 15r/ min. only 1 out of 60 trials showed an "off" response and this could have been the result of coincidence. Surgical removal of the eye stalks abolished the response to both light and x-rays. In the initial studies a transparent plastic chamber was used and subsequently it was found that the plastic flouresced emitting visible light (visible to dark adapted human). Light emission by the plastic was dose-rate dependent. In subsequent experiments a black, non flourescing chamber was used and the animals still exhibited the characteristic "off" response. Although chamber flouresence can be eliminated as a variable, flouresence of the crystalene lens or other tissues may be possibly involved in the x-ray activation of the photoreceptors.

SURFACE FORCES, COMPLIANCE AND AIRSPACE CONFIGURATION OF THE LUNG. D. F. Tierney and J. A. Clements (intr. by M. B. McIlroy). Cardiovascular Research Inst., Univ. of Cal., San Francisco, Cal.

Lung compliance (C_L) of excised rat lungs at low transpulmonary pressure (P_{TP}) decreased during shallow ventilation, but atelectasis did not occur and the airways did not collapse. On the basis of lung extract studies, we attributed the low C_L to increasing surface tension (ST). The possible configuration of alveolar ducts at low (A) and high (B) ST is illustrated below. Surface forces retract the mouths of the alveoli, decreasing their volume and area but increasing their radii. The other figure illustrates the surface-tension dependent pressure-volume relationships during inflation of an alveolus. (Mead, Am. Rev. Resp. Dis. 81:739, 1960). Alveoli that exceed a hemisphere (A) can expand (slope 2) without added pressure. Expansion of alveoli of less than hemispherical shape (B) requires increasing pressure (slope 1). C_L may be decreased because some alveoli which are less than a hemisphere change volume only slightly unless the "opening pressure" (point 3) is exceeded. Results of preliminary studies comparing excised rat lungs frozen with propane immediately after and 20 minutes after deflation from maximal volume to a low P_{TP} support this concept. (Supported in part by USPHS grant HE-06285.)

A FLOWMETER USING CHANGES IN ELECTRICAL RESISTANCE. Stepen R. Topaz* and W.J. Kolff. Department of Artificial Organs, Cleveland Clinic Foundation, Cleveland, Ohio.

In 1962, Moulopoulos and Topaz reported at the ASAIO meeting an electrokinetic flowmeter which showed a flow curve which could be standardized and duplicated, but the underlying principle was not understood. Three electrodes were placed at equal distances in a tube through which fluid flowed. An alternating current was fed into the middle and was picked up by the outer electrodes. Thus, simultaneously one arm of the current is going upstream, the other downstream. By using an alternating current polarization was excluded. The electrical resistance balanced in the two arms at standstill changed when mercury or saline flowed through the tube. The differential resistance is explained with electron flow in flowing fluids. It correlated with flow rather than velocity. Width of the tube does not disturb the end result. Later, three electrodes were mounted on a cardiac catheter. Calibration was done in mock circulations and with calibrated artificial hearts in animals. A linear correlation was found between resistance differential in Ohms and ml. of fluid flow. Diagrams and tracings will be presented to show the stability immediately after insertion into an animal and over long-term flow studies with natural hearts, artificial hearts and extracorporeal pumps.

THE RENAL EXCRETION OF TRITIATED DIGOXIN. E. J. Towbin, I. E. Doherty* and C. B. Ferrell*. VA Hospital and University of Arkansas School of Medicine, Little Rock, Arkansas.

Stop-flow and clearance techniques were used to study renal excretion of tritiated digoxin in anesthetized dogs after the I.V. injection of 0.5 mg of pharmacologically active glycoside having a specific activity of 61 μc/mg. Urine radioactivity and "cold" digoxin migrate identically when chromatographed. This observation permits the use of urine and plasma radioactivity as a measure of digoxin content. In four experiments ureteral stasis was applied for five minutes before tritiated digoxin and a marker of filtration, $Na_4Fe(CN)_6$, were rapidly and simultaneously injected I.V. Two minutes later the clamp was removed and urine samples secured. Digoxin and $Na_4Fe(CN)_6$ concentration curves were superimposable, indicating that digoxin is freely filtered. In a second experimental protocol, creatinine, urea, glucose and tritiated digoxin in Ringer's solution were infused at a constant rate. Subsequent to equilibration, the ureteral catheter was clamped for 3-6 minutes, then 1/2 cc serial urine samples were collected. Eighteen such experiments showed that filtered digoxin is reabsorbed by the proximal tubule just distal to the site for maximal glucose reabsorption. There is no evidence for tubular secretion of digoxin. Average clearance per kidney during free flow was 9.5 cc/min for digoxin and 16 cc/min for creatinine, clearance ratio 0.66 ± 0.03. Control and post digitalization electrolyte stop-flow patterns were observed in 29 experiments; of these, 19 showed inhibition of distal tubular reabsorption of potassium after digitalization. The sodium pattern was not changed by digoxin.

Effects of Changes in Peripheral Vascular Resistance on Cardiac Performance in Normal and Cardiac Denervated Dogs Studied Without Thoracotomy. A. G. Tsakiris*, W. Rutishauser*, N. Banchero*, D. E. Donald and E. H. Wood. Mayo Clinic, Mayo Foundation, Rochester, Minn.

Cardiac responses to pressure and volume load induced by changes in peripheral vascular resistance were studied in 5 normal dogs and in 5 dogs with chronic cardiac denervation (regional neural ablation) under morphine-pentobarbital anesthesia. Observations were made with spontaneous and with constant heart rates maintained by driving the atria and ventricles with electronically coupled pacemakers. Vasoconstriction or vasodilatation were produced by step-wise infusion of Angiotensin II or Acetylcholine into the ascending aorta about 3-4 cm. above the aortic valves. Pressures were measured in the cardiac chambers, ascending aorta, femoral and pulmonary arteries and cardiac output determined by dye dilution. Angiocardiograms obtained by the injection of 2.5 to 5.5 ml. Renovist into the left ventricle were recorded on videotape (the silhouette of the left ventricle was used as an index of end-diastolic and end-systolic volumes). Mean aortic pressures ranging from 40 to 200 mm. Hg and cardiac output from 0.9 to 7.0 L./minute were obtained. Cardiac output and stroke volume in both animal groups were maintained or slightly decreased with increased resistance to ventricular ejection; however, left ventricular end-diastolic pressure and left atrial pressure increased more in normal (11-25 cm. H_2O) than in denervated animals (3-8 cm. H_2O). In contrast during vasodilatation, denervated dogs were unable to increase cardiac output and maintain aortic pressure to the same degree as normals. These differences are thought to reflect the extent to which the basic response of the heart, as found in the chronically denervated group, is modified by vagal and sympathetic influences. (Supported in part by research grants: NIH H-3532, AHA CI 10, AHA 63-9.)

FUNCTIONAL ACTIVITY OF OLFACTORY NERVE IN BIRDS. Don Tucker (intr. by L. M. Beidler). Florida State University, Tallahassee, Florida.

Responses to odors were recorded from various parts of the olfactory apparatus in many species of animals, including mammals, amphibians, reptiles and birds. We have been struck by the lack of obvious species differences which, in the case of taste, are easily evident. The presence of a functional olfactory organ and nerve implies, but does not prove, that birds can smell. The role of olfaction in the behavior of many birds is still unknown. It is interesting to note, however, that the amyl acetate thresholds recorded for chicken and sparrow hawk were better than that for the average rabbit preparation. The anatomy of the adult bird is very favorable for recording from small olfactory nerve twigs in response to olfactory receptor stimulation. The nerve seems to be unusually resistant to the effects of stretching during dissection, and thus makes bird olfactory preparations attractive for study. The following birds have been used in successful olfactory preparations:

Blue jay	*Cyanocitta cristata*
Night hawk	*Chordeiles minor*
Yellow-throat warbler	*Geothlypis trichas*
House sparrow	*Passer domesticus*
Ring-billed gull	*Larus delawarensis*
White leghorn chicken	*Gallus domesticus*
Sparrow hawk	*Falco sparverius*
Homing pigeon	*Columba livia*
Bob-white quail	*Colinus virginianus*
Embden goose	*Anser anser*

Supported by U.S.P.H.S. Grant No. 5T1 NB 5258-05

VOLUME HISTORY OF SUBCUTANEOUS GAS POCKETS. Robert Tucker* and S. M. Tenney. Dept. of Physiology, Dartmouth Medical School, Hanover, N. H.

The subcutaneous gas pocket represents an *in vivo* tonometry system useful to the study of respiratory gas exchange. In air breathing animals, the history of pockets of foreign, inert gases is complicated by the simultaneous influx of nitrogen and efflux of the foreign gas. The ratio of these two rate processes is the important determinant, and its value can be predicted from the physical properties of the gases and physiological characteristics of the pocket wall. Differential equations were set up and solved in terms of parameters which could be evaluated with a high speed computer. With these results, theoretical curves of volume as a function of time were constructed for a variety of foreign gases and conditions, and these were then compared with experimental results in rats using the following foreign gases: Argon, Nitrogen, Hydrogen, Helium, Nitrous Oxide, Cyclopropane, and Sulfur Hexafluoride. The theoretical curves provided a satisfactory fit of the data in all cases if correction was made for initial influx of CO_2 and O_2, and an assumption was made about changing surface:volume ratio of the pocket. The relative importance of diffusion and perfusion to the exchange process could be evaluated in each case. [Supported by P.H.S. Grant HE-02888-08]

ACTIVITY OF LARYNGEAL MUSCLES ELICITED BY HEMORRHAGE AND VASODILATATION
J. K. Turner (intr. by H. L. Batsel) V. A. Hospital, Long Beach, California and Department of Physiology, U. C. L. A.

Evidence from previous studies with dogs under pentobarbital indicates that steady state activity of abdominal muscles is reflexly elicited by reduction in volume of blood in the low pressure portion of the cardiovascular system (Am. J. Phys. Med. 42: 1, 1963). In studies described here activity of the sphincteric portion of the larynx during bleeding and administration of nitroglycerin was studied in conscious dogs and in dogs lightly narcotized with thiopental or methohexital. Removal of blood or administration of nitroglycerin first elicited a selective lengthening of the expiratory phase and steady state contractions of abdominal muscles. With additional bleeding or nitroglycerin, a closure of the glottis was elicited. As a result of this activity of the laryngeal muscles, expulsion of air was slowed and intra-abdominal, intrapleural, and intrapulmonic pressures showed similar and nearly equal rises during the prolonged expiratory phase. The significance of this laryngeal activity would seem to be in its effecting an equalization of distribution of pressure generated by trunk compressing muscles and in the effects of this pressure upon capacity of vasculature of the thoracic and abdominal cavities. That activity of the abdominal and laryngeal muscles have profound effects on cardiac filling is indicated by experiments with lightly narcotized dogs. While administration of gallamine triethiodide has little effect on arterial pressure in animals showing no activity of abdominal muscles it produces a profound drop in animals when this activity is present.

HYPOTENSION EVOKED BY STIMULATION OF THE MEDULLA OF THE COMATOSE CAT. Richard S. Tuttle, Masonic Medical Research Laboratory, Utica, N.Y.

In the comatose cat preparation, a brief period of stimulation of the medulla in the region of the calamus scriptorius causes a severe and prolonged hypotension, far outlasting the period of stimulation and occasionally leading to death. The response was composed of two phases. The initial phase was potentiated by cholinesterase inhibitors and by the infusion of norepinephrine; it was prevented by either atropine or chlorpheniramine (Chlor-Trimeton). The second phase was potentiated by increased vasoconstrictor tone (resulting from carotid occlusion) and was attenuated or prevented when vasomotor tone was reflexly reduced by infusion of norepinephrine. The response appears to consist of an active (cholinergic-histaminergic?) early component, plus a delayed passive component consisting of inhibition of adrenergic vasoconstrictor activity.

Supported by USPHS Grant NB04337-02

RECOVERY OF INTRINSIC ACTIVITY IN ISOLATED PACEMAKERS FOLLOWING OVERDRIVE.[1] J. Ushiyama*, H. H. Lu*, G. Lange and C. McC. Brooks. Department of Physiology, Downstate Medical Center, Brooklyn, New York.

Intracellular recordings were obtained from cells of the isolated sinoatrial node tissues of the cat heart. Different types of intrinsic activities were observed. These varied from rhythmic subthreshold changes in resting potential, occasionally producing spike potentials, to the classical picture of pacemaker activity in which a regular gradually rising diastolic depolarization resulted invariably in propagated action potentials. When typical pacemaker cells were located and their rates of discharge determined,degrees of overdrive were produced by applied stimuli. It was found that after termination of this overdrive a period of quiescence preceded resumption and gradual acceleration of spontaneous pacemaker action. Duration of the postdrive suppression was related to the duration and to the rate of the overdrive. Cells differed considerably in the quantitative aspect of their reactions. In most instances an initial suppression was followed by an acceleration above the pacemaker's resting rate. This was greater at faster rates of overdrive. Longer periods of imposed acceleration prolonged the suppression phase more significantly. It was found that overdrive produced a hyperpolarization of the pacemaker cell during the stimulation. This hyperpolarization persisted following drive, disappearing as pacemaker activity was resumed. Atropine did not abolish the phenomenon. During the period of asystole there was a gradual depolarization, usually exponential in form. On occasion small subthreshold oscillations in potential were recorded before a propagated response was initiated. [1]Supported by a grant PN-5621 from the New York Heart Association.

BEHAVIORAL EVIDENCE FOR DREAMING IN RHESUS MONKEYS. Charles J. Vaughan (Intro. by H. E. King) School of Medicine, University of Pittsburgh, Pittsburgh, Pa.

The simultaneous occurrence of rapid eye movements (REMs) and low-frequency fast activity (LVFA) EEG provides an indication of dreaming in the sleeping man. In the sleeping rhesus monkey both REMs and LVFA have also been observed, but objective behavioral evidence for oneiric activity has been lacking. Rhesus monkeys were placed in restraining chairs and were maintained and trained under continuous white noise and a relatively unchanging visual field. They were avoidance conditioned to bar press continuously (minimum rate of 3000 resp/hr) only when any training stimuli appeared on an otherwise homogeneously illuminated panel. Failure to respond resulted in repeated shocks which were avoided only by bar pressing. The stimuli were chosen to generate an extremely broad stimulus generalization gradient; any of a very wide variety of light points, colors, shapes, scenes, etc. or varying intensities was sufficient to elicit the rapid responding. Following conditioning to criterion four rhesus males had translucent corneal contact lenses applied binoccularly. Within 5-19 hours, and in the absence of any introduced external stimuli, three Ss began responding spontaneously at rates similar to those of their criterion periods when stimuli were introduced. In every instance observed the spontaneous responding was either preceded or accompanied by closed eye movements. Both slow eye movements (SEMs) and REMs were observed but REMs were associated with spontaneous responding and characteristic facial movements. It appears that some kind of dream activity had occurred giving rise to the same type of responding which the animals had been previously conditioned to perform only in the presence of actual visual stimuli.

A SEALED SYSTEM FOR CHRONIC RECORDINGS OF CSF PRESSURES IN THE AMBULATORY OR ANESTHETIZED ANIMAL.

J. Verdura, M.D.*, R. J. White, M.D., Ph.D. and M. Albin, M.D.*
Section of Neurosurgery, Cleveland Metropolitan General Hospital and Western Reserve University School of Medicine, Cleveland, Ohio.

We have developed a method for measurements and recordings of cerebrospinal fluid (CSF) pressures for protracted periods of time in the awake unrestrained animal. A small silicone rubber tube is introduced into the subarachnoid space immediately beneath the brain stem via a small perforation in the ventral surface of the occipital bone near the foramen magnum. A sealed watertight system results from fixing the tube in the bony opening with an adhesive, methyl-2-cyanoacrylate, and leading the catheter to the skin surface. The cutaneous end of the catheter is sealed with a rubber diaphragm which needs only to be punctured to permit recording of CSF pressures. Using a venous pressure strain gauge transducer connected to an oscillographic recorder CSF pressure has been repeatedly measured in 20 dogs in whom silicone rubber catheters were chronically implanted for periods ranging up to 3 months. Records were obtained in the awake unrestrained state as well as under anesthesia with and without assisted respiration. In addition, changes in CSF pressures were studied during acute airway obstruction. The average CSF pressure measured in the awake, ambulatory unrestrained animal was between 135-150 mm.H_2O; during barking or straining the values rose from 60-80 mm.H_2O above baseline. Under pentobarbital anesthesia with spontaneous respiration the average CSF pressure values ranged between 109-122 mm.H_2O. With acute complete tracheal obstruction CSF pressure rose to 400-475 mm.H_2O within one minute. No evidence of infection or damage to contiguous brain structures was observed in the ten animals autopsied. Supported by NIH Grants NB 03859-02 and NB 03859-02S1.

ADRENAL CORTICOIDS AND VASCULAR REACTIVITY DURING RECOVERY FROM SURGERY

Veselin Vujovic, M.D.*, Misa Albrecht, M.D.* & G.H.A. Clowes, Jr., M.D.
Medical College of South Carolina, Charleston, South Carolina

Further to understand the importance of adrenal cortical hormones in recovery from the stress of surgical procedures, the postoperative hemodynamic and metabolic patterns of adrenalectomized dogs were compared with those of intact controls and with adrenalectomized animals given various forms of substitute therapy. Cardiac output determinations, blood pressure measurements, and blood sampling for gasses and electrolytes were done serially without pain in conscious animals before and after bilateral flank adrenalectomy incisions. The 11 untreated adrenalectomized animals died between six and 25 hours postoperatively. The cardiac output declined to 60% of the basal value at three hours and to 20% just before death. Although there was little change in central venous pressure, the arterial blood pressure fell proportionately to the output with little evidence of increased peripheral vascular resistance. The average blood potassium concentration rose terminally to 6±1mEq/L with little change in sodium. The buffer base deficit increased to 11 mEq/L, but was compensated by a pCO_2 of 26 mm Hg until the terminal period when it rose somewhat. Ten adrenalectomized animals treated with infusion of glucose and water and ten given glucose and saline solution survived for slightly longer periods. They exhibited the same vascular and metabolic behavior as untreated animals. The administration of DOCA to 14 animals altered the course but little. Two which drank water survived two and five days respectively. The remainder died within 15 hours. By contrast, the 12 animals given hydrocortisone 1 mgm/kg wt/24 hours behaved similarly to the 12 sham operated control dogs. Their cardiac outputs were slightly lower but remained near the basal preoperative values.

THE CIRCULATORY EFFECTS OF PULMONARY ARTERIOVENOUS FISTULAE. John A. Waldhausen* and Francis L. Abel. Depts. of Surgery and Physiology and the Heart Research Center, Indiana Univ. Sch. of Med., Indianapolis, Indiana.

The acute effects of pulmonary arteriovenous fistulae on cardiac output and pulmonary vascular resistance were studied in eleven dogs. Fistulae were made between the pulmonary artery and left atrial appendage. Cardiac output and fistula flow were simultaneously measured using an electromagnetic flowmeter. Pressures were recorded in the left atrium, pulmonary artery and aorta. In 14 experiments cardiac output increased by only 11% in response to opening a 7 mm I.D. pulmonary arteriovenous fistula carrying an average of 30% of the right heart output. However, left atrial pressure rose by 44% in response to opening the fistula and resistance of the pulmonary bed (excluding fistula flow) decreased by 13%. Following denervation of the lungs, pulmonary vascular resistance increased by 22% (excluding fistula flow) when the 7 mm I.D. fistula was opened. Fistula flow now was 55% of cardiac output which increased by 46% in response to opening the fistula. Left atrial pressure increased by 111%. Clamping the right pulmonary artery tended to merely accentuate the changes seen in both the normal and denervated lungs. These studies suggest that the response to opening a pulmonary arteriovenous fistula differs from that to a systemic one in that pulmonary vascular resistance decreases and cardiac output increases only slightly. However, in the denervated lung the response appears similar to that with a systemic fistula, showing a greater increase in cardiac output accompanied by an increase in pulmonary resistance.

CONTRACTILITY AND FINE STRUCTURES IN TENOTOMIZED RAT MUSCLE. S. M. Walker, G. R. Schrodt*, X. T. Truong*, and B. J. Wall*. Depts. of Physiology and Pathology, Univ. of Louisville School of Med., Louisville, Ky.

After 2 to 4 weeks of tenotomy gastrocnemius muscles of mature rats show a 50 to 60% decrease of contractility and a small percentage of lesions usually located near the center of the muscle fibers. These lesions are about 4 to 10 μ in diameter and 10 to 40 μ in length with the long axis situated parallel to the long axis of the fiber. Electron micrographs of the lesions reveal remnants of myofilaments and sacroplasmic reticulum in various states of dislocation and degeneration. In some cases the sarcoplasmic reticulum is completely absent in the center of the lesions and dislocated in the peripheral border. A rather sharp line of demarcation separates the lesions from apparently normal muscle. This line of demarcation shows a change of appearance in fine structures rather than a separation or break of these structures. Glycogen granules appear to be more numerous in tenotomized than in normal muscle. The glycogen granules in normal and tenotomized muscle are frequently attached by densely stained stems to membranes of the sarcoplasmic reticulum. It is concluded (1) that lesions formed in tenotomized muscle do not appear to be sufficient in quantity to account for the marked decrease of contractility, (2) that lesion formation is an insidious process not involving a break between normal and abnormal fine structures, and (3) that structural connections may exist between the membranes of sarcoplasmic reticulum and glycogen granules. (Aided by USPHS (NIH) Grant HE-00697-14S1 and by NSF Grant GB-2009.)

THE EFFECT OF CHANGES OF THE IONIC ENVIRONMENT UPON THE RUBIDIUM LOSS FROM FROG SARTORIUS MUSCLES. Raymond R. Walsh and Alexander J. Montoya*. Department of Physiology, University of Colorado School of Medicine, Denver, Colorado.

In order to evaluate the relative rates of loss of rubidium from frog sartorii, desaturation data were obtained from muscles that had been previously incubated in Ringer's solutions containing trace amounts of Rb-86. Increasing $(K^+)_o$ from 2.4 to 34.0 meq/L accelerates the rate of rubidium loss from muscle. Up to 34.0 meq/L there is a fairly direct relationship between the desaturation rate and $(K^+)_o$ -- and, presumably, the degree of membrane depolarization. Varying the $(Ca^{++})_o$ from 0 to 3.2 meq/L does not significantly alter the increased rubidium efflux which is brought about by increasing $(K^+)_o$. Thus, within the concentration limits specified, the loss of rubidium from muscle is a function of $(K^+)_o$ and is very nearly independent of $(Ca^{++})_o$. The foregoing is consistent with the concept that the principle impediment to the efflux of a cation from frog sartorius muscle is the electrical field associated with the transmembrane potential. Increasing $(K^+)_o$ above 34.0 meq/L does not further increase the rate of rubidium loss. This suggests that, as the membrane is appreciably depolarized, the electrical field consequences of the transmembrane potential no longer provide the chief impediment to the efflux of rubidium. An additional consideration is that the structural integrity or "functional porosity" of the membrane might be substantially altered by higher levels of potassium in the external medium.

(Supported by USPHS Grant No. NB 02772)

ELECTRODERMAL REFLEX OF NONANESTHETIZED NORMAL CATS UNDER DIFFERENT AMBIENT TEMPERATURES. G.H. Wang, Lab. of Neurophysiology, Univ. of Wisconsin Med. School, Madison, Wisconsin.

As stated elsewhere (Wang, G.H., The neural control of sweating, 1964, Madison, Wis., Univ. of Wisconsin Press), The amplitude of the electrodermal reflex of even the same nonanesthetized normal cat varies to a great extent from one stimulation to another and from day to day. Recently we have, however, found that the amplitude of the reflex is definitely decreased, both when the ambient temperature is raised from 25° to 40° C and when it is lowered from 25° to 10° C. The latency of the reflex is slightly shorter at 40° C, and much longer at 10° C, than at 25° C. Our work on the excitatory and inhibitory sweat centers, summarized in the above-mentioned monograph, and our recent observations on the potential waves under different ambient temperatures in the footpads of nonanesthetized striatal, thalamic (Chun,R.W.M. and Wang, G.H., 1963, Fed. Proc., 22:282), and low spinal cats (Wang, G.H., 1964, Fed. Proc., 23:304), suggest that the changes in the amplitude and latency of the electrodermal reflex with ambiant temperatures may be interpreted on the following two assumptions. 1) Ambient temperature of 40° C stimulates both the high excitatory and inhibitory sweat centers, and 2) ambient temperature of 10° C stimulates the higher inhibitory centers alone. (Supported by the NIH grant 732)

THE PHYSIOLOGICAL SIGNIFICANCE OF THE "ANAEROBIC THRESHOLD"
K. Wasserman, G.G. Burton* and A.L. Van Kessel* Respiratory Function Lab., Stanford Medical Center, Palo Alto, California.

The "Anaerobic Threshold" defined as the work level (oxygen consumption) above which the subject develops metabolic acidosis, was measured from the increase in the ventilatory respiratory quotient (R) during graded cycle ergometer exercise in ten normal subjects. Each subject was re-studied on another day at three different fixed work levels for 50 minutes or until he could no longer continue the exercise. Two hour rest intervals separated each level. The lowest work load was just below the anaerobic threshold, the medium and high loads were approximately 700 and 1500 ml. oxygen consumption/min. above the low, respectively. The order of performance was random. All subjects were able to complete the sub-threshold work load without difficulty while only 40% were able to complete the medium and none were able to complete the high work load for the 50 minute period. An early "steady state" in ventilation, heart rate and oxygen consumption could only be achieved at the sub-threshold level. R remained constant during the entire 50 minutes of the sub-threshold load except for the first few minutes when there was transient hypoventilation. For the work loads above the anaerobic threshold, R increased to a maximum in 4 minutes and subsequently decreased to a constant value. The increase in R correlated with the rate of increase in blood lactate and decrease in serum bicarbonate. The oxygen debt was relatively small following the sub-threshold work load and was paid back within a few minutes. In contrast the oxygen debt at heavier work loads was large and required more than 30 minutes for repayment. These studies indicate that the anaerobic threshold is a level of work below which a subject can exercise for prolonged periods in a steady state without developing metabolic acidosis. (Supported by P.H.S., Grant no. 06591)

NORMALIZATION OF FROG SKIN ELECTRICAL IMPEDANCE. Don W. Watkins* and Warren H. Dennis. Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Investigation of the electrical impedance of active tissues led Cole and co-workers to conclude that the limiting membrane of cells could be represented electrically by a pure resistance shunted by a polarization element. The polarization element is a reactive element characterized by a constant phase angle. The impedance locus of these tissues are the arcs of circles. Cole showed for Nitella and the squid axon that activity changed only the resistance. Hodgkin showed that changes in the time constant of squid axon produced by changes in the external potassium indicated that only the pure resistance changed. Cole's polarization theory has been extended to show that normalization of the impedance results in a circular arc dependent solely on the polarization element. This technique has been applied to frog skin under a variety of conditions. With four-fold changes in the low frequency impedance during the recovery period after mounting and the changes produced by the application of copper ion, the normalization procedure results in a single circular arc. These results show that these impedance changes occur as the result of changes in the pure resistance only and that the polarization element is unchanged.

LOCAL AND SYSTEMIC EFFECTS OF EPINEPHRINE IN FROG. C. O. Watlington*, P. K. Burke and E. G. Huf. Medical College of Virginia, Richmond Virginia.

In this study attention is called to the fact that urethanized frogs (Rana pipiens) were very sensitive to small doses, and yet extremely tolerant to massive doses of epinephrine (E). Physiological responses could be elicited with a few ug of E when given intravenously. One or two ug of E., e.g. brought about noticeable changes in the dynamics of the frog heart. I.V. injection of 7.5 ug of E lead to in vivo changes in skin P.D. and short circuit current. The P.D. decreased, and the current showed a transient rise and fall to the original level, or below it. - One mg or more of E produced more pronounced effects on heart and skin. The mucous glands were found empty shortly after E, but they partly refilled later in spite of continued E treatment. Consistent skin erythema with sludging in the subepidermal capillary plexus was noted. Blood sugar remained unaltered. Noticeable changes in the ECG occurred with alterations in the V, P and T waves, and in P-Q and S-T intervals. It is noteworthy that no arrhythmia or QRS changes occurred. A variable moderate increase in heart rate was seen in most instances. Total oxygen consumption was elevated for 10 to 15 minutes. These massive doses of E, however, were not lethal to the frog. It is not known why frogs can tolerate E at a dose which, both absolute and relative to body weight, would kill warm blooded mammals, although, in frogs as in mammals, E has its pronounced physiological effects at ug levels. The situation is compared with the known great tolerance of frogs to injections of thyroxine and insulin, although in the latter case, violent convulsions, followed by death of the frog can be produced. (Supported by NIH Grants RG 3545 and AM 6481.)

SECOND DEGREE ATRIO-VENTRICULAR BLOCK IN THE HORSE. C. Watsabaugh*, C. R. Smith, D. L. Smetzer*, and R. L. Hamlin*. Department of Veterinary Physiology and Pharmacology, The Ohio State University, Columbus 10, Ohio.

Second degree atrio-ventricular block occurs in approximately 15% of healthy horses at rest. In unanesthetized horses simultaneous registration of pneumograms, electrocardiograms, and carotid and pulmonary artery pressures demonstrated a direct relationship between cyclic variation in carotid artery pressure and blocked ventricular beats. Carotid pressure rises in step-wise fashion over three or more ventricular beats, block occurs, carotid pressure falls, and is followed by a repetition of the sequence. No simple relationship between block and phases of respiration is evident. Block appears to be the result of variations in vagal tone induced reflexly via fluctuations in arterial blood pressure. Pressure in the pulmonary artery fluctuates with the phases of respiration.

REVERSIBILITY OF HEMORRHAGIC SHOCK FOLLOWING TREATMENT WITH CORTICOSTEROID. Max H. Weil and Howard Whigham*. Dept. of Med., Univ. of So. Calif. School of Med., Los Angeles, Calif.

Adrenal cortical hormones are effective for the treatment of shock produced by bacterial endotoxins. The purpose of the present study in 120 animals was to define the potential value of these drugs for treatment of late shock following hemorrhage. A femoral artery was cannulated in male Wistar rats weighing an average of 322.3 grams. The cannula was connected to a reservoir maintained at 30 mm Hg. An average of 9.2 (range 8.4 to 11.2) ml bled into the reservoir. Blood was reinfused after 240 minutes. Hydrocortisone phosphate (240 mg/kg), methylprednisolone sodium succinate (40 mg/kg), dexamethasone phosphate (8 mg/kg), d-aldosterone (0.05, 0.1, and 0.2 mg/kg), or saline, each adjusted to a volume of 1 ml, were injected intra-arterially following reinfusion of the blood. After 48 hours only 3 of 30 saline control rats survived, but all 10 rats treated with either hydrocortisone or dexamethasone survived ($p < 0.001$). Significantly better results were obtained with dexamethasone than with hydrocortisone in terms of early alertness and survival at the end of 7 days ($p < 0.01$). Ten of 20 animals treated with methylprednisolone survived ($p < 0.01$). The largest of the three doses of d-aldosterone gave the best results with survival of 6 of 10 rats ($p < 0.03$). This investigation demonstrates that corticosteroids effectively improve survival in experimental hemorrhagic shock. As in the case of endotoxin shock, best results were achieved with pharmacological doses of glucocorticoid. (Supported by The John A. Hartford Foundation and the USPHS Grants HE 05570 and HE 07811.)

A THEORETICAL ANALYSIS OF THE INDICATOR DILUTION CURVE YIELDING CIRCULATING BLOOD VOLUMES. H. Weinstein, R. Anderson, T. J. Fitzgerald, H. Weisberg, and A. B. Shaffer. (intr. by L. N. Katz) Dept. of Chemical Engineering, Illinois Institute of Technology and Cardiovascular Institute, Michael Reese Hospital and Medical Center, Chicago, Illinois 60616.

A new method of analyzing dilution curves is presented. The analysis is developed for a recirculating system and therefore makes use of the entire curve. Blood volume and mean transit time are determined from sampling to injection site and vice versa, making possible the measurement of circulating blood volume from a standard dilution curve. The model uses the principles of Chemical Reaction Engineering. A system is hypothesized consisting of perfect delays and perfect mixers in series with complete feedback or recirculation. Five units are employed necessitating evaluation of five parameters from the circulation curve, which are time constants of the units. The response of the model system to slug injection of dye closely resembles the experimental curve. When the model response is fitted to the experimental curve the values for the time constants of the model are used to obtain the mean transit times and blood volumes. In preliminary testing, circulating blood volumes as calculated from dilution curves in normal man, fell within the predicted range. The modeling technique and analysis presented are only first steps in using this concept to evaluate circulation curves. The methodology is ideally suited to analog computation and such computers would enable analysis of a circulation curve in minutes. It may also be possible to extend this technique to analyze flow in various major organs of animals and man.

THE EFFECT OF INSPIRATORY AND EXPIRATORY LOADS ON THE CO_2 RESPONSE CURVE OF BIRDS. Stephen A. Weinstein, Stanley Freedman, and Bruce Northrup (intr. by John T. Fales), The Johns Hopkins University, Baltimore, Md.

Eldridge and Davis, Cherniack and Snidal, and Milic-Emili have demonstrated a depression of the slope of the CO_2 response curve in the presence of either inspiratory or expiratory loads in man. The present studies were performed on 8 pigeons to determine the effects of inspiratory or expiratory loads on the CO_2 response curves of birds. Continuous pressures of plus 10 or minus 10 mm. Hg, were applied around the bird's body, the head being exposed to atmospheric pressure. Thus, in each condition, one phase of respiration was loaded and the other facilitated. Inspiratory loading (positive pressure around the chest) produced a depression of respiratory frequency and tidal volume, and consequently a depression of the CO_2 response curve. Expiratory loading (negative pressure around the chest) produced no change in tidal volume or respiratory frequency and hence did not alter the slope of the CO_2 response curve.

ANTIRENIN IN THE DETERMINATION OF THE ROLE OF RENIN IN RENAL HYPERTENSION IN THE RAT. R. Weiser* and S.W. Hoobler. Dept. of Int. Med., The University of Michigan, Ann Arbor, Michigan.

A substance** produced in dogs in response to hog renin has been shown, in the following ways, to be an effective renin antibody in rats: 1) The pressor response of the rat to the injection of an incubated mixture of rat renin and plasma was blocked by the addition of this substance to the incubation mixture. 2) The pressor response of the rat to rat renin injected i.v. was blocked when the antirenin substance was mixed with the injected renin. 3) The elevation of blood pressure maintained by constant infusion of exogenous renin in the rat was reduced to near control levels after injection of antirenin. 4) In the rat the elevated blood pressure caused by endogenous renin released by removing clamps which had blocked the renal pedicles, was effectively lowered by injection of antirenin. The antirenin did not induce a non-specific depressor effect, and it was further established that the antirenin was not exercising its effect on angiotensin since the antirenin did not block the pressor response of the rat to angiotensin. Though this antirenin was found to be effective in blocking renin activity, it did not reduce the elevated blood pressure of rats made chronically hypertensive (4 to 14 weeks) by the Goldblatt method. These results indicate, then, that renin is not the factor primarily responsible for the elevated blood pressure of the chronic renal hypertensive rat.

** Kindly supplied by Dr. A.G. Johnson, University of Michigan

(Supported by grant HE-02578 from the National Institutes of Health. Richard Weiser is a Trainee, on the Cardiovascular Research Training Program, HTS-5465, National Institutes of Health.)

EVIDENCE CONCERNING MECHANISMS IN THE RENAL RESPONSES TO ACUTE INTRAVASCULAR VOLUME EXPANSION. M.L.Weisfeldt*, A.R.Ugel* and J.P.Gilmore. Lab. Cardiovasc. Physiol. National Heart Institute, Bethesda, Maryland.

The influence of carotid sinus denervation or vagotomy upon the renal responses to the intravenous administration of 6 per cent clinical dextran in an amount equal to 3 per cent body weight has been studied in the anesthetized dog. In the intact animal dextran produced a substantial increase in urine flow, sodium and osmolar excretion, and endogenous creatinine clearance. Eight of the 11 animals in this group showed a U/Posm of one or less following dextran infusion. The diuresis was significantly less in the vagotomized and carotid denervated groups while the increase in sodium excretion and creatinine clearance was not significantly different from that found in the intact animals. Three of the 10 vagotomized and 1 of the 9 carotid denervated animals showed a U/Posm of one or less following dextran infusion. Little diuresis or natriuresis occurred in intact animals in which hemodilution was produced by an equal exchange of dextran and blood. The data are consistent with the position that receptors in the left atrium, carotid sinus and aortic arch can influence free water excretion. The receptors in the carotid sinus and aortic arch may exert their influence primarily under conditions of acute hypovolemia whereas those in the atrium under conditions of hypervolemia. The experiments also indicate that the natriuresis is (1) not secondary to dilution of a circulating hormone; (2) not secondary to a change in renal blood flow distribution resulting from a decline in hematocrit; (3) not dependent upon the integrity of the vagi or carotid sinus nerves and thus not mediated via receptors in the carotid sinus, aortic arch, atria, or ventricles. The natriuresis appears to be best explained by a change in glomerular filtration rate.

THE REACTIVE COMPONENT OF IMPEDANCE DURING SPREADING DEPRESSION AND ANOXIA IN RELATION TO OHMIC RESISTANCE, DC POTENTIAL, EEG AND SURFACE TEMPERATURE OF THE CORTEX. T. Weiss*, R. T. Kado* and W. R. Adey. Dept. of Anatomy and Brain Research Institute, Univ. of California, Los Angeles.

The reactive and resistive components of impedance were recorded from the exposed neocortex of anesthetized (pentobarbital sodium 50 mg/Kg) or locally anesthetized and immobilized (gallamine triethiodide) rats in acute experiments using microvolt signals at 1000 c/sec together with cortical DC potential levels, EEG and temperature. The resistive impedance component increased in the majority of cases during spreading depression, as previously shown by others. However, the reactive component regularly showed a reversible decrease in this condition. Its duration corresponded well with the depression of spontaneous EEG activity, but lasted in the majority of cases longer than the electronegative shift of DC potential recorded from an adjacent region. Sometimes a dissociation between the occurrence of the DC potential and impedance shifts was observed. The phase relationships between different parameters of spreading depression were analyzed. A drop in the reactive component was also observed during anoxia. The decrease in reactive impedance may arise from decreased ionic concentration gradients on the neuron membranes occurring in both situations.

EFFECTS OF REPETITIVE CONTRACTION RATE ON GLYCOGEN METABOLISM IN PERFUSED, ISOLATED DIAPHRAGM. George W. Wermers, * H. Mead Cavert, James D. Harris * and Carril F. Quello. * Physiol. Dept., Univ. of Minn., Minneapolis

The effects of muscle contraction on glycogen metabolism were studied in the perfused, "intact" diaphragm muscle of the fasted rat. This isolated muscle preparation is perfused in a retrograde manner through the inferior vena cava with a Krebs-Ringer bicarbonate solution containing glucose-U-C^{14} (100 mg%) and insulin (0.5 units per ml.) at 37°C. All muscles were preperfused for 15 minutes prior to the 60 minute perfusion period. A control glycogen value of 1.24 mg per gm of wet weight was obtained for muscles which had been preperfused only. Muscles contracting at rates of 1 or 2 times per second exhibited final glycogen values of 4.45 (N = 16) and 4.70 (N = 5) mg per gm of wet weight, respectively. The final glycogen value obtained for resting muscles (N = 9) was 4.97 mg per gm wet weight. The glycogen radioactive data obtained from resting and contracting muscle indicate that the glycogen increase, found when glucose and insulin are present, is due to synthesis of new glycogen with apparently little or no turnover of initial, preformed glycogen. Muscles contracting 5 times per second show a final glycogen content of 1.44 mg per gm; not significantly different from the control level. However, the radioactivity found in glycogen isolated from these rapidly-contracting muscles indicates a replacement of about 40% of the control glycogen by new glycogen formed from medium glucose-C^{14}. (Supported by USPHS Grant GM-07305)

INTESTINAL ABSORPTION OF SUGAR AND EFFECTS OF Co^{60} IRRADIATION IN GROUND SQUIRREL, CITELLUS TRIDECEMLINEATUS. D.D. Westhoff* and X. J. Musacchia, Dept. of Biology, St. Louis Univ., St. Louis, Mo.

Sacs of everted duodenum, jejunum, and ileum were incubated (in vitro) in Warburg flasks, and measurements of sugar absorption, transfer, and oxygen consumption were made. Incubation for 30 minutes in an isotonic TRIS-saline medium with 100 mg% D-glucose initially present on the mucosal and serosal sides of the sac was selected as the basic experimental procedure. Intestinal preparations were made from non-hibernating, 0 - 48 hours post-hibernation, and irradiated (Co^{60} whole body, 1000r) squirrels. Results indicate that: (1) duodenal and jejunal segments made from animals 12 hours post-hibernation have a greater ability for mucosal absorption than those from active animals, (in micromoles/gm dry wt/30 min, 219.6 and 125.6 compared with 96.9 and 99.8 respectively); (2) oxygen consumption is greatest in all intestinal areas in animals 48 hours post-hibernation and least in animals immediately upon arousal, (micromoles/gm dry wt/30 min, 21.7 vs. 51.3 (duodenum), 13.5 vs. 54.0 (jejunum), and 21.8 vs. 48.1 (ileum); (3) in terms of oxygen consumption/micromole glucose absorbed, values from various animals were comparable; (4) although there is variation, oxygen consumption and final serosal concentration show some direct relationship; (5) following irradiation, typical values for middle and lower segments were, respectively, 8.5 and 20.2 micromoles/gm dry wt/30 min (10 days), and 3.4 and 13.6 micromoles/gm dry wt/30 min, (28 days); (6) phlorizin inhibits transfer of D-glucose in intestinal sacs taken from both active and hibernating squirrels. (Supported by NASA Grant NsG 271.)

APPLICATION OF LUNG LAVAGE TO PROBLEMS OF DIFFUSION, MIXING, AND WASHING IN A FLUID FILLED LOBE. Rita Wetton* and Arthur B. DuBois. Dept. of Physiol., Grad. Sch. Med., Univ. of Pa., Philadelphia, Pa.

A modification of the technique employed by Kylstra in lavaging one lobe of one lung of a dog was used to evaluate the following: 1. The alveolo-capillary transfer of antibiotic (sodium oxacillin) when given systemically and when placed in the fluid filled lobe. 2. The effectiveness of mixing in the fluid filled lobe. 3. The transfer of CO_2 from the blood to the fluid filled lobe. 4. The uptake of O_2 from the fluid filled lobe. 5. The effectiveness of removing or "washing out" the surface-active material. The basic solution used in all experiments was 1.5% Glucose in 0.9% NaCl. The following results were obtained. When the antibiotic solution was placed in the lobe the concentration of oxacillin remained at high levels (2,500 -15,000 mcg/cc) compared with circulating blood levels of 1-3 mcg/cc (courtesy of E. L. Foltz) over the four hour test period. When oxacillin was given intravenously the blood levels reached peak values (50-60 mcg/cc)in five minutes and had dropped below 5 mcg/cc in one to two hours. The concentration in the fluid filled lobe did not exceed 6 mcg/cc during the test period. Concentrated dye (T-1824) was introduced into the fluid filled lobe and showed poor distribution in thirty seconds and uniform distribution in two minutes. O_2 equilibrated CO_2-free solution was introduced and showed a sharp fall of O_2 and rise of CO_2 in the fluid. By flushing the basic solution in and out of the lobe it was possible to "wash out" some of the surface-active material. The technique is innocuous to the animal and the same dog can be used repeatedly. The technique is useful for evaluating diffusion, mixing, and "washing" in a fluid-filled system and may ultimately have therapeutic applications (i.e. exposure of lung tissues to chemical and biologic agents).

VENTRICULAR OUTPUT IN THE IGUANA. F. N. White* and R. R. Sonnenschein. Department of Physiology, UCLA

Flow in the pulmonary artery, right and left systemic arches and common aorta were measured with the electromagnetic flow meter in specimens of Iguana iguana (1.5-2.2 Kg) under Tricaine anesthesia at 23-25°C body temperature. Pressure was measured in the femoral artery throughout, and occasionally in the pulmonary artery and systemic arches. Cardiac output (sum of flows in pulmonary artery and systemic arches) ranged from 17 to 37 ml/min/Kg; heart rate 36-54/min; total ventricular stroke volume 1.2 to 2.1 ml. Distribution between the pulmonary and systemic circuits was variable; the former could exceed, equal or be less than the latter. Similarly, the right and left arch flows could equal or differ from each other. Occlusion of any of the three major vessels led to redistribution between the remaining two. It is evident that, contrary to Ewer's statement (Amer. Naturalist 84:215-220, 1950), the pulmonary circuit can accomodate a flow equal to or greater than the systemic flow. (Supported by NSF Grant GB-923).

HYPOTHERMIC BRAIN STORAGE WITH ELECTRICAL AND METABOLIC RECOVERY
R. J. White, M.D., Ph.D., J. Verdura, M.D.*, M. Albin, M.D.*, and H. Brown, M.D.*. Section of Neurosurgery, Cleveland Metropolitan General Hospital; Western Reserve University School of Medicine, Cleveland Ohio.

These experiments were designed to examine the possibilities of prolonged survival of cerebral tissue deprived of blood supply at extremely low temperatures.

In 20 anesthetized, heparinized dogs, the brain was vascularly isolated from the body but neurogenically connected via the vagi and spinal cord. Following heparinization (3 mgm./kg. body wt.) the brain was cooled to intracerebral temperatures of 6-8°C. within 25-30 minutes by pumping blood from a femoral artery through a miniature heat exchanger to T-cannulae placed in the carotid arteries. To facilitate cooling, extensive bilateral craniectomies were performed and the dura covered with sterile snow. At cardiac arrest, further reductions in brain temperatures were accomplished by perfusing the carotid system with 300 cc. of 0°C. heparinized Ringer Lactate solution. The cord was ligated and divided and the brain was stored at 3°C. in a humidified refrigerator for periods of 2, 4, 8 and 12 hours. An identical extracorporeal system was used to rewarm the brain utilizing a donor dog. A thermistor and 6 intracerebral electrodes were positioned in brain substance.

Brains stored for 2 and 4 hours demonstrated excellent EEG activity and significant mean A-V O_2 (7.1 vols.%) and V-A CO_2 (5.3 vols.%) above 20°C. After 8 and 12 hours of storage, marked cerebral edema (easily reduced with intra-arterial Urea) developed during rewarming. While no EEG activity could be recorded after 8 hours of storage, A-V O_2 (2.7 vols.%) and V-A CO_2 (1.7 vols.%) differences were measured.
(Supported by NIH Grants #NB 03859-02, #NB 03859-02S1)

BRAIN HYPOTHERMIA BY VENTRICULAR PERFUSION. A.J.Whitty* and P.P.Foà. Division of Research, Sinai Hospital and Department of Physiology and Pharmacology, Wayne State University School of Medicine, Detroit, Michigan.

Total body hypothermia may cause acidosis and profound myocardial changes leading to ventricular fibrillation and necrosis. For this reason, various methods of regional hypothermia have been developed. Cooling of the canine brain was achieved by circulating an artificial cerebrospinal fluid into the lateral ventricles and out through the cisterna magna. At cortical temperatures of 28-30°C, respiration ceased and artificial respiration was begun. At temperatures of 23-25° C, there was marked increase in hematocrit, decrease of systolic, diastolic and pulse pressures, an inversion of the T wave, a decrease in serum K and P_{CO_2} and an increase in blood glucose, pH and O_2 saturation. The latter was attributed to artificial respiration. There was no consistent change in serum Na. In lightly anesthetized dogs, cooling caused a deepening of anesthesia as judged by corneal and other reflexes. It would appear that the most remarkable change due to brain hypothermia is respiratory arrest, immediately reversible upon rewarming. This procedure appears to avoid cardiac difficulties and profound metabolic changes typical of total body hypothermia.

	Blood					Serum	
	Hematocrit	O_2 sat.	pH	P_{CO_2}	Glucose	Na	K
	%	%		mmHg	mg%	mEq/L	mEq/L
Control	41.5	91.7	7.27	54	88	152	4.2
Hypothermia	51.5	97.6	7.47	26	109	150	3.4

RECEPTIVE FIELDS OF MONKEY GENICULATE CELLS IN THE DARK ADAPTED STATE. T.N.Wiesel & D.H.Hubel. Dept. of Pharm.,Harvard Med. School, Boston.

Twelve cells in the dorsal layers of the lateral geniculate body of the Rhesus monkey were examined with monochromatic light-spot stimulation in both the light and dark adapted state. All cells had their receptive fields 3° to 18° from the fovea. Four cells with opponent-color center-surround receptive fields showed an increase in the sensitivity of the center responses by about 3 log units; the peak spectral sensitivity of the center responses came to lie at about 500-520 mu,instead of at 540 or 580 mu in the light adapted state. The opposing surround showed no corresponding increase in sensitivity. Hence in the scotopic state at threshold levels these cells showed no opponent color mechanism, the spectral sensitivity was similar to that of rhodopsin, and the field had no center-periphery arrangement. These cells thus seemed to be supplied by both rods and cones; the rods seemed to play little part in the responses in the light adapted state, but dominated the responses at low intensities in the scotopic situation.In 6 other cells,also ones with opponent-color center-surround receptive fields, the threshold of both on- and off-components fell with full dark adaptation by only 1-1.5 log units, and there was little or no change in spectral sensitivity. This would be expected under our experimental conditions if all receptors supplying these cells were cones. Of the other type of opponent-color cell, in which the two antagonistic components had the same spatial distribution(i.e.,overlapped completely), only two were studied in the dark-adapted state. These seemed to receive input from cones only, since they showed only a moderate decrease in threshold and no change in spectral sensitivity of the two components. In summary, some geniculate cells appear to be connected to both rods and cones, others to cones only.

Roentgen Videodensitometric Study of Efficacy of Mitral Valve Closure in Dogs Without Thoracotomy. J. C. P. Williams*, T. P. B. O'Donovan*, R. E. Sturm* and E. H. Wood. Mayo Clinic, Mayo Foundation, Rochester, Minn.

Dogs under anesthesia and IPP respiration were positioned for fluoroscopy in a half-body cast so that the mitral-valve ring was parallel to the x-rays (modified left posterior oblique). Renovist (4 ml. 69%) was injected into the left ventricle (LV) through a spray-tip #5 catheter and angiograms recorded on videotape while the atria and ventricles were driven at constant rate by coupled pacemakers. Vagal "tone" was varied by bilateral stimulation of the distal vagi after section in the neck. Roentgenovideodensographic dilution curves (Fed. Proc. 23:303, 1964) were recorded from a 5x6 mm. sampling window juxtaposed to the mitral valve 2 and 5 mm. upstream (over the left atrium (LA)) and downstream (over the LV). The efficacy of valve closure during effective atrial contraction, EAC, (A-V stimulus interval: 0.05-0.14 sec.) and "ineffective" atrial contraction, IAC, (A-V interval: -0.003 sec.) was assessed as the regurgitant index: ratio of areas under immediately appearing portion of simultaneous LA and LV curves. In the control state, i.e. no vagal tone, and pacing about 15 beats above spontaneous rate of 105 to 185 beats/min., slight regurgitation was usually seen in dogs with EAC. During IAC, regurgitation was unchanged or slightly increased. At this paced rate, moderate and severe vagal stimulation (sinus rates below 90 and 60) had no systematic effect on regurgitation with EAC but usually increased any regurgitation with IAC. When, during the control state, severe circulatory depression was produced with pentobarbital, regurgitation increased during EAC, and still more during IAC, in proportion to the severity of hypotension. In unpaced dogs at slow sinus rates induced by vagal stimulation, the regurgitant index increased due mainly to retrograde flow in diastole. (Supported in part by research grants: NIH H-3532, NASA NsG-327, AHA CI 10, and BNZ.)

CHRONIC TOTAL EXTRINSIC DENERVATION OF THE HEART IN PRIMATES. V.L. Willman*, C.R. Hanlon*, G.C. Kaiser* and T. Cooper. Department of Surgery, St. Louis Univ. and St. Louis Univ. Surgical Service, V.A. Hospital, St. Louis, Mo.

In preparation for homotransplantation of the heart in sub-human primates, we have studied circulatory performance in eight normal baboons and three baboons after total extrinsic cardiac denervation. Denervation was accomplished by mediastinal neural ablation in two animals, and by excision and reimplantation (autotransplantation) of the heart in one. Under light anesthesia, cardiac output (CO) in 4 normal females (9-12 kg) averaged 0.15 l/kg; heart rate (HR) 115/min; blood pressure (BP) 145/95 mmHg; stroke volume (SV) 13.8 ml; blood volume (BV) 65 ml/kg and hematocrit (HT) 39%. In 4 normal males (16-24 kg), CO averaged 0.12 l/kg; HR 82/min; BP 150/100 mmHg; SV 30.4 ml; BV 62.4 ml/kg and HT 49%. After cardiac denervation, the baboons showed hemodilution (BV 76 and 116 ml/kg; HT 29 and 33) and weight gain in spite of reduced appetite. CO remained in normal range, although SV was depressed (30%) and HR elevated (25%) during the phase of water retention. Completeness of the denervation was demonstrated by a fall in myocardial catecholamine content to zero and lack of response to intravenously administered tyramine. Thoracotomy and mediastinal dissection were well tolerated. These studies demonstrate the capacity of the primate heart for adaptation to loss of extrinsic nervous regulation and define problems associated with loss of innervation in cardiac transplant.

Aided by grants from the John A. Hartford Foundation and USPHS.

SIMULTANEOUS MEASUREMENTS OF HEART RATE AND DEEP BODY TEMPERATURE FOR PROLONGED PERIODS OF TIME IN GALLUS DOMESTICUS. C. M. Winget and T. B. Fryer (intr. by E. Ogden). NASA, Ames Research Center, Moffett Field, California.

A reliable and versatile system for measuring heart rate and deep body temperature over relatively long periods of time (approximately 90 days) has been developed and evaluated for class Aves. A subcarrier modulated telemetry system is used to transmit the temperature and heart rate data from the animal. Details of the electronic system will be published later (Fryer, in preparation). Placement of the sensors was found to be critical and to obtain maximum voltage response (approximately 1 mv) for heart rate measurements each bird was individually evaluated. A thermister (0.10 cm. dia.) along with the transmitter was sutured to the sternum through an abdominal incision of approximately 8 cm. in length. The periodicity of the data was evaluated by: 1) Fourier analysis; 2) Schuster's periodogram; 3) Correlogram.

A COMPARISON OF THE MECHANICAL PROPERTIES OF IN VIVO AND EXCISED DOG LUNGS. M.E.B. Wohl* , J. Turner* and J. Mead, Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

Static volume-pressure curves of dog lungs were obtained in living paralyzed animals and on the same lungs after excision. In the living animal pressure was recorded from an esophageal balloon, and, in some instances, simultaneously from an air-filled pleural catheter. Pressures recorded from the two sites were not systematically different and the differences were small. The measurements in the excised lungs were made under approximately the same conditions of volume history. The excised and in vivo lungs were distended to the same pressure over the same time intervals. Total gas volume of in vivo and excised lungs were similar, both at 30 cm. H_2O and at 0 cm. H_2O pressure. However, there were small but consistent differences in the static volume- pressure characteristics. Excised lungs exhibited greater static hysteresis and on deflation from 30 cm. H_2O pressure contained a larger fraction of gas at low distending pressures. We feel that the most likely explanation of these results is an alteration in surface forces, alveolar surface tension being decreased in the excised lungs during deflation and increased during inflation compared to that in vivo.

MODIFICATION OF RENAL TUBULAR PHOSPHATE SECRETION IN THE HEN BY ACUTE ACIDOSIS, ALKALOSIS OR CALCIUM LOADING. Robert A. Wolbach and Donald J. Marsh*, Department of Physiology, University of Utah, Salt Lake City, Utah, and Department of Physiology and Biophysics, New York University, New York.

In hens, net phosphate secretion by the renal tubules may occur naturally and can be induced by phosphate loading or by parathyroid hormone (PTH) injection (Levinsky & Davidson, Am. J. Physiol., 191: 530, 1957). In contrast, net phosphate reabsorption is typical of acutely acidotic hens, whether plasma phosphate concentration (Pphos) is normal or artificially elevated (Wolbach, Am. J. Physiol., 181: 149, 1955). Appropriately, we now find that phosphate secretion can also be induced or enhanced by $NaHCO_3$ infusion. These changes in tubular transport of phosphate which are secondary to acid-base alterations, are independent of changes in Pphos. However, plasma dialyzable calcium concentration (P_{DCa}) does change: $NaHCO_3$ infusions decrease P_{DCa}, while HCl infusions increase it. Likewise, phosphate infusions decrease P_{DCa}. Now, when calcium chloride infusions are used to directly increase P_{DCa}, net phosphate secretion decreases, again independent of changes in Pphos. Even when P_{DCa} is elevated, injected PTH enhances phosphate secretion. Changes in P_{DCa} probably reflect changes in ionized calcium concentration which, in turn, modify endogenous PTH release. Thus, all stimuli of phosphate secretion in these experiments are associated with high PTH availability and phosphate reabsorption with low PTH availability.

Aided by Grants H-1172 and AM-06973, National Institutes of Health.

RELATIONSHIP OF ACIDEMIA TO CEREBRAL EDEMA. S.K. Wolfson, Jr., P.A. Moscovitz and S.B. Prusiner (intr. by J.E. Rhoads). Harrison Dept. of Surg. Res., School of Med., Univ. of Penna., Phila., Pa.

Cerebral edema has been associated with respiratory acidosis. Previously we noticed signs of cerebral edema in animals having severe metabolic (hypoxic) acidosis following prolonged circulatory arrest with deep hypothermia. Since cerebral edema has not been reported due to hypothermia alone, a causal relationship between acidosis and cerebral edema seemed possible. Experiments were carried out to study the effect of increased blood H^+ alone upon cerebral water content. Male rats (250gm) were anesthetized with pentobarbital. Their inferior vena cavae were cannulated and solutions infused for 45 min.They were decapitated, brains removed, blotted, weighed and placed in a vacuum oven. They were dried at 62°C and 0.9mmHg to constant weight (48 hrs). Controls were decapitated after 45 min anesthesia alone. HCl (3N) was infused in the experimental group to produce a venous pH of 7.0 after 45 min. Distilled water infusion tested the adequacy of the method.

Group	No. Anim.	Infusion	% H_2O (Brain)	Value of p	Final venous pH
A	16	control	77.78±0.28	----	7.35-7.38
B	12	HCl(3N)	77.78±0.22	1.00	6.91-7.10
C	10	H_2O	78.90±0.18	<0.001	7.35-7.39

Group C shows that cerebral edema produced by water infusion could be detected by the method used. The comparison of Groups A and B indicates that HCl infusion, producing blood pH of 7.0, did not produce cerebral edema. Thus, it may be concluded that if cerebral edema was present in the acidotic animals mentioned earlier, it was more likely secondary to the effects of hypoxia than to acidemia per se. It would also seem likely that the cerebral edema observed in respiratory acidosis is due to elevated CO_2 or factors other than hydrogen ion.
Supp. by N.I.H. Grant #HE-08066 and a U.S.P.H.S. Career Devel. Award.

A REVISED METHOD FOR THE DETERMINATION OF TOTAL CHOLESTEROL IN BLOOD. Harry Y. C. Wong, Halina C. Mendez*, Sara R. Geer*, and Harold H. Orvis*[1], Department of Physiology, Howard University College of Medicine, Washington, D. C. and Department of Preventive Medicine[1], University of Illinois, Chicago, Illinois.

Questions have been raised as to the accuracy of blood cholesterol determined by Bloor's or Sackett's method. As a result there has been a tendency to dismiss these methods for cholesterol measurement. This study was undertaken to compare total cholesterol values obtained by the methods of Sackett (which is a modification of Bloor's method), Sperry-Webb and Vahouny. Our modification of Sackett's method was to allow the specimens to stand overnight to precipitate out the proteins rather than raise the temperature of the contents in the flask to boiling by placing over a water bath as outlined by Sackett. The results of cholesterol measurement in normal and hypercholesterolemic men and chickens were quite similar for each of the methods. The total cholesterol for Sackett's method, with a modification by us, showed that normal chickens had an average of 103.2 mg% as compared to 111.6 mg% by the method of Sperry-Webb. Present values compare favorably with Vahouny's method. Chickens on an atherogenic diet of 2% cholesterol plus 5% cottonseed oil added to plain mash showed an increase of total cholesterol, but there were no significant differences in cholesterol values as determined by the above methods. The ease for determining total cholesterol by our method permits an individual to run as many as 90 - 100 samples per day as compared to the more laborious method of Sperry-Webb or Vahouny. In addition, this method is not as costly as the other methods since it does not require digitonin precipitation of cholesterol. (Supported by grants HE-02420-07, HE-08649-01, Amer. Heart Assoc. and Hunt Foods and Industries, Inc.)

RELATIONS BETWEEN ALTERATION IN MEAN SKIN AND TYMPANIC MEMBRANE TEMPERATURE TO VASOMOTOR AND SUDOMOTOR RESPONSES. R.D. Wurster*, R.D. McCook and W.C. Randall, Stritch School of Medicine and the Graduate School, Loyola University, Chicago.

The nude subject on a copper screen bed was placed alternately in independently temperature controlled climate chambers. Five areas of cutaneous blood flow and eight areas of sweating were continuously sampled while measuring tympanic membrane temperature (T_{tm}), oral temperature and 12 areas of skin temperature from which a weighted mean skin temperature (T_{ms}) was electronically computed. To evaluate the relative importance of T_{tm} and T_{ms} in the control of sudomotor and vasomotor responses, T_{ms} and T_{tm} were varied independently. With T_{ms} constant at levels between 33 - 34°C, T_{tm} was raised as much as .3°C (by ingestion of hot fluids) without appearance of sweating. With T_{ms} constant at 37°C and T_{tm} elevated above control levels, complete sweat recruitment and increased volume pulse amplitudes were recorded. Under the latter conditions, T_{tm} was rapidly lowered (by ingestion of cold fluids) and sweating was reduced but not abolished with some decrease in volume pulse amplitudes. In a third experiment, T_{tm} was decreased while T_{ms} was rising: even so, sweat recruitment was initiated. In the last procedure T_{tm} was maintained .4°C above control and sweating stopped immediately upon reduction in T_{ms}. Thus, it is apparent that recruitment of sudomotor responses may vary independent of T_{tm} changes and points out the importance of skin temperature in thermoregulatory responses. (Supported by grant no. HE 08682-01 from NIH.)

STUDY OF VENTILATION-PERFUSION RATIO DISTRIBUTION IN ANESTHETIZED DOG BY MULTIPLE INERT GAS WASHOUT. T. Yokoyama* and L.E. Farhi. Dept. Physiol., State Univ. New York at Buffalo, Buffalo, N. Y.

The theoretical basis for this work is presented elsewhere in this issue (Farhi and Yokoyama). In order to determine the $\dot{V}_A/\dot{Q}$ distribution in the anesthetized, artificially ventilated, supine dog, the animal was first allowed to breathe for 20 minutes a mixture of methane, ethane, nitrous oxide (having Bunsen solubility coefficients of 0.04, 0.10, and 0.42, respectively) and oxygen. During the subsequent washout the concentration of the tracer gases was measured at intervals in the expired gas and in the arterial and mixed venous blood, using a gas chromatograph. When the results were analyzed in terms of a two-compartment system, one of these received 15% of the ventilation and 25 to 50% of the perfusion. Such a distribution pattern, easily detectable by the present method, would be difficult to demonstrate by O_2 and CO_2 pressure differences. A different treatment of the data allows to demonstrate in each case the presence of elements having a $\dot{V}_A/\dot{Q}$ of less than 0.1.
(Supported in part by the U.S. Air Force)

MAGNETIC FIELD AND VAGAL EFFECTS. Wei Young, John W. Gofman*, Jack Hitchman*, Michael Kelly*, and Gerald Molino*. Bio-Medical Division, Lawrence Radiation Laboratory, University of California, Livermore, California.

Vagal inhibitory effects are readily observed in the isolated vagal heart preparations of Rana pipiens. The normal inhibitory effect was partially blocked by exposing the preparation to about 4,500 Gauss. When the preparation subjected to higher field, the effect appeared to be pronounced. Higher intensity (15,000-16,000 Gauss) of magnetic field not only increases the activity of Acetyl-cholinesterase but also induces arrhythmic contractions afterwards. It suggests that there is impairment of the conducting system. Physostigmine at concentration of 2×10^{5} gm. blocks magnetic effect completely, indicating that the effect is on the active sites; more likely the anionic site of Acetyl-cholinesterase.

METABOLISM AND THE PROTECTIVE ACTION OF ANESTHESIA AGAINST TOXICITY OF OXYGEN AT HIGH PRESSURE(OHP), D. Zee†, J.W. Bean, R. Hendrix†, B. Thom†, Depts. of Physiol. & Path., Univ. of Mich., Ann Arbor. An attempt was made to determine whether the protective action of anesthesia (Na-pentabarbital) against the toxicity of OHP is due to the attendant depression of metabolism as has been claimed. Young adult male rats were used as subjects. After determining the resting metabolism of individual rats, first unanesthetized then anesthetized, the dosage of a drug (di-nitrophenal, L-thyroxine) or direct tetanic stimulation of muscle, needed to return the metabolism of an anesthetized rat to about or above normal resting value, was ascertained. Exposures to OHP(75psi) were made in groups of 3, one unanesthetized and one anesthetized control and one anesthetized whose metabolism had been returned to about or above normal resting level as described above. Observations were made throughout the exposure which was carried to onset of neuromuscular reaction in any animal. Following stage decompression gross and microscopic examination was made of lungs and livers. It was found that all anesthetized rats, including those whose metabolism had been elevated to about or well above normal levels by drugs or tetanic stimulation during the OHP exposure, remained free of convulsions; gross and microscopic damage changes were entirely absent or minimal, whereas all unanesthetized controls, including those in which overt seizures were intentionally avoided by short exposures, suffered significant lung damage. The most severe lung damage occurred in the severely convulsed rats. The data support the conclusions, 1. that the protection afforded by anesthesia against OHP is not due simply to the attendant decrease in metabolism; 2. that while the possibility of a direct toxic action of OHP on the lungs is not denied, the greater part of this damage is mediated by other means, most probably of neurogenic nature;3.convulsive seizure is conducive to but not essential to lung damage. (Supported in part by NIH)

PRODUCTION OF AN APERISTALTIC URETERAL SEGMENT IN DOGS.
Paul D. Zimskind*, Paul L. Lewis* and M.H.F. Friedman.
Jefferson Med. Coll., Philadelphia, Pennsylvania

As a continuation of earlier work on ureteral dynamics, the present study is an attempt to produce adynamic hydronephrosis in dogs by abolishing peristalsis in a localized segment of the ureter. The technique consisted of exteriorization of the bladder, passage of a small balloon catheter into the ureter and inflation of the balloon to a diameter of 1.5 cm. for 2 minute periods at intervals of 3 days. Pressure recordings of the ureter were obtained from one week to 3 months after the balloon inflation procedure by means of intraluminal non-obstructing catheters connected to strain gauge pressure transducers. The effects were confined to the areas of balloon distension, and consisted of flattening of the peristaltic contraction recordings. At least four successive balloon inflation procedures were required to produce lasting ureteral dysfunction. Intravenous urograms and retrograde pyelograms showed progressive dilatation of the ureter and renal pelvis above the treated segment. Histologic examination of the affected site showed rupture of the muscle layers, but the lumen of this area remained widely patent. The results support the concept that urinary obstruction can be of an adynamic, as well as mechanical, nature.

(Supported in part by USPHS Postdoctoral Fellowship #5-F2-HE-19,220-02.)