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ABSTRACTS OF PAPERS

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

METABOLISM OF MITOCHONDRIA AND OTHER CYTOPLASMIC FRACTIONS OF DEVELOPING RAT BRAIN. A. A. Abdel-Latif* and L.G.Abood. State of Ill. Pediatric Inst. and Dept. Psychiatry and Biochem., U. of Illinois, College of Med., Chicago, Ill.

It has been possible by means of continuous gradient centrifugation in a medium of Ficoll-sucrose-EDTA to further fractionate the conventionally prepared "mitochondrial fraction" of rat brain into 4 distinct fractions (A-D) (Tanaka and Abood, J. Neurochem., in press). When isolated from adult brain fractions, C and D contain virtually pure mitochondria, while A consists largely of myelin, axonal, and glial fragments and B largely of terminal boutons. The present study reports on metabolic findings on similarly prepared particulates of embryonic and 10-day old rat brains. The lightest fractions (A+B) of embryonic brain contained mainly unmyelinated axons, microsomes, glial processes, terminal boutons, and a few mitochondria. In the case of the 10-day old the A fraction contained, in addition, myelinated axons, while the B fraction was distinctly separated and contained largely terminal boutons. Mitochondria were found in the C and D fractions at both ages. Both embryonic and 10-day old brain are capable of oxidative phosphorylation with all the activity in C and D; whereas glycolytic activity resides only in A and B. The specific activity of phosphorylation in embryonic brain was the same or higher than that of the 10-day old, suggesting a rapid, early maturation of brain mitochondria. (Supported by Mental Health Fund, State of Illinois.)

INTERNAL IMPEDANCE OF THE LEFT VENTRICLE. F. L. Abel (intr. by L. K. Knoebel). Indiana Univ. School of Med., Indianapolis, Indiana.

The ability of the left ventricle to adjust to a changing work load was studied by measuring the changes in stroke volume, heart rate, and aortic pressure that occurred in response to experimental increases or decreases in TPR. By analyzing the slope of the aortic pressure-cardiac output graph at any particular point, a measure of the internal impedance of the ventricle at that point, analogous to the same variable in an electrical generator, is obtained. The results show a curvilinear relationship between cardiac output and TPR, with most of the change in cardiac output being due to changes in stroke volume in the lowered TPR animals, and to changes in heart rate in those animals in which TPR was experimentally increased. The plot of pressure drop versus flow across the systemic bed indicates a very high left ventricular internal impedance for increased resistance loads, and a somewhat lower internal impedance for decreased resistance loads. These results indicate that the left ventricle functions primarily as a constant current generator.

HYPOTHALAMIC TEMPERATURE IN UNANESTHETIZED ALBINO RATS. Robert Abrams* and H. T. Hammel (Intr. by R. O. Rawson). Dept. of Physiology, School of Medicine, Univ. of Penna., Phila. and John B. Pierce Foundation, New Haven, Connecticut

Stainless steel and polyethylene reentrant tubes were implanted permanently in the brain and abdominal cavity of anesthetized male albino rats. Several days later thermocouples were placed in the tubes and the leads were counterweighted above the rat cage. Temperatures were recorded continuously for up to 4 hrs during the day in unanesthetized, unrestrained rats. A decrease in temperature of the preoptic area usually accompanied sleep. Temperature increases were often associated with arousal from sleep and activity. Following a 24 hr fast, feeding was consistently associated with an increase in temperature of the preoptic area, piriform cortex and abdominal cavity of about 0.1° C/min. Changes in temperature in the preoptic region either paralleled or slightly preceded the temperature changes in the abdominal cavity. Marked thermal gradients of over 2°C were demonstrated by manually changing the position of the abdominal cavity thermocouple. The caloric content and S.D.A. potential of the diet did not appear to be important in determining the degree of temperature rise. A 60-80% increase in metabolic rate occurred simultaneously with the rise in temperature of the preoptic area during the first 10 minutes of a feeding period. The activity associated with eating is postulated to account for the increase in brain and other body temperatures.

CHANGES IN OXYGEN UTILIZATION BY RATS DUE TO ACCLIMATIZATION TO SIMULATED ALTITUDE. Eugene Ackerman. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Many experiments dealing with biochemical changes during acclimatization to simulated altitude are based on the hypothesis that the rate of utilization of oxygen is changed by acclimatization. The experiments described represent an attempt to detect and quantify any such changes. Rats were divided into four groups: (1) controls; (2) exercised; (3) acclimatized to simulated altitude of 20,000 feet; (4) exercised and acclimatized. The exercised animals were required to run on a treadmill in order to obtain food. Animals were exercised 10 days before the start of acclimatization. Animals were acclimatized for 2 weeks. All were maintained at room temperature, and all oxygen utilizations were measured at pO_2 = 0.2 at. For the studies of rate of oxygen utilization, the rats were placed in a closed, rotatable cage shaped like a wheel. The air in the cage was circulated, and the pO_2 was monitored with a polarigraphic sensor. Measurements were made with rats at rest and with rats running as the wheel-cage revolved. (Some rats attempted to avoid running and used more oxygen thereby than when running; results from rats not running had a greater variability and were not used.) Results indicated that all groups used less oxygen per minute per kg when at rest as they became older. However, rats in groups (3) and (4) used less extra oxygen per minute per kg when running after acclimatization than did rats in groups (1) and (2). Accordingly it is concluded that the animals acclimatized to simulated altitude conditions did have a lower rate of oxygen utilization per kg when running than did the control animals. These experiments, which were performed with the technical assistance of R. G. Slabaugh and A. Hildestad, were aided by NIH grants GM-08280 and FR-00007.

CARDIO-PULMONARY RESPONSES IN CHILDREN DURING PHYSICAL EXERCISE. Goran Agnevik*, Jack Daniels*, and Robert T. Clark, Oklahoma City University, Oklahoma City, Oklahoma.

Secondary and elementary school children were tested on both a treadmill and bicycle ergometer. The treadmill speed was set at 3.4 mph and the grade was increased 1% each minute with the subject continuing to a maximum pulse rate of 210. Blood samples were taken before and after work on the treadmill for biochemical measurements. Blood pressures and pulse rates were determined each minute during work on the treadmill. Resting ECG's and working radioelectrocardiograms were recorded. During the last minute of the treadmill test respiratory air samples were collected and total ventilation measured. Parallel studies were carried out on the bicycle ergometer for each subject. Results for boys and girls were: Min. on treadmill, 19.0 and 11.3; V.C., 4.4L and 3.0L; M.B.C., 149L and 112L; working B.P., 189/59 and 151/76; total ventilation STPD, 79L and 48L; T.V., 2.3L and 1.4L; Oxygen in ml/KGBW/min., 47 and 32; oxygen pulse, 15 ml and 9 ml; Total ventilation/L oxygen, 32L and 37L; R.Q., 1.007 and 1.063. Work on the treadmill and bicycle was best correlated with oxygen consumption in ml/KGBW/min. The results indicate inefficient use of oxygen by children who are relatively inactive as compared to children and adults who regularly exercise.
(Supported by NIH Grant #GM 10381-01)

CORRELATION OF THE VIBROCARDIOGRAM WITH THE HEMODYNAMIC EVENTS OF THE CARDIAC CYCLE IN THE DOG. C.M. Agress, H.M. Estrin* and S. Wegner.* Cedars of Lebanon Hospital, Los Angeles, California.

The vibrocardiogram was recorded with a capacitance microphone (Altec Model 165A) in dogs simultaneously with intracardiac chamber pressures and pulmonary artery or aortic pressures. The transducer tip catheter (Statham Model SF-1) was utilized to minimize the time delays of previous methods. A correlation of 2 milliseconds or better was made possible by displaying the pressure curves and the vibrocardiographic tracings on a high-speed Tektronix oscilloscope (Model 532) with camera attachment (Tektronix Model C-12). It was found that the H wave of the vibrocardiogram occurred at the onset of left ventricular pressure rise and the J_2 with aortic valve opening, the interval H-J_2 thus defining isometric contraction. The L_1 wave marked the end of ejection, the interval J_2-L thus measuring the duration of ejection. The J_1 marks the onset of the isometric pressure gradient, J_3 the peak of ejection, and L_4 the end of isometric relaxation. L_1 marks the onset of protodiastole, M the aortic incisura and the interval L_1-L_4, the duration of isometric relaxation. All these vibrocardiographic measurements correspond to the catheter measurements within 2 milliseconds.

Modifications of pressure-volume curves in rat lungs after inhalation of surface active extracts and agents. Yves Alarie* and Eugène Robillard. Département de Physiologie, Faculté de Médecine, Université de Montréal, Canada.

Rat lung alveolar lining extracts prepared after the Bondurant and Miller method (J. Appl. Physiol. 17, 167, 1962) were administered by inhalation to rats . The isolated lungs of these animals were used to establish stepwise filling and emptying volume-pressure curves with saline solution or with air. Curves obtained with saline solution did not significantly differ from the normal control curves. Curves obtained during filling and emptying with air after inhalation of the alveolar lining extract were markedly deviated to the left of the normal control curves. An aerosol containing 0.125% of synthetic L-Alpha Lecithin induceed the same effects. These results indicate that lower surface forces are present in the lung in the treated groups. When an aerosol containing 0.5% of synthetic L-Alpha Lecithin was used, a region of the lung rapidly opens when filling with air and a leak from this region was observed during the following inflation process. In this last condition, leaking happens between 2 to 4 ml. of intrapulmonary volume and from 8 to 14 cm. H_2O of pressure. This phenomenon of leaking,was also observed in other conditions namely: after inhalation of high concentrated (1%) aerosol of isoproterenol, adrenaline, n-adrenaline and dopamine, and also in some series of rat lungs after inhalation of microparticules (<0.2 microns) of aluminum oxide. Aluminum oxide inhalation was also reported to lower surface forces in the lung. (Can. J. Biochem. and Physiol. 40, 1359, 1962 and 41, 1257, 1963).

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THE PROFILE OF pH, PRESSURE AND POTENTIAL DIFFERENCE AT THE GASTRODUODENAL JUNCTION IN MAN. Sven Andersson* and Morton I. Grossman. Veterans Adm. Center, Los Angeles.

A probe containing a water-filled balloon (5 mm in diameter) for pressure recording, an open tipped KCl-agar tube for potential difference (PD), and a miniature glass electrode for pH was introduced by nasal route into the distal duodenum of 15 human subjects. Skin electrodes were used to complete the pH and PD circuits. Records of respiration and the outputs of the sensors were continuously recorded on a multi-channel oscillograph while the probe was withdrawn 1 cm at a time through the stomach into the esophagus. Position of the probe was repeatedly checked roentgenographically. A sharp rise in PD (19 to 33 mV) occurred when the electrode moved from the duodenum into the stomach and the PD fell as the gastroesophageal junction was traversed to approximately the same level as that found in the duodenum. Pressure changes characteristic of the gastroesophageal sphincter were always seen at the junction of these organs but there were no characteristic pressure changes at the duodeno-gastric junction. When gastric pH was below that in the lower duodenum, the fall in pH was first detected in the duodenal bulb.

THE EFFECT OF LUNG VOLUME ON PULMONARY SHUNT FLOW. N. R. Anthonisen (intr. by S. M. Tenney). Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

Relative pulmonary shunt flow ($\dot{Q}s/\dot{Q}t$) was measured in denitrogenated open chested cats during apnea over the full range of lung volumes. The particular lung volume and transpulmonary pressure were also measured. When completely collapsed lungs were inflated, $\dot{Q}s/\dot{Q}t$ decreased sharply to 3% at total lung capacity (TLC). During deflation from TLC $\dot{Q}s/\dot{Q}t$ was insensitive to changes in lung volume. $\dot{Q}s/\dot{Q}t$ remained low during re-inflation after deflation from TLC. These changes in shunt flow can be interpreted as due to either recruitment or collapse of gas exchange units during lung volume change. It appears that completely collapsed lungs inflate very unevenly but that deflation from TLC proceeds remarkably evenly. Reinflation after deflation from TLC also seems to proceed evenly, and the manifest pressure-volume hysteresis is most likely due to hysteresis of the surface active properties of the alveolar lining material.

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THE 5-HYDROXYTRYPTOPHAN DECARBOXYLASE-MONOAMINE OXIDASE AND CHOLINEACETYLASE-CHOLINESTERASE SYSTEMS IN SEVERAL DISCRETE AREAS OF THE AVIAN BRAIN. M. H. Aprison, T. L. Folkerth* and Ryo Takahashi*. The Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, Ind.

In our expanding neurochemical correlates of behavior project (with pigeons) it became necessary to determine the activities of the synthetic and catabolic enzymes systems for 5-hydroxytryptamine (5-HT) and acetylcholine (ACh), compounds thought to be neurohumoral agents. The enzyme 5-hydroxytryptophan decarboxylase (5-HTP-D) synthesizes 5-HT (and 3-hydroxytyramine) while choline acetylase (ChAc) synthesizes ACh. Monoamine oxidase (MAO) and cholinesterase (ChE) are the enzymes which contribute to the regulation of the physiological levels of 5-HT and ACh. These 4 enzyme activities were determined (with published methods) in 4 specific brain areas: telencephalon, diencephalon (plus optic lobes), cerebellum and medulla oblongata-pons. When the specific enzyme activities were expressed as μM substrate formed or destroyed per gm of wet tissue per hr, the MAO and ChE activities of all 4 brain areas were of the order of 100 or more times the activity of the respective synthetic enzymes. The 5-HTP-D and MAO activities were relatively constant in the brain parts analyzed. Greater variation between brain areas was found for ChAc and ChE. The ChE and ChAc activities of each part were much higher than the MAO and 5-HTP-D activities, respectively.
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PANCREATITIS IN THE RAT. T. Arai* and H. Necheles. Department of Gastrointestinal Research, Michael Reese Hosp., Chicago.

With rare exceptions when a duct may run directly into the duodenum, all pancreatic ducts join the common bile duct in the rat. Because of this common channel the rat offers itself as a good animal for the production of experimental pancreatitis by ligation of the common duct at the duodenum. Because contradictory results have been reported we have conducted such experiments in rats, and have been able to invariably produce an acute hemorrhagic pancreatitis with extensive fat necroses and biliary ascites. Intravenous injection of secretin hastened the development of these changes. Chronic preparations of these animals died between one and ten days with similar pathologic changes. Measurements of the increasing pressure of biliary and pancreatic secretion in the obstructed common bile duct were carried out and a considerable increase was observed within 6 hours. In previous work, no pancreatitis developed after the common bile duct was intubated above the entrance of the pancreatic ducts, with bile permitted to drain, and the bile duct below the entrance of the pancreatic ducts was ligated; this procedure only caused stasis within and distension of the pancreatic duct system. Rats with ligated common bile duct may be useful for investigation of effects of drugs on pancreatitis.

Supported by a grant from the Hartford Foundation.

POTENTIATION OF THE OLFACTORY RECEPTOR AFTER REPETITIVE STIMULATION. H. Aréchiga. O. Longoria. J. Torres and C. Alcocer-Cuarón. (spon: J.J. Izquierdo) Nat. Univ. of México, Sch. of Med.

Slow electric responses from olfactory receptors in eminentia olfactoria of isolated frog heads, following Ottoson's technique, were recorded through glass micropipettes filled with 3M KCl; 10-30 MΩ resistence. Repetitive stimulation with amyl acetate at lesser intervals than one minute, resulted in depression of the response. But if a longer resting period followed depression, responses to new stimuli were of greater amplitude, up to twice the control potentials, and this effect lasted for several minutes. The enhancement effect thus resulting, both in intensity and duration of the generator potential, was found to be a function of the frecuency in the conditioning train of stimuli and of the intervals mediating between those stimuli and the test stimulus. Similarity of this potentiation with others described for other excitable structures, including pacinian corpuscle, suggests that this corresponds to a general property of excitable structures and not to a particular one of synaptic junctions, as currently supposed.

X-RAY MICROSCOPY, A TOOL IN VASCULAR RESEARCH. Kenneth A. Arendt, B. W. Beaton* and C. V. Ettari*. Department of Physiology, Loma Linda University, Loma Linda, California.

The projection x-ray microscope has been applied to in vivo studies of vascular physiological phenomena in opaque tissues, primarily skeletal muscle. Although the beam intensity is relatively low, fast film emulsions and high contrast development permit exploitation of the excellent depth of field characteristics of this instrument. The most frequently employed site of investigation has been the hind limb of the hamster. The abdominal aorta is cannulated and the muscle vasculature is perfused under physiological pressures with Thorotrast. The effect of a hyaluronidase-like spreading factor in moccasin snake venom has been shown by means of intramuscularly introduced solutions of venom in 50% Hypaque. A 0.2 cc bleb of Hypaque alone remains relatively localized for several minutes at the site of injection, whereas the same quantity of the substance containing 0.1% venom is widely, uniformly dispersed throughout the thigh musculature within 5 minutes. The vasoconstrictor influence of intramuscular injections of snake venom is readily discernable in Thorotrast perfused blood vessels. Among other observations provided by the microradiographic technique are the increase in vascular tone by nor-epinephrine and the decrease of intramuscular vascular resistance by infused epinephrine and topically applied lactic acid. Respired amyl nitrite elicits a marked vasodilation. X-ray microscopy has previously been used successfully in delineating blood vessels of non-living compact bone. It is now suggested that this method may be employed to good advantage in vascular studies involving a variety of living tissues which do not readily lend themselves to observation by visible light techniques. (Supported by Grant A-1762, National Advisory Council on Arthritis and Metabolic Diseases, N.I.H.).

MODIFICATION OF CARDIOGENIC SHOCK BY RESERPINE. G. Ascanio*, F. Barrera*, and M. J. Oppenheimer, Temple University, School of Medicine, Philadelphia, Pennsylvania.

Previously reported results, (Federation Proceedings, 22:640, Part I, #2, March-April, 1963) when myocardial infarction was produced by intracoronary artery injection of a necrotizing agent, tetrafluorohexachlorobutane, indicated that much of the morbidity and many of the 33% fatalities might be explained by the sudden release of catecholamines at the moment of infarction. To test this hypothesis dogs were premedicated with reserpine, 0.1 mgm/Kg. subcutaneously, 24 hours before the acute experiment was performed under pentobarbital sodium, 35 mgm/Kg. intravenously. At the time of the latter experiment the following parameters were measured simultaneously: left ventricular systolic and diastolic pressures, femoral artery mean pressure, first derivative of the ventricular pressure pulse, and cardiac outputs at 10, 30, and 60 minutes after infarction and 5, 10, and 20 minutes after positive inotropic or peripheral vasoconstrictor agents. EKG was monitored throughout. pH, pO_2 and pCO_2 of arterial and coronary sinus were controlled by a respiratory pump and observed at frequent intervals in one series of experiments. Dogs, with catecholamines depleted by premedication with reserpine, were almost free of arrhythmias, did not fibrillate even when some of them died, and had only a small fall in blood pressure or even a rise at the time of infarction.

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RATE OF PROTEIN LEAKAGE IN INFLAMED SKIN. Emil Aschheim and Eugene M. Farber, * Stanford Univ. Med. Center, Stanford, Cal.

Inflammation was produced in female anesthetized rats by the topical application of xylene onto the clipped abdominal skin. At specified times thereafter, about 2 uc of I^{131} labeled serum albumin were injected through a previously inserted jugular cannula and washed in with 0.5 ml of saline. Exactly one minute after the injection of the tracer, the heart action was stopped with 1 ml of saturated KCl solution. Skin and blood samples were obtained and clearance determined (equal to the ratio of c/m/g dry skin to c/m/ml blood). This value represents the quantity of blood cleared of the label by one gram of dry skin during one minute. Clearance of the normal skin is due to the label which is contained intravascularly. Subtracting the clearance of the normal skin from that of the inflamed skin, one obtains the minute clearance induced by the phlogogen during a particular stage of the inflammatory reaction. The results indicate that during the initial rising phase the rate of protein extravasation increases linearly with time (0.0468 ml plasma/g normal skin/min^2). The peak is reached 4.5 minutes after the initial application of xylene. From then on the minute rate of protein leakage decreases exponentially with time (k = 0.2236). The linearity of the first phase is thought to result from the continuous operation of a constant phlogogenic activity. The first order kinetics of the second phase probably reflects the combined action of a number of processes which increasingly limit the blood flow to the inflamed skin. Supported by U.S.P.H.S. N.I.H. research grant #HE-03833-04.

OXYGEN DELIVERY AND MYOCARDIAL PERFORMANCE, Marvin Bacaner, Maurice Visscher, Franco Lioy*, Richard Stish*, Henry Ballin*. Dept. of Physiology, University of Minnesota, Minneapolis.

Heart metabolism is generally considered to change in passive response to altered work demands which change heart performance. In intact dogs it was noted that increasing coronary blood flow (CBF) caused heart work to increase without an imposed increase in work load. (Am. J. Med. 30:392, 1961). The implication that an increase in blood supply enables the heart to contract more forcibly was studied on totally isolated dog hearts contracting without doing external work. Left ventricular resting tension and contractile tension were monitored with a force gauge mounted on a moveable rack gear (to vary resting tension) connected to the heart apex. The base was fixed by a clamp on the aortic perfusion cannula through which CBF was controlled for either constant pressure or constant flow blood perfusion. 1) Changing resting tension resulted in an immediate change in contractile tension to a new plateau (Starling effect). 2) At constant resting tension stepwise increases and decreases in CBF (25-300 ml/min) provoked respective stepwise increases and decreases in contractile tension. Changes in contractile tension resulting from a change in CBF were progressive (rather than immediate) gradually reaching a new plateau in about 90 seconds. O_2 consumption was found to be lineraly related to contractile tension independent (within limits) of arterial pO_2 (metabolic effect). 3) The contractile tension developed at any resting tension was proportional to the O_2 delivery to the myocardium over a wide range of imposed variations in CBF and pO_2.
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VASCULAR CAPACITY CHANGES IN THE DOG FORELIMB. C. H. Baker and L. J. O'Brien. Dept. of Physiology, Medical College of Georgia, Augusta, Ga.

Vascular volumes were estimated by arterial injections of Cr^{51}-labelled red cells and I^{131}-albumin in an isolated dog forelimb preparation. Changes in vascular volume were also measured by changes in weight of the limb. Flow was controlled by means of a constant infusion pump and measured with a Medicon flowmeter or by collection of venous outflow in a graduated cylinder. Perfusion pressure and venous outflow pressure were measured and radioactivity was monitored by means of a probe and ratemeter connected to an oscillographic recorder. Vascular volumes were determined with the indicators, 1) at the control time, 2) following dilation of the vasculature with an acetylcholine infusion (2μg/kg/min) with no change in rate of blood flow, and 3) after increasing the flow rate until the control pressure was reached. The changes in vascular volume measured by the Cr^{51}-red cells closely followed the changes in volume as measured by changes in limb weight. Vascular volume changes measured by I^{131}-albumin agreed with those calculated from the weight changes only after the vasculature had been dilated. (Supported by USPHS grant HE-04573-04).

UPTAKE OF α-AMINOISOBUTYRIC ACID BY SKELETAL MUSCLE OF NORMAL AND DYSTROPHIC MICE. R. David Baker. Department of Physiology, University of Texas Medical Branch, Galveston.

Uptake of the non-metabolized amino acid, AIB-1-C^{14}, into skeletal muscle of normal and dystrophic mice (Bar Harbor strain 129) was studied both in vitro and in vivo. In the in vitro studies, sheets of abdominal muscle (2 from each animal) were incubated in 2.0 ml of Krebs-Ringer-bicarbonate at 37°. AIB was present initially at 0.089 μmoles/ml (0.46 μc/ml). Insulin was present (0.37 units/ml) with one hemiabdominal muscle from each animal. After incubation the muscles were rinsed, blotted, weighed, extracted in boiling water and the concentration ratios (radioactivity/gm of muscle:radioactivity/ml of medium) were determined. At all time intervals studied (1,2,3 and 4 hrs.) the dystrophic muscles accumulated more AIB than the normal muscles. Both dystrophic and normal muscles were responsive to insulin. In the in vivo studies, mice were injected, I.P., with 48.5 μ moles/Kg (35.7 μc/Kg) of AIB. At various times after injection the mice were decapitated, blood was collected from the neck, and samples of abdominal and leg muscles were obtained. The muscles were weighed, extracted in boiling water, and the concentration ratios (muscle activity/gm:plasma activity/ml) determined. Diphasic uptake curves were obtained; a plateau was maintained between about $1\frac{1}{2}$ and $4\frac{1}{2}$ hours, followed by a secondary rise which usually reached a peak at 12 hours. At all times studied the concentration ratios were greater for the dystrophic than for the normal muscles. At 12 hours, over a 5-fold difference was noted for the leg muscles. The cell type within dystrophic muscle responsible for increased AIB accumulation has not been determined; however, these results do not support the view that muscle fibers in general are more "leaky" in dystrophics than in normals. (Supported by the Liberty Muscular Dystrophy Research Foundation.)

EFFECT OF URETERAL STOP FLOW AND FILTERED SODIUM ON RENAL TISSUE UREA, CREATININE AND PAH IN DOGS. A. Louise Baldwin* and Gaspar Carrasquer. Dept. of Med., Univ. of Louisville, Louisville, Kentucky.

Creatinine and PAH concentrations increased in renal tissue, during ureteral stop flow, more in oliguric than in mannitol diuresis dogs. More NaCl available for reabsorption from the lumen may have contributed to higher accumulation in oliguria. To test this hypothesis, nembutalized dogs were injected with 0.5 M NaCl to produce urine flows of over 5 cc/min. per kidney. One kidney was removed during free flow of urine. The other kidney was removed after 50 min. of ureteral stop flow. In the free flow kidney, urea concentration was higher in medulla than in cortex, and creatinine and PAH concentrations were higher in cortex than in medulla as in mannitol diuresis. During ureteral stop flow the concentration of urea increased in inner medulla, contrary to what was observed during mannitol diuresis. The high increase in PAH and creatinine concentrations in medulla caused a reversal of the concentration gradient to one increasing from cortex towards papilla. In mannitol diuresis the PAH and creatinine gradients were not reversed; i.e. concentrations remained higher in cortex. Abundant reabsorption of NaCl from Henle's loop during stop flow might result in liberation of "free" water → water reabsorption → hydrostatic gradient → filtration and intraluminal multiplication of non-reabsorbable material (creatinine, PAH and urea). Collecting ducts are apparently the only suppliers of urea to the I.S. The intraluminal multiplication of urea in mannitol diuresis and oliguria is not great enough to compensate for its drainage from I.S. Consequently, a decrease of medullary tissue urea is observed. Mild increase of urea in cortex in all experimental conditions studied should proceed from persistent filtration. (NIH and AHA support).

CARDIOVASCULAR EFFECTS OF CHLORALOSE. Berl Bass* and N.M.Buckley. Albert Einstein College of Medicine, New York.

During an investigation on cardiovascular responses in acute hemorrhage, a detailed comparison of the effects of chloralose vs. pentobarbital anesthesia on cardiac output, arterial blood pressure and heart rate was made in control dogs. Three groups of experiments included determinations of (1) effects of duration of anesthesia alone, (2)cardiovascular responses to continuous infusion of epinephrine or norepinephrine, and (3) inotropic effects of the two anesthetics in the dog heart-lung preparation. In 5 intact dogs anesthetized with chloralose, the above parameters of cardiovascular function were observed at 30-minute intervals for 150 minutes, and revealed a rise in heart rate and a fall in stroke volume. In 20 dogs anesthetized with pentobarbital there were no apparent differences in the mean values of cardiac index, stroke index, heart rate and arterial pressure, as compared to 18 dogs anesthetized with chloralose. However, cardiac index decreased in response to epinephrine in 5 of 7 dogs under pentobarbital, while it rose in all 7 dogs under chloralose; the rise in blood pressure was greater under chloralose than under pentobarbital. In response to norepinephrine, cardiac output decreased in all 7 dogs under pentobarbital and rose in 4 of 6 dogs under chloralose, with no consistent change in heart rate. Both pentobarbital and chloralose were negatively inotropic in dog heart-lung preparations, producing a decrease in ventricular stroke work and contractility. These studies confirm the importance of the choice of anesthetic agent for any study of cardiovascular responses, and the need for determining time-course controls before interpreting experimental results. (Supported by N.I.H.Grant HE-03008).

DISTRIBUTION OF THE TRAVERSAL TIMES OF BLOOD FLOWING THROUGH AN ARTERY. J. B. Bassingthwaighte*, E. H. Wood and H. R. Warner, Mayo Clinic, Mayo Foundation, Rochester, Minnesota and Latter-Day Saints Hospital, Salt Lake City, Utah.

Time-concentration curves were recorded simultaneously at the femoral and dorsalis pedis arteries of men following dye injections of varied form into the superior vena cava or thoracic aorta. A dispersion process was simulated by the equation for a single washout superimposed on a random distribution of transit times about a mean time (Physiologist 4:8, 1961). Using a digital computer, the upstream curve was convoluted with this process to produce a theoretical downstream curve and the three constants of the equation adjusted so that a close fit to the recorded downstream curve was attained. Optimal values of the constants of the dispersing process were similar for curves recorded in sequence even though the recorded curves were of quite different form (e.g. conventional curves following single injections into right atrium or aorta, or double-peaked curves following double injections into aorta). Applications of the convolution integral assumes that the system can be represented by linear equations; these results indicate that this assumption is reasonable for a branched arterial segment. From this calculated dispersion process, making assumptions that the axial velocity is greatest and that the sampling is "volume averaged", an "average" velocity profile may be computed ignoring the variation over the cardiac cycle. In all cases, the profile is more blunt than parabolic. The mean transit time/appearance time ratio was less than 1.7 as compared with 2.0 for parabolic flow. (Supported in part by NIH Grant H-4664).

OBSERVATIONS ON PERIPHERAL BLOOD ELEMENTS DURING CHRONIC ETHANOL ADMINISTRATION IN DOGS. James D. Beard*, George Barlow and Arliss H. Tuttle*. Clinical Physiology Laboratories, University of Tennessee College of Medicine, Memphis, Tennessee.

The influence of comparatively long-term alcohol administration on peripheral blood elements has been studied in dogs. Sixteen dogs were given varying doses of ethanol (2-4 g/kg) by gastric tube daily for periods up to twelve weeks. All animals were maintained on an adequate diet. The parameters measured on a weekly basis were: hematocrit, hemoglobin concentration, erythrocyte count, reticulocyte count, erythrocyte sedimentation rate, leucocyte count and the differential. All groups gave evidence of prolonged reduction in hematocrit, hemoglobin concentration and in leucocyte count. In general, there were no appreciable alterations in sedimentation rate or in reticulocyte count. No changes were seen in the derived mean corpuscular values. Although leucocyte counts were depressed markedly in all groups of dogs, this reduction could not be attributed to a disproportionate alteration of individual white blood cell components; however, definitely abnormal-appearing white cells were noted. The most striking change occurred in the lymphocytes, which exhibited an increase in the number of binucleated forms, marked cytoplasmic vacuolization and pyknosis. These changes in peripheral blood elements will be related to other ancillary measurements (plasma and blood volumes) made in these animals. It would appear that ethyl alcohol in the doses employed might have exerted a depressing influence on leucopoietic and erythropoietic tissues. (This investigation was supported in whole by Public Health Service Research Grant No. MH-04440 from the Institute of Mental Health.)

DIVING BRADYCARDIA IN THE IGUANA. Daniel A. Belkin (intr. by A. B. Otis). Dept. of Physiol., Coll. of Med., Univ. of Florida, Gainesville.

When threatened by a potential predator, the lizard Iguana iguana often dives to the bottom of a stream and remains submerged, in a state of tonic immobility, for over an hour. Electrocardiograms recorded during voluntary diving of unrestrained lizards show that the bradycardia associated with this submergence is the most profound yet observed in any vertebrate. At the onset of a dive, the heart rate is immediately reduced to less than one percent of its pre-dive level: at a body temperature of 22°C, the interval between submergence and the first heartbeat is usually 4 to 5 minutes. The slowing of the heart is due almost entirely to lengthening of the T - P interval (or T - T interval when the P wave is absent). The early part of the dive is characterized by complete atrial arrest and heart rates of less than 0.5 beats per minute; double beats and QRS-P-T sequences are common. P waves appear with increasing frequency during the later part of the dive, and heart rate gradually increases. Bradycardia is completely abolished by light doses of atropine sulfate (0.08 mg/kg 1 hour before the dive); the only other effect of this drug on diving behavior appears to be a decrease in the duration of voluntary submergence. Disturbance during a dive (tapping on the aquarium or roughly handling the animal) elicits a further slowing of the heart. During short voluntary dives not initiated in response to the appearance of a potential predator, bradycardia may be slight or absent. Injection of water into the nares of iguanas fails to elicit bradycardia. It is tentatively concluded that diving bradycardia in the iguana is mediated principally through the vagus, and that it is a response to external factors, rather than to internal physiological changes associated with apnea. (Supported by grant G 9817 from N.S.F.)

IONIC SHIFTS ACROSS THE INTACT URINARY BLADDER OF THE DOG

by

Morris Phillip Bellard,* William B. Grondolfo,* C. Allen Wall* & Kathleen E. Roberts

A mathematic technique has been presented for the study of unilateral renal disease. Its accuracy assumes that water does not shift across the bladder mucosa. These experiments were designed to determine if water or electrolytes did shift across the bladder membrane.

Utilizing female dogs under nembutal anesthesia the ureters were ligated, distally, and ureteral catheters inserted for total collection of urine from the kidneys. The bladder remained "in situ" but separated from the ureters. Fifty cc of various concentrations of Dextrose(i.e.0-5%) containing radioactive hippurate(RAI) was placed in the bladder. 4 cc aliquots were removed at intervals for analysis of electrolytes and RAI. Urines and blood were also collected for the analysis of RAI at appropriate intervals. The results showed that no RAI appeared in the ureteral urine or plasma and all injected material was recovered in the same concentration, thus, indicating that water did not shift across the bladder. There was, however, a gradual increase in sodium concentration to 10-20 mEq within a twenty minute interval.

These experiments propose an excellent preparation for the study of isolated bladder function and define shifts of electrolytes, but not water into the bladder and thus, strengthening studies of unilateral renal function.

PHYSIOLOGICAL EFFECTS OF ACTIVE AND PASSIVE EXERCISE. Fred B. Benjamin, L. Peyser* and G. Albright*. Life Sciences Laboratory, Republic Aviation Corporation, Farmingdale, L.I., New York

In 1888 Geppert and Zuntz found that passive exercise increases pulmonary ventilation. In 1961 Dixon and co-workers found that: "In passive exercise, ventilation is stimulated in excess of demand indicated by the oxygen consumption." Balke and co-workers showed that jet pilots experience marked hyperventilation which, according to Dixon's findings, may be due to the effect of passive jolting. As the mechanism of this change was never clarified, this study was undertaken to determine changes in heart rate, respiration, and body temperature in active and passive exercise. In 14 tests on 7 human subjects, it was found that active exercise produces a greater increase in heart rate and tidal volume, while passive exercise produces a greater increase in respiratory rate, respiratory minute volume, and body temperature.

ADENINE NUCLEOTIDES AND THEIR DERIVATIVES IN ANOXIC CARDIAC AND SKELETAL MUSCLE. R. M. Berne, S. Imai* and A. L. Riley,* Dept. of Physiology, Western Reserve U. Sch. of Med., Cleveland, Ohio.

An hypothesis has been proposed suggesting that coronary vasodilation seen in reduced oxygen supply to the heart or in increased metabolic activity of the myocardium is mediated by the release of adenosine from the myocardium (Fed. Proc. 20: 101, 1961; Am. J. Physiol. 204: 307, 1963). In an attempt to test the validity of this hypothesis the adenine nucleotides and their derivatives were enzymatically quantitated in the normal and anoxic rabbit heart. The amounts of ATP, ADP, AMP and Adenosine (Ads) in normal ventricular myocardium were 4.04, 0.67, 0.48 and 0.28 μM/g wet wt., respectively. Inosine (In) and hypoxanthine (Hx) could not be detected. In preparations of the intact heart in which the coronary circulation was maintained there was a large decrease of ATP, increase of ADP and AMP, decrease of Ads and appearance of In and Hx with progressively increasing periods (up to 3 min.) of anoxia (respirator stopped in open chest animal). With interruption of the coronary circulation anoxia produced an increase in Ads followed by a decrease associated with increases in In and Hx in the myocardium. These findings are compatible with the idea that Ads is the vasodilator mediator. In view of the high myocardial Ads deaminase content, compartmentalization of the Ads in the normal heart appears likely. In ischemic skeletal muscle Ads was not increased, AMP was slightly increased, and inosinic acid was greatly increased. These findings indicate a different degradative pathway of adenine nucleotides in skeletal muscle and suggest a different regulatory mechanism in skeletal muscle than that hypothesized for heart.

THE RELATION OF AGE TO SPINAL CORD REGENERATION IN THE ADULT GOLDFISH. Jerald J. Bernstein*, Laboratory of Neuroanatomical Sciences, N.I.N.D.B., N.I.H., Bethesda, Maryland.

In the fish and amphibia the regenerative capacity of the spinal cord decreases from the embryonic stages of life to adulthood. The present experiments examine the relationship between age and the regeneration of severed spinal elements in the adult goldfish. The spinal cord of 1, 2, and 3 year old fish (2, 2, and 7 inches long respectively) was transected in the mid dorsal fin region. Behavior. The operation resulted in paralysis caudal to the lesion. Normal swimming and turning movements occurred in 20-25 days for 1 year olds, 25-30 days for 2 year olds, and 35-40 days for 3 year olds. Electrophysiology. In all age groups stimulation of the cervical spinal cord 30 days postoperatively elicited electromyographic responses in the myotomes caudal to the lesion. Anatomy. By 7 days postoperatively, small branching nerve fibers had grown from both proximal and distal stumps into the connective tissue scar in the gap. By 90 days postoperatively regeneration was complete. At this time there was a 26% decrease in cord diameter in the 2 year olds ($P<.001$), a 28% decrease in the 3 year olds ($P<.005$), but only 0.5% decrease in 1 year olds ($P>.50$). In the region of transection the percentage of fibers was significantly greater in the 1 year olds than in the 2 and 3 year olds ($P<.01$); in the 1 year olds the number of fibers was 90% of normal whereas in the 2 and 3 year olds it was 50% of normal. There were no motor horn cells in the regenerated area, and Mauthner's axon did not regenerate. It is concluded that spinal cord regeneration in the goldfish is age dependent; however, regeneration was sufficient in all age groups studied to result in complete restitution of function.

PRESSURE-VOLUME CHARACTERISTICS OF LUNG-THORAX OF RELAXED, NORMAL, HUMAN MALES. Leon Bernstein, Harold H. Phillips*, and Richard B. Paddock*. VA Hosp. & Cardiovasc.Res.Inst., UC Med.Ctr., San Francisco, Calif.

Although indirect evidence suggests that compliance of the human lung-thorax at or just above functional residual capacity (FRC) is increased after inflation to near vital capacity, this has not been demonstrated directly, as has been done for other species. In these experiments, patients without overt respiratory disease, awaiting minor surgery, were anesthetized 2 hr before its scheduled start, were relaxed with i.v. tubocurarine, and were ventilated artificially at constant (500 c.c.) tidal volume. After they had been 1 hr on this regime, we determined pressure-volume curves of their lung-thorax, as follows: A - by discrete inflations to sequentially increasing volumes above FRC; B - in repetion of A without delay; C - in repetition of B after intervening periods of from 10 to 60 min of ventilation with the original tidal volume; and D - in stepwise deflation from the greatest volume reached in A,B, or C. Pressures were recorded with an aneroid manometer, after equilibration periods of 10 sec for each injection and 5 sec for each withdrawal of air. Curve A consisted of two straight segments intersecting about 1,000 c.c. above FRC; above this volume compliance was greater: B and C were co-terminous with A, and, with pressure as ordinate, lay wholly below A; C lay between B and A, and approached A as the delay was increased; D closely resembled B, returning through the origin at FRC and barometric pressure. Generally, the forms of and the relations between these curves resemble those reported for other species. They confirm the occurrence of a temporary increase of compliance at or just above FRC following large inflations.

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ORIGIN OF SOME VISUAL CORTEX AFTERDISCHARGES IN ANESTHETIZED CATS. K. E. Bignall* and L. T. Rutledge. Dept. of Physiology, Univ. of Mich., Ann Arbor, Michigan.

In anesthetized cats, the visual cortex response to a brief flash consists of a short latency positive-negative primary complex, usually followed by a second complex of similar waveform and cortical distribution. Under Nembutal this second complex can represent the first of several waves of a "multiple" response; under chloralose, normally only the primary and second complexes are present. Investigation of the origin of the second complex in cats under Nembutal or chloralose anesthesia has shown: 1) It survives removal by suction of mesencephalon and most of thalamus, including non-specific and association nuclei but excluding lateral geniculate. 2) It is present in subcortical white matter before and after aspiration of visual cortex. 3) It is depressed more than the primary by brief retinal anoxia produced by raising intraocular pressure. 4) It reverses polarity within cortex in the same manner and at the same depth as the primary. 5) It, like the primary, facilitates the cortical response to optic pathway shock. 6) Correlated long latency responses are usually seen in lateral geniculate and can be detected in retina, but are seldom present in optic tract. 7) Most cortical cells discharging during the second complex fire also during the primary "on" and/or "off" response. The second complex of the photically evoked visual cortex response thus apparently originates within the specific afferent system, below cortex and possibly in retina, and occupies elements in common with the primary "on" and "off" cortical responses. The second complexes seen under Nembutal and under chloralose are evidently generated by the same mechanism.

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EFFECTS OF UNILATERAL HEMISPHERIC AND OPTIC TECTAL ABLATIONS ON VISUAL DISCRIMINATION LEARNING IN PIGEONS. Richard L. Binggeli*, Robert D. Tschirgi, and Bernice M. Wenzel. Univ. of Calif. Sch. of Med., L. A.

Damage to the central nervous system usually produces deficits rather than enhancement of some aspect of performance. However, in the following study it was observed that learning rate was augmented for certain visual discrimination tasks after unilateral lesions in the optic tectum. Adult blue and racing homer pigeons were used; 7 had one entire hemisphere removed by suction, 9 had varying degrees of unilateral lesions in the mid-lateral optic tectum, 3 had the retina of one eye destroyed, and 6 were normal. The birds were trained to peck at either a red or green key depending on the position of a preceding white cue light. The red and green keys were randomly interchanged from trial to trial. All birds were first practiced to a predetermined pecking proficiency and then given equal amounts of pre-training in the various components of the final task. In the final discrimination task 85 trials of white cue light followed by red and green response keys were given per day. Performance was measured as per cent correct responses per day. The results show that: (1) the hemispherectomized birds learned most slowly (more than 26 days to criterion); (2) the normal and retinal damaged birds learned at an intermediate rate (14.6 and 13.0 days, respectively); and (3) the tectal damaged group (with two histologically definable exceptions) learned most swiftly (7.7 days). All ablated animals were subsequently killed and examined histologically for direct and degeneration effects. Supported by grant USPHS 2M-6415 from the National Institute of Mental Health.

EFFECTS OF SUPINE AND SITTING EXERCISE ON CIRCULATORY AND METABOLIC ALTERATIONS IN PROLONGED BED REST. N. C. Birkhead, G. J. Haupt*, J. J. Blizzard*, P. A. Lachance and K. Rodahl. Div. of Research, Lankenau Hospital, Philadelphia, Pa.

Prolonged bed rest (6 weeks) resulted in increased urinary excretion of calcium (Ca) but not nitrogen (N), orthostatic intolerance and decreased maximal O_2 uptake. To further study these effects, similar metabolic and hemodynamic measurements were made in 4 healthy trained men before, during and following 24 days' continuous bed rest, except for one hour daily of bicycle exercise in supine (2 subjects) or sitting (2 subjects) position. Urinary Ca increased by the second week and reached levels twice control values. Decreased tolerance to 70° head-up body tilt also developed, but maximal O_2 uptake and pulse response to exercise were unaltered. One hour of daily supine or sitting exercise was sufficient to maintain physical work capacity but did not prevent orthostatic intolerance or increased urinary Ca loss resulting from bed rest. (Supported in part by U.S. Air Force Contract No. AF 33(657)9049.)

INFLUENCE OF INTRAPULMONARY PRESSURES ON THE ACTIVITY OF THE ABDOMINAL MUSCLE AND DIAPHRAGM. Beverly Bishop. Department of Physiology, State University of New York at Buffalo, Buffalo, N. Y.

It has been demonstrated previously that continuous positive pressure breathing (CPPB) in the anesthetized cat (1) excites expiratory activity in the abdominal muscle, and (2) inhibits the diaphragm. In this investigation we have tried to determine whether these activities are linked or separate. It was found that when a given pressure has to be overcome during expiration (P_E) the activity of the abdominal muscle (AMR) is recruited to the same extent regardless of the pressure to which the animal was exposed during the preceding inspiration. This occurs although changes in lung volume and blood pressure accompanying CPPB are different from those seen when the increase in pressure occurs only during expiration. On the other hand, the inspiratory activity of the diaphragm is augmented if the pressure is applied only during expiration and decreases with each increment in pressure applied during inspiration. Vagotomy abolished the AMR under all conditions as well as the inhibitory response of the diaphragm to CPPB, but did not interrupt the augmented inspiratory activity of the diaphragm to P_E. It is concluded that abdominal muscles respond selectively to an increase in airway pressure during expiration, while the diaphragm activity is regulated specifically by the difference between pressures during inspiration and expiration. (Supported in part by U. S. Air Force Contract AF 33(657) 10082.)

AN EXPLANATION FOR GLYCOLYTIC FAILURE IN STORED HUMAN RED CELLS. Charles Bishop. (intr. by Fred R. Griffith, Jr.). State University of New York at Buffalo, Buffalo, New York.

Since human red cells derive all their energy from glycolysis, the gradual failure of glycolysis in red cells on storage leads to cell death. Hexokinase, which catalyzes the first step in glycolysis has long been regarded as a critical factor in failing glycolysis. An assay was devised for hexokinase activity in the intact cell. This was based on O_2 uptake in the presence of methylene blue, utilizing alternately glucose or inosine as substrate. As hexokinase activity decreased in the stored cell, O_2 uptake with glucose decreased while O_2 uptake with inosine remained unaltered. This was not due to failure of the enzymes, however, but was because of a shortage of ATP, the other factor required for glucose phosphorylation. This was demonstrated by showing that in the presence of an ATP-generating system it was possible to restore the stored red cell to its initial hexokinase activity level. (Supported by NIH Grants AM-06367 and A-5581).

STUDY OF THE VIBROCARDIOGRAM ON ATHLETES DURING MAXIMUM EXERCISE. D. J. Bleifer*, C. M. Agress, and H. M. Estrin.* Cedars of Lebanon Hospital, Los Angeles, California.

Previous studies have demonstrated the accuracy of the vibrocardiogram in the measurement of isometric contraction and ejection. Furthermore, the relationship of the duration of isometric contraction to ejection, when expressed as a ratio, decreases after exercise in patients with angina and in coronary insufficient dogs. It was desired to study these ratio changes in college athletes at maximum exercise on a bicycle ergometer. The pulse, blood pressure, respiration, electrocardiogram and oxygen consumption were determined at rest and at the peak of exercise and five minutes after recovery. Oxygen consumption often reached 15 times the control levels while the vibrocardiographic interval ratio increased over 100 per cent. The constant increment up to maximum effort indicated (1) that isometric contraction and ejection can be measured accurately by an external technique during vigorous exercise and (2) that these intervals expressed as a ratio, parallel the pulse rate and oxygen consumption.

RADIOISOTOPIC RADIODENSITOMETRY: A NEW METHOD FOR DETERMINING BLOOD FLOW AND CIRCULATION TIMES BY THE INDICATOR DILUTION PRINCIPLE. William T. Blessum* and Alfred W. Brody, The Creighton Univ. School of Medicine, Omaha, Nebraska.

Uncalibrated variations in radiodensity of the heart following injections of contrast material have been described previously utilizing angiography and cinefluorographic film densitometry. With a ten millicurie Lead 210 encapsulated collimated source of low energy gamma rays and a scintillation tube and countrate meter as the detection system, we have continuously recorded radiodensitometric indicator-dilution curves in a model system and in dogs, and compared flows calculated by this method with those obtained simultaneously with the dye-dilution technique. Instantaneous concentration was computed from $I = I_0 e^{-KC}$, where I = Instantaneous count rate, I_0 = baseline rate, K = absorbance constant, and C = indicator concentration. Each curve was calibrated from the concentration of an "equilibrium" sample drawn after thorough indicator mixing in the system when concentration was changing very slowly; this concentration with equilibrium and baseline count rates substituted into the above formula gave the absorbance constant. In fifteen experiments in a recirculating model system, flow comparisons between radiodensitometric and Indigo Carmine dilution curves demonstrated close agreement with no systematic difference between the two methods (Diff. in Av. $<1\%$, $p>.95$). Distinct right and left heart curves may be inscribed at low and localized radiation exposure without the necessity of handling radioactive solutions. (*Trainee USPHS HTS-5506 and Post sophomore Fellow USPHS Gen. Res. Support Grant; Study supported in part by Nebraska Heart Association Heart Chair Grant.)

COMPARISON OF AEROBIC AND ANAEROBIC ACTIVE TRANSPORT BY DIFFERENT REGIONS OF THE YOUNG CHICK INTESTINE. P. H. Bogner, I. A. Haines,* and P. L. McLain, Jr.* Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

Active transport of galactose by the upper, middle, and lower thirds of the small intestine from embryos (3 days from hatching) and 0-, 2-, and 9-day-old male chicks was measured by means of the in vitro tissue accumulation method. In an oxygen atmosphere none of the embryonic tissues accumulated galactose whereas all areas from the hatched chicks actively transported this sugar. Transport increased in all intestinal regions between 0- and 2-days of age. Although activity was greatest in the middle third in both these age groups, it only slightly exceeded that in the upper (duodenal) third. At nine days of age the concentrating power of the middle third was considerably higher in the midportion than in the other two sections. In a nitrogen atmosphere all intestinal areas from the hatched chicks concentrated galactose, but to a lesser extent than occurred in the presence of oxygen. In a number of experiments the anaerobic active transport of the upper third clearly exceeded that in the other two areas. Galactose utilization was also somewhat greater in this section in the nitrogen atmosphere although it was not accompanied by an increased production of lactic acid. The galactose, therefore, seems not to have entered the glycolytic pathway. There is thus reason to believe that the upper or duodenal region of the intestine possesses the greatest metabolic potential under anaerobic conditions while the middle third appears to be most active when oxygen is available. (Supported by N. I. H. grant A-2353)

TESTS OF HUMAN CARDIAC PERFORMANCE BEFORE AND AFTER CARDIAC SURGERY. Clorinda S.-S. Bohler*, Robert G. Ellison, and Philip Dow. Depts. of Physiology & Thoracic Surgery, Medical College of Georgia, Augusta.

These studies are part of a broad effort to identify the factors involved in promptness and completeness of improvement of cardiac function after corrective surgery. Most of the patients in this series were having mitral repair or replacement. Output and pressure data for an index of cardiac performance were obtained immediately before and immediately after the bypass procedure, immediately upon awakening, and up to 24 hours later in the recovery room. Output data without pressures were obtained on many of the patients before operation and up to several days afterward. Outputs were done by central injection and arterial sampling of Cardiogreen (Gilford densitometer). Left ventricular end diastolic pressures were obtained by intraventricular catheter and a Statham strain gauge during the operation, and left atrial pressures were gotten during the recovery period by a polyethylene tube through the chest wall. Flow usually increased after the corrective surgery and pressures often varied spontaneously or with drugs administered during the post-operative period. Left ventricular work was calculated from the left ventricular output and the pressure rise from left atrium to aorta, and the plot of this figure against LVEDP or mean LAP furnished an index of cardiac performance. The vector of this performance index regularly swung in the direction representing improvement. Aided by grants from the Life Insurance Medical Research Fund and the National Institutes of Health (H-240, H-5432, HE-07266).

EFFECTS OF HYDROGEN PEROXIDE INFUSION ON IRRADIATED BONE. William R. Bond, Jr.*, James W. Finney*, and J. L. Matthews. Baylor Dental College and Baylor Medical Center, Dallas, Texas.

Osteoradionecrosis was induced in monkey mandibles by radiation through two 16 mm diameter ports on each side. A total of 2700 R absorbed dose was given to each side of the mandible with a 250 KVP unit at 30 MA at a focal skin distance of 20 CM. Infusion of 0.12% hydrogen peroxide was effected by cannulation of the right carotid artery. The left side was used as the non-infused control side. Clinical and radiological examinations were made at weekly intervals. A biopsy of the mandibles was made at two months and histological examinations of the mandibles were made following sacrifice at 117-119 days. Both sides demonstrated previously described characteristics of osteoradionecrosis. The infused side demonstrated a marked increase of both periosteal and endosteal cancellous bone, while the marrow of the infused side was less fibrous, suggesting an osteogenic effect of peroxide with inhibition of fibrous tissue displacement of myeloid elements.

ROLE OF CARDIOPULMONARY BYPASS IN TREATMENT OF ENDOTOXIN SHOCK. Bor, Naci M.*, Brecher, Gerhard A., Boles, Margaret A.* and Martinez, Patricia, D.*. Research Institute, Presbyterian Hospital, Philadelphia, Pennsylvania and Department of Physiology, Emory University, Atlanta, Georgia.

In anesthetized closed chest dogs peripheral arterial, venous and pulmonary arterial pressures, electrocardiogram and temperature were continuously monitored. Arterial pH, hematocrit, total oxygen uptake, oxygen and carbon dioxide contents of the arterial and mixed venous blood were determined. Cardiac output and peripheral resistance were calculated. E. coli endotoxin was injected intravenously, 6 mg/Kg., and the animal observed for three hours while profound shock developed and all measured parameters became abnormal ($P < 0.01$). Cardiopulmonary bypass was then begun, draining blood from caval veins and after oxygenation returning it to femoral arteries. Perfusion rate was gradually increased to 147 $\pm$ 28 ml/Kg/min. and sustained for two hours. Maintenance of a physiological arterial blood pressure was the primary consideration. It was found that all the pathological trends established in shock were reversed by perfusion ($P < 0.01$): Arterial pressure increased from 55.1 to 119.3 (mean) mmHg. Venous oxygen content rose from 5.41 to 16.33 vol. % and arteriovenous oxygen difference declined from 12.6 to 3.6 vol. %. pH increased from 7.12 to 7.28 as did the carbon dioxide excretion rate from 1.90 to 3.73 ml/Kg/min. Oxygen uptake returned to its control level, 5.19, from 3.08 ml/Kg/min in shock.

THE EFFECT OF INTRAVENOUS INFUSION OF KCl ON CANINE URETERAL PERISTALSIS IN VIVO. S. Boyarsky, J. Sharkey* and P. Catacutan-Labay*, Albert Einstein College of Medicine, N. Y.

Ureteral peristaltic pressures in dogs with explanted bladders recorded by catheters and transducers have been previously shown to be influenced by histamine, benadryl and hydrodynamic load. KCl, 0.6 meq/min. i.v., increased the peristaltic rate in a manner analogous to histamine and unlike that due to diuresis. Electrocardiographic Lead II, T-wave elevation paralleled this ureteral effect. The rate of serum K^+ rise seemed to govern, rather than the absolute level. The change in ureteral frequency was inversely proportional to the change in calculated, intracellular-extracellular K^+ ratio. (Total body water estimated as 54% body weight and intracellular water as 32% body weight: serum K^+ and administered K^+ were measured.) A decrease in this ratio from 35 to 17 led to a doubled frequency in four experiments. Variations in this ratio to a greater or lesser extent were inversely proportional to the change in frequency of peristalsis. Intravenous histamine (40 mcg/kg) during hyperkalemia produced a further independent rise in frequency. Histamine administration alone was followed by concomitant biphasic fluxes in serum K^+ levels, possibly due to losses from muscle cells during contraction. Peristaltic changes in the ureter may be associated with alterations in intracellular-extracellular K^+ gradients, whether the changes are induced by histamine or by K^+ administration. [Supported in part by Public Health Service Research Grant GM 05986-05 from the NIH.]

CONTROLLED-DEPTH ANESTHESIA FOR RESPIRATORY STUDIES. Bernard Brandstater, Edmond I. Eger, II, and Gerald Edelist (intr. by John W. Severinghaus). Cardiovascular Research Inst., Univ. of Calif. Med. Center, San Francisco.

Respiratory depression from anesthetic drugs introduces an undefined variable into many experiments. This study was designed to test whether the degree of depression from halothane could be kept constant by maintaining an unvarying concentration in arterial blood. To approximate this in dogs anesthetized with halothane and oxygen in a semi-closed circle, alveolar (end-tidal) concentration of halothane was kept constant using a Beckman infrared halothane analyser. The ventilatory response to CO_2 was recorded awake and at several fixed alveolar concentrations of halothane after allowing sufficient time for blood-brain equilibration. Increments in halothane concentration resulted in a shift to the right and a diminished slope of the $\dot{V}_E/P_{A_{CO_2}}$ response curve. The slope of the response curve diminished in direct proportion to the alveolar halothane concentration, from the awake state, where the slope was steepest, through all levels to deep anesthesia, where the slope became negative. With halothane concentration kept constant, the response to CO_2 remained essentially unchanged for periods up to 12 hours. In 4 dogs the effect of intravenous thiopental was determined after first establishing a control $\dot{V}_E/P_{A_{CO_2}}$ curve. With the halothane concentration kept constant, a minimal "sleep" dose of thiopental caused a significant shift of the response curve towards higher $P_{A_{CO_2}}$. Between 3 and 4 hours elapsed before the response returned to control values. It was concluded that induction of anesthesia with an intravenous barbiturate, though technically desirable, would in some degree distort any respiratory response data obtained during the ensuing several hours. (Supported in part by USPHS HE-6285 and 2G 63.)

ROLE OF RATE OF CHANGE OF SKIN TEMPERATURE IN HUMAN TEMPERATURE REGULATION. G. L. Brengelmann* and A. C. Brown. Dept. of Physiology & Biophysics, Univ. of Washington School of Medicine, Seattle, Wash.

Interaction between the rate of change of skin temperature and the levels of skin and central temperature is a factor in the control of metabolism. The object of these studies has been to analyze the extent of this interaction quantitatively. Skin temperature (Ts) was controlled by immersing subjects in a well-stirred water bath, and was uniform over the body surface within 0.1 C. The tympanic membrane and rectal temperatures were recorded continuously within 0.02 C. Heat production was calculated from the rate of O_2 consumption. The sensitivity to rate of change of Ts was tested by rapidly shifting the temperature of the bath (steps) and by changing it more slowly at various rates (ramps). In response to step decreases, an appreciable overshoot in O_2 consumption was seen only when the final Ts was below about 31 C, and amounted to as much as 50% more than the final steady state value upon a decrease to 28 C. Increasing steps produced the inverse response pattern. Central temperature decreased in response to a step increase from 28 to 31 C. The pattern of responses to ramp decreases depended on the rate of fall of Ts. At rates of 1 C/5 min to 1 C/10 min, central temperature was maintained throughout the ramp, but it and O_2 consumption dropped to a new steady value after the ramp was terminated at 28 C. In ramps slower than 1 C/20 min central temperature decreased and O_2 consumption increased continuously with no discontinuity in response when the ramp ended at 28 C. Increasing ramps with rates greater than 1 C/15 min resulted in depressed O_2 consumption and central temperature. These results can be approximated by a first order differential equation in which dTs/dt is summed with both Ts (to indicate the stimulus from surface temperature) and a response in the form of $\tau d(\dot{V}_{O_2})/dt + \dot{V}_{O_2}$ to account for the lag in metabolic rate.

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MEASUREMENT OF SYSTEMIC VASCULAR COMPLIANCE B. Bromberger-Barnea, S. Permutt, and R.L. Riley. Johns Hopkins University, Baltimore, Md.

To measure the compliance of the systemic vascular bed (Cs), it is necessary (1) to change the blood volume of that bed by a known amount (ΔVs) and (2) to determine the change in mean systemic pressure (ΔPs). To accomplish (1), we add a known amount of blood (ΔV) to intact, anesthetized dogs under conditions where we can be relatively certain that no change in intrathoracic blood volume can occur; thus, $\Delta V = \Delta Vs$. We keep the intrathoracic blood volume constant by increasing intrapleural pressure (Pip) and adding blood in such a manner as to keep transatrial pressure (Pra-Pip) constant. At the same time, tracheal pressure (Pt) is increased by the amount necessary to keep transpulmonary pressure (Pt - Pip) constant. Under these conditions, it is reasonable to assume and has been shown experimentally that blood flow (Q) and blood volume of the intrathoracic structures are unchanged. Furthermore, since Q is unaltered, the pressure gradient between periphery and the thorax is unaltered, even though Pip and Pra are increased; and it is reasonable to assume that the rise in Pip has been paralleled by an equal rise in pressure everywhere in the peripheral circulation. Thus, Δ Pip = Δ Ps. Therefore, $\Delta V/\Delta$ Pip = Cs. Average values of Cs were 2 ml/kg/cm H_2O (range 1.2-2.7). Increases in venous tone from hemorrhage or epinephrine were not accompanied by significant decreases in Cs. Surprisingly, with hemorrhage there was a slight increase in Cs. We conclude that an increase in the tension of smooth muscle in the walls of the veins acts as a pressure equivalent (like a G-suit), rather than through altering the elastic properties of the veins.

CONTROL OF ACTIVITY IN SUPRAOPTIC NUCLEUS NEURONS. Chandler McC. Brooks, Tomoe Ishikawa* and Kiyomi Koizumi. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Single unit activities were recorded from supraoptic nucleus or nearby regions by microelectrodes in chloralose anesthetized cats or cats decerebrated under ether. Only neurons which were sensitive to osmotic changes in blood produced by intra-carotid injection of hypertonic sodium chloride solution were considered to belong to the supraoptic nucleus. Stimulation of the cingulate gyrus or somatic afferents from a leg most often excited these neurons while stimulation of cerebellar posterior lobe tended to inhibit the activity. Acetylcholine given intra-arterially or intravenously augmented the neuron discharges, but large doses of the same drug inhibited them temporarily, possibly due to the lowering of blood pressure. Stimulations of motor and frontal cortex sometimes caused an increased activity in supraoptic neurons but were less effective than other stimuli employed. Isolation of supraoptic region from other neural tissues abolished all effects from stimulating neural structures. Unit discharge continued and chemical stimulation still caused the changes described above. (Supported by a grant from USPH-NB-00847(08))

ENERGY RELEASE BY ELECTRON TRANSFER, THE TRIGGER MECHANISM IN LIVING CELLS. Matilda M. Brooks. Univ. of California, Berkeley, California.

The basic principle controlling all biological reactions in animal and plant life, termed, "trigger mechanism" is the electron attraction for atoms more positively charged than the one to which the electron is attached, whereby energy is released. The fertilization of eggs by sperm or artificially is the result of the electron attraction of the negatively charged unfertilized egg by the positively charged sperm or chemicals used, as shown in marine eggs, by producing the correct energy release which begins cell division. In the aerobic respiratory mechanism each enzyme on the scale is at a higher energy state so that the electron is able to release energy stepwise to the region of the cytochromes and oxygen, forming water. In green plants, the high energy from the sun's rays, absorbed at the exact wave length of chlorophyll, raises the electrons to a high energy level as they are attracted to the positively charged nuclei radiated from the sun. This results in the separation of the oxygen atom from water and one from CO_2. The two remaining hydrogen atoms from water unite with the carbon atom to complete the 4 valences left incomplete by the removal of one oxygen atom. This rearrangement results in the formation of CH_2O as the first step in the reduction process. The CH_2O becomes further reduced through biochemical combinations in seconds as the electrons lose their high energy state and drop back to normal in the dark. The two oxygen atoms unite to form molecular oxygen.

TWENTY-FOUR HOUR CYCLES IN URINARY NITROGEN AND ELECTROLYTES IN MEN. Gerald E. Brooksby * and Donald R. Young. National Aeronautics and Space Administration, Moffett Field, Calif.

Urinary excretion of electrolytes is known to vary systematically during a 24 hr. period. To further examine the phenomenon of periodicity, particularly in its relationship to electrolyte and protein metabolism, measurements were made over a 7 day period on men consuming a constant diet. Urinary samples were obtained every 4 hrs. and examined for their content of Na, K, Ca, total nitrogen, and amino acids. The excretion of electrolytes and total nitrogen showed similar frequencies, 1 and 2 cycles per day, and in general were in phase with each other. There was no correlation between the excretion of these substances and the feeding schedule or the work-rest cycle. The average content of nitrogen in the 4 hr. urine samples was 2 gm. and the mean amplitude or displacement from the mean was 1 gm. Urinary glycine, histidine, methyl histidine, lysine, threonine, methionine, and isoleucine followed closely the pattern of total nitrogen excretion. It is concluded that periodic cycles of protein as well as electrolyte metabolism are related to basic body rhythms.

THE SIGNIFICANCE OF HEART RATE CHANGES IN DOGS WITH EXPERIMENTAL NEUROGENIC HYPERTENSION. William E. Brown*, W. Linell Murphy* and Edward W. Hawthorne. Howard University College of Medicine, Washington, D. C.

The chronic neurogenic hypertension which follows resection of buffer nerves in dogs is generally believed to be due to a chronic increase in cardiac output. The latter is presumed to be due solely to the chronic and significantly increased heart rate in such animals. In normal dogs and in dogs with complete heart block a significant rise in mean arterial pressure (60 mm Hg +) follows debuffering. In control dogs the rise in pressure is invariably accompanied by increases in heart rate of 100 beats/minute or more while in dogs with complete heart block no change in heart rate is seen. Thus, alterations other than changes in heart rate are involved in the pathogenesis of neurogenic hypertension.

AN ERYTHROPOIETICALLY ACTIVE FRACTION IN "ALTITUDE" GOAT MILK. T. R. Bullard* and J. C. Stickney. Department of Physiology, West Virginia University Medical Center, Morgantown, W. Va.

Milk was obtained from goats which had been exposed to a simulated altitude of 22,000-24,000 feet and ground controls. Casein, fat, and lactose were removed and the whey was lyophilized. The dried whey was dissolved in buffer and eluted through a DEAE cellulose column 4x31 cm. using first an acetate buffer (0.01M, pH 4.8), then a 0.5M NaCl acetate buffer gradient, and finally a salt-alkali gradient of 1M NaCl and 1N NaOH. Three absorption peaks were obtained in both control and altitude whey. Sialic acid was determined using the diphenylamine reaction and was found in greatest quantities in the second peak (peak B). Starved male rats were given i.p. injections of altitude and control peaks A and B, and saline daily for four days. On the fifth day reticulocytes and hemoglobin were determined. There was no difference in the hemoglobin values for the experimental and control animals. Rats given peak A showed no significant difference over controls while those receiving peak B had a significant increase in reticulocytes with a p: 1% and an F value of 6.656 significant at the 5% level. The evidence indicates that altitude goat milk whey contains a reticulocyte stimulating factor which is found in peak B. It is possible that this factor is erythropoietin.

LEFT VENTRICLAR WALL TENSION IN MAN CALCULATED FROM ANGIOGRAPHIC VOLUMES. I. L. Bunnell*, C. Grant* and D. G. Greene. State University of New York at Buffalo, Buffalo, N.Y.

Angiographic determination of left ventricular volume plus simultaneous pressure permits calculation of developed wall tension. Calculations have been based both on a thin-walled spherical and thick-walled ellipsoidal reference model. From the ellipsoidal model, two values of tension can be calculated at the waist, one in the polar and one in the equatorial plane. Both latter values take into account measured wall thickness. Twenty-five conscious human subjects have been studied: 7 with normal ventricles, 10 with predominant dilatation, 5 with hypertrophy and 3 with primary myocardial disease. From the thin-walled spherical model, tension in the normal ventricle is significantly less than that in dilatation, hypertrophy or primary myocardial disease. Tension in the polar plane of the ellipsoidal model is not significantly different from that calculated from the spherical model except for a 30% increase in 3 of the 5 hypertrophied ventricles. Wall thickness therefore appears to modify calculated tension only with significant hypertrophy. Tension in the equatorial plane of the ellipsoidal model is 2/3 greater than that in the polar plane of normal, dilated or hypertrophied ventricles, but with primary myocardial disease is only 1/3 greater. In primary myocardial disease the ventricle is of nearly spherical proportions and the effect of ellipsoidal shape on wall tension is minimized. The integrated systolic wall tension, Tension Time Product (TTP) is lower in normal and hypertrophied ventricles than in dilated or diseased ventricles. However, when allowance is made for the stroke work done per unit TTP, it can be seen that hypertrophied ventricles are capable of twice the normal amount of work per unit of systolic tension; dilated ventricles are similar to the normal while diseased ventricles are capable of only half the normal amount.

OXY-HEMOGLOBIN AFFINITIES AND HEMOGLOBIN PATTERNS IN TWO SPECIES OF BASSES. Jack D. Burke (intr. by Ernst Fischer). Univ. of Richmond and Med. College of Va., Richmond, Va.

Hemoglobin solutions of pooled samples from Micropterus dolomieui (smallmouth bass) and Micropterus salmoides (largemouth bass) were made up in phosphate buffer (u = 0.3; pH 7.4 and 6.8); spectrophotometric readings were made at 25 ± 1° C. At pH values of 7.4 and 6.8, 50 % saturation with oxygen of smallmouth bass hemoglobin occurs at 14 and 93 mm Hg whereas the largemouth hemoglobin is 50 % saturated at 9 and 30 mm Hg. Electropherograms were made on cellulose acetate membranes after electrophoresis in an electrocab containing a barbital buffer (u = 0.05; pH = 8.6) for 1 hr. at 250 V. The patterns were developed by staining with brom phenol blue or amido black 10B, clearing in dilute acetic acid solution, and drying in air. The patterns showed distinctly the presence of 3 hemoglobins in the smallmouth bass and 4 hemoglobins in the largemouth bass. These hemoglobin differences - oxy-hemoglobin affinities, Bohr effects, and electrophoretic patterns - seem to be important in establishing the limits, sometimes overlapping, of the habitats occupied by populations of smallmouth and largemouth basses. This work is part of an investigation supported by the National Institutes of Health, Bethesda, Maryland under Grant No. H-4708.

INTERRELATIONSHIPS OF THYROID HORMONE AND EPINEPHRINE IN TISSUE CULTURE H. Burlington, Department of Physiology, University of Cincinnati College of Medicine, Cincinnati, Ohio

The nature of thyroid hormone-epinephrine interrelationships is unclear. Difficulty in precisely defining their interaction stems partly from the multiple effects of each and fluctuating variables in the intact organism. Tissue culture provides the opportunity to examine one aspect of the interaction in the absence of complicating variables. The effects of Triiodothyronine (T_3), epinephrine, and nor-epinephrine on oxygen consumption (QO_2), and aerobic glycolysis (QCO_2) in primary cultures of dog kidney cortex was studied. The hormones, alone or in combination were included in the medium throughout the period of cell growth. When harvested the cells were rinsed free of hormone. T_3 stimulates both QO_2 and QCO_2 whereas epinephrine inhibits QO_2 while stimulating QCO_2 slightly. In combination the effects are additive. Hormonal effects on individual enzyme systems involved in the response were also studied. For example, succinic dehydrogenase, cytochrome oxidase, and malic dehydrogenase respond in a manner which indicates that the endocrine interaction at this level is minimal and apparently indirect.

HEAT EXCHANGE IN MAN FOLLOWING INTRAVENOUS INJECTION OF ENDOTOXIN. E. R. Buskirk, R. H. Thompson*, S. M. Wolff* and M. Rubenstein*. National Inst. of Arthritis and Metabolic Diseases and National Inst. of Allergy and Infectious Diseases, National Insts. of Health, Bethesda, Md.

This investigation was designed to assess heat exchange during the course of an induced febrile episode following injection of endotoxin. Seventeen experiments were performed on thirteen young and middle aged normals or patients with recurrent fever of both sexes. They were given I.V. either saline or a dose of one or two millimicrograms (ng) of Lipexal (the lipopolysaccharide of Sal. abortus equii) per kg body weight approximately 15 minutes before being exposed for 3 to 6 hours to 27.7°C (82°F) air in the Metabolic Chamber while wearing minimal clothing. Continuous measurements were made of: oxygen consumption, carbon dioxide production, core temperatures (ear, esophagus, rectal), skin temperatures, muscle surface temperature (beneath subcutaneous adipose tissue of the forearm), and heat flow from the lateral surface of the upper and lower arm and the back of the hand. Three distinct patterns of reactivity were found in those given 1 ng endotoxin per kg body weight: a) non-reactors (n = 3), b) those in whom chills and elevated heat production preceded a rise in core temperature (n = 8), and c) those in whom vasoconstriction and thermal redistribution were responsible for a rise in core temperature prior to an increase in heat production (n = 4). Although saline produced no response, a dose of 2 ng per kg invariably produced a febrile episode. One normal subject, who failed to become febrile with a 1 ng dose, consistently responded to a second and third 2 ng injection of endotoxin by exhibiting pattern "c". The results suggest that endotoxin may produce fever by alteration of either vasomotor control of heat redistribution or heat production at rates that are independent and characteristic of the individual.

LIPID AND PROTEIN METABOLISM IN RATS IN OXYGEN UNDER SIMULATED HIGH ALTITUDE CONDITIONS. Charles L. Cahill*, John Patrick Jordan*, John B. Allred*, Robert T. Clark, (intr. by A. Kurt Weiss). Oklahoma City University, Oklahoma City, Okla.

The effect of a simulated space capsule environment (5.22 psia and 93% O_2) on the metabolism of 350-420 gm rats was studied after an exposure of 8 hours per day for 34 days. No significant differences were observed in body weight or organ weights when compared with control animals which were maintained under normal atmospheric conditions. Experimental animals contained approximately one-half as much serum lipoprotein as the control animals although no other differences in serum proteins, as determined by paper electrophoresis, were observed. After injecting pairs of rats with acetate-2-C^{14}, at varying times prior to sacrifice, the turn-over rates of lipid, carbohydrate, and protein pools were studied in liver, heart, kidney, brain, and muscle tissue. The expiration rate of radio-CO_2 was also determined. In general, the metabolic rate of the experimental animals was reduced at least 10%; metabolically the animals did not appear to be adapting to the environment. Major alterations were observed in the metabolism of lipids particularly fatty acids. It was concluded that both anabolic and catabolic rates were decreased in the experimental animals. (Supported by NASA Grant SC NsG 300-63)

ARTERIAL LACTATE AND EXCESS LACTATE IN AWAKE, HYPOXIC DOGS.
S. M. Cain and J. E. Dunn*, USAF School of Aerospace Medicine, Brooks AFB, Texas.

Blood lactic acid levels have been reported by some to be elevated during exposure to altitude and by others to be unaffected. Both the hyperventilation caused by hypoxia and tissue hypoxia itself should cause a rise in blood lactic acid, the latter factor being reflected primarily as excess lactate. After a 3-hour control period at ground level, unanesthetized dogs were exposed for 8 hours to 21,000 feet simulated altitude (P_B = 335 mm. Hg). Arterial blood samples were drawn frequently from a special teflon T-cannula surgically placed in a carotid artery one or two days before the experiment. Lactic and pyruvic acid concentrations, P_{CO_2}, P_{O_2}, and pH were measured. The average P_{O_2} immediately after ascent was 32 mm. Hg and was 34 mm. Hg just prior to descent. At these times, P_{CO_2} decreased from 25 to 21 mm. Hg and pH increased from 7.48 to 7.52. All control values were in normal ranges. The changes in lactic acid after ascent were quite variable, but the consistent pattern was a peak within the first one or two hours with a gradual decline toward control levels while still at altitude. Excess lactate changed in a similar manner. The decline in lactic acid, in spite of a continuing severe arterial hypoxia and hypocapnia, remains unexplained.

Arterial Oxygen Unsaturation in Pulmonary Embolism
P. Caldini (intr. by I. L. Trapani). Department of Physiology National Jewish Hospital, Denver, Colorado

In thoracotomized dogs, ventilated with a constant volume respirator, the right heart was substituted with a venous reservoir and a mechanical pump. The airway pressure during expiration was maintained at 2-3 mm. Hg. by means of a Starling valve connected to the expiratory line of the respirator. Serial injections of glass microspheres (80-120μ in diameter) or autologous clots (2-3 mm. in diameter) were injected into the main pulmonary artery until the mean pulmonary artery pressure rose from 16-21 to 80-100 mm. Hg. Significant changes in cardiac output and systemic arterial pressure were prevented by the pump-reservoir system. During emboli administration, systemic arterial oxygen saturation decreased from 95% to 82%, arterial P_{O_2} fell from 84 to 53 mm. Hg., arterial P_{CO_2} rose from 21 to 32 mm. Hg. and venous admixture rose from 4% to 30% of the total cardiac output. After the stabilization of these changes the airway pressure during expiration was raised to 12 mm. Hg. This maneuver was coincident with a return of arterial oxygen saturation and arterial P_{O_2} to normal values and a decrease of venous admixture to control levels. The inhalation of 99.5% oxygen during the anoxic period of observation did not influence the mean pulmonary artery pressure. Essentially the same results were obtained with glass microspheres as were with autologous clots. These findings suggest that arterial hypoxemia associated with pulmonary embolism is due to perfusion of poorly or nonventilated areas of the lung, and not to a significant blood flow through arteriovenous anastomoses. This work confirms the studies done by Gootman et al (Circulation 26:722, 1962).

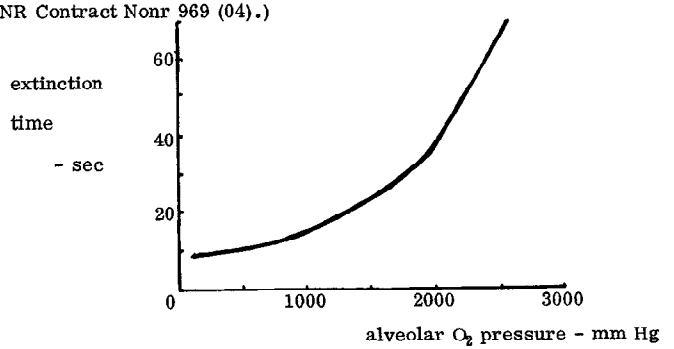
THE CELLULAR COMPARTMENTALIZATION OF ARGININE METABOLISM IN THE HEPATOPANCREAS TISSUE OF THE LAND SNAIL. J.W. Campbell and Suzanne Gaston (intr. by L. Kraintz). Rice University, Houston, Texas.

A survey of the distribution of arginase activity in members of the phylum Mollusca has shown that the high levels of arginase activity previously found in two snails (Helix and Otala) is not characteristic of all species of land gastropods. The activity is, however, widely distributed among the various species and high levels are common, ranging to an activity of 50,000 umoles arginine hydrolyzed per g. hepatopancreas per hr. at 25° under optimum conditions. The activity has also been found to be present in organs other than the hepatopancreas and kidney.

Because of the wide distribution of arginase, the high rate of arginine breakdown both in vitro and in vivo, and the fact that arginase is normally localized in the soluble fraction of the cell, the question of the origin of the protein arginine was raised. Two species of land snails were compared: Otala, with high levels of activity and Bulimulus, a species with 1/50 the activity of Otala. The substrates used included C^{14}-labelled bicarbonate, urea, ornithine, citrulline and arginine. Following aseptic incubations of the tissue with these substrates, the protein was isolated and purified by known methods. Arginine was isolated from acid hydrolysates as the monoflavianate derivative and was recryst. to constant radioactivity. Although certain differences were noted in the metabolism of these substrates by the two species, both were found to incorporate exogenous arginine into protein as well as to synthesize protein arginine from precursor molecules via the arginine pathway previously documented in Otala. These results and others indicate a high degree of compartmentalization of arginine breakdown vs. its synthesis and incorporation into protein in these tissues.
(Supported by USPH Service Grant AI 05006-01)

OXYGEN UNDER HIGH PRESSURE AND ISCHEMIC VISUAL BLACKOUT TIME. Raymond Carlisle*, Hermann Rahn and Edward H. Lanphier. Dept. of Physiology, State University of New York at Buffalo, Buffalo, N. Y.

Digital pressure on the eyeball sufficient to produce retinal ischemia causes extinction of central vision in approximately 8 seconds in healthy subjects breathing air. Extinction times were determined at alveolar oxygen pressures up to 2500 mm Hg (obtained by oxygen breathing in a high pressure chamber) and are shown in the figure below. The change in extinction time appears to be proportional to the increase in retinal venous oxygen tension as computed with an assumed a-v oxygen content difference of about 6 volumes per cent. (Supported by National Institutes of Health Grant HTS 5508 and ONR Contract Nonr 969 (04).)



EFFECTS OF BOILING AND OF LYOPHILIZATION UPON THE ABILITY OF FROG KIDNEY IMPLANTS TO FORM ACCESSORY LIMBS IN URODELES. Bruce M. Carlson* and Charles F. Morgan. University of Minnesota, School of Medicine, Minneapolis, Minnesota.

Subcutaneous implants of pieces ($1mm^3$) of frog kidney (Rana pipiens) into the forelimbs of adult newts (Triturus viridescens) have been shown by Ruben (Anat. Rec. 128:612, 1957) to induce the formation of accessory limblike structures. In a group of 30 newts normal pieces of kidney were similarly implanted into the dorsal area of the left forelimbs above the elbow whereas pieces of kidney which had been placed in boiling water for 10 minutes were implanted in comparable sites in the right forelimbs. On the control side 20 of 30 limbs developed accessory structures ranging from nodular growths to rod-like structures. Gross examination of the experimental side revealed one limb of the 30 which demonstrated an enlargement which could be interpreted as growth. In another series of 20 animals the left forelimb was used as a control and pieces of kidney which had been lyophilized for 15 hours were implanted into the right forelimbs. Of the 20 control limbs 19 exhibited reactions which grossly indicated accessory growth. The 20 experimental limbs also produced 19 accessory structures. The results indicated that there was some property of the kidney implant, destroyed by boiling but not by lyophilization, which induced the host limb to form accessory structures.

Supported by USPHS Grant GM-07762.

HEAT EXCHANGE DURING A STEP CHANGE IN ENVIRONMENTAL TEMPERATURE. L. D. Carlson, T. Sasaki, W. V. Judy. Heat loss and heat production as well as body and skin temperature, and an index of peripheral blood flow (peripheral pulse) were measured in the sitting position in a calorimeter at 30°C and following a step change (within 2 minutes) in temperature to 25°C. The measurements were made on four subjects over two - three hour periods; one starting at 0630 the other at 1330. The morning experiment was performed with the subject basal and the afternoon experiment followed one can of Metrecal at 1200.

Temperature effects on peripheral circulation and peripheral temperatures were analogous at the two times of day but offset by the difference in initial core and peripheral temperature. Heat production and heat loss were proportionately greater in the afternoon. The peripheral pulse response is rapid in onset and develops toward its maximum over a period of 20 minutes. Blood flow (as indicated by pulse height) is proportional to the temperature of the region tested and has a different relationship to mean skin temperature.

ANTI-MULTIPLIER EFFECT OF VASA RECTA IN THE DOG KIDNEY. Gaspar Carrasquer. Dept. of Med., Univ. of Louisville, Louisville, Kentucky

Some authors have proposed that vasa recta might perform as active multipliers, producing renal tissue concentration gradients. Impairment of nephron function by ureteral stop flow, in dogs producing concentrated urine, should outline the contribution of vasa recta to the concentrating mechanism. Dehydrated dogs were nembutalized. One kidney was removed during free flow of urine. The other kidney was removed while the ureter remained connected to a mercury manometer. The hydrostatic pressure of the clamped ureter was recorded and its kidney was removed 15-20 min. after the pressure reached a plateau. Kidneys were sliced in three regions: cortex, outer medulla and inner medulla. Homogenates were analyzed for Na, Cl, urea and osmolality. Renal concentration gradients increasing towards medulla observed in the free flow kidney, decreased markedly in the stop flow kidney. The time necessary to lower the osmolality gradient by simple diffusion, calculated from Fick's equation, is 6-7 times higher than the time required to lower the osmolality gradient to similar levels during ureteral stop flow. Therefore, vasa recta perform as an anti-multiplier factor that is uncovered when the counter-current multiplier mechanism (i.e. the nephron) is impaired by ureteral stop flow. (NIH and AHA support).

OXYGEN: ITS ROLE IN LOCAL AUTOREGULATION. Oliver Carrier, Jr.*, James R. Walker* and Arthur C. Guyton. Univ. Med. Center, Jackson, Miss.

Many studies have been made to uncover the mechanism and the controller of local autoregulation of blood flow. One theory suggests that a major controlling factor is the blood Po_2. The present studies investigated this possible role of oxygen by using isolated arterial segments. Using constant flow and constant pressure systems to perfuse a total of 60 arterial segments 1 cm. in length and 0.5 to 1.0 mm. in diameter with blood of various Po_2 levels, a definite decrease in vascular resistance always occurred on decreasing the Po_2, and an increase occurred when the Po_2 was raised. In one series of ten vessels, perfused under constant pressure of 100 mm. Hg, blood Po_2 was changed stepwise from 100 mm. Hg to 30 mm. Hg. A graded response was obtained with an average maximum decrease in resistance of individual vessels being 72.9 per cent (S.E.M. $\pm$ 0.6 per cent). This degree of change is sufficient to keep a physiological supply of oxygen available to tissues despite very low blood Po_2. In all of these experiments pH and Pco_2 were monitored and kept at physiological levels. Our results indicate oxygen could well be one of the major controllers, if not the major controller, in local autoregulation. (Supported by a grant from NIH.)

CARDIAC OUTPUT IN THE EXERCISING DOG. Paolo Cerretelli and Johannes Piiper (intr. by H. Rahn). Dept. of Physiology, University of Milan, Milan, Italy.

The cardio-circulatory changes induced by muscular exercise were studied in dogs running on a treadmill at different speeds (5 to 16 km/h) and at different inclines (0 to +20%). The cardiac output (thermo-dilution method) increased with increasing energy expenditure (calculated from the O_2 consumption and the lactate production) up to a maximum value about 3 to 3.5 times the resting value. This maximum value was reached at an energy expenditure of about 300 cal per minute per kg body weight. At further increases of the energy expenditure the cardiac output remained constant. As the maximum increase in the stroke volume was only 40% the increase in the cardiac output was mainly due to an increase in the heart rate, from 110 per minute at rest to 300 per minute at maximum work. The time course of the adjustment of the cardiac output was determined after an abrupt onset or cessation of the exercise. The half reaction time seemed to be independent of the work load and equalled about 20 seconds for both processes. The fact that with increasing energy expenditure the cardiac output reaches a maximum plateau value, while the O_2 consumption still increases without significant changes in arterial P_{O_2} and relatively small lactate production, suggests that it is the cardiac output which is the most important factor limiting the aerobic working capacity in exercising dogs.

OXYGEN BALANCE DURING HEMORRHAGIC SHOCK. E.A. Chasnow*, H.S. Small*, J.H. Henry*, E.M. Papper* and G.G. Nahas. Dept. of Anesth., Coll. of Phys. & Surg., Columbia University, New York, N.Y.

"O_2 balance" describes the cumulative change in O_2 uptake during an experimental period as compared to the control level. Continuous spirometric records of O_2 uptake were made in 79 dogs during hemorrhagic shock. Hypotension (50 mm Hg) was produced by bleeding, and O_2 balance was calculated for the 150' of hypotension. Thirty dogs were given either local anesthesia, or local anesthesia and intravenous morphine during hypotension, or local anesthesia with meperidine premedication. Twenty-two dogs failed to survive and had positive O_2 balances (+28 to +900 ml/kg). Three of the 8 dogs with negative O_2 balances (-1 to -950 ml/kg) survived. Fourteen of 17 dogs anesthetized with thiopental and 8 of 10 dogs premedicated with morphine had negative O_2 balances (-13 to -863 ml/kg) and failed to survive. The survivors had O_2 balances ranging from -206 to +153 ml/kg. Administration of buffer (0.10M THAM and 0.05M $NaHCO_3$) to dogs receiving thiopental or local anesthesia resulted in negative O_2 balances (-16 to -1077 ml/kg) but an increased survival rate (15 of 22). These results contrast with those of Guyton and Crowell (Fed. Proc. 20: 51, 1961) who related changes in O_2 uptake during shock with survival. Since O_2 requirements may change during shock, alterations in O_2 uptake ("O_2 balance") are not a true measure of O_2 debt and cannot be correlated with survival.

A COMPARATIVE STUDY OF TWO PREPARATIONS OF SECRETIN AND PANCREOZYMIN-CHOLECYSTOKININ IN MAN. Woo Yoon Chey* and Harry Shay. Fels Research Institute, Temple University School of Medicine, Philadelphia, Penna.

Effect of Boots' and of Vitrum's secretin and cholecystokinin-pancreozymin in similar unit amounts on biliary-pancreatic secretion was studied in 7 subjects. Two consecutive doses of the same preparation given more than an hour apart produced similar results in duodenal contents. Sandwiching one or the other preparation in a series of 3 injections demonstrated differences in their action. Injection of Boots' secretin always produced a dark bile rapidly, Vitrum's secretin did not. Boots' secretin produced larger volume and amylase output. Bicarbonate was similar for both. The contamination of Boots' secretin by pancreozymin-cholecystokinin is apparent. Cecekin produced greater mean values for volume, HCO_3^-, amylase and bilirubin outputs than did Boots' pancreozymin but difference was statistically significant only in volume. Cecekin also caused more variation in amylase output. In patients with T-tube in common bile duct the two preparations of secretin produced similar choleretic effects. There was no significant choleretic effect following both Boots' pancreozymin and Cecekin. Importance of these findings will be discussed.

EFFECTS OF ENDOTOXIN ON THE TRANSFER OF MACROMOLECULES FROM PLASMA TO LYMPH. Shu Chien*, D. G. Sinclair*, C. Chang*, R. J. Dellenback*, B. Peric*, S. Usami* and M. I. Gregersen. Columbia Univ. College of Physicians and Surgeons, New York, N. Y.

In dogs under pentobarbital anesthesia, the thoracic duct was cannulated. Dextran with mean molecular weight of 250,000 (Dx) and I^{131}-albumin (RISA) were injected intravenously and their concentrations determined in the plasma (P) and the thoracic duct lymph (L) at 20-min. intervals for 100 min. E. Coli endotoxin (3 mg/kg i.v.) was then administered. As the arterial pressure decreased, the lymph flow from the thoracic duct increased within 5 min. after endotoxin and reached a peak (approximately double the control) in 10 min. At the same time $(Dx)_L$ and $(RISA)_L$ increased markedly. Since $(Dx)_P$ and $(RISA)_P$ usually decreased slightly, the L/P ratio for these macromolecules increased. Eighty min. after endotoxin injection, the L/P ratio remained high (0.65 for Dx and 0.85 for RISA) although the lymph flow already declined to within 10% of the control. In control dogs not given endotoxin, the L/P ratio was only 0.35 for Dx and 0.55 for RISA at 180 min. after the injection of these macromolecules. The results indicate that endotoxin caused a marked increase of the outward passage of fluids rich in macromolecules across the capillary membrane of the splanchnic area. Since the increase in lymph flow after endotoxin was associated with rises in portal and wedged hepatic venous pressures and decreases in central venous pressure and hepatic blood flow, the outward movement of fluid can be explained by an increase of hydrostatic pressure in splanchnic capillaries due to hepatic venular constriction. When the inferior vena cava was obstructed, similar increases in lymph flow and macromolecule concentration were observed as in endotoxin shock. (Supported by U. S. Army Contract DA49-193MD2272 and USPHS Grants HE-06139 and 2G257).

CONDITIONED REFLEX STUDIES IN EXPERIMENTAL EPILEPSY. Raymond W. M. Chun* and Francis M. Forster. Department of Neurology, University of Wisconsin Hospitals, Madison, Wisconsin.

Studies were carried out to determine the possibility of inducing focal convulsive seizures in animals by the use of conditioned stimuli. Seizures were produced by chronic implant electrodes in non-anesthetized cats. The conditioned stimuli used in the experiments consisted of sound and intermittent light (stroboscope). In cats with intact brains it was not possible to produce convulsive seizures by conditioning alone with either sound or intermittent light as conditioned stimuli. Behavioral responses obtained were preparatory movements for the unconditioned stimulus. Electroencephalographic changes were also induced but these were not true convulsive patterns. After the preparatory response and EEG changes had been elicited, acute chemical "lesions" were made by placing analeptic drugs upon the cerebral cortex. This considerably modified the responses. Some convulsive movements were obtained by conditioning and these were similar to those produced by the unconditioned stimulus (electrical stimulation of the motor cortex). In chronic epileptic lesions, seizure could be reproduced by the condition stimulus alone after months of conditioning trials. Our studies show that in the absence of structural lesion it is not possible to produce seizures by conditioning techniques alone.

GENESIS OF KOROTKOFF SOUNDS

D. Chungcharoen (Intr. by B. R. Boone)
Department of Physiology, Temple University School of Medicine.

Korotkoff sounds were reproduced in dogs and registered by means of a pulse-sound microphone on an electronic recorder (Electronics for Medicine). Blood flowing through the compressed arterial segment was studied cinefluorographically (64 and 270 frames/sec.). The relation of Korotkoff sounds to pulse waves, heart sounds and vibrations of the arterial wall was also studied. As the cuff pressure was gradually released, a series of Korotkoff sounds were recorded. These sounds began at the onset of each pressure pulse and their amplitude and duration varied with blood flow. The Korotkoff sounds were not derived from heart sounds because the heart sound appears before the upstroke of the aortic pressure while the Korotkoff sound coincides with this same upstroke. Furthermore, if recording amplitudes are reduced, heart sounds disappeared when Korotkoff sounds are still recorded. Blood flowed through the compressed artery at a velocity higher than that of the control and gave rise to turbulence downstream. The vessel wall at that downstream area vibrated. When the arterial segment was replaced by constricted glass tubing, similar sounds could be produced. These findings suggest that the arterial wall at the site of compression is not essential for sound production and that Korotkoff sounds are generated by the turbulent blood flow.

INFLUENCE OF KINETIC BEHAVIOR OF SURFACE FILMS ON PULMONARY ELASTICITY. J.A. Clements, D.F. Tierney*, and H.J. Trahan*. Cardiovasc. Res. Inst., Univ. of California Medical Center, San Francisco, California.

Pressure-volume relationships in excised lungs depend reversibly on the temperature at which lungs are examined. Differences in elastic properties are attributed to alterations in alveolar surface tension (ST) since temperature (from 20 to 50°C) affects air-filled but not liquid-filled specimens. The difference in transpulmonary pressure with gaseous and liquid media when volume is reduced to 40% of maximum rises from 1 cm H_2O at 27°C to 6 cm H_2O at 47°C. Most of this increase occurs at temperatures above 40°. Heating causes a similar rise in minimal ST of lung extracts. The rate of rise of ST of extracts is found to increase smoothly with temperature; these rates approximate first-order reaction kinetics, and rate-constants plotted against reciprocal temperature give an estimate of about 22 kcal/mole for the heat of activation of the surface reaction. Kinetic analysis of pressure-volume data gives a comparable result for intact lungs. Two pure phospholipids (dipalmitoyl lecithin and erythrocyte sphingomyelin) which lower ST nearly to zero when spread as films on isotonic saline and compressed, were subjected to similar analysis. Both substances give lower rates of change of ST than are estimated for saline extracts and alveolar surfaces but comparable heats of activation. This information is consistent with the hypothesis that ST below about 24 d/cm represents an unstable state of alveolar or extract surfaces; that rate of attainment of equilibrium depends on temperature; and that long-term stability of the lungs requires periodic replenishment of surfactant. The effect of prolonged apnea or shallow breathing in reducing compliance and causing progressive non-obstructive atelectasis may be explained by this mechanism.

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RECURRENT AND ANTAGONIST INHIBITION IN VESTIBULO-OCULOMOTOR PATHWAYS. B. Cohen*, J. Suzuki*, S. Shanzer and K. Goto*. Dept. of Neurology, Mt. Sinai Hospital, New York, N.Y.

Inhibition of ocular muscle activity induced by semicircular canal stimulation was studied in encephale isole' cats. Recurrent inhibition occurred during anterior or posterior canal nerve stimulation producing a transient decrease in tension in activated eye muscles 10-15 msec. after the onset of stimulation. Inhibitory effects were most prominent after submaximal stimulation of ampullary nerves and disappeared during repetitive supramaximal stimulation or strong alerting. Prominent recurrent inhibition was never seen during lateral canal stimulation. This reflects one difference between lateral and vertical semicircular canals. Strong antagonist inhibition was produced by stimulation of every canal nerve. Relaxation of antagonists occurred at the same time as contraction of agonists. Canals in the same plane induce opposite ocular reactions. During simultaneous activation of both lateral canal nerves inhibition predominated and all contractions were blocked. Trains of pulses were delivered to both lateral canal nerves during continuous stimulation of one of these nerves. The amplitude of contraction and relaxation in activated muscles produced by the testing pulse trains increased as the muscles contracted. By balancing the strength of the repetitive stimulation of one lateral canal nerve against the strength of the pulse trains to the other, typical jerky nystagmus could be formed at the frequency of the pulse train repetition rate between 2 and 10 cps. These data show that pathways carrying excitation and antagonist inhibition to any one eye muscle are simultaneously facilitated during vestibularly-induced contraction of that muscle. These changes in facilitation of inhibitory and excitatory pathways appear to play an important role in the formation of vestibular nystagmus.

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UNALTERED OSTEOBLASTIC FUNCTION IN THE PRESENCE OF ENDOGENOUS PARATHYROID SECRETION. Cary W. Cooper*and Roy V. Talmage. Rice University, Houston, Texas.

By microradioautographic analyses at the cellular level, tritiated amino acid precursors of bone collagen have been shown to be initially incorporated into the bone-forming cells (osteoblasts) and subsequently released to the prebone or osteoid. Glycine, proline, and histidine all have been employed in this manner. Radioautographic experiments with tritiated proline were conducted in order to determine whether or not endogenous parathyroid secretion influences osteoblastic function in the rat. Varying degrees of parathyroid stimulation were elicited by peritoneal lavage and by bilateral nephrectomy, and the animals were sacrificed at 30 minutes and 4 hours post-injection. Femora were removed and prepared for histological and radioautographic examination. Control and parathyroidectomized animals were also studied under all conditions employed for parathyroid stimulation. Microradioautographs of the femoral endosteum and distal metaphysis were examined, and the osteoblastic labelling indices (% labelling) and grain counts determined. In agreement with previous reports, most of the osteoblasts are labelled at 30 minutes post-injection; whereas, 4 hours after injection most of the labelling has passed from the cells into newly formed matrix. While the turnover of labelled proline is more rapid in the metaphysis than in the endosteum, the labelling indices were not significantly altered under any of the experimental procedures used. Although the labelled compound employed in these studies does not preclude cellular transformations involving osteoblasts, the results indicate that the amount of parathyroid hormone that can be endogenously evoked in the rat apparently does not retard or increase the production of bone collagen by active osteoblasts.

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RESPONSES TO SYMPATHOMIMETIC AMINES AFTER CHRONIC CARDIAC DENERVATION. T. Cooper, V.L. Willman*, L.T. Potter*, and C.R. Hanlon*, St. Louis University, St. Louis, Mo. and NIMH, Bethesda, Md.

Surgical denervation of an organ frequently enhances its responses to certain chemical substances. Whether the heart reacts in this manner has been questioned. We have studied the chronotropic and inotropic (strain gauge arch) responses to sympathomimetic drugs in 10 dogs 8 to 300 days after total extrinsic cardiac denervation. Denervation was accomplished by mediastinal neural ablation or by excision and reimplantation of the heart. The drugs tested were: epinephrine and norepinephrine, (0.01-0.5 μg/kg); H^3-norepinephrine (0.5 μg/kg); dopamine (4-32 μg/kg); tyramine (30-60 μg/kg); amphetamine and ephedrine (300 μg/kg); and mephentermine (1.0 mg/kg). The degree of cardiac acceleration is similar after intravenous injection of epinephrine and norepinephrine. However, there is 100% augmentation of the inotropic responses to epinephrine and twice this degree of augmentation with norepinephrine. The capacity to bind H^3-norepinephrine was 8% of normal. Chronotropic and inotropic responses to tyramine, amphetamine, ephedrine and mephentermine were minimized or eliminated, although modest pressor activity usually persisted. Denervation attenuated by a half the inotropic and pressor responses to dopamine. These studies indicate: 1) the totally denervated heart is more reactive than the normal heart to norepinephrine and epinephrine 2) enhancement in inotropic activity to norepinephrine is greater than to epinephrine 3) the cardiac responses to dopamine, tyramine, amphetamine, ephedrine and mephentermine are attenuated or eliminated after chronic cardiac denervation.

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THE EFFECTS OF pH ON ISOLATED VESSEL TONE. Meredith K. Cowsert, Jr.*, Oliver Carrier, Jr.*, John C. Hancock* and Arthur C. Guyton. Univ. Medical Center, Jackson, Miss.

The effects of high and low pH on vascular resistance have been studied by many investigators, but the results have been equivocal or non-quantitative, because the methods used either estimated or calculated blood pH rather than measuring it. In the present studies isolated arterial segments, 1 cm. in length and 0.5 to 1.0 mm. in diameter, were perfused with Tyrode's solution titrated to various levels of pH. Po_2 and Pco_2 were held at physiological levels, the perfusion pressure was held at 100 mm. Hg, and flow was measured by a drop counter. There was a linear increase in flow as pH was decreased from 7.4, 0.05 units at a time, with an increase of 100 per cent obtained at pH 7.15. When the pH was raised, initially there was a 35 per cent decrease in flow by the time pH of 7.50 was reached, followed by an increase as the pH was further increased up to 7.65, at which point flow was 50 per cent above control level. Consistent results were obtained on 35 vessels using Tyrode's solution titrated to the desired pH with lactic acid, hydrochloric acid, acetic acid, sulfuric acid, nitric acid, sodium hydroxide, or sodium bicarbonate. These results indicate that vessels have a very narrow pH range in which to maintain physiological tone, and such changes in pH can become a serious problem in interpretation of both clinical and experimental hemodynamic data. (Supported by a grant from NIH).

AUTOREGULATION OF CORONARY BLOOD FLOW. Cecil E. Cross St. Joseph Hospital, Burbank, Calif.

An active change of regional coronary vasomotor tonus (i.e., autoregulation) was observed when the performance of the heart was kept constant and when the coronary driving pressure (CDP) in separately, cannulated coronary vessels was varied. However, when CDP varied together with aortic pressure and cardiac performance, as is normally the case, evidence for coronary autoregulation was not observed. In all innervated hearts coronary tonus remained constant over a wide range of CDP and systemic arterial pressures; coronary vasodilation was seen only when the mean blood pressure exceeded about 100 mm Hg, corresponding with myocardial oxygen consumption of 9 ml/100 g heart/min. In the semi-intact circulation the relative importance of hydraulic, metabolic, and neurogenic factors that influenced coronary vasomotor tonus was not known to us. Clear evidence of autoregulation was seen only under experimental conditions that imitated disease (coronary stenosis) or that cannot occur in vivo (coronary overperfusion).

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REGULATION OF BREATHING AT THE BEGINNING OF EXERCISE.
E. G. Cummings and F. N. Craig. U. S. Army Chemical Research and Development Laboratories, Edgewood Arsenal, Maryland.

In initial 20 second periods of running on the treadmill, raising the slope to 12 per cent increased by 50 per cent the integrated muscle action potential recorded from the underside of the thigh without affecting the ventilation in four men. Five men worked for one minute at four tasks, two on the treadmill and two on the horizontal bicycle ergometer. Each pair of tasks consisted of slow and rapid leg movement at the same rate of work. Ventilation often continued at about the resting rate for the first few seconds of work unaffected in any significant way by the frequency of leg movement. In the subjects responding to the onset of exercise by a sudden sharp involuntary increase in ventilation the nature of the nervous respiratory drive is not clear. Whatever drive arises from the work itself may be strongly modified by training or by complexities in the work situation.

LOCAL EFFECTS OF VASOACTIVE AGENTS ON INTESTINAL BLOOD FLOW AND MOTILITY. J. M. Dabney and J. B. Scott (intr. by F. J. Haddy). University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

Vascular smooth muscle of the intestine is surrounded by visceral smooth muscle. Since these two types of muscle are affected oppositely by certain vasoactive agents, the resulting blood flow may be affected by the sum of these two influences. Lumen pressure was measured in an *in situ* closed length of ileum (avg wt 51 g). Concurrently, venous outflow was measured while infusing acetylcholine chloride or serotonin creatinine sulphate (1 to 20.5 μg salt/min); epinephrine hydrochloride or levarterenol bitartrate (0.1 to 2.1 μg base/min) into the arterial inflow. Average control blood flow was 0.28 g/min/g intestine at an arterial pressure of 100 mm Hg. Infusion of epinephrine or levarterenol decreased blood flow and lumen pressure. On stopping the drug infusion, blood flow greatly exceeded control while lumen pressure remained low. With acetylcholine, lumen pressure and blood flow increased as a function of infusion rate up to 5 μg/min. At higher rates of infusion lumen pressure rose more but blood flow fell. On stopping the infusion, lumen pressure fell to control while flow rose to 246% of control. Infusion of serotonin produced a definite increase of lumen pressure while blood flow was little changed. On stopping the infusion, flow fell while lumen pressure remained elevated. These studies indicate that the activity of the intestinal smooth muscle, by passively affecting vessel caliber, is an important determinant of intestinal blood flow.

STUDIES ON VAGAL ESCAPE AND CERTAIN VAGAL INDUCED ARRHYTHMIAS. Willard M. Daggett and Andrew G. Wallace (intr. by S. J. Sarnoff). Natl. Insts. of Health, Bethesda, Md.

In dogs, bipolar electrograms were recorded from the SA node and His bundle to localize pacemaker sites during vagal escape, to study the effects of isuprel on escape mechanisms, and to characterize certain vagal induced arrhythmias. Vagal escape can result from the development of rhythms of supranodal, nodal, or idioventricular origin. Isuprel shortened the period of asystole prior to the onset of vagal escape, increased the rate of escape rhythms at all pacemaker sites, and occasionally changed the pacemaker to a higher focus in the conduction system. Atrial re-excitation (echo responses) was observed in all animals with vagal stimulation. During echo responses the sequence of activation at the SA node and atrial septum was reversed, i.e., similar to idioventricular beats with retrograde conduction. This suggests that echo beats re-enter the atrium from the AV node or His bundle. Atrial re-entry was also observed in the presence of complete heart block (in the absence of recorded activity from the His bundle) further localizing the source of the echo to the AV node. While the presence of a dual AV conduction system is not precluded by these experiments, the pathways for the electrical responses observed appear to be limited to the upper AV node. Atrial flutter and fibrillation occurred frequently and in all cases followed early atrial re-entry. This suggests that re-entry beats may in certain instances initiate atrial fibrillation.

THE EFFECT OF HYPOTHERMIA ON THE VECTORCARDIOGRAM OF DOGS. R. W. Dahlen (intr. by D. F. Opdyke). Seton Hall College of Medicine and Dentistry, Jersey City, N. J.

Anesthetized mongrel dogs on positive pressure respiration were cooled by an extracorporeal circulation until ventricular fibrillation occurred (esophageal temperature 20-25°C). Three simultaneous electrocardiographic leads were recorded using the lead system described by Horan et al. (Am. Heart J. 61:503, 1961) at a paper speed of 200 mm/sec. The resultant vectors of these leads were photographed on both stationary and moving film. The latter procedure overcomes the blurring due to superimposing of the image that occurs around the isoelectric potentials. The spatial vector was calculated at 2.5° or 5° intervals of body temperature. The data showed a progressively reduced duration and a counter-clockwise shift in the direction of the ventricular depolarization vector under hypothermia. This was most marked at the end of the loop, corresponding to the H wave which occurs in hypothermia. (Supported by NIH Grant HE 07624-02).

EFFECTS OF CHRONIC PULMONARY VASCULAR CONGESTION ON POSTURAL CHANGES IN PHYSIOLOGIC DEAD SPACE AND DIFFUSING CAPACITY IN MAN. Walter J. Daly* and Joseph C. Ross. Indianapolis, Indiana

Pulmonary diffusing capacity (D_{LCO}), pulmonary capillary blood volume (V_C), and physiologic dead space (V_D) were determined in normal subjects and patients with pulmonary congestion and hypertension due to mitral stenosis (PA mean > 20 mm Hg) before and after tilting 60° head up. In 10 normal subjects, D_{LCO} decreased, 39.2 ± 7.7 to 31.5 ± 6.7 ml/min/mm Hg (p=0.001), and V_C decreased, 99 ± 17 to 75 ± 19 ml (p=0.001). In 10 patients with mitral stenosis, no change in V_C (97 ± 24 ml) or D_{LCO} (20.7 ± 6.0 ml/min/mm Hg) was observed during tilting. In 16 patients with normal pulmonary vascular pressures, V_D increased from 142 ± 40 to 201 ± 55 ml (p=0.001). In a similar group of patients with pulmonary congestion, V_D increased from 192 ± 81 to only 208 ± 84 ml (p=0.05). This difference in the effect of posture on V_D was not the result of a difference in the overall ventilatory response to tilting. These data are compatible with observations that the normal upright lung is evenly perfused and its capillaries are unevenly filled; that this gravity dependent unevenness is not present in pulmonary congestion; and further that the normal pulmonary vascular pressure is not sufficient to produce even perfusion and capillary filling in upright postures.

HUMAN EVOKED CORTICAL RESPONSES TO AUDITORY STIMULI. H. Davis and N. Yoshie*. Central Institute for the Deaf, St. Louis, Missouri.

Averaged evoked responses to filtered clicks are conveniently recorded from the vertex of the human head. The typical pattern is triphasic: vertex positive (P_1, 60 msec) then negative (N_1, 110 msec), then positive (P_2, 190 msec). These are mean peak latencies. They are invariant with intensity of stimulus, its acoustic frequency and the degree of recovery following the previous response. Complete recovery requires several seconds. Voltage (N_1 to P_2) is often a linear function of decibels of sensation level, although the input-output curve may be concave upward at high levels. The responses are obtained while the subjects sit and read, and are only slightly affected by closing the eyes, attending to the sounds or counting them, but they are greatly depressed by drowsiness. There are clear individual differences in the slope of the input-output functions, and unidentified factors may cause considerable fluctuations and even changes in wave form. (The usual pattern consists of at least three independently variable components.) Most subjects give a very similar pattern of response to electric shocks, of equal subjective intensity, to the median nerve. The response to shocks is usually of greater voltage, particularly near the start of a session. There is, on the average, no reduction of response when a click is closely preceded (0.5 sec.) by a shock or a shock by a click. (NINDB Grant B-3856)

PHYSIOLOGICAL AND BIOCHEMICAL MEASUREMENTS OF AGED POPULATIONS. R. L. Davis* and A. H. Lawton, VA Ctr., Bay Pines, Fla., Study Group on Aging and Accidents, PHS, DHEW, St. Petersburg, Fla.

Many of our physiological and biochemical measurements of an aged population are based upon determinations made utilizing hospital patients. Thus, the impact of pathology on these values may be considerable. Studies were initiated on several populations of domicile members and hospital patients residing at the VA Center, Bay Pines, including one group of 62 domicile members of average age 87. All subjects except for hospital patients were free from overt manifestations of acute disease and presumably maintaining normal physiological function. Single or serial determinations were performed on these groups. The measurements included various biochemical, hematological, enzymatic, metabolic, physiological and others. Some of the observations were: Blood urea nitrogen and uric acid levels were higher than those of a younger "normal" population, 26.0 and 6.2 mg% respectively, whereas cholesterol, hematocrit, hemoglobin, thymol turbidity, lactic acid and others were within normal limits. Serum B_{12} levels were depressed but the absorption of orally ingested Vitamin B_{12} appeared unimpaired in the aged. Serum cholinesterase was depressed, phosphohexoisomerase and other enzymes were not. Certain of these values obtained from domicile members were compared with those obtained from hospital patients. Differences were observed in several instances, such as serum cholinesterase.

FROG'S GASTRIC MUCOSA IN POTASSIUM FREE SOLUTIONS. T.L. Davis*, J.R. Rutledge*, and W.S. Rehm. Dept. of Physiology & Biophysics, Univ. of Louisville, School of Med., Louisville, Ky.

Secreting mucosae (histamine) were mounted between chambers with appropriate bathing solutions. The potential difference, resistance, (Δ PD/applied current) and H^+ rate (pH stat method) were measured. Replacing usual Cl^- solutions with K^+- free solutions results in a rapid increase in PD of about 8 mv which is followed by a gradual decrease in PD and H^+ rate and by an increase in resistance. PD is still finite when H^+ rate reaches zero. Addition of K^+ to the secretory side (to very high levels) with zero K^+ still on nutrient does not reverse the decrease in H^+ rate but does increase positivity of nutrient and decrease resistance. Restoration of K^+ to normal on nutrient side may restore characteristics to approximately their original values. With Cl^-- free solutions (SO_4^{--} for Cl^-) the PD is inverted (nutrient negative). Elimination of K^+ from Cl^-- free solutions results in a decrease in H^+ rate and a return of PD to normal orientation (nutrient positive) and increase resistance. The PD in absence of Cl^- and K^+ and with identical solution on both sides is between 3 to 10 mv, is maintained for hours (short-circuit current 5 to 8 $\mu a\ cm^{-2}$) and is depressed to zero by anoxia. Readmission of O_2 results in an overshoot of PD and then a return to control level. It is concluded that the mucosa can transport ions other than H^+ and Cl^- against their electrochemical potential gradients (NSF and NIH support).

THE EFFECT OF SIMULATED ALTITUDE ON THYROID FUNCTION IN THE RAT. Domenic A. DeBias and Wang Yen.* Departments of Physiology and Radiology, Jefferson Medical College, Philadelphia 7, Pa.

Thyroidectomy or administration of thiourea have been known to increase the resistance of the rat to simulated altitude, presumably because hypothyroidism reduces the oxygen requirements of the animals. We have previously reported that thyroidectomy did not significantly increase the survival time of adrenalectomized rats exposed to simulated altitude, and that a single injection of 3 mg. cortisol, which was inadequate to sustain adrenalectomized rats, increased the survival time of thyroidectomized-adrenalectomized rats (DeBias, D.A., Am. J. Physiol., 203:818, 1962). We proposed that a possible mechanism whereby lesser amounts of cortisol become effective in prolonging the survival time of thyroidectomized rats exposed to altitude may be a decreased catabolism of the steroid in the hypothyroid animals. In support of this concept, present data indicate that induced hyperthyroidism decreases the survival time of animals exposed to altitude, and that larger amounts of cortisol are required to protect such animals. Also, measurements on various parameters of thyroid activity indicate that thyroid function of normal rats is increased during exposure to altitude. Measurements of thyroid function which were found to be increased were: thyroidal uptake of I^{131}, release of thyroidal I^{131}, erythrocyte uptake of triiodothyronine-I^{131}, and blood PBI^{131}.

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ALTERATION OF MYOCARDIAL FUNCTION CAPACITY BY ALCOHOL. I. Unal Degerli* and Watts R. Webb. Department of Surgery, Univ. of Miss. School of Medicine, Jackson.

Much evidence indicates that alcohol increases susceptibility to shock. This experiment evaluated the effects of alcohol on myocardial function. METHODS: Cardiac output was recorded from the ascending aorta by an electromagnetic flowmeter, and aortic and left atrial pressures were recorded. Myocardial function curves (Sarnoff) were obtained before and after alcohol administration in three different dosages. OBSERVATIONS: Following 0.5 gm./Kg. I.V., blood pressure and cardiac output increased slightly, and left atrial pressure remained constant. Function curves showed myocardial depression even to severe failure, and two of 20 dogs died in shock. After a moderate dose (1.5 gm./Kg.) left atrial pressure, cardiac output and blood pressure all rose while peripheral resistance decreased. Myocardial function curves showed more marked depression. Three dogs of 12 died in shock. After 2.5-5 gm./Kg. of alcohol, the animals died during the infusion period of 30-40 minutes with left atrial pressure rising to a mean of 15 mm. Hg while cardiac output and blood pressure progressively declined. Prophylactic Ouabain given before the alcohol protected the animals from myocardial failure, or if given after alcohol restored the function curves to normal. These observations suggest that shock in alcoholism is primarily myocardial failure.

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MITOCHONDRIAL SWELLING CAUSED BY DINITROPHENOL. Frederick D. DeMartinis (intr. by H. R. Hafkesbring), Woman's Medical College of Pennsylvania, Philadelphia, Pennsylvania.

Dinitrophenol (DNP) has been reported to inhibit the swelling of rat liver mitochondria occurring in 0.25 M sucrose in 0.02 M tris buffer (pH 7.4). This effect distinguishes DNP from other uncoupling agents, such as thyroxine, which promote mitochondrial swelling in this medium. In this laboratory, it was found that DNP will promote swelling of mitochondria. However, to demonstrate this effect requires a concentration of DNP (10^{-3}M) that is much higher than that required to cause uncoupling ($5x10^{-5}$M). It is necessary too that sucrose be eliminated from the medium. Using either 0.125 M KCl in 0.02 M tris buffer (pH 7.4) or only 0.2 M tris buffer (pH 7.4), it has been found that DNP will greatly increase swelling of mitochondria. Such swelling can be reversed after 45 min. by the addition of ATP ($2x10^{-3}$M). It can be partially prevented by the addition of serum albumin (4 mg/ml) initially to the medium, but EDTA (10^{-3}M) has no effect. Inhibition of the electron transport sequence with Amytal ($2x10^{-3}$M), Antimycin A (1 µg/ml) or cyanide (10^{-3}M) in the presence of DL-β-hydroxybutyrate (10-3M) has no effect on the swelling induced by DNP. (Supported by PHS Grant AM-03143-04 from the Institute of Arthritis and Metabolic Diseases, Public Health Service.)

IONIC ASPECTS OF ELECTROGENESIS IN THE SOMATIC MUSCLE CELLS OF ASCARIS LUMBRICOIDES. W. C. de Mello*, J. del Castillo and T. Morales*, Lab. of Perinatal Physiol. and Dept. of Pharmacol. Sch. of Med. San Juan 22, Puerto Rico.

(1) Although the transmembrane potential decreases in these cells when the extracellular concentration of K^+ ions ($[K^+]_o$) is increased while keeping $[Na^+]_o$ and $[Cl^-]_o$ low and constant, our results show that the surrounding Cl^- ions are more important than those of K^+ in maintaining the resting potential. Furthermore, the cell surface membrane has a relatively high Na^+ conductance, the resting potential increasing by 15 mV or more, probably to the E_{Cl} level, when the outside Na^+ is removed. This hyperpolarization is accompanied by the abolition of the spontaneous spike potentials in most cells. (2) The muscle inhibitory potentials elicited by nerve cord stimulation appear to be due to a transitory enhancement of the Cl^--conductance of the cell membrane, being abolished by removal of external Cl^- and increasing if a fraction (10%) of these ions is replaced by the smaller NO_3^- anions. (3) When, in the absence of nerve cord stimulation, all the external Cl^- is substituted for NO_3^- the resting potential increases and the spike activity is blocked. The hyperpolarizing current is presumably transported by the NO_3^- ions through the pre-existing Cl^- channels. (4) The flaccid paralysis induced by piperazine in Ascaris, is due to a hyperpolarization caused by an increased Cl^--conductance of the cell membrane. The conductance changes involved in both drug and neural inhibition are restricted to the syncytial region of the muscle, the resulting potential changes spread electrotonically to the rest of the cells. (Supported by Grant No. NB 02021-05 of the U.S.P.H.S.).

EFFECT OF CATION ON CHLORIDE MOVEMENT ACROSS GASTRIC MUCOSA. Warren H. Dennis and Susana R. Kruglicoff*. Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Previously it was reported that chloride and sodium ions are absorbed into the blood in equimolar amounts from 0.16 M NaCl solutions in contact with the acid secreting portion of the canine gastric mucosae using Rehm's chambered gastric segment preparation (Bornstein, Dennis and Rehm, Am. J. Physiol. 197, 332-336, 1959). In similar experiments the movements of chloride and osmotically active particles from 0.16 M NaCl and 0.16 M KCl solutions were determined. In the case of the sodium chloride solutions the disappearance of the chloride ions was confirmed (106 microEq/30 min-31 cm^2) but the rate of disappearance of osmotically active materials was less than would be predicted from the chloride ion disappearance (50 microOsm/30 min-31 cm^2). An osmotically active material therefore must have moved from the blood to the lumen. In the case of the potassium chloride solutions there was a net outflow of water (0.11 gm/30 min-31 cm^2), and essentially no change in the total amount of chloride (outflow 7 microEq/30 min-31 cm^2) or total amount of osmotically active particles (outflow 7 microOsm/30 min-31 cm^2). Two hypotheses for the movement of sodium chloride across the resting mucosa were proposed: 1) separate electrogenic transport processes electrically coupled for the chloride and the sodium ion and 2) the movement of ion pairs down their chemical potential gradient. The electrogenic hypothesis is compatible with the data on the potassium chloride solutions while the ion pair hypothesis requires other assumptions. (Supported by the USPHS central support grant to the University of Wisconsin and American Heart Association - Established Investigatorship.)

MYOEPITHELIAL CELL FUNCTION DURING EXPERIMENTALLY-INDUCED INVOLUTION OF THE MAMMARY GLANDS OF LACTATING RATS. David J. DeNuccio* and Clark E. Grosvenor, University of Tennessee, Memphis, Tennessee.

Little information is available concerning the functional activity of the myoepithelial cells of the mammary gland during lactational decline or failure. We have investigated whether these cells function during experimentally-induced involution of the mammary glands of lactating rats. The litters of primiparous lactating rats were removed on postpartum day 4 and the function of the myoepithelium assessed in groups of rats 1, 3, 5 or 7 days later. This was done by inserting a cannula intraductally, injecting rat milk through the cannula to expand the alveoli of the mammary gland, connecting the milk-filled cannula to a pressure transducer, and recording the magnitude and duration of the intramammary gland pressure rise following intravenous oxytocin (50mU). We also visually noted whether the alveoli of the exposed mammary gland contracted following topical administration of oxytocin (2mU). Average intramammary pressures of 31, 27, 15 and 7 cm H_2O were obtained in rats undergoing mammary involution for 1, 3, 5 and 7 days, respectively. The amount of time required for the pressure to return to pre-injection levels was similar for rats involuting 1 or 3 days (>24 min.) but was reduced to 11 and 5 minutes for rats involuting 5 and 7 days, respectively. Injection of prolactin (2 mg subc 3 X daily) for 7 days after removal of the litter resulted in a pressure rise of 23 cm H_2O requiring 14 minutes to return to normal. Rats in each group responded to topically applied oxytocin by localized contraction of alveoli. Gross inspection of entire mammary glands which were injected intraductally with india ink indicated that the number of alveoli was drastically reduced after 5-7 days of non-suckling. There was marked retardation in loss of alveoli in rats receiving prolactin.

PREVENTION OF THE ACUTE ETHANOL-INDUCED FATTY LIVER BY ANTIOXIDANTS. N. R. Di Luzio. Dept. of Physiology, Univ. of Tennessee Medical Units, Memphis, Tennessee.

Previous studies from this laboratory have demonstrated that the pathogenesis of the acute ethanol-induced fatty liver is a depression in the intrahepatic utilization of triglyceride. Since antioxidants have been demonstrated to maintain both the structural integrity of the liver following carbon tetrachloride and a normal DPN-DPNH ratio, a study of the effect of α-tocopherol and N,N'-diphenyl-p-phenylenediamine (DPPD) on the ethanol-induced fatty liver was undertaken. α-tocopherol acetate (10mg/100g) or DPPD (60mg/100g) was given intraperitoneally 48, 24, and 2 hrs. prior to the oral intubation of ethanol. Control rats received isocaloric glucose. In contrast to the control group, ethanol administration produced a 4-5 fold elevation in liver triglycerides. α-tocopherol pretreatment produced a 40% reduction. Plasma triglycerides were unaltered in either group. The administration of DPPD did not alter liver triglycerides in the control group but completely prevented the fatty liver in the ethanol-treated group. Plasma triglycerides were unaltered. These studies demonstrate the complete prevention of fatty metamorphosis by chemical means and suggest the employment of suitable antioxidants as specific therapy for parenchymal liver disease resulting from exposure to certain hepatotoxins. (Supported by a grant from the C. D. Smithers Foundation.)

GLYCOLYTIC METABOLISM OF THE HEART IN HEMORRHAGIC SHOCK. J. Doersching* B. Coleman and V. V. Glaviano, Stritch Sch. of Med., Loyola Univ., Chicago, Ill.

Arterial blood levels of lactate and pyruvate in addition to the myocardial concentrations of lactate, pyruvate, glycogen and phosphorylase were determined in 25 mongrel dogs anesthetized with Nembutal. Fifteen of the 25 dogs were subjected to hemorrhagic shock. Shock was induced by lowering mean arterial blood pressure by rapid bleeding to 40 mm Hg. This level of pressure was maintained for approximately 4 hrs., after which the total bled volume was reinfused. Myocardial glycogen levels in normal dogs (av. 932 mg%) did not differ significantly from those determined in the hypervolemic state of shock (av. 852 mg%). However, myocardial phosphorylase activity increased markedly from 63 to 73%, an effect most likely due to the elevated blood levels of catecholamines. Blood lactate rose from 15 to 68 mg/100 ml,(354%), while cardiac muscle level increased 38 to 55 mg/100 gm (31%). Myocardial pyruvate was elevated to 2.29 mg from a control level of 1.84 mg/100 gm, an increase of 24%. Blood levels of pyruvate increased from 0.56 to 0.96 mg/100 ml. The cardiac muscle levels of lactate and pyruvate are not comparable to the anoxia often postulated for the heart in shock. In an additional study, 10 dogs in the normovolemic state of hemorrhagic shock were treated with 500 μg of l-norepinephrine. This group was observed to have decreases in myocardial glycogen (11%) and lactate (17%), while pyruvate increased 32%. In addition to its glycogenolytic action, l-norepinephrine gave evidence of an effect on the lactate dehydrogenase system. (Supported by ONR contract 3502 01)

MOMENT TO MOMENT CARDIOVASCULAR RESPONSES TO EXERCISE IN NORMAL DOGS AND DOGS WITH CHRONIC CARDIAC DENERVATION. David E. Donald and John T. Shepherd, Mayo Clinic, Rochester, Minnesota.

The average stroke volume, pulmonary blood flow (electromagnetic flowmeter), heart rate, mixed venous saturation (cuvette oximeter) and aortic blood pressure (indwelling catheter) were measured over periods of 6 seconds during 4 minutes of exercise (8-fold rise in oxygen consumption) in 3 normal dogs and 5 dogs with cardiac denervation. Oxygen uptake was measured over intervals of 20 seconds for the first 2 minutes of exercise and the first 2 minutes of recovery. In both groups uptake reached a steady value after 1 to 1½ minutes of exercise and returned to pre-exercise levels in the same time; arterial blood pressure usually declined 20-30 mm. Hg on starting to run and returned to control levels by 1 to 1½ minutes with an occasional overshoot of 10 to 20 mm. Hg when exercise ceased; pulmonary artery saturation declined from 50 to 60 per cent in light exercise to 25 per cent during severe exercise. In normal dogs, heart rate and cardiac output reached maximal values 15 to 30 seconds after the start of exercise, stroke volume remaining unchanged or showing a decrease initially. In dogs with chronic cardiac denervation, stroke volume increased with the onset of exercise to reach a peak value some 30 seconds later, whereas maximal values of heart rate and cardiac output were not obtained until 1 to 1½ minutes from the onset of exercise. However, the similar patterns of oxygen uptake in the two groups demonstrated the adequacy of the denervated heart to meet the metabolic demands of severe exercise. Supported in part by NIH grant H-6143.

EFFECT OF INCREASED METABOLISM ON OXYGEN TENSION IN THE GINGIVA

H. L. Dorman and J. G. Bishop
Baylor Dental College, Dallas, Texas

Vascular changes have been associated with chronic bone loss from the alveolar crest in periodontal disease. Vascular occlusion, on the compression side of the tooth during orthodonic treatment may initiate bone loss and allow movement. Since periodontal inflammation increases metabolism in the area, oxygen tensions were measured in order to determine if the gingiva becomes hypoxic with increased metabolic rate. Oxygen tensions were measured with a Beckman oxygen microelectrode using the polarographic technique and body metabolism was increased by intravenous dinitrophenol (8 mg/kg). Arterial blood saturation was continuously monitored by means of a flow through cuvette oximeter. The saturation was maintained at 99.5% by manipulation of positive pressure breathing equipment. Normal dog gingiva average 56 mm/Hg° oxygen tension before dinitrophenol and averaged 54 mm/Hg° oxygen tension following dinitrophenol infusion. Gingival oxygen tension was not significantly changed even though whole body metabolism was increased three fold. These results indicate that the gingival vascularity is sufficiently adaptable to maintain normal oxygen tensions following greatly increased metabolic demands.

ABILITY OF MONKEYS TO DISCRIMINATE ELECTRICAL STIMULATION OF THE BRAIN. R.W. Doty, Center for Brain Research, University of Rochester, Rochester, New York

A conditioned stimulus (CS) of 1-msec, 50/sec pulses applied to neocortex, or 0.2-msec, 300/sec pulses subcortically, elicited conditioned reflexes (CRs) of shock avoidance by lever pressing from 4 cynomolgus and 2 pig-tailed macaques (Macaca irus and M. nemestrina). No significant differences in effectiveness were found for 31 widely distributed cortical and 17 subcortical points. Thresholds were less for elicitation of CRs than for inherent movement, even from "motor" cortex (average threshold for CRs: 0.27 mA, cortex; 0.21 mA, subcortex). The animals unhesitantly made CRs to stimulation of area striata or precentral gyrus upon first presentation of the unreinforced CS if they had previously been trained to respond to stimulation, respectively, of another striate or precentral point. Such "stimulus generalization" did not occur between "heterogeneous" cortical areas, although CRs were established, usually within 1-5 trials, for a new CS after reinforcement was begun. One M. nemestrina was trained to make one CR upon CS_1 to obtain food, another upon CS_2 to avoid shock. After training for about 1200 trials this animal was able to respond with better than 90% accuracy when CS_1 and CS_2 consisted of identical stimulation, or stimulation randomly varied as to intensity and/or frequency, applied to the foveal region of striate cortex at pairs of points only 3 mm apart. (Supported by USPHS Grants #B-1068 and B-3606).

THE PHYSIOLOGY OF ERUCTATION IN RUMINANTS. RECENT WORK ON THE PHYSIOLOGIC DISPOSITION OF ERUCTATED GASES. R. W. Dougherty, C. H. Mullenax*, and M. J. Allison*. National Animal Disease Laboratory, Ames, Iowa.

It has been estimated that approximately two liters per minute of gas are formed in the rumen and reticulum of a one-thousand pound bovine animal. Proper functioning of the eructations mechanism is so important that the life of the ruminant depends on efficient gas elimination. A short section of cinefluorographic movie film will be shown which illustrates the mechanics of eructation. A brief description of esophageal innervation, sphincter action and the eructation inhibitory reflex will be given. Previous work has shown that eructation is an active and forceful process involving the following: (1) complicated maneuvers of the rumen and reticulum which force ingesta away from the cardia, (2) opening of the cardia and prediaphragmatic sphincter, while the pharyngo-esophageal sphincter remains closed permitting gas to enter and distend the esophagus, (3) closure of the cardia and prediaphragmatic sphincter and opening of the pharyngoesophageal sphincter with a rapid wave of esophageal antiperistalsis forcing the gas into the pharynx with a closed nasopharyngeal sphincter and oral cavity and an open aditus laryngis, (4) this forces over half of the eructated gases into the lungs where absorption of certain components occurs. Graphic illustrations will be made of the seemingly unphysiologic process that occurs during normal eructation; i.e., the "shunting" of a large proportion of the eructated gas and its aerosolized components into the lungs. The physiologic significance of this unusual mechanism will be discussed in the light of (1) recent work in which $C^{14}O_2$ placed in the rumen is traced in blood, saliva, milk and tissues; (2) recovery of marker microorganisms and volatile chemical agents transported from the rumen to the respiratory tract.

TWO FACTORS AFFECTING THE CIRCULATING RED CELL MASS. Ben H. Douglas*, Oliver Carrier, Jr.* and Jack W. Crowell. Univ. Med. Center, Jackson, Miss.

Changes in the hematocrit ratio are often assumed to reflect changes in plasma volume; the concept is based on the assumption that the red cell mass remains constant. The present study reveals that there are two factors which can cause variability in apparent red cell mass as determined by the hematocrit measurements. These factors are: (1) sequestration of red cells by the spleen in dogs under sodium pentobarbital anesthesia, and (2) fluid shifts across the red cell membrane resulting from changes in blood pH. Ten normal and ten splenectomized dogs were anesthetized with 30 mg/kg sodium pentobarbital and their hematocrits followed serially. It was found that the sodium pentobarbital caused an average drop of 18.6 while in the splenectomized animals the hematocrit decreased only 6 per cent ($p < 0.01$). The hematocrit as a function of pH was investigated in nineteen normal dogs and in ten *in vitro* experiments. The pH was decreased by lactic acid or increased by sodium hydroxide or sodium bicarbonate. A decrease in pH of 0.1 units increased the hematocrit approximately 3.0 per cent and an increase in pH of 0.1 units decreased the hematocrit by the same percentage in both the *in vivo* and the *in vitro* experiments. The amount of hematocrit change caused by the pH and the sodium pentobarbital is sufficient to necessitate rigid control of these factors during experiments involving blood volume studies.

SYSTOLIC PRESSURE GRADIENTS IN ASCENDING AORTA. Thomas E. Driscol* and Richard W. Eckstein, Departments of Medicine and Physiology, Western Reserve University, Cleveland, Ohio.

It was reported (The Physiologist 5: 132, 1962) that during ejection left ventricular pressure exceeded or equaled that recorded in the aorta at the valves. However, during middle and late systole, ventricular pressure fell below that registered at more distal sites in the aorta. Experiments were designed to test whether there is an actual mean negative pressure gradient in the ascending aorta during ejection. A cannula was constructed from a 60 cm length of 17 gauge needle tubing. Two side openings were placed 1 cm apart in the central section and the segment between the holes was closed. In anesthetized dogs with open chests the cannula was passed through the apex into the aorta and to the exterior via an opening in the left common carotid artery in the neck. Statham gauges attached to both ends of the cannula were connected by the method of Spencer to record pressure difference. Mean and phasic pressure differences were recorded when the cannula was advanced from a position where both openings lay in the ventricular cavity to that where the cephalic opening entered the carotid artery. Cannulae with openings 2 and 3 cm apart were also employed. It was found that the mean gradient in the ascending aorta is slightly negative. Integration of the phasic records indicates that this is due to a large negative gradient during the latter 1/2 to 2/3 of systole. In a model similar negative pressure gradients were also measured for a distance of several cm beyond a constriction which produced a jet. (Supported by Grant H-4156 from the NIH.)

SINGLE UNIT ACTIVITY IN ASSOCIATION CORTEX OF THE CAT. R. Dubner* and L. T. Rutledge. Dept. of Physiol., Univ. of Michigan, Ann Arbor.

Single unit responses in middle suprasylvian gyrus to light flash, click, contralateral forepaw and contralateral homotopic cortical stimulation were studied in both the chloralosed and unanesthetized states. In chloralose preparations (35-50 mg/kg), approximately two-thirds of the units fired to photic stimuli, with a decreasing order of responsiveness found for cortical, auditory and somatic stimuli. The latency of the photically evoked unit response usually occurred between the onset and the peak of the positive component of the surface evoked potential. Convergence of sensory input on single cells was found in less than fifteen percent of the units examined, though a high degree of convergence was noted between the transcallosal response and the photically evoked response. Conditioning-test interactions of different inputs on polysensory neurons revealed a lack of reciprocal effectiveness between modalities. In unanesthetized cats, spontaneous cellular activity was higher and the responsiveness of cells to sensory stimulation was lower than in the chloralosed cats. The proportion of units activated by contralateral cortical stimulation was the same in both preparations. The data support the concept of imperfect convergence of peripherally and centrally elicited input on neurons in an association area of cat cerebral cortex.

(Supported by grant B-2978 from NIH)

VENTILATORY RESPONSE TO INTERMITTENT INSPIRED CARBON DIOXIDE R.E.Dutton*, V. Chernick*, H. Moses*, B. Bromberger-Barnea, S Permutt & R.L. Riley. Dept. of Environmental Medicine, The Johns Hopkins Univ., Baltimore,Md.

This experiment was designed to test the hypothesis that the intermittent administration of carbon dioxide will produce an additional stimulus to respiration beyond that produced by the steady administration of carbon dioxide. Oscillations of alveolar carbon dioxide tension were produced by the intermittent administration of 20% CO_2 for one breath every seven to twelve breaths. The increment in ventilation per mm Hg rise in mean arterial carbon dioxide tension ($PaCO_2$) during the intermittent administration of CO_2 was compared to that produced by steady 3% CO_2 breathing in nine dogs anesthetized with pentobarbital. In all except one animal the increase in ventilation per mm Hg change in mean $PaCO_2$ was greater during intermittent CO_2 than during steady CO_2. In five experiments oscillation of CO_2 caused a ventilatory response great enough to lower the mean $PaCO_2$ below control values. The mean slope for the steady administration of CO_2 was 0.58 (S.E. 0.034) and for the intermittent administration of CO_2 was 2.28 $L/min/\frac{mm}{Hg}$ (S.E. 0.108). The differences between the means is statistically significant ($P<.001$). This increase in ventilation with oscillations is of the same magnitude as the increase found during preliminary experiments in man in this laboratory.

These findings support the concept that chemoreceptors may be stimulated by the rate of change of $PaCO_2$ as well as the absolute level of $PaCO_2$. While the frequency of oscillations produced during this experiment was necessarily much less than that produced by respiration, the response obtained is consistent with the suggestions of Rossier (Respiration, C.V.Mosby 1960), Yamamoto and Edwards (J. Appl. Physiol. 1960), and Grodins (N.Y.Acad.Sci. in press) that oscillations of $PaCO_2$ may be an additional stimulus to ventilation during muscular exercise.

ELECTRICAL CALIBRATION OF THE MERCURY STRAIN GAUGE PLETHYSMOGRAPH, C. J. Eagan (intr. by D. A. Vaughan).
Arctic Aeromedical Laboratory, Fort Wainwright, Alaska

The unique features of a mercury strain gauge matched to an appropriate amplifier and recorder system have made it useful for limb and digital plethysmography in both research and clinical applications. Quantification of volume changes has been a problem, however, because of the lack of a precise and convenient method of calibration. The fact that the percentage change in volume of a cylinder (which changes in transverse dimensions only) equals the percentage change in resistance of a mercury strain gauge encircling the cylinder is the basis for the simple method of electrical calibration which is described. The calibration device consists of precision ganged potentiometers, P_1 and P_2, connected in parallel. The resistance of P_2 is exactly ten times that of P_1 for any setting of P_1. The effect of resistance of connecting leads is eliminated by making those to the calibration unit equal to those connecting to the mercury column of the gauge. For calibration of a gauge balanced in its circuit the calibration unit is connected in place of the gauge and the resistance of P_1 and P_2 in parallel is adjusted to equal that of the gauge. Opening P_2 causes a 10% increase in resistance which is equivalent to a 10% increase in volume applicable to the part encircled by the gauge. Thus, in less than one minute, it is possible to effect precise and convenient calibration without making any resistance or extension measurements on the gauge or any dimension measurements on the limb or digit.

A COMPARISON BETWEEN RYANODINE AND DINITROPHENOL ON OXYGEN CONSUMPTION AND CONTRACTURE IN FROG MUSCLE. Leslie E. Edwards and Anne C. Brehme.*
Department of Physiology, Medical College of Virginia, Richmond, Va.

This study was designed to show that drug-stimulated oxygen uptake is altered by muscle length changes as well as by metabolic inhibitors. Oxygen consumptions of paired sartorious muscles are measured in the standard Warburg apparatus. All inhibitors are added from the sidearm. Inhibitors are analyzed to see if they influence both muscle length and oxygen uptake. At high dose levels both ryanodine and dinitrophenol cause first a high oxygen consumption followed by a decrease. This decrease is associated with a slow developing contracture. Azide inhibits the oxygen uptake from dinitrophenol-treated muscles without producing shortening of muscles. In ryanodine-treated muscles, azide inhibits the oxygen uptake but also produces some shortening of the muscle. Iodoacetate at most dose levels tested decreases both muscle length and oxygen consumption. The degree of shortening of the muscle caused by a combination of drugs is usually greater than the sum of shortening produced by each drug measured separately. Oxygen consumption of a muscle has a component related to confirguration of the muscle as well as related to the metabolic pathways involved. All inhibitors should be checked to see if they influence muscle length at the time oxygen measurements are taken.
(Supported by NIH Grant AM-06252)

CORTICAL STEADY POTENTIAL DEPENDENCE ON IONIC ENVIRONMENT. E. Eidelberg. Barrow Neurological Institute and Arizona State University, Phoenix, Arizona.

Experiments were carried out on young albino rats, anesthetized with pentobarbital and/or ethanol. D. C. recordings were taken from the exposed cortex via reversible electrodes. Increasing the concentration of K+ ions, in a saline solution perfusing the cortical surface, caused a linearly-related increase in the negativity of the cortex to a remote reference lead, up to a "threshold" level, beyond which a wave of spreading depression was triggered. This "threshold" could be raised very considerably by Ca++ ions. Anoxia caused first a graded negative shift and then a further rapid shift very similar to spreading depression (S. D.). The K+-induced S. D. wave showed clear "refractoriness", although graded shifts could still be induced by KCl during the "refractory" phase. These data seem to indicate that depolarization of the superficial neuropil in the cortex may be induced in two stages resembling - on a very different time scale - that of neuronal membrane depolarization.

MECHANISMS OF ACTION OF THE INSECTICIDE ENDRIN. T. E. Emerson, Jr., C. M. Brake and L. B. Hinshaw. Civil Aeromedical Research Institute and Dept. of Physiol., Okla. Univ. School of Med., Okla. City, Okla.

Cardiovascular effects during the early phase of lethal endrin poisoning are obscure. Experiments to investigate these phenomena were carried out in a variety of intact dog preparations. Systemic arterial blood pressure, heart rate, cerebrospinal fluid pressure (CSFP) and cerebral venous pressure (CVP) were monitored continuously with Statham pressure transducers connected to a Sanborn recorder. Rectal temperature, leukocyte counts and differentials, blood pH and hematocrits were also determined before and after endrin stress. Acute endrin administration produces bradycardia, hypertension, copious salivation, hyperexcitability, tonic-clonic convulsions, increased body temperature, leukocytosis (neutrophilia), hemoconcentration and decreased pH. Large increases of CSFP and CVP were also prominent features. Preventing the convulsions with Anectine did not affect the hematological findings. Bradycardia, reversible with atropine, was independent of the hypertension and usually preceded it and the increase in CSFP and CVP. Elevation of CVP occurred after the onset of bradycardia, but before the hypertension and could have been caused by cerebral arteriolar dilatation or cerebral venous constriction. Results indicate that CVP elevation preceded the increase in CSFP. Lowering the elevated CSFP or preventing its rise did not affect the bradycardia, hypertension or elevated CVP. Both sympathetic and parasympathetic nervous systems appeared to be simultaneously stimulated by endrin. Although most of these effects appear to be caused by endrin acting directly on the central nervous system, some may be due to altered cerebral hemodynamics. (Research supported in part by USPHS grant H-1889.)

ROLE OF THE THALAMIC NUCLEUS FOR TASTE IN MODIFYING CALCIUM INTAKE IN RATS MAINTAINED ON A SELF-SELECTION DIET. R. Emmers* and M.R. Nocenti, Department of Physiology, Columbia University, New York City.

Previous experiments conducted in this laboratory have revealed that male Sherman rats, housed individually, can select their diet from 10 different foodstuffs in a manner which results in a normal body weight gain and growth rate. Such an arrangement is suitable for studying the importance of gustatory cues utilized in meeting dietary needs with respect to fats, proteins, carbohydrates, salts, vitamins, and water. In the following experiment an evaluation of gustatory involvement in the selection of a single substance, calcium, was made. In order to induce an increase in the intake of a 2% calcium gluconate solution against which the effects of any changes in taste acuity could be evaluated, a group of rats, previously adapted to the self-selection diet, were parathyroidectomized (Ptx); other animals remained unoperated to serve as controls. Approximately 30 days later, thalamic lesions were made to destroy taste in a portion of the Ptx and control animals. In a few rats lesions were made in the thalamic region for somesthetic input from the tongue or snout to assess the influence of tactile cues. The Ptx rats increased their calcium intake by as much as four times the preoperative amount. This elevated calcium ingestion after Ptx was maintained when the lesion destroyed the thalamic tactile region for tongue or snout; similar results were obtained in sham operated rats. Destruction of the thalamic nucleus for taste in Ptx animals caused an abrupt fall in calcium intake to levels found during their adaptation period. When this nucleus was only partially destroyed, calcium ingestion returned to a high level after an initial post-operative drop. These results indicate that taste has an important role in self-selection of dietary calcium. (Supported by grant B-3266, NINDB)

STUDIES OF TSH STIMULATION ON THYROID GLUCOSE OXIDATION AND NUCLEOTIDE COFACTOR CONCENTRATIONS. S.M. Epstein,* A.K. Remer,* and J.B. Field, Dept. of Medicine, University of Pittsburgh, Pittsburgh, Pa.

The increased glucose oxidation (G.O.) of thyroid slices, mediated by TSH, is associated with increased TPN levels and equivalent decreases of DPN. This suggested a TSH effect on thyroid DPN kinase which converts ATP and DPN to TPN. Levels as low as 10^{-12} moles of TPN were measured enzymatically. With excess 6-phosphogluconate-1-C^{14} (6PG) and excess 6-phosphogluconic dehydrogenase, TPN is rate limiting in the reaction 6PG $\xrightarrow{TPN}$ $\xrightarrow{TPNH}$ ribulose-5-PO_4 + $C^{14}O_2$. The production of $C^{14}O_2$ is thus proportional to the TPN present. A new assay sensitive to 10^{-12} moles of DPN, measured this nucleotide after conversion to TPN in the presence of excess ATP and DPN kinase. Reduced nucleotides are assayed after oxidation with α-ketoglutarate and glutamic dehydrogenase. Fractionation of TSH stimulated thyroid slices has localized the major TPN increase in the supernatant portion of the cell. In vitro pre-incubation of thyroid slices with carzinophilin which decreases DPN synthesis (Fed. Proc. 22:532, 1963) reduced basal, and TSH stimulated G.O. Thyroids from rats injected with ethionine, which decreases tissue ATP (J. Biol. Chem. 238:1757, 1963), show diminished TSH responsiveness. Thus reduction of substances used in TPN synthesis decreases TSH responsiveness. Addition of TPN and DPN in vitro does not increase thyroid slice G.O., probably because of lack of permeability. The G.O. of dog stomach mucosa and submaxillary gland slices, tissues which concentrate iodine, shows no TSH influence. Actinomycin-D has no effect on basal G.O. or TSH responsiveness. These data are consistant with an early, and perhaps initial, specific TSH stimulation of thyroid DPN kinase.

SINGLE NEURON INVESTIGATION OF SOMESTHETIC THALAMUS OF THE OPOSSUM. R. P. Erickson*, J. A. Jane*, R. Waite* and I. T. Diamond, Department of Psychology, Duke University, Durham, N. C.

The purpose of this study was to determine the functional properties of the somesthetic region of the opossum thalamus by means of microelectrode recording, and to compare the results with those obtained in investigations (e.g., Poggio & Mountcastle's) of single neurons in VP, Po and GM of the cat. Clicks, light flashes, and electrical and mechanical skin stimuli were delivered to animals anesthetized with dial-urethane. Glass micropipettes and fine (25 μ) nichrome wires served as electrodes. The placement of the electrodes was later established by a study of serial sections through the thalamus. A major finding was that many of the active neurons in VP had extensive somatic receptive fields, such as four paws. Neurons of this type in the cat are found in Po, but not VP. The remaining active units of VP had restricted fields, such as one paw. In the area intercalated between VP and the geniculate bodies, some neurons were responsive to both auditory and somatic stimuli, while others responded to only one of these classes of stimuli. Neurons of both types showed either extensive or restricted somatic receptive fields, so that functionally this region resembles Po in the cat. The finding that neurons of the opossum thalamus located in the area corresponding to the Po region of the cat show functional properties like Po, suggests that these thalamic subdivisions of the two species are homologous. (Supported by USPHS Grant M4849 and NSF Grant G18124.)

MEASUREMENTS OF INTRAFOLLICULAR PRESSURES IN THE RABBIT OVARY. Lawrence L. Espey* and Harry Lipner. Florida State Univ., Tallahassee, Fla.

Pressures within rabbit Graafian follicles have been determined by direct cannulation with micropipettes. The average pressure in the antrum of 60 maturing follicles was slightly over 17 mm Hg. There was no difference in the pressures in pre-coital and post-coital follicles. The average pressure of 15 blood follicles (pre-atretic) was 50 mm Hg. A direct proportionality was observed between the blood pressure and follicle pressure, suggesting that colloid osmotic pressure contributes little to the total hydrostatic pressure in the follicle. Blebbing preceded the appearance of the ovulation cone. In six measurements made during ovulation, intrafollicular pressure dropped instantly from about 15 mm Hg to 5 mm Hg at the time of rupture. Visible muscle-like contractions of the follicle, concomitant with recorded pressure changes, were seen in two of six ovulating follicles. A hypothesis explaining the mechanism of ovulation includes the concept that structural changes in the thecal wall result in ballooning and the appearance of an ovulation cone. Rupture of the ovulation cone occurs under the force of a steady pressure in the antrum. This investigation was supported in part by PHS Research Grant AM-01904 from the NIAM, Public Health Service.

EFFECT OF EXERCISE ON RENIN CONTENT OF PLASMA OF NORMOTENSIVE AND HYPERTENSIVE SUBJECTS, Alfred F. Fasola and Oscar M. Helmer (intr. by K. G. Kohlstaedt). Lilly Laboratory for Clinical Research, Marion County General Hosp., Indianapolis, Ind.

Renin has been found in high concentration in peripheral blood of patients with either renal vascular occlusive disease or with malignant hypertension. Renin cannot be demonstrated in the plasma of some patients with essential hypertension in the resting state, although, renin can be demonstrated in peripheral plasma of normotensive subjects. Renin was determined by the method of Helmer and Judson before and after exhausting exercise in the supine position. Control samples were drawn after 1/2 hour rest, at the heighth of exercise and 1 hour after the end of exercise. All normotensive subjects, except one, show an increase in renin as a result of exercise. In contrast only 4 of 12 hypertensives show an increase in renin as a result of exercise. Renin could not be demonstrated in 5 hypertensives in either the control plasma or as a result of exercise. Renin substrate (angiotensinogen) was higher in hypertensives than in normotensives. Some normotensive children of hypertensive parents showed the same response to exercise as the hypertensive parent.

ADAPTATION TO SUCROSE LOADING IN THE RAT. Vincent Fiorica,* P. F. Iampietro, and Russell Moses.* Civil Aeromedical Research Institute, Federal Aviation Agency, Oklahoma City, Oklahoma.

Unanesthetized male white rats, bearing chronically indwelling carotid catheters, were infused I.A. with 1.5 M sucrose solutions to determine 1) tolerance to sucrose, 2) effect of prior sucrose exposure on tolerance, and 3) patterns of urinary solute excretion during repeated sucrose loading. Injection volumes between 0.5 and 4.5 ml/100 gm body wt. were used to establish the load tolerance curve: loads between 0.5 and 2.0 ml/100 gm were tolerated without death; beyond 2.0 ml/100 gm mortality rate increased with dose to 100% at 4.5 ml/100 gm. Animals previously exposed to a standard sucrose load (2.0 ml/100 gm) demonstrated an increased tolerance to loads which were normally toxic to unadapted animals. At these high loads sucrose is relatively slowly excreted, suggesting that the protective effect may involve an increased tissue tolerance for the disaccharide. Effect of repeated sucrose loading on urinary solute excretion was determined by infusing four groups of animals with 0.5, 1.0, 1.5 or 2.0 ml/100 gm. Urine was collected at intervals over a seven hour test period. Six days later each group was retested at the same load. In each case a second loading resulted in a reduced total urine volume and the excretion of a smaller fraction of the total load. The smaller urine volume was primarily the result of a marked decrease in urine flow during the first 30 minutes following the second loading. Only small differences were noted in either sucrose or total solute concentration of urine following a second exposure to sucrose.

DENSITY-GRADIENT CENTRIFUGATION IN ANGLE-HEAD ROTORS. W. D. Fisher,* G. B. Cline,* and N. G. Anderson. Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee.

The widely used technique of banding materials by isopycnic density-gradient centrifugation is often limited by the small capacity of available high-speed swinging-bucket rotors. Therefore, we have investigated the use of higher capacity angle-head rotors for isopycnic separations, in essence, replacing the mechanical transitions of swinging-bucket rotors by a fluid transition as the rotor comes to rest. This transition is made with little mixing as shown by the recovery of preformed gradients and sample zones without distortion after acceleration and deceleration. Banding was done in self-formed CsCl gradients in a Spinco Model L ultracentrifuge. The tubes were scanned by an automatic recording device consisting of a quartz flow cell in a Beckman DB Spectrophotometer, a Water Model 34H refractometer and a Brown 12-point recorder. Good resolution was obtained with T3 bacteriophage in the Spinco #30 and #40 rotors. The half-height volumes were 3.5 ml and 1 ml, respectively. Native and heat-denatured calf thymus deoxyribonucleic acid were resolved in the #40 rotor. These results demonstrate that banding of viruses and macromolecules by isopycnic density-gradient centrifugation can be done with high resolution in angle-head rotors. Angle-head rotors were used instead of swinging-bucket rotors because: (1) a special rotor is not required, (2) more samples can be run, and (3) larger samples can be used. In the present experiments the gradients were self-formed; however, fluid transitions occurring during acceleration do not cause appreciable mixing and preformed gradients may be used to shorten centrifugation time.

INFLUENCE OF CALCIUM ON PERMEABILITY AND SECRETORY CHARACTERISTICS OF BULLFROG GASTRIC MUCOSA. J. G. Forte and A. H. Nauss (intr. by D. Scott,Jr.) Dept. Physiology, Sch. of Med., Univ. of Pennsylvania.

Isolated bullfrog gastric mucosae were mounted between two chambers. On the nutrient or serosal side was placed bicarbonate Ringers solution; on the secretory or mucosal side was placed either bicarbonate Ringers or a similar solution in which the $NaHCO_3$ was replaced by an isosmotic amount of NaCl. (The latter solution was used when acid secretion was measured.) Both sides were gassed with 5% CO_2 and 95% O_2. Elevation of the calcium concentration from 2-12 mM in the solution bathing the secretory side of the gastric mucosa resulted in a consistent decrease in the rate of acid secretion and an increase in the transmucosal potential difference (P.D.). Similar concentrations of calcium on the nutrient surface had little significant effect on these parameters. Mucosal conductance was not significantly altered in either instance. Removal of calcium by serial washing in calcium-free solution or by addition of citrate or ethylenediaminetetraacetic acid caused a fall in P.D., a rise in mucosal conductance and an apparent decrease in acid secretion as measured by the pH-stat method. Unless the P.D. fell to values very nearly zero, the short-circuit current was little altered ($\pm$ 10% of control values). Unidirectional movement of Na^+, K^+, Cl^- and sucrose were increased when the above effects of calcium depletion were noted, but the net flux of Cl^- was not significantly altered. All effects of calcium depletion were reversible by the addition of calcium, but not by Mg^{++}, Ba^{++} or Sr^{++}. The data suggest that calcium removal does not measurably interfere with active Cl^- transport. It is postulated that the observed decrease in acid secretion may be due to the neutralization of H^+ by HCO_3^- which may occur as a result of the increased leak of materials between the cells. Supported by USPHS.

THE IN VITRO INTESTINAL TRANSPORT OF MAGNESIUM IN THE AGING RAT. William C. Foster, Lab. of Clin. Chem., Misericordia Hosp., Philadelphia, Pa.

The magnesium content of bone has been shown to decrease markedly with age. An attempt was made to relate this observation to alterations in the absorption of magnesium from the gastro-intestinal tract in the aging process. Wistar-Strain Albino rats of approximately two months and two years of age, on a diet of laboratory chow, were lightly anesthetized with ether and sacrificed by transection of the spinal cord. The small intestine was removed, flushed with saline solution, everted, and sacs of the upper and lower jejunum and ileum were made by the technique of Wilson and Wiserman[1]. Krebs-Ringer-bicarbonate solution, containing approximately 1.2 mEq/l magnesium was instilled into the sacs as serosal fluid. The sacs were suspended in saline-bicarbonate solution containing approximately 6.0 mEq/l. magnesium for one hour at 37°C. The magnesium of the serosal and mucosal fluids was determined by the fluorometric method of Schachter[2], using an 8-hydroxyquinoline-magnesium complex. In all experiments the transport of magnesium to the serosal side was greater in the ileum than in the jejunum. A slight difference in transport was noted in the young and older rats. (Supported by U. S. P. H. Grant D-930, N. L. H.)

1. J. Physiol. 123:116-125 (1954)
2. Lab. Clin. Med. 54:763-768 (1959)

Experimental Analysis of the Cholinergic Properties of the Primary Afferent Pathway. D. T. Frazier* and L. L. Boyarsky. Dept. of Physiology and Biophysics, University of Kentucky, Lexington, Kentucky.

The effect of the anticholinesterases, DFP and eserine, on evoked unit and slow responses of somesthetic cortical, thalamic and cuneate neurones have been studied in the cat. The responses were evoked by stimulation of the radial nerve and, in the case of the thalamus and cortex, by direct monosynaptic excitation. Various routes of infusion were chosen so as to deliver as high a concentration of the drugs as possible to the area under study. Typically, all three areas were sensitive to the anticholinesterases; the cortex and thalamus being much more sensitive than the cuneate. DFP was the more potent inhibitor, usually depressing the response within 30 seconds after infusion. Eserine, on the other hand, had a longer time course with its initial effect being a potentiation of the slow wave followed by a depression. In each case the slow wave was affected first; the unit activity often persisting after the disappearance of the slow wave. Differential effects of the drugs on the positive and negative components of the slow potentials were also observed. Although the results were variable, atropine antagonized the effect of both DFP and eserine. The results are consistent with the presence of cholinergic fibers in all relay junctions of the primary afferent system. (Supported in part by Public Health Service Grants---9101 and GPM-10,554-C3.)

EFFECT OF o,p'-DDD AND SU-4885 ON DEVELOPMENT OF RENAL HYPERTENSION IN RATS. M. J. Fregly, Dept. Physiology, Univ. Florida, Sch. Med., Gainesville, Florida.

The adrenal cortex is often implicated in the development of experimental renal hypertension in the rat. The aim of these studies was to test the effect of the "adrenocorticolytic" compounds o,p'-DDD (2,2 bis (2-chlorophenyl, 4-chlorophenyl) 1,1-dichloroethane) and SU-4885 (2 methyl-1,2-bis-(3 pyridyl)-1-propanone) on development of renal hypertension in rats whose kidneys were bilaterally encapsulated with latex envelopes. Administration of 0.1 to 0.3% o,p'-DDD by weight in food during 18 weeks reduced cardiac hypertrophy and prevented a rise of systolic blood pressure to the level of untreated, renal hypertensive controls. The highest dose level appeared to offer greatest protection but all dose levels allowed modest rises to occur. o,p'-DDD is not toxic as defined by normal food and fluid intakes and growth rate. At autopsy treated rats showed a tendency toward smaller ratios of adrenal weight to body weight and thymus weight to body weight than untreated controls. Other tests of adrenal function were unaffected by treatment with o,p'-DDD and include serum sodium and potassium concentrations and spontaneous intake of NaCl solution. SU-4885, at dose levels of 0.1 and 0.2% in the diet, decreased growth rate and failed to protect against development of renal hypertension in rats.

HYDRODYNAMICS OF AORTIC BLOOD FLOW. E. D. Freis and W. C. Heath* Veterans Administration Hospital, Washington, D.C.

This study examines the question of disturbed versus streamlined flow in the thoracic aorta. A thermistor mounted in a hypodermic needle to permit aortic puncture in open chest dogs was used to record the temperature at 2 mm. intervals along the cross sectional diameter of the aorta. Simultaneously, cold saline solution was infused continuously from a catheter placed in various upstream locations. The results indicated that with infusion into the ascending aorta the indicator mixed more or less uniformly across the greater part of the cross sectional diameter. With infusion into the descending aorta a temperature gradient was maintained across the aortic diameter the greatest temperature drop occurring in the streamline occupied by the orifice of the infusion catheter. When two thermistors were stationed in different positions in the aortic root, and when cold saline was injected suddenly in their vicinity, the temperatures recorded by the two thermistors equalized immediately following the onset of the next systole. Using an intravascular microphone, sound waves were detected during the systolic interval in the proximal 2 cm. of the aorta but not in the descending portion. These various observations are consistent with the presence of disturbed but not necessarily turbulent flow in the ascending aorta, and with predominantly streamlined but not necessarily completely laminar flow in the descending portion.

DISSOCIATION OF MECHANICAL AND ELECTRICAL MANIFESTATIONS OF THE HEART BEAT. Steven A. Friedman*, M. D. Strong*, R. C. Mackowiak*, Z. Pober* and M. H. F. Friedman. Dept. of Physiology, Jefferson Med. Coll., Philadelphia, Pennsylvania

Experiments were performed on dogs under anesthesia. Aortic pressure, right atrial pressure, ventricular muscle contraction, phonocardiogram and ECG were monitered continuously. The heart was made hypodynamic and ultimately brought to standstill by several methods, such as overdosage with sodium pentobarbital by intravenous drip. Electrical activity as seen in several leads persisted for some time after apparent cessation of mechanical activity as confirmed by absence of pressure and contraction tracings and by direct inspection. Early after cardiac arrest the ECG appeared only slightly altered in configuration and voltage. First degree and complete heart block but rarely fibrillation preceded total electrical silence. In the heart poisoned by barbiturates, measures for cardiac resuscitation often restored electrical activity which, however, was never accompanied by restoration of the ventricular beat.

CAUDATE EFFECTS ON EVOKED ACTIVITY IN N. VENTRALIS LATERALIS. T. Frigyesi* and D. P. Purpura, Columbia Univ., N. Y.

Low-frequency (8/sec) caudate stimulation elicits 35-60 msec latency diphasic (negative-positive) focal potentials in n. ventralis lateralis (VL). Overt characteristics of caudate evoked activity in VL differ from those initiated by 8/sec midline thalamic (CM) stimulation in terms of latencies, magnitude and effects on VL responses to brachium conjunctivum (BC) stimulation. Whereas paired CM-BC and caudate-CM stimulation reveals prominent inhibitory-facilitatory-inhibitory interactions with progressive increases in conditioning-testing intervals, activity cycles of caudate-BC evoked responses in VL are predominantly inhibitory. Blockade of VL-focal negativity is accompanied by augmentation of focal positivity of both caudate and CM evoked responses. Inhibitory after-effects of variable duration (100-400 msec) are demonstrable on caudate evoked responses in VL following termination of CM stimulation and vice versa. Relayed pyramidal tract (PT) discharges associated with BC-evoked activity in VL are abolished by appropriately timed CM stimulation, but are only conditionally affected during the inhibition of VL activity by caudate stimulation. Effects observed in motor cortex, VL and PT during caudate activation are dependent on sites of stimulation. Such effects are clearly differentiated on the basis of temporal relations and polarities of evoked activities in these structures. These and other data suggest that caudate effects in VL are mediated in part by synaptic pathways involving rostral components of the thalamic-reticular-system.

PLASMA THIOCYANATE OF RATS, MEASURED BY THE BOXER AND RICKARDS METHOD. Cullie F. Funderburk* and L. Van Middlesworth, University of Tennessee, Memphis, Tennessee.

Boxer and Rickards (Arch. Biochem., 39:292, 1952) have presented an extremely sensitive and potentially specific test for thiocyanate in biological fluids. Their results suggest the normal thiocyanate concentration in human plasma is 100 times as great as the normal concentration of iodide; this, it would seem, should interfere with iodide metabolism.

The method of Boxer and Rickards was tested for specificity by addition of $S^{35}CN$ to plasma of rats, dialysis of the mixture, and chromatography of the crystalloids which passed through the dialysis membrane. The dialyzed plasma and the $S^{35}CN$ spots from the chromatograms were assayed for chemical thiocyanate using the Boxer and Rickards method. The thiocyanate passed freely through the dialysis membrane and the $S^{35}CN/S^{32}CN$ ratio was equal on both sides of the membrane. When all the $S^{35}CN$ was dialyzed from the plasma, no thiocyanate could be detected in the dialyzed plasma with the Boxer and Rickards procedure, indicating the absence of a measurable "false positive" reaction from plasma colloids. These results show the Boxer and Rickards method to be substantially specific for thiocyanate.

Preliminary studies on rat plasma show the thiocyanate concentration to range between 200-400 μg%. The lowest values have been observed in low iodine Remington diet fed rats having hyperplastic thyroids, whereas the highest values have been seen in rats fed Purina laboratory chow.

SIZE OF VENTRICULAR CAVITIES DURING ISOVOLEMIC PARTIAL HEART-LUNG BYPASS. P.M. Galletti, E. Lüthy* and C.R. Salgado*. Dept. Physiology, Emory Univ. Atlanta, Ga.

The size of the heart is one of the main determinants of the work load and energy expenditure of the myocardium. Thus to assist a failing heart, artificial circulation procedures ought to bring about a significant decrease in the size of ventricular cavities. Partial heart-lung bypass creates a particular hemodynamic situation characterized by a decrease in venous return to the heart, a reduction in pulmonary blood flow and maintenance of normal systemic flow. In 16 closed-chest dogs, cardiac output, stroke volume, left and right end-diastolic ventricular volume were measured using a thermodilution technique. When the cardiac output was reduced by isovolemic partial heart-lung bypass from 100 to 30 ml/kg/min, the end-diastolic volume shrunk to 48% of control for the right ventricle versus 67% for the left ventricle. Since no important change in heart rate was observed, the decrease in stroke volume was proportional to the decrease in cardiac output. In the control conditions, the right ventricle ejected a higher proportion of its end-diastolic content than the left ventricle (33% versus 24%). During bypass, the fraction ejected decreased more markedly for the left ventricle, which pumped against an unchanged systemic pressure, than for the right ventricle, which had to overcome a much decreased pulmonary artery pressure. These results were confirmed in a second series of experiments, where a decrease in the size of the cardiac shadow and diameter of the pulmonary artery was established by cineangiographic techniques. In conclusion isovolemic partial heart-lung bypass causes an acute reduction in the size of the heart in proportion to the amount of flow carried by the extracorporeal circuit.

Arousal and detection to x-rays. John Garcia* and N. A. Buchwald, Department of Psychology, Long Beach State College, and Department of Anatomy and Brain Research Institute, UCLA.

Threshold intensities for arousal and detection of x-rays were determined by two methods, changes in the electroencephalogram and behavioral discrimination. To study arousal, EEG's were recorded from chronically implanted cortical electrodes. Changes from a high-amplitude slow or spindling record to a low-voltage fast record were observed as a consequence of total x-ray doses as low as 0.1 r. An instrumental conditioning technique in which x-ray served as the conditioned stimulus (CS) was used to provide a behavioral measure of x-ray detection. Rats learned to detect total doses as low as 0.050 r by this method. The probability of response in both cases appeared to be a function of the log of the x-ray intensity. These data will be used to support a theory for x-ray perception by mechanisms intrinsically similar to those responsible for perception of other sensory modalities.

EFFECTS OF ANGIOTENSIN ON THE VASCULTURE OF THE KIDNEY, INTESTINE, AND LEG OF THE DOG. W. F. Geber, and J. M. Schwinghamer* Univ. of South Dakota Medical School, Vermillion, South Dakota.

A comparative study of angiotensin, epinephrine, norepinephrine, and serotonin effects on several vascular beds has indicated that angiotensin has unique and somewhat unpredictable properties. It produces a consistant, prolonged increase in blood pressure under all conditions. Blood flow and heart rate responses are variable. Data indicate that a possible reevaluation of the implications of the term "pressor substance" is in order at this time.

THE EFFECTS OF pH CHANGES UPON VENTRICULAR FIBRILLATION THRESHOLD.* Paul H. Gerst, William H. Fleming and James R. Malm (intr. by H. G. Barker). Department of Surgery, Presbyterian Hospital and Columbia University, N.Y., N.Y.

The purpose of this study was to evaluate the effects of variations in acid-base balance upon the susceptibility of the heart to ventricular fibrillation.

Metabolic acidosis and alkalosis and respiratory acidosis and alkalosis were produced in anesthetized and artificially ventilated dogs. Ventricular fibrillation thresholds were measured as originally described by Wiggers and Wegria. The fibrillation threshold levels were determined in each animal, first under normal conditions, and then during the above states of acid-base imbalance.

The data indicate that metabolic acidosis leads to a reduction in the ventricular fibrillation threshold, while metabolic alkalosis raises the threshold to ventricular fibrillation. When blood pH changes equivalent to those induced by the metabolic changes were produced solely by respiratory variations, there was no discernable change in the ventricular fibrillation threshold. With existing metabolic acidosis, the administration of sodium bicarbonate or THAM, sufficient to restore the pH to normal, returns the ventricular fibrillation threshold to the control value.

These results suggest that the susceptibility of the heart to ventricular fibrillation is directly related to the excess of fixed acids, and that a base excess protects the heart against fibrillation. Hypercapnia and hypocapnia, when not associated with other alterations in acid-base balance, do not appear to influence the fibrillation threshold.

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BIOCHEMICAL OBSERVATIONS IN EXPERIMENTALLY PRODUCED CONGESTIVE HEART FAILURE: Menard M. Gertler, M. D., N. Y. U. School of Medicine.

Congestive heart failure was produced in male guinea pigs weighing 300-400 grams by restricting the flow of the aorta just above the aortic valves. After a ten-day period the animals were sacrificed. Studies were made of oxidative phosphorylation on the mitochondrial preparations derived from both normal and experimentally produced failure in guinea pig hearts, liver and kidney. Various substrates were employed in these studies such as α ketoglutarate, succinate, malate, citrate, pyruvate, glutamate and β hydroxybutyrate. It was observed that in the liver little change occurred with the substrates except with α glutarate. The kidney preparations also showed very little change. There was phosphorylation accompaniment in all oxidations in the liver and kidney. Citrate was oxidized in heart muscle but there was no phosphorylation accompanying it. The startling change occurred, however, during coenzyme stimulation of α ketoglutarate with CoA, DPN and TPN when the oxidative rates of the failing cardiac mitochondrial preparation increased from 1032 to 1524 and the P/O ratio fell from 2.91 to 1.95. These results were not observed to the same extent in the normal cardiac mitochondrial preparations where the oxidative rates increased from 1170 to 1480 and the P/O ratio fell only slightly from 2.90 to 2.32. In spite of these changes the total energy yield appeared the same in both the normal and failure preparations.

PATTERN OF BRAIN HEATING PRODUCED BY SUBCORTICAL ELECTRODES. Philip L. Gildenberg (intr. by E. A. Spiegel). Departments of Experimental Neurology and Neurosurgery, Temple Medical School, Philadelphia, Pa.

The size and shape of subcortical lesions produced by the application of heat by means of an implanted electrode depend upon the pattern by which heat is carried away from the site of the electrode. A specially designed electrode was used, with a high resistance heating element at the tip through which 60 cycle A.C. was passed, so that it was possible to heat the electrode without the necessity of passing current through the surrounding brain tissue; the effect of radio frequency was also studied. Measurements were made of temperature changes in brain tissue at various distances from the electrode tip, as well as at various points along the electrode sheath. Thus, it was possible to judge the amount of heat dissipated via the electrode sheath, through the surrounding brain tissue itself, and via the blood stream (by repeating the procedure on a dead animal). When the 60 cycle heating electrode was brought to 70° C., for example, the brain tissue 2 mm away did not exceed 46° C., the temperature at which irreversible thermal damage supposedly begins to occur. Therefore, under these conditions, the lesion was confined to a width of 4 mm; measurement of the fixed brain demonstrated an area of coagulation with a width of 2.2 + 0.5 mm. The pattern of heating on application of radio frequency was compared.

TUBULAR PHOSPHATE ABSORPTION IN MAGNESIUM DEFICIENT AND PARATHYROIDECTOMIZED RATS. H Earl Ginn. Veterans Administration Hospital and University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

Previous studies revealed increased urinary phosphate excretion in magnesium deficient rats. To study tubular phosphate absorption in magnesium deficient and control rats 1-C^{14}-carboxyl labelled inulin was used to measure G.F.R. Following timed collections of urine and blood samples at endogenous plasma phosphate levels from 6 to 25 μM of phosphate buffered at pH 7.4 was infused per min. Test animals had a mean Tm for phosphate of 0.9 μM/min/ml of C_{In} compared to 1.9 in controls. Another group of pairs was similarly studied 7 to 10 days following parathyroidectomy. Parathyroidectomized magnesium deficient animals' Tm for phosphate averaged 1.7 μM/min/ml of C_{In} compared to 4.2 in parathyroidectomized controls. These data suggest that magnesium deficiency interferes with renal tubular phosphate absorption separate from an influence on parathormone.

BRAIN STEM TRANSECTIONS AND GALVANIC SKIN REFLEX ACTIVITY. Richard L. Glasser, Mario Perez-Reyes*, and Joe W. Tippett*. Departments of Physiology and Psychiatry, Univ. of North Carolina School of Medicine, Chapel Hill, N. C.

Other investigators have reported that galvanic skin reflex activity virtually disappears after intercollicular decerebration and significantly recovers after high cervical spinal cord transection. The virtual absence of the galvanic skin reflex in the midmesencephalic animal has been attributed to the inhibitory activity of the medullary ventromedial reticular formation. In the present study, galvanic skin reflex activity was recorded in cats subjected to vagotomy and serial decerebration procedures. Decerebration levels were judged by physiological criteria and by anatomical examination of the brain. Spontaneous and reflex galvanic skin activity largely disappeared after midmesencephalic decerebration, but significantly recovered in low pontile and high medullary animals. Cervical spinal cord transection in these animals typically produced further potentiation in the activity. These data indicate that the lower brain stem contains an extensive galvanic skin reflex inhibitory system consisting of an important pontile component in addition to a medullary component. Maximal suppression of galvanic skin reflex activity in the decerebrate animal requires the integrity of both components of this system. (Supported by USPHS Grant HE 03755.)

EFFECT OF ENVIRONMENTAL TEMPERATURE ON CHRONIC EXPOSURE TO OXYGEN. Armand J. Gold, Elaine C. Silver* and Harry E. Hance*. Martin Co., Baltimore, Md., General Electric Co., King of Prussia, Pa. and Univ. of Pennsylvania School of Veterinary Medicine, Philadelphia, Pa.

Experiments to determine effects of temperature on chronic exposure to atmospheric O_2 were carried out in separate studies on the mouse, Bar Harbor Strain C-57, and on the giant amoeba, Pelomyxa carolinensis. In the former, groups of 12 or 13 male mice were placed in a chamber containing 98-99% O_2 and subjected to temperatures ranging from 75° to 115°F. Results indicated increased sensitivity to O_2 with increased temperature, LT_{50}'s for O_2-75° and O_2-100° groups being 100 hours and 30 hours, respectively. However, high temperatures appeared to dominate the effect of O_2, LT_{50}'s for groups exposed to O_2 or air between 110° and 115° being 30-60 minutes. Evidence of O_2 toxicity (pulmonary edema, atelectasis, pulmonary hemorrhage) was found in the lungs of mice exposed to temperatures below 100°. Pulmonary hemorrhage commonly seen with high heat stress was observed in mice exposed to O_2 or to air at 100° or above, tending to substantiate the LT_{50} data. In the second study, small chambers containing culture solutions of Pelomyxa were exposed to streams of O_2 or air passed over the solutions for 72 hours at temperatures of 35°-100°F. Whereas air-75° controls increased their number by 90% after 3 days, the increase was attenuated to 20% in the O_2-75° group. High temperatures in combination with either O_2 or air resulted not only in growth attenuation but nearly 100% disintegration of the amoeba population. Low temperatures in the presence of O_2 or air produced a much lower incidence of disintegration. The data suggest that O_2 effects (growth attenuation), evident at normal and near-normal temperatures, were abolished or replaced primarily by high-temperature and to some extent low-temperature effects (cell disintegration).

Intrinsic and Extrinsic Inhibition of the Reactivity of the Toad Bladder to Vasopressin. D.C.Goldberg*, M.A.Schoessler* and I.L.Schwartz, Med. Res. Centr.,Brookhaven Natl. Lab. and Dept. Physiol.,U. of Cin. Coll.Med.

The effect of arginine vasopressin (AVP) to increase the permeability to water of the toad bladder has been studied as a function of time, dosage, previous challenges and history of the buffered (pH 7.4), oxygenated Ringer fluid bath (250 milliosmolal) in which the bladders were mounted. The bladders were filled with diluted Ringer fluid (50 milliosmolal). Following prolonged (4 to 14 hrs.) exposure of bladders to AVP with or without changes of the serosal bathing fluid, the hormone-induced increase in water permeability reached an early maximum and then declined exponentially with a half time of 150-250 min. In 15 experiments the AVP-induced increase in permeability was allowed to decline to various levels in the presence of hormone after which the bladders were thoroughly washed in hormone-free Ringer fluid until baseline impermeability was regained. At this point they were rechallenged with an identical dose of hormone. The second response was always significantly less than the initial response; in fact, the maximum response to the second challenge approximated the level to which the initial response had been allowed to decline before washing in hormone-free Ringer. The fact that the wash served to arrest the diminishing hormone effect without reversing it suggested that the intrinsic reactivity of the bladder wall had decreased.

Other experiments indicated that an extrinsic factor contributed to the decline in hormone effect: bladders were exposed overnight to Ringer fluid containing AVP (10 mu/ml) and then discarded. Fresh bladders, which were then placed in this overnight serosal bath, exhibited little or no response even when a fresh dose of 10 mu/ml of AVP was added, suggesting that an inhibitor had been released from the bladder tissue into the serosal bath.

SOME DYNAMICS OF BODY HEAT STORAGE. Ralph F. Goldman (intr. by G. Clark). U.S. Army Research Institute of Environmental Medicine, Natick, Mass.

Ten subjects were exposed for 3 hours on each of 5 days in an uncompensably hot environment (104°F dry bulb, 98°F wet bulb temperature, 80% relative humidity). Despite maximal vasodilatation and sweat production by the subjects, this environment could not carry away all of the resting metabolic heat production. Therefore, a relatively linear rise in mean body temperature occurred; at rest at a rate of 0.35°C per hour. On 3 of the days, at one point in the 3 hour exposure, each subject walked on a treadmill for 15 minutes. Treadmill speed and grade were set to require an energy expenditure rate which would add, in the 15 minute period, 20, 40 or 55 kcal per square meter of body surface to the resting heat production. Thus, an essentially square pulse of metabolic heat was added to the resting heat production.

The change in the rate of rise of skin and rectal temperature varied with the different heat increments. However, when body heat storage was calculated, the total increment appeared in the calculated heat content of the body eventually. This "stirring time" was again dependent on the level of heat increment.

Some rectal and skin temperature responses to a sinusoidally varying metabolic heat production at frequencies of 1/2 to 3 cycles per hour will also be presented. The forcing function was generated by varying the treadmill speed sinusoidally between 1.5 and 4 miles per hour.

DIRECT RELATION BETWEEN PULSATILE BLOOD FLOW AND ELECTRICAL IMPEDANCE OF THE BRAIN. Frank Gollan and Richard Namon*. VA Hospital and University of Miami School of Medicine, and Physical Instruments Inc., Coral Gables, Florida.

With the recent interest in cranial plethysmography or rheoencephalography, as applied clinically by F. L. Jenkner, it has become important to prove the validity and accuracy of this technique to measure cerebral blood flow. It has been suggested by Nyboer that a relative change in blood flow can be calculated from the electrical plethysmogram by multiplying the amplitude, extrapolated to zero time, by the pulse rate. To test this proposition, the cerebral circulation of dogs was isolated by draining venous blood into a pump-oxygenator and returning it into both carotid arteries. The heart of the animal was arrested by external electrical fibrillation, so that cerebral blood flow, pulse rate, pulse pressure and gas tensions could be controlled. Blood flow was monitored with an electromagnetic flowmeter, blood pressure with a strain gauge, and electrical impedance with monopolar electrodes attached to contact lenses of the eyes. These studies prove that changes in electrical impedance of the brain are actually caused by pulsatile blood flow, whereas continuous flow abolishes electrical impedance changes. The electrical impedance changes reflect pulse volume and flow velocity, and are independent of pressure. Nyboer's assumption is correct, since the amplitude of the rheoencephalogram from corneal leads could be linearly related to pulsatile blood flow.

EFFECT OF pH ON CANINE GASTRIC WALL RESISTANCE
R. L. Goodale, Jr., M. D.,* J. P. Delaney, M. D.,* A. J. Madsen, M. D.,* and O. H. Wangensteen, M. D. (intr. by N. S. R. Maluf, M. D.)

Gastric wall resistance to perfusion of the stomach with 0.1N HCl at 44°C. was observed under variable conditions of systemic acid-base balance to evaluate whether abetment of ulcer provocation occurs if the alkaline reserve of the gastric wall is depleted. Gastric perfusion was performed with an open end-hole and also with multiple side-hole vents for dispersion of the perfusate in order to evaluate the jet-thrust effect. Results:

Systemic Condition	Average time (min.) to perforation, and incidence of perforation (in parentheses)	
	Single End-hole Tube	Multiple Side-hole Tube
Normal pH	69 (11/12)	200 (2/8)
Metabolic Acidosis	51 (11/12)	190 (2/4)
Metabolic Alkalosis	72 (9/11)	236+ (0/5)
Respiratory Acidosis	20 (9/11)	175 (2/13)
Respiratory Alkalosis	71 (8/11)	161 (5/10)

There is no appreciable difference between the normal and alkalotic animal in ulcer development and perforation, while acidosis, particularly of the respiratory type, appears to enhance the ulcer-provocation of such perfusions.

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Dept. of Surg., University of Minnesota Med. School, Minneapolis 14

INHIBITION OF ADENOSINE PHOSPHATE BREAKDOWN IN BLOOD BY CITRIC ACID BUFFER David B. Gordon Mt. Sinai Hospital Cleveland, Ohio

It has long been suspected that adenosine compounds may be secreted into the blood stream by such organs as skeletal muscle, heart or kidney. ATP, as well as ADP and AMP, when added to whole blood or plasma is degraded to compounds of lower energy content. In order to detect small amounts of adenosine phosphates in blood plasma it is necessary to prevent their breakdown. We investigated the possibility of preventing this breakdown by the addition of non-volatile organic acids to the blood. Citric acid buffer (acid + K salt pH 6.3) added to whole blood in the proportion 1 ml. buffer: 10 ml. blood was found to be effective. For example, without buffer less than 10% of added ATP was recovered after incubation with whole blood at 35° C for 3 minutes. With buffer, under the same conditions, over 50% was present and conversion to AMP was greatly reduced. Breakdown of ADP and of AMP is also reduced in the presence of citric acid buffer. Whether the buffer capacity or the chelating effect of the citrate is responsible for its protective action is being investigated.

(This work was done during the tenure of an Advanced Research Fellowship of the American Heart Association.)

RESPONSE TO STIMULATION OF VASODEPRESSOR AREAS IN CONSCIOUS AND ANESTHETIZED MONKEYS. R. J. Gorten*, O. A. Smith and R. F. Rushmer Department of Physiology & Biophysics and Regional Primate Research Center, University of Washington, Seattle, Wash.

Most of our understanding of the cardiovascular regulation provided by diencephalic and lower brain structures is based on studies with anesthetized animals. Chronic implantation of bipolar electrodes in diencephalic vasodepressor areas of five pigtail monkeys permitted evaluation of certain regulatory functions which are altered by light anesthetic doses of α-chloralose or sodium pentobarbital. On repeated occasions after recovery from the operations, diencephalic stimulation in the conscious animals was accompanied by elevation of arterial pressure, cardiac rate, and peak velocity of flow in the abdominal aorta. However, when an anesthetic agent was administered, vasodepressor and cardioinhibitory responses were elicited by stimulation through the same electrode in each animal on every occasion. Although motor activity usually accompanied stimulation in conscious animals, there were indications that the reversals in pressure and rate responses involved unidentified special functions of the nervous system which counteract influences tending to lower arterial pressure and inhibit cardiac activity in the conscious animal. Presumably, these special functions are removed during even light anesthesia, so that central stimulation can partially inhibit the sympathetic nervous system. (Aided by grants HTS5147 and HE04741 from the National Heart Institute.)

A STUDY OF EXCITABILITY CYCLES IN THE CAT CEREBRAL CORTEX. L. J. Greenbaum, Jr. and J. K. Merlis (intr. by W.D. Blake). University of Maryland, School of Medicine, Baltimore.

A study has been made of the electrical responses to direct electrical stimulation of the exposed cerebral cortex of cats under a variety of conditions. The excitability cycles of the suprasylvian, lateral and ectosylvian gyri have been studies and compared in unanesthetized and anesthetized cats using submaximal, maximal and supramaximal stimuli. The paired stimuli were delivered at intervals ranging from 2 to 400 msec. These paired shocks of equal magnitude were delivered at 2 second intervals. The test response amplitude was compared to the conditioning response amplitude and was expressed as a ratio. In general, the excitability cycles for the three cortical gyri in the unanesthetized state (succinyl choline, encéphale isolé and cerveau isolé) were characterized by an initial period of facilitation (F_1) which was followed by a brief depression (D) at 5 msec. A longer lasting facilitation (F_2) followed D and sometimes exceeded 400 msec. Pentobarbital (plus $MgSO_4$) increased the magnitude and duration of depression and decreased the magnitude of F_2. No consistent relationship between the magnitude of F_1,D and F_2 and strength of stimulus could be established in the unanesthetized and anesthetized cats. The difficulty of evoking responses in the ectosylvian gyrus was obviated by pentobarbital anesthesia and/or decerebration. It is suggested that F_1 reflects intrinsic changes in dendrite excitability while D and F_2 are considered to involve synaptic mechanisms.

CIRCULATORY RESPONSES TO ABRUPT RELEASE OF BLOOD ACCUMULATED IN THE LEGS. A.D.M. Greenfield*, E. Brown, J.S. Goei*, and G.C. Plassaras*. Cardiovascular Res. Inst. and Dept. of Med., U.C. Sch. of Med., San Francisco, Calif.

Recumbent subjects were exposed below the hips to pressures 70 mm Hg below atmospheric for periods of 0.5 to 10 min to simulate a leg down tilt. The arterial pressure fell briefly and recovered, the heart accelerated, and the forearm blood flow decreased. Following abrupt (0.3 sec) release of suction, there was (1) a headward shift of center of gravity of 45,000 g cm in 3 sec, estimated to correspond to the transfer of about 500 g of blood from below to above the hips, (2) an almost immediate brief rise of arterial pressure to above control level, (3) a very brief but pronounced slowing of the heart (slowest at 4.4 sec after release) and (4) a transient marked increase in forearm blood flow reaching its maximum 15.5 sec after release, by which time arterial pressure was normal. All of these effects were greatly reduced if the return of blood from the legs was impeded by the inflation of cuffs around the thighs. Flow changes in the forearm were unaffected following injection of 0.4 mg of atropine into the brachial artery but were abolished by 12.5 mg of bretylium tosylate. Thus they appear to be mediated by changes in activity of adrenergic vasoconstrictor nerves. Massage of one carotid sinus which caused similar slowing of the heart failed to affect forearm blood flow. Neither the bradycardia nor the increase in forearm blood flow could be reproduced by raising the mean arterial or the mean and pulse pressures by voluntary respiratory maneuvers. It appears that the responses have an origin other than in the carotid sinus baroreceptors. (Supported by USPHS Grant HE-06285.)

CUTANEOUS DIFFUSION OF N_2 DURING N_2 WASHOUT. A. C. Groom* and L. E. Farhi. Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, N. Y.

N_2 washout from the body of the dog during O_2 breathing was studied by following the level of N_2 in mixed venous blood. The data suggested that atmospheric N_2 diffuses across the skin into the blood and this affects substantially the later part of the washout curve. This effect was quantitated by experiments in which the gaseous environment was controlled. The apparent half-life of the slowest washout compartment of dogs surrounded by air is more than twice that of dogs placed in O_2. This effect must be of even greater importance under hyperbaric conditions. Change of the environment during an experiment allows calculations of "effective skin perfusion" and of the rate of cutaneous gas transfer. This rate can actually exceed that at which N_2 is washed out from the tissues at 5 hours. It is therefore essential to provide a gaseous environment of the same composition as the inspired gas in order to obtain an accurate description of inert gas washout from the body stores. (Supported by U. S. Air Force Contract AF 33(657) 10082.)

EFFECT OF TRANSFORMING A PAVLOV TO A HEIDENHAIN POUCH ON RESPONSE TO GASTRIN AND HISTAMINE. Morton I. Grossman and Sven Andersson*. Veterans Adm. Center, Los Angeles.

In 3 dogs with Pavlov pouches (PP) the maximal responses to histamine were 1.22, 1.49 and 1.09 mEq/15 min. After transformation of the PP to a Heidenhain pouch (HP) the maximal responses to histamine were 1.32, 1.53 and 1.13 mEq/15 min. In these same dogs the maximal responses to gastrin were 1.34, 0.95 and 0.82 mEq/15 min. from the PP and 0.52, 0.52 and 0.24 mEq/15 min. from the HP. Thus vagal denervation did not significantly alter the maximal response to histamine but greatly depressed the maximal response to gastrin.

MAINTENANCE OF MILK SECRETION IN RATS FOLLOWING DENERVATION OF THE MAMMARY GLANDS. Clark E. Grosvenor. Univ. of Tennessee, Memphis, Tennessee

Experiments were performed to test the essentiality of the nervous component of suckling in maintenance of milk secretion in the lactating rat. The milk ducts of the 6 anterior mammary glands of primiparous rats were ligated on postpartum day 2. After 1-2 days the 6 young nursed only the 6 posterior mammary glands. On postpartum day 9 or 10 the posterior glands were denervated by pithing the spinal cord caudal to T-12 and removing it by suction. Some mothers were injected with oxytocin (Group 1) and some with saline (Group 2) subc. 3-4 times a day for several days. Other rats (Group 3) had their spinal cords removed caudal to T-12 but were otherwise untreated. Litter body weights of rats in groups 1 and 3 were reduced 1-10g the day after cord removal though milk could be seen in their stomachs through the semitransparent skin. Thereafter, group 3 litters gained weight at a normal rate and group 1 litters at a rate 60-75% of normal. The litters of group 2 rats lost 11-28g of weight the day after cord removal; little or no milk could be seen in their stomachs. However, the litters of group 2 thereafter secured enough milk to retard the loss, to maintain, or to gain in body weight. Milk was visible in their stomachs by the 3rd day after cord removal. Autopsy revealed only milk in the stomachs of the young in each group. Intramammary pressure recordings from denervated glands of ether anaesthetized rats in each group showed that the pressure rose quickly and was maintained for several minutes in response to tapping the skin over the gland or compressing the skin and underlying gland. Similar manipulations applied to the contralateral gland were without effect. These results suggest that the nervous component of suckling is not indispersable for maintenance of milk secretion or milk removal in the rat. Supported by a grant from the USPHS during tenure as a Research Career Development Awardee of the USPHS.

STUDIES ON THE "TROPHIC" RELATIONSHIP BETWEEN NERVE FIBERS AND TASTE BUDS. Lloyd Guth. Laboratory of Neuroanatomical Sciences, N.I.N.D.B., N.I.H., Bethesda, Maryland.

Total denervation of the rat's circumvallate papilla results in disappearance of taste buds and epithelial atrophy. This has been attributed to a loss of trophic nerve function. Inasmuch as partial denervation of skin, muscle, CNS, and sympathetic ganglion elicits functional collateral sprouting of the residual nerve supply, the present experiment was performed to determine the changes in trophic nerve function following partial denervation of the circumvallate papilla. Unilateral or bilateral glossopharyngeal nerve transection was performed on rats. Histological examination of the circumvallate papilla was made on 7 and 35 day postoperative specimens. Unilateral transection resulted in a 12% rather than a 50% decrease in the number of taste buds, which is interpreted as indicating bilateral innervation of the remaining taste buds. The number of taste cells per bud diminished 25% after unilateral denervation, but in view of the methods employed the true decrease was probably greater. The epithelium atrophied less after unilateral than after bilateral denervation; mitotic counts on bilaterally denervated specimens revealed changes that were not sufficient to account completely for the epithelial atrophy. The effect of partial denervation on each of these parameters (taste buds, cells per bud, and epithelial atrophy) was the same at 7 as at 35 days postoperatively. Consequently, even if collateral sprouting occurred after partial denervation, it was not manifested by changes in trophic nerve function, i.e., by histological changes in the end organs.

THEORY FOR AUTOREGULATION OF GLOMERULAR FILTRATION RATE AND BLOOD FLOW IN EACH NEPHRON BY THE JUXTAGLOMERULAR APPARATUS. Arthur C. Guyton. Dept. of Physiology, Univ. Med. Center, Jackson, Miss.

The macula densa of the distal tubule lies in apposition to the juxtaglomerular apparatus which surrounds the afferent arteriole. Therefore, it is reasonable to believe that some factor in the distal tubule might control blood flow to the glomerulus and thereby control glomerular filtration rate. A theory has been formulated based on the concept that osmolarity of the distal tubular fluid controls blood inflow to the glomerulus and thereby autoregulates the GFR. This theory utilizes observations by several investigators that the osmolarity of the tubular fluid at the macula densa is regulated at a very low osmolarity under widely varying conditions and that rapid flow of fluid through the loop of Henle causes water absorption to lag behind sodium chloride absorption, thereby diluting the fluid entering the distal tubule. The theory assumes that too dilute fluid at the macula densa causes the juxtaglomerular apparatus to swell or to release a vasoconstrictor substance, perhaps renin, either of which effects could cause afferent arteriolar constriction. This would decrease the GFR which in turn would increase the osmolarity of the fluid at the macula densa back toward its normal control value. Too concentrated fluid would cause converse effects. This theory explains many known functions of the kidney such as (1)autoregulation of both GFR and renal blood flow, (2) failure of these two types of autoregulation at high and low arterial pressures and during vasoconstriction, (3) high GFR's during mannitol, urea, or hypertonic sodium chloride diuresis, and (4) low osmolarity of the urine during water diuresis or diabetes insipidus. The remarkable fit of this concept with many known functions of the kidney makes it important to examine the theory further.

THE RELATION BETWEEN RENAL LYMPH VESSEL PRESSURE AND AUTOREGULATION OF RENAL BLOOD FLOW. F. J. Haddy and J. B. Scott*. University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

We previously reported that resistance increases as a function of flow in capsulated or decapsulated live kidneys but not in dead kidneys, that the onset of the increase correlates better with flow than perfusion pressure, that elevation of venous pressure at constant flow raises resistance in intact kidneys and decreases it only slightly in dead kidneys, and that a change in venous pressure produces 25 times more change in renal lymph flow than the same change in arterial pressure (Am. J. Physiol. 195:97 and 111, 1958). We concluded that autoregulation results from active vasomotion initiated by change in flow and the response to venous pressure results from both active and passive vasomotion. The present study shows the effect of a square wave change in flow rate (F) and of change in venous pressure (Pv) at constant F upon perfusion (Pa) and lymph (P_l) pressures. Doubling F immediately raises Pa. It may then remain constant at the new level or gradually rise, never reaching a steady state (autoregulatory phenomenon). P_l, however, rises slightly and remains constant at the new level regardless of the behavior of Pa. If F is doubled for 2 seconds and then returned to the control value, Pa sometimes remains slightly elevated for a short period of time. This raised pressure is unassociated with a change in P_l. Elevation of Pv at constant flow produces an almost equivalent increment in P_l, but often a greater increment in Pa. These studies indicate that tissue pressure does not have an important role in autoregulation but does participate in the response to changed venous pressure. Autoregulation results from active vasomotion due to change in metabolite concentration and, possibly, in transmural pressure, whereas the response to changed venous pressure is a composite of active and passive vasomotion.

UREA TRANSPORT ACROSS DOG INTESTINAL MUCOSA IN VITRO: UPHILL MOVEMENT OF UREA. Ali A. Hakim* and N. Lifson, Dept. of Physiology, University of Minnesota, Minneapolis.

It has frequently been suggested that solvent flow and consequent solvent drag (fluid circuit, osmosis, pinocytosis, etc.) occurs during intestinal absorption. If a solvent stream carries a passively transported solute from low to high concentration more rapidly than its return in the direction of diffusion, uphill movement of the solute should occur. The data to be presented indicate that this is the case for urea in a dog mucosal membrane preparation recently described, and that, moreover, such uphill transport can occur in either direction across the membrane. Mucosal membranes from the small intestine were stripped and mounted for study as previously described (J. Appl. Physiol. 18:409, 1963). The bathing fluids were Krebs-Ringer bicarbonate containing 500 mg% glucose and urea in suitable concentrations. They were maintained at 38°C and gassed with 5% CO_2-95%O_2. During normal absorption of water, net urea transport was found from a 10 mM mucosal fluid concentration to a serosal one of 20 mM. When the direction of water transport was reversed by serosal pressure and the concentration relationship also reversed, uphill movement of urea took place from serosal to mucosal fluid. The relationship between urea and water transport in these experiments, as well as in others under a variety of conditions (downhill transport of urea with or against the direction of water movement, transport without a concentration difference) was indicative of bulk flow plus a small diffusion component. If sieving is present, it is minor. Results with D_2O, treated as a solute, were comparable to those for urea.

PULMONARY INACTIVATION OF ENDOGENOUS VASODILATOR MATERIAL. George H. Hall and Marvin A. Sackner. (intr. by A.B. DuBois). Department of Physiology, Grad. Sch. Med., University of Pennsylvania, Phila., Pa.

The pulmonary function of inactivation of naturally occurring vasoactive substances has received little attention. The purpose of this study was to determine the physiologic significance of this function, and whether the substances removed from the venous blood were predominantly vasodilator or vasoconstrictor in action. The hind limb of an anesthetized dog was perfused either with arterial blood, or venous blood from the superior vena cava, hepatic vein or pulmonary artery, by a peristaltic pump alone or in combination with a sponge oxygenator. The oxygenator produced 100% oxygen saturation with minimal changes in Pco_2 and pH of the blood passing through it. Vascular resistances in the whole limb and the paw were calculated from pressure and flow measurements and these results expressed as a percentage of the resistances prior to the perfusions. In six dogs, there was no significant difference in paw resistance between the perfusion of arterial blood and arterial blood after passage through the oxygenator nor a significant difference between the perfusion of venous blood and venous blood after passage through the oxygenator. However, the mean paw resistance, was 94% for all the arterial perfusions but only 44% for all the venous perfusions ($p < 0.005$). In three of these dogs, the mean limb vascular resistance was 110% for all the arterial perfusions and 68% for all the venous perfusions ($p < 0.05$). A fall in vascular resistances with venous blood also occurred after administration of tetraethylammonium chloride, a ganglionic blocking agent, to one dog. It is concluded that, 1) venous blood has vasodilatory activity; 2) this property is not affected by saturation with oxygen; and 3) this property is lost after passage through the lungs.

OXIDATIVE PHOSPHORYLATION IN MITOCHONDRIA FROM ADRENALECTOMIZED RATS. James C. Hall and Bengt S. Liljeroot*. Rutgers-The State University, Newark 2, N. J.

This study was undertaken since previously reported experiments have shown that P:O ratios are reduced in diabetic and hypophysectomized rats. Male Sherman rats, 200-250 grams in weight, were adrenalectomized bilaterally, maintained on a regular diet and sacrificed after 3-4 days. The liver mitochondria were isolated and oxidative phosphorylation measured by standard procedures. Mitochondrial protein was depressed by 25%. The mitochondria appeared to be shrunken, but their number was not greatly decreased. Four substrates were used. P:O ratios in the normal controls were 2.2 with pyruvate, 2.2 with βOH butyrate, 3.0 with citrate and 3.0 with glutamate. Comparable values in the adrenalectomized group were 1.5, 1.5, 1.8 and 1.9 respectively. This is caused by a decrease in the rate of phosphorylation in most cases and not by altered O_2 consumption. The addition of various hormones "in vitro" was found to cause various degrees of improvement in the P:O ratios. Thus, with glutamate as a substrate, the values were: 2.2 with insulin, 2.15 with epinephrine, 2.35 with cortisone, 2.45 with insulin and cortisone, and 2.8 with insulin, cortisone, and epinephrine combined. This pattern was apparent with each substrate. The three hormones combined were always the most effective, but phosphorylation never reached the values of the normal controls. Their effect was primarily on ATP synthesis and not upon O_2 uptake. Since this stimulation occurred "in vitro", it is logical to conclude that all of these hormones probably interact in some manner with the mitochondrial membrane and so alter its phosphorylating capacity. The effects of mineralcorticoids and of NaCl maintenance will be reported later.

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Experimental circumstances modifying polyvinyl alcohol-induced hypertensive vascular disease, anemia and tissue infiltration. O. Hall* and C. E. Hall. Univ. of Texas Medical School, Galveston, Texas.

Groups of female rats were given daily 1 ml injections of a 5% aqueous solution of 133,000 MW polyvinyl alcohol (PVA) and 1% NaCl to drink. Unilaterally nephrectomized animals were compared with intact and the subcutaneous route of administration was compared with intraperitoneal. Unilaterally nephrectomized subcutaneously injected rats rapidly developed severe hypertension and anemia and often edema and ascites. Hypertension was later in onset and more slowly progressive among intact subcutaneously treated animals, anemia was milder and edema or ascites negligible. Intraperitoneally treated intact rats characteristically did not demonstrate hypertension, edema or ascites, although they developed anemia as severely as did subcutaneously injected rats. Organ weights revealed that only hypertensive rats had statistically enlarged kidneys and hearts, although both organs showed heavy PVA infiltration. The spleens and livers were infiltrated by PVA and enlarged in all treated animals. However enlargement was significantly greater when it was given intraperitoneally than subcutaneously. The liver showed extensive foam cell infiltration with intraperitoneal but not with subcutaneous PVA. Anemia was independent of the route of administration but aggravated by hypertension. Hypertension appeared to be dependent upon subcutaneous administration but was enhanced by removal of a kidney, circumstances which also provoked edema and ascites. (This study was supported by grants from the USPHS.)

EFFECTS OF RAPID INJECTION OF HEPARINIZED BLOOD INTO RIGHT AND LEFT VENTRICLES OF DOGS. F. J. Hallermann,* C. C. Rastelli,* and H. J. C. Swan, Mayo Found. and Mayo Clin., Rochester, Minn.

Injections of 18-160 cc. of heparinized homologous blood at a rate of 3.9-14.4 ml./sec./10 kg. body weight into right and left ventricles were performed in 5 dogs. Only injections during and after which no extrasystoles or irregular heart action were observed were evaluated. After R.V. injection there was a small rise (1-2 mm. Hg) in R.A. pressure. R.V. systolic pressure increased by 1-12 mm. Hg and smaller increases in L.A., L.V. and femoral artery pressures were observed, the magnitude of which was related to both the total volume of injectate and the rate of injection. L.V. injection was followed by an increase in R.A. (1-4 mm. Hg) and R.V. (1-19 mm. Hg) pressures which occurred at the time of injection. There was an increase in L.A. (1-7 mm. Hg) and L.V. (5-60 mm. Hg) pressures. L.V. output was monitored continuously by electromagnetic flowmeter placed on the ascending aorta. When the absolute volume added to the circulation was less than 60 ml., cardiac output increased transiently to "repay" 20-30% of injected volume during injection and the remainder over the following 20-30 seconds. A more sustained increase in cardiac output was observed after injection of larger volumes. Injection into the L.V. at times resulted in transient bradycardia and decreased arterial blood pressure 8-10 seconds after injection. Injection of fluid into each ventricle tends to restrict the inflow of blood from the respective atria. The added volume is ejected from the central circulation over 20-30 seconds. Reflex effects or effects of hemolyzed blood on the peripheral circulation may play a part in the response of L.V. injections.

HEPATIC ARTERY PRESSURE-FLOW RELATIONSHIPS IN THE IN SITU DOG LIVER. Kenneth M. Hanson* and Paul C. Johnson. Dept. of Physiology, Indiana Univ. Med. Center, Indianapolis, Ind.

Studies were begun on the hemodynamics of the dog liver to determine whether the pressure-flow relationships seen would give any evidence for autoregulation of hepatic blood flow as we have seen in isolated intestine and hind limb preparations treated similarly. The hilum was dissected free and the major vessels stripped, leaving only the hepatic artery (HA), portal vein (PV), vena cava and bile duct. All visible nerves and collateral vessels were sectioned. Absence of any significant collateral flow was established by an injection technique. The common HA was cannulated and supplied with blood from the femoral artery through PE tubing. Perfusion pressure (P_{HA}) was taken at the cannula, venous pressure (P_{HV}) in the vena cava at the level of the hepatic vein orifices and portal vein pressure (P_{PV}) in one of its primary branches by passing a catheter up the pancreatico-duodenal vein, with the hilum as zero reference. Flow (F_{HA}) measurements were with a 400 cps sine wave electromagnetic flowmeter. Vascular resistance (R_{HA}) was calculated as $P_{HA} - P_{HV}/F_{HA}$, mmHg/ml/min/100 gm. As P_{HA} was reduced stepwise from c.a. 90 down to 20 mmHg, R_{HA} increased over the entire pressure range in about 60% of the experiments done to date. The remainder showed some evidence of autoregulation. Initial F_{HA} ranged from 15 to 30 ml/min/100 gm. Except for a slight reduction in R_{HA} shunting of the portal flow had no significant effect on the behavior of the HA. The 70% reduction in P_{HA} was accompanied by only 2 to 5% reduction in P_{PV}. Supported by grants from the American Heart Association and the National Institutes of Health (HE-05200 C3).

EFFECT OF GUANYLIC ACID AND CORTISOL ON METABOLIC RESPONSES TO HIGH ALTITUDE. John L. Hartman, Capt., USAF(MSC)* and Estelle R. Ramey, Georgetown University School of Medicine, Washington, D. C.

Four series of male albino Sprague-Dawley rats weighing 200-300 Gm. were subjected to 282 mm. Hg barometric pressure (25,000 feet) for four hours. This constitutes a severe stress. The four groups were pretreated one hour prior to exposure to altitude as follows: (1) untreated controls, (2) 1 mg./kg. cortisol, (3) 1 mg./kg. cortisol plus 15 mg./kg. guanylic acid, and (4) 15 mg./kg. guanylic acid. At the end of the exposure to high altitude conditions, blood glucose, NEFA, and cholesterol levels were determined. As in other stresses, the plasma NEFA levels were elevated in the untreated animals, while blood glucose and blood cholesterol were relatively unchanged. Cortisol alone did not prevent the elevation of plasma NEFA levels. However, guanylic acid pretreatment with or without added cortisol significantly lowered plasma NEFA levels during the stress and simultaneously raised blood glucose levels. Plasma cholesterol levels were ambiguous and require further work.

	(1) Untreated	(2) Cortisol	(3) C + GA	(4) GA
Glucose (mg.%)	129.5±10.7	124.2±11.6	142.5±8.6	140.5±13.4
NEFA (mEq./L)	0.932±.207	0.852±.149	0.458±.104	0.545±.146
Cholesterol (mg.%)	70.6±8.01	69.0±10.7	64.1±8.81	58.6±7.45

These data are consistent with our earlier results suggesting that guanine nucleotides may be released during lymphatic involution and act to maintain homeostasis in a stressful situation.

AUTOREGULATION OF GLOMERULAR FILTRATION RATE. Rodney B. Harvey, Dept. of Physiology, University of Minnesota, Mpls.

Isolated dog kidneys were perfused with arterial blood by a heparinized donor dog. Glomerular filtration rate was continuously estimated as the product of renal plasma flow and the extraction of exogenous creatinine. Renal plasma flow was estimated from renal vein outflow measured by a displacement flowmeter and the interpolation of serial arterial blood hematocrit determinations. Renal artery and renal vein creatinine concentrations were continuously measured using two technicon autoanalyzer systems and a 2-channel recorder. It was found that the time course of autoregulatory changes in RBF and GFR were very similar. There were only small or brief changes in the extraction of creatinine or filtration fraction with large changes in perfusion pressure. ATP infused into the renal artery usually produced a large increase in blood flow, always reduced the extraction of creatinine, and always reduced urine flow. The magnitude of the fall in creatinine extraction with ATP is similar to that produced by ureteral clamping. In all cases the depression of creatinine extraction by ATP was promptly reversible. ATP was also found to reduce the stop flow ureteral pressure. It was concluded that ATP reduced effective filtration pressure by producing efferent arteriolar dilatation.

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RELATIONSHIP OF CHANGES IN SARCOPLASMIC RETICULUM TO DURATION OF THE LATE AFTER-POTENTIAL OF FROG SKELETAL MUSCLE. D. C. Hellam*, D. A. Goldstein*, L. D. Peachey*, and W. H. Freygang, Jr., Natl. Insts. of Health, Bethesda, Md., and Columbia Univ., New York.

Adrian and Freygang (J. Physiol. 163: 61, 1962) have described a theoretical model of ionic movement in frog fast skeletal muscle fibers which can explain changes in membrane conductance during the flow of hyperpolarizing and depolarizing constant current pulses applied across the membrane. It has been demonstrated that the model, extended to allow for the flow of chloride current, can also approximate the properties of the late after-potential which follows a train of impulses in fibers of the frog sartorius (Hellam, Goldstein, and Freygang, Biophysical Soc. Abstr., 1963). In Ringer's fluid made twice isotonic by the addition of sucrose, the late after-potential is strikingly prolonged. This effect can be explained by assuming that v, the volume per unit area fiber surface of compartment 2 in the model, is increased. Electron microscopic examination of muscles in hypertonic solution has shown that the size of the intermediary vesicles of the sarcoplasmic reticulum is increased when the muscle is in hypertonic solution. The electrical changes and the change in size of the intermediary vesicles are reversed when the muscle is returned to isotonic Ringer's fluid.

TEMPERATURE-SENSITIVE NEURONES IN THE DOG'S HYPOTHALAMUS. R. F. Hellon*, J. D. Hardy, and Kerstin Sutherland*. John B. Pierce Foundation Laboratory, New Haven, Connecticut

A search has been made in the anterior hypothalamus of dogs under urethane for thermosensitive neurones which could play a part in temperature regulation. Recording with tungsten micro-electrodes, single units have been studied while local brain temperature was changed with thermodes. Many of the neurones did not appreciably alter their firing rate with changes of temperature. A number however showed a marked sensitivity to temperature when this was changed between 36 and 40°C. Two types of neurones were found in about equal numbers: one set increased their firing rate with rising temperature while the others fired faster when the temperature was lowered. The approximate Q_{10} value was at least 8 for both types and they were all found close to the midline between the anterior commissure and the optic chiasma. It seems probable that these cells are responsible for the thermoregulatory responses which are seen when this region of the brain is heated or cooled in the conscious dog.

THE EFFECT OF AMPHETAMINE ON BODY TEMPERATURE AND MORTALITY OF COLD EXPOSED ANIMALS. Roger H. Helmendach, James A. Thomas* and G. H. Wade*. Department of Physiology, Loma Linda Univ., Loma Linda, Calif.

It is known that amphetamine enhances heat induced hyperthermia of rats and mice. Aggregation of these animals increases mortality. Amphetamine injected mice survive better in the cold when aggregated than when individually caged. These studies were performed to determine whether amphetamine alters body temperature drop of cold exposed animals and whether restraint alone in lieu of aggregation has a protective effect against cold exposure in amphetamine treated animals. Amphetamine treated animals were compared with untreated controls using four different preparations. Three groups of rats exposed to cold ambient air (8°C) included restrained rats, lightly nembutalized rats and conscious unrestrained rats. The fourth group consisted of lightly anesthetized rabbits subjected to immersion hypothermia. Cooling rates as determined by rectal temperature measurements were more rapid in all four experimental groups than in controls. Amphetamine treated rabbits died at lower rectal temperatures but earlier in the course of cooling than did control animals. The rectal temperature drop of amphetamine treated rats was approximately the same for all three groups. Restrainedcontrol animals exhibited the greatest drop of all control groups. Mortality rate of amphetamine treated animals was greatest in all three groups of rats. The mortality of amphetamine treated lightly nembutalized unrestrained rats at 180 minutes was 50% as compared with zero for controls at 360 minutes and 5.6% at 180 minutes in amphetamine treated restrained rats. Amphetamine increases body cooling due to cold exposure. This decrease in body temperature is probably due to increased heat loss. Light dosages of nembutal which of themselves did not increase mortality rate caused death in all amphetamine treated animals. (Supported in part by Grant No. 5171 of the U.S. Public Health Service.)

INTRACAROTID VALIDATION OF BLOOD PRESSURE MEASUREMENTS IN MICE WITH FURTHER OBSERVATIONS ON ABSENCE OF AGE CHANGES. J. P. Henry, J. P. Meehan*, G. A. Santisteban*, P. Stephens*. Dept. Physiology, USC. Sch. of Med.

A small mammal with its short life cycle is of potential value in the study of the factors associated with the age linked changes in vascular reactivity. Using a rapid simple oscillometric method of estimating caudal blood pressures in the mouse (Fed. Proc.22:455,1963), systolic pressures were measured in CBA mice. A 12mm occlusive cuff averaged 106 mmHg for 2 month old males and females; 114 mmHg for a 14 month old group and 96 mmHg for mice aged 20 months. A 6mm cuff having a breadth/diameter ratio standard in human sphygmomanometry gave higher values averaging within 10mm of the systolic peaks as recorded in 7 mice by a 3mm long, 0.5mm ID carotid cannula. Pulse pressures ranged from 50-25 mmHg: mean 36 mmHg and were transduced by a P23 Db Statham gage. The 6 mm cuff figures of 124 mmHg for mice 2 months old, 128 mmHg for 14 month and 126 mmHg for the 20 month groups show no change with aging of the CBA colony.

ORAL AMINO ACID TOLERANCE IN THE ALLIGATOR. T. Hernandez and R. A. Coulson*. Louisiana State University School of Medicine, New Orleans, La.

In previous amino acid tolerance studies in the rat and the alligator in which 10 mmoles/kg were injected intraperitoneally, the non-essential amino acids were utilized much more rapidly than the essential ones (Biochem. J. 79:596, 1961). To determine the effect of the intestinal mucosa on amino acid metabolism, the experiments were repeated by giving the same quantity of each of 19 amino acids to alligators by stomach tube. In contrast to the rapid absorption following i p injection, those amino acids which are only sparingly soluble (tyrosine, tryptophane, leucine) were absorbed by the gut wall so slowly that the plasma level was only slightly elevated at any one time. Even the soluble amino acids were absorbed slowly enough to prevent the plasma concentration from reaching the levels observed in the intraperitoneal experiments, and in those cases in which the rate of metabolism was about equal to the rate of absorption, the tolerance curves were flattened. Methionine, a compound metabolized very slowly, had identical tolerance curves by either route. Lysine, glutamic acid, and to some extent aspartic, were apparently converted into other compounds in the intestinal wall. The intestinal destruction of lysine by the alligator was a surprise and may be linked to a natural adaptation to the plentiful supply in the diet. Irrespective of the route of administration, most of the essential amino acids were metabolized more slowly than the non-essential ones. The role of the fecal flora appeared to be insignificant in amino acid degradation.

MECHANISMS OF AUTOREGULATION IN THE INTACT DOG KIDNEY. L. B. Hinshaw, T. E. Emerson*, C. M. Brake*, M. S. Brown*, and F. D. Masucci*. Environ. Physiol. Branch, Civil Aeromed. Res. Inst.; Dept. of Physiol., Univ. Okla. Med. Sch., Oklahoma City, Oklahoma.

Mechanisms involved in the autoregulation of blood flow in the isolated perfused kidney have been previously reported from this laboratory. The present study has been carried out on the intact kidney as a logical extension of the earlier reports. Adult dogs were anesthetized with sodium pentobarbital, and the left kidney was exposed via a flank approach. The kidney was freed from the peritoneal layer, and denervated surgically and chemically. The renal vein was cannulated and venous outflow was measured with cylinder and stopwatch. Venous blood was returned to the dog by means of a Sigmamotor pump. Systemic arterial blood pressure was varied in some experiments by infusion of blood. Tissue pressures were estimated by three independent procedures: value of needle pressure; value of increased large vein pressure which results in a detectable decrease in blood flow; and value of increased ureteral pressure which results in a detectable decrease in blood flow. These procedures showed close agreement. In nine dog kidneys, tissue pressures averaged 39 mm. Hg at an average renal arterial pressure of 119 mm Hg. Increases in renal artery pressure resulted in significant elevations of tissue pressure. The rise in total resistance with increased arterial pressure was produced in large part by an increase in venous segment resistance. These findings strongly suggest that autoregulation of blood flow in the intact kidney may be accounted for in large measure by changes in tissue pressure (Research supported in part by USPHS grant #A-6313.)

TIMING OF POST-PARTUM OVULATION IN THE RAT. Joan C.Hoffmann* and Neena B.Schwartz. Dept.Physiol., Univ.Ill. Coll.Med.,Chicago, Ill.

It is well-known that the female rat ovulates within 36 hours after delivery. In the cycling rat LH is released between 2 and 4pm on the day of proestrus followed by ovulation in 10 to 12 hours. This study was designed to determine the time of post-partum ovulation in comparison to cyclic ovulation, and its relation to time of delivery. Primiparous adult rats were observed for delivery at 8am, 10am, 12N, 2pm, 4pm, and 6pm. Ovulation was ascertained by the presence of ova in the oviduct. Of animals delivering between 4pm (Day 1) and 8am (Day 2), 0/4 had ovulated by 10am(Day2); 0/6 had ovulated by 4pm(Day 2); and 8/8 had ovulated by 10am(Day 3). Of animals delivering between 8am and 4pm(Day 1), 0/5 had ovulated by 4pm (Day 1), and 9/16 had ovulated by 10am(Day 2). This suggests that animals delivering after 4pm (Day 1) but before 8am (Day 2) release LH during Day 2 and ovulate during the ensuing night. Animals delivering between 8am and 4pm show more variation, some ovulating the same night and others presumably ovulating the following night. Therefore, in the rat there is not a constant parturition-to-ovulation interval. Rather, time of ovulation may depend on the relationship between time of delivery and the occurrence of the next "2-4pm facilitation." The variability in time of ovulation in animals delivering between 8am and 4pm may be related to the proximity of delivery to the facilitatory period, possibly necessitating a 24 hr. wait until the next facilitation. In a preliminary study, "blocking" drugs were given to animals delivering between 4pm and 8am. In contrast to its effects in cycling animals, pentobarbital(30mg/kg) injected at 2pm on Day 2 failed to block ovulation in 4 of 5 rats. Morphine sulfate (50 mg/kg) injected at 12 N or 2pm blocked ovulation in 3 of 5 rats. Further drug studies are in progress. (Supported by Grant AM-06145, PHS).

ESTIMATION OF THE FORCE-LENGTH CONSTANT OF THE LEFT VENTRICLE OF HORSES, CATTLE, SWINE, DOGS AND RABBITS. J. P. Holt, E. A. Rhode* and H. Kines*. Heart Research Laboratory, Univ. of Louisville, and Univ. of California School of Veterinary Medicine.

Serial determinations of left ventricular end-systolic pressure, P, and end-diastolic, EDV, end-systolic, ESV, and stroke volumes were carried out following plethora and hemorrhage in 17 animals. Since the force-length relationship of contracted cardiac muscle over a limited range is similar to that of rubber, the force per unit area of wall cross-section, F/A, and middle-mass radius, R_m, of the equivalent thick-walled sphere were calculated, as described by us in another paper, for each animal over a wide range of ESV and P. A linear relationship between F/A and R_m was found. The force-length constant, which mathematically is identical to the elasticity constant, was 779 ±247 Gm./cm^2 for all of the animals. A pattern of function described by the equation: $F/A = 1107\ R_m\ R_{om}^{-1} - 1107$ exists from the small (rabbit) to the large (bovine) ventricle in which the ratio of the wall thickness to the internal radius of the undistended ventricle is 1.16. R_{om} is the middle-mass radius of the undistended ventricle. Since F is a function of P and R_m is a function of internal volume, V, an equation relating P and V has been derived:

$$P = \bar{V}^{\frac{2}{3}}\left(497V_o^{-\frac{1}{3}}(2V+9V_o)^{\frac{1}{3}}-1107\right)\left((V+9V_o)^{\frac{2}{3}}-V^{\frac{2}{3}}\right).$$

The integral of this equation between the limits V_o, volume when distended with zero P, and any value of V, equal to an EDV, is the total potential energy developed by the ventricle; that part of the area between the EDV and an ESV is the potential energy which is converted to mechanical energy with the ejection of the stroke volume. (Supported in part by USPHS Grant #2075; and the Ky. and Lou. Heart Assns.)

THE POSSIBLE RELATIONSHIP BETWEEN CYCLIC 3'5'AMP AND SOLUBLE CARDIAC RELAXING SUBSTANCE. Carl R. Honig and Claire Van Nierop*. University of Rochester School of Medicine and Dentistry, Rochester, New York.

Both cyclic 3'5'AMP (AMP) and soluble cardiac relaxing substance (RS) are synthesized by muscle granules in the presence of ATP, and appear to be normal tissue constituents. It therefore seemed reasonable to suspect that RS and AMP are identical, an idea already suggested by Uchida and Mommaerts (Biochem. Biophys. Research Comm. 10:1,1963). To test this possibility the effects of cardiac RS and AMP on the Mg-stimulated ATPase of canine cardiac myofibrils were examined. In 10 experiments 10^{-8} to 10^{-4}M AMP was without effect on 4 preparations of fibrils known to be capable of vigorous responses to RS. At 10^{-3}M AMP 10% inhibition of the enzyme was observed. Results were the same for freshly isolated unglycerinated fibrils, fibrils stored in 50% glycerol-succinate for 6 to 170 days, and for fibrils tested in the presence and absence of 2.5 mM oxalate and/or 10^{-5} to 10^{-3}M Ca. Thus AMP alone is not identical to cardiac RS. Tested in the presence of muscle protein, however, AMP did enhance the activity of a labile, Ca sensitive, preformed RS extracted directly from the muscle. It is therefore suggested that AMP and an unidentified protein together may constitute a cardiac relaxing system. A second relaxing system insensitive to AMP and Ca, and stable on prolonged storage at -15°C also exists.

Cortical spindles evoked by stimulation of caudate nucleus and internal capsule. F. Horvath*, S. Soltysik* and N. A. Buchwald, Department of Anatomy and Brain Research Institute, UCLA.

Experiments were performed on 50 cats to test for the caudate nuclear or internal capsular "origin" of spindles recorded from the pericruciate region of the cortex. EEG recording and electrical stimulation were carried out on acutely prepared cats immobilized with Flaxedil (R) after suitable local anesthesia. The results of these experiments follow: (1) The stimulus intensity necessary to evoke spindles from either the caudate nucleus or the internal capsule varies with the recording site. For example: (a) with increasing intensity, stimulation of the caudate nucleus evokes spindles first from the medial surface of the pericruciate cortex and second from its dorsolateral surface, while with stimulation of the capsule, the situation is reversed; (b) caudate nucleus stimulation evokes spindles in the contralateral cortex at much lower thresholds than does stimulation of the capsule. (2) Spindle thresholds are lowest at the border between capsule and caudate, but loci in the caudate several mm. from the capsule elicit spindles at thresholds too low to be attributed to current spread. In contrast, currents required to elicit cortical spindles from points 1 or 2 mm. dorsal to the head of the caudate nucleus may be 10 times those required from points within the nucleus. These data indicate that spindles elicited by stimulation of the caudate nucleus and of the adjacent internal capsule must involve different pathways.

Diuresis By The Infant Rat After Intravenous Loading. P.A. Hoy (intr. by E.F. Adolph). Dept. Physiology, Univ. of Rochester, Rochester, N.Y.

The newly born rat is slow and conservative in its excretion of fluid loads placed in its stomach. Is it possible to increase urine production by loading through a different route? Can any changes in chloride concentration of resultant urine and plasma be seen? Urethral catheterization of the bladder of female infant rats allowed continuous observation of urine flow. Four per cent of the body weight (b.w.) of distilled water (A) or 4% b.w. 1 M (4.00 meq./100 gm. b.w.) sodium chloride solution (B) was given to rats 6 hours to 6 days of age through a polyethylene catheter, o.d. 0.2 mm. placed in the femoral vein (I.V.). Other rats received A or B by intraperitoneal (I.P.) injection. By 1-1/2 hours after loading $I.V._B$, rats $\leq$ 1 day old produced urine equivalent in volume to B, but after $I.V._A$, only 1% b.w. of urine. In contrast, both $I.P._A$ and $I.P._B$ elicited but 0.6% b.w. urine. Chloride concentrations of urine and of plasma did not differ after I.V. or I.P. Consequently, total chloride excretion was increased 6-fold (0.75 meq./100 gm. b.w.) after $I.V._B$, 3-fold after $I.V._A$ above that after I.P. These data suggest that increase of urine production during diuresis by infant rats is closely associated with intravascular factors and not solely with renal incapacity.

THE EFFECTS OF IMMERSION OF THE HAND IN COLD WATER ON BLOOD FLOW THROUGH THE FINGERS. A. C. L. Hsieh, T. Nagasaka and L. D. Carlson. (Dept. of Physiology and Biophysics, Univ. of Kentucky.) The temperatures of the tip of the middle fingers (T_s) of nine comfortably warm subjects have been recorded during immersion of all the fingers of one hand in a 27 l bath containing slowly stirred water at temperatures ranging from 4.6 to 40°C (T_w). Blood flow (F = ml/cm^2/min.) was estimated from the average T_s for the last 15 min. of a 20 min. period, T_w and body temperature (T_b) by using the equation: $F = 1087 \times K(T_s - T_w)/(T_b - T_s)$. K was found to be 0.0134 kcal/cm^2/min./°$(T_s - T_w)$. F was lowest when T_w = 10° but increased at lower values of T_w. The increase in F per °C reduction in T_w below 10°C was 0.164±0.077 ($B<.05$). This value gives a measure of the vasodilatation occasioned by immersion in water below 10°C. The sample regression equation of F on T_w was: $F = 4.1 - .164T_w \pm 0.17$ (n = 27; range of T_w = 4.6 to 10°C). This method of estimating blood flow at several levels of T_w describes more fully the peripheral circulatory response to cold than methods in which only one level of T_w is used. Supported in part by Contract AF 41(657)-335 from the Arctic Aeromedical Laboratory USAF.

CHANGE OF THORACO-ABDOMINAL RESONANT FREQUENCY WITH DRIVING PRESSURE. W. E. Hull and E. C. Long, Dept. of Physiology and Pharmacology, Duke Medical Center, Durham, N. C.

Resonant frequency of the anesthetized apneic dog contained in a whole-body respirator was determined by studying the phase relationship between forcing pressure and trachial volume-flow. By means of a cylinder attached to the respirator and containing a piston having an adjustable position, the driving pressure applied to the dog's body was alterable. The equation $P = \log S + 0.8$ approximately describes the relationship between driving pressure (centimeters H_2O) and resonant frequency (cps). Because thoracic compliance has been shown to be independent of respiratory frequency, within narrow limits, it appears likely that inertance is variable. Meade demonstrated the role of gas density in determining pulmonary inertance. It would appear that factors related to the tissues themselves must also contribute.

SOME EFFECTS OF SIMULTANEOUS APPLICATION OF OPPOSING AUTONOMIC STIMULI IN ANESTHETIZED CATS. J. Hyde and M. Gogate*, Brain Research Institute and The Center for Health Sciences, University of California, Los Angeles, California.

An increase or a decrease in respiration or blood pressure is known to result upon stimulation in various areas of the central nervous system. The present study was designed to determine the result of simultaneous stimulation of two opposing sites in cats anesthetized with nembutal or chloralose. When stimulation of two sites (in hypothalamus, midbrain or medulla) elicited opposite effects, the sites were stimulated simultaneously. Under nembutal anesthesia, simultaneous stimulation of pairs of sites individually exerting opposing effects on respiratory depth resulted in: algebraic summation (6 cases); a response equivalent to that seen upon stimulation of one site alone, representing simple dominance (7 cases); or a response of markedly greater magnitude than that seen upon single stimulation (4 cases). Under chloralose anesthesia, simultaneous stimulation of pairs of sites separately exerting opposite effects on blood pressure resulted in either algebraic summation (8 cases) or an exaggerated response in one direction (3 cases). Simultaneous stimulation of pairs of sites with opposite effects on respiratory rate resulted in algebraic summation (3 cases) or exaggeration (4 cases). While both simple dominance and algebraic summation have been reported by others to result from simultaneous application of opposing autonomic stimuli, there has been no previous report of elicitation of an exaggerated response in one direction.

DETERMINATION OF THE PULMONARY DIFFUSING CAPACITY FOR O_2 (D_{LO_2}) BY A BREATHHOLDING TECHNIQUE. R.W. Hyde* and R.E. Forster, Department of Physiology, Grad. School of Medicine, Univ. of Pennsylvania, Phila.,Pa.

Measurements of the rate of disappearance of the stable isotope $O^{16}O^{18}$ (designated O_2^*) and C_2H_2 in relation to neon from the alveolar gas during breathholding from 3 to 14 sec. have been used to calculate D_{LO_2} in two subjects. They first rebreathed rapidly for 10 sec. from a 2 liter bag containing initially 10% CO_2 and 90% N_2 in order to equilibrate alveolar and mixed venous O_2 and CO_2 tensions, thereby maintaining pulmonary capillary O_2 saturation constant at about 75% during subsequent breathholding. Next a gas mixture containing 6% O_2, 0.2% O_2^*, 6% CO_2, 0.5% neon, 0.5% C_2H_2, 0.4% CO, and 86.4% N_2 was inspired maximally, held for a predetermined time and an alveolar sample collected. Total O_2 and O_2^* were measured on a mass spectrometer and the other gases measured on a gas chromatograph. The O_2^* in excess of natural abundance disappeared exponentially with rate constants of 0.037 and 0.027 sec^{-1}. The "effective" solubility of O_2^* in the blood was calculated from the exponential disappearance constant, the effective alveolar volume, and pulmonary capillary blood flow ($\dot{Q}_c$) obtained from the C_2H_2 disappearance curve. The ratio of this "effective" solubility to the true solubility, calculated as $[O_2Hb]$ divided by alveolar P_{O_2}, equals the fractional equilibration of O_2^* between end capillary blood and alveolar gas. An average of 74% equilibration was found. Since P_{O_2} and P_{CO_2} were constant along the capillary, the exchange of O_2^* with capillary blood is a simple exponential process obviating the Bohr integration, and the fractional equilibration at the end of the capillary equals: $1-\exp[-D_{LO_2}/(\dot{Q}_c \times \text{solubility of } O_2^*)]$. In one subject at an alveolar P_{O_2} of 42 mm Hg, D_{LO_2} was 37 ml/mm x min (simultaneous $D_{LCO} = 44$); in another at a P_{O_2} of 48 mm, D_{LO_2} was 23 ($D_{LCO} + 40$).

EVIDENCE FOR THE SHIFT OF BLOOD TO THE NUTRITIVE CIRCULATION DURING REACTIVE HYPEREMIA. Chester Hyman, Kathryn Ballard,* and Patricia Fielding.* University of Southern California School of Medicine, Dept. of Physiology, Los Angeles, California.

Blair et al. report elimination of the hyperemia after arterial occlusion in the human forearm if the circulation to the arm is restricted to normal levels immediately following the arrest. They measured total blood flow using plethysmographic techniques. We have suggested that in spite of a normal total blood flow following arrest there had been an internal redistribution so that a larger fraction of the blood perfuses the nutritive circulation. To test this hypothesis simultaneous measurements were made of blood flow and of clearance of iodide from the muscles of the skinned leg of cats. The isotope was introduced during a temporary dilatation so that the entire tissue was labeled. After 3 or 4 minutes of normal unobstructed flow, the artery was occluded and ischemia was maintained for 5 minutes. Then the pre-occlusion level of flow was restored using a pump for another period of 5 minutes. Following this, blood was allowed to flow freely to the leg. In 30 experiments there was a marked increase in tissue clearance during the period of pump perfusion. Examination of the curves suggests that the nutritional blood flow debt had been repaid by the end of the period of pumping. The results of these experiments confirm the implications of our original argument and provide further evidence for the redistribution of blood from the "shunt" to the "nutritional" circulation in a preparation of pure muscle tissue.
(Supported by U.S.P.H.S. Grant #HE-00352-13.)

THROMBOTIC AND SURFACE FACTOR STUDIES IN RABBITS. Sotirios G. Iatridis*, Panayotis G. Iatridis* and John H. Ferguson. Physiology Dept., Univ. of North Carolina, Chapel Hill, N. C.

Surface factor (SF), from human $Al(OH)_3$ plasma, was obtained as a kaolin-NaCl (7%) eluate from the precipitated euglobulin, dialysed, and concentrated in 1/10 original volume. 54 anesthetized rabbits received SF 1 ml/Kg intravenously, SF injections: (a) ear vein (20 rabbits), (b) portal vein (20 rabbits) and (c) ear vein, after ligation of portal vein and hepatic arteries (14 rabbits). Controls: 67 rabbits, including the above 54 before injection. Ten others given inactive materials also gave negative results. Thrombotic activity in vivo (Wessler's technique) was studied by occluding a venous segment for 10 min. The incidence of thrombosis was: (1) Controls: 96% negative; (2) 1 min. post-injection: (a) 95% positive, (b) 85% positive, and (c) 100% positive; (3) 10 min. post-injection: (a) all negative, (b) 20% positive, and (c) 21% positive. Thrombelastograms (whole blood): r and k values were all significantly shorter than controls in 1 min. post-injection samples; ma values, in (a) and (b), were greater than controls, suggesting a relationship between ma and blood SF activity. Anti-SF activity in rabbits (unlike dogs) was high in controls and did not increase after SF injections. It is concluded that a "progressive" action of plasma anti-SF accounts for inhibition of the SF in the 10 min. post-injection samples. The data do not indicate participation of the liver directly in this inactivation of SF. (Supported by USPHS Research Grant HE-01510-10)

ESTERIFIED FATTY ACIDS IN EXERCISE. B. Issekutz, Jr., H. Miller, P. Paul* and K. Rodahl. Div. of Research, Lankenau Hospital, Philadelphia, Pa.

Palmitic acid-1-C^{14} was infused i.v. for 3 hours or administered orally 18 hours before work into normal and pancreatectomized dogs with indwelling arterial and venous catheters who were trained to run on a treadmill. During exercise, it did not make any difference whether the turnover of the plasma FFA decreased, as in the normal dogs, or increased as in the diabetic dogs, the specific activity of EFA remained constant. The incorporation of FFA into EFA was inhibited during exercise and accelerated during recovery. When a 3 hour infusion of radiopalmitate was stopped 5 minutes before exercise began, the FFA S.A. decreased sharply in the normal dog. At the end of 40 minutes of exercise, the "apparent oxidation" of plasma FFA (expired $C^{14}O_2$ / FFA S.A.) was many fold higher than the total turnover of plasma FFA. It was concluded that the intramuscular fat pool plays an important role as an energy source, whereas the plasma EFA did not seem to participate in the 5-6 fold elevated metabolism to any considerable extent.

PLACENTAL TRANSFER OF EPINEPHRINE. B.T. Jackson,* G. J. Piasecki,* and R.H. Egdahl, Dept. Surgery, Medical College of Virginia, Richmond.

In previous reports the conclusion that epinephrine does not cross the placenta has been based on the following: fetal administration of epinephrine caused specific hemodynamic changes; maternal administration fails to cause the same changes in the fetus. The problem is, however, complex and requires further study. Methods. Experiments were performed in pregnant dogs, ECG electrodes and venous and arterial canulas were placed in the fetus without its removal from the uterus or loss of amniotic fluid. Blood flow was measured with an electromagnetic flowmeter. Data were recorded on an 8 channel Sanborn recorder. Catechol amines were determined by the method of Weil, Marlherbe, and Bone with the Saranow modification. Results. 1. Epinephrine to fetus, rise in arterial pressure. 2. Epinephrine to mother,a) 85 -95% decrease in uterine artery blood flow b) fall or no change in fetal arterial pressure.3. N,N-dibenzyl-B-chloroethylamine (Dibenamine) to mother and epinephrine to fetus, rise (less than in 1.above) in fetal pressure.4. Dibenamine and epinephrine to mother,a) 0-20% decrease in uterine artery flow b) no change or slight rise in fetal arterial pressure. 5. Epinephrine to mother with chemical assay a) maternal epinephrine levels high (ca200γ/l) b) slight increase in fetal epinephrine levels,moderate increase in norepinephrine (e.g. 6 to 25γ/l). Conclusions.1. Maternally administered epinephrine a) may inhibit placental transfer by decreasing uterine blood flow b) may mask the effect of epinephrine on the fetus by tending to depress fetal pressure.2. Dibenamine "protects" uterine blood flow but appears to decrease fetal sensitivity to epinephrine. 3. The small rise in fetal pressure occasionally occurring with maternal injection of epinephrine may be due to the endogenous release of norepinephrine by the fetus.5. The question of the placental transfer of epinephrine is complex and remains unclear.

SET TEMPERATURE DECREASE IN EXERCISING DOGS. D. C. Jackson* and H. T. Hammel, Dept. of Physiology, School of Medicine, Univ. of Penna., Phila. 4, and John B. Pierce Laboratory, New Haven, Conn.

Experiments were performed on dogs to test the hypothesis of an elevated set point temperature in exercise. Thermodes were surgically implanted in the hypothalamus for both local heating and cooling and temperature recording. Measurements of rectal, hypothalamic, and skin temperatures and respiratory evaporative heat loss were made on dogs at rest and during exercise on level treadmill at 4 mph. The relation between hypothalamic temperature and evaporative heat loss during rest and exercise was compared and it was found that in both cases evaporative heat loss increased with increasing temperature but during exercise the rates of heat loss were much greater than during rest at the same hypothalamic temperatures. In experiments at low ambient temperatures (11°C-15°C), internal body temperatures were often the same or lower during exercise than during the preceding rest period although panting and vasodilatation were observed during exercise in contrast to shivering and vasoconstriction during the rest period. These observations lead to the conclusion that the set point temperature in trained, exercising dogs is lowered from the resting level. Local hypothalamic heating and cooling was performed on two dogs during exercise to confirm the temperature sensitivity of the hypothalamus during exercise. Heating caused a mild increase in heat loss while cooling caused a pronounced rise in heat retention.

EVIDENCE FOR A BIPOLAR DETECTOR SYSTEM INVOLVED IN HUNGER AND SATIETY

Harry L. Jacobs, Psychol. Lab., Univ. of Illinois, Urbana.

Food dilution experiments suggest that intake is modulated by the nutrient qualities of diet. Adjustment to dilution has been reported to be independent of the sensory qualities of diet with ad libitum feeding (Jacobs; Epstein and Teitlebaum). Food deprived rats cannot adjust to diluted diets; this fact has been attributed to bulk limitation (Smith, et. al.). However, hungry rats increase saccharine intake (Snyder, et. al.), suggesting that failure to adjust to dilution may be due to the taste potentiating effects of hunger and not to bulk. The work reported here was designed to evaluate the sensory and nutrient qualities of food as a function of hunger. Rats were presented with cellulose or corn oil and water diluted diets under conditions of food deprivation or ad libitum feeding. Hungry animals responded to flavor, non-hungry animals to nutrient quality of food. Bulk was not important. Preliminary results on normal and hypothalamic hyperphagics with different dilution diets show similar trends. These data are compatible with the hypothesis that hunger and satiety control systems have different classes of detector mechanisms, the former responding to sensory qualities (taste, smell, texture, etc.) and the latter to nutrient qualities (calories, SDA, glucose, protein, fats, etc.). Thus, the state of energy balance controls the bias of this dual system; energy deficits shifting the critical modulator from nutrients to flavor. (Supported by grant M5754, USPHS, and by a grant-in-aid from the Corn Products Institute of Nutrition.)

PRESSURE AND WORK DUE TO CONVECTIVE ACCELERATION OF GAS IN THE AIRWAYS.

Marc J. Jaeger*, Richard L. Parker* and A. B. Otis, Dept. of Physiology, Coll. of Medicine, Univ. of Florida, Gainesville, Fla.

According to Bernoulli's theorem the pressure gradient between two points of a nonuniform pipe is not only dependent on frictional losses related to viscosity but also on the linear velocity of the fluid at the site of the pressure measurement. Furthermore, the lateral pressure measured at the outlet of a pipe is equal to the ambient pressure, whereas the lateral pressure at the inlet of a pipe has a negative value that is dependent on convective acceleration. These facts would indicate: 1) that measurements of intraesophageal pressure vs. ambient pressure and measurements of alveolar pressure based on body plethysmography include a pressure gradient due to convective acceleration; 2) that measurements of intraesophageal pressure vs. lateral pressure at a mouthpiece include a gradient due to convective acceleration for the expiratory phase only; 3) that the pressure gradient due to convective acceleration mentioned under 1) and 2) is primarily dependent on the diameter of the mouthpiece. Pressure and work due to convective acceleration are appreciable; during a forced expiration using a mouthpiece of 2 cm ID, the pressure was found to be 8 cm H_2O at peak flow and the work 0.10 kgm. This work is dissipated as heat when the airstream produces turbulence in the environment. Supported by Contract AF 41(609)-1553 with School of Aerospace Medicine.

EFFECT OF CHOLESTEROL FEEDING ON CERTAIN ORGANS IN THE RABBIT. Ralph G. Janes, State University of Iowa, Iowa City, Iowa.

A diet containing 0.75 % cholesterol was fed rabbits for periods up to six months. Three organs were examined histochemically for distribution of lipoid substances and for pathological changes. Liver lobules could be distinguished grossly in such animals. Histochemically the liver usually showed normal amounts of glycogen, but increased amounts of lipoid material. In addition, lipoid material was found in the Kupffer cells. In one instance there was a central lobular fibrosis. All parts of the secretory tubules of the kidney contained lipoid droplets. The cells of the collecting tubules had fine droplets. In certain rabbits the glomeruli showed xanthomatosis. Lipoid distribution in the eye was mostly limited to the anterior segment. Grossly the iris had radially oriented streaks of cholesterol-like material. These extended into the outer margins of the cornea. Microscopically the outer margins of the cornea (substantia propria) contained lipoid-filled macrophages and there was neovascularization in this area. The muscular parts of the ciliary body were crowded with lipoid bearing cells. Lipoid material deposited in the eye apparently did not affect mydriasis but it would be surprising if accommodation could occur in some animals.

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HYPOPHYSEAL INFLUENCE ON MYOCARDIAL CALCIFICATION. Gaëtan Jasmin and Edrs Bajusz. Lab. of Exper. Path. Univ. of Montreal, Canada.

Interference with venous coronary circulation produces myocardial calcification in rats (Bajusz, E. and Jasmin, G.: Proc. Soc. Exp. Biol. Med. 112: 752, 1963). This dystrophic calcification of the damaged myofibers — unlike the onset of necrotizing processes — was completely prevented by hypophysectomy (Hyp-X) performed 12 days before ligature of the two main coronary veins. Replacement therapy with a crude anterior pituitary extract — given at doses of 10 mg, twice daily, during 10 days — effectively compensated for the effect of hypopituitarism. It is also significant that none of the purified anterior-lobe hormones so far tested (TSH, LTH, ACTH and/or STH), when given to Hyp-X animals, showed any replacement value that would duplicate the action of the anterior pituitary extract. It is concluded that the type of myocardial calcification studied is influenced by some, as yet unidentified, pituitary factor. Results of calcium and inorganic phosphorus determinations in serum and heart muscle will be presented in an effort to explain the above findings. Here, we simply emphasize that Hyp-X and injection of anterior pituitary extract merely influenced calcification and not the occurrence of cardiac necrosis. Thus, a dissociation between calcification and structural myocardial damage could be demonstrated, which opens new avenues for studies on factors involved in soft-tissue calcification. (Supported by the Medical Research Council of Canada and the Quebec Heart Foundation.)

GASTRIC MOTILITY WITH CENTRAL VAGUS STIMULATION. N.C. Jefferson, T. Arai*, T. Geisel*, Y. Kurovanagi*, and H. Necheles. Department of Gastrointestinal Research, Michael Reese Hospital, Chicago.

After bilateral vagotomy in the neck of dogs and stimulation of the central end of one or of both vagi, gastric contractions were observed. Of 30 dogs, 20 were positive, 5 negative, and 5 were doubtful. It appears, that in long haired mongrel dogs of predominantly collie type, the phenomenon occurs more frequently than in other types of animals. In a number of dogs, reversal of a negative into a positive response was seen after vagi and esophagus were sectioned above the diaphragm; section of the esophagus was necessary in order to ensure a complete vagotomy. It appears that, in the dog, there is an extra-vagal cholinergic innervation of the stomach.

Supported by USPH A6078-01

ANALYSIS OF THE FROG SARTORIUS MUSCLE FIBER ACTION CURRENT. Howard Jenerick. Emory University, Atlanta, Georgia.

If a propagated spike is recorded in a phase plane(V, dV/dt), it can be shown that, $\frac{I}{C} = \frac{dV}{dt}\left(\frac{m}{k} - 1\right)$, where I= ionic current density, C= membrane capacitance, m= slope of the trajectory at any point, dV/dt= magnitude of the first time derivative at that point, and k= rate constant of spike potential foot. By analysis of spikes recorded under a variety of conditions, (altered pH and varied Na, K, and Ca concentration), evidence was obtained that Na ion carries the major fraction of the inward current, and that the sodium potential, the peak sodium conductance, and the peak inward and outward currents may be obtained directly from various portions of the phase plane trajectory. It was consistently observed that the inflow of charge ($q_i = \int I_i dt$) exceeded the outflow of charge ($q_o = \int I_o dt$) during the spike. A relation exists between the resulting charge imbalance ($q_i - q_o$) and the negative after-potential, and suggests the latter is caused by the temporary accumulation of a portion of this charge on the membrane capacitance. (Supported by a grant (B-3272) from the NIH.)

THE EFFECT OF INTRA-ALVEOLAR FLUID UPON PULMONARY SURFACE TENSION PROPERTIES J.W.C. Johnson, J.H. Sipple, E.S. Salem, (intr.by R.L. Riley) The Johns Hopkins University, Baltimore, Maryland

Many of the pulmonary conditions in which lung extracts are reported to exhibit abnormally high surface tensions are also characterized by the presence of intra-alveolar fluid. The purpose of this investigation was to study the effect of intra-alveolar saline and human amniotic fluid upon the pressure-volume and surface tension characteristics of the normal dog lung. In 17 anesthetized dogs, 50-150 ml. of fluid were instilled into a degassed lobe. After spontaneous or artificial ventilation for 2 - 6 hours, the lobes were excised. Static pressure-volume deflation curves were then determined on a fluid- and a non-fluid-instilled lobe from each animal. Subsequently, surface tension was measured on extracts from 3 gram samples of each lobe using a modified Wilhelmy surface tension balance. In the fluid-instilled lobes these samples were taken selectively from areas that appeared grossly to contain fluid or to collapse prematurely. In the non-fluid-instilled lobes the samples were taken at random. During deflation the fluid-instilled lobes had proportionately smaller total volumes than the controls at transpulmonary pressures between 5 and 40 cm H_2O ($p<.001$). The extracts of the selected tissue from the fluid-instilled lobes had higher surface tensions on compression than the controls ($p<.001$). There was a significant negative correlation between the volumes during deflation and the surface tensions on compression ($p<.001$). It is proposed that intra-alveolar fluid may inactivate or displace the surface-active material from the alveolar lining membrane.

ALTERED HEAT EXCHANGE IN NORMAL MEN BEFORE AND AFTER CHRONIC COLD EXPOSURE. Robert J. T. Joy, (Intr. by D. E. Bass), USA Research Institute of Environmental Medicine, Natick, Massachusetts.

An attempt was made to resolve some of the contradictory findings in the literature on the effect of cold acclimatization on skin temperatures. Ten normal young men had five weeks of semi-nude exposure to 5°C, 8 hours/day, 5 days/week. A standard cold exposure test, consisting of one hour at 5°C following a 30-minute basal period at 27°C, was performed immediately before and after the 5-week period. Mean skin temperature (T_S), rectal temperature (T_r), heat production (M), and quantitative electromyography (EMG) of the deltoids and quadriceps were measured continuously. Body heat content (H_c) was calculated from average body temperature (T_B) using $0.8\ T_r + 0.2\ T_S$ in the warm and $0.5\ T_r + 0.5\ T_S$ in the cold. Heat loss (H_L) was calculated as $M+\Delta H_c$ (where ΔH_c is heat debt). After 5 weeks of cold exposure there were no changes in the basal state or in cold T_r. Cold T_S, T_B and H_c were significantly increased, and M, ΔH_c, H_L, and EMG significantly decreased. Analysis for critical difference demonstrated that these differences are not significant for any parameter until after the 10th minute of cold exposure, and not for all parameters until the 25th minute, which may indicate the lag times for acclimating mechanisms to respond to a cold stimulus. From the 25th to the 60th minute in the cold all parameters are significantly different and the functions are nearly parallel, so that the presence of a new steady state is suggested, with a warmer "shell", an identical "core" and paradoxically decreased heat production. However, when the 10 men are divided into 2 groups of 5 by their final EMG, the low shiver group is found to account for all the significant changes of the entire group. This raises the possibility that all findings may be due to changes in convective heat loss.

PLASMA AND CARDIAC REDUCING CAPACITY IN STRESSED ADRENALECTOMIZED AND HYPOPHYSECTOMIZED RATS. John Kabal* and E. R. Ramey, Georgetown Univ. Sch. Med., Washington, D.C. (Intr. by John C. Rose).

Rats exposed to stress show a marked rise in plasma and cardiac muscle reducing capacity as measured by Boda's method. Previous work suggests that the catecholamines may be important factors in this elevation. The role of other hormones in this system was studied. Adrenalectomized and hypophysectomized male Sprague-Dawley rats were exposed to Metrazol stress (100 mg Metrazol/Kg). Ten minutes after the injection, the rats were sacrificed and plasma and cardiac muscle reducing capacity was determined and compared with Metrazol treated controls. Neither the adrenalectomized nor the hypophysectomized animals showed any significant elevation in plasma reducing capacity as compared to control elevations. The adrenalectomized animals differed from the hypophysectomized animals in the response of the cardiac muscle. Unstressed adrenalectomized animals have an abnormally high cardiac reducing capacity and stress produces no further elevation. Hypophysectomized rats have normal unstressed cardiac levels but they, too, are not capable of the normal cardiac elevation during a stress. These results suggest that the adrenal steroids participate with the catecholamines in this metabolic response to stress. The total cardiac response seems to require, in addition, other target gland hormones such as thyroxine.

Red.Cap in mEq O/L	Contr.	Contr.& Metr.	Adrenex	Adrenex & Metr.	Hypox.	Hypox. & Metr.
Plasma	4.8±0.8	17.9±1.9	7.3±1.2	6.7±1.2	6.1±0.9	7.5±1.7
Heart	19.4±1.3	34.3±1.4	38.3±1.5	35.6±2.5	17.2±0.4	18.4±0.3

HYPOTHERMIC HEMOCONCENTRATION. G.S. Kanter Albany Medical College, Albany, New York.

Increase in hematocrit is a common finding during hypothermia in dogs. Recent measurements, in this laboratory and others, of plasma protein concentration in hypothermic dogs indicate that the alteration in protein concentration does not parallel the change in hematocrit. Similarly the decrease in plasma volume does not parallel the change in hematocrit. Hypothermic hemoconcentration is therefore not due to a simple loss of protein free plasma to the interstitial compartment nor is it due to bulk sequestering of whole plasma. The purpose of this investigation was to re-examine the basis of hemoconcentration during hypothermia in dogs. Some 23 acute experiments on anesthetized dogs were conducted. All dogs were made progressively hypothermic by packing in ice and rectal temperature was reduced from normothermia control of 38C to 27C. In series 1, 10 dogs thus handled showed an increase in hematocrit of 28.6 ± 3.7%. Total protein determined by refractometry and by the biuret method showed respective increases of only 10.9 ± 1.5% and 11.3 ± 1.7%. In series 2, 7 dogs were acutely splenectomized and treated as in series 1. The increase in hematocrit was 7.8 ± 1.5% while total protein increased 4.1 ± 1.3% and 4.7 ± 1.0% by the methods described above. Four dogs chronically splenectomized and then tested as in series 1 showed results similar to series 2. Lastly 2 dogs were tested for 4 hours under normothermic conditions. Only a minimal alteration in hematocrit, total protein, albumin and globulin was found. It may therefore be concluded that the major cause of hemoconcentration in hypothermia is due to splenic contraction. (Supported by Contract AF 41(657)393, School of Aerospace Medicine, Brooks Air Force Base, Texas.)

CALCIUM AND LENGTH DEPENDENCE OF EPINEPHRINE INOTROPY. Frederic Kavaler and Martin Morad*. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

The augmentation of contractile tension (in atrial muscle) with increasing driven rate has been correlated by Winegrad and Shanes with an increase in tissue calcium uptake. It has also been shown that, in a medium sufficiently rich in calcium (7.2 mM., sodium 75 mM.), staircase and related rate-rhythm inotropies are abolished, suggesting that a maximum is attained for whatever mechanism mediates these inotropies if calcium influx into the cell is sufficiently augmented in some other way. Tension was recorded from 1 to 2 mm lengths of cat papillary muscles or trabeculae (diameter 0.4 to 1.0 mm). The length-tension relationship is not abolished in the "high-calcium" medium, developed tension increasing, in fact, more steeply with stretch than in normal Tyrode's solution. When added to "high calcium" Tyrode's, epinephrine causes little or no increase in contractile tension when the muscle length has been previously adjusted to give maximal contractile tension (before epinephrine). At shorter muscle lengths the epinephrine inotropy in "high-calcium" medium is considerable. Staircase is abolished in "high-calcium" Tyrode's at all muscle lengths. The inotropic action of epinephrine is thus influenced by two apparently separate factors: the extracellular calcium level (presumably governing calcium influx into the cell); and muscle length.

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CAROTID SINUS DEPRESSOR REFLEX DURING HYPOTHERMIA. J. E. Kendrick (intr. by R. C. Wolf). Dept. of Physiology, Univ. of Wisconsin, Madison, Wis.

Dogs anesthetized with morphine-chloralose were cooled by total body immersion in an ice-water bath. One carotid sinus was isolated and perfused with a pulsatile flow. Carotid sinus reflexes were elicited by raising the mean pressure to 200 mm Hg in this sinus. The vagi were cut and the remaining sinus inactivated. Reflex changes in systemic blood pressure and heart rate were observed at the following rectal temperatures: 37°, 30°, 28°, 26°, 24° C. At hypothermic temperatures the reflex fall in blood pressure was decreased in magnitude and became more gradual but was still quite prominent at 24° C. The heart rate decreased with cooling as did the heart rate response to sinus hypertension. In order to determine which components of the baroreceptor reflex arc were influenced to the greatest extent by cooling the following experiments were conducted. (1) Local cooling of the carotid sinus. (2) Local cooling of the vascularly isolated, perfused leg. (3) Body cooling while the isolated perfused leg was maintained at nearly normal temperature. The results of these experiments suggest that: (1) Baroreceptor activity is not decreased at the temperatures employed. (2) The more gradual nature of the depressor response at the lower temperatures is due to changes in the peripheral vascular bed. (3) Cooling the vascular bed may affect the baroreceptor reflexes as greatly as does cooling the central nervous system. (Supported by grants from USPHS and Wisconsin Heart Association.)

INTRATHORACIC PRESSURES DURING ACUTE PERICARDIAL TAMPONADE IN DOGS STUDIED WITHOUT THORACOTOMY. H. M. Kenner*, D. E. Donald, A. C. Edmundowicz*, and E. H. Wood, Mayo Clinic, Mayo Foundation, Rochester, Minnesota.

Intrapericardial infusions and pressure measurements were made through a 1.2 mm. diameter catheter positioned percutaneously via an olive-tipped needle advanced along the ventral margin of the trachea. Simultaneous intrapleural and intracardiac pressure measurements were made through similar catheters positioned via percutaneous needles. Mean end-expiratory pericardial pressures referred to catheter-tip level were increased by an average of 16.3 (10 to 24) cm. H_2O by intrapericardial infusion of an average of 11.2 (9.5 to 16.0) ml./kg. of isotonic fluid (170 to 320 ml.) in 6 supine anesthetized dogs. Mean right atrial pressures increased by 13.3 (8.0 to 21.5) cm. H_2O, average transatrial pressures diminishing from 3.0 to -0.5 cm. H_2O. Right ventral pleural pressures were unchanged and average transpericardial pressures increased from 1.3 to 17.4 cm. H_2O. Increased atrial pressure and reduced transatrial pressure were followed by a decrease in systemic blood pressure in all dogs with marked hypotension in some. This limitation of cardiac function due to increased pericardial pressure is in contrast to the absence of systematic increases in pericardial pressure in these dogs during acute right or left heart failure produced by balloon obstruction under conditions of normal blood and pericardial fluid volumes (Fed. Proc. 22:459, 1963). These studies, coupled with Holt's findings of increased pericardial pressure during heart failure produced by plethora, suggest that the position of the intrapericardial volume on its pressure-volume curve may be of importance in determining whether or not the restrictive capability of the pericardium plays an important role in the reaction to various types of cardiac stress. (Supported in part by Life Insurance Grant).

NEW ACTIVITY PATTERNS AFTER AROUSAL FROM HIBERNATION. Barbara B. Kent* and V. P. Popovic, Dept. Physiol., Emory Univ., Atlanta 22, Georgia.

Spontaneous locomotor activity of diurnal homeotherms follows a 24 hr. rhythm, reaching on the same day a peak and a trough value. Even when external clues are absent, the same pattern of periodicity is maintained for several weeks. But when nonhibernators are artificially cooled and kept 7 hrs. at a body temperature of 24°C, their biological clock is retarded (Rawson,K.S., Symp.Quant.Biol.25:105,1960). What is happening to the biological clock of a hibernator during hibernation is not known. To investigate this problem, patterns of spontaneous running activity of ground squirrels were studied before hibernation and compared with patterns obtained in the same animals after an induced arousal. The first group of ten animals, exposed to controlled illumination for 11 hrs. each day, were aroused at 8AM, 12 AM, and 6 PM. The activity of the animals began as soon as they were aroused and persisted for the same period of time as it had before hibernation. Animals which were aroused several hours after the usual time for onset of activity (as observed before hibernation) slowly shifted during the next four days toward the pattern they had before hibernation. Their circadian rhythm was, therefore, shorter than 24 hrs. By the fourth day after arousal the spontaneous activity of ground squirrels came back to the same periodicity and the same phase as the pattern recorded before hibernation. The second group of nine ground squirrels were kept in complete darkness. Their activity began also immediately after arousal. During the 3 days sequential to arousal the onset of the spontaneous running activity was delayed as much as it was the first day. The free running cycle found after hibernation was as long as the cycle recorded before hibernation but was not in phase with it. We interpret the results in both groups as a new circadian rhythm being induced by arousal from hibernation.

120-DAY STUDY OF CARDIAC OUTPUT IN UNANESTHETIZED RATS. Kenneth M. Kent* and V. P. Popovic, Dept. Physiol., Emory Univ. Medical School, Atlanta 22, Georgia.

The technique of permanent cannulation of the aorta and right atrium (Popovic, V., and P. Popovic: J. Appl. Physiol.,15:727,1960) was successfully employed when the simultaneous sampling of arterial and venous blood in unanesthetized small laboratory animals was desirable or when one cannula was used to inject a substance into the blood stream of the animal while the other one was employed for simultaneous sampling of the blood. The patency of the venous cannula was 40 days. This technique has been modified so that the venous cannula is inserted in the right ventricle (Popovic,V., K.M. Kent, and P. Popovic:Proc.Soc.Exptl.Biol.& Med.,in press) and the patency of the cannulas is increased to well over 100 days. Moreover, such a technique can be used for cardiac output determinations based on the direct Fick principle in unanesthetized animals as was done in this study. The oxygen consumption (open circuit technique), the oxygen content of the blood (Roughton, F. J. W. and P. F. Scholander: J. Biol. Chem. 148:541,1943) and the cardiac output (Fick principle) were measured on 94 adult male rats 7 times during a period of 120 days. The mean value of the cardiac output was 238 ±21 ml/min Kg. remaining unchanged throughout the experiment. The results obtained on individual animals show a good reproducibility. Two measurements done on the same day at a 1-hour interval differed only slightly; the average difference from the mean was 2.6% (0.7 to 4.8%). In summary, our results indicate that the technique of permanent cannulation of the aorta and the right ventricle offers a reliable and reproducible method for cardiac output determinations in unanesthetized and unrestrained rats during a period of several months after the cannulation.

VENOUS ADMIXTURE AND HEMODYNAMIC EFFECTS OF HYPOXIA IN DOGS WITH CHRONIC PULMONARY HYPERTENSION DUE TO INFESTATION WITH DIROFILARIA IMMITIS. D. Kentera*, C. R. Wallace*, W. F. Hamilton and L. T. Ellison. Depts. of Physiology & Pharmacology, Med. Coll. of Georgia, Augusta.

Dirofilariasis (heartworm disease) causes changes in the small vessels of the lungs which increase the pulmonary peripheral resistance and produce pulmonary arterial hypertension with only occasional and small increase in the left atrial pressure. Correlated with the hypertension is the degree of arterial unsaturation. Since the unsaturation persists with breathing high oxygen mixtures, and since the pulmonary diffusion capacity for CO is normal, it is concluded that the unsaturation is due to venous admixture, probably in the peripheral pulmonary vascular bed (right to left shunting). The amount of venous admixture is found to be closely proportional to the pulmonary arterial hypertension. Hypoxia due to breathing of low oxygen mixtures (10% oxygen in nitrogen) causes equivocal results which on statistical analysis tend to show that hypoxia increases pulmonary peripheral resistance to the same degree as it does in control groups. The normal animal maintains or increases output but the infested animals do not maintain their cardiac output during hypoxia and the pulmonary arterial pressure does not change significantly. These conclusions were based, so far, on the study of eight infested dogs as compared with ten normal controls. All animals were under pentobarbital anesthesia. Ventilation was held constant by means of a pump. (Supported by a USPHS fellowship (D.K.) and USPHS grant H-240).

DETERMINATION OF A FORCE-LENGTH CONSTANT FOR THICK-WALLED RUBBER SPHERES AND RUBBER MODELS OF THE LEFT VENTRICLE. H. Kines*, S. Hassold* and J. P. Holt. Heart Research Laboratory, Univ. of Louisville.

Since, over a limited range, rubber has elastic properties similar to contracted cardiac muscle, a method for determining an elasticity, or force-length, constant of rubber left ventricle models has been developed. The pressure-volume relationship was determined on a series of hollow rubber spheres having different wall thicknesses, and on exact rubber models of the left ventricle of rats, rabbits, dogs, sheep and cattle. A linear relationship was found between the force per unit area of wall cross-section (F/A) and the middle-mass radius (R_m) of the rubber spheres. R_m is the radius of the internal volume plus one-half of the wall volume. From this relationship the elasticity constant was calculated by means of the equation: $e = \frac{F}{A_o} \frac{R_{om}}{\Delta R_m}$, where A_o is the wall cross-section area and R_{om} is the middle-mass radius when the sphere is undistended. The value of this elasticity constant differs from the true elasticity constant, determined on a strip of the same rubber, in a predictable manner depending on the wall-thickness ratio, i.e., the ratio of the wall thickness to the internal radius of the undistended sphere. When F/A and R_m are calculated for a rubber ventricle, assuming the ventricle to be a sphere of equivalent internal volume and wall mass, a linear relationship similar to that above is obtained; the force-length constant calculated from this line is in good agreement with that obtained on an equivalent sphere. A pattern of function exists for the force-length relationship of rubber ventricles from the smallest (rat) to the largest (bovine) described by the equation:

$F/A = 17{,}692\ R_m\ R_{om}^{-1} - 17{,}692$. (Supported in part by USPHS Grant #2075; and the Ky., Lou. and Jefferson County Heart Assns.)

EVIDENCE OF INHIBITIVE ROLE OF HIPPOCAMPUS IN NEURAL REGULATION OF ACTH RELEASE. Karl M. Knigge and Myron Hays*. Department of Anatomy, University of Cincinnati, Cincinnati, Ohio.

Several studies have indicated that portions of the limbic system may participate significantly in the neural mechanisms regulating adenohypophyseal secretion of ACTH. Bilateral electrolytic lesions were placed stereotaxically in amygdala and midbrain reticular formation of rats. Two weeks later, adrenocortical response to ether anesthesia and heart puncture was tested. One-half of these animals now received additional bilateral lesions in hippocampus; two weeks later all animals were again subjected to ether anesthesia and heart puncture. Plasma corticosterone of the blood obtained by heart puncture was determined fluorometrically.

The pituitary-adrenal axis of normal rats, as reflected by plasma corticosterone levels, is activated acutely by the stress of ether anesthesia and heart puncture. Bilateral lesions in portions of the midbrain reticular formation or the amygaloid nuclei suppress or block this acute response. In such lesioned, unresponsive animals, placement of an additional lesion in hippocampus negates the block created by the first lesion in reticular formation or amygdala and permits a maximal adrenocortical response. The results support the opinion that hippocampus contributes an inhibitory component to the neural mechanisms regulating ACTH release.

ANDROGEN REGULATION OF NUCLEIC ACIDS IN TISSUES OF THE GUINEA PIG. C. D. Kochakian and J. Hill; Univ. Alabama Med. Ctr. Birmingham, Ala.

Skeletal muscles of guinea pig show a wide variation in their dependence on androgen for growth. Since nucleic acids are intimately associated with synthesis of protein, RNA and DNA of representative muscles, seminal vesicles and prostate have been determined after castration and testosterone treatment (5-34 days). Seminal vesicles:Castration produced characteristic decrease in weight accompanied by decrease in DNA less than and in RNA greater than percent loss in tissue weight. Administration of testosterone increased DNA in direct proportion with increase in weight. RNA increased at a greater rate than tissue. Prostate:Castration and testosterone produced effects essentially same as those in seminal vesicles except that increase in DNA after testosterone occurred later than increase in weight and RNA. Temporal muscles:Castration produced a decrease in RNA in direct proportion with decrease in weight but did not change total DNA. Administration of testosterone produced a progressive increase in weight, with no change in DNA but a very rapid increase in RNA to nearly maximal level within 5 days. Masseter muscles:Responses were practically identical with those in temporal muscle except that RNA increased to a maximum after 5 days of testosterone treatment and gradually decreased with continued treatment. Gastrocnemius muscles:Castration and testosterone treatment had no effect on weight, DNA or RNA.

EFFECT OF A GASTRIN PREPARATION ON GASTRIC SECRETION IN CHRONIC FISTULA RATS. S. A. Komarov, L. J. Schoenfield,* and H. Siplet.* Fels Research Institute, Temple University Medical Center, Philadelphia, Penna.

Volume, acid concentration and output, and pepsin concentration and output were measured in response to gastrin extract administered subcutaneously to chronic fistula rats. This highly purified extract was kindly supplied by R. M. Gregory and its potency was about 40 times that of histamine phosphate in stimulating acid output in dogs. The experimental design was two 4 x 4 latin squares using graded doses of gastrin. Volume, acid concentration, and acid output increased markedly during the first 3 of the 4 hours of observation after injection of the extract. In the fourth hour there was a significant depression of secretion below preinjection values; also with a greater than maximal response dose there was a significant decrease in secretion. These effects are believed to be due to the presence of inhibitory impurities in the extract. Pepsin concentration and output diminished sharply in the first hour and slowly returned to preinjection levels during the subsequent 3 hours of observation. The difference in average pepsin output between control hours and 4 hours after injection was highly significant; there was a 28 and 47 percent decrease in pepsin output in the 2 latin squares respectively. There was no significant difference among doses in the effect on pepsin.

THE QUANTAL NATURE OF MONOSYNAPTIC TRANSMISSION IN SPINAL MOTONEURONS OF THE CAT. M.Kuno (intr. by C.Eyzaguirre). Physiol. Dept. Univ. Utah Coll. Med. Salt Lake City, Utah.

A lumbosacral motoneuron innervating the triceps surae muscle was impaled with a microelectrode. The triceps surae muscle nerve was then dissected into a fine filament containing only one or a very small number of Group Ia afferent fibers. Electrical stimulation of such a filament produced a monosynaptic excitatory post-synaptic potential (EPSP) in the motoneuron. During repeated stimulation at 0.5/sec the EPSP showed a considerable fluctuation in size, including some failures of response. Since the amplitude of the afferent impulses monitored was constant throughout the observations, fluctuations in the EPSP size were not due to changes in the number of afferent fibers stimulated. The statistical analysis showed that the distribution of sizes of the observed EPSPs could be described by Poisson's law. The average size of the smallest or 'unit' response was in the range of 0.13-0.24 mV. The afferent impulse, besides evoking the monosynaptic EPSP, often induced a recruitment of miniature EPSPs. The mean size of the miniature EPSPs was approximately the same as the unit EPSP. The mean number of units responding to single afferent impulses (the quantum content) was approximately 1 or even less. It is concluded that the synaptic transmission in spinal motoneurons occurs in quantal steps, and that one impulse in single Group Ia afferent fibers may release, on the average, only one quantum. (Supported by NIH Grant B-1320).

INTERACTION OF MECHANICAL AND CHEMICAL STIMULI ON VENTILATION. T. W. Lamb*, D. Bartlett, Jr.*, and S. M. Tenney. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

The ventilatory responses to graded total body vibration, hypoxia and to CO_2 were studied singly and in combination in human subjects. When corrected for the increased metabolism associated with vibration, the combined stimuli produced responses greater than the sum of the responses found individually in $PACO_2$ ranges above the normal resting value. This was taken as an indication of interaction of mechanical and chemical stimuli at some point in the ventilatory control system. (Supported by PHS Grant HE-02888-07)

Studies on the Renal Tubular Site of Adrenal Steroid Action. D. M. Landwehr* and S. J. LeBrie. Dept. Physiol.,Tulane Univ., School of Med. New Orleans, La.

Gunnebault, M.(Proc.Internat.Union Physiol.Sci. 2:246, 1962,Leiden) reported that aldosterone administration over a period of 2 days restored the renal counter-current gradients in adrenalectomized hamsters. These results were interpreted as indicating that aldosterone plays a role in the active process of concentrating the urine, presumably in the ascending limb of Henle's loop. Since aldosterone administration increases plasma Na^+ concentration, the above results might alternatively be ascribed to an elevation of plasma Na^+ concentration rather than to a direct action of the hormone on the ascending limb of Henle's loop. We have tested this interpretation by maintaining adrenalectomized dogs for 4 days on a 2 gram per day NaCl supplement. Cortical and medullary tissue slices were analyzed for Na, K, Cl and urea. Osmotic pressures were also determined. The data indicates that under the conditions of the experiments, normal medullary gradients are maintained and there is a production of a concentrated urine (over 1000 mOsm/Kg water). Presumably maintenance of adequate plasma Na^+ concentrations and consequently filtered Na^+ levels prevents loss of concentrating ability. It is well documented that adrenal steroids increase Na^+ reabsorption by about 2% in adrenalectomized dogs. Aldosterone administration over a period of days would tend to raise plasma Na^+ irrespective of its site of action (loop of Henle, distal tubule or collecting duct). Our results indicate that maintenance of plasma Na^+ results in a secondary maintenance of the counter-current gradients. Therefore chronic aldosterone administration can not be used to prove the site of action of this hormone. (Supported by U.S.P.H.S. Grant AM 05050-02)

APPARENT OPPOSITION TO LAMINAR FLOW IN THE RENAL CIRCULATION AS INDICATED BY PLASMA LABELED DILUTION CURVES. Ramon L. Lange and James T. Botticelli*. Marquette Univ. School of Med., Milwaukee, Wisc.

Geometry and flow rates of organ vascular beds yield Reynolds numbers which should insure laminar flow. Such flow implies a distribution of transit times for each pathway so that the mean transit time (t) is twice the shortest transit time, appearance time (a). The presence of vascular pathways with different flow/volume ratios (F/V) would cause t/a to exceed 2. In normal human and animals Indocyanine green dilution curves sampled from the renal artery input and renal vein following femoral venous injection consistantly showed t/a of < 2 ($t = 4.07$ sec., $a = 2.88$ sec., $t/a = 1.41$; mean values in 24 curves from 6 dogs). This indicates that the dispersing effects of laminar flow and unequal F/V is significantly opposed by a mechanism which tends to maintain constant indicator concentration in all flow lamina. i.e. radial diffusion. Arterial and venous sampling system - densitometer - galvonometer system time constants were identical. Response times of 0.4 sec. (dog) and 1.2 sec. (human) affected both input and output curves equally. Sampling rates employed did not cause a fall in arterial pressure during the period of curve recording. Model studies employing flow tagging - mean flow concentration sampling, thereby simulating the in vivo conditions, show similar deviations in that $t/a < 2$. Using straight conduits and plasma, a only is delayed, t is appropriate, while coiling of the conduit further delays a and t is greater than the measured F/V would indicate. This suggests a second effect which acts primarily on the axial lamina. Whole blood systems show more deviation than plasma systems. These effects should be considered when description of organ flow patterns is attempted from plasma labeled curves.

EFFECT OF DISTENTION PRESSURE, MOTILITY AND LYMPHATIC CONTRACTILITY ON WATER AND SOLUTE TRANSPORT FROM THE INTESTINE. J.S. Lee, Dept. of Physiol., University of Minnesota, Minneapolis.

Fluid is mainly transported via the lymphatic system from rat intestine in vitro and the lymphatic pressure due to accumulation of the absorbed fluid has been called "lymphatic absorption pressure" (LAP) (Am. J. Physiol. 204:92, 1963). LAP has been repeatedly determined to be correlated with the net absorption rate. In a rat upper jejunal preparation, it was found that LAP increased with distention pressure on the mucosal side (DP), motility and lymphatic contractility. At DP of 3-5 mmHg with vigorous motility the average LAP was 16 mmHg. At DP above 10 mmHg, most motility was prevented and LAP was lower than or equal to DP. Serotonin (0.2 mg%) and eserine (0.2 mg%) increase motility and increase LAP. Epinephrine (0.1 mg%) and Na pentobarbital (10-15 mg%) abolish motility and decrease LAP. These drugs were added to the serosal bathing fluid. In segments with little motility, epinephrine may also cause an increase of LAP by 20 to 40% and an increase of mesenteric lymphatic contractility. The lymphatic fluid contains equal concentrations of Na^+ and K^+ and higher concentrations of glucose than the mucosal fluid. These observations seem to indicate that DP, motility and mesenteric lymphatic contractility play an important role in fluid and solute transport from intestine into the lymphatic system and then into the systematic circulation. (Supported by U.S.P.H.S. Grant AM-05073)

POTENTIATION OF THE CARDIOVASCULAR EFFECTS OF NOREPINEPHRINE BY TETRAHYDRO-β-CARBOLINE. Allan M. Lefer* and Gordon L. Farrell, Dept. of Physiology, Western Reserve U. School of Medicine, Cleveland, Ohio.

The cardiovascular actions of n-acetyl-1-methyl-6-hydroxy-1,2,3,4-tetrahydro-β-carboline, a substance which stimulates the secretion of aldosterone in the decerebrate dog, were tested. The compound, when given by itself, had no significant effect on cardiac contractile force, arterial blood pressure, aortic and femoral blood flow, venous pressure or heart rate in sympathetic blocked (pentolinium), or surgically debuffered dogs. However, when given with norepinephrine, it potentiated the contractile force, blood pressure and blood flow responses to a test dose of 1 μg/kg of the intravenously injected catecholamine. The duration of these responses was markedly prolonged (80% increase); the amplitude of the responses slightly increased (10 to 15%). Very small doses (0.075 to 0.75 μg/min) of the carboline were necessary to achieve this effect, indicating a high level of potency. Higher doses of the carboline (150 to 300 μg) seemed to render the cardiovascular system virtually refractory to exogenous norepinephrine. The data suggest that the alkaloid acts as a monoamine oxidase inhibitor at low doses, but as a sympatholytic agent at high doses.

The Uptake of Thyroxine by the Liver of Rats Under Various Hormonal Conditions. F. B. Leftwich* and Samuel R. Tipton, Dept. of Zoology and Entomol., University of Tennessee, Knoxville. The uptake of I-131 labeled L-thyroxine (T_4^*) by the isolated perfused rat liver was followed over a 3-hour period. The T_4^* was added to the perfusate of diluted rat blood in concentrations ranging from 0.94-2.45 x 10^{-8} M. Samples of perfusate were withdrawn from the perfusing system at one half hour intervals. The uptake of hormone by the liver reached a maximum by 90 minutes and amounted to 32 to 65% of the total initial dose added to the perfusate. Free and protein-bound T_4 measured in a Sephadex column decreased rapidly in the perfusate with time. The plasma iodide did not rise above 0.14% of the total, initial dose. No other degradation products of thyroxine were detected in the perfusate. L-Triiodothyronine labeled with I-131 was not bound to protein in the perfusate and entered the liver very rapidly. Most of this hormone appearing in the bile was a conjugate of glucuronide. It appears that the rate of penetration of the thyroid hormone into the liver is determined by the level of free hormone in the perfusate. Binding of T_4^* was studied also in the plasma and subcellular fractions of the livers of partially hepatectomized rats. The level of free hormone was higher in the plasma of these animals than in normals which suggests that the rate of entry of hormone into the liver would be greater in them. (Supported in part by grant NSF-G21534 from the National Science Foundation.)

BURST PATTERNS IN VISUAL CORTICAL NEURONS AND CAUDATE STIMULATION. D. Lehmann and M. Koukkou (intr. by C. D. Clemente). Dept. of Anat., UCLA and Neurophysiologie, Universität Freiburg i.B., Germany.

The caudate nucleus was stimulated (0.4-1.0 msec shocks) in 20 encéphale isolé cats, and units were recorded extracellularly in the visual cortex. After caudate stimulation (100-600 msec trains of 50-100/sec), 57 of 105 neurons exhibited increased neuronal spike discharge frequency for periods of 100-1500 msec. The duration of activation after each stimulation was fairly constant for an individual neuron. About 60% of the activated neurons showed a change in their discharge pattern following caudate activation. Instead of single spike activity (spike intervals greater than 6 msec) or occasional double spike discharges, high frequency 'bursts' of 3-7 spikes appeared with spike intervals from 1.5-3 msec and long inter-burst intervals. This 'burst' activity at times changed back to the single spike firing pattern spontaneously 150-1900 msec later, or it was interrupted by the next activating caudate stimulation. Auditory or noxious stimuli, which induced EEG desynchronization, also caused pattern changes from 'burst' discharges to single spikes. Spike 'bursts' also tend to occur in 'light on' responding visual neurons when the light is turned off (and vice versa). Spike 'bursts' were also observed spontaneously in cortical neurons during rhythmically recurring periods when another neuron recorded in an adjacent or different cortical field showed decreased single spike frequency (Naturwissenschaften 49: 611-612, 1962). Cortical neuronal 'burst' periods 1) after induced activation, 2) during specific inhibition and 3) during periods of decreased single spike frequency in other cortical neurons might be a characteristic of resting neuronal discharge.

TRANSMEMBRANE POTENTIALS OF TRYPSIN-DISPERSED CHICK HEART CELLS CULTURED IN VITRO. D. Lehmkuhl* and N. Sperelakis. Western Reserve Univ., Cleveland, O.

Trypsin-dispersed ventricular cells from 6 to 8 day old chick embryo hearts were cultured 1-7 days. Single cells reassembled into various communities of cells which usually contracted synchronously. Many cells were spontaneously active; quiescent cells could be driven. The average magnitude of the action potentials after microelectrode sealing was 71.2 ± 1.5 mV (range, 40 to 108 mV) and that of the resting potentials 59.0 ± 1.2 mV (range, 40 to 84 mV). These values are larger than the values previously reported by Crill, et al. (1960) and by Fänge, et al. (1956). Maximum velocity of depolarization varied between 1 to 5 V/sec; positive after-potentials were often found. The duration of the action potential varied between 150 to 500 msec. Plateaus were observed in only a few of the cells; often a second component appeared on the repolarization phase of the spike. Many cells had pacemaker potentials of about 10 mV. However, even though a pacemaker potential was present, the cell in a number of instances was fired by transmission of excitation from neighboring cells; a prepotential was often observed as a step in the rising phase of the action potential. The data from trypsin-dispersed cells were compared with those of non-dispersed clumps and with non-cultured intact embryonic hearts. The results indicate that the electrophysiological properties of cultured myocardial cells are similar to those of cells in intact embryonic or adult hearts and indicate the feasibility of using such a system for study of the nature of cell to cell interaction. (Supported by grants from the Cleveland Area Heart Society and the Public Health Service, H-5087.)

THE EFFECT OF INSULIN ON MYOCARDIAL CONTRACTILITY. Eugene A. Lentini and Richard I. Park*. Univ. of Oregon Medical School, Portland, Oregon.

Investigations of the glucose uptake of contracting rat heart muscle lead to studies designed to examine the influence of insulin on myocardial contractility. The myocardial preparations were stimulated at a frequency of one per second and bathed with 45 ml of Ringer's salt solution. The substrate of the control group contained amino acids and glucose. The bathing solution of the other experimental groups contained only glucose with and without insulin at various specified times. The recording of the developed tension was accomplished by using a strain gage transducer. The muscles were placed under a resting tension of one gram and aerated with 95% O_2 + 2% CO_2. It was noted that muscles bathed in a Ringer's glucose (75 mgs %) solution, containing amino acids, revealed a constant developed tension. However, muscles bathed only with a Ringer's glucose solution exhibited a marked decline in the developed tension over a comparable period of time. The addition of insulin to the bathing solution decreased the rate of decline in the isometric tension. Insulin exhibited a positive inotropic effect on muscles made hypodynamic. The experimental data support the contention that insulin does influence the contractile activity of rat heart muscle. (Supported by PHS H-4562 and O.H.A.)

HEMOLYTIC PROPERTIES OF FAT INFUSIONS. Harry H. LeVeen and Prudence Giordano*. Veterans Administration Hosp., Brooklyn, N. Y., and State Univ. of N. Y., Downstate Med. Center.

Mild hemolytic anemia occurs after prolonged intravenous injection of emulsified fat. Does the infusion of neutral fat produce sufficient concentrations of NEFA during clearing to cause a hemolytic anemia? Hemolysis did not occur until 11,000μ Eq/L of fatty acid were liberated during in vitro clearing in the presence of erythrocytes. This concentration of NEFA was never reached in 38 hospital patients given infusions of 500 cc of 15% fatty emulsions. Elevation of circulating NEFA is not the explanation for anemia. Patients and animals did not remove injected fat by the normal clearing process. Most of the injected fat is removed from the blood by the RE system. Neutral fat might be split in the RE cell. This might lead to NEFA concentration in the tissues of the RE system sufficient to cause hemolysis. Average NEFA in the spleen of normal animals was found to be approximately 6,900μ Eq/Kg. of wet tissue. After a series of fat infusions, NEFA levels in the spleen can be raised over tenfold, depending upon the amount of emulsion administered. Since these values are far beyond the critical level which produces hemolysis, lysis of erythrocytes in the spleen is possible under these circumstances. Emulsifying agents can also cause hemolysis. Phospholipid caused distortion of red cells and hemolysis of red cells and hemolysis of erythrocytes suspended in saline. Plasma albumin protected against this hemolysis. These experiments disclosed that plasma binding of emulsifying agents is an important factor if emulsions are to be non-hemolytic. Nonionic emulsifying agents cause hemolysis even in presence of plasma. Low circulating plasma proteins and saturation of the binding sites of plasma albumin can contribute to hemolysis.

ELECTRICAL POTENTIAL PROFILE OF THE DOG THYROID. Harold A. Levey and Antonio Paes de Carvalho*. State U. of N.Y., Downstate Med. Ctr., Bklyn.

Electrical potentials of dog thyroid slices (1.2-1.5 mm thick) were recorded with glass capillary micropipettes with tip diameters of less than 0.5 μ and resistances of about 20 megohms. The depth of electrode penetration was determined by the voltage drop across a 10-turn potentiometer coupled to the fine-control knob of the micromanipulator. Potential and depth were recorded simultaneously on a Sanborn 2-channel recorder. The electrode tracks were located histologically and correlated with the observed potentials. As the electrode tip was advanced into the slice, potentials of -20 to -60 mV appeared and persisted for as much as 150 μ of tip excursion. Many of these electronegative regions were found to be co-extensive with follicles of comparable diameter. Recordings also were carried out on rat thyroids, both *in situ* in anesthetized animals, and *in vitro* in a temperature-controlled bath. The observed potentials were -70 to -100 mV in the former and -40 to -60 mV in the latter. The potentials in the rat thyroids also were co-extensive with follicular diameter. Recordings from propylthiouracil-treated rat thyroids yielded electronegative regions which, in some cases, persisted for over 200 μ, compatible with the greater follicular diameter in the goitrous glands. These findings suggest that follicular fluid is negative with respect to extracellular fluid and apparently is isopotential with the interior of the follicular cells (assuming that the latter is electronegative). If the foregoing is substantiated, it must follow that the polarization of the basal membrane of the thyroid follicular cell is far greater than that of the apical membrane. Future theories on the thyroidal iodide-trapping mechanism accordingly must accommodate the movement of the iodide anion against the electrical, as well as the chemical, gradient.

THE SURFACE ACTIVITY OF SALINE EXTRACTS FROM INFLATED AND DEGASSED NORMAL LUNGS. BERNARD E. LEVINE* AND RUDOLPH P. JOHNSON* (INTRO. BY F.N. CRAIG). U.S. ARMY CHEMICAL RESEARCH AND DEVELOPMENT LABORATORIES, EDGEWOOD ARSENAL, MARYLAND

A CONFLICT EXISTS IN RECENT REPORTS DEALING WITH THE EFFECT OF ATELECTASIS UPON THE SURFACE ACTIVITY OF SALINE LUNG EXTRACTS. NORMAL RABBIT LUNGS HAVE BEEN EXTRACTED IN AERATED AND IN VITRO DEGASSED STATES TO SEE IF ALVEOLAR COLLAPSE ALONE ALTERED EXTRACT ACTIVITY. THREE EXTRACTION TECHNIQUES, CHOPPING, MINCING, AND PESTLE-HOMOGENIZATION WERE COMPARED. AERATED LUNG SAMPLES YIELDED HIGHLY ACTIVE EXTRACTS BY ALL EXTRACTION METHODS. EXTRACTS FROM AIRLESS LUNGS PREPARED BY CHOPPING OR MINCING INVARIABLY SHOWED HIGHER MINIMUM SURFACE TENSIONS, LOWER STABILITY INDICES, AND TOOK MORE TIME TO REACH MINIMUM TENSIONS THEN DID EXTRACTS OF THE SAME LUNG WHEN AERATED. DIFFERENCES COULD BE DUE TO DECREASED AREA OF SALINE-ALVEOLAR CONTACT DURING EXTRACTION, AS IT WAS NOTED THAT INCREASING THE WEIGHT OF THE LUNG SAMPLE OR DIVIDING THE LUNG MORE FINELY (I.E., PESTLE HOMOGENIZATION) INCREASED EXTRACT ACTIVITY. IF SALINE EXTRACTS OF ATELECTATIC LUNG ARE STUDIED, QUALITATIVE STATEMENTS ABOUT PRESENCE OF SURFACTANT SHOULD TAKE INTO ACCOUNT WEIGHT OF LUNG TISSUE AND TECHNIQUE OF EXTRACTION.

FURTHER STUDY OF THE EFFECT OF GLUCAGON ON MEAL--HISTAMINE--GASTRIN--AND SHAM FEEDING--INDUCED GASTRIC HCl SECRETION.

LILLY RESEARCH LABORATORIES, INDIANAPOLIS

T. M. Lin, D. N. Benslay,* and R. H. Tust*

The results of this study confirm the findings that gastric HCl secretion induced by meal, gastrin and sham feeding can be completely abolished by the administration of glucagon. The question of whether glucagon also inhibits histamine-induced HCl secretion has been controversial. This controversy has been partially resolved by this study. The augmenting or inhibitory effect of glucagon on histamine-stimulated secretion depends on the relative dose ratio of glucagon to histamine, the manner by which glucagon is given and also on the presence or absence of vagal innervation. In dogs with innervated and denervated gastric pouches, the effect of glucagon on gastric HCl secretion is determined along with changes in electrolytes and glucose in the blood and urine. Part of the inhibitory effect of glucagon on gastric HCl secretion may be related to its effects on elevation of blood sugar and loss of electrolytes from the body.

INCREASED CAPILLARY BLOOD FLOW IN DIBENZYLINE TREATED SHOCK DOGS. E. Lindseth, J. Merickel and J. Vick (intr. by E. W. Humphrey). V.A. Hospital, Minneapolis

Nembutalized adult mongrel dogs were subjected to hemorrhagic shock (50 mm.Hg.) for 3 hours using a Lamson-Fine technic. Five animals were at this point given 1 mg/kg Dibenzyline (DBZ). Seven other dogs served as untreated control group. Hourly arterial and venous blood samples were drawn and O_2, CO_2 content, arterial pH and hematocrit were determined for 6-10 hours. A marked increase in A-V O_2 and in V-A CO_2 was noted during this prolonged hypotensive period. This increase was due mainly to a precipitous fall in the venous O_2 (V O_2) and arterial CO_2 (A CO_2). The changes in A O_2 and V CO_2 contributed much less to make up the change in the difference. Dibenzyline restored these parameters, the acidosis and hemoconcentration to near normal values within 2 hours with the BP at 50 mm.Hg. This study corroborates well with previous studies of total peripheral vascular resistance, distributional blood flow and survival rate in similar preparations. The combined data are interpreted as a DBZ vasodilatory effect, release of pooled blood, increased capillary pertusion with a resultant near normal O_2 and CO_2 transport in tissue and relief of tissue anoxia. Previous evidence of protected kidney function with DBZ in such preparations suggests a renal mechanism responsible for the correction of the acidosis. Maintenance of capillary blood flow rather than unilateral concern for BP with vasopressors appears to be both rational and logical.

STUDIES ON THE METABOLISM OF 3-SULFANILAMIDO-6-ETHOXYPYRIDAZINE. W. H. Linkenheimer (intr. by W. C. Grant). Agricultural Division, American Cyanamid Company, Princeton, New Jersey.

The metabolites of sulfaethoxypyridazine (3-sulfanilamido-6-ethoxypyridazine) were isolated from the urine of treated pigs, sheep, and heifers by paper and column chromatography. Separation of metabolites from whole and blood plasma was achieved by solvent extraction followed by chromatography. In most cases, butanol:ammonia:water (4:1:5) and 5% aqueous pyridine were used as the solvent systems. Four metabolites plus the parent compound were isolated from the urine of pigs and sheep. Two metabolites plus the parent compound were isolated from the blood of pigs, sheep, heifers, and the urine of heifers. The parent compound was found in the blood and urine of all treated animals. The N^4 acetylated sulfaethoxypyridazine appeared to be the predominant urinary metabolite, but present in minor concentration in the blood probably due to high renal clearance. A glucuronide of unknown structure was found to be the other major metabolic product observed in the urine and, to a lesser extent, in the blood. A minor metabolite, found only in the urine, was isolated and identified as the N^4 glucuronide of sulfaethoxypyridazine. Furthermore, it was established that this metabolite was formed non-enzymatically *in vitro* by the addition of sulfaethoxypyridazine and glucuronic acid to urine or water, followed by incubation at 37°C. The fourth metabolite was found in the urine only and also appeared to be formed non-enzymatically *in vitro*. The structure of this metabolite is unknown; however, it has been established that the compound is not sulfanilic acid and that both ring systems of the parent compound and the ethoxy group remain intact.

THE EFFECT OF ACUTE CHANGES IN LEFT ATRIAL PRESSURE ON THE URINE FLOW OF THE UNANESTHETIZED DOG. Helmut Lydtin* and W. F. Hamilton. Depts. of Physiol. and Pharmacol., Med. Coll. of Ga., Augusta, Georgia.

We have been able to confirm the results of Gauer, Henry, O'Connor and others in showing that a rise in intraatrial pressure brings about a marked diuresis in the hydrated chloralosed dog. Following the technique of Ellison, an externally controlled purse-string was used around the mitral annulus to minimize thrombosis. In order to extend these observations to unanesthetized animals, chronically implanted Teflon catheters were placed in the left atrium and superior vena cava. The femoral artery was cannulated percutaneously. Pressure changes in these locations were monitored with strain gauge manometers. Urine was collected at 10 min. intervals. The unanesthetized dogs were suspended in a hammock and trained to remain quiet for up to 8 hours while the left atrial pressure was observed for a 30-110 min. control period, followed by a 30-120 min. (mean 56) period when the left atrial pressure (LAP) was elevated about 20 cm H_2O above control level. This was followed by a second control period. The experiment was repeated under different conditions from 2-19 times on each of 7 trained unanesthetized dogs. The chronic dogs always increased arterial pressure throughout the period of LAP increase. This increase in LAP was almost always accompanied by a diuresis with reduced urine specific gravity (falling drop method) whose absolute volume and percentage increase above control level varied directly with the state of hydration. Since the diuretic response occurred immediately after the LAP was increased with or without anesthesia, since it occurred in the presence of vasopressin infusion and since it was accompanied by a 296% mean increase in sodium excretion, it is felt that it cannot be explained entirely by changes in the level of antidiuretic pituitary hormone. Supported by USPHS grant HTS-5044 and American Heart Association.

TSH AND IN VITRO IODINE METABOLISM IN THE THYROID. Robert E. Mack. Wayne State University, Detroit, Michigan.

Thyroid stimulating hormone (TSH) has been demonstrated to increase the uptake of iodine and its incorporation into protein in several in vitro systems. In the present study, the effect of TSH on in vitro iodine metabolism in the rat thyroid, when injected prior to sacrifice is compared to the results obtained when TSH is added to the incubation media. Rat thyroid slices were incubated in buffer containing I^{131}. The addition of 25 m.u./ml TSH resulted in an increase in I^{131} uptake and the fraction of the tracer incorporated into protein. Labeled mono- and diiodotyrosine were present in increased amounts in the TSH-supplemented tissue. When thyroid slices from rats injected with 1 u. TSH 24 hrs. prior to sacrifice were incubated with I^{131}, iodine uptake was not appreciably altered when compared to sham-injected controls. The protein bound I^{131} fraction was similar to the control value or diminished. Labeled mono- and diiodotyrosine were not significantly increased. It is postulated that these observations might be explained by the presence of larger amounts of inorganic iodine in the thyroid, resulting from the TSH-induced hydrolysis of thyroglobulin.

THE INFLUENCES OF CHANGES IN VENOUS RETURN ON CERTAIN ASPECTS OF HUMAN CARDIAC FUNCTION

Ian F. S. Mackay, José Berrios*, Francisco Ramos-Morales* - Depts. of Physiology and Medicine of the University of Puerto Rico

The technique used was modified from that of Mackay (J. Physiol. 1947).

A reduction in venous return is obtained by the following procedures: (1) The subject is tilted into a head-down position and the arms are elevated. This allows drainage of the veins of the four limbs, (2) A supra-systolic pressure is applied to pressure cuffs on the four limbs, (3) The subject is tilted into a head-up position, (4) The cuff pressures are allowed to fall rapidly to 60 mmHg. This allows a rapid inflow of blood into the four limbs which is temporarily prevented from returning to the right heart by the venous occluding cuffs.

An increase in venous return may be caused by (1) placing the subject in the head-down position, (2) applying venous obstructing cuffs at 60-90 mmHg, (3) Following the filling and distension of the limb vessels, the venous obstructing cuffs are released causing a surge of blood into the right side of the heart. The volumes and flow rates involved in these procedures were estimated plethysmographically.

With the aid of this technique investigations were carried out to experimentally analyze the components of the classical polygraph. The changes in the heart rate and electrocardiograph were also studied.

GAS DENSITY AND MECHANICS OF BREATHING IN MAN.

Domenic Maio* and Leon E. Farhi. Dept. of Physiology, State University of New York at Buffalo, Buffalo, N. Y.

The effects of changing the density of the inspired gas on the mechanics of breathing and the extent to which these could affect performance were studied in man. A low resistance Wedge spirometer was used. Gas densities were varied by either (1) the density of the inspired mixture (80% N_2, He, or SF_6), (2) the ambient pressure (which ranged from 380 to 5700 mm Hg), or (3) a combination of both. Thus, in relation to air at sea level gas densities from 0.22 to 8.46 could be obtained. The alveolar pressure required for a given gas flow rate was essentially proportional to gas density and independent of the nature of the inert gas used which had an almost identical viscosity. The maximum breathing capacity as well as the maximal inspiratory and expiratory flow rates decreased as density increased. A relative density of 4 caused a drop of the MBC and maximal flow rates to approximately one-half the control value (breathing air at ground level.) Extrapolation of the experimental data to a theoretical gas density of zero yields maximal flow rates of approximately twice control value. This indicates the limitations of the respiratory pump which are not dependent on gas flow in the airway.
(Supported by the U. S. Air Force.)

VENO-VENOUS OXYGENATION IN HYPOXIC DOGS. F.J.Martinez† P.M.Galletti and D.Aidan*. Dept. Physiology, Emory Univ., Atlanta, Ga.

In ten closed-chest dogs, veno-venous oxygenation was carried out in an extracorporeal shunt from jugular vein to femoral vein. A 9" rotating disc oxygenator and 2 roller pumps were employed. Once the extracorporeal flow reached 100 ml/kg/min, the animals were made to breathe 6% CO_2 in N_2 for a period of 3 hours. The gas transfer capacity of the artificial lung was regulated so as to arterialize the blood infused into the femoral vein at a pO_2 of about 110 mm Hg and a pCO_2 of 40 mm Hg. After one hour, the pO_2 of mixed venous blood and arterial blood became equal and stabilized between 50 and 60 mm Hg. The pO_2 of peripheral venous blood varied between 30 and 40 mm Hg. Alveolar and arterial pCO_2 remained around 40 mm Hg, while the blood pH was essentially unchanged. Pulmonary ventilation was markedly increased owing to an increase in respiratory rate and tidal volume. A moderate degree of pulmonary and systemic hypertension developed. After 3 hours of hypoxia, the animals were permitted to breathe oxygen, emerge from anesthesia and recover. These experiments demonstrate that adequate substitution for pulmonary function can be achieved by veno-venous oxygenation. Complete functional pulmonary bypass with gas exchange at the pre-pulmonary level appears compatible with the maintenance of tissue oxygenation and acid-base balance.

MUSCULAR VS. CEREBRAL SOURCES FOR THE SHORT-LATENCY HUMAN EVOKED RESPONSES TO CLICKS. Truman Mast (intr. by H. Davis) Central Institute for the Deaf, St. Louis, Missouri

Short-latency components of human evoked responses to clicks are known to include an inion response presumed to originate in muscle. We sought for early non-muscular responses. Scalp responses were averaged by a digital computer. Responses from a bipolar (P_1-C_Z) electrode placement not overlying muscle were compared to the inion-ear placement known to yield a response that is markedly increased by the tension put on the posterior neck muscles by forward traction on the head. Using a 1/sec. stimulus rate, the most prominent part of the early responses is a P_1-negative wave, (peak latency of 30 ($\pm$ 5) msec.) and an inion-negative wave of approximately similar latency. Recovery may not be a simple monotonic function of stimulus repetition rate, and varies among subjects. The peak-peak amplitude of the P_1-C_Z response was proportionately much less increased by forward traction than was the inion response. In some subjects. backward traction abolished the inion response, but it never abolished the P_1-C_Z response. The inion response showed a much more rapid rise in amplitude at high stimulus intensities (70-90 dB above threshold) than did the P_1-C_Z response. Evidently the P_1-C_Z response contains components (probably cerebral) other than those originating in the posterior neck muscles. Both responses appear to arise from both "cerebral" and muscular sources, but at slow stimulus rates, the "cerebral" source usually predominates for P_1-C_Z. (NINDB Grant B-3856)

INCORPORATION AND RETENTION OF TRITIATED ALDOSTERONE BY TISSUES OF NORMAL RATS. Connie S. McCaa, L. L. Sulya, Virginia H. Read, and Donald L. Bomer (intr. by William A. Neely). Univ. of Miss. Medical Center, Jackson, Miss.

The calculated "volumes of distribution" for the body compartments which aldosterone is assumed to occupy exceed that of total body water, indicating that aldosterone is selectively taken up by some region or regions of the body. The present investigation was designed to determine which tissues incorporate and retain the hormone. H^3-1,2-d-Aldosterone was intravenously administered to rats maintained on a constant sodium and potassium dietary intake. At varying periods after injection, animals were sacrificed, the desired tissues excised, and homogenates prepared. Concentrations of total dichloromethane extractable radioactivity and H^3-aldosterone in the homogenates were determined using a liquid scintillation spectrometer. Fifteen minutes following injection, liver, lung, duodenum, aorta, kidney, heart, spleen, and skeletal muscle contained a higher concentration of radioactivity than did blood, while brain and adipose tissue had a lower concentration. From blood, kidney, heart, brain, spleen, lung, and skeletal muscle, radioactivity disappeared logarithmically with time. The kidney and duodenum had a higher level of radioactivity 90 minutes following injection than any other tissues studied. This possibly reflects the role of aldosterone in sodium reabsorption in these tissues. Subcellular fractions of liver were separated by preparative ultracentrifugation and analyzed for dichloromethane soluble radioactivity. Seventy-five per cent of the radioactivity in the total homogenate was found in the supernatant fraction.

THE EFFECT OF ANION SUBSTITUTION ON INTRACELLULAR CARDIAC POTENTIALS IN A MOTH. Frances V. McCann, Dartmouth Medical School, Hanover, N.H.

Previous experimental data have demonstrated that bioelectric potentials generated in single cells of the moth myocardium are insensitive to alterations in the extracellular Na^+ concentration. Action potentials average 60 mv with 12 mv of overshoot when exposed to a Na^+-free bathing medium. Measured resting potentials average 50 mv, inside negative to outside, a value exceeding that of 11 mv predicted by the Nernst Equation employing the ratio of intracellular to extracellular K^+ concentrations. This report considers the possibility that an anion may be functioning in the role of the major current-carrying ion. Intracellular electrical activity in single cells of the myocardium of the moth S. cecropia was measured with conventional microelectrodes. The heart was bathed with physiological solutions in which the normal chloride content was replaced with nitrate or sulfate. The replacement of the normal chloride content with nitrate produces an initial increase in frequency with a marked shortening of the plateau. This effect occurs within three minutes, and if exposure to this solution is prolonged to two hours, recovery to the initial frequency is not observed. The resting potential is not appreciably altered. The substitution of sulfate for chloride ions produces an initial increase in frequency of heart beat followed by a gradual slowing. Some hearts exhibit an exquisite sensitivity to the sulfate solution, and within two minutes the heart ceases to beat as action potential activity ceases. The resting potential is only slightly reduced. Supported by P.H.S. Research Grant HE-06132-03.

VASOMOTOR AND SUDOMOTOR RESPONSES TO HEATING OF RESTRICTED PORTIONS OF THE BODY SURFACE. Robert D. McCook, Robert Wurster*, and Walter C. Randall, Department of Physiology, Loyola Univ., Chicago, Ill.

Employing twin climate chambers separated by an insulated partition, young, male, nude subjects lay on a copper screen bed with a sponge rubber diaphragm fitted around the abdomen in such a way that the portion of the body below the umbilicus was in one chamber (A), while the portion above the umbilicus was in the second (B). While the ambient temperature in B was maintained relatively constant, the temperature of A was progressively increased. Sweating, cutaneous blood flow, cutaneous and deep body temperatures were simultaneously and continuously recorded. Mean skin temperature was measured by means of a simple analogue computor employing small, matched thermistor surface probes and calibrated potentiometers. The weighted output from each of eight to twelve thermistors was summated by means of an operational amplifier and continuously recorded, together with blood flows, on a six channel Grass Polygraph. When the upper portion of the body was maintained at 25 ±1°C while the temperature in chamber A was progressively elevated to approximately 50°C, cutaneous vasodilation and sweating occurred on the foot, calf and thigh as much as 90 minutes in advance of that on the upper extremities and head. In many subjects neither vasodilation nor sweating occurred on the upper extremities under these conditions. Elevation of the ambient temperature in chamber B to 30 ±1°C reduced the period of sweat recruitment over the entire body surface to a period of 10 to 15 minutes. Rapid cooling of chamber A following establishment of sweating on all cutaneous surfaces resulted in prompt diminution or cessation of sweating with much slower alterations in vasomotor activity.

TWO MECHANISMS OF $Na_2S^{35}O_4$ LABELING OF RAT BLOOD PLATELETS. T. P. McDonald* and T. T. Odell, Jr., Biology Div., Oak Ridge Natl. Lab., Oak Ridge, Tenn.

The nature of the association of S^{35} with rat blood platelets was investigated during the 32-hour period after single injections of S^{35}-sulfate. Radioactivity of saline-washed platelets declined from 18 x 10^{-7} count/min/platelet at 1 hour to about 7 x 10^{-7} count/min/platelet at 12 hours, and then rose by 24 hours to 11 x 10^{-7}. These results suggested two different mechanisms of platelet labeling: (1) an immediate uptake by, or adsorption to, circulating platelets, and (2) labeling of platelets in another compartment, which subsequently enter the circulatory system. The disappearance half-time of platelets labeled in the blood was about 12 hours, whereas platelets labeled while still part of megakaryocytes in the marrow gradually increased in the circulation, reaching a peak at 72 hours. About half of the S^{35} could be released as free sulfate by water lysis at early time periods (1 and 3-1/2 hours), whereas very little free sulfate was found at 24 hours. At later times, a significant proportion of the activity was associated with a sulfated acid mucopolysaccharide (MPS), but there was no labeled MPS in platelets harvested immediately after sulfate injection. MPS was separated from platelets by alkaline hydrolysis and identified by (1) comparing the electrophoretic patterns with known samples of chondroitin sulfate and heparin, (2) staining with Alcian blue, and (3) measuring radioactivity.

Electrolyte and Acid Secretory Studies One Year After Freezing of Isolated Canine Gastric Pouches.

A.S. McFee, M.D.*, E.F. Bernstein, M.D.* and O.H. Wangensteen, M.D. Department of Surg., Univ. of Minn. Minneapolis 14, Minn.

A single episode of freezing, for one hour, at inflow temperatures of -17°C is usually adequate to produce prolonged achlorhydria in isolated canine Heidenhain and Pavlov pouches. However, histologic studies reveal that following a short period of acute edema and hyperemia Heidenhain pouch mucosa appears essentially normal. A relatively slight amount of inflammatory change with patchy evidence of arteritis may be seen. In spite of this, achlorhydria commonly persists for over one year. Biopsy studies at this interval reveal mucosal atrophy. Many parietal cells appear intact but fail to respond, even to augmented doses of histamine.

Following freezing, Heidenhain pouch electrolyte secretion is also strikingly altered. Potassium concentration is approximately double the pre-freeze values, and an associated decrease in chloride concentration to about 60% of control values has been observed. Sodium concentration tends to increase, but relatively slightly, and not in all animals.

Some of these animals have now been followed over 20 months since freezing, and have continued to be achlorhydric, with persistent electrolyte secretory alterations.

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SOME HORMONAL EFFECTS OF ELECTRICAL "SELF STIMULATION" IN THE LATERAL PREOPTIC REGION. **P. R. McHugh, W. C. Black and J. W. Mason (intr. by F. Strumwasser). Walter Reed Army Institute of Research, Washington 12 D. C.**

A study of hormonal changes in "self stimulating" animals was undertaken to elucidate their metabolic state and possibly to illuminate emotional qualities of the experience. Five chair-confined rhesus monkeys with bipolar electrodes in the lateral preoptic region could press a lever for up to five days and obtain for each response a 0.5 sec train of biphasic rectangular pulses (1.0-3.0 mamp, 0.5 msec, 100c/sec). Urinary and plasma 17OH corticoids rose consistently with stimulation. In one case urinary corticoids rose from a control of 1.0 to 3.7, 4.0, 5.7 mg/24 hours on three successive days. In another plasma 17OHs rose from 48 to 168 ug % during three hours of rapid stimulation. Urinary catechols and plasma BEI rose while estrogen and androgen levels tended to fall. This is the hormonal pattern of intense emotions such as fear, rage, anticipation. Through the lateral preoptic region pass neurons which have major connections to the hypothalamic neuroendocrine nuclei and which are thought to be important in emotional arousal. Their stimulation appears to produce 1) hormonal effects similar to those of great excitement and 2) an experience that the subjects seek to continue.

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MIXING OF INDICATOR WITH BLOOD IN THE LEFT ATRIUM AND VENTRICLE. M.B. McIlroy, Cardiovas. Res. Inst. & Dept. of Med., Univ. of Calif. Med. School, San Francisco.

When a deep breath of nitrogen is followed by a breath of oxygen, the resulting changes in arterial oxygen saturation measured with an ear oximeter inscribe a reduced hemoglobin dilution curve. This paper reports a comparison of reduced hemoglobin dilution curves with indicator dilution curves obtained after injection of Coomassie Blue dye into the left atrium or ventricle.

The time constant of the exponential clearance of both indicators from the circulation was measured in 9 patients with heart disease during left heart catheterization. The dye was injected into the left atrium in 3 patients and into the left ventricle in 8. The clearance of indicator was more rapid in all but 2 of the patients when it was introduced into the pulmonary capillary bed. These results suggest that indicator introduced into the blood in the lungs mixes with a smaller volume of blood in the left side of the heart than when injected directly into the left atrium or ventricle. In view of this finding, the assumption of complete mixing of indicator with blood in the left side of the heart seems likely to be incorrect.

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WATER AS A BLOOD SUBSTITUTE. Frances McLean* and Jack W. Crowell. Univ. Med. Center, Jackson, Miss.

Thirty dogs anesthetized with 30 mg/kg sodium pentobarbital were bled until their arterial pressure was 30 mm. Hg and their blood pressure was maintained at this level for 15 minutes by additional small bleedings. Ten of the animals were given no fluid and only one animal survived. An additional ten of the animals were given 50 cc/kg saline, and five of these animals survived. The remaining ten were given 50 cc/kg of distilled water and eight of these animals survived. Whereas blood, plasma, and dextran are undoubtedly the replacement fluids of choice, in mass casualty situations or in remote areas these are not always readily available. Saline is of value because the survival rate was much higher than that of the untreated control. However, distilled water proved to be effective and the survival rate was higher than that of the saline treated dogs. Non-protein crystalloidal fluids leave the vascular system very rapidly. Water differs in that it lowers the osmotic pressure of the animal and causes an expansion of the erythrocytes to increase blood volume.

VENOUS DISTENSIBILITY OF THE HAND AND FOREARM AS AFFECTED BY PASSIVE TILTING AND ACUTE PAIN. John P. Meehan (intr. by P. O. Greeley) and James P. Henry. Dept. Physiology, USC. Sch. of Med.

Venous distensibility of the hand and forearm was determined in eight human subjects using an occlusive cuff technique, an air filled plethysmograph and direct venous pressure measurements of the limb segment under study. Control data was obtained while the subjects were resting and supine. Experimental data was obtained while subjects were supine and performing a cold pressor test, while being passively tilted to an angle of 50°, and while being passively tilted and performing a cold pressor test. Venous distensibility curves were obtained by plotting limb segment volume changes against the directly measured venous pressure. Consistent decreases in forearm venous distensibility were noted in the passively tilted subject and in the tilted subject performing the cold pressor test. The cold pressor test alone did not significantly alter forearm venous distensibility. At a venous pressure of 35 mmHg the control increase in limb volume was 1.64 ml/100 ml tissue. Passive tilting gave 1.20 ml/100 ml tissue and tilting plus the cold pressor test gave 0.90 ml/100 ml limb volume. The venous distensibility of the hand under control conditions gave an increase of 2.1 ml/100 ml limb volume at 35 mmHg venous pressure. The increase in hand volume at 35 mmHg venous pressure was 1.6 ml/100 ml tissue volume for all experimental conditions. The differences noted between the hand and forearm may be in part due to the differences in relative amounts of skin and muscle in these two regions and in part due to the different circulatory function in these two tissues. (Supported by Los Angeles County Heart Grant 293-C1)

PROPAGATION OF IMPULSES IN RAT MYOMETRIUM. Carlton E. Melton, Jr. and Julian T. Saldivar, Jr*; Civil Aeromedical Research Institute, F.A.A., Oklahoma City, Oklahoma

Uteri from estrogen-primed rats show impulse propagation but uteri from spayed rats do not. Eight hrs after injection of 50 µg of estradiol conducted spikes appear throughout the uterus; the effect lasts 2-3 mos. Velocity increases from 2.54 ± 0.25 cm/sec at 8 hrs to 4.83 ± 0.12 cm/sec at one week and remains at 3.4-3.9 cm/sec through the 9th week. Evidence for separate conduction paths is: (1) impulses going in opposite directions can pass, (2) response amplitude increases with stimulating voltage, (3) components of the action potential separate with conduction distance. During recovery from refractoriness, each response is seen to propagate farther. When the tissue is fatigued by a succession of shocks, each response is seen to propagate less distance. Soaking in isotonic sucrose up to 1 hr 17 min slowed the velocity to 1.51 ± 0.22 cm/sec. Soaking for 10-15 min in sucrose containing Ca and K abolished impulse conduction and tone was greatly increased. Effects of isotonic sucrose and of sucrose-Ca-K were reversed by Ringer-Locke. When LiCl was substituted for Na in Ringer solution, conduction slowed but did not persist as long as in isotonic sucrose. Impulses were slowed but not abolished after 2 hrs in isotonic LiCl. LiCl is apparently toxic as there was no recovery in Ringer-Locke. Impulses in the uterus travel in separate bundles, facilitation can be demonstrated suggesting a junctional process, the tissue continues to conduct impulses after prolonged soaking in Ca-free solutions, and Li is apparently irreversibly toxic.

PREPARATION OF VASCULAR BED FOR GENERAL PERFUSION TECHNIQUE IN MICE. Zygmunt Menschik. Schools of Medicine and Dentistry, Georgetown University, Washington, D.C.

For the purpose of successful perfusion of all tissues in mice it is essential to prepare the vasculature adequately so that the perfusing fluid replacing the blood would circulate freely. Preparation of the vascular bed consists of: 1. vasodilation, 2. prevention of thrombosis, 3. maintenance of physiologic pH, osmotic and oncotic pressure and 4. maintenance of adequate and continuous hydrostatic pressure. (1) The vasodilating agents histamine, Regitine and Dibenamine (N,N-dibenzyl-chloroethylamine HCl) were not satisfactory. Sodium nitrite in a two per cent aqueous solution, 0.25 ml per adult animal injected intracardially gave satisfactory general vasodilation and carbon dioxide anesthesia provided an additional dilation of cerebral blood vessels. (2) As an anticoagulating agent, heparin sodium solution (100,000 units in 25 ml distilled water) 0.25 ml per adult mouse injected intracardially was adequate. (3) For maintaining the most physiologic conditions of capillary wall function trials were made with the following clearing solutions: normal saline, Ringer's, Hanks' balanced salt solution 10X concentrate, Lactate-Ringer's (Hartman's) H-S, suspension of gum acacia, Polyvinyl-pyrrolidone (PVP), Plasdone and TC Medium 199. The Lactate-Ringer's with a pH of 7.2 and warmed to 43°C provided the most satisfactory results in maintaining adequate osmotic pressure, preventing damage to the vascular tree and preventing undesirable hydration or dehydration of tissue. (4) Hydrostatic pressures varying from 16 to 200 mm Hg were tried; 80 mm Hg was found to be the most satisfactory for perfusing with the clearing solution. (Supported by U.S.P.H.S. grants NB-01120 and DE-01509.)

AUTORADIOGRAPHIC DISTRIBUTION PATTERNS REFLECTING THE CONCENTRATING MECHANISM IN RAT KIDNEY. P.F. Mercer*, N.H. Mercer* and R.H. Wasserman Dept. of Physical Biology, N.Y. State Vet. Coll., Cornell Univ., Ithaca, N.Y.

The countercurrent multiplier system has been used as an explanation for the formation of a concentrated urine by the mammalian kidney. Active sodium reabsorption out of the loops of Henle into the interstitial areas has been suggested as the source for the concentrating effect seen in urine passing through the collecting ducts. In this study, frozen sections from rats receiving Na^{22}, inulin-C^{14}, and Cl^{36} were mounted in the frozen state on non-screen x-ray film, and exposed for varying periods of time to show the pattern of these substances in the kidney. The sodium and chloride appeared to be uniformly distributed throughout the cortex. In the outer medulla the concentration of both ions increased. At the junction between the outer and inner medulla, the concentration fell and then increased again toward the tip of the papilla. The inulin-C^{14} concentration was comparatively low throughout the cortex and outer medulla, and increased abruptly at the junction between the outer and inner medulla, increasing further toward the papillary tip. From these experiments it would seem that the single increasing pattern of Na concentration from outer medulla through to the papillary tip, expected from the countercurrent hypothesis, did not exist as such. There appeared to be two areas of sodium concentration: one in the outer medulla, not associated with water reabsorption, and one in the inner medulla, showing a similar concentration effect as seen with inulin. This would place water reabsorption primarily in the inner medulla, the same areas in which the thin parts of Henle's loops and collecting ducts are located. (Supported by NIH and USAEC)

HIGH ARTERIAL P_{CO_2}, LOW pH AND THE ACh-AChE SYSTEM IN THE BRAIN. Bernard Metz. Medical College of S. Carolina, Charleston, S.C.

Previous experiments produced suggestive support for the concept that a cholinergic factor may participate in central respiratory reflex activity. Gesell postulated that CO_2 and other acids, by changing the intracellular pH of the respiratory neurons produce their effects by inhibiting the destruction of acetylcholine(ACh), i.e. the CO_2 acts as an anticholinesterase. To test this "acid-humoral" theory, and since CO_2 and H^+ are important "centrally acting" stimuli to breathing, these studies examine the relationship between these stimuli, the total ACh content, and the acetylcholinesterase(AChE) activity in the medulla, employing respiratory responses to Hering's N. stimulations as a parameter. During eupneic breathing, Hering's N. in dogs was stimulated electrically, until steady state control values were obtained. Then the animals were exposed to gas mixtures of 0.5 to 31.7% CO_2 + 30% O_2 for 33 minutes, following which the medulla was instantly immersed in liquid N_2. Significant changes occurred in the ACh levels (17-18% increase, $P<0.01$) when the arterial P_{CO_2} increased over 100 mm. Hg, and the pH declined below 7.150, accompanied by a small but significant decrease of 16% ($P<0.01$) in the AChE activity of the medulla, at these same levels. Concurrently, there was no marked change in the magnitude of the respiratory reflex until the pH fell below 7.150 and the P_{CO_2} was above the 100 mm. Hg mark. In both cases the end result was depression of the reflex. There most probably exist factors other than those of a cholinergic nature in respiratory control, but the results are compatible with the "acid-humoral" theory that the high arterial P_{CO_2} and/or the low pH may affect ACh content and AChE activity in the medulla, and which in turn possibly influences central respiratory reflex activity. (Supported by N.I.H. Grant NB-00954-06).

THE RELATIONSHIP BETWEEN FATTY ACID OXIDATION AND PLASMA FFA CONCENTRATION. H. Miller, B. Issekutz, Jr. and P. Paul*. Div. of Research, Lankenau Hospital, Philadelphia, Pa.

Palmitate-1-C^{14} was infused i.v. for 3 hours into unanesthetized dogs with indwelling arterial and venous catheters. The apparent "oxidation" of plasma FFA was calculated from the ratio $C^{14}O_2$ output (mμc/kg/min)/FFA specific activity (S.A.). While norepinephrine infusion increases the plasma FFA concentration, it decreases the S.A. The apparent oxidation of plasma FFA was considerably increased. When the infusion rate of the radiopalmitate was suddenly reduced, the S.A. decreased without changing the plasma FFA level, which gave a similar rise in the oxidation. Radiopalmitate dissolved in corn oil was orally administered to the animal, 5-8 hours later heparin was infused i.v. This induced a rapid increase of the plasma FFA without causing any marked change in the S.A. However, in this case the calculated oxidation of plasma FFA did not change. It is concluded that the rise of plasma FFA per se does not increase the fat oxidation. It may enter an intracellular fat pool, and therefore the FFA S.A. cannot be related to the $C^{14}O_2$ output.

CSF pH IN HUMAN RESPIRATORY REGULATION DURING METABOLIC ACIDOSIS AND ALKALOSIS. R.A. Mitchell and M.M. Singer (introduced by J.M. Felts) Cardiovascular Research Inst., Univ. of Calif. Med. Center, San Francisco.

Acute metabolic acidosis, to a base deficit of 6 mM/l was induced by an initial oral dose of 20 gms NH_4Cl and sustained for 5 days by 3 gms q6h. pH_a fell from 7.417 to 7.339 in 4 hours. $\dot{V}_E$ increased from 6.2 to 8.4 l/min, Pa_{CO_2} fell from 39.8 to 37.1, CSF pH increased from 7.318 to 7.334 and the CO_2 response curve shifted 2.8 mm Hg to the left. At 24 hours, CSF pH was 7.322 with CSF Pco_2 and HCO_3^- reduced to 42.4 mm Hg and 21.0 mEq/l respectively (control 48.6 mm Hg; 24.0 mEq/l). $\dot{V}_E$ increased to 9.85 l/min, arterial pH increased to 7.371, Pa_{CO_2} fell to 36.4 mm Hg and the CO_2 response curve was 5.0 mm Hg to the left of control. Acute increase in pH_a to 7.449 in 2 hrs. by $NaHCO_3$ ingestion decreased $\dot{V}_E$ to 6.8 l/min, increased Pa_{CO_2} to 39.5 mm Hg, decreased CSF pH to 7.299 and shifted the CO_2 response curve back 4.9 mm Hg to the right. CSF pH was normal in chronic acidosis. It was restored to normal in acute metabolic acidosis by elevating Pa_{CO_2} to normal. In both acute and chronic states at a constant CSF pH, $\Delta\dot{V}_E = -150\ (\Delta pH_a)$. Assigning the remainder of the drive to ventilation to changes in CSF pH, we were able to express the observed changes in $\dot{V}_E$ by the equation $\Delta\dot{V}_E = -150\ \Delta pH_a - 525\ \Delta pH_{CSF}$. This study suggests that the peripheral chemoreceptors initiate and sustain alterations in $\dot{V}_E$ in metabolic abnormalities. Acute acidosis increases $\dot{V}_E$ by stimulating the peripheral chemoreceptors. The Pa_{CO_2} falls and CSF pH increases, decreasing medullary (H+) chemoreceptor activity. Active transport restores CSF pH and the medullary (H+) chemoreceptor activity to normal causing a further increase in ventilation which partially compensates for the metabolic acidosis. (Supported in part by USPHS 2G-63 and GM 05881.)

THE POSSIBLE RELATIONSHIP OF CATECHOLAMINES TO BLOOD PRESSURE RESPONSES FROM HYPOTHALAMUS ELECTRICAL STIMULATION. Woodrow Mitchell*, S.N. Pradhan* and Walter M. Booker. Howard Univ., Col. of Med., Wash., D.C.

Attention has been directed in increasing intensity toward the influence of the central nervous system on changes in B.P. The present work is presented to show B.P. responses to electrical stimulation in various parts of the hypothalamus in anesthetized cats treated and untreated with reserpine. Our efforts are directed toward determining the possible role of catecholamine release, either centrally, or at postganglionic sympathetic sites, on the responses to hypothalamic stimulation. Cats weighing 1.8 to 3.0 kg were anesthetized with chloralose (50 to 70 mg/kg) following which they were arranged on a modified Horsley-Clark stereotaxis apparatus and the brain exposed by trephination. B.P. was recorded on a Grass recorder from the femoral artery. The areas of the hypothalamus were stimulated with currents of 6 volts, frequency 20/sec., duration 0.5m sec. over a period of 15 secs. Control blood samples were drawn from the external Jugular vein; and samples were drawn during the course of stimulation from the same site. Reserpine was admin. in doses ranging from 0.75 to 1.25 mg/kg 24 hrs., 2hrs. and 12hrs. prior to the experiment. Results show that: 1) B.P. markedly increases upon stimulation of the ventral medial nuclei. There was also increase in B.P. when in the anterior dorsal nuclei were stimulated. The 2hr. reserpinized cats show marked increased in B.P. responses over the untreated control. The 24hr. reserpinized cat, however, showed little or no response to stimulation. It appears that the first effect of reserpine on the cardiovascular mechanism is one of stimulation or sensitization to stimulation, and failure to obtain response at 24hrs. may be due to peripheral depletion of catecholamines. (Supported by a grant from National Heart Institute.)

THE QUANTITATIVE EFFECT OF OXYGENATION ON CO_2 CAPACITY AND BUFFER POWER OF WHOLE BLOOD. J.C.Mithoefer, T.Peters,Jr.* G.D.Mead*. Mary Imogene Bassett Hospital,Cooperstown, N. Y.

It is well established that reduction of hemoglobin increases both its capacity for CO_2 and its buffer power and that this property is of importance in gas transport (C-D-H effect). In previous work a quantitative value has been assigned to this property based upon data from nomograms and has been assumed to be independent of the level of P_{CO_2} or pH and to apply over the entire range of hemoglobin reduction. The problem has been re-studied using oxygenated and reduced whole dog blood over a range of P_{CO_2} from 0-190 mm (pH 8.4-6.9). It has been shown that the increased capacity for CO_2 resulting from reduction of oxyhemoglobin varies with the pH or level of P_{CO_2}. At levels of normal alveolar CO_2 tension reduction of hemoglobin expressed in terms of reduction of 1 Vol.% increases the CO_2 content by greater than 0.4 Vol.%. This is a maximal value which falls to below 0.1 as P_{CO_2} of 0 is approached and to 0.2 at high levels of P_{CO_2} (190 mm). It has further been shown that the increased CO_2 capacity resulting from reduction of oxyhemoglobin is a non-linear function of the amount of hemoglobin reduced. The physiological implications of these findings will be discussed.

HEMODYNAMIC EFFECTS OF ANGIOTENSIN INFUSION IN THE RAT BEFORE AND AFTER AUTONOMIC BLOCKADE. D. Montague and R. Rosas (intr. by P. A. Rondell). Dept. of Physiol., Univ. of Mich., Ann Arbor, Mich.

Cardiac output (CO)(thermodilution technique), mean arterial pressure (MAP), and heart rate (HR) were measured during angiotensin infusion (0.125 μg/kg/min. and 0.250 μg/kg/min., i.v.) in 8 sodium pentobarbital anesthetized rats before and after autonomic blockade (pentolinium bitartrate, 5 mg/kg, i.p.). Elevations in MAP due to angiotensin were in excess of 30 mmHg and were about the same in magnitude before and after blockade. Before blockade CO decreased from 267 to 227 ml/kg/min., low dose and from 249 to 221 ml/kg/min., high dose. After blockade CO increased from 197 to 231 ml/kg/min. and from 214 to 241 ml/kg/min. for the low and high doses respectively. These effects of angiotensin on CO were all statistically significant ($p < 0.05$). No change in HR was found. These findings are interpreted as indicating that the positive inotropic action of angiotensin (Kuschinsky, G. and Luelmann, H., Klin. Wochschr. 37: 928, 1959) is masked in the intact rat by the activation of the baroreceptor mechanism which causes a reduction in CO. In the blocked rat, however, this action of angiotensin is unmasked and the CO is increased. (Supported by grant H-2578 C7 from the National Institutes of Health. D. Montague is a Trainee, Cardiovascular Research Training Program, HTS-5465, National Institutes of Health.)

CARDIAC ARRHYTHMIAS PRODUCED BY NOREPINEPHRINE IN ANESTHETIZED DOGS. E. N. Moore,* H. T. Morse* and H. L. Price. Department of Anesthesiology and Comparative Cardiovascular Studies Unit, Schools of Med. and Vet. Med., University of Pennsylvania, Philadelphia, Pennsylvania.

Dresel and associates have proposed that in the presence of thiopental-cyclopropane anesthesia (20 mg/Kg and 20 per cent respectively), both bigeminal rhythms and monofocal "ventricular" tachycardias produced by small doses of catecholamines originate in the A-V node or bundle of His. The evidence for this view was indirect. In the present study lead II of the electrocardiogram was recorded simultaneously with bipolar electrograms from the right atrial appendage, bundle of His, right Purkinje-papillary junction and right ventricle. Under conditions similar to those described by Dresel, we have observed both coupled and monofocal ventricular rhythms. In these dysrhythmias, the origin of the abnormal ventricular complexes appeared to lie distal to the His bundle. In the monofocal rhythms the His potentials were usually inverted and were frequently observed to precede both right ventricular and atrial activation. Moreover, the onset of ventricular depolarization observed on the electrocardiograph always preceded the appearance of the His potential. During coupled rhythms the His electrogram of the abnormal beat was either 1) inverted, 2) not distinguishable, or 3) present with normal configuration and atrial-His interval. However, in 3) the lead II electrocardiogram showed that ventricular depolarization preceded His activity; the His-ventricular septal interval was considerably shortened. Further evidence that monofocal tachycardias and coupled rhythms may originate distal to the bundle of His was obtained in studies employing intracellular electrodes.

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INDUCTION OF LIGHT AND DEEP SLEEP IN CATS BY CHOLINERGIC STIMULATION OF THE LIMBIC FOREBRAIN-LIMBIC MIDBRAIN CIRCUITRY. P. J. Morgane and R. Hernandez-Peon*. Brain Research Unit, Mexico City, Mexico.

A systematic chemical mapping of the trajectories of hypnogenic neural pathways in the brains of cats has been carried out by means of chronically implanted exploring cannula devices. In addition to gross behavioral observations recordings of olfactory bulb activity, cortical EEG, eye movements, and neck EMG were made in all animals. In the fully awake animal crystals of cholinergic agent tamped into the cannula evoked a progression from alertness through a phase of light sleep into deep sleep with latencies varying from 15-125 sec. Sleep persisted for periods of 2-4 hours provided the animal was undisturbed. Nociceptive stimulation aroused the animal momentarily followed by resumption of sleep. Electrical stimulation of the lateral mesencephalic reticular formation always aroused the cholinergic sleeping animal in a completely stimulus-bound manner. Lesions bilaterally in the medial forebrain bundle posterior to cannula sites from which sleep was previously obtained prevented induction of sleep on subsequent cholinergic restimulation. When two cannula systems were implanted from which cholinergic stimulation evoked sleep, a lesion between the cannulae in the medial forebrain bundle blocked induction of sleep from the anterior cannula but did not affect induction of sleep from the posterior cannula. Since the medial forebrain bundle has been shown to be concerned with motivated behavior in several spheres the present studies may be considered in terms of activation theories of motivation and shed light on several types of behavioral deficits seen following lateral hypothalamic lesions. A consideration of the function of the limbic forebrain-limbic midbrain circuitry relevant to states of activation, arousal, and focusing of attention may be important in defining a neurology of all motivated behavior. (Supported by Grants from the U.S. Airforce.)

EFFECTS OF VASODILATORS ON THE CIRCULATORY CHANGES DURING ENDOTOXIN SHOCK. J. A. Morris*, R. W. Smith*, L. D. Longo*, R. G. Beck* and N. S. Assali. Univ. of California School of Medicine, Los Angeles.

Systemic and regional circulatory changes to intravenous E. Coli lipopolysaccharide and to the subsequent use of vasodilator agents were studied in 10 dogs anesthetized with pentobarbital. Cardiac output (ascending aorta), renal and superior mesenteric flows were measured simultaneously with electromagnetic flowmeters, and pulmonary, portal and aortic pressures with strain gauges. Endotoxin produced a precipitous and equivalent fall in cardiac output, renal blood flow and systemic pressure within 5 minutes followed by a 30 minute period of partial recovery. Thereafter, a relapse occurred during which the animal slowly deteriorated. Total peripheral and renal resistances changed insignificantly during the hypotensive and recovery phases. Mesenteric artery flow decreased significantly more than the cardiac output indicating increased mesenteric resistance. During the relapse, all resistances decreased. Pulmonary artery pressure changed inconsistently while portal pressure remained elevated through the experiment. Infusion of a ganglionic blocking agent (Arfonad) or intravenous injection of hydralazine during the relapsing period of endotoxin shock resulted in further decline in the systemic pressure, cardiac output, renal and mesenteric flows with rapid deterioration of the animal's condition. These findings indicate that blockade of the sympathetic vasoconstrictor impulses or the administration of a vasodilator agent do not reverse or improve the hemodynamic alterations in endotoxin shock.

TUMORS INDUCED IN PRIMATES BY CHICKEN SARCOMA. J. Spencer Munroe (intr. by W. F. Windle) Sloan-Kettering Institute for Cancer Research, New York, and Laboratory of Perinatal Physiology, NIH, San Juan, Puerto Rico.

Four adult and 10 newborn rhesus monkeys were injected with a strain (Zilber) of Rous sarcoma virus. A premature died and one was killed day 6 after injecting tumor suspension and cell-free supernate respectively. Virus was demonstrated at injection site (thigh) and in liver of the one suspension-injected, the technique being inoculation of chicken wing-web. The tumors which developed were histologically similar to the original Rous sarcoma. One adult monkey was killed for histology and blood and tissues searched for virus. None of the 3 remaining adults developed tumors after 13 weeks. All the other 8 newborn monkeys developed tumors. Three were histologically fibrosarcomas. One tumor appeared 6 weeks after inoculation, was excised for histological and virus recovery studies, and recurred in 14 days. Two other monkeys in which fast-growing tumors appeared 3 weeks after injection were killed because of debility. Tumors and organs were studied by light and electron microscopy, for chromosome evaluation, for demonstration of virus by the chick wing-web technique and serologically for detection of circulating antibodies; in the tumors of these, virus was demonstrated by 3 serial passages in chicks. Survivors are being observed for ultimate fate of animals and of tumors, and for evidence of tolerance to cell-free supernate of the tumor material. This may be the first time sarcomas have developed in primates after virus injection. Originally this virus could not be passed by Dr. Peyton Rous to birds not blood-related to the flock in which he discovered the virus. Immaturity of immunity mechanisms in the monkey at birth may account for crossing the species barrier from bird to primate.

Spatial Summation of Cutaneous Pain. D. Murgatroyd* and J. D. Hardy, John B. Pierce Foundation and Department of Physiology, Yale University Medical School, New Haven, Connecticut

Cutaneous pain thresholds were determined for four trained subjects by exposing skin areas of various sizes on the face (5-200 cm^2) to thermal radiation from a large area (60 cm X 160 cm) quartz lamp source. Exposures were also made of the thorax, back, and posterior and anterior aspects of the legs as well as the entire posterior and anterior body surfaces. Measurement of the variation in radiation intensity over the small areas indicated uniformity of irradiance within 5%. Over the larger areas a variation of 15% was observed. The intensity of the radiation was maintained constant and the exposure time varied randomly; reports of pain or no pain were given by the subjects. Skin temperatures were measured prior to each test with a radiometer. Thresholds were calculated in terms of the skin temperature reached at the end of the exposure for which 50% of reports were "pain". Skin reflectance was measured during irradiation by direct observation of skin heating with a chopped-beam radiometer provided with an indium-arsenide filter. Results showed subject to subject differences in pain threshold level but there was no consistent lowering of threshold with increasing size of area stimulated. It is concluded that spatial summation of pain is not appreciable in homogeneous skin areas for which the senses of warmth and cold summate well.

TRANSCALLOSAL INFORMATION TRANSMISSION IN THE PRIMATE. Ronald E. Myers. Spring Grove St. Hosp., Baltimore, Md.

In the chiasma-sectioned cat visual experiences acquired through one eye cannot be reversed by subsequent conflicting experiences through the other eye. It was concluded that the effectiveness of direct sensory stimulations predominates over that of transcallosal transmissions. In the present experiment similar studies were carried out in the tactual system using the monkey. Eight monkeys were taught a specific tactual roughness discrimination task using their right hands. After response establishment they were retrained on the reversed task through their left hands. Finally, they were tested again through their right hands on the initial task. The animals required from one to three hundred trials to reestablish response, three exhibiting early complete reversal of the initially acquired task. It is concluded that in the monkey transcallosal effects are sufficiently developed to bring about disruption or, in some cases, reversal of directly developed learned tactual responses. Supported by the US Public Health Service.

EFFECT OF LUNG INFLATION ON TRACHEAL VOLUME IN DOGS. J.A. Nadel and J.G. Widdicombe* University Laboratory of Physiology, Oxford, England.

We measured volume changes in an isolated segment of cervical trachea whose nerve and blood supply were intact in dogs anesthetized with chloralose and urethan or pentobarbital. Transient lung inflation(200-600ml) increased tracheal volume in each of ten spontaneously breathing dogs (mean, +7.7%;range +1.0-+16%)and in each of eight artificially ventilated dogs (mean, +7.6%;range +1.7-+14%). The degree of dilation varied with inflation volume and with resting 'tone' of the tracheal muscle. Pulmonary denervation caused maintained tracheal constriction and blocked tracheal dilation during lung inflation in four spontaneously breathing and four artificially ventilated dogs. Cooling the cervical vagi to temperatures between 7-12°C had the same effect. Both of these procedures blocked the Hering-Breuer inflation reflex, but the trachea still constricted following carotid body chemoreceptor stimulation by KCN, indicating that conduction in vagal efferent fibers to the trachea was still intact. In each of four paralyzed dogs, right heart injection of veratrine (25-100ug) increased tracheal volume (mean, +11.3%; range, +4.4-+22%), presumably by stimulating pulmonary stretch receptors. Left heart injection dilated the trachea much less. The former effect was abolished by pulmonary denervation. These studies establish the reflex nature of tracheal dilation during transient lung inflation and suggest that Hering-Breuer stretch receptors are the responsible end-organs.

(Supported by Medical Research Council and USPHS grant HE-06285.)

HISTOLOGICAL STUDY ON THE DEGANGLIONATED SMALL INTESTINE OF THE DOG. T. Nagata* and F. R. Steggerda. Dept. of Physiology, University of Illinois, Urbana, Illinois.

Deganglionated loops of the small intestine were prepared in 15 dogs, according to the modified technique of Hukuhara et al. The duration of ischemia varied from 1 to 4 hours. Immediately after the operation, small tissue blocks were cut out from both the normal control intestine and the adjacent deganglionated loops for study. At intervals from 2 to 100 days, the animals were reoperated upon and similar blocks of normal and deganglionated intestine were removed for study. The tissue blocks were fixed and sections stained in a number of ways for appropriate histological and histochemical study. In general, desquamation of epithelial cells from the tops of the villi to the roots was prominent in accordance with the duration of ischemia. The muscle fibers of the two muscular layers became loosened after 4 hours' treatment. No significant change was observed in the tunica propria mucosae and the serosa. These cells show complete recovery within one week after the operation. The ganglion cells of the Auerbach's plexus showed various degenerative changes in accordance with the duration of ischemia. After 4 hours ischemia, most of the ganglion cells of the plexus were completely destroyed. The ganglion cells of the Meissner's plexus were less sensitive to the ischemia. The degeneration changes observed in Auerbach's plexus, after 4 hours ischemia, was irreversible. Meissner's plexus recovered completely even after 4 hours ischemia. PAS positive substances decreased in all the layers except the goblet cells in the epithelia. The DNA content of ganglion cells showing degeneration gave no change, while the RNA content did change shortly after the ischemia.

ACTIVE SYMPATHETIC VASODILATION DUE TO AFFERENT VAGAL STIMULATION IN BULLFROGS. H. Naito* and K. Kotsuka* (Spon: F. R. Steggerda). Dept. of Physiology, Kansai Medical School, Osaka, Japan.

In a single pithed bullfrog in which both the vagus nerves and anterior spinal roots III-IX had been cut, stimulation of the central cut end of the vagus nerve with a "glycerine spot method" (Kotsuka) resulted in a definite dilation of small arteries of isolateral M. gracilis. However, in a similar preparation in which the posterior roots III-IX or the sympathetic chain had been previously cut, no vasodilation occurred following the afferent stimulation of the vagus nerve. The above results demonstrate that the vasodilation resulting from a reflex activation is brought about by efferent vasodilator fibers travelling via posterior roots and sympathetic chain, and that it can be elicited by depressor type of reflex from the afferent stimulation of the vagus nerve. Experimental evidence supports the hypothesis that there are active vasodilator fibers via the posterior roots to the bullfrog's hindlimb. Evidence is available to show that the reflex vasodilation in bullfrog's hindlimb muscle is not due to an inhibition of the sympathetic vasoconstrictor tone as maintained by Swedish investigators.

INHIBITION OF FIBRINOLYSIS. L. B. Nanninga* and M. Mason Guest. Univ. Of Texas Medical Center, Galveston, Texas.

Immediately after physical lysis of a clot by fibrinolysin (Fl) (plasmin) the turbidity of the system, measured after the addition of 25% sat. $(NH_4)_2SO_4$ to diluted samples, decreases linearly with time during the first 6 minute period. Clots containing Fl, purified fibrinogen and thrombin were lysed at 37°C. Viscosity studies, ultracentrifuge studies and temperature dependence demonstrated that the change in turbidity following lysis results from continued action of Fl. Saline or saline containing antifibrinolysin (AFl), trypsin inhibitor (TI) or other substances to be tested were added at the point of complete lysis. With a specified concentration of fibrinogen and Fl the rate of decrease in turbidity was then dependent upon the amount of the inhibitor added. The method can thus be used as a rapid assay for inhibitors of fibrinolysis. The addition of mercurials (parachloromercuribenzoate, mercurihydrin) and iodoacetate caused the inhibition by AFl or TI to disappear, but the effect was reversed by the addition of cysteine or glutathione. Oxidizing agents such as iodine and dichlorophenolindophenol also decreased inhibitory effects of AFl and TI on Fl and this decrease in inhibition was found to be overcome through the use of such reducing agents as $NaHSO_3$ and reduced glutathione. Thus the inhibitory effects of both AFl and TI on Fl appear to be dependent upon an intact SH-group which is easily oxidizable. The binding is strong; calculations were made on the Michaelis constant of Fl and on the inhibition constants of the inhibition with AFl and TI. Fibrinolysin does not appear to be a SH-enzyme since its activity is hardly affected by mercurials. The blocking effect on AFl may have significance with respect to the control of in vivo fibrinolysis.

RENAL HEMODYNAMICS DURING URETERAL OCCLUSION IN THE INTACT DOG KIDNEY.
F. D. Nash* and E. E. Selkurt, Dept. of Physiology and Heart Research Center, Indiana Univ. Medical Center, Indianapolis, Indiana.

Increased RBF during stop-flow (S-F) in saline-loaded dogs has been previously reported (Selkurt, E. E., Fed. Proc. 22:173, 1963). This is confirmed in oliguria and urea diuresis. Rate of elevation of ureteral pressure or rate of urine flow do not alter the directional response. The time course of pressure-flow transients following rapid elevation of ureteral pressure and after release of occlusion suggest a myogenic response. It is speculated that increased intrarenal pressure reduces the afferent arteriolar transmural pressure gradient, eliciting vasorelaxation, reduction in intrarenal vascular resistance, and increase in RBF. If, as in severe osmotic diuresis, extravascular pressure is so high that additional increases, as in S-F, prevent further arteriolar dilation, the vasculature is physically compressed as extravascular pressure exceeds intravascular pressure, and RBF is reduced. The reduction in E_{PAH} seen during S-F, which was reported previously, may be due to one, or a combination, of the following factors: with slowed tubular fluid flow, the limiting gradient for transfer of PAH from cell to lumen may be reached, reducing net transport of PAH and increasing venous concentration; augmented passive, non-ionic back diffusion; pyelo-venous reflux; increased volume-flow rate past the transport site decreasing the efficiency of a rate-limited system; or diversion of blood flow away from extracting tissue such as by the opening of arteriovenous communications or by increased medullary perfusion. The evidence for each possibility will be evaluated. (Supported by grants from the National Heart Institute and the Heart Research Center, Indiana University Medical Center.)

INDUCED DELAYED PARTURITION IN SWINE AND CATTLE.
John E. Nellor, Endocrine Research Unit, Department of Physiology and Pharmacology and Department of Animal Husbandry, Michigan State Univ., East Lansing.

Levels of orally administered 6-methyl-17 acetoxyprogesterone (.7 mg/pound body weight daily) not capable of suppressing follicular growth in the ovaries of normal cycling gilts over a long duration (30 to 60 days) effectively block parturition. The duration of normal pregnancy (although parturition is blocked, the ovaries in an inactive state, and the uterus quiescent) is accurately designated by a copious letdown of milk. Fetal growth and welfare, as ascertained by Caesarian delivery or laparotomy, is apparently normal when parturition is delayed for as long as two weeks from the date of milk letdown. A graded fetal death occurs from this time. Fetuses have survived 23 days of delayed parturition, although the majority of the same litter are dead. Delayed parturition in cattle follows the same sequence (.5 mg/pound body weight daily). Although parturition was blocked, a copious milk letdown occurred near expected term. The fetus was alive and apparently normal 10 days over term, and fetal death occurred the 13th day over term. Parturition was not normal if sows were removed from treatment later than 2 days after milk letdown. Uterine and abdominal contractions were marked 14-18 hours after the end of the twice-daily treatment but the cervix did not relax. Fetal death occurred during this activity. Cervical dilation and presentation of dead young occurred 24 hours after termination of treatment. (Supported by a grant from the Benson and Henry Fords.)

THE EFFECT OF REDUCED ARTERIAL PRESSURE AND FLOW ON GUT LUMINAL PH AND K CONTENT IN CANINE SMALL INTESTINE. R. Nelson and R. Beargie (intr. by J. W. Werle). Geo. H. Scott Res. Lab., Fairview Park Hosp., Cleveland, O.

Luminal pH and K content were studied before, during and after periods of reduced pressure and flow in the abdominal aorta in 13 dogs. A Tyrode solution of pH 2.5 was instilled into duodenal segments with and without intact pancreatic and bile ducts. A neutral solution of Tyrode and neutral solution of mannitol were instilled into jejunal segments. Constriction of the abdominal aorta proximal to the celiac axis reduced blood pressure and flow approximately 75%. In duodenal segments the pH of luminal contents steadily increased during control tests. When the aorta was constricted, the pH of gut contents in both duodenal segments did not increase as rapidly and contents were always more acid. After release of aortic constriction, pH regulation returned to normal. Also, in jejunal segments, the pH of luminal contents was always more acid than control values when aortic blood pressure was reduced but returned to control levels when blood pressure was restored. K concentration in duodenal segments increased slightly as pH became more alkaline. When blood pressure was reduced, the concentration of K doubled in gut contents. When blood pressure was restored, concentration of K returned to control values. Similar changes were seen in jejunal segments, K concentration increased in luminal contents when aortic blood pressure was low and returned to normal when blood pressure was restored. It was concluded that acute reduction in aortic blood pressure and flow increases the acidity and K content of gut luminal solutions.
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CLEARANCE OF EXOGENOUS VITAMIN K_1 FROM THE BLOOD. T. E. Nelson, Jr. and L. B. Peck.* Dept. of Pharmacology, Univ. of Colorado Med. Ctr., Denver 20, Colorado.

A ten-fold difference in the rate of clearance of two dosage forms (Mephyton and Aqua Mephyton, M.S.D.) of vitamin K_1 (phytonadione) from the blood stream of anesthetized intact rats was recently reported by us; Fed. Proc. 22: 434, 1963. This difference in rate of removal appears to be almost entirely due to the pinocytotic efficiency of the liver parenchyma in removing the vitamin in the emulsified state as compared to the more limited uptake of the aqueous suspension. Previous reports have indicated that the reticuloendothelial, R.E., cells of the liver were responsible for the selective clearance of large doses of vitamin K_1 from the blood stream. However, comparison of the effects of R.E. blockade by I.V. injection of thorium dioxide (Thorotrast, Heyden Chem. Co.) and pinocytotic blockade by an I.V. fat emulsion (Lipomul, Upjohn) on the blood clearance and tissue uptake of both forms of vitamin K_1, suggest that phytonadione has no unusual attraction for the liver in excess of any other emulsion. It is also concluded that the reticuloendothelial system can no longer be considered important in the removal of this naphthoquinone from the blood stream. (Supported by grants from the Colorado Heart Association and the Univ. Colo. Med. Ctr. General Research Support Fund.)

THYROID ACTIVITY IN CARCINOGEN TREATED RATS. W. C. Newman* and R. C. Moon, Department of Physiology, Univ. of Tennessee, Memphis, Tennessee.

Little is known of the effect of chemical carcinogens on thyroid activity. Fifty day-old Sprague-Dawley females received daily feedings of 10 mg 3-methylcholanthrene (MCA) in sesame oil for 30 days. Controls received only sesame oil. Thyroid activity was estimated using thyroid secretion rate (TSR) method. TSR of each rat was determined prior to, during, and after MCA treatment. Average TSR of sesame oil controls did not change either during or after feeding. Average TSR of MCA treated rats decreased approximately 25% during the feeding period when compared to the average TSR obtained prior to the MCA treatment. Average TSR after MCA treatment was comparable to that obtained before administration of the carcinogen. The rate of thyroidal I^{131} release was also determined. Beginning 24 hours after the administration of I^{131}, each rat received daily intragastric feedings of 1 ml sesame oil for 3 days followed by daily feedings of 10 mg MCA in 1 ml sesame oil for another 5-7 days. Average hourly release of thyroidal I^{131} was significantly less during the MCA feeding period than during the control period in which the rats received only sesame oil. These data indicate MCA depressed thyroid activity and this, in turn, may influence the rate of tumor induction by this compound. (Supported by grant CA 05397 from NIH.)

AV-BLOCK AS A CONDITIONAL RESPONSE FOLLOWING FARADIC SHOCK REINFORCEMENT. Joseph E. O. Newton. Pavlovian Lab., Johns Hopkins School of Med., Baltimore, Md.

A beagle dog was found to have 1% frequency of dropped beats (absent QRS complexes with P-waves present) during a control study of orienting to 88 presentations of 256 cps tones at 2 min. intervals. Subsequent procedure consisted of: A sequence of 20 tones reinforced with 1-5 volts faradic shock to a foreleg and 80 additional tones unreinforced with shock. Frequency of dropped beats rose after shock to 10% during subsequent intertrial intervals and to 37% during tones (conditioning). Extinction was noted in a further series of 72 unreinforced tones during which all occurrences dropped to $< 5\%$. Subsequent constant reinforcement (each tone followed by shock) produced dropped beats during 30% of 140 tones, bigeminy during some tones, but only 5% random frequency of dropped beats. EKG changes were not related to respiration. Atropine abolished and CNS stimulants potentiated them. One sibling of this dog had no dropped beats during either control periods or 100 orienting tones (no shock) but after a single shock trial developed 15% conditional dropped beats. The other 3 littermates also showed dropped beats at onset of tones, possibly related to respiration.

CONCLUSION: In animals with congenital predisposition, partial AV-block may become a conditional response to what are not usually considered adequate cardiac stimuli.

GLUTAMIC DEHYDROGENASE ACTIVITY FOLLOWING HYDROCORTISONE ADMINISTRATION M.T. Nishikawara and J.G. Bricker (intr. by F.A. Hitchcock) Ohio State U. Columbus, Ohio

Amino acid oxidation in mammalian tissues is considered to proceed mainly via the coupled reactions:1. Transamination to α-ketoglutarate and 2. Oxidative deamination of the glutamate formed. Transamination has been studied under a wide variety of nutritional and physiologic conditions. Glutamic-pyruvic transaminase (GPT) of liver has been shown to be related to the level of dietary protein and therefore to the level of amino acid metabolism. GPT activity has also been shown to increase in conditions leading to increased protein catabolism and gluconeogenesis. Reaction 2 which is catalyzed by glutamic dehydrogenase (GDH) has not been investigated as extensively under similar conditions. The first of a series of experiments designed to investigate reaction 2 was concerned with the effect of hydrocortisone on the GDH activity of rat liver. The time course of the effect of two dose levels of hydrocortisone (2 and 5 mg. per rat per day) was investigated. The lower dose of hydrocortisone stimulated a significant increase in the GDH activity in 24 hours. This increase was maintained for the experimental period. The higher dose level promoted an increased activity for 48 hrs. but at 7 days the activity had fallen to normal. This decrease in activity was attributed to a significant reduction in food intake by the hormone-treated animals. These results are in partial agreement with those of Fazekas and Domján (Enzymologia 24, 267, 1962), whose results appeared while our work was in progress but at variance with those of Kruskemper (Z. Vitamin-Hormon u. Fermentforsch 9, 213, 1957 - 1958).

GLUTAMINE AND KETO ACIDS IN AMMONIA AND AMINO ACID BIOSYNTHESIS IN KIDNEY. Daniel J. O'Donovan (intr. by W. D. Lotspeich). Univ. of Rochester Med. Center, Rochester, N.Y.

Previous studies from this laboratory have indicated that the amide nitrogen of glutamine may behave in a manner similar to NH_4Cl in the formation of amino acids from α-keto acids. To extend these observations homogenates of guinea pig kidney cortex were incubated with pyruvate, α-ketoglutarate or oxaloacetate in the presence of either glutamine or NH_4Cl. The formation of new amino acids under these conditions was studied. Kreb cycle inhibitors were used to prevent the interconversion of one keto acid to another. The pattern of new amino acid formation was similar with both glutamine and NH_4Cl, but quantitatively greater with glutamine. These studies supported the concept that the amide nitrogen of glutamine behaves like inorganic ammonia in amino acid biosynthesis. To investigate this hypothesis more definitively experiments were performed utilizing $N^{15}H_4Cl$ and glutamine labeled with N^{15} in its amide position. New amino acids formed were significantly labeled with N^{15} when either glutamine or NH_4Cl was present, indicating that the amide group of glutamine can participate in amino acid biosynthesis in a manner similar to inorganic ammonia in the amination of Keto acids. More of the label was recovered in each new amino acid when glutamine was employed. These results may also relate to the changing equilibrium in kidney between glutamine, free ammonia, and keto acids during changing acid-base balance.

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

RESPIRATORY VARIATIONS IN THE ABDOMINAL SYMPATHETIC ACTIVITY OF THE DOG. H. Okada*, L. J. Fox*, (intr. by C. Terzuolo. University of Minnesota, Minneapolis.

In dogs (nembutal anesthesia) activity recorded centrally to the cut end of the abdominal sympathetic chain or from splanchnic, renal and splenic nerves was recorded while respiratory center activity was monitored by recording from phrenic nerve. Femoral artery pressure and blood flow in the renal and other intra-abdominal and femoral arteries were recorded continuously by strain gauge and electromagnetic flowmeter respectively. Only 16 of 71 animals breathing spontaneously showed grouping of the sympathetic impulse activity; contrary to previous reports, discharges occurred during expiration and were absent in inspiration. The fact that this pattern of activity was abolished by bilateral but not unilateral vagal section, suggests reflex inhibition of the vasomotor centers during pulmonary inflation in quiet breathing by increased afferent vagal impulses. Activity in the respiratory centers is not essential to this phenomenon since sympathetic activity still presented the same pattern even after cessation of discharge in the phrenic nerve by hyperventilation (artificial respiration and flaxedil). Abolition of the pattern under artificial respiration required pneumothorax (ineffective alone) in addition to bilateral vagotomy. There is apparently no relation between grouping of sympathetic activity and normally occurring fluctuations in systemic arterial blood pressure and flow since: 1) Respiratory grouping of sympathetic activity occurred only infrequently. 2) The normal relation between sympathetic activity, arterial blood pressure and respiratory center activity was able to be reversed by flaxedil. Therefore it is suggested that fluctuations in systemic arterial pressure and flow during spontaneous breathing are due to mechanical effects of ventilation rather than being central in origin.

THE EFFECT OF CONTROLLED PRENATAL ASPHYXIA ON THE PULMONARY FUNCTION AND LUNG SURFACTANT OF NEWBORN LAMBS. M.M. Orzalesi† C.D. Cook, J.M. Craig† D.J. Hollister† H.N. Jacobson, Y. Kikkawa† E.K. Motoyama† E.O.R. Reynolds† Harvard Medical School, Boston, and Albert Einstein College of Medicine, New York.

Retrospective studies have suggested that the respiratory distress syndrome of newborn infants may follow intrauterine asphyxia. The present investigation was undertaken to see if such a relation might be established in lambs. Twelve fetal and 13 newborn lambs of varying gestational ages provided control data on the time of appearance of surfactant, the water content of the lungs, and pulmonary function as well as the related histology shown by light and electron microscopy. Prenatal asphyxia lasting 2-3 hours was induced in 9 lambs with gestational ages above 120 days by hypoventilating the ewe. Measurements of PaO_2, $PaCO_2$, and pH in the ewe and lamb, and continuous monitoring of the blood pressure and heart rate enabled the degree of asphyxia to be observed and regulated. The lambs were then resuscitated and allowed to breathe. Results: 1. Control animals: lung surfactant was present after approximately 115 days gestation in the non-asphyxiated lambs. During the first three hours of breathing there was a progressive decrease in water content of the lungs but no change in surfactant. 2. Asphyxiated animals: all three asphyxiated lambs with gestational ages between 120 and 131 days developed chemical and pathological features of respiratory distress including loss of surfactant. Only one of the six asphyxiated animals over 132 days gestational age showed some of the features of the respiratory distress syndrome. It is concluded that respiratory distress and the decrease of surface activity of lung extracts in the lamb results from prenatal asphyxia and that premature animals are particularly susceptible. (Supported by N.I.H. Grants #HE 05339-03, 2A-5276, A-2967-C3, CA 5683 and Ass. Aid Crippled Child.)

RELATIONSHIPS BETWEEN RESTING POTENTIAL, RATE OF RISE AND OVERSHOOT OF ACTION POTENTIALS OF A-V NODE, ATRIUM AND HIS BUNDLE[1]. A. Paes de Carvalho*, W.B. Langan* and B.F. Hoffman. State University of New York, Downstate Medical Center, Brooklyn, New York.

It has been suggested (Fed. Proc. 22(2):765),that there may be two mechanisms for depolarization of cardiac fibers: one, a change in P_{Na}, causing the rapid upstroke of the action potential and the other, normally masked by the first, causing an Ach-sensitive slow upstroke like that of nodal fibers. The magnitude of the maximum inward Na+ current is known to bear an S-shaped relationship to membrane potential:attempts to demonstrate this relationship in atrium and node have been inconclusive because of tissue geometry. We have attempted to control membrane potential in a circumscribed area by means of local application of Tyrode solution varying only in KCl concentration. Graded depolarizations of atrium, His bundle and nodal fibers were produced in this manner and maximum rate of rise of the action potential and overshoot were measured at each level of membrane potential. Single fibers of atrium and His bundle showed the expected S-shaped relationship between maximum rate of depolarization and level of resting potential; however overshoot was maintained until near failure of propagation. This overshoot corresponded to phase 2 of the original action potential, not to phase 0. The maximum rate of rise of A-V nodal action potentials changed little when resting potential was decreased by potassium. The maximum rate of rise of A-V nodal fibers was much lower than that recorded from atrium or His bundle at a similar take-off level. Phase 2 behaved similarly in all three tissues. Progressive depolarization of atrium or His bundle decreases the initial, rapid depolarization, presumably due to Na+ current, and unmasks the slower depolarization mechanism which may carry membrane potential to or beyond zero. Supported in part by grants HE-05148-03 and HE-03916-05 from the USPHS.

MUSCLE AS A NEURAL SIGNAL MODIFIER. Lloyd D. Partridge. Dept. Physiol., Univ. Tenn., Memphis

Muscle converts a nerve impulse pattern into a time-varying tension and in the process introduces other changes in the signal received from its nerve. The nature and magnitude of such signal modifications must be known in order to analyze the motor system. Tests were made by replacing the normal, complex pattern of motor nerve impulses generated by the CNS with a motor nerve stimulus pulse pattern generated by an analog computor. Cat muscles with intact circulation were stimulated and isometric tension recorded. A stimulus pulse rate varying sinusoidially between physiological limits results in tension patterns roughly sinusoidal in form. Comparison of input pulse rate cycles with output tension cycles provides information concerning the effect of muscle on the signal it transfers. Thus the cyclic responses lag significantly behind the stimulus cycles. Wave summation in the muscle appears to be the main basis of this lag. The size of the lag, from one to two orders of magnitude larger than the sum of conduction and synaptic delays in spinal and peripheral paths, is great enough to profoundly affect clonus and voluntary and involuntary movements. The relative and absolute values of the lag are influenced by the cyclic frequency of the stimulus rate. Response amplitude also depends on cyclic frequency, decreasing markedly with increase frequency. Both lag and amplitude effects occur at cyclic frequencies common in motor activity and are of magnitudes which should be of considerable physiological significance.

D.C. RECORDINGS OF OCULAR MOVEMENTS AFTER EYE EVISCERATION IN THE MONKEY. Pedro Pasik, Tauba Pasik and Morris B. Bender. Dept. of Neurology, The Mount Sinai Hospital, New York, N.Y.

We have previously demonstrated that electrooculograms of caloric nystagmus could be obtained in the monkey after ablation of the retina and choroid if enough time was allowed for recovery. Our method of recording, however, did not provide for measurement of potential differences between the anterior and posterior poles of the globes. Therefore, a relative decrease after evisceration could not be detected with precision. In the present study, passive eye movements under anesthesia and caloric nystagmus in wakefulness were recorded in 3 monkeys before and after bilateral evisceration. D.C. recordings were made through silver-silver chloride disc electrodes applied to the shaved temples. Skin was tattoed for reproducibility of electrode position. Results: (1) Passive eye movements from the extreme right to the extreme left in normal animals produced deflections of 1-2 mV. Deflections persisted for as long as the eyes were kept in a deviated position. Caloric nystagmus was recorded as a sawtooth with shift of the baseline according to the general location of the globes. (2) After bilateral evisceration, recordings were flat for 2-3 days. Then, passive movements caused maximal deflections of 0.07 mV. Recordings in successive days showed a steady growth of this potential reaching preoperative values on the 28th day. Again the deflections remained during the deviation of the eyes and their sign indicated that, as in the normal, the posterior poles of the globes were negative with respect to the anterior poles. Recordings of caloric nystagmus showed a similar recovery. Conclusion: These findings indicate that the bioelectric field of the eye may recover to normal values after total ablation of the retina and choroid. Whether this potential is of the same or different origin in the intact and the operated eye remains to be investigated. (Aided by U.S.P.H. Grant # MH-02261).

DIFFERENTIAL THRESHOLDS FOR VISUAL PATTERN DISCRIMINATION IN NORMAL AND BRAIN DAMAGED MONKEYS. Tauba Pasik, Pedro Pasik and Peter Schilder*. Dept. of Neurology, The Mount Sinai Hospital, New York, N.Y.

We have previously shown that monkeys with bilateral aspirations of temporal neocortex exhibit a deficit in visual discrimination of small patterns and a significant improvement when same targets were enlarged. This suggested that a visual field alteration was present in these animals. To quantify the disturbance more precisely, 5 macaques were tested pre and postoperatively on the discrimination of a square (log Ratio between two normal sides [log R]=0.00) and a rectangle (log R=1.40) of same area (25 cm^2) presented frontally at a minimum of 5 in. from the monkey's eyes. Illumination at the center of the figures was 3.15 mL. After achieving criterion, animals were given 25 sessions in which the square was paired with rectangles of decreasing log R in 0.05 log steps or smaller for each correct response, and of increasing log R in same amounts for each incorrect response. Daily thresholds were obtained by averaging the means of trends occurring in each day. Results: (1) Normal monkeys achieved criterion on the 1.40 log R difference with a mean of 153 errors. Mean threshold was 0.088 log R. (2) Postoperatively, the 1.40 log R difference was performed significantly better with a mean of 14 errors ($P < 0.005$). Although 4 animals showed increased thresholds, significancy was reached in only two, and the group mean of 0.120 log R did not differ significantly from the preoperative value. Conclusion: Monkeys with bilateral aspirations of temporal neocortex failed to show significant deficits on a pattern discrimination at supraliminal and liminal levels under the described new conditions of testing. These findings support the view that the method of testing is a crucial variable in defining a visual deficit and suggest that other manipulations of the technique are needed to reveal such alteration in these animals. (Aided by U.S.P.H. Grant # MH-02261).

PROLONGED PRESYNAPTIC DEPRESSION FOLLOWING OPTIC NERVE TETANIZATION IN THE CAT. A. L. Pearlman*, N. L. Morlock*, and W. H. Marshall. Natl. Insts. of Health, Bethesda, Md.

Tetanic stimulation of the optic nerve in Nembutal anesthetized cats produces 1) an initial subnormality of the post-synaptic portion of the lateral geniculate response lasting a few seconds; 2) post-tetanic potentiation lasting 30-60 sec., followed by 3) a second subnormality (SS) lasting for hours (Hughes, Evarts, and Marshall, Am. J. Physiol. 186: 483, 1956). Curtis and Eccles (J. Physiol. 150: 374, 1960), utilizing the separate afferent innervations of gastroconemius motoneurones, demonstrated that the effects of tetanization on EPSP's occurred only in the afferents tetanized, and that the EPSP's evoked by stimulating the untetanized nerve remained constant. In the present study KCl-filled glass microelectrodes were employed to obtain large (5-60 mV) extracellular potentials from single lateral geniculate cells in an attempt to determine whether the events underlying SS were occurring in pre- or post-synaptic elements. Following optic nerve stimulation at 400/sec. for 20 sec., EPSP's evoked by single stimuli were markedly decreased in amplitude for 3-5 sec., were increased for about 30 sec., and then were again decreased over a time course corresponding to SS. "Spontaneous" discharge rate was also studied and no significant change occurred following tetanization, thus implying no change in the excitability of geniculate cells. This evidence suggests that the prolonged changes underlying SS occur in the presynaptic endings of the optic nerve.

EFFECT OF RESPIRATORY GASES ON COMPLIANCE OF INTRAPULMONARY ARTERIES AND VEINS S. Permutt, E.S. Salem*, J.W.C.Johnson*, and R.L. Riley. The Johns Hopkins University, Baltimore, Maryland

We have attempted to determine whether changes in alveolar concentrations of CO_2, N_2, or O_2 can affect directly the compliance of the intrapulmonary arteries or veins. Horizontal burettes were connected to the pulmonary artery and vein of excised lobes of dog lungs. The capillaries were collapsed by keeping the level of the burettes well below the lobe so that alveolar pressure was considerably higher than vascular pressure. Under these conditions, any change in the volume of fluid within the arteries and veins could be studied independently. An increase in transpulmonary pressure caused an increase in the volume of the arteries and veins, presumably through an increase in radial traction from surrounding alveoli. We measured the ratio of the change in vascular volume to the change in transpulmonary pressure ($\Delta V/\Delta P_{TP}$) following inflation of the lobe with various gas mixtures. 100 per cent CO_2 caused $\Delta V/\Delta P_{TP}$ for the arteries to fall to 13% $\pm$ 4% S.E. of its value on room air. Qualitatively similar changes were found for the veins. CO_2 concentrations as low as 8 per cent caused a significant decrease in $\Delta V/\Delta P_{TP}$. No effect on $\Delta V/\Delta P_{TP}$ could be detected with changes in O_2 or N_2. A change in $\Delta V/\Delta P_{TP}$ must have been due either (1) to a change in the compliance of the blood vessels or (2) to a change in radial traction. The P-V curves of the airspaces were identical on all gas concentrations, suggesting that there was no change in radial traction with CO_2. We conclude, therefore, that CO_2 caused a decrease in vascular compliance. Since the only pathway by which CO_2 could get to the arteries and veins was through diffusion from adjacent alveoli and since all central reflex pathways were abolished, it appears likely that alveolar CO_2 acted directly on the pulmonary arteries and veins.

The Protective Effect of Saliva on Experimentally Produced Peptic Esophagitis. E. T. Peter, M. D. *, A. I. Walder, M. D. *, A. J. Madsen, M. D. *, H. Sosin, M. D. * and O. H. Wangensteen, M. D. (intr. by L. Tobian, M. D.) Dept. of Surg., Univ. of Minn., Minneapolis 14, Minn.

This study was undertaken to determine the role which saliva plays in protection of the esophagus against reflux acid-peptic digestion. Fourteen mongrel dogs were subjected to a Wendel cardioplasty on the esophago-gastric junction plus bilateral truncal vagotomy. This procedure produces delayed emptying of the stomach and free reflux of gastric juice into the esophagus. Eight of these dogs (Group 2) also underwent cervical esophagostomy. The remaining six dogs comprised the Control Group, or Group I. Gastric secretion was stimulated in both groups with daily injections of 30 mgm. of histamine in beeswax. Esophagostomies in Group 2 were opened to divert saliva on the dog on the same day that histamine injections were commenced. These animals were supported by tube feeding through the esophagostomy. Average survival post-histamine injection in Group I was 10.7 days, whereas the mean survival in Group 2 was only 2.2 days. Esophagitis, grossly and microscopically, was more severe in those dogs whose saliva had been diverted than in those dogs with esophageal continuity intact. The short survival time in these animals appeared to be directly related to the esophagitis with some dogs dying of hemorrhage and others of perforation of the esophagus. It is concluded that saliva does help protect the esophagus from experimentally produced peptic esophagitis.

Supported by a USPHS Grant and the Donald J. Cowling Fund for Surgical Research

EFFECT OF HYPOTHERMIA AND PHOTIC STIMULATION ON NERVOUS REGULATION OF SKELETAL MUSCLE IN THE DEVELOPING CHICK, Joseph J. Peters, Xavier University, Cincinnati, Ohio.

The objective of these experiments was to reveal some physiological components involving the visual apparatus, nervous pathways, and skeletal muscles, for it was correctly assumed that during progressive maturation some of these components would manifest different degrees of resistance to cooling. Electrical recordings were made from the shank muscles, eye, and cerebrum of developing chicks of various ages while the body temperature was lowered from normal to about 16°C. It was found that as body temperature dropped, photic stimulation of the eyes modified the amplitude of muscle potentials by first producing a reduction in amplitude (35 to 25°C), then brief augmentation (20 to 24°C), then prolonged augmentation (20 to 16°C), first, with the onset, and later with the cessation of photic stimulation. These effects appear between the 20th day of incubation and about one week after hatching. The results seem to provide further evidence for the views that the eye has separate components for discerning the onset, persistence, and cessation of photic stimulation, and that these receptors are associated with nervous pathways capable of either reducing or augmenting the amplitude of muscle potentials.

CARDIAC OUTPUT, VENOUS ADMIXTURE, AND RESPIRATORY DEAD SPACE DURING POSITIVE OR NEGATIVE MEAN INTRAPULMONARY PRESSURES. Johannes Piiper (intr. by H. Rahn). Max Planck Institute, Gottingen, West Germany.

The effects of variation of the mean intrapulmonary pressure (IPP) from -60 to +20 cm H_2O upon circulation and pulmonary gas exchange were investigated in anesthetized dogs ventilated by a Starling pump. The cardiac output (measured with the thermo-dilution method) increased at negative IPP and decreased at positive IPP. As the cardiac frequency was little affected the changes in the cardiac output were due to changes in the stroke volume, which were attributed to the Starling mechanism of the heart and to limitation of the venous return by collapse of central veins. The venous admixture (determined from alveolar-arterial P_{O_2} differences in hyperoxia) was found to increase up to 46% at negative IPP. This increase in venous admixture, which could be completely eliminated by inflation of the lungs, was explained by formation of atelectatic areas. The physiologic dead space (calculated from P_{CO_2} in arterial blood, inspired and expired gas) increased both at positive and negative IPP. The changes of the physiologic dead space appeared to be mainly due to corresponding changes in the "series" dead space. The combined effect of these changes was such that both the effective pulmonary capillary flow and the alveolar ventilation (at constant tidal volume and frequency) were maximal if the IPP was maintained at zero during artificial ventilation.

PRE-SYNAPTIC EVENTS DURING POTENTIATION OF THE SYNAPTIC POTENTIAL. G. Pilar* and A. R. Martin. Department of Physiol., University of Utah College of Medicine, Salt Lake City, Utah.

Intracellular records have been obtained from both pre-and post-synaptic elements in the ciliary ganglion of the chick. In most of the ganglion cells the excitatory post-synaptic potential (e.p.s.p.) is preceded by a 'coupling potential', which usually initiates the spike (Martin & Pilar, 1963). When a conditioning shock is applied to the presynaptic nerve trunk, the e.p.s.p. produced by a second, or 'test' shock is enhanced. This facilitation of the e.p.s.p. is produced over a range of intervals between the two shocks of 8 - 150 msec. During this period there is no change in the amplitude of the coupling potential. Much greater enhancement of the e.p.s.p. is produced by a brief conditioning tetanus. During post-tetanic potentiation, the amplitude of the e.p.s.p. may reach more than 500% of normal and remain greater than normal for more than 5 minutes. Again, there is no change in the amplitude of the coupling potential. When recording from presynaptic nerve terminals, neither a single conditioning shock nor a conditioning tetanus applied to the presynaptic nerve produces any increase in the amplitude of the presynaptic spike. It is thus concluded that facilitation and post-tetanic potentiation of the e.p.s.p. in this preparation are not associated with an increase in presynaptic spike amplitude. Reference: A. R. Martin & G. Pilar (1963). Dual mode of synaptic transmission in the avian ciliary ganglion. J. Physiol., 167, (in press).

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STUDIES OF RESPIRATORY FUNCTIONS IN MEDICAL STUDENTS.[1] James O. Pinkston and Frederick F. Kao.[2] Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Studies of respiratory functions were carried out in 139 first year medical students, including 125 males and 14 females. It was found that the ventilatory capacity was affected by the size of the lungs, the force available to the subject and the resistance prevailing in the total pulmonary system. This was revealed by the significant correlation coefficients of ventilatory capacity with vital capacity, maximal expiratory pressure, and with the diameter of the breathing tube. There are quite a few variables that showed differences between the male and female subjects, but when ratios were used, e.g. capacity ratio, total pulmonary compliance, ventilatory equivalent for oxygen, etc., there was little or no difference between the subjects of different sexes. The ventilatory capacity was greatly reduced when resistance in the air flow system was increased. The relationship between the ventilatory capacity and diameter of the breathing tube is a curvilinear one simulating that of an S shaped curve.

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[2]Recipient of Career Scientist Award of Health Research Council of the City of New York under Contract #I-194.

FAILURE OF 3,3',5'-TRIIODO-DL-THYRONINE TO INHIBIT CALORIGENIC ACTION OF 3,5,3'-TRIIODOTHYROACETIC ACID. J. A. Pittman*, C. S. Pittman and R. W. Brown*. Department of Medicine, University of Alabama Medical Center, the Medical Service and the Radioisotope Laboratory, Veterans Administration Hospital, Birmingham 3, Alabama.

It is known that 3,3',5'-triiodo-DL-thyronine (T'_3) can block the calorigenic action of thyroxine, T_4, (Am. J. Physiol., 1961) and that T_4 is metabolized *in vitro* to 3,5,3'-triiodothyroacetic acid (TRIAC) and other substances (Endocrin., 1959). It has been postulated that TRIAC is the "active form" of the thyroid hormones to which T_4 must be converted in order to exert its calorigenic action. Thyroidectomized Sprague-Dawley rats weighing approximately 200 gm each were divided into three groups of 6 rats each, and the post-absorptive oxygen consumption (Q_{O_2}) of each rat was measured daily for three months. After an initial baseline period, the rats of Group 1 were given daily injections of T_4, 10 ug/kg/day, and those of Group 2 and Group 3 were given daily injections of TRIAC, 30, and 15, ug/kg/day, respectively. After the Q_{O_2} had stabilized, injections of T'_3 were given for 10 days, 5 mg/kg twice daily. When the T'_3 was given, the Q_{O_2} of the T_4 group immediately dropped to approximately the baseline levels, but there was no change in the Q_{O_2} of the TRIAC groups. Repetition of the experiment gave comparable results. These results are consistent with the postulate that T_4 must be converted to TRIAC to act, but other explanations are possible, especially that the difference in susceptibility to blockade results from relatively stronger binding of TRIAC by intracellular substances.

PREACCLIMATIZATION OF MEN TO HEAT BY TRAINING. R.W.Piwonka*, Sid Robinson, V.L.Gay*, and R.S.Manalis*. Anatomy-Physiology Dept., Indiana University, Bloomington, Indiana.

During April, 1963 five distance runners from the Indiana University track team, ages 18-29, performed 85-minute walks on a treadmill at 3.5 mph on a 5.6% grade in a hot environment (40 C d.b.; 23.5 C w.b.). Although none had been exposed to work in heat since the preceding summer, all made responses typical of heat acclimatized men. Untrained subjects of comparable ages failed to regulate body temperature effectively when exposed to the same stresses. In the heat the rectal temperatures of the trained men became nearly constant at an average of 38.2 C, whereas those of the untrained men continued to rise throughout the experiment, averaging 39.5 C at the end. The men's heart rates near the end of the exposure averaged 119 and 173 respectively for the trained and untrained groups. In both groups there was a small rise of mean skin temperature, terminating at 36.2 and 36.5 C in the trained and untrained men, respectively. Thus the heart rates of the untrained men in the heat were more closely related to the central temperature than to changes of peripheral temperature. Sweating during the exposures was nearly the same for both groups. Heat production per surface area in the runners was 15% less than in the untrained men. The difference between the groups in heat storage was nearly equal to the difference in heat production. The preacclimatized state of the trained men is probably dependent on the daily elevations of central temperature during their strenuous workouts. Skin temperature is not elevated during strenuous exercise in a cool environment. (Supported by U.S.Army Medical Research & Development Command Grant DA-MEDDH-60-10.)

EFFECTS OF SIMULATED POSTURAL BLOOD SHIFTS ON THE CAPACITY FUNCTION OF THE LIMB VESSELS. G.C. Plassaras*, E. Brown, J.S. Goei*, and A.D.M. Greenfield*. Cardiovascular Res. Inst. and Dept. of Med., U.C. Sch. of Med., San Francisco, Calif.

The legs below the iliac crests of 8 recumbent subjects were exposed to pressures 65-72 mm Hg below atmospheric to simulate postural blood shifts. Blood flow was measured in one forearm and venous distensibility simultaneously in the other. For this, the changes in local venous pressure and in arm volume were recorded during deflation of a collecting cuff at 1 mm Hg/sec after a period of controlled congestion, in a plethysmograph pressurized to 20 mm Hg (Fed. Proc., 22:344, 1963). With 6 to 8 min of suction, average heart rate increased from 60 (range 51-75) to 92 (range 84-103) beats/min and blood flow decreased from 4.0 (range 2.7-6.5) to 2.6 (range 1.6-3.9) ml/100 ml/min. Distensibility was not affected. (Average change from control determination -1.1%, range +6% to -13%.) Slightly more severe (-80 mm Hg) or prolonged (17 min) suction caused syncope on 2 occasions without changing distensibility. These results provide no evidence that changes in vascular distensibility play an active role in regulating the blood content of the limbs during gravitational stress. Changes in the irrigation of the capacity vessels caused by changes in arterial inflow are probably more important. (Supported by USPHS Grant HE-06285.)

EARLIER PERFORMANCE OF COOLED RATS AFTER ADAPTATION TO HYPOTHERMIA. V. P. Popovic, J. A. Panuska and Pava Popovic; Dept. Physiol., Emory Univ. Med. School, Atlanta 22, Georgia.

Inexperienced rats cooled to a body temperature of 29 C learn and perform a simple technique for obtaining external heat within 48 min. This permits them to rewarm to euthermia and to survive a situation in which otherwise they would perish (Panuska, J. A. and V. P. Popovic: Fed. Proc. 22: 224, 1963). Rats learn to perform for heat even in deeper hypothermia, but after longer exposure and after more accidental reinforcements than at the body temperature of 29 C. The body temperature of 25 C was the lowest at which rats were able to learn and perform in a 3-hr. experiment (Panuska, J. A. and V. P. Popovic: Proc. Internat. Congr. Zool. 1963). In present experiments seven white rats were cooled to a body temperature of 15 C twelve times in 30 days. The thirteenth time the rats were cooled to a body temperature of 22 to 25 C and placed in a dimly illuminated cage of a constant temperature of 2 C, with the possibility of using a heat reinforcement apparatus. The rats accidentally pressed the lever of the heat reinforcement apparatus an average of 0.8 times per min. After an average of 74 (34-116) min., all hypothermia-adapted rats suddenly began to use the heat reinforcement apparatus an average of 5.2 times per min. and rewarmed themselves to euthermia. Of a group of seven control rats five failed to perform even though they were exposed to more accidental heat reinforcements during a 3-hr. experiment than hypothermia-adapted rats. The two non-adapted rats which performed did so after 132 and 175 min., later than any of the hypothermia-adapted rats.

STRESS RELAXATION AND STRESS RELAXATION RECOVERY IN THE EXTERNAL JUGULAR VEIN. Camilo I. Porciuncula*, George G. Armstrong, Jr. and Arthur C. Guyton. Univ. Med. Center, Jackson, Miss.

The time course and magnitude of stress relaxation (SR) and stress relaxation recovery (SRR) in the external jugular vein were studied in 17 dogs. A 2 ½ inch segment of the vein was perfused in a chamber with arterial blood from a dog included in the "perfusion cycle." Volume changes due to distention or narrowing and elongation or shortening of the vein segment were recorded with a Grass volumetric pressure transducer following step alterations in pressure. Transmural venous pressure (TVP) was also directly measured using paired Statham strain gauge pressure transducers. All measurements of volume were compared to the initial volume of the vein at 0 pressure (Vo). SR was found to be both time and pressure dependent with a longer time of progression at higher TVP. The magnitude in relation to Vo and the initial elastic stretch V_1 was much greater at lower than at higher pressures. The SRR time course was twice as long and the magnitude 1 ½ to 2 ½ more than SR. It is concluded that SR plays a buffering role in maintaining normal cardiac output and blood pressure during moderate increases in blood volume and that SRR is a significant factor in maintaining normal or near normal cardiac output and arterial blood pressure following decreases in blood volume.

EFFECT OF SHAM FEEDING ON BILE FLOW IN CONSCIOUS CHOLECYSTECTOMIZED DOGS. Keith C. Powell*, Leonard D. Miller*, and Frank P. Brooks. Depts. of Medicine, Surgery, and Physiology, School of Medicine, Univ. of Pennsylvania, Philadelphia, Pennsylvania.

This study was done to determine the relationship of the response to sham feeding to the choleresis induced by a meal or insulin hypoglycemia reported by Fritz and Brooks (Am. J. Physiol. 204:825, 1963). Four cholecystectomized mongrel dogs were equipped with a gastric fistula, a duodenal fistula opposite the common bile duct (Thomas), and an esophagostomy (Komarov and Marks). Bile was collected at hourly intervals for 5 hours through a cannula in the common duct (Snape and Thomas). The volume, bilirubin and total solid output were determined in control experiments and compared with the results when the dogs were sham fed for 10-12 minutes with 100 gm of Ken-L Burger at the end of the first hour. Continuous gastric suction was applied to the gastric fistula. A mean volume of 52 ml was collected from the stomach during the hour after sham feeding with a mean total acid concentration of 105 mEq/L. There were no significant differences in volume of bile flow, bilirubin nor total solid outputs between the sham feeding and control experiments. Therefore the "cephalic" phase of bile secretion is not a significant factor in meal-induced choleresis. The failure of sham feeding to reproduce the response to insulin-induced hypoglycemia remains to be explained.

THE DRIVING PRESSURE REQUIRED TO ATTAIN MAXIMAL EXPIRATORY FLOW. N.B. Pride*, S. Permutt, and R.L. Riley. Johns Hopkins University, Baltimore, Md.

Fry and Hyatt (Am. J. Med. 29:672, 1960) have shown that expiratory gas flow increases as the difference between alveolar and mouth pressure (ΔP) is increased until at a critical pressure difference ($\Delta P'$) maximum flow is attained. By measuring iso-volume ΔP-flow curves by a new method, we have obtained an estimate of $\Delta P'$ in 13 normal subjects, 8 men with irreversible airway obstruction and 10 asthmatic subjects. Our results confirm that $\Delta P'$ decreases in the normal as lung volume is reduced. The $\Delta P'$ near full inflation was approximately equal in the two groups of subjects with airway obstruction, but was considerably less than $\Delta P'$ in the normal. In most subjects when ΔP was greater than $\Delta P'$ flow remained essentially unchanged from that at $\Delta P'$. The slopes of the ΔP-flow curves at full inflation were similar in the three groups at low values of ΔP. A simple model to explain these results is proposed in which a portion of the airway is considered as the collapsible tube in a Starling resistor, the input pressure of which is alveolar pressure (P_{alv}). The collapsing pressure around this airway is regarded as $P_{alv} + P_{bm} - P_{rt}$, where P_{bm} and P_{rt} are the pressure equivalents of bronchomotor tone and radial traction respectively. In this system $\Delta P'$ would equal $P_{rt} - P_{bm}$. An increase in P_{bm} might then account for the reduction in $\Delta P'$ at full inflation in the subjects with asthma and a reduction in P_{rt} account for the reduction in $\Delta P'$ in the subjects with emphysema. It would appear that the mechanism which limits flow at full inflation in both asthma and emphysema is the same --collapse of the airways at a lower than normal ΔP.

SOMATIC SENSORY REPRESENTATION OF FORELIMB IN DORSAL ROOTS OF RACCOON, COATIMUNDI, AND CAT. B. H. Pubols Jr.,* W. I. Welker, and J. I. Johnson Jr.* Laboratory of Neurophysiology, University of Wisconsin Medical School, Madison, Wisconsin.

In order to gain some understanding of the neural bases of interspecific differences in use of the forepaw as a tactile organ, the electrical activity of 2211 dorsal root fibers was investigated by microelectrode recording in raccoons, coatimundis, and cats. Single unit activity was recorded in dorsal roots C-6 through T-2. Units were driven by mechanical stimulation of cutaneous and deep receptors in forelimb and particularly digits. Cell counts in dorsal root ganglia C-6 through T-2 were also made. Raccoons, which make prominent use of the forepaw as a tactile organ, possess a greater number of DRG cells supplying forelimb than do the other two species. Further, in raccoons a significantly greater proportion of units examined were found to be cutaneous as opposed to deep in origin than was the case in either coatimundis or cats. However, cutaneous receptive fields located on the digits have similar areas in raccoons and cats. In both species, mean cutaneous receptive field area is a positively accelerated, increasing function of distance from apex of forelimb to center of receptive field. In cats, mean field size of dorsal root units is considerably smaller, for a given body locus, than field size of cortical units (Mountcastle, 1957). The above results suggest that differences in innervation density, rather than in field size, are correlated with interspecific differences in tactile behavior. (Supported by NIH grants BT-824, M-2786, and B-3249.)

EFFECT OF BREATHING HIGH AND LOW OXYGEN MIXTURES ON THE VENTILATION & HEART RATE OF UNANAESTHETISED NEW-BORN LAMBS. Michael Purves* (Intr. by Julius H. Comroe, Jr.) Cardiovasc. Res. Inst. San Francisco, Calif.

29 lambs aged 50 minutes to 7 days have been studied to determine whether they have tonic peripheral chemoreceptor activity breathing air and at what level of reduced inspired and arterial oxygen tension, sustained changes in ventilation and heart rate could be observed. We measured ventilation (body plethysmograph), heart rate, femoral artery blood pressure and PO_2. End-tidal CO_2 was recorded continuously with an infra-red analyser, sampling from a tracheotomy tube. The lamb remained quiet given local anaesthesia, regular feeding and attention. Nitrogen/oxygen mixtures were humidified, the PO_2 being measured regularly, and led to the tracheotomy tube at a constant flow of 3 liters per min. After a stable period, the inspired PO_2 was suddenly raised and maintained for 5 - 10 mins. The ventilation of all lambs fell abruptly by 5 - 72% of control, (mean 31%). The heart rate fell by a mean of 9%: the blood pressure fell only slightly or remained constant. Hypoventilation usually lasted for 1-3 minutes but, in 11 of the lambs, persisted as long as high oxygen was administered. There was no relation between the degree or length of hypoventilation and the age of the lamb or the resting P_ACO_2 or P_aO_2. Reducing the inspired PO_2 from ambient to 125 mmHg. resulted in a fall of arterial PO_2 of 7-15 mmHg. and, in 89% of the lambs, in a sustained and reproducible rise in ventilation (mean 8% of control) and heart rate (mean 6%): all lambs responded to a P_IO_2 of 115 mmHg. with a mean increase of ventilation of 11%. In 10 lambs, there was a marked hypoventilation below control when the P_IO_2 was returned to ambient levels. It is concluded that new-born lambs have peripheral chemoreceptor activity at least as marked as that reported in adults.

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ANALYSIS OF WATER METABOLISM IN MAMMALS. E. P. Radford, Jr., Department of Physiology, Harvard School of Public Health, Boston, Massachusetts.

On the assumption of minimum voluntary water intake for mammals (Radford, E. P. Jr., Am. J. Physiol. 196:1098,1959), water turnover under various environmental conditions may be analysed. First, one may define the relationships between food intake and output of urine solutes, L_u, and extrarenal water. When renal concentrating capacity is expressed by the maximum rate of excretion of solutes(L_c) in excess of solutes which would be present if the urine were isotonic, then urine water, W_u, is

$$W_u = \frac{(L_u)^2}{P_o(L_c+L_u)}$$

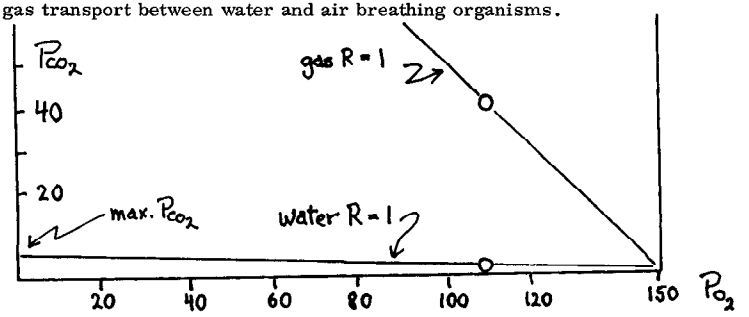
where P_o is plasma osmolality. L_u depends on solute load from food, L_f, and L_c is dependent on nitrogen and possibly electrolyte intake. Explicit balance equations can be written on the assumptions that L_c, L_f, metabolic water and extrarenal water loss are constant for constant food intake. Water intake may be from 1) free water, W_f, (osmolality essentially zero) and 2) water containing electrolytes, W_s, at osmolality C. The equations may be used to: a) evaluate long-range ("whole body") osmotic effects on taste preferences between solutions of different concentrations, b)define conditions of minimum free water requirements for various diets, and c) determine the maximum concentration of W_s at which water balance can be maintained with limited W_f. For example, the saving in free water by drinking salt solutions is determined by

$$\left(\frac{\partial W_f}{\partial W_s}\right)_{C,F} = \frac{C}{P_o}\left[1-\left(\frac{L_c}{L_c+L_f+CW_s}\right)^2\right]-1$$

This equation defines conditions where small amounts of sea-water may decrease free water requirements for men on life rafts.

AQUATIC GAS EXCHANGE: PREDICTION OF ARTERIAL GAS TENSIONS AND "VENTILATION" OF GILLS. H. Rahn and J. B. West*. State University of New York at Buffalo, Buffalo, N. Y.

When a respiratory surface exchanges CO_2 for O_2 at a given R the simultaneously occurring gas tensions will differ depending on whether the gas exchanges in air or water (which is saturated with air.) The figure shows the possible gas tensions at an R = 1. The gas R line has a slope of -1.0. The water R line has a slope of $-\alpha O_2/\alpha CO_2$ (at 20°C). For the same capillary blood P_{O_2} of 110 the alveolus will have a $P_{CO_2} = 40$, the gill a $P_{CO_2} = 1.4$. In order to absorb 1 ml of O_2 at comparable O_2 tensions the gills must extract a volume of water which is 28 times larger than the alveolar ventilation. These considerations imply large differences in the role of CO_2 and mechanics of gas transport between water and air breathing organisms.



SPINAL MEDIATION OF THERMALLY INDUCED SWEATING. Walter C. Randall, Ludwig Guttmann* and John Silver*, Department of Physiology, Loyola Univ., Chicago and the Spinal Injuries Center, Stoke-Mandeville Hospital, Aylesbury, England.

Most modern concepts of temperature control include participation of both cutaneous and central thermal sensors although the predominance of the hypothalamus has received recent emphasis. The demonstration of thermal sweating in paraplegic patients has been criticised on the basis that efferent sudomotor fibers could conceivably take exit from the cord above the lesion, descend in the sympathetic trunk, and innervate cutaneous regions via segmental nerves. Employing both the quinizarin and the starch-iodine-paper methods simultaneously, patients with physiologically complete lesions at C5 or C6 were exposed to elevated temperatures in a climate chamber. Because of demonstrated influences of increased bladder pressure on autonomic functions, the patients were catheterized. Positive although frequently sparse sweating responses were elicited on each of the test areas of all patients studied. In those who were completely free of sweating during the control period, sparse sweating was induced on the lower extremities with more profuse sweating on the upper trunk and head. Such sweating was generally not sufficient to prevent a rise in oral temperature. The sweating progressively increased during the heating period and decreased or stopped promptly upon cooling of the chamber. If urinary bladder distension occurred, sweating became more profuse. The ability of the "isolated" spinal cord to independently mediate sweating was thus conclusively established. Sweating in response to a cutaneously applied thermal stimulus was also proved. The precise pattern of sweat recruitment over the body surface is significantly modified by the level of the spinal lesion.

RIGHT VENTRICULAR HYPERTROPHY AND CARDIOVASCULAR RESPONSE IN DOGS. G. C. Rastelli,* J. W. Kirklin,* J. L. Fellows,* H. J. C. Swan. Mayo Found. and Mayo Clin., Rochester, Minn.

Right ventricular hypertension and hypertrophy were induced in 14 dogs by constricting the main pulmonary artery to an average area of 0.26 cm^2 (normal 2.0 cm^2) measured by cineangiocardiography (average period 5 months). Cardiac performance was assessed during graded exercise on a treadmill before and at different intervals after removal of the band. Five dogs were restudied up to a maximum of 3 times from 2 weeks to 11 months postoperatively in an attempt to correlate hemodynamic changes in the cardiovascular system with changing degrees of right ventricular hypertrophy. Before removal of the band, R.V. systolic pressure at rest averaged 98 mm. Hg and R.V. maximal thickness, measured by cineangiocardiography, 12 mm. (normal 6.0 mm.). After debanding there was a residual narrowing of P.A. (0.61 cm^2) which did not undergo further increase with time. Averages of cardiac parameters are summarized as follows:

	Conscious dogs at rest					During exercise			
After deband.	H.R.	R.V. syst. mm.Hg	C.O. L./min./m^2	S.V. ml.	R.V. hypertr. mm.	H.R.	R.V.	C.O.	S.V.
2 wk.	126	72	4.7	24	11.3	248	116	10.7	29
2 mo.	115	47	3.6	21	9.1	230	88	8.0	22
5 mo.	110	36	3.7	21	7.5	220	72	8.3	24

The progressive decline in R.V. pressure which parallels reduction of the hypertrophy is not related to a change in the obstruction to outflow but appears to occur gradually over a period of months.

EFFECT OF pH ON RENAL NITROFURANTOIN EXCRETION DURING STOPPED FLOW. B. M. Razon* and L. P. Sullivan, Department of Physiology, University of Kansas Medical Center, Kansas City, Kansas.

Excretion of the weak acid, nitrofurantoin, was studied in successive stopped flow procedures performed on dogs first made acidotic by HCl infusion and then alkalotic by $NaHCO_3$ infusion. The stopped flow patterns showed distal tubular reabsorption in all occlusions and proximal tubular secretion in 6 of 12 occlusions. The secretory peak was always slightly proximal to the PAH peak. In successive occlusions, on any one dog, the peak U/P nitrofurantoin ratio in the proximal secretory area increased with decreasing difference between blood and urine pH. In the distal tubular reabsorptive area, the minimum U/P nitrofurantoin ratio also increased with decreasing difference between blood and urine pH. The effect of pH on nitrofurantoin excretion was more pronounced during stopped flow in both distal and proximal areas than during free flow. These observations suggest that nitrofurantoin is actively secreted by the proximal tubules and passively reabsorbed in both proximal and distal tubules in response to H^+ gradients between blood and urine. (Supported by USPHS Grant HE-06974).

EFFECT OF TAURINE ON THE POTASSIUM LEVEL OF THE HEART. W. O. Read and J. D. Welty* Dept. of Physiology, School of Medicine, University of South Dakota, Vermillion, South Dakota.

Previous reports from this laboratory have shown that taurine, present in high concentration in heart tissue, will prevent the development of epinephrine or digoxin induced premature contractions. Additional work has demonstrated that the active compound is the deaminated analogue of taurine, isethionic acid. The present report demonstrates that, the conversion of taurine to isethionic acid by heart slices is increased 39 per cent by 10^{-8}M epinephrine and is increased 47 per cent by 1.25×10^{-6}M digoxin. Taurine, in the presence of 10^{-8}M epinephrine or 1.25×10^{-6}M digoxin, increased the intracellular potassium concentration of heart slices by 30 per cent. In open chest dog preparation, taurine administration prevented the efflux of potassium from the heart which commonly accompanies epinephrine administration. These results suggest that taurine, by forming isethionic acid, acts to retard the efflux of intracellular potassium associated with some cardiac arrhythmias.

THE ACUTE AND CHRONIC EFFECTS OF THE INSECTICIDE ENDRIN ON THE DOG KIDNEY. D. A. Reins, D. D. Holmes, and L. B. Hinshaw. Environ. Physiol. Branch, Civil Aeromed. Res. Inst., Oklahoma City, Oklahoma.

The renal effects of lethal injections of the insecticide Endrin are poorly understood. In the present study, endrin was administered intravenously in acute experiments. In chronic studies it was administered intramuscularly dissolved in cottonseed oil. Hemodynamic parameters and renal functions were studied. Results showed minimal changes until animals reached the moribund state. No significant histological damage was apparent.

In a second series of experiments, isolated kidneys were perfused by dogs acutely poisoned with endrin. Changes in renal artery pressure and blood flow were recorded. Renal vascular resistance increased markedly within ten minutes in most experiments. The increase in resistance was abolished by injection of phentolamine into the renal artery. It appears that the early renal effects of endrin are due to the release of constrictor agents.

HYPOTHALAMIC LESIONS AND PULMONARY EDEMA. R. W. Reynolds, Dept. of Psychology, University of California, Santa Barbara.

Rats were observed for the incidence of pulmonary edema following the placement of hypothalamic lesions. In 74 rats lesions were produced electrolytically by anodal DC current. In 54 rats the lesions were produced by radio frequency thermocoagulation. Electrodes were stainless steel insect pins insulated except at the tip. In the animals with electrolytic lesions 31% (23) died with pulmonary edema and marked signs were observed in another 20% (15). Marked signs of pulmonary edema, therefore, appeared in 51% of the animals with electrolytic lesions. Moderate transient signs appeared in only 3.7% (2) of the animals with radio frequency lesions, and there were no deaths attributable to this syndrome in this group. The relative failure of the syndrome to appear after radio frequency lesions may be attributable to the fact that such lesions are relatively clean, leaving little foreign debris in the tissue, and cauterizing blood vessels in the vicinity. Electrolytic lesions, on the other hand, characteristically leave large metallic deposits and frequent small hemorrhages in the tissue surrounding the lesion. These can serve as foci for the irritation of the surrounding tissue. Pulmonary edema, therefore, is quite likely an irritative consequence of the lesion process rather than a "release" phenomenon.

CHANGES IN MALIC DEHYDROGENASE ACTIVITY FOLLOWING FEEDING. R. A. Rhoades and R. R. Nielson (intr. by W. C. McNelly) Miami U., Oxford, O.

In a previous study (Fed. Proc. 19:45, 1960) tissue from rats accustomed to a feeding regime allowing 5 hours of feeding each 24 hours were assayed for changes in succinic dehydrogenase activity during and following feeding. Significant variations in succinic dehydrogenase activity of cardiac and psoas muscles, liver and kidney during a 24 hour period and during a subsequent fast were noted. In the present study Malic dehydrogenase activity (MDA) of the same tissues from rats on a similar feeding schedule were assayed at 15 selected times over a 57 hour period following the beginning of a feeding period to determine the effect of feeding and fasting on MDA. All tissues studied showed a minimal enzyme activity 8 hours following the opening of the feeding cage (i.e., after 5 hours of access to food and 3 hours of fast). During the 24 hour period and the subsequent fasting period liver showed significant variations in MDA. The variations observed during the 24 hour period are referred to as cycling since they repeat themselves each 24 hour period. The cycling shown by the other tissues was not significant. During the 24 hour period MDA fell from 150% of the 8 hour low at the beginning of the feeding period to the 8 hour low value and then increased back to the same value at the end of the 24 hour period. Percentages are based on QO_2 values. When the next regular feeding period was missed, extending the fasting period, liver MDA remained high and increased to a maximum value of 165% of the 8 hour assay at the 29th hour. Changes in enzyme activity of a rather large magnitude and short duration correlated to the time after feeding have been demonstrated for a second citric acid cycle enzyme.

STUDIES ON THE ACCURACY OF VENTRICULAR VOLUME MEASUREMENTS BY THE INDICATOR DILUTION TECHNIQUE. E. A. Rhode*, H. Kines* and J. P. Holt. Heart Research Laboratory, Univ. of Louisville, and Univ. of Calif., Davis.

Evidence has been presented that ventricular volumes measured by the indicator dilution technique are not accurate because of inadequate mixing of indicator with blood in the ventricle. Such volume determinations are dependent on the accurate measurement of ventricular residual fraction and stroke volume. The simultaneous determination of indicator concentration at the aortic root and femoral artery following ventricular injection of indicator should give a measure of any error in stroke volume resulting from inadequate mixing at the aortic root if indicator and blood are assumed to be completely mixed by the time they traverse the aorta and reach the femoral artery. We have carried out 115 simultaneous determinations of indicator concentration at the aortic root and femoral artery on 15 horses, cattle, swine and dogs. In 80 of these injections were made into the left ventricle and in 35 into the right ventricle. Assuming that the measurements at the femoral site are correct, the average deviation and one standard deviation were respectively ±16% and ±20% for left injection and ±13% and ±15% for right injection. It is concluded that the error in the stroke volume measured by the indicator dilution technique at the aortic root is not large, but a more accurate value can be obtained if aortic root and femoral strokes are determined simultaneously. (Supported by USPHS Grants #2075 and HE 05622; and the Ky., Louisville and Jefferson County Heart Associations.)

DIFFERING EEG SLEEP STAGES AND THEIR RESPONSE TO TONE STIMULATION IN THE CHIMP, John M. Rhodes*, W. Ross Adey, Raymond T. Kado*, Martin L. Reite* Space Biology Laboratory, Brain Research Institute, UCLA Medical Center, Los Angeles 24, California.

By the use of stereotaxically implanted electrodes in subcortical areas of the brain and screw electrodes over the cortex it has been possible to study the relationships between cortical and subcortical areas during 30 all-night sleep sessions with three chimpanzees. Clicks were presented at different stages of sleep and averaged evoked responses calculated. The general pattern of sleep stages is similar to that found in humans. In contrast to that found with lower animals, hippocampal leads failed to show reciprocal rhythms with the cortical leads. During "paradoxical" stages two patterns were noted, and could be differentiated primarily by the presence or absence of amygdaloid "spindling". The responses to clicks varied with the different stages and, though decreased, continued to be seen in the "paradoxical" stage. The results suggest: (1) the possibility of a higher level of sleep control for primates than previously thought, and (2) "Paradoxical" sleep may have at least two types, one of which may involve internalization of attention rather than deep sleep. Supported by the following grant: AF-AFOSR 61-81.

MEASUREMENT OF NORMAL MEAN SYSTEMIC AND MEAN PULMONARY PRESSURES IN DOGS. T. Q. Richardson (intr. by Arthur C. Guyton), Dept. of Physiology, Univ. Med. Center, Jackson, Miss.

Mean systemic (MS) and mean pulmonary (MP) pressures have been measured in eight mongrel dogs. One week before measuring MS and MP pressures, the dogs were anesthetized with sodium pentobarbital, and an incision was made along the fourth intercostal space on the left side of the thorax. A large polyethylene loop was placed around the aorta and pulmonary artery immediately adjacent to the heart with one end tied to an anterior rib for anchorage, and the other end placed just under the skin of the back. A small catheter was secured in the left atrium with the distal end placed subcutaneously. Approximately seven days following the surgery, the animals were again anesthetized with sodium pentobarbital, and catheters were placed into the pulmonary artery, right atrium, and femoral artery to measure the respective pressures. A pump was connected to the animals by catheters in the left femoral artery and right femoral vein. Small incisions were made in the skin and the catheter in the left atrium along with the polyethylene tube were brought to the exterior. Pressures were recorded on a Grass polygraph recorder. To measure MS and MP pressures, the dog's heart was fibrillated, and the loop tightened to occlude both the pulmonary artery and aorta. Blood was pumped from the aorta into the inferior vena cava until the pressures reached equilibrium. The equilibrated point was considered to be the MS pressure. The MP pressure was obtained by permitting the left atrial and mean pulmonary arterial pressures to reach equilibrium. These preliminary studies indicate that the normal MP pressure averaged $9.8 \pm .7$ mm. Hg, and the normal MS pressure averaged $6.2 \pm .54$ mm. Hg.

NUCLEOTIDE CHANGES ASSOCIATED WITH UNCOUPLED OXIDATIVE PHOSPHORYLATION IN THE PERFUSED RABBIT HEART. Harold G. Richman, Ulysses S. Seal and Leigh Wyborny (intr. by Y. C. P. Lee). Veterans Admin. Hosp. and Univ. of Minn. Med. School, Minneapolis, Minn.

Albino rabbit hearts were perfused by the Langendorff method in a constant temperature, constant flow system at pH 7.4 with Krebs-Henseleit solution. Perfusate and tissue extract studies were undertaken in both control hearts and hearts in which uncoupling of oxidative phosphorylation was accomplished by use of bishydroxycoumarin. During uncoupled respiration, oxygen uptake increased from resting levels of 1.8 to 4.3 cc/gm/hour. Within ten minutes following loss of respiratory control myocardial nucleic acid efflux occurred without apparent protein breakdown as measured by 260/280 mμ absorption ratios. Spectral analysis of the perfusate indicated presence of varying ratios of adenine and hypoxanthine or their derivatives. Further identification of efflux nucleic acids by chromatography revealed predominantly adenosine. Inosine and occasionally hypoxanthine were also detected in smaller concentrations. Chromatographic analysis of tissue extracts of uncoupled hearts as compared to controls revealed an absence of adenosine despite marked reduction in nucleotide. It would appear that progressive dephosphorylation to adenosine is the primary metabolic alteration of nucleotide metabolism in rabbit myocardium during uncoupled oxidative phosphorylation. Absence of this nucleoside in tissue despite its presence in perfusate would indicate a rapid substantial loss of adenine derivative from the intact cell. No evidence of nucleotide efflux was observed.

PITUITARY-ADRENAL FUNCTION ASSOCIATED WITH AGING IN CATTLE. Gail D. Riegle*, and John E. Nellor. Endocrine Research Unit, Department of Physiology and Pharmacology and Department of Animal Husbandry, Michigan State University, East Lansing.

Pituitary-adrenal function was estimated in dairy and beef bulls, ranging from one month to fourteen years in age, by biological assay of plasma adrenocorticotropic activity and chemical assay of glucocorticoid hormones. Levels of adrenocorticotropic activity were consistently low (less than 1.4 μU ACTH activity/100 ml plasma) and in most instances barely detectable in bulls from one to thirty months of age. Adrenocorticotropic activity increased with age, reaching a peak value of 15.4 μU ACTH activity/100 ml plasma. Substantial amounts of plasma adrenocorticotropic activity were assayed in all animals above three years of age. Levels of plasma Cortisol and Corticosterone ranged between 5 and 12 μg/100 ml plasma and exhibited no consistent alterations related to increased adrenocorticotropic activity. These data are interpreted to reflect abnormal adrenal function during aging, and concomitant increased adrenocorticotropic secretion in order to maintain blood levels of glucocorticoids within the normal range. (Supported by grants from the Benson and Henry Fords; and Smith, Kline & French Laboratories).

ACCLIMATIZATION OF OLDER MEN TO WORK IN HEAT. S. Robinson, H.S. Belding, F.C. Consolazio*, S.M. Horvath and E.S. Turrell*. Indiana University, University of Pittsburgh, U.S. Army Med. Res. and Nutr. Lab., University of California, and Marquette University.

In March 1963, five men, ages 45 to 60, subjected themselves to a repetition of the protocol by which they had demonstrated rapid acclimatization to work in a hot climate in daily exposures 21 years earlier (AJP 140: 168, 1943). The work, heat stress and duration of exposure were those originally found to cause marked hyperprexia and circulatory strain in unacclimatized men on the first day in the heat: 65 to 85 minutes of walking up a grade on a treadmill (metabolism about 6 x basal); 8 oz. cotton twill clothing; ambient temperatures 40°C d.b. and 23.5° w.b.; air turbulent at 55 m/min. Under these conditions, the subjects sweated at 1.3 to 1.5 kg/hr. Tolerance of the men on the first day of exposure was no less than when they were younger; individual patterns of elevation of pulse rate differed somewhat from those of the earlier experiments, but elevations of rectal and skin temperatures were quite similar. Body temperatures and heart rates of the older men were lowered in successive days of exposure and the work was judged progressively easier. Final values reached after 5 to 7 days of exposure were about the same as observed originally after the same number of exposures. Thus, these older men exhibited about the same degree of strain during work in the heat as they did 21 years earlier and acclimatized about as well. (Supported by U. S. Army Medical Research and Dev. Command Grant DA-MD-49-193-63-G91.)

INFLUENCE OF TOTAL BODY RADIATION ON ALKALINE PHOSPHATASE LEVELS IN THE RAT.[1] Leonard M. Rosenfeld*[2], M.H.F. Friedman and Simon Kramer*, (Departments of Physiology and Radiology, Jefferson Med. Coll., Phila.)

An inbred strain of young male Wistar rat of 125 gm. body weight was used. Following total body radiation with LD50/30 dose of gamma rays (725 r. at 79 r. per minute) there was a steady fall in activity of intestinal mucosa alkaline phosphatase. A 40% depression in intestinal mucosa levels of the enzyme was found by the third post-radiation day, with normal values restored by the 10th day. Pretreatment of the animals with dietary supplements of inert bulk materials prevented these changes. After radiation, serum magnesium levels decreased in parallel with intestine alkaline phosphatase but intestinal magnesium levels were slightly elevated. The marked reduction in intestinal mucosa weight which occurred following radiation was also prevented by inert dietary supplements. The post-radiation decrease in intestinal weight could be duplicated by hypophysectomy but not the changes in intestinal alkaline phosphatase.

[1]Supported by U.S. Army Quartermaster, DA-19-129

[2]N.I.H. Predoctoral Fellow in Physiology

METHOD FOR QUANTITATIVE SEPARATION OF MONKEY SKELETAL MUSCLE LIPIDS. Loring B. Rowell*, Edward J. Masoro and Rosa Mae McDonald*. Univ. of Wash. School of Med., Seattle, Wash.

Ninety nine per cent of the total lipid from perfused muscle was extracted by 3-fold blending in chloroform-methanol (1:1). Water soluble contaminants were removed by a specifically developed wash system. Column silicic acid chromatography of the purified lipids yielded 5 fractions. Fraction I contained neutral lipids and was subfractionated into cholesterol, cholesterol esters, triglycerides, diglycerides, and monoglycerides by further silicic acid column chromatography. Fraction II contained phosphatidic acid-polyglycerophosphatide class of lipids and phosphatidylethanolamine. Quantitative separation was by means of specifically developed thin layer chromatography (TLC). Fraction III contained phosphatidylserine, phosphatidylinositol, glycolipid, and phosphatidic acid-polyglycerolphosphatide class of lipids. Quantitative separation was by means of specifically developed TLC. Fraction IV contained only lecithin. Fraction V contained lecithin and sphingomyelin which were quantitatively separated by TLC. Skeletal muscle contained about one per cent lipid (wet weight). Approximately fifty per cent of this is neutral--primarily cholesterol and triglyceride. The predominant phospholipids are lecithin and phosphatidylethanolamine. There were also considerable quantities of phosphatidylinositol, phosphatidylserine, sphingomyelin, and some glycolipid. The plasmalogen to lipid phosphorous ratio is approximately 0.2. Plasmalogen was found primarily in phosphatidylethanolamine and to a lesser extent in lecithin.

BOUND NUCLEOTIDES IN STRIATED MUSCLE. Jacob Sacks. Department of Chemistry, University of Arkansas, Fayetteville.

Resting and stimulated muscles of cats were frozen in situ and the frozen powder extracted with 80 per cent ethanol containing 0.001 M EDTA, at low temperature, to extract the free nucleotides and other free P compounds. The protein-bound nucleotides were extracted by treating the residue with trichloroacetic acid. It was found that essentially all the ADP and the greater part of the ATP were apparently bound to protein. Tetanic stimulation did not lead to any increase in the proportion of free nucleotides. The amount of ADP present is consistent with the literature value of one mole of ADP bound per mole of actin monomer. Since only F-actin binds ADP, this suggests that all the actin present in resting muscle is as F-actin, and therefore that the conversion of G-actin to F-actin is not a factor in the contraction process. The amount of bound ATP is much greater than can be accounted for on the basis of 1:1 binding with the lowest molecular weight protein of the contractile elements. The indication of multiple binding sites of ATP can be taken as a mechanism for maintaining the ordered structure of the fiber indicated by electron microscope studies. This work is supported by grant No. AM-07273 of the National Institutes of Health.

LACTATE CONCENTRATION OF THE INNER MEDULLA OF THE RAT KIDNEY. Peter R. Scaglione* and Robert W. Winters. Dept. of Pediatrics, Columbia Univ., College of Physicians & Surgeons.

Previous work in in vitro systems indicates that the inner medulla of the kidney relies largely upon anaerobic glycolysis for energy needs. In an effort to study metabolic activities of this tissue in vivo, concentrations of lactate in inner medulla and cortex have been measured under varying conditions of urine flow and concentration. In antidiuretic control rats, medullary lactate concentration was nearly twice that of the cortex. During osmotic diuresis induced with either mannitol or urea, cortical lactate remained unchanged while medullary lactate showed a nearly two fold increase over control values. In water diuresis both cortical and medullary lactate were not significantly different from values observed during antidiuresis. Blood lactate did not vary under any of the conditions studied. Theoretical considerations suggest that the concentration of lactate in the inner medulla is directly related to the rate of glycolysis and inversely related to the nth power of the blood flow where n is between 1 and 2. Thurau et al. (Pflug. Arch. Physiol., 270:270, 1960) have shown that the rate of medullary blood flow increases in both osmotic and water diuresis. Our observations that inner medullary lactate in water diuresis is not different from control, indicate that lactate production is increased. The fact that medullary lactate actually rises in osmotic diuresis indicates a striking augmentation of glycolysis in this condition. Conceivably these increased rates of glycolysis reflect increased rates of sodium transport by the loops of Henle secondary to augmented delivery of sodium to the loops or to a "washout" of medullary interstitial sodium effected by the increase in medullary blood flow. (This work was supported by the Health Research Council of the City of New York under contract #U-1127).

INFLUENCE OF PILOCARPINE ON Na-22 EXCHANGE IN SUBMAXILLARY GLAND SLICES. L. H. Schneyer and C. A. Schneyer. Univ. of Alabama Med. Ctr., Birmingham, Ala.

Slices of rat submaxillary gland show appreciable net gain of sodium and loss of potassium during incubation for 20 min at 37 C in Krebs-Ringer-phosphate gassed with N_2 (Phase I). During subsequent incubation with O_2-gassing (Phase II), but with other conditions unchanged, slices actively extrude sodium and reaccumulate potassium (Am. J. Physiol. 203: 567, 1962). With pilocarpine present during Phase II, net extrusion of sodium and reaccumulation of potassium appear reduced (Fed. Proc. 22: 445, 1963). The effect of pilocarpine on exchange of sodium during Phase II has now been examined using Na-22. It was ascertained, first, that tissue total sodium was essentially at steady state levels by 10 min after start of Phase II in absence of pilocarpine, and by 30 min when 2×10^{-5} M pilocarpine was present. When slices were loaded with Na-22 during Phase I and washout was followed during Phase II, it was apparent that pilocarpine did not affect rate of loss of Na-22 between 30 and 60 minutes after washout was started. Inward movement of Na-22 during Phase II, however, was affected by pilocarpine. Loading of cells during 10 min exposure to Na-22 was generally increased 50-100 percent by pilocarpine. It is concluded that the observed reduction in net efflux of sodium, produced by pilocarpine during Phase II, results principally from an increase in inward transcellular movement of sodium. (Supported by a grant from NIH.)

A THYROID REBOUND PHENOMENON. E. Schönbaum*, V. Row*, E. A. Sellers and McA. Johnston*. Depts. of Pharmacol. and Medicine, Univ. of Toronto, Canada.

Male Wistar rats were fed a diet of powdered chow (total I 1.6 μg/g) and 1.25% of $KClO_4$ (PC) for more than 1 year. 48 hrs. after 50 μc of I-131 the rats were killed and serum extracted with n-BuOH. Paper chromatography of the purified extracts showed values of T_4 - 21%, T_3 - 14% of the I-131 on the paper. Values for rats fed 25 μg% T_4 (in diet) plus PC were 26% and 8%. Rats on chow only yielded 4% as T_4, but T3-I-131 was not detectable. Serum PBI's of similar rats were 2.0, 3.1 and 3.3 μg%; approx. I-131 uptakes (48 hrs) of thyroids were 0.6%, 0.2% and 7.3%. Results obtained with a diet of Ken-L-Kibble, salt-free + 1% NaCl, total I 0.25 μg/g were: PC alone - 13% T_4 and 11% T_3; PC + T_4 in diet - 4% T_4 and 5% T_3. In the group fed chow + PC, T_4 reduced thyroid weights from 142 to 98 mg, while in the Ken-L-Kibble group T_4 increased weights from 98 to 173 mg per rat. These data form part of a long-term study of effects of goitrogens, with and without T_4, on thyroid function and TSH levels. They generalize the finding, reported earlier for PTU, that T_4 can enhance thyroid growth. It is apparent that the feed-back mechanism may be positive as well as negative. Supported in part by a grant from the J. P. Bickell Foundation.

NEUROMUSCULAR ACTIONS OF SEROTONIN FOLLOWING PARTIAL CURARIZATION. Robert T. Schopp and Elaine M. Rife*. Department of Physiology, University of Colorado School of Medicine, Denver, Colorado.

Serotonin possesses the ability to influence transmission at a variety of junctional sites although it is reported to be without effect at the skeletal neuromuscular junction. We are in general agreement with the latter observation as applied to a normal system, however, pretreatment with curare provides a preparation sensitive to the influence of serotonin. When a small amount of serotonin creatinine sulphate (0.1 μg/Kg) is administered by close intra-arterial injection in the partially curarized, indirectly stimulated, dog peroneal-tibialis anticus nerve-muscle preparation a slight to mild antidepressant action on muscle contractions is noted. Increasing the dose level to 1.0 μg/Kg yields a prominent long-lasting anti-curare response. Injection of 1.0 mg/Kg induces first a transient depression of muscle contractions followed by an appreciable anti-curare action of long duration. Thus, although serotonin is essentially without effect on nerve-skeletal muscle transmission in the control preparation it does increase muscle contractions after partial curarization at rather low dose levels and larger amounts of serotonin cause an immediate transient curariform response succeeded by a longer-lasting anticurare action.

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

A METHOD TO STUDY MICROCIRCULATION IN MAN. M. Stephen Schwartz*, Harbans Singh*, Edward Messina* and Walter Redisch. NYU Res. Service, Goldwater Mem. Hosp., Welfare Island, New York, N.Y.

Revival of capillary microscopy and photography in man appeared warranted with increasing evidence of small vessel disease in mesenchymal disorders. With up to 220 x magnification and 1/1000 of a second exposure, good color pictures are obtained from any part of the body integuments. First, range of physiologic variations in the appearance of surface capillaries in man has been established. In Systemic Progressive Sclerosis (Scleroderma) minute vessels show persistent morphologic and flow deviations from the norm; the same deviations (giant loops, sluggish flow) are seen in certain cases of Raynaud's. Evaluation of distinctive peculiarities of microcirculation in Rheumatoid Arthritis and Systemic Lupus Erythematosus will only be possible after accumulation of a larger series. In untreated and in "brittle" diabetics, a lake-like widening of the transitional limb has been found persistently, possibly related to "microaneurysms"; correlation with clinical and laboratory parameters is attempted. The number of microvessels is markedly increased in Polycythemia, the channels are choked with cells and flow is extremely slow, its pulsatile quality lost; after bleeding, the number of vessels diminishes and flow rate increases. Studies of microcirculation in pulmonary osteo-arthropathy and in experimental homografts are under way. It is expected that basic patterns of disturbances in microcirculation may be established from this type of study.

EFFECT OF ACUTE OVARIECTOMY DURING THE RAT ESTROUS CYCLE ON PITUITARY LH. Neena B. Schwartz. Dept. Physiol., Univ. Ill. Coll. Med., Chicago, Ill.

Indirect evidence indicates that a neural facilitation for release of the ovulatory surge of LH occurs daily between 2 and 4pm in the rat but LH release occurs between 2 and 4pm only on the day of proestrus. To test the hypothesis that a positive ovarian hormonal feedback synergizes with the "clock" facilitation to cause LH release, advantage was taken of the observation that pituitary LH drops between proest 10am (9.3γ) and est 10am(3.8γ), accompanied by vaginal cornification(VC) and ovulation at est. The procedure followed was to ovariectomize at proest 10am, or at 4pm or 10am of the preceding day(diest), and autopsy at "est"10am(24,42,48 hrs. post-op) to see if the normal drop in LH between proest and est was prevented. Preliminarily it was shown that pentobarbital (30mg/kg) given at proest 2pm blocked ovulation in 8/8, correlating with a LH content at "est" 10am of 8.1γ. Ovariectomy at proest 10am yielded "est"LH contents of 6.6γ, 13/15 showing VC. Ovariectomy at diest 4pm yielded LH contents at "est" of 7.8γ, 3/12 showing VC. Ovariectomy at diest 10am yielded LH contents of 9.0γ at "est", 0/10 showing VC. Sham ovariectomy at proest 10am or diest 4pm did not alter the usual est VC, ovulation or low LH. However, sham ovariectomy at diest 10am gave variable results with respect to all three measures at est. As "time after ovariectomy" controls rats were ovariectomized at 24,42, or 48 hrs. before autopsy at diest. These rats showed a consistent gain of 3γ/pit from met to diest, suggesting that increasing time after ovariectomy *per se* could not account for the changes in pituitary LH occurring when ovariectomy is carried out at increasing intervals before the proest"2-4pm" facilitation. These results suggest that the ovary must be *in situ* during the day of diest in order for the proest LH release to occur. (Supported by Grant AM-06145,PHS.)

RETINOTOPIC PROJECTION OF THE OPTIC TECTUM IN FISH. Horst Schwassmann* and Lawrence Kruger. Dept. of Anatomy, UCLA Center for Health Sciences, Los Angeles, Calif.

Several fresh-water fish were studied in an apparatus designed to reduce refractive errors when visual stimuli were presented. Animals were anesthetized and the optic tectum was exposed for exploration in 0.5 mm steps, by recording massed unit discharges with a large steel microelectrode. A precise point-to-point projection of visual fields was found for all points on the tectum. The dorsal fields are represented on the dorsomedial surface, ventral fields on the lateroventral surface, nasal fields anteriorly and temporal fields posteriorly. Within the receptive field for a given recording point, shortest latencies were found in the center of the field and an independent late discharge (over 100 msec.) was found in the surround. Stimulus properties for driving single units were also studied. (Supported by USPHS Grants B-2684, NB 4578 and Fellowship BPD 15,886)

AUTOREGULATORY, REACTIVE HYPEREMIC, AND THE VENOUS-ARTERIOLAR RESPONSES IN THE INTESTINAL VASCULAR BED OF THE DOG. J. B. Scott and J. M. Dabney (intr. by M. J. Keyl). University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

The effect of perfusion pressure, venous pressure, and flow upon resistance to flow and gut activity was studied in the ileum. Pressure was measured in the lumen of an *in situ* closed length of ileum (avg wt 51 g) while measuring venous outflow or controlling arterial inflow (pump). With both techniques, blood flow averaged 0.28 ml/min/g at an arterial pressure of 100 mm Hg. In 7 of 12 pump perfused preparations, resistance increased as a function of flow rate. Following a period of no flow (pump off), perfusion pressure was less than control. The magnitude and duration of the post-ischemic hypotension progressed with the duration of ischemia. Periods of ischemia often produced increased intestinal activity which tended to decrease the amount of post-ischemic hypotension. On the average, elevation of venous pressure by 17 mm Hg at constant arterial inflow failed to decrease resistance. Elevation of venous pressure by 14 mm Hg while measuring venous outflow at constant arterial pressure also failed to decrease resistance. Sometimes arterial occlusion failed to produce reactive hyperemia in the venous outflow preparation. These findings indicate that the intestinal vascular bed autoregulates, exhibits a venous arteriolar response, and exhibits reactive hyperemia. The degree of the latter is often influenced by increased intestinal muscle activity.

FUNDAMENTAL FUNCTION OF Ac-GLOBULIN AND LIPID IN BLOOD CLOTTING. Walter H. Seegers, Edmond R. Cole* and Nobuo Aoki.* Dept. of Physiol. and Pharm., Wayne State Univ., Coll. of Med., Detroit, Mich.

To find out more about the way Ac-globulin and lipids function work has been directed toward the isolation of Ac-globulin from bovine plasma. A 1000-fold purification has been achieved, and nearly a single component is represented. Ac-globulin is a co-autocatalyst. It was studied with the use of purified prothrombin, thrombin, autoprothrombin C, and autoprothrombin J. The conversion of prothrombin to thrombin is fundamentally an autocatalytic process in which either enzyme from prothrombin may be the catalyst. The Ac-globulin alters the substrate specificity of the enzyme so that there are different degradation products of prothrombin in the presence of Ac-globulin than in its absence. The lipids are nonspecific in their function and accelerate the complex interactions of the enzyme with substrate. Thrombin and autoprothrombin C come from prothrombin and catalyze the conversion of prothrombin to thrombin providing Ac-globulin is present. Ac-globulin is a co-autocatalyst. It cannot properly be called a coenzyme since these generally are small molecules and Ac-globulin is a protein.

ORGANIZATION OF NEURONAL GROUPS INFERRED FROM ANALYSIS OF SPONTANEOUS ACTIVITY PATTERNS. J.P. Segundo and G.P. Moore. Brain Research Inst. and Dept. of Anatomy and Physiology, UCLA.

Extracellular recordings of spikes per se tells us nothing about the sub-threshold activity of the monitored cell or the intrinsic connectivity of the region. Intracellular records obtained in isolated visceral ganglia of Aplysia californica permitted simultaneous observation of spike and subthreshold (PSP, pace-maker) potentials of single neurones. By identifying separate PSPs it was possible to describe the activity of each cell influencing the impaled unit. From these observations and from previous knowledge of the types of activity present in the ganglion one could infer the existance of cell-groups the organization of which could be specified in terms of inter-connections, signs (excitatory, inhibitory) and spike activities (pace-maker, burst-like, etc.). The following examples are illustrative of the inferences that are possible. 1) That the output from the observed cell influences its own input. 2) That one or more input sources, and the observed cell itself, interact with each other. 3) That a single neurone constitutes an input source for many neurones. 4) That the observed cell was under the influence of a pre-synaptic cell, itself subject to a third cell, whose activity could be specified in terms of temporal distribution and sign. Relations observed in Aplysia may be applied, tentatively at least to situations where only the spike discharge is visible. USPHS # M-5183; NSF # G-21497.

THE IN VIVO EFFECTS OF HISTAMINE AND BENADRYL ON THE PERISTALSIS OF THE CANINE URETER AND PLASMA POTASSIUM LEVELS. J. Sharkey*, S. Boyarsky and J. Martinez*, Albert Einstein College of Medicine, New York (61).

Ureteral peristaltic pressures were recorded on electronic recorders in anesthetized large female dogs with previously explanted bladders. The potent stimulating effect of histamine upon ureteral peristalsis and a similar effect by benadryl has been reported previously. Further comparison of the effects of the two drugs showed that to raise ureteral peristaltic frequency 1.5—2x requires 500x the dosage of benadryl over that of histamine mol. for mol. Benadryl effect (0.61 mgm/kg i.v.) includes shortening of the interperistaltic interval with unchanged duration of contraction. Histamine (5–40 mcg/kg i.v.) increases frequency 2-3x with shortening of the duration of contraction and interperistaltic interval. Fifteen seconds to two hours before histamine, in i.v. doses below 2 mgm/kg, benadryl had no demonstrable effect on peristaltic frequency but did inhibit histamine action. Benadryl did not alter the histamine effect once commenced. Above an i.v. dosage of 2 mgm/kg, both the ureter-stimulating effect and the histamine-inhibitory effect appear. The histamine and benadryl dose-response curves and double-reciprocal plots were analogous to the Michaelis-Menten equation for enzyme-substrate interaction, and enzyme-substrate inhibition. Benadryl shows competitive inhibition as a weak, sluggish histamine agonist. Both substances caused temporary elevation of serum K^+ immediately following the muscular response. [NIH Grant # GM 05986-05.]

GASTRIC-CAUDATE RELATIONSHIP: ITS IMPLICATIONS IN FOOD INTAKE K. N. Sharma and S. Dua (intr. by Harry L. Jacobs), Dept. of Physiology, All India Institute of Medical Sciences, New Delhi.

Electrical activity from caudate was recorded through chronically implanted bipolar electrodes in Nembutal anaesthetised and in freely moving cats. Test solutions were administered through intragastric tubes and a water filled balloon system was used for gastric distention. Graded distention of the stomach caused a marked drop in voltage with or without an accompanying increase in frequency. The change in activity appeared within a second or so of the gastric distention and continued from about 10 sec to 1-3 min. Infusion with 10-12 ml of 5.4% glucose solution evoked a similar response but the latency and the duration were, in general, longer than that obtained after gastric distention. Electrical activity remained unchanged after intragastric infusions of 0.9% NaCl solutions. The changes observed after gastric distention or infusion with glucose were obtained from medio-marginal regions of the head of the caudate; and were observed in freely moving cats but were not seen in the anaesthetised preparations. Moving the gastric tube up and down the oropharyngeal regions often evoked spike discharges recorded from medial regions of the head of the caudate. The results indicate that caudate may be involved in short term satiation of hunger via "stomach receptor" mechanisms. Further studies are in progress to investigate the relationship between caudate and the hypothalamic hunger and satiety "centers."

DISTRIBUTION OF EEG ACTIVITY CYCLE EFFECTS ON AUDITORY EVOKED RESPONSES. Guy C. Sheatz (Introduced by Felix Strumwasser) WRAIR, Wash., D.C.

Auditory evoked waveforms averaged from the spontaneous EEG (by the computer of average transients, "cat") reveal diverse patterns of structure and amplitude throughout cortical and subcortical areas. These patterns undergo repeatable alterations in wakefulness and sleep. In most areas, amplitudes increase during sleep. An attempt has been made to correlate amplitude changes with a factor derived from amplitude-frequency measurements of corresponding samples of spontaneous EEG. Failure to correlate is more marked at cortical than at subcortical levels. Examples from all functionally defined areas of the brain will be presented.

ABILITY OF DENERVATED HEART IN VIVO TO MAINTAIN OUTPUT AGAINST INCREASED RESISTANCE. J. T. Shepherd and D. E. Donald, Mayo Clinic, Mayo Foundation, Rochester, Minnesota.

The intrinsic ability of the heart to maintain output when confronted with a sudden increase in aortic pressure was studied in dogs with chronic cardiac denervation. Increases in aortic pressure were obtained by bilateral occlusion of the common carotid arteries in awake and anesthetized dogs, and by obstructing the aorta at the arch with a balloon catheter in anesthetized dogs. During carotid occlusion there was sustained elevation of arterial systolic and diastolic pressure (mean pressure rise 40 mm. Hg or more), a sustained elevation of left atrial pressure (mean pressure rise 5 cm. H_2O) but little change in right atrial pressure. Cardiac output (dye dilution and electromagnetic flowmeter around pulmonary artery) remained at or above the control level. In the normal dog during carotid occlusion, left atrial pressure was unchanged and cardiac output was maintained at the preocclusion value. With obstruction of the aorta, there was a sustained doubling of systolic but little change in diastolic pressure proximal to the balloon. Left atrial pressure rose by 8-12 cm. H_2O but returned to near control values after 25 seconds of obstruction. There was little change in right atrial pressure. Cardiac output was maintained at control level throughout the period of test. (Supported in part by NIH Grant H-6143).

EFFECTS OF ACUTE POTASSIUM DEPLETION ON RENAL CATION EXCRETION, Robert R. Siegel* & William D. Lotspeich, Dept. of Physiology, U. of Rochester Med. Sch. (Spon: A.B. Craig, Jr.)

Investigations initiated to determine the effect of rapidly-induced hypokalemia on renal ammoniagenesis, revealed early changes limited mainly to Na and K excretion. Dogs under pentobarbital anesthesia were dialyzed on a Kolff artificial kidney, (1) against control bath, then (2) low (K^+) bath, at constant weight, during mild mannitol diuresis. Pump regulation of ventilation, prevention of blood volume changes, and maintenance anesthesia by constant infusion limited GFR and blood pH variation. During control periods, urinary (K^+) remained stable, K excretion varied with urine flow; urinary Na varied directly with GFR. Urinary (K^+) decreased promptly on starting depletion, and declined in parallel with plasma (K^+). Urinary Na rose as K fell. When filtered Na load remained stable during K depletion, the sum of Na + K excretions tended to remain at starting values, and urine osmolality did not vary significantly. Urine pH and ammonia did not change in response to K depletion over 160-240 minutes. The reciprocal, and apparently equivalent changes in Na and K excretion suggest interference with a tubular Na-K exchange site as K depletion advances. The promptness of the response argues against hormonal mediation but this remains to be tested experimentally. (supported by a Buswell Found'n Senior Post-Doctoral Fellowship and USPHS grant #1-GS-103).

CORTICOTROPIN INDUCED INCREASE IN THE MITOCHONDRIAL RIBONUCLEIC ACID IN RAT ADRENALS. Morton B. Sigel* and J. Thomas Dowling
King County Hospital and University of Washington School of Medicine, Seattle, Washington.

The widespread effects of corticotropin (ACTH) on adrenal intermediary metabolism suggests that many are adaptive cellular responses to an antecedent primary stimulus. Several are not specific for ACTH since other peptide hormones and humoral agents evoke them. Considering the importance of nucleotide metabolism to enzyme production, the specificity of the *in vivo* response of adrenal nucleic acids to ACTH was assessed. Ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) were measured in subcellular fractions of pooled adrenals removed from rats 4 hours after injection of several agents. After 2 units of ACTH mitochondrial RNA, in terms of gland weight, increased 30% over that of saline injected animals and 74% over uninjected controls. Nuclear DNA and nuclear and microsomal RNA were unchanged under these conditions. Thyrotropin (2 u) growth hormone (1 u), chorionic gonadotropin (500 u), triiodothyronine (25 ug.) and p-dinitrophenol (50 ug.) failed to affect either nucleic acid. The mitochondrial:adrenal weight ratio increased only in ACTH treated animals. The percentage increment of mitochondrial RNA exceeded that of the weight increment three-fold. A part of the sequential response of adrenal intermediary metabolism to ACTH thus includes alterations in nucleic acid content of the organelle associated anatomically with steroidogenesis.

CARBONIC ANHYDRASE INFLUENCE ON CALCIFICATION. R. Simpson* (Spon: A. B. Taylor). Dept. of Physiology, University of Illinois, Urbana, Illinois.

Recent in vitro work suggests that carbonic anhydrase may influence calcification. Experiments were carried out to ascertain whether this system functioned in vivo. Rickets were induced in rats and subsequently calcification was initiated by administration of vitamin D. Test groups were treated with various dosages of acetazolamide. After the treatment period, calcification in the tibial epiphyseal plate was assessed by measuring the width and brightness of the calcium deposit on radiographs of the rats' legs. The width was measured by using vernier calipers, and the brightness by comparison with an x-ray of an aluminum step gauge. The arbitrary intensity figure was multiplied by the width in millimeters for obtaining values useful in statistical analyses. Using the Mann-Whitney 'U' test, inhibition was observed which was significant at the 0.1 level in 5 of the groups. Biochemical analysis was carried out and carbonic anhydrase was found to be present in costal cartilage. The evidence seems to indicate that carbonic anhydrase does influence the calcification process in the mammalian skeleton.

EFFECT OF HIGH AND LOW FREQUENCY STIMULATION OF LIMBIC STRUCTURES ON PLASMA CORTICOSTEROID LEVELS IN UNANESTHETIZED RATS. Margaret A. Slusher. Brain Research Institute and The Center for Health Sciences, University of California, Los Angeles, California.

In unanesthetized, unrestrained male rats bearing a chronically implanted electrode in the CNS, blood was collected through a previously implanted venous catheter for the fluorimetric analyses of plasma corticosteroid levels. On each of three experimental days, individual samples were taken at 9 and 10 a.m. and 5 p.m. On day 1, normal circulating corticosteroid levels were determined for each of these time periods. On days 2 and 3, blood samples were taken at 9 a.m. for determination of control levels; at 9:45 a.m. rats were stimulated for 1 minute, in one of several structures of the limbic system or associated areas, at 0.5 volts with either low (6/sec.) or high (200/sec.) frequency. Plasma corticosteroid levels were determined 15 minutes post stimulation (at 10 a.m.), and at 5 p.m. Preliminary results indicated high frequency stimulation through electrodes aimed for the hippocampal commissure, septum, or habenulo-peduncular tract was more effective than low frequency in eliciting a significant rise in corticosteroid levels 15 minutes post stimulation. On the other hand, stimulation with either low or high frequency, through some similarly placed electrodes, while ineffective in increasing corticosteroid levels at 10 a.m., resulted in an inhibition of the normal 5 p.m. rise (diurnal). These data suggest that various components of the limbic system involved in the rapid release of ACTH are specifically activated by high frequency stimuli, whereas those involved in modulation of the diurnal variation of plasma corticosteroid levels are responsive to stimuli of both high and low frequency.

THE EFFECT OF HEMORRHAGIC HYPOTENSION ON OXYGEN CONSUMPTION OF DOGS. Elvin E. Smith* and Jack W. Crowell. Univ. Med. Center, Jackson, Miss.

The effects of hematocrit, Dibenzyline, and epinephrine on oxygen consumption have been studied in 209 dogs whose arterial pressure was lowered to and maintained at 30 mm. Hg. Oxygen consumption was recorded previous to and during the period of hypotension. The average oxygen consumption was 7.20 cc/kg/min. prior to hemorrhage. After 30 minutes of hypotension the oxygen consumption was 4.70 cc/kg/min. (65% of control) and the oxygen consumption increased to 5.33 cc/kg/min. (74% of control) after one hour. Dibenzyline increased the oxygen consumption during the early stages of hypotension but had little effect in the latter stages. Epinephrine decreased the oxygen consumption during the entire hypotensive period. Previous studies have shown that the oxygen utilization coefficient approaches its maximal value during the hypotensive period; therefore, oxygen uptake becomes limited by the blood flow and the changes in oxygen consumption indicated changes in flow rate to active tissue. Simultaneous studies showed that the hematocrit influenced oxygen transport by effects on both the blood oxygen content and the blood flow. The results illustrate that animals with hematocrits of 35-39 are able to transport more oxygen than animals with other hematocrits. When the hematocrit is lower than this range the flow is high, but the oxygen content is low. When the hematocrit is higher than this range, the oxygen content is high, but the flow is low. (Supported by the U. S. Army Medical Research and Development Command, Dept. of the Army, Research Contract No. DA-49-193-2219.)

THE ACIDITY OF GASTRIC CONTENTS OF MACACA MULATTA. G. P. Smith and J. W. Mason (intr. by F. Strumwasser). Walter Reed Army Institute of Research, Washington, D. C.

Three Macaca mulatta male monkeys (4-5 kg.) were equipped with chronic gastric fistulae and maintained in restraining chairs within completely enclosed booths for 6 to 9 months. We collected their gastric contents for periods of 3 to 8 hours, using constant suction. During a minimum total of 30 one-half hour collection periods obtained on at least 6 different days, the following secretory profiles emerged for the 3 monkeys respectively: Volume in cc./30 min.: 5.2 ± 0.4*, 3.7 ± 0.8, 5.0 ± 0.3; pH: 1.6 ± 0.1, 2.6 ± 0.1, 2.1 ± 0.7; "free" acid (pH 3.5) in mEq./l.: 71.4 ± 4.2, 24.7 ± 3.2, 33.1 ± 0.5; and "total" acid (pH 7.0) in mEq./l.: 85.3 ± 11.9, 46.9 ± 3.1, and 43.5 ± 2.5. No seasonal variation of the acidity occurred in one monkey studied from August through April inclusive. Less extensive observations in 3 other mulatta macaques with chronic gastric fistulae and in 2 others with innervated fundic pouches revealed similar acidity of gastric contents. Our method of collection of gastric contents produces little or no increase in urinary 17-OH corticosteroid values. Our data suggests that when the gastric contents of M. mulatta are collected under conditions of minimal environmental disturbance, "free" acid is usually present.

*values are the mean ±S.E. of the mean.

The Effect of Ions on the Birefringence of Electrically Polarized Crayfish Nerve. H. M. Smith and Samuel Gaston*, U. Arkansas Med. Center, Little Rock, Arkansas.

Electrical polarization of crayfish nerve results in a prompt decrease in positive birefringence at both anode and cathode with metatropic reversal at the anode. The rate and degree of this decrease depends upon the strength of current. The development of the loss of birefringence also depends in part upon the ionic species in the ambient salt and water medium. In a chloride-free medium the decrease occurs promptly; in sodium-free medium the anodal decrease is delayed for 5 to 10 minutes. In a potassium-free medium the cathodal phenomenon is enhanced in degree and rate of development, but there is a delayed change at the anode. In calcium-free solution the anodal change develops most rapidly and extensively whereas there is no decrease at the cathode. In 0.2 M KCl the birefringence decreases uniformly, with a further decrease at the anode when the nerve was electrically polarized. In 0.16 M $CaCl_2$ the change was similar to the control. Hydrogen ion over a pH range of 4.5 - 8.5 does not influence the usual polar changes. Calcium in association with a positive ion migrates to the anode during polarization. It is concluded that the polar changes in the nerve protein structure are in part a function of potassium and calcium concentration. Supported by a grant from NIH.

Antral Humoral Mechanisms: Inhibition of Atropine Induced Gastric Antral Inhibition by Pontocaine. H. Sosin, M. D. *, E. F. Bernstein, M. D. *, and O. H. Wangensteen, M. D. (intr. by Dr. J. King) Dept. of Surgery, Univ. of Minn. Hospitals, Minneapolis 14, Minnesota

Acid inhibition of acetylcholine (ACH) induced secretion has recently been shown to be blocked by local application with pontocaine. These studies depict the site of action of ACH and assess the effect of pontocaine upon atropine inhibition of ACH induced secretion. In dogs with Heidenhain pouches and antral fistulas, HCl secretion was studied during (1) control periods of 0.2% ACH stimulation by continuous antral irrigation and (2) test periods of 0.2% ACH stimulation with and without 5% pontocaine hydrochloride (5 cc/15 min) added to the irrigating solution. Local antral atropinization with 0.1% atropine (15 cc.) for 15 minutes intervened between control and test periods. ACH induced gastric secretion is markedly inhibited by local application of atropine. When 5% pontocaine is added to the ACH following atropinization, secretion returns toward control values (12/18), and in some instances attains levels higher than control values. Pontocaine is not a gastric secretory stimulant, as shown by experiments using only saline and pontocaine. Cocaine and procaine have not been observed to have this effect. The mechanisms of these effects are as yet unknown. These effects are not systemic but originate locally within the gastric antrum. These findings provide a useful tool for the further elucidation of antral humoral mechanisms.

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The Absorption of Calcium in Osteoporosis. H. Spencer, J. Menczel*, I. Lewin* and J. Samachson*. Metabolic Sec., V.A. Hosp., Hines, Ill.

The metabolic effects of adding calcium to the diet for time periods ranging from 1 1/2 to 4 years were studied under controlled dietary conditions in 3 patients with osteoporosis. The mineral and protein metabolism of these patients was studied first in the low calcium control phase. Thereafter, calcium was added in the form of calcium gluconate tablets to the constant diet. In both phases of calcium intake, balances of calcium, phosphorus and nitrogen were performed as well as radioisotope studies using Ca^{45} and Sr^{85} as tracers. The endogenous fecal calcium excretion was determined by the balance and radioisotope technique. The addition of calcium to the diet resulted in a very high excretion of calcium with the stool. The high fecal calcium excretion during calcium supplementation was due to the passage of unabsorbed calcium, suggesting poor absorption of calcium from the intestinal tract. The utilization of the added calcium was low and ranged from 11 to 15% as compared to the utilization of 30% in patients of the same age group without clinical and roentgenological signs of osteoporosis. Calcium 45 absorption decreased during high calcium intake in all three patients.

IDENTIFICATION OF THE ORGANELLE WHICH SYNTHESIZES THE STABLE CARDIAC RELAXING SUBSTANCE. Allan C. Stam, Jr.*, Bernard J. Panner* and Carl R. Honig. Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Canine cardiac granules produce a soluble relaxing substance (RS), stable on prolonged storage at -15°C. We sought to determine the optimum G-time product for granule isolation and to characterize the granules by electron microscopy. Lt. ventricular homogenates were centrifuged at $9x10^3$Gxmin. and granules collected from the supernatant at 8 G-time products between $6x10^4$ and $1.2x10^7$Gxmin. Granules were incubated with 5 mM ATP for 20 min then separated from the RS elaborated during incubation by centrifuging at $1.8 x10^8$Gxmin. RS activity was assayed as inhibition of Mg-stimulated cardiac myofibrillar ATPase. The optimum range for collection of the active granule was $6x10^4$ to $5x10^6$ Gxmin., but all preparations produced some activity. Granules were heterogeneous, and varied in proportion of mitochondria, myofilaments, and small single and double membraned vesicles. Homogenized mitochondria do not provide either the active particle or an essential soluble co-factor. Activity was not influenced by incubation with KF or low Mg. Although the origin of the small vesicles could not be determined by microscopy alone biochemical and morphologic observations together suggest that the endoplasmic reticulum synthesizes a stable cardiac RS.

STUDIES ON ACUTE PULMONARY EDEMA DUE TO ELEVATION OF VASCULAR PRESSURE
N.C. Staub, H. Nagano*, M.L. Pearce*, Y. Sagawa*, and T. Nakamura*. Cardiovasc. Res. Inst., Univ. of Calif. Sch. of Med., San Francisco.

We previously reported that acute pulmonary edema induced by alloxan appears to alter pulmonary capillary permeability directly. (H. Nagano, Fed. Proc. 22:396, 1963). In the present series we induced acute edema by infusions of dextran, blood and epinephrine. Using CO techniques, we measured pulmonary diffusing capacity (D_L), pulmonary capillary blood volume (Vc) and alveolar capillary membrane diffusing capacity (D_M). We also monitored pulmonary arterial (P_{pa}) and left ventricular end diastolic (LVED) pressures and measured cardiac output ($\dot{Q}$) and extravascular water space (ΔQ_{THO}) by indicator dilution methods. We froze some lungs with liquid propane at the end of the experiment to determine the structural basis for the functional changes observed. In 5 control dogs Vc, $\dot{Q}$ and ΔQ_{THO} remained stable for the duration of the experiment (2 hours). In 9 experimental dogs control measurements were followed by rapid intravenous infusions and slower maintenance infusions. Vc and $\dot{Q}$ increased and D_M decreased as soon as measured after the initial infusions. Changes in Vc correlated well both with LVED and mean P_{pa}. ΔQ_{THO} increased slightly at first, but after 1 hour large changes were measured. Histologic studies revealed some clear fluid in alveoli and perivascular lymph channels (primary fluid), but this was often masked by gross hemorrhage into the lower zone of the lung. Finding that D_M decreased and ΔQ_{THO} increased slightly while Vc increased suggests that there is a stage of interstitial edema or an increase in the alveolar fluid lining layer before gross alveolar filling occurs. (Supported in part by PHS Grant HE-06285 and ONR contract 222 (55).

THE EFFECT OF BRAIN LESIONS ON EEG CORRELATES OF ALIMENTARY BEHAVIOR.
M. B. Sterman*, S. Roth* and C. D. Clemente, Sepulveda V. A. Hsptl. and Depts. of Anatomy and Psychology, Univ. of Calif. at Los Angeles, Los Angeles, Calif.

In a cat trained to manipulate a lever in order to receive liquid food, discrete periods of EEG synchronization are observed to occur during and after consumption of the food. This phenomenon has been termed "post-reinforcement EEG synchronization" (Sterman, Roth and Clemente, Fed. Proc. 22: 399, 1963). Experiments have recently been performed to determine the effects of specific brain lesions upon this EEG pattern and its behavioral correlates. Limited destruction of the intralaminar nuclei of the thalamus results in an immediate increase in the frequency of occurrence of the post-reinforcement synchronization, whereas lesions placed in the preoptic and basal telencephalic region results in a gradual decrease in the frequency of occurrence. No gross behavioral alterations are observed following thalamic damage; however, basal forebrain lesions were followed by the emergence of a motor hyperactivity and a hyperphagic condition. No motor or sensory decrement is apparent with either lesion. Although additional subcortical and cortical sites must be sampled in order to complete the present study, it is important to note that the midline thalamic areas have been associated with the arousal mechanisms of the brainstem, and the basal forebrain region with hypnogenic mechanisms. Physiologic alteration of such basic functions may influence the animal's level of satiation, which may be reflected in the post-reinforcement EEG pattern.

In Vitro Respiration of Normal & Pathologic Human Lung. B. Strauss (intr. by A.Cournand). Rockefeller Inst., N.Y.

Earlier studies of in vitro respiratory rates of human lung have, with few exceptions, employed homogenates, a choice dictated in part by difficulty encountered in producing uniform slices of intact cells. Thus, little is known about the oxidative metabolism of normal and pathologic pulmonary tissues whose cells and architecture remain undisturbed. To circumvent the difficulty of slicing, the present study utilized rods of tissue prepared with the McIlwain chopper. Such rods, cut from normal and pathologic sections of the lungs of patients undergoing thoracotomy for carcinoma or tuberculosis, were pipetted as suspensions into Warburg flasks. Respiratory rates were measured using the direct method of Warburg. A second difficulty encountered in studying pathologic tissue lies in the resolution of the specimen into normal and abnormal components. This problem was obviated by using the point-counting method of Chalkley to partition the weight of the tissue into its component parts. These approaches were applied to specimens from 12 patients with tuberculosis and 12 with carcinoma. The results showed that the qO_2 of normal lung was 2.1 μL/mg. dry wgt./hr.; of tuberculous tissue 5.4; and of malignant lung, 8.6. Hence it may be concluded that the presence of tuberculosis or carcinoma may augment the oxidation of the lungs.

EFFECT OF URINE AND BLOOD pH ON RENAL AMMONIUM EXCRETION DURING STOPPED FLOW. L. P. Sullivan, Department of Physiology, University of Kansas Medical Center, Kansas City, Kansas.

The effect of blood and urine pH on peak ammonium concentration developed during stopped flow was studied in successive occlusions on chronically acidotic dogs first infused with HCl and then with $NaHCO_3$. The relationship of peak ammonium concentration to urine pH in successive occlusions performed on any one dog closely followed the theoretical slope predicted by the theory of non-ionic diffusion and the buffer equation (i.e., a ten-fold increase in ammonium concentration for each ten-fold increase in hydrogen ion concentration) in the urine pH range 6.2-7.3. When stopped flow urine pH was below 6.2 in successive occlusions, the slope was significantly less than the theoretical. In the latter experiments, increasing occlusion time from 5 to 10 mins. resulted in only a small increase in peak ammonium concentration. Infusions of the impermeant anions, sulfate and ferrocyanide increased ammonium concentration but did not change the slope. In preliminary experiments infusions of glutamine also increased ammonium concentration and shifted the slope towards the theoretical at urine pH's down to 5.6. In other experiments renal arterial injections of creatinine-hydrochloride during stopped flow lowered blood pH and the peak urine ammonium concentration developed. (Supported by USPHS Grant HE-06974.)

UNIT ACTIVITY IN VISUAL CORTEX OF PUPPIES AND KITTENS. Dwight Sutton (intr. by Thelma T. Kennedy). Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle, Wash.

Responses to light were studied in acutely prepared animals 5-45 days old. Brief flashes of light produced firing of inactive neurons or modified the activity of spontaneously firing neurons in all animals. Some spontaneously active units were unaffected by light. "On" and "on-off" firing patterns were most commonly encountered. A slow rate of stimulation was necessary to maintain optimal effects on the unit responses. Since the ocular media are cloudy for the first 20-25 days of life, accurate refraction of the eye, permitting presentation of patterned visual stimuli on the retina was not possible in the very young animals. The location of the stimulus in the visual field did not influence the firing patterns in the youngest animals. As age increased, the maximum firing rates occurred when the stimuli were presented in progressively smaller regions of the visual field. Preliminary testing with stimuli of various geometric forms indicated slight differential sensitivity to the different configurations. The results suggest that the connections of field-specific units found in adult animals develop gradually in young animals. [Aided by a grant (B5082) from the National Institute of Neurological Diseases and Blindness.]

A COMPARATIVE STUDY OF THE EYE MOVEMENTS INDUCED BY STIMULATION OF THE NERVES OF VERTICAL SEMICIRCULAR CANALS. J. Suzuki*, B. Cohen*, K. Goto* and M.B. Bender. Dept. of Neurology, Mt. Sinai Hospital, New York, N.Y.

When individual anterior or posterior semicircular canal nerves were stimulated electrically in the monkey, cat, dog, and rabbit, disconjugate eye movements were induced which were characteristic and different for each canal nerve stimulated in each species. This is in contrast to eye movements from lateral canal nerve stimulation which were always conjugate and horizontal regardless of species. To demonstrate the relationship of the disconjugate eye movements from vertical canals to ocular compensatory movements, ocular deviations were calculated which would precisely oppose head rotations in vertical planes. The planes of these rotations were at 45, 0, and 90 degrees from the midplane of the head and their axes lay in the plane of the lateral canals. These rotations corresponded to head movements which would excite single anterior or posterior canals, bilateral anterior or posterior canals, or unilateral anterior and posterior canals, respectively. The eye movements evoked by vertical semicircular canal nerve stimulation showed close correlation in direction and degree of movement with the eye movements predicted to oppose head rotation in the planes of the semicircular canals. These data indicate that the degree of ocular dissociation and direction of the eye movements can be mathematically approximated if the plane of the excited semicircular canal and the lateral or frontal positioning of the eyes in the head are known. They also show that disconjugate eye movements induced by anterior or posterior semicircular canals provide ocular opposition to head rotation and tend to maintain the visual axis in space.

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HYPOXEMIA IN EXPERIMENTAL PULMONARY THROMBOEMBOLISM. Edward W. Swenson, Roberto Llamas*, and Judith Winkler*. VA Hosp., and Univ. of Miami, Coral Gables, Fla. (Supported in part by USPHS grant H-5027).

Cyanosis is frequently seen in patients with massive pulmonary embolism and arterial hypoxemia has been described as its basis. These findings are not in keeping with certain clinical and experimental work in which the occlusion of a main branch of the pulmonary artery resulted in an enlarged "dead space-effect" although arterial oxygenation was rarely encountered. We have re-examined this problem in dogs using autologous clot as the embolizing material. Results are given as averages. 7 dogs weighing 28 kg received 41 ml of clot I-V(particles 2-7 mm in diameter). Arterial pO_2 fell from 83 mm Hg control down to 71 after embolization; the corresponding values during oxygen breathing were 568 and 459. These changes were associated with a 210% rise in mean pulmonary arterial pressure and a 13% decrease in cardiac output. In 3 of the dogs, generalized pulmonary edema was noted. In a second group of 6 dogs weighing 29 Kg we used a balloon catheter to block the artery of one lung while an average of 42 ml of clot were given and swept to the other lung. Under these circumstances the changes were similar to, but more severe than those described in the first group. The arterial pO_2 fell to 51 on air and 323 on oxygen. If the balloon were deflated the pulmonary pressure fell but arterial oxygenation remained poor. Hypoxemia was severe only in 4 of the 6 dogs; in these 4 we afterward found bilateral pulmonary edema in spite of the presence of a tracheal divider. We interpret these findings to indicate that massive pulmonary thromboembolism leading to severe precapillary pulmonary hypertension can be accompanied by generalized pulmonary edema. The latter is associated with arterial hypoxemia based in large part on anatomic shunting.

TREMOR INDUCED BY AUTOSTIMULATION IN CATS. E. G. Szekely and G. V. Jacoby*. Department of Experimental Neurology, Temple Univ. School of Medicine, Philadelphia, Penna.

The difficulty of producing tremor in the cat has been a serious hindrance to gaining experimental data about such tremor. In previous experiments, tremor was elicited by electrical stimulation of the mesencephalic or pontine tegmentum. This type of tremor evoked in acute experiments only was utilized for exploration of additional tremor influencing structures, e.g. destruction of the contralateral nucl. ventralis lateralis diminished or abolished the tegmental tremor. A miniature transistorized unit permitting amplification and changes in frequency of the stimulating pulses has been built and used for brain stimulation in chronic preparations. The potentials elicited by the heart beats serve as the power source. The subcutaneously placed apparatus is able to sufficiently amplify and modify the cardiac potentials so that the threshold of cerebral structures is reached. The tremor produced by such autostimulation permits studies of facilitatory and/or inhibitory systems by applying certain drugs or by stereotaxically placing lesions in various parts of the cerebrum in chronic experiments. Such a successfully developed method of autostimulation lends itself to many uses in biological research.

(Aided by a General Research Support Grant from Temple Univ. School of Medicine).

THE EFFECT OF ATP ADMINISTRATION IN IRREVERSIBLE SHOCK. Samir M. Talaat *, Walter H. Massion and John A. Schilling. Depts. of Surgery & Anesthesiology, Univ. of Okla. Medical Center, Oklahoma City, Okla.

Studies of myocardial metabolism during hemorrhagic shock have shown that rapid dephosphorylation of high energy phosphate will occur as a result of myocardial hypoxia. The loss of ATP and the destruction of coenzymes which require ATP for resynthesis may contribute to the irreversibility of shock after restoration of blood volume. Three groups of dogs were heparinized and connected to a reservoir via the femoral artery. Mean arterial pressure was maintained at 35 mm Hg by adjusting the reservoir level. The shed blood was retransfused after 5 hours of shock or after spontaneous uptake of 20% of the shed volume. In the control group blood loss averaged 47.2 ml/kg; the survival rate was 22%. The second group received 6.2 mg/kg ATP-Na with the retransfused blood and an equal amount IM 2 hours after retransfusion. Blood loss in this group was 49.8 ml/kg; 55% of the animals survived. The third group received 6 mg/kg ATP-Na IM one hour before the experiment and an equal amount in the retransfused blood. Average blood loss was 52.5 ml/kg and the survival rate was 80%. A fourth splenectomized group is currently under study. The results of this study indicate that administration of adenosine triphosphate preceeding hemorrhage may prevent or reduce the incidence of the irreversible phase of shock in this standard preparation.

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BRONCHOCONSTRICTION IN EXPERIMENTAL AUTOLOGOUS PULMONARY EMBOLISM. G. Tanabe*, V. Rege*, D. Thomas* and M. Stein. Beth Israel Hospital and Harvard Medical School, Boston, Massachusetts.

Fresh autologous peripheral venous thrombi were released to the lungs of 26 anesthetized spontaneously breathing dogs. Embolization produced significant increases in total lung resistance, lung elastance, respiratory rate and arterial-alveolar (a-A) CO_2 tension difference which were unrelated to changes in lung volume. Intravenous heparin (5000 units) administered 30 minutes before release of preformed thrombi completely prevented increases in lung resistance and elastance although post embolic tachypnea and increases in the a-A CO_2 tension difference still occurred. Acute bronchoconstriction produced by intravenous histamine, acetylcholine and serotonin was not effected by the prior injection of heparin. When l - methyl lysergic acid butanolamide (MLA), an antiserotonin agent, was administered intravenously during embolization, the increases in lung resistance and elastance were completely prevented. Examination of lung emboli immediately after release revealed that significant amounts of thrombin could be eluted. The following conclusions can be made: (1) The effects of heparin and MLA demonstrate that neither the physical presence of emboli in the lung nor the reduced alveolar CO_2 tension are responsible for post embolic bronchoconstriction; (2) The failure of heparin to prevent the bronchoconstriction due to intravenously injected serotonin indicates that heparin does not block this action of serotonin directly; (3) Thrombin on fresh pulmonary emboli induces the release of serotonin from blood platelets with subsequent bronchoconstriction; and (4) Heparin prevents the release of serotonin by its anti-thrombin action.

THE CUTANEOUS SLOWLY-ADAPTING MECHANORECEPTOR OF THE CAT. Daniel N. Tapper (intr. by E.L. Gasteiger), Cornell Univ., Ithaca, N.Y.

Analysis of nerve-receptor interactions and mechanical transducing characteristics of this anatomically discrete receptor indicates a marked dependence of receptor function on the properties of the afferent fiber. From recordings of isolated fibers of dorsal root and by use of controlled mechanical and electrical stimuli on the tactile prominence within which the innervating fibers ramify, it was determined that: (1) The tactile unit consists of from 1 to 5 terminals. (2) The peripheral field size is no greater than 1 cm^2. (3) There appears to be no convergence of units in the skin. (4) The mechanical threshold for 3 msec duration displacements was 9 to 58 microns. (5) Summation of short duration displacements was not obtainable. (6) Short duration voltage stimulation evoked a single action potential. By use of dual electrical and electrical-mechanical sequences, the changes in mechanical threshold from 0.5 to 60 msec after the conditioning stimulus coincided with those observed by using a second electrical pulse. Mechanical transduction time varied from 1.3 to 0.4 msec depending on the displacement. Upon sustained suprathreshold mechanical stimulation, two rate processes were evident in the spike train; one was displacement-rate sensitive and associated with the rising phase and the other was displacement sensitive and coincided with the plateau phase of the stimulus.

CLICK-EVOKED RESPONSES FROM ELECTRODES IMPLANTED IN CAT.

Don C. Teas[+], Center for Comm. Sciences, Res. Lab. Elect., MIT and Nelson Y-S. Kiang, also of Eaton-Peabody Lab., Mass. Eye and Ear Infirmary, Boston, Mass.

At the cortex (AI) of the awake cat, the evoked response to an acoustic click shows an early (8 - 12 msec) surface-positive deflection, a second (22 - 29 msec) surface-positive deflection, and a later (60 - 80 msec) surface-negative deflection. The three deflections show different properties in relation to variation in stimulus parameters and variation in organismic parameters. The late deflection is labile and is absent when the electrocorticogram and the electromyogram (neck muscles) indicate that the cat is not awake.

In contrast the early deflection (8 - 12 msec), while less sensitive to change in organismic variables, can be manipulated by stimulus variables, in particular background noise. Thus the early and the late components can be selectively eliminated from the complex evoked response.

[+]Now at the University of Pittsburgh

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ANTRAL INHIBITION OF GASTRIN-STIMULATED GASTRIC SECRETION. James C. Thompson, Warren D. Davidson, and James H. Miller (intr. by Jonathan E. Rhoads). Surgical Research Laboratory, Pennsylvania Hospital, and the Departments of Surgery and Biochemistry, University of Pennsylvania School of Medicine, Philadelphia.

Gastrin was prepared from hog antral mucosa according to Grossman's modification of Gregory's method. One ml. of the resultant material contained approximately 10 mg. of protein and was equivalent to 10 gm. wet weight hog antral mucosa. We have repeatedly confirmed Grossman's observation of the inhibitory effect of single large intravenous injections of "gastrin" on gastric secretion. Gastrin was diluted to 200 ml. with normal saline and administered intravenously to dogs prepared with Heidenhain and denervated antral pouches. Either 2 or 4 ml. of the gastrin was given over a 3-hour period, the rate of gastrin administration being equivalent to 6.7 or 13.3 gm. antral mucosa per hour. This dosage produced a sustained acid secretion from the denervated fundic pouches. In this study of the effect of antral acidification on gastrin-stimulated gastric secretion, 15 paired control-test studies were performed on 8 dogs; the sequence of the studies was varied. Paired control-test studies were identical except that in test experiments, the isolated antra were irrigated with N/10 HCl, beginning 30 minutes prior to the administration of gastrin. The average 3-hour control acid output was 1.75 mEq., while the average test output was 0.58 mEq. The average percentage difference was 60%, with a P value of < 0.02. Conclusion: Antral acidification was shown to suppress gastrin-stimulated gastric secretion. This supports the concept of an antral inhibitory hormone. (Supported by grants from the John A. Hartford Foundation, Inc. and by U.S.P.H.S. grants #A-4265 and #A-5845).

Bone Cellular Activity Associated with Skeletal Atrophy. P. A. Thornton (Spon: F. W. Zechman) University of Kentucky Medical School, Lexington, Kentucky.

The effect of immobilization on bone metabolism was studied in young male rats. The right rear leg was fixed for one or two weeks with a plaster of paris cast with the left limb serving as a control. After sacrifice, metaphyseal area bone samples were taken for metabolic studies and various chemical determinations. The results indicated that total bone mass was not reduced until after one week of immobilization but that cellular nitrogen was markedly reduced at one week. The bone citric acid level was elevated in the experimental limbs at one week but subsided by the end of the second week. The output of lactic acid by incubating bone tissue followed a similar pattern. Glucose utilization by incubating bone was sharply increased in the immobilized limbs at both time periods. The results suggest that bone atrophy resulting from disuse is preceeded by either a reduction in cell number or a shift in cell type. This change is accompanied by an increased metabolic rate which tends to decrease as atrophy progresses.

LOOSELY-BOUND MEMBRANE MAGNESIUM AND CALCIUM AS REGULATORS OF INTESTINAL PERMEABILITY. C. S. Tidball and R. Hairston*
Physiol. Dept., The George Washington Univ., Washington, D.C.

The absorption of phenolsulfonphthalein (phenol red) was used as a measure of intestinal permeability in rats anesthetized with sodium pentobarbital. All solutions placed in the intestinal lumen were adjusted to pH 7.0 and 300 mOsm/L. When 5 ml. of a 1 mM solution of phenol red were placed in either proximal or distal halves of the small intestine, the hourly absorption ranged from 0.0 to 3.9% with a mean of 1.4% for 70 determinations. The presence of 25 mM/L EDTA as the calcium salt did not alter the phenol red absorption from these control values. With 25 mM/L of sodium ethylenediaminetetraacetate (NaEDTA) present in the lumen, the absorption of phenol red ranged from 5.1 to 27.2% with a mean of 14.8% for 38 determinations. After NaEDTA had been present for one hour, rinsing the lumen produced results which varied with the ionic composition of the rinsing solution. Balanced physiologic saline did not reverse the increased permeability. A $CaCl_2$ rinse produced a permeability intermediate between NaEDTA and control levels. A $MgCl_2$ rinse reinstated normal permeability in most experiments. A combined $CaCl_2$-$MgCl_2$ rinse invariably returned the permeability to control levels. It is concluded that loosely bound magnesium and calcium in the structure of the membrane regulate the aqueous permeability of the intestinal epithelium.
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INCREASE IN VENOUS ADMIXTURE DURING BREATHING 100% OXYGEN. G. E. Torres*, C. T. Huang*, and H. A. Lyons. State University of New York, Brooklyn, N. Y. Aided by P. H. S. Grant HTS-5485.

Any increase of venous admixture during breathing of 100% O_2 can be related to increase in direct shunting. Decrease of ventilatory units was thought the cause (Finley et al 1960). The present study was designed to observe the effect of breathing 100% O_2 on venous admixture and dynamic pulmonary compliance. Any decrease in expected arterial oxygen tensions during nitrogen washout studies were considered due to increase of venous admixture. Twenty subjects studied during breathing of 100% O_2 had end-tidal and mixed expired nitrogen concentrations, and arterial oxygen tensions (every 5 mins.) continually measured. $\dot{V}_E$ was continually measured. Arterial oxygen tensions decreased 50 - 300 mm.Hg. within 5 to 10 mins. The decrease was evident before completion of the nitrogen washout. Measurements of dynamic compliance with control of frequency and tidal volume were made on 3 subjects. Compliance lowered to 50% of control. PaO_2 became elevated after 5 full inspirations and for the 3 subjects compliance returned to control values. Increase of venous admixture occurs during 100% O_2 breathing and is due to reduction of units of ventilation of the lung.

EFFECTS OF RENAL VEIN OCCLUSION ON URINE OUTPUT IN DOGS. Louis A. Toth. Dept. of Physiology, Louisiana State University School of Medicine, New Orleans, Louisiana.

Urine rates were determined by recording drops from catheters tied into ureters of anesthetized dogs (intraperitoneal Dial-Urethane) receiving slow intravenous infusions of Locke's solution. Unilateral renal vein occlusions of one minute or less resulted in oliguria from the experimental kidney in 96 of 99 trials in 16 dogs. Thirty-five trials produced an immediate oliguria; 20 a polyuria followed by oliguria during the occlusion; 26 a polyuria during the occlusion followed by oliguria after release of the vein; and 15 showed no change in urine rate from the control during occlusion but oliguria after release of the vein. In no experiment did the urine rate in the contralateral control kidney change during the venous occlusion. Direct blood flow measurements on the experimental kidney (renal vein-femoral vein anastomosis) were made in 6 dogs. Immediately after release of venous occlusion the blood flow exceeded the pre-occlusion blood flow significantly but returned to the latter rate within 2 minutes.

STOP FLOW STUDY OF RENAL EXCRETION OF TRITIATED VASOPRESSIN. Eugene J. Towbin and Carl B. Ferrell.* Research Lab, VA Hosp., Little Rock, Ark.

Stop flow techniques were utilized to study renal excretion of tritiated arginine vasopressin in 30 anesthetized dogs. 50 μgm of biologically active peptide with a specific activity of 46 μc/mg was injected intravenously. Antidiuretic activity of the urine correlated well with radioactivity; validating the use of urinary radioactivity as a measure of its hormone content. After induction of a brisk solute diuresis, two protocols were used. Stop Inject - The ureteral catheter was clamped and after 5 to 12 minutes a dose of radioactive hormone, along with a filtration marker (e.g. C^{14} inulin or creatinine), was rapidly injected intravenously. The ureteral clamp was released 3 to 5 minutes later and 1/2 cc serial samples of urine were collected. The concentration of vasopressin was proportional to the concentration of the filtration marker, indicating the hormone is only filtered. Inject Stop - Following priming doses, continuous infusion of tritiated vasopressin and creatinine was maintained. After 5 minutes of urinary stasis, creatinine clearance ratios ($\frac{U/P\ Tritium}{U/P\ Creatinine}$) were constant throughout the serial urine samples which represent the anatomic sites of the nephron. This constancy means that vasopressin is neither secreted nor reabsorbed by the renal tubule. Though constant in any one experiment, clearance ratios varied from 0.2 to 0.8 with a mean of 0.6. Plasma protein binding of tritiated vasopressin would account for the clearance ratio being less than one. Average clearance per kidney was 25 cc/min for creatinine and 15 cc/min for vasopressin.

THE USE OF VELOCITY OF ELASTIC WAVES IN THE DETERMINATION OF ELASTIC CONSTANTS IN FROG MUSCLE. X. T. Truong*, S. M. Walker, and B. J. Wall*. Dept. of Physiology, Univ. of Louisville School of Med., Louisville, Ky.

Measurements of velocity of propagation of elastic waves were used to study the elasticity of leg muscles in the frog under various conditions of stretch and contraction. The isolated muscle was mounted on an isometric myograph to allow the recording of resting and isometric tensions. An electro-dynamic transducer was used to produce low frequency mechanical pulses at one end of the muscle and a piezoelectric transducer was used to pick up the propagated electric waves at the other end. Both sending and receiving signals were displayed on a double-beam oscilloscope and the traveling time measured. Measurements were made in the resting and contracting states at various muscle lengths from 80% to 130% of resting length. The linear longitudinal moduli of elasticity were calculated from the velocity equation. Comparison with constants derived from the length-tension data showed good correlations. (Supported by the National Institute of Neurological Diseases and Blindness.)

DIARRHEA CAUSED BY ENDOTOXIN IN MICE. Mary Marshall Turner* and L. Joe Berry. Bryn Mawr College, Bryn Mawr, Pa.

One of the earliest symptoms to appear in mice after endotoxin injection is diarrhea. Loose stools and soiling of fur usually begin within the first half hour after injection and are seen in nearly all mice receiving an LD_{50}. The ED_{50} (dose causing diarrhea in 50% of the animals) is between 1/10 and 1/100 of the LD_{50}, for three endotoxins tested. Blood plasma from endotoxin-injected donor mice causes diarrhea in recipients even after dialysis but loses activity when heated at 56° C. for one hour. This suggests that diarrhea is mediated by a protein or heat-labile complex present in the blood of endotoxin-poisoned mice.

INDEPENDENCE OF GFR AND THE ABNORMALLY SUSTAINED RENAL RESPONSE TO THE SODIUM-RETAINING ACTION OF ELECTROLYTE-ACTIVE STEROIDS

J. Urquhart, J. O. Davis, and J. T. Higgins, Jr.*, NIH, Bethesda, Md.

Chronic Na retention in dogs with cardiac failure or thoracic inferior vena caval constriction depends not only upon hypersecretion of aldosterone, but also upon an abnormally sustained renal response to the Na-retaining action of aldosterone. Previous studies eliminated the adrenal cortex, renal nerves, and renal venous hypertension as necessary for the abnormal response to steroids. The present study evaluates the role of GFR in this phenomenon. Four dogs were uni-nephrectomized 6-20 weeks prior to study. After a control period of Na and K balances and measurement of postabsorptive renal clearances of Cr and PAH, the renal artery was constricted. Na balance was achieved postoperatively after 3-5 days. GFR was chronically reduced by 9-18 ml/min below previous values of 38-58 ml/min, and RBF was reduced by 50-119 ml/min. Each dog was treated with 25 mg desoxycorticosterone acetate (DOCA) per day, but achieved Na balance during treatment after an initial few days of retention. Thus, a reduction of GFR did not provide the changes necessary for the sustained renal response to the steroid. Each of 2 dogs which maintained Na balance despite a large A-V fistula was treated with 25 mg DOCA daily and retained Na nearly completely for the duration of treatment. GFR was measured after feeding both prior to and during DOCA treatment. In each dog, the maximum postprandial increment in GFR was 20 ml/min above fasting values. Prior to DOCA this increment coincided with a rise in Na excretion from 7 and 25 to 119 and 102 μEq/min, respectively; during DOCA treatment, similar increments in GFR coincided with maximum Na excretion rates of 33 and 3 μEq/min. These findings indicate that the abnormally sustained renal response to electrolyte-active steroids is independent of GFR, and appears by exclusion to be dependent upon a humoral mechanism.

THEORY OF TRANSPORT ACROSS A MEMBRANE.

V. S. Vaidhyanathan*, W. H. Perkins*, and E. J. Towbin. VA Hosp., Little Rock, Ark.

Recent years have witnessed the development of a unified statistical mechanical theory of transport in liquid mixtures and electrolytes. To understand the passive nature of transport of small ions and solvent molecules across a membrane, one needs essentially a molecular theory of transport applicable at least for certain idealized systems. We have developed such a theory for a precisely defined system. The membrane is considered permeable for several small ions as well as solvent molecules. The membrane separates 2 solutions of different concentrations of a single electrolyte and develops an electrical potential due to the preferential absorption of one kind of ion. The system is considered rigorously as composed of 5 regions of which 3 are distinct from a theoretical point of view; namely, bulk solution where the membrane potential has a negligible effect, diffuse double layer, and the interior of the membrane. We have attempted to develop adequate expressions for diffusion in these 3 regions under steady state conditions in the absence of any chemical reactions or temperature gradient. A procedure for explicit calculations from experimental data of passive transport of solvent and ion molecules is described. Many of the results of linear statistical mechanical theory of transport have been incorporated.

NEUROHYPOPHYSIAL PRINCIPLES IN RATS WITH FAMILIAL HYPOTHALAMIC DIABETES INSIPIDUS. H. Valtin, W.H. Sawyer and H.W. Sokol*. Dartmouth Medical School, Hanover, N.H., and College of Physicians and Surgeons, Columbia University, New York, N.Y.

Assays were done on three female rats with diabetes insipidus (D.I.) and three normal females. Acetone-dried tissues were homogenized in 0.05 M acetic acid containing 0.5% chloretone. The homogenates were placed in boiling water for five minutes, cooled, and centrifuged. The supernatants were assayed for antidiuretic activity by intravenous injection into ethanol-Inactin anesthetized rats, and for oxytocic activity on rat uterus in vitro suspended in magnesium-free van Dyke-Hastings solution. The pituitaries of all D.I. rats contained large amounts of oxytocic activity. Two of the rats with D.I. showed antidiuretic activity in pituitary and hypothalamus of 1.0-1.5 mU/rat (normal about 500 mU/rat for pituitary and 15 mU/rat for hypothalamus). This small amount of antidiuretic activity could have resulted from the oxytocin in these tissues, and the pattern of antidiuresis did in fact resemble the response to oxytocin rather than to arginine vasopressin. The third rat with D.I. showed antidiuretic activity of 6 mU/rat in pituitary and 2.5 mU/rat in hypothalamus. Although much less than normal, this amount of antidiuretic activity was more than one would have predicted from the oxytocin content. Furthermore, the antidiuretic activity from this rat resembled that of arginine vasopressin rather than of oxytocin. In fluid balance studies done just before sacrifice, no difference could be detected between the D.I. rat showing vasopressin-like activity and the two D.I. rats showing none. It is concluded that the deficiency causing D.I. in these rats is specifically a lack or dearth of arginine vasopressin. The small amount of vasopressin-like activity found in one of the D.I. rats may reflect a genetic variant or contamination.

AN ESTIMATE OF REFLECTION COEFFICIENTS IN CAPILLARIES OF RABBIT HEARTS. Fernando Vargas* and J. A. Johnson. Dept. of Physiology, University of Minnesota Medical School.

Isolated, perfused, continuously weighed rabbit hearts have been studied in order to characterize their capillary bed with respect to estimated reflection coefficients and equivalent pore radii. Urea, sucrose, raffinose, inulin and albumen were used as test substances which were introduced into the perfusing solution. The reflection coefficients obtained were 0.1, 0.3, 0.38, and 0.69 for urea, sucrose, raffinose and inulin respectively. By assuming that the reflection coefficient for albumen was one, a filtration coefficient could be estimated which turned out to be $8 \times 10^{-8} \frac{cm}{sec\ cm \text{ of } H_2O}$. The equivalent pore radius was calculated to be 35 Angstroms.

CHANGES IN SUBSTRUCTURES OF A FILAMENTS IN NORMAL AND DENERVATED RAT MUSCLE. S. M. Walker, G. R. Schrodt*, X. T. Truong*, and B. J. Wall*. Dept. of Physiology, Univ. of Louisville School of Med., Louisville, Ky.

In electron micrographs of normal rat gastrocnemius muscle the substructures within A filaments are compact and difficult to observe. On the other hand, substructures within A filaments of denervated gastrocnemius muscle are more loosely held together and more easily observed. Apparently the substructures are held together by a lattice-like network of fine threads. Fragmentation of substructures is revealed in A filaments near the plasma membrane of denervated muscle fibers. The normal position of projections from the A filaments is preserved in the center of the fiber where the normal hexagonal arrangement of the A filaments persists. These projections form bridges between the A filaments in the H zone. In the zone of overlap between A and I filaments these projections from A filaments show a 30-degree shift of position where bridges between A and I filaments are seen. (Aided by Research Grant HE-00697-14 from the National Heart Institute and by a grant from the American Heart Association.)

EVIDENCE FOR A SINGLE TRANSPORT SYSTEM FOR MONOVALENT ANIONS. Mackenzie Walser and W. Joseph Rahill.* Johns Hopkins University School of Medicine, Baltimore, Md.

If a group of solutes is in equilibrium with a cell constituent X, along the course of the tubule, and if the rate of transport of the solutes at every point is proportional to the amount of each combined with this constituent, the ratios of excreted/filtered quantities, R, for each will be powers of one another. The exponent relating clearances of any two solutes is the ratio of k_1k_3/k_2 for one solute to that of the other, where

$$A + X \underset{2}{\overset{1}{\rightleftharpoons}} AX \xrightarrow{3} \text{Reabsorbed A.}$$

Simultaneous clearances of inulin, the monovalent anions Br^{82}, I^{131}, F^{18}, NO_3, or SCN, and chloride were determined in dogs salt depleted or receiving NaCl, NaI, NaBr, $NaNO_3$, NaSCN, $NaClO_4$, or mannitol i. v. For each anion, R_A/R_{Cl} varied with R_{Cl}, approaching unity as R_{Cl} increased. The ratio $\log R_A/\log R_{Cl}$ was, however, constant, and was unaffected by urine flow, urine pH, plasma concentration, filtration rate, or the presence of other anions of this group. The exponents, indicating relative transport rates, are in the sequence $SCN>Br>Cl>I>NO_3>F$. These exponents predict the relative clearances with moderate precision. Absolute clearances are determined (in part) by the proportion of more permeant as opposed to less permeant anions in the plasma. Thus I and NO_3 are chloruretic, but SCN and Br are not. These results indicate that monovalent anions (below a certain size) share a common transport system. Other kinetic models may yield the same results.

MUTUAL INFORMATION OF TWO PHYSIOLOGICAL RECORDS, Donald O. Walter and Daniel Brown*, Space Biology Laboratory, Brain Research Institute, UCLA.

The mutual information connecting two partially random functions is a general measure of interaction, and can be numerically estimated from physiological data. For two Gaussian processes, i.e., those whose distribution of amplitudes follows the normal curve, the only relations possible are linear ones; here the cross-correlation function is sufficient to define the mutual information. Correlation, however, underestimates the mutual information for other distributions of amplitudes, or for such physiologically interesting relationships as non-proportional response, or modulation of one signal by another. Lagged mutual information generalizes the cross-correlation function, and can be assembled into a cross-information function. Additional insight is provided by calculating the multivariate mutual information at several lags at once, these lags to be selected on the basis of the cross-information function. The degree of relationship indicated by cross-correlation versus that indicated by lagged and multivariate mutual information, between pairs of related electroencephalographic traces, will be compared, and the additional insight due to the new technique explained. The direct extension of such calculations to process additional parameters derived from EEG traces, such as filter outputs, will be shown to provide material for direct study of the cerebral coding of information transfer. Supported by the following grants: USPHS B-1883, NASA NsG 203-62, AF-AFOSR 61-81.

SUDOMOTOR ACTIVITY INDUCED BY SINGLE SHOCK STIMULATION OF HYPOTHALAMUS IN ANESTHETIZED CATS. G. H. Wang and Gastone Celesia*.
Lab. Neurophysiol., Univ. Wisconsin, Madison 6, Wisconsin

Since the time of Karplus and Kreidl (Pflügers Arch., 1909, 129-138) to the present, studies of the effects of stimulation of hypothalamus on vegetative functions seem to have been performed exclusively with tetanic stimulation. We have found that a single shock applied to the hypothalamus is sufficient to elicit a potential change in the sweat glands of the footpads in anesthetized cats. With this type of stimulation we delimited the excitatory sweat center in the hypothalamus to its rostral portion, excluding, however, the preoptic area. Furthermore, the sudomotor reflex (GSR) to single shock stimulation of the central stump of a divided afferent or mixed nerve was facilitated by appropriate single shock stimulation of the hypothalamus. A single shock applied to the rostral hypothalamus was also found to be sufficient to cause inhibition of the heart beat. Single shock stimulation may, therefore, prove to be a new method to study the functions of the hypothalamus. Supported by Grant B1460 of the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland.

STUDIES OF THE RETENTION AND DISTRIBUTION OF CESIUM-137 IN CITELLUS LATERALIS[1]. James W. Warren* and M. L. Riedesel. Biology Dept., University of New Mexico.

The rate of excretion of radioisotopes may serve as an index of the physiological state of an animal. These studies are designed to determine the effect of environment on the retention and excretion of Cs^{137}. One ml of buffered ringers solution containing approximately 0.3 microcuries of Cs^{137} in the chemical form of CsCl was injected into the peritoneal cavity of the experimental animals. All measurements of radioactivity were made with a 4 pi liquid scintillation small animal whole body counter. The mean biological half times ($BT_{\frac{1}{2}}$) of Cs^{137} in C. lateralis were as follows:

	Animals active at 22°C			Animals active at 10°C		
	n	mean (days)	range (days)	n	mean (days)	range (days)
First $BT_{\frac{1}{2}}$	9	2.13	1.6-3.2	2	2.6	2.1-3.1
Second $BT_{\frac{1}{2}}$	6	4.7	3.7-5.7	2	6.3	6.2-6.4
Third $BT_{\frac{1}{2}}$	3	7.0	5.8-8.8	2	10.0	9.7-10.4

The specific activity of blood, heart, stomach, liver, lung, kidney, spleen, gastrointestinal tract, bone, and muscle were determined after the first, second and third $BT_{\frac{1}{2}}$. The distribution of Cs^{137} in the tissues of cold exposed animals differed from the distribution in control animals.

1. This study was supported in part by NSF grant GB 216.

BLOOD FLOW-VOLUME ALTERATIONS DURING EMBOLIC-INDUCED PULMONARY EDEMA. H. Weisberg, R. Jortner, A. Ellis, I. Kline and A. Shaffer, (intr. by L. N. Katz). Cardiovascular Institute, Michael Reese Hospital and Medical Center, Chicago 16, Illinois.

Bilateral edema has been shown to occur, in our previous studies, after unilobar starch emboli injected in a pulmonary artery wedge position. This has been attributed to neurohumoral mechanisms, on the basis of experimental results. The present study demonstrates that during embolic pulmonary edema a marked increase in calculated pulmonary vascular resistance occurs, unaccompanied by significant elevation of pulmonary artery pressure because of the associated reduced cardiac output. Cardiac output was measured by an indicator-dye technique. No evidence of increased pulmonary vascular resistance was seen over a similar time period in control animals. Left ventricular end-diastolic pressure did not rise in the starch embolic dogs, ruling out left heart failure. At present we are studying the changes in blood volume which accompany pulmonary edema. A method has been developed by us for this purpose.

INCUBATION AND HATCHING OF CHICKEN EGGS IN AN ATMOSPHERE ALMOST DEVOID OF NITROGEN. Harold Weiss, Ronald Wright* and Edwin Hiatt. Ohio State Univ., Columbus, O.

Fertile eggs were incubated in a closed chamber containing an atmosphere of helium (about 79%) and oxygen (about 21%). The nitrogen content of this atmosphere did not exceed 2% and was usually less than 1%, relative humidity was 65-75%, CO_2 less than 0.5%. Total pressure was that of the ambient atmosphere and temperature was maintained at 98-101° F. The control eggs were incubated in an identical chamber containing air. Both groups were turned three times daily. Eggs opened on the 4th and 7th days of incubation showed similar development in the two groups. However the rate of hatching of the eggs in the helium-oxygen atmosphere was about half that of the control eggs. After hatching, some chicks were maintained for 4 weeks in the same atmosphere as that in which they were incubated. Although the chicks in the He-O_2 atmosphere grew at a slower rate for a few days after hatching they later grew at the same rate as the controls. Oxygen consumption measurements made on 4 day embryos showed no difference between those incubated in He-O_2 atmospheres and the controls. It is concluded that the almost complete substitution of helium for nitrogen in their gaseous environment is not incompatible with embyronic development and post-hatching growth of chickens. (Supported by a grant from NASA).

EFFECTS OF INTRACAROTID INFUSIONS OF POTASSIUM CHLORIDE AND SODIUM CHLORIDE ON LEARNED BEHAVIOR IN GOATS. Bernice M. Wenzel, Basil A. Baldwin*, and Robert D. Tschirgi. Univ. of Calif. Sch. of Med., L. A.

In view of the well-known sensitivity of neuronal function to changes in environmental $[K^+]$, the effects of transient increases in plasma $[K^+]$ on learned behavior were studied. The subjects in these experiments were adult female goats prepared with carotid loops as previously described by Baldwin, Wenzel, and Tschirgi (Fed. Proc., 22:639, 1963). The goats were trained in a visual discrimination task, viz., pressing the brighter of two transilluminated lucite panels with their noses. The composition of the blood perfusing the brain was changed by infusions through an indwelling polyethylene cannula in one carotid artery. The effects of these infusions remained ipsilateral unless accompanied by occlusion of the opposite carotid loop. Each testing session consisted of two infusions of 4% KCl, one ipsilaterally and one bilaterally distributed, and two infusions of an equimolar concentration of NaCl. The order of infusions was systematically balanced over sessions. All infusions continued for 2 minutes at a rate of 7.75 ml/min. The number of correct and incorrect responses was recorded during the minute immediately before infusion, the first and second minutes of infusion, and the first minute of steady responding after infusion. These data show: 1) almost complete cessation of responding during KCl infusion and maintenance of steady responding with NaCl; 2) resumption of steady responding a few minutes after termination of KCl infusions; 3) no difference between ipsilateral and bilateral conditions; 4) no effect on response accuracy. Supported by Grant No. G-21521 from the National Science Foundation.

IN VITRO PERFUSION OF THE ISOLATED MONKEY BRAIN. Robert J. White, Maurice Albin*and Javier Verdura*, Section of Neurosurgery, Western Reserve University, Cleveland, Ohio.

Ten Rhesus monkey brains have been surgically isolated and perfused for periods ranging from 30-180 minutes utilizing a simplified extracorporeal circuit incorporating a large, blood compatible donor monkey. Operative isolation was accomplished by removing all anatomic structures of the skull, including the lower jaw and orbits, until the brain was attached only to a small basal plate of bone. The brain was separated from the cord and vertebral column at the first cervical level. Extracorporeal circulation maintained blood flow to the brain via bilateral carotid perfusion through two small "T" cannulae. Only the internal carotid arteries and the internal jugular veins were preserved. Perfusion pressures in the carotid "T" cannulae ranged from 150/120 - 120/90 mm. Hg.; and average of 40 mm. Hg. below the brachial pressure of the donor animal. Blood flows of 25-50 cc./min. were recorded in brains weighing 80.5-85.0 gms. "Normal" function of the isolated brain preparation was evidenced by significant mean A-V differences of O_2 (5.8 vols.%) and V-A differences of CO_2 (5.0 vols.%), as well as good electrical activity measured with cortical electroencephalograms. (Supported by Grant 5455M3817 from the National Institute of Neurological Diseases and Blindness).

INFLUENCE OF TEMPORAL SEQUENCE OF ATRIAL AND VENTRICULAR CONTRACTIONS ON CLOSURE OF MITRAL VALVE IN DOGS STUDIED WITHOUT THORACOTOMY. J. C. P. Williams* and E. H. Wood, Mayo Clinic, Mayo Foundation, Rochester, Minnesota.

A concentric catheter assembly was passed into the left heart via a 13-gauge needle inserted through the fossa ovalis from the right external jugular vein of dogs under morphine-pentobarbital anesthesia. The inner catheter (outside diameter: 0.8 mm.) used for ECG synchronized injections of indocyanine green into the left ventricle was positioned so that its spray tip was 0.5 to 2.0 cm. downstream to the mitral valve. The outer catheter (O.D.: 2.0 mm.) used for sampling of dilution curves was positioned so that its tip was 0.5 to 1.0 cm. upstream to the valve. With these catheter positions, slight retrograde flow of indicator could be detected uniformly in dogs with normal sinus rhythm, but not when they were separated appreciably further. In contrast, in dogs with surgically created mitral incompetence, the position of the tips of injecting and sampling catheters has little effect on the regurgitant fraction (Circulation Res. 19:1196, 1961). The atria and the ventricles were driven by coupled pacemakers in any desired temporal sequence using the transseptal needle tip and electrode catheter tip in the right ventricular outflow tract as the respective stimulating sites. Varying the sequence of atrial and ventricular contractions from normal to synchronous, or reverse sequence, over the heart rate range of 60 to 200 beats/minute caused increases in atrial pressures and decreases in cardiac output (Physiologist 5:211, 1962). However, a systematic effect on the efficiency of mitral valve closure could not be demonstrated. Similarly when the atria were fibrillating, no increase in retrograde flow was detected if a regular ventricular rate was maintained by electrical driving. (Supported in part by American Heart Grant 61G-111 and Minnesota Heart Grant).

USE OF THE SINGLE BREATH DIFFUSION TEST AS AN INDEPENDENT VARIABLE IN THE PREDICTION OF DEGREE OF PULMONARY DISABILITY. R. H. Wilson, B. Hargis*, Dept. of Research VAH, Southwestern Medical School, Dallas, Texas.

The need for a systematic and uniform classification of pulmonary disability (DPD) for therapeutic, diagnostic, industrial compensation and pension purposes is great. At present there is no uniform system in use by the clinicians, physiologist, pension and rating boards throughout the country. The most commonly used pulmonary ventilation tests of lung volume measurement and the single breath pulmonary diffusion test of Forster were used to obtain data to compare with a clinical classification in which there were 5 degrees of pulmonary disability based upon the most frequently occurring clinical signs and symptoms of pulmonary disease in 56 patients. There were 30 normal persons in the study. The data was used to obtain a 'least squares' formula for the prediction of DPD by the multiple regression technic. It was found that the pulmonary diffusion data correlated with DPD; r was 0.70. These data indicate that the pulmonary diffusion test correlates only moderately well with the degree of pulmonary disability. The MVV the FEV 1 second correlated to a greater degree; the correlation coefficient being greater than 0.8. The correlation coefficient between the DPD and RV/TLC was -0.68. It was concluded that it is not feasible nor necessary to perform pulmonary diffusion test on all patients to establish pulmonary disability because the simple tests such as MVV, FEV 1 second, RV/TLC and FEF 25-75% inserted into a nomogram predicted the degree of pulmonary disability to a high degree and the pulmonary diffusion test should be used in instances where there is clinical evidence of a pulmonary diffusion defect.

KERNICTERUS PRODUCED EXPERIMENTALLY IN RHESUS MONKEYS. W. F. Windle, R. E. Behrman*, E. Hibbard*, Ofelia Esquivel de Gallardo*, and J. F. Lucey*. Laboratory of Perinatal Physiology, NIH, San Juan, Puerto Rico.

Newborn monkeys have "physiologic jaundice", reticulocytosis, lower liver-level of glucuronyl transferase and slower bilirubin clearance time than adults. Infants were delivered near term by cesarian section of healthy females with known conceptual dates and subjected to hyperbilirubinemia alone, asphyxiation alone, or asphyxiation followed by hyperbilirubinemia. Hyperbilirubinemia was induced in 14 infants by injecting indirect-reacting bilirubin, 2 mg/100 g, iv, every 6 hours from 1-3 hours after birth for as long as 4 days; continuous bilirubin levels of 20-30 mg % in the blood were attained. Marked jaundice developed in 6 hours; slight lethargy but no other clinical neurological signs and no kernicterus were seen. Fifteen monkeys were asphyxiated for 12 min at birth by encasing the head in a fluid-filled condom while clamping the umbilical cord. After resuscitation all displayed clinical neurological deficits; nonhemorrhagic bilaterally symmetrical circumscribed lesions occurred in the thalamus and brain stem. Six asphyxiated monkeys were infused with indirect-reacting bilirubin from 2-4 hours to 30-50 hours of life. Another was inadvertently partially asphyxiated at cesarian section. All showed clinical neurological signs, abnormal EEG, and kernicterus. Three most severely affected were lethargic for 12 hours, then suddenly developed tremors, focal seizures and prolonged opisthotonus. Brain slices showed selective yellow staining of certain nuclei of basal ganglia, brain stem, cerebellum and cerebrum. Microscopical examination revealed pigment in neurons and neuroglia cells of the colored nuclei. Asphyxia may be one of several agents causing cellular damage to bring about kernicterus in the presence of excess bilirubin in the blood.

CIRCULATORY ARREST OF 30-90 MINUTES UTILIZING PREFERENTIAL CEREBRAL HYPOTHERMIA WITHOUT EXTRACORPOREAL CIRCULATION. S.K. Wolfson, Jr.*, W.Y. Inouye*, A.R. Kavianian*, W.M. Perkins.

Circulatory arrest was induced in 35 anesthetized and heparinized dogs by transthoracic electrical fibrillation. The right common carotid artery was then perfused with saline (60 cc/kg. at a rate of 10 cc/kg/min); 6 were perfused with 37°, 0.15 M. saline (controls), eleven with 0° saline and heads packed in ice, 18, precooled to 29-31°C.(R), by ice bags around the body, were also perfused with 0° saline. In the latter group an intracerebral temperature of about 20° was recorded within 5 minutes of onset of arrest and 8-20° after 45 min. Resuscitation by manual cardiac massage and electrical defibrillation was aided by I.V. epinephrine and neo-synephrine. Moderate metabolic acidosis was controlled in some animals with I.V. sodium bicarbonate. One of 3 controls survived 10 min. arrest but none of 3 regained consciousness after 15 min. Cerebral hypothermia alone prevented injury after 15 or 20 min. arrest but there was spinal cord damage in half of the 30 min. and 40 min. animals. With combined cerebral and general hypothermia all 18 survived periods of up to 90 min. of total arrest. One animal had 25 min. arrest, one 30 min., seven 45 min., and five had 60 min. circulatory arrest all of which were apparently normal. These animals have survived periods of 2-4 months before sacrifice. One of two 75 min. and both 90 min. dogs exhibited neurological or personality changes but the 75 min. animal was apparently normal within a week. Residual deficits were observed in the 90 min. dogs. Microscopic analysis of autopsy specimens is being undertaken.

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania. Supported in part by NSF Post-Doctoral Fellowship, U.S. Army Contract 511, and N.I.H. Grant HE-08066-01.

A REFINEMENT OF THE BAKKE THYROTROPIN ASSAY. James W. Woods and Peter G. Burch*. Johns Hopkins Medical School, Baltimore.

Four changes have been made in the procedures described by Bakke, et. al. In this laboratory we: (1) use smaller beef thyroid slices to increase the number of assays which may be done with the thyroid gland from one animal, (2) incubate the slices 30 hrs. which improves precision, (3) store slices overnight while doing a sensitivity run on several glands making it completely unnecessary to deal with the problem of assay failure, and (4) filter plasma through a Sephadex column which removes the inhibitory material in one step. Measurements have been made on normal human, beef and cat plasma, on plasma from hypophysectomized or thyroidectomized cats, and on human plasma taken after one week of triiodothyronine (T-3) treatment. TSH in normal individuals of all three species varies between 100 and 400 μu/ml. In hypophysectomized cats and in the human after T-3, it is undetectable. In four thyroidectomized cats values of 450, 500, 750, and 790 μu/ml. were recorded. These values (normal and experimental) are based upon over 70 experiments in which Armour's Thytropar was used as a standard. Data from recent assays in which USP Reference Standard TSH was used suggest that the quoted values are slightly low. One recovery experiment has been carried out in which TSH was added to human plasma taken after T-3 treatment. Recovery of five different concentrations averaged 90%. Efforts have been made to study the inhibitory material. It is apparently a small molecule which absorbs at 280 mu and has basic properties. It is not dialysable and withstands mild heating. No in vivo activity has been demonstrated.

BIMODAL RESPONSE OF THE FUNCTIONAL STATE OF THE RETICULOENDOTHELIAL SYSTEM (RES) FOLLOWING GLUCAN ADMINISTRATION. W. R. Wooles* and N. R. Di Luzio. Dept. of Physiology, Univ. of Tennessee Medical Units, Memphis, Tennessee.

The daily administration of glucan for three days to normal mice resulted in a marked phagocytic and proliferative response of the RES, particularly of the RE cellular elements of the liver, lung and spleen. In relation to control values, liver weight was increased 84% ten days after the last glucan injection and by 20 days returned to control levels. However, at 25 and 30 days liver weight of RE stimulated mice was decreased below control values. Lung hypertrophy persisted for 10 days and by 15 days had returned to control levels with maximum hypertrophy (43%) occurring at the 5th day. Maximum splenic hypertrophy (533%) occurred 10 days after the last glucan injection and by 30 days had returned to control values. Hyperphagocytosis, determined by the intravascular clearance of colloidal carbon, was present one day after the cessation of glucan treatment. Maximum RE function, indicated by a mean t/2 of 1.1 mins., occurred at 10 days and coincided with maximum hepatic and splenic hypertrophy. Regression of liver and spleen weight was associated with decreased phagocytic activity, and at 20 days both liver weight and phagocytic activity were similar to those of the control group. The decreased liver weight of glucan-treated mice at 25 and 30 days was associated with a marked reduction of phagocytic activity, as indicated by a mean t/2 of 25 and 15 mins. as opposed to 6 and 7 mins. respectively in the saline control group. The marked similarity in the response of the weight of the liver and the corresponding degree of phagocytic activity reflects the importance of the liver in the phagocytic response. (Supported in part by the Atomic Energy Commission.)

ALTERATIONS IN ELECTRICAL ACTIVITY OF THE PREPYRIFORM CORTEX DURING SHORT-TERM ALTITUDE EXPOSURE. Dorothy E. Woolley, Anthony J. Silva* and Paola S. Timiras. Dept. of Physiology, Univ. of Calif., Berkeley.

Effects of exposure to simulated 12,500 ft altitude (480 mm Hg) on cortical electrical activity were determined in unanesthetized, unrestrained rats chronically implanted with bipolar recording electrodes in the prepyriform cortex and bipolar stimulating electrodes in the lateral olfactory tract (LOT). The cortical evoked response, produced by single shock (3-10 volts, 30 μsec or less duration, 4 per sec) stimulation of the LOT, was a high amplitude, damped, sinusoidal oscillation. A minimum of 250 responses was averaged electronically at 3 stimulus intensities for each rat before, during and after altitude exposure. Within 10 min after reaching altitude the number and frequency of the oscillations in the response decreased. For example, the number of surface negative-surface positive waves decreased from 4 or 5 to 3 and the duration of the final oscillation was markedly prolonged. Hence, the terminal waves of the response were more susceptible than the initial ones to depression by altitude exposure. These alterations persisted throughout the 2-hr period of altitude exposure, but disappeared 10 min after return to sea level pressures, when the evoked response reverted to normal. Thus, short-term exposure to simulated 12,500 ft elevation reversibly alters cortical electrical responsiveness. (Supported by USPHS Grant GM-9267.)

The Action of Procaine on the Single Nerve Fiber. A Hypothesis Correlating Membrane Structure and Function. Ernest B. Wright and J. Maruhashi, Physiol.Depart.,Coll. of Med., Univ. of Fla., Gainesville, Florida.

Procaine applied to a single Ranvier node or single crustacean axon abolishes the Na spike selectively. The resting membrane potential and resistance are uneffected. Depolarization by K-rich media is markedly reduced or entirely prevented. 0.2% procaine prevents depolarization by 60 mM K solution. Remarkably, it is possible to record the prolonged K response from a narcotized fiber or node in a K-rich solution without the applied hyperpolarizing inward current. This response may even occur spontaneously. To explain these and other data in support of the separate activities of the Na+ and K+ carrier systems in a nerve membrane, the following hypothesis is proposed. The unit membrane comprises two protein-phospholipid layers back to back. The assumption is made there exists between these layers a compartment or space for ionic sites. Thus across the entire membrane there are three compartments; the extracellular Na, the intra membrane and the intra cellular K compartments. During Na+ carrier activity, the Na potential is developed across and controlled by the outer monolayer. The K or resting potential is developed across and controlled by the inner monolayer. Procaine effectively seals the outer layer to Na+ flow abolishing that potential, but does not affect the inner layer or the K currents across it and the resting potential. A similar result obtains with replacement of Na by sucrose or choline in the extracellular compartment. Pump and carrier systems continue to function within the intra membrane compartment to extrude chloride to the extracellular and concentrate K+ in the intra cellular compartments. Conversely, variation of K concentration within the axoplasm compartment (Moore, 1963) affects only the resting potential across the inner layer, the outer Na layer continuing to function normally. This theory has numerous applications and implications. NSFG 24013

RECEPTIVE FIELDS OF SINGLE NEURONS IN THE OPTIC TECTUM OF THE PIGEON. Richard M. Wylie (intr. by G. Eisenman). Department of Physiology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

There is a topographic representation of the retina on the optic tectum of the pigeon. In the present work, tungsten microelectrodes were used to record the activity of single tectal neurons when visual stimuli were projected onto a screen in front of the animal's eye. Most neurons responded to a stationary spot of light turned ON or OFF within their receptive fields. The receptive fields of these neurons consisted of a center and a concentric peripheral surround. Illumination of the center evoked either an ON, an ON-OFF or an OFF response. Illumination of the peripheral surround evoked either ON or OFF responses but never both. Inhibitory interaction takes place between the central and peripheral areas of these receptive fields and diffuse illumination evokes either a weak response or no response. All of these units responded to moving spots of light regardless of their direction of movement. Other units were found which responded selectively to the direction of movement of spots of light. Many of these units responded to spots moving within a central area but not to elongate bars of light which extended out of this central area. It was found that this central area is flanked by an inhibitory surround. Movement in this surround evokes no response but can inhibit the response generated within the center of the receptive field.

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LACK OF PHASE CONTROL IN THE DIPTERAN FLIGHT MOTOR SYSTEM

Robert J. Wyman* and Donald M. Wilson
Dept's. of Biophysics and Zoology, Univ. Calif., Berkeley

The pattern of sensory input and motor output in diptera is largely unknown. Even though it appears from the previous studies of others that the muscles would not respond to a phasic pattern in the motor output, a pattern may yet exist. The elucidation of this point is the purpose of this study. The experiments were carried out by attaching several species of flies (Eucalliphora, Musca, etc.) to a support and inserting fine wire electrodes into the flight muscles so as to allow free movement of the wings. During steady flight the activity of the individual neurons does not maintain a special phase relationship to the wing movements. Maintained phase relations are also not seen in comparisons between simultaneous trains of spikes in different muscles. From these observations it is argued that information for gradation of flight parameters is probably conducted to the flight muscles by a frequency modulated pulse code in which specific timing of any one pulse is unimportant. Our records show an increase in frequency of nervous stimulation to the power muscles when wingbeat frequency increases. Increases in power output may be due to a generalized increase in the frequency of all nervous units due perhaps to a generalized increase in the excitation to the flight control system.

TOOTH PULP PRESSURE AND HYDROSTATIC PERMEABILITY. David Yankowitz and George Brengelmann (intr. by A. C. Brown). Departments of Endodontics and Physiology & Biophysics, University of Washington, Seattle, Wash.

The object of these experiments was to establish whether the hydrostatic forces normally existing within the pulp cavity can be described as a "pressure" and to evaluate the hydrostatic permeability of the vascular system of the pulp. In canines and third incisors of anesthetized mongrel dogs a 370 μ hole was drilled through the enamel and dentine until the pulp chamber was just penetrated. A stainless-steel threaded tube, filled with mammalian Ringer's, was screwed into the hole and connected to a pressure transducer of very low compliance and a microsyringe. Pressure was recorded as the tube first penetrated the pulp. Then, small amounts (about 0.05 μliter) of fluid were injected. The pressure rose during injection but decreased toward a steady level following injection. Similarly, when fluid was withdrawn, the pressure decreased and then rose. Referred to tooth level (which was approximately heart level) the mean steady pressure obtained in these measurements was 62 mm Hg (range 45-70 mm Hg in nine teeth). However, the equilibrium pressure reached after an injection of fluid was systematically about 5 mm Hg higher than that reached following withdrawal of fluid. This hysteresis set a limit upon the accuracy of pulp tissue pressure measurement, and perhaps was a result of local tissue distortion. The hydrostatic permeability was calculated from the rate of fluid flow when the pressure was above or below its steady state value. When the pressure was high (fluid being forced into the pulp and presumably into the capillaries), flow averaged about 0.03 μliter/min for a 15 mm Hg driving force. When the pressure was low (fluid being withdrawn from the tooth), flow averaged about 0.01 μliter/min at this driving force. Thus, except for the hysteresis effect, the hydrostatic forces in the pulp can be classified as a pressure, although the magnitude of this pressure was much greater than expected on the basis of similar measurements in other tissues. In addition, the hydrostatic permeability is not constant but depends strongly upon the direction of flow. (Aided by grant DE7103 from the National Institute of Dental Research.)

A DEFECT IN URINARY AMMONIUM FORMATION FROM GLUTAMINE IN PRIMARY GOUT. T. F. YÜ AND A. B. GUTMAN*. MT. SINAI HOSPITAL, NEW YORK, N. Y.

WHEN GLYCINE-N^{15} IS ADMINISTERED TO GOUTY SUBJECTS, IT IS FOUND THAT INCORPORATION INTO URIC ACID-N^{15} MAY OR MAY NOT BE GREATER THAN NORMAL BUT THAT INCORPORATION OF ISOTOPE INTO THE TWO URIC ACID NITROGENS DERIVED FROM GLUTAMINE, N-9 AND N-3, INVARIABLY IS DISPROPORTIONATELY INCREASED. THUS IN 3 NONGOUTY SUBJECTS, THE MEAN TOTAL URIC ACID-N^{15} WAS 0.05 ATOM % EXCESS, IN 6 GOUTY SUBJECTS (3 NORMO- AND 3 OVEREXCRETORS OF URIC ACID) 0.205 ATOM % EXCESS, A 4-FOLD INCREASE; WHEREAS THE MEAN N^{15}-9,3 WAS 0.007 ATOM % EXCESS IN THE NONGOUTY SUBJECTS AND 0.078 ATOM % EXCESS IN THE GOUTY, A 10-FOLD INCREASE. THESE RESULTS INDICATE DIVERSION, PARTICULARLY OF GLUTAMINE, TO DE NOVO PURINE BIOSYNTHESIS FROM SOME COMPETING METABOLIC PATHWAY FOR ITS UTILIZATION, A DIVERSION OF SPECIAL SIGNIFICANCE FOR OVERPRODUCTION OF URIC ACID BECAUSE THE FIRST AND RATE REGULATING STEP IN DE NOVO PURINE BIOSYNTHESIS IS DONATION OF N-9 BY THE AMIDE-N OF GLUTAMINE. THE COMPETING PATHWAY HAS BEEN IDENTIFIED AS RENAL PRODUCTION OF AMMONIA, OF WHICH GLUTAMINE IS THE VIRTUALLY SOLE SOURCE (PITTS ET AL. 1963; OWEN AND ROBERTSON 1963). THE MEAN % DOSE OF GLYCINE-N^{15} EXCRETED AS URINARY $N^{15}H_4$ IN 5 CASES OF PRIMARY GOUT ON DAY 1 WAS 1.61% AS COMPARED TO 2.85% IN 2 NONGOUTY SUBJECTS WITH COMPARABLY ACID URINE, MOST OF THE DEFICIT $N^{15}H_4$ APPEARING AS URINARY UREA-N^{15}, SOME AS URINARY URIC ACID-N^{15}. IN 77 GOUTY SUBJECTS WITH OTHERWISE APPARENTLY NORMAL RENAL FUNCTION, ACID URINE AND NORMAL TITRATABLE ACIDITY, THE MEAN URINARY NH_4/CREATININE RATIO WAS 0.27 ± 0.09 AS COMPARED TO 0.41 ± 0.10 IN 17 NONGOUTY SUBJECTS. THE RESULTS INDICATE A BLOCK IN FORMATION OF URINARY AMMONIUM FROM GLUTAMINE IN PRIMARY GOUT (?GLUTAMINASE DEFICIENCY), AND BY-PASS OF THE GLUTAMINE NOT UTILIZED FOR THIS PURPOSE TO ALTERNATE PATHWAYS FOR DISPOSAL OF AMINO ACID NITROGEN, BY WAY OF UREA AND URIC ACID.

Relation of Glucose to Platelet Histamine Release: Effects of Epinephrine and Insulin

M.H. Zaidenberg* and M.E. Tidball
Pharm. Dept., The George Washington Univ., Washington, D.C.

Platelets were obtained from male albino rabbits by cannulation of a femoral artery allowing rapid removal of blood into a siliconized tube containing EDTA. The platelets were separated by differential centrifugation, washed in saline, and resuspended in a volume of pH 7.4 Krebs-bicarbonate buffer equal to that of the plasma from which they were isolated. Aliquots of platelet suspension were incubated with glucose, glucose and insulin, and glucose and epinephrine for 30 min at 37°C with gentle shaking. After incubation and separation of platelets from the medium, histamine in the supernatant fluid was analyzed fluorometrically and the results expressed in percent of total histamine present in an equal aliquot of the original suspension. Spontaneous and complete release of platelet histamine occurred in the Krebs buffer. Release was reduced by half if glucose (100 or 200 mg%) was present in the medium. Further inhibition occurred when 1.2 U/ml regular insulin were added. Partial reversal of glucose inhibition was effected by 200 µg/ml epinephrine. Thus it has been demonstrated that histamine is released spontaneously from rabbit platelets suspended in a glucose-poor medium. A measure of platelet histamine is retained in the presence of glucose, this effect being enhanced by insulin. It has also been shown that epinephrine stimulates histamine release which has been inhibited by glucose. The data suggest that glucose metabolism is implicated in the regulation of the level of intracellular histamine.

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RELATION BETWEEN BLADDER FILLING, URINE FLOW AND URETERAL PERISTALSIS. Paul D. Zimskind*, M. H. F. Friedman and David M. Davis*. Jefferson Med. Coll., Philadelphia, Pennsylvania

The effects of changes in urine flow and of bladder filling upon peristaltic activity of the ureter were studied in human subjects by the method of Kiil. Using intraluminal non-obstructing catheters connected to strain gauge pressure transducers, simultaneous pressure recordings of the ureter and bladder were obtained. Findings were as follows: Peristaltic activity was diminished when urine formation was decreased. Infusion of the renal pelvis caused a prompt increase in frequency of ureteral peristalsis. Increasing the intravesical pressure to a level approximating the contraction pressure of the ureter caused a gradual rise in the ureteral resting pressure, and ureteral peristalsis was practically abolished. Reduction of the intravesical pressure was followed by resumption of ureteral peristalsis. The ureter retained its ability to contract following nephrectomy. Peristalsis was induced by distension of ureteral stumps with fluid. Ureteral peristaltic activity appears to be dependent on the volume of urine to be transported at a given time. Peristalsis appears also to be dependent on intravesical pressure and is inhibited when the pressure is elevated.