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ABSTRACTS OF PAPERS

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

POSSIBLE MAMMILLOTHALAMIC TRACT INVOLVEMENT IN FEEDING BEHAVIOR

F.D.Abraham, BRI & NPI, UCLA, and N.M.Weinberger, Psychobiology, UCI
(intr. by D.O.Walter)

The possibility that the mammillothalamic tract (VDA) may be another diencephalic area similar to the lateral hypothalamus (LH) in importance for feeding behavior was revealed in a pilot study of hypothalamic lesions and weight change. Bilateral lesions (direct current and radio frequency) centered on the ventromedial nucleus of the hypothalamus (VM) were made in 16,4 mo old, 447-597 gm, male Wistar rats. Ad lib feeding and blind weighing techniques were used from 2 mo preceding to 120 days after surgery. Final weights ranged from an aphagic 235 gm to a hyperphagic 982 gm. Coronal brain sections were rated for extent of damage to several ventral diencephalic structures, and these were correlated to final weights. Extensive VM damage occurred in all animals and was related to hyperphagia, but additional damage to VDA in some animals was best correlated to aphagia, a syndrome which appears similar to LH aphagia in predominating over VM hyperphagia.

Preliminary stochastic analyses of EEG activity in these diencephalic areas in cats have subsequently revealed a good electrophysiological relationship of VDA to hypothalamic areas. They revealed the possibility of a thalamo-mammillothalamo-hypothalamic centrifugal system sharing a broad frequency band of EEG activity with maximum coherences about 40 Hz. Some relationship of this activity to feeding behavior and conditions was also found.

Others have shown that stimulation of VDA (Hess,1954) and anterior thalamus and mammillary bodies (Maire,1956) elicits eating behavior which also implicates the importance for feeding of this system, which is in a good position to integrate many neural areas important for this behavior. (Supported by Calif. Grant 64-2-36).

PLACENTAL TRANSFER OF IRON IN SHEEP. David C. Abramson, * Demetrius H. Bagley*, Edward J. Zapolski, * and J. V. Princiotto (intr. by T. A. Strike). Dept. of Physiology and Biophysics, Georgetown University Schools of Medicine and Dentistry, Washington, D.C.

The placental transfer and fetal distribution of iron bound to transferrin and iron chelates was studied in sheep during the last trimester of pregnancy. Cannulation of fetal arterial and venous vessels and the maternal vessels directly monitored iron transfer across the placenta over a 90 minute period when radioactive iron compounds were administered to either the fetus or ewe. Iron bound to fetal transferrin, remained in the fetus, when injected in this compartment and was distributed in liver, spleen, and marrow. A measurable portion of iron, administered to the fetus as ferric ethylene di(o-hydroxy phenyl glycine), transferred to the ewe. The placenta incorporated 50-70% of this dose. When administered to the ewe, iron bound as transferrin, or chelate, appeared in the fetal circulation and was distributed in the fetal liver. Chelated iron was not accumulated by the placenta when administered via this route.

IRON ABSORPTION IN NORMAL AND ANEMIC RAT MUCOSAL CELLS. Betty S. Adelman,* David C. Abramson,* Martin Rubin* and J. V. Princiotto. Dept. of Physiology and Biophysics and the Dept. of Biochemistry, Georgetown University Schools of Medicine & Dentistry, Wash., D.C.

Iron absorption in normal and anemic rats has been studied by an examination of the iron distribution in subcellular fractions of intestinal epithelial cells following either 1 ug or 30 ug of intragastric Fe^{59}. The fraction of administered iron localized in tissue and cellular components was essentially the same at the two dosage levels with the exception of an increased iron absorption in the anemic animals by the mucosal layer at the 30 ug dosage. The subcellular distribution of the absorbed iron was also distinctive in the anemic animals in that the "nuclear" cellular fraction showed a rapid, high and sustained iron deposition compared to the normal group. This represented approximately 40-60% of the total mucosal iron. The soluble cytoplasmic iron was essentially the same for both normal and anemic animals. The time sequence of the data suggest that a nuclear pool of iron is rapidly and initially repleted in iron deficient animals. This process occurs in the first fifteen minutes following iron administration and is followed by transmucosal migration.

CARBON MONOXIDE DISAPPEARANCE DISTAL TO PULMONARY ARTERY OCCLUSION. E.W. Ahlgren*, V.E. Doty* and R.L. Johnson, Jr. U. Tex. Southwestern Med. Sch. and VA Hosp., Dallas, Texas.

After occluding the left pulmonary artery in a dog, we have inflated that lung with a gas mixture containing 5.0% CO and 0.5% neon in oxygen and nitrogen; the CO disappearance with respect to neon was measured after various intervals of breath holding or rebreathing ranging from 15 seconds to 20 minutes. There is an initial rapid equilibration of alveolar CO with the capillary blood volume (V_C), which is theoretically 99% complete within 10 sec, followed by a very slow linear fall of alveolar CO concentration related to collateral blood flow ($\dot{Q}_C$). From the slope of the linear CO disappearance average $\dot{Q}_C$ was estimated to be 1.7 ml/min during breath holding and 2.2 ml during rebreathing in 4 dogs weighing from 11.1 to 14.3 kg. Average V_C in 8 dogs weighing 9.5 to 14.3 kg was estimated from the zero time intercept to be 9.4 ml during breath holding and 9.5 ml during rebreathing. By repeating these measurements at different levels of pulmonary venous pressure in two dogs, pulmonary capillary bed compliance was estimated to be 0.6 ml/mm Hg. (Supported by USPHS grant HE 07744.)

THE EFFECT OF CO_2 BREATHING ON BRONCHOMOTOR TONE. S. Ahmed*, M. Weiss*, and H.A. Lyons. Downstate Med. Center, S.U.N.Y., Brooklyn, N.Y.

The bronchomotor response to increased concentration of CO_2 in inspired air has been reported with divergent results in animal experiments. Reports of studies on conscious human subjects are scanty. The present study was performed to elucidate this problem further.

Six young normal subjects were studied using volume displacement plethysmograph. Tidal volume, transpulmonary pressure change and airflow were recorded simultaneously at one minute intervals during control period breathing room air and during 6% CO_2 breathing. Concentration of CO_2 in expired air was continuously monitored. Thorasic gas volume (TGV) was determined prior to and towards the end of CO_2 breathing. Pulmonary compliance and non-elastic resistance was computed from these data.

Conductance per unit lung volume increased to a mean value of 65% and specific compliance decreased to an average of 23%. TGV increased to a mean of 0.3456L. There was a positive linear relationship between conductance and alveolar concentration of CO_2.

The present study in contrast to that of Butler et al (1960) demonstrated an increase in conductance in response to 6% CO_2 breathing.

AN OPEN-LOOP ANALYSIS OF THE AORTIC ARCH AND BRACHIOCEPHALIC BARORECEPTOR REFLEX. James L. Allison* and Kiichi Sagawa. Dept. of Physiology & Biophysics, Univ. of Miss. School of Medicine, Jackson, Miss.

In contrast to the study of the carotid sinus baroceptor reflex, surgical difficulties in isolating the aortic baroceptor area have impeded servo-analytical study of this region. The authors have succeeded in isolating the aorto-brachiocephalic region from the dog's circulatory system, and the reflex effects of controlled pressure changes in this area on the entire circulatory system have been determined. The ascending aorta was cannulated with an EMF probe which led blood into a damping chamber, followed by a servo-resistance regulator controlling the chamber pressure at 100 mm Hg. Perfusion of the common carotid arteries and descending aorta was maintained by a constant flow pump. The carotid sinus nerves were ligated and pressure in the isolated area (AAP) was varied stepwise (30 mm Hg) from 0 to 300 mm Hg. Systemic perfusion pressure (SPP) showed a transient, rate-sensitive response marked in the AAP range of 90 to 180 mm Hg. SPP decreased as much as 30-40 mm Hg transiently, to a 30 mm Hg increase in AAP. The steady-state response was less pronounced in magnitude (approximately 10 mm Hg) over the AAP ranging from 120 to 210 mm Hg and even smaller at lower or higher AAP ranges. The latency in SPP response was 2 to 3 sec., whereas, the time to the peak transient was 10 to 15 sec. The cardiac responses are characterized by decreased heart rate, increased stroke volume, and decreased minute outflow. Tenative conclusions are: (1) the baroreceptor reflex operates from 75 to 300 mm Hg, (2) the vascular and cardiac responses have rate-sensitive and proportional elements, (3) the rate-sensitivity is asymmetrical, but not unidirectional, and more prominent in lower AAP ranges, and (4) the overall reflex gain is less than that of the carotid sinus reflex. (Supported by NIH Grant HE 09644).

COMPARISON OF ELECTRICAL IMPEDANCE PLETHYSMOGRAPHY WITH CONVENTIONAL BLOOD FLOW MEASURING TECHNIQUES

Robert D. Allison*, (Intr. by N. C. Hightower, Jr.) Department of Clinical Physiology, Scott and White Clinic, Temple, Texas.

Electrical impedance determination of blood pulse volumes and flow rates were compared with results of blood flow meter studies on exposed arteries of anesthetized dogs and confirmed by direct bleed out procedures. In addition, electrical plethysmograph results were compared with hydroplethysmograph blood flow studies on finger and leg segments of healthy subjects and venous occlusion plethysmograph studies on calf segments using a mercury and rubber strain gage. Results of the comparison of methods with the impedance system are:

Method	Location	Number of Studies	Average* % Diff.	Range of* % Diff.
Electromagnetic Flowmeter	Exposed Vessel	90	7	- .54- + 18
Direct Bleed out	Exposed Vessel	85	13	- 1.1 - + 32
Hydroplethysmograph (No venous occlusion)	Fingers	40	4	- 7.0 - + 20
	Calf segments	25	4	- 0.4 - + 20
Mercury gage plethysmograph (with venous occlusion)	Calf segments	35	12	-11.0 - + 22

* % Diff. between listed method and calculated impedance blood flow values.

CATION-BINDING AND ACTIVITY OF BRAIN NA-K ATPASE STUDIED BY A TWO-PHASE SEMI-RAPID REACTION METHOD. G. Alonso* and M. Walser. Johns Hopkins University School of Medicine, Baltimore, Md.

Particulate enzyme supported on a membrane filter and perfused with substrate-containing media of constant composition yields an effluent containing the reaction products at constant concentration. When influent composition is suddenly altered, uptake or release of substrates and cofactors and changes in product formation can be detected by sampling the effluent at short time intervals. Using a filter chamber of ~120 µl volume containing ~1mg. of rat brain ATPase protein, perfused at 105 µl/sec, 95% washout of tritiated water, ATP or Na can be achieved in less than 2 sec. Wash-in curves are even steeper. Phosphate production, measured five times per sec., during perfusion with ATP 5 mM, Mg3 mM, Na 100mM, K 20 mM, tris 20 mM, pH 7.4 at 37°, is constant at ~5 nmoles/sec. It starts immediately on adding ATP but persists a few seconds after ATP washout, probably owing to residual bound substrate. Ouabain inhibition, and reactivation on washing out ouabain, are considerably slower; here H^3-ouabain curves establish slowness of uptake and removal, despite mol. wt. near that of ATP. No uptake or release of calcium^{45} can be detected under these conditions.

Perfusion with a Na-free medium, interrupted by a 2 sec. pulse of Na-containing medium of the same ionic strength produces a burst of phosphate production coextensive with the Na in the effluent, beginning less than 0.3 sec. after Na arrival. At the same time or even earlier, calcium is released. In 5×10^{-6} M Ca, total release is ~50 pmoles from 1 mg. The presence of ouabain in all the solutions does not eliminate this release, despite enzyme inhibition.

BLOOD COAGULATION AND LEUKOCYTES IN ENDOTOXEMIA: THEIR RELATIONSHIP TO THE PROGRESSION OF THE SYNDROME IN THE RAT. Burton M. Altura and S.G. Hershey*. Albert Einstein College of Medicine, New York, N.Y.

Correlation of the clinical sequence of events with the mechanisms leading to cardiovascular collapse in endotoxin shock is difficult and uncertain. The usual cardiovascular parameters are less reliable in endotoxemia than in other types of shock. The present study represents an attempt to develop relatively simple clinical indices of the course of experimental endotoxemia; these data to serve as a basis for therapy. Rats were given single i.v. LD_{85} or LD_{50} doses of S. enteritidis endotoxin and serial (q. 30 min.) total and differential white blood cell (WBC) counts and whole blood clotting times were determined for a minimum of 6 hrs. (most fatalities occur within 7-8 hrs.). Arterial BP and mesenteric microcirculation (direct microscopy) were monitored in representative experiments. All animals were grouped as survivors or deaths for purposes of analysis. Blood changes within and between each group in relation to time were analyzed statistically. In addition lymphocyte to granulocyte ratios (L/G) were calculated serially. Four distinct phases of change in blood pattern interrelationships emerged as identifiable parameters of the progression of endotoxic shock in rats. L/G ratios decreased progressively in survivors from 1.0 to 0.4 but remained at unity (1.O.) in animals which subsequently died. Blood coagulability followed a predictable course to incoagulability toward 5-6 hrs., only in non-survivors. The observations suggest that sequential adjustment of specific therapy, based on the blood picture and coagulation may aid in the rational development of therapeutic regimes in endotoxic shock. (Supported in part by USPHS Grants HE-09042 and HE-11391.)

FRACTIONAL DISTRIBUTION OF CARDIAC OUTPUT TO THE BRAINS OF HYPOTHERMIC RATS. Peter M. Andrews* and J. A. Panuska. Georgetown University, Washington, D.C.

An "indicator fractionation technique" (Sapirstein, L. A. and G. E. Hanusek, Amer. J. Physiol., 193:272, 1958; Sapirstein, L. A., Gastroent., 52:365, 1967) was used to determine the fractional distribution of cardiac output to the brains of normothermic and hypothermic rats. Female albino rats, 230 - 310 g, were anesthetized i.p. with 40 mg/kg pentobarbital sodium. Thirty-five animals were cooled in 2°C air to a colonic temperature of 25°C. Forty-eight were maintained at a colonic temperature of 36°C. At specific time intervals, 1 - 60 sec, after femoral intravenous injection of 5 uc of I^{131} - iodoantipyrine, the rats were decapitated. The brains were removed, weighed, and radioactivity measured in a well-type crystal scintillation counter. This study, as indicated by the pattern of isotope accumulation and stabilization in the brains of the hypothermic animals, succeeded in confirming Sapirstein's technique as being theoretically applicable to hypothermic rats. A value of 1.20 $\pm$ 0.02 (SE) % of I^{131} - iodoantipyrine was found in the brains of normothermic rats as opposed to 1.09 $\pm$ 0.04 % in hypothermic subjects. These results indicate that the fractional distribution of cardiac output to the rat's brain was slightly reduced (about 9%) at a colonic temperature of 25°C. (Supported in part by DA-49-193-MD-2668 and ES-00087.)

RELATIONSHIP OF RENAL SODIUM AND CALCIUM TRANSPORT. L. D. Antoniou,* G. M. Eisner,* L. M. Slotkoff,* and L. S. Lilienfield. Georgetown University School of Medicine, Washington, D. C.

The effects of several diuretics on the urinary excretion of Na^+ and Ca^{++} were studied in mongrel dogs in an effort to determine the relationship between the renal transport mechanisms of Na^+ and Ca^{++}. After control periods, furosemide 0.5 mg/Kg or chlorothiazide, 20 mg/Kg was given in a single intravenous injection. In another set of experiments diuresis was produced by infusion of normal saline. In all studies, the urinary losses were replaced by the intravenous administration of a comparable quantity of Ringer's lactate solution. The clearance of inulin, Na^+, and Ca^{++} were measured. Saline infusion, which is known to have a proximal tubular effect, caused a proportionate increase in Na^+ and Ca^{++} clearance. Furosemide, which acts primarily on the ascending limb of Henle's loop, caused a consistently greater increase in the clearance of Ca^{++} than Na^+. There was no appreciable effect on Ca^{++} clearance following chlorothiazide administration, whereas the clearance of Na^+ was significantly increased. The results are interpreted as follows: 1. Although Na^+ and Ca^{++} reabsorptive mechanisms are closely linked in the proximal tubule, different transport mechanisms may operate in other segments of the tubule. 2. Chlorothiazide appears to act on a reabsorptive mechanism for Na^+ alone. 3. It appears that in the loop of Henle the cation pump may normally have a greater avidity for divalent (Ca^{++}) than monovalent (Na^+) cations. An alternative explanation would be that furosemide changes permeability to a greater extent for Ca^{++} than Na^+ at this site.

ENHANCED ASCENDING MONOSYNAPTIC RESPONSES TO ACTIVATION OF GROUP I AFFERENTS FROM TENOTOMIZED, DE-EFFERENTED MUSCLES. R.S. April* and W.A. Spencer, NYU Med. Schl. NYC (Supp. USPHS NB-05980, NB-1113-02).

Previous studies (Beranek et al. 1961; Kozak and Westerman 1961)have shown that, several weeks after tenotomy, there is enhanced potency of monosynaptic reflexes and monosynaptic dorsal spinocerebellar tract relayed responses to stimulation of tenotomized muscle nerves. This has been attributed a) to disuse and b) on the contrary, to excessive use from increased suprasegmental drive to gamma motoneurons. To eliminate postulated changes in gamma bias, and to disuse stretch afferents maximally, we combined Achilles tenotomy with ventral root transection in cats, and, weeks later, measured the monosynaptic ascending mass discharges to activation of group I afferents of the tenotomized, de-efferented gastrocnemius muscles after acute spinal transection under pentobarbital. Corresponding responses on the normal side served as controls. Afferent volleys were symmetrical. Throughout acute experiments lasting up to 10 hours the ascending monosynaptic response to group I activation was enhanced on the side of tenotomy and de-efferentation. Moreover, this asymmetry persisted during PTP following brief (10 sec) tetani to gastroc. nerves of each side. Monosynaptic ascending responses to sural nerve volleys were symmetrical, indicating experimental conditions did not artifactually favor one side. In control animals all ascending monosynaptic group I responses were symmetrical. Our data suggest that increased effectiveness of monosynaptic ascending group I actions in the operated animals is due to synaptic disuse, rather than excessive use. Although it will be necessary to measure tonic activity of group I afferents from muscles which have been both tenotomized and de-efferented, the data available from muscles subjected to each of these procedures alone (Hnik et al. 1963; Hnik and Payne 1965) are compatible with the disuse hypothesis.

HEMOVASCULAR RESPONSES TO MOCCASIN SNAKE VENOM. Kenneth A. Arendt and Norman M. Case*. Department of Physiology and Biophysics, and Department of Anatomy, School of Medicine, Loma Linda University, Loma Linda, California.

Studies of the petechial hemorrhagic phenomenon by conventional light microscopy have been supplemented with electron microscopic observations, in an attempt to further elucidate the mechanisms of initiation and arrest of erythrocyte extravasation. Topical applications of moccasin venom in concentrations ranging from 0.1% to 1.0% in Ringer's solutions, or in buffered Krebs' solution produced petechial hemorrhages in an apical lingual preparation in the frog and in the hamster cheek pouch. Electron micrographs of frog microvasculature indicate endothelial alterations with an apparent increase in porosity. Characteristic of the frog preparation is a partial transmural protrusion of erythrocytes rather than the localized extravascular accumulation typical of the hamster petechial response. Frog microvessels appear blistered with great numbers of protruding cells. The physical mass of the nucleus is evidently the retarding factor. There is less obvious damage to the hamster endothelium. Sections through arrested hemorrhagic areas show no evidence of platelet accumulation, but leucocytes are seen lining the intravascular surface. Among other venom-induced phenomena is the transformation of erythrocytes from biconcave discs at the arteriolar end of a given capillary segment, to crenated and ultimately spherocytic cells when they arrive at the venular end. (Supported by Grant HE 09453, National Heart Institute, N. I. H.)

FUNCTIONAL ROLE OF VESTIBULO-OCULAR REFLEXES: OBSERVATIONS IN HUMAN SUBJECTS. A. Atkin* and M.B. Bender. Dept. of Neurology, Mount Sinai Hospital, New York City.

The role of the vestibular system in sensing head position and movement is well known. Vestibular inputs are involved in various postural reflexes, and in particular, in adjustments concerned with maintenance of ocular stability during head movements. We have compared ocular stabilization reflexes of normal subjects with those of patients with nonfunctioning vestibular systems by recording velocity of compensatory eye movement and angular velocity of the head during transient head rotations that fall within the normal physiologic frequency range. This approach is consistent with recent work (e.g., Jones & Spells 1963) indicating that within this frequency range the semicircular canals are best considered angular velocity transducers, rather than acceleration transducers. As was expected, ocular stabilization became defective at much lower head velocities in subjects lacking vestibular function than in normal subjects: nevertheless some of the former maintained accurate stabilization at the lowest head velocitites. (A) This residual stabilization did not depend strongly upon inputs from cervical joint receptors, since head rotations performed with these joints immobilized by splinting (body and head turning as a unit) gave similar results; we conclude that the residual stabilization represented the optokinetic component of normal ocular stabilization. (B) When subjects lacking vestibular function reached the range of head velocities at which their ocular stabilization became defective they noted illusory movement of the entire visual surroundings. This perceptual concomitant gradually disappeared over several months following loss of vestibular function, but there was no corresponding improvement in ocular stabilization, and there was a persisting reduction of visual acuity during head movements.

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INHIBITION BY ATROPINE IN CHOLINERGIC NEURONS OF APLYSIA. **G. Austin, M. Sato*, and H. Yai*. Division of Neurosurgery, University of Oregon Medical School, Portland, Oregon.**

Using two intracellular microelectrodes we have recorded changes in membrane conductance in D and H-type neurons of Aplysia Californica, in response to locally applied ACh in vitro. Having previously shown that the increases in conductance are mainly due to an increase in P_{Na} in D-cells, and P_{Cl} in H-cells, we assume that these changes, ΔP_{Na} and ΔP_{Cl} are proportional to the concentration of substrate-receptor complex which determines the enzymatic reaction velocity. A Lineweaver-Burke type of plot for various concentrations of ACh gives the usual straight line relationship between $V^{-1} = \left(\frac{\Delta G}{G_o}\right)^{-1}$ and $[ACh]^{-1}$, for moderate concentrations between 10^{-4} and 5×10^{-3} gm./cm^3. The slope of the above straight line increased with increase in concentration of Atropine. All straight lines for varying concentrations of Atropine appeared to converge to a point at high [ACh], suggesting a competitive type of inhibition. Control applications of Atropine alone, at the same concentrations, cause no change in conductance or resting potential.

EVALUATION OF THYROTROPIN-RELEASING FACTOR (TRF) ACTION BY INTRAPITUITARY INFUSION IN RATS. R. L. W. Averill* (intr. by D. M. Keller). Dept. of Physiol. & Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

Intrapituitary infusion was used to study the time course of action of TRF in 80 Holtzman rats. Endogenous TSH secretion was depressed by phenobarbital anesthesia and raised ambient temperature (34°C). Three, 4, or 5 days prior to anesthesia each rat was given 10 μc 131-I i.p., and 19 hr. after the start of anesthesia a stainless steel cannula was implanted with its tip in the adenohypophysis. Control infusions of 0.85% NaCl for 3-hr. at 5-7 μl/hr. did not elevate blood 131-I, nor did they damage the cells of the infused pituitary lobe. Three-hour intrapituitary infusions of extracts of porcine stalk median eminence (SME) caused an increase in both the total 131-I level and the TCA-precipitable 131-I level in blood samples drawn at hourly intervals from the onset of infusion. (Responses were expressed as % increase in blood 131-I levels over the mean pre-infusion level). One hour from the onset of infusion of SME, 131-I levels had already risen above control values ($p < .05$). From 2 hr. onward the responses were highly significantly increased by SME ($p < .001$) being maximal at 3, 4, 5 and 6 hr. with no significant peak. Time courses were compared following infusions lasting 1 vs. 3 hr. for three concentrations of SME. At the highest concentration the duration of infusion did not alter either the level of response or its time course, suggesting maximal pituitary activation. With 4- and 16-fold dilutions of SME, peak responses were lower and occurred one hour earlier after 1 hr. than after 3 hr. infusions. The patterns of response closely paralleled those following i.v. infusions of TSH suggesting that there is virtually no time lag between entry of TRF at high concentration into the pituitary and the release of thyrotropin. Supported by USPHS Grant AM-11379.

EFFECT OF DEHYDRATION AND ENVIRONMENTAL TEMPERATURE ON ANTIMONY TOXICITY. Anna M. Baetjer, The Johns Hopkins School of Hygiene and Public Health, Baltimore, Md.

Rats, dehydrated to a loss of 11% in body weight for 48 hours before intravenous injection of potassium antimony tartrate, had a higher mortality rate and shorter survival time than their nondehydrated controls. Injection of blood immediately preceding antimony administration prolonged survival time but saline was without effect. Antimony produced a marked increase in heart rate in dehydrated rats whereas it caused a slight fall in nondehydrated rats as did also dehydration per se. Electrocardiograms showed T wave changes characteristic of antimony toxicity equally in both groups. The effects on the heart were not due to potassium since similar results were obtained with the sodium antimony compound. Intracellular dehydration produced by substitution of 2% saline for drinking water for two weeks before and one week after antimony injection increased mortality and rate of dying but shorter periods on saline were without effect Exposure of rats and mice to 35°C. temperature with 90% R.H. for 48 hours preceding and continuously following injection of antimony caused higher mortality, earlier onset of deaths and shorter survival time.
(Supported by USPHS grants 5R01OH00005 and ES001444.)

RECORDING OF THE CHEMOMECHANICAL TRANSDUCING EVENT IN SINGLE VASCULAR SMOOTH MUSCLE CELLS IN SITU. Silvio Baez. Albert Einstein College of Medicine of Yeshiva University, New York.

It has been the aim to record the pattern of response of single smooth muscle cells, in the wall of precapillary arterioles, to the action of some well known vasoconstrictor drugs in situ. Microvessel walls in the mesentery of the anesthetized rat were magnified up to 6000 x, using a Bausch & Lomb zoom microscope in line with a television camera. The electronically enhanced image of a segment of the microvessel wall projected in the video screen permitted a clear-cut separation of cells outline for photography and micrometric measurements. Accurate measurements, both of total wall thickness and single muscle cell width under steady state and during drug stimulation were carried out utilizing the image splitting-television microscope system (J.Appl.Physiol.21:299,1966). Forty four measurements in eleven single muscle cells alone, in three rats, gave an average cell diameter of 2.08μ (range 1.9μ to 2.4μ). The calculated muscle cell diameter derived from sixty eight measurements of wall thickness (endothelial and muscle cell) in four rats, gave an average diameter of 2.54μ (range 2.3μ to 3.2μ). Topical application of epinephrine in gradients ranging from 0.1 μg/ml to 10 μg/ml resulted in a proportionate increase both in the width of the effector cell, during shortening, and of the time-course duration of response. Thus, the pattern of the chemomechanical transducing event was recorded from a single vascular smooth muscle cell in situ, in the living animal. These results and the pattern of responses of the single smooth muscle effector cell to epinephrine, pitressin, and angiotensin, before and after topical Dibenzyline will be presented for discussion.

(Supported by NIH grant HE-06736.)

Respiratory Responses to CO_2 During Exercise in Awake Dogs. C.R. Bainton*, R.A. Mitchell, and J.M. Senapati*. Dept. of Anesth. and Cardiovasc.Res.Inst. University of California Medical Center, San Francisco, California.

This study was initiated to investigate the role of the carotid body in the hyperpnea of active exercise. Steady state and transient changes in ventilation produced by exercise will be evaluated during high $P_{I}o_2$ and acute and chronic hypoxia. Results, presented here, represent partial control data prior to denervation in two awake dogs with tracheostomies and carotid loops. Temperature of the animal was controlled and panting prevented by a preliminary washing and application of isopropyl alcohol during exercise. Panting, through the tracheostomy, could also be prevented by holding the mouth shut. Four point steady state CO_2 response curves with $P_{I}o_2 > 500$ mm Hg were obtained at rest, during one hour of 9 MPH exercise and after recovery. Sitting at rest, $(a-A)Pco_2$ was .5 mm Hg in both dogs.

	$P_A co_2$ mm Hg	V_E L/min	f	pulse	O_2 consumption cc/min	Slope, L/min /mm Hg CO_2
Dog 1 (N = 9)						
Rest	43.0±2.0	2.2±.5	8±2	80±5	138	1.2
Exercise	38.1±1.5	9.0±.9	25±4	132±5	520	1.3
Dog 2 (N = 8)						
Rest	40.6±1.5	2.6±.7	16±4	76±5	118	1.5
Exercise	38.3±1.5	8.2±1.9	42±15	136±6	405	1.5

Our results differ from those reported in man in that resting $P_A co_2$ is reduced with active exercise but agree with those that report the slope of CO_2 response at rest and exercise to be parallel.

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LIGHT FLASH INTENSITY DEPENDENCE OF LATERAL GENICULATE NEURONS. Frank H. Baker and Eugenio Riva Sanseverino (intr. by V. B. Mountcastle). The Johns Hopkins University School of Medicine.

As part of a survey of the transient response to light flashes of lateral geniculate neurons of the unanesthetized cat, a study was made of response dependence on stimulus intensity. Receptive fields were localized, their topology determined and centers or peripheries studied with positive going light flashes. Stimulus time histograms were used as an estimate of the stimulus locked probability density of firing which was taken as a sufficient measure of neural activity. For light stimulated excitation, greater intensities produced greater peak firing densities up to a saturation point, greater durations of increased firing rate, decreased duration of peak firing, and decreased latency of the response. Neurons are separable into two classes on the basis of whether or not a depression of activity occurs following the initial peak firing burst at higher flash intensities. Correlation of time histogram microstructure with knowledge of the latency of surround inhibition supports the notion that this post peak activity depression may be inhibitory in origin. Units tested for intensity-duration dependence in the range of 10-40 msec. were in general not found to demonstrate a Bunson-Rosco law identity of response to equal stimulus energy under the measures we have used. Finally, some characteristics of stimulus intensity dependence of inhibition are comparable to excitation.

RAPID METHODS FOR DETERMINATION OF PBI AND SERUM IODOTHYRONINES. H. J. Baker* and J. W. Woods. The Johns Hopkins Medical School, Baltimore.

Anion exchange column chromatography (Dowex resin AG1X2) and chloric acid digestion of the column effluent permit rapid determination of thyroid hormones (T3-T4) in human and animal sera. Removal of inorganic iodide from serum with another ion exchange resin (Hycel Products, #226) followed by chloric acid digestion allows routine PBI determination in less than three hours. Both methods may be used in the presence of relatively high concentrations of inorganic iodide. The concentrating properties of the column method may be used to quantitate T3-T4 in samples containing extremely low concentration of iodothyronines. The columns also allow quantitative differentiation of iodotyrosines and non-hormonal iodoproteins. PBI values obtained on sera from 48 hospital patients differed from those obtained by the commercial laboratory which ordinarily performs this test for our hospital by -0.22 μgms/100 ml. (mean difference). The range of values in this series was from 1.6 to 10.7 μgms/100 ml. The standard deviation in each of two series of PBI determinations on two lots of human serum was 0.27 (mean PBI values, 4.5 and 6.6; N=41 and 46, respectively). Our determinations of T3-T4 by column chromatography on 3 lots of human serum were within ± 0.2 μgms/100 ml. of those obtained by the commercial laboratory (mean values of 4.0, 4.8 and 5.1). The highest and lowest values obtained by us in this series (N=33) were within 10% of the mean. Both methods have been used to evaluate thyroid function in monkeys, horses, dogs, cats and rats. Under ordinary laboratory conditions we have found that one individual can comfortably perform 50-60 determinations in a normal day using either method.

THE REGULATION OF BRAIN TEMPERATURE IN THE RABBIT IN SLEEP AND AROUSAL. Mary Ann Baker* and J.N. Hayward. Dept. of Anatomy and Brain Research Institute, UCLA, Los Angeles, Calif.

Temperature fluctuations in the blood perfusing the brain appear to underlie the thermal changes which we have observed in the brainstem of the rabbit. Temperatures were measured in the aortic arch, the brainstem, and on the skin of the ear in unrestrained rabbits at 25°C ambient temperature. The animal and the EEG were observed continuously. Temperature changes in the brain were preceded by similar changes in the blood. Thermal shifts in the subarachnoid space near the vessels of the circle of Willis rapidly reflected the oscillations in aortic blood temperature. Deep brain sites were warmer than the arterial blood and showed damped oscillations. Blood temperature fluctuations were correlated inversely with fluctuations in ear temperature. The most dramatic thermal events of sleep-waking cycles were those observed during paradoxical sleep. The transition from slow-wave sleep to paradoxical sleep was always accompanied by a vasoconstriction of the ear and a warming of the blood and brain. Whether they were followed by wakefulness or by slow-wave sleep, the terminations of the paradoxical sleep episodes were associated with vasodilatation of the ear and a drop in blood and brain temperatures. Alternating episodes of slow-wave sleep and arousal usually were not associated with significant thermoregulatory changes. These studies indicate that the temperature changes in the brain of the freely-moving rabbit depend upon temperature shifts of the arterial blood related to cutaneous vascular activity.

(Supported in part by USPHS Grant NB-05638-03)

RESPONSE OF TRANSMURAL ELECTRICAL POTENTIAL OF RAT INTESTINE TO RAPID INCREASE IN TEMPERATURE. R. David Baker and Malcolm J. Wall*. Univ. of Texas Med. Br., Galveston, Texas.

As is well known, a relatively steady potential difference (PD) of about 1 mV exists across the wall of everted rat jejunum in Krebs-Ringer-bicarbonate without sugar at 37°. At 0° the PD was only about 0.4 mV. During sudden warming from 0° to 37° the PD promptly increased in two phases to 4-5 mV, then gradually declined over a period of several minutes to its steady value of 1 mV. Upon subsequent cooling and rewarming a second transient response was obtained but of much less magnitude. Ouabain had no consistent effect. Phlorizin blocked the usual response to glucose but had no effect on the transient thermal response. When uneverted segments were suddenly warmed from 0° to 37°, the PD rose in two phases to about 6-8 mV and was maintained at this high value. Upon subsequent cooling and rewarming of uneverted segments the original large PD's were re-established. The failure of everted segments to maintain a respectable PD may be due to an increase in passive permeability (with internal short circuiting) upon warming. Uneverted segments are apparently better able to maintain their integrity. (Supported by USPHS Grant AM-05778).

RENAL TUBULAR SECRETION OF p-AMINOHIPPURATE IN THE DOG : EFFECTS OF α-KETOGLUTARATE. Sulamita Balagura and William J. Stone, intr. by Richard H. Kessler. Cornell Univ. Med. Col. New York, N.Y.

The accumulation of p-aminohippurate (PAH) by rat renal cortical slices, and the renal extraction of PAH in the dog are depressed by certain Krebs cycle intermediates. The present work includes a systematic study of the nature of the inhibition of PAH secretion by α-ketoglutarate (α-KG) in the dog. Following is a summary of the results obtained in twenty-three experiments performed in anesthetized dogs, using renal clearance and extraction procedures: Inhibition of PAH secretion by α-KG occurs at all levels of tubular loading with PAH, below and above those necessary for saturation (Tm). Renal titration curves for PAH at high plasma levels of α-KG are essentially flat when compared to those obtained at normal plasma levels of the intermediate. The degree of depression of Tm_{PAH} correlates well with the magnitude of the renal loads of α-KG relative to those of PAH. The process is not overcome by increasing the tubular loading of PAH during administration of α-KG at constant rates. Administration of acetate, which enhances Tm_{PAH} in normal conditions, neither prevents nor overcomes the inhibition of PAH secretion by α-KG. Since α-KG depresses both the affinity (Km) and the maximal capacity (Vmax) of the PAH transport system, we conclude that inhibition is non-competitive. This contrasts with the nature of the inhibition of tubular transport of PAH also produced by a large variety of compounds, which has been described as competitive inhibition, or as one due to decrease in the energy supply to the PAH transport system.

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CARDIODYNAMICS OF ENDOTOXIN SHOCK. Basdeo Balkissoon and Robert L. Simmons*. College of Medicine, Howard University, Washington, D.C.

Endotoxin shock is a difficult therapeutic problem in clinical medicine. The current therapeutic management even with the recent use of phenoxybenzamine and large electrolyte and colloid replacement is still attended by a high mortality. To study the changes in cardiac performance produced by endotoxin (E. Coli polysaccharide) shock, we implanted mercury-rubber Whitney strain gauges around the left ventricle and pressure cannulas into the ascending aorta and left ventricle of mongrel dogs. After the dogs had completely recovered, left ventricular circumference and pressure and aortic pressure were chronically recorded in the awake state and after the administration of endotoxin (4 mg/kg). The left ventricular end-diastolic, end-systolic and stroke circumference decreased markedly and left ventricular and aortic pressures fell precipitously. The maximum velocity of left ventricular circumferential shortening decreased markedly and suggested the depletion of myocardial catecholamines. As confirmatory evidence the myocardial catecholamines will be determined. Cardiac output will be measured both before and after endotoxin shock. It appears that one mechanism of action of endotoxin in production of shock is profound myocardial depression by depletion of myocardial catecholamines.

MODIFICATION OF TRANSCAPILLARY EXCHANGE BY NON-PARTICULATE PERFUSION MEDIA. K.W. Ballard (Introduced by R.L. Paldino). Dept. of Physiol. U.S.C. School of Medicine, Los Angeles, California.

It has been suggested that cellular elements in whole blood foster the exchange function of the circulation by physical stirring of plasma in capillaries. The effect of blood-borne particulate matter on the effective flow in skeletal muscle was examined empirically in the skinned hind limb of cats with normal arterial blood supply, perfused with whole blood, or with cell-free iso-oncotic media. Effective circulation was assessed from clearance of radioactive sodium iodide after intra-arterial administration. Perfusion with oxygenated or oxygen-depleted whole blood, plasma, or oxypolygelatin did not change clearance from that observed with the normal arterial supply. However, perfusion with 6% dextran consistently increased clearance in some cases by as much as 98%. Only those preparations perfused with oxygenated whole blood consistently failed to show post-perfusion hyperemia. It was concluded that the rate of movement of solutes across vessels perfused with particulate-free media was not diminished. The increased clearance frequently found during perfusion with cell free media may be in part explained by the relatively greater solvent perfusion if one assumes that the volume occupied by red cells is not available to carry any solute. This possibility is currently being evaluated. (Supported by U.S.P.H.S. Post-Doctoral Fellowship #1-F2-HE-5896-01.

PULMONARY VASOCONSTRICTION IN HYPOVOLEMIC LOW FLOW STATES: T. Van N. Ballentine*, W. Zuschneid*, George H. A. Clowes, Jr. Sears Surgical Laboratory, Boston City Hospital, Harvard Medical School, Boston, Massachusetts

To avoid the effects of anesthesia, the pulmonary vasomotor reactions were studied in healthy intact animals. Needles were inserted painlessly into the pulmonary artery and left atrium through conduits implanted several weeks before. Cardiac output was measured by dye dilution curves. Dogs were trained to lie quietly. By bleeding, the blood pressure was reduced to 45mm Hg mean and the cardiac index to 1.2L/M^2/min. for two hours. In 12 complete experiments the average pulmonary artery and left atrial pressures fell 8cm. and 7cm. H_2O respectively. The transpulmonary vascular pressure (ΔP) remained nearly constant. The pulmonary vascular resistance (PVR) increased 256%, whereas, the total peripheral vascular resistance (TPVR) rose but 76% above the resting basal values. That pulmonary venoconstriction may play a part in the elevation of PVR is suggested by a discrepancy of 2 to 4cm. H_2O between the "wedge pressure" and the left atrial pressure. Arterial pO_2 was 95mm Hg. Upon reinfusion of blood there was a slight but sustained elevation of both left atrial and pulmonary artery pressures, although PVR returned within 5 minutes to the basal value. However, 24 hours later PVR was elevated 58% and remained so during the next 3 days, accompanied by a moderate reduction in arterial pO_2. It is concluded that active arteriolar constriction or cut off and possibly venomotor constriction are present in the intact animal during low flow states. Both may play a part in the subsequent morphological and functional changes.

BRADYKININ AND 5-HYDROXYTRYPTAMINE (5-HT)'S EFFECTS ON THE MICRO-CIRCULATION. T. A. Balourdas (intr. by E.M.K. Geiling). Dept. of Pharmacology, Medical School, Howard University, Washington, D.C.

Microvascular effects of synthetic Bradykinin (BRS) on the microcirculation, namely, vasodilatation, hypotension, increased capillary permeability, vascular hyperreactivity, venoconstriction, stases and petechial hemorrhages were reported (Balourdas, T.A., Proceedings III Internat. Pharmacological Congress, Sao Paulo, Brazil, July 1966, p.199 & Extra-Congress Symposium on Vaso-active Polypeptides, Ribeirao Preto, Brazil, Aug. 1966(In Press); The Pharmacologist, 8:174, 1966.) The present investigations are concerned with the effects of Serotonin (5-HT) on the microvessels and the interactions with BRS. The rat mesocaecum bioassay was used and the mesoappendiceal microvessels were examined by in vivo microscopy. Results: Vasodilatation, increased capillary permeability, increased capillary fragility with petechial hemorrhages, slowing blood flow, stases, venular constriction, microvascular hyperreactivity were observed. Hypotension was found both with small and higher doses of 5-HT intravenously injected in the rats. The effects of BRS following Serotonin were enhanced and vice versa. Especially the venospasm and the sensitization of microvessels apparently were found markedly increased. These observations indicate the interaction of Bradykinin and Serotonin in regard to microcirculatory effects. Whether this interaction is synergistic or other underlying mechanisms, directly or indirectly being involved, will be discussed. The variability of pharmacodynamic responses of the cardiovascular system with Serotonin directly produced and/or reflexly mediated, does not permit conclusive interpretation of the microvascular findings. Changes in enzymatic activity and local action of other vasoactive amines and agents might be involved. (Supported by grant from NHI).

THE KINETICS OF I^{131}-DIODRAST® PENETRATION INTO CANINE RED BLOOD CELLS. R. O. Banks* and C. V. Paganelli. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Diodrast (3,5-diiodo-4-pyridone-N-acetic acid) is a lipid insoluble organic acid (pK_a = 2.9) with a molecular weight of 404.94. If Diodrast were to enter red cells by simple diffusion, it should do so quite slowly in view of its size and solubility properties. However, we found that Diodrast entered washed dog red cells, incubated in vitro at 37°C, with a half-time of 5.5 min. Diodrast influx displayed saturation kinetics (V_{Max} = 4 mM/L cells/hr; K_m = 1.12 mM) and was competitively inhibited by phenol red. Countertransport of Diodrast was induced in a Diodrast-equilibrated cell suspension by adding phenol red to the medium. At a medium pH of 7.4 the steady-state ratio (R) of cell water Diodrast concentration to medium Diodrast concentration was 0.72 ± .04. In contrast, when cell suspensions were incubated with Diodrast and 10^{-4}M iodoacetic acid (IAA), R values averaging 1.13 ± .03 were obtained. In the presence of IAA a steady-state cell Diodrast concentration was attained in about 90 min. Either glucose depletion or 10^{-3}M sodium fluoride produced effects similar to IAA. Equilibrium ultrafiltration of hemolysates from Diodrast-containing cells showed that the increase in cell Diodrast concentration with IAA could be accounted for by binding of Diodrast to hemoglobin (Hb). The binding did not result from a direct effect of IAA on Hb. We conclude that Diodrast uptake by dog red cells is carrier-mediated and that intracellular Diodrast binding induced by IAA is in some manner dependent on red cell metabolism.

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COMPARATIVE STUDY OF RECEPTIVE FIELD SIZES FOR SINGLE UNITS INNERVATING THE RHINARIUM IN COATI AND RACCOON. David J. Barker* and W. I. Welker, Laboratory of Neurophysiology, Univ. of Wisconsin, Madison.

The coatimundi's more prominent use of its rhinarium for tactile exploration of the environment, coupled with a higher rhinarial receptor density, when compared with that of the raccoon, prompted a study to determine if there were corresponding distinctive features in the coding of information in first-order somatosensory neurons which innervate the rhinarium. In acute experiments, under surgical levels of pentobarbital anesthesia, the left Vth ganglion in 9 coatis and 8 raccoons was exposed by hemispherectomy and dissection of dura, and explored with tungsten microelectrodes. Receptive field sizes of single units were delineated with a series of "von Frey" wire probes, ranging in diameter from 150 to 25 microns. Fields so determined were drawn on photographs of relevant skin surfaces. Modality of isolated units was classified in terms of wire probe threshold, rate of application of adequate stimulus and nature of unit response. Of 115 units examined in coati and 91 in raccoon, approximately half of these were studied with the Vth root severed in both animals. Four modality classes were distinguished: low and high threshold touch, pressure, vibration, and temperature, with a distribution of 46%, 12%, 30%, and 12% respectively in the coati and 58%, 14%, 24% and 4% in raccoon. Average differences in touch receptive field sizes between coati (N=46) and raccoon (N=45) were not significant, but touch field sizes in both animals were signficantly smaller when the Vth root was intact. Vibratory field sizes were also smaller in the intact root preparation. (N=35 and 22). Similarity in rhinarial touch field sizes in coati and raccoon agrees with the previously reported similarity in forepaw touch field sizes in these two animals. (Supported by USPHS Grants 5326 and 06225)

THE CORRELATION OF RUPTURED NEXUSES AND ELECTRICAL DECOUPLING IN A SMOOTH MUSCLE. L. Barr, M. M. Dewey* and W. Berger*. Departments of Physiology and Biophysics, and Anatomy, Woman's Medical College, Philadelphia, Pa.

Action potentials propagate throughout the taenia coli of guinea pig by way of electrical transmission between the smooth muscle cells with a large safety factor. Large bulbous, end-to-end nexuses and numerous smaller side-to-side nexuses occur between these cells. Theoretically narrow strips of taenia coli are electrically like single core conductors with a single space constant. In such situations the side-to-side nexuses are irrelevant to the tissue's behavior. In all situations propagation seems to occur by way of local circuit current flow across the nexuses between cell interiors. When the nexuses in a sucrose gap are ruptured by treatment with hypertonic sucrose solutions the longitudinal resistance of a muscle strip across the gap increases. In other experiments when physiological saline solutions are made hypertonic the propagation of action potentials is blocked even in the presence of spontaneous activity.
(Supported by USPHS grants HE-10084 and AM-11327.)

FREQUENCY DISTRIBUTION OF URETERAL PERISTALSIS.

William F. Barry, Jr.*, and Saul Boyarsky, Duke University Medical Center and V.A. Hospital, Durham, North Carolina.

Ureteral peristalsis is described classically to be regular, rhythmic and progressive. Ureteral pressure tracings, sensed through indwelling catheters, from two different types of in vivo dog preparations have been analyzed with respect to the frequency of these contractions. One animal preparation consisted of a chronic bladder explant receiving a slow intravenous (0.1 cc/min) infusion. The second preparation had a chronic explant and nephrostomy with inflow to the ureter controlled by a constant infusion pump (0.2-1.3 cc/min). The time interval between pressure events was converted to "instantaneous rate". Frequency distribution plots, mean, standard deviation, and range were obtained from this data for each individual study and for each group of similar studies. Analysis of 3600 events in 57 tracings from 11 dogs show that ureteral peristalsis occurs in a very arrhythmic sequence. The frequency distribution curves tend to show a bimodal distribution, occasionally a multimodal curve. The frequency distribution curves change with increasing urine flow with possible limitation in the maximal response. Peaks in the frequency distribution tend to occur in multiples of a basic frequency for any given ureter. (Supported by grants from the National Institutes of Health, the American Medical Association and the Veterans Administration).

NORMAL BLOOD pH OF THE TOAD AT DIFFERENT TEMPERATURES AS A FUNCTION OF THE IONIZATION CONSTANT OF WATER.

F. W. Baumgardner* and H. Rahn. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Blood pH of unanesthetized, unrestrained toads (Bufo marinus) was measured at their body temperature after acclimatization to several temperatures between 10° and 37°C and was shown to decrease from 7.99 to 7.57, while the pH of water at neutrality (pH = 1/2 pKw) decreased from 7.27 to 6.81. As has been previously reported from this laboratory for other poikilotherms, observed blood pH changes parallel the pH changes of water at neutrality. Thus observed blood pH can be expressed as pH = 1/2 pKw + Constant, where Kw is the ionization constant of water. Therefore a constant relative alkalinity is demonstrated and appears to be the parameter in blood acid-base balance which is maintained, independent of body temperature. The preceding studies were carried out with animals which were presumed to be in a steady state after 3 days' acclimatization to a given temperature. In additional experiments short term pH changes were measured during imposed diurnal temperature cycles (15° to 30°). The same constant difference between blood pH and water pH was maintained, indicating that blood pH changes seem to be sufficiently rapid to preserve a constant relative alkalinity in the blood during daily temperature fluctuations.

REGIONAL BRAIN BLOOD FLOW AS INFLUENCED BY CO_2, ANESTHESIA, LIGHT, AND O_2 AT HIGH PRESSURE. J.W. Bean and N.E. Leatherman*Physiology Dept., Univ. of Michigan, Ann Arbor. Needle thermo-flow probes (Fed. Proc. 26:437, 1967) modified after Gibbs and others and our earlier models (Fed. Proc. 25:700, 1966 shown by in vitro and in vivo tests to reliably monitor regional blood flow changes in brain and kidney were used to study regional changes in brain blood flow in rats. The prompt flow increase in the geniculate and rostral reticular thalamic regions induced by CO_2 in unanesthetized rats was sometimes intermittent and the pronounced initial increase was not maintained throughout the administration. Under anesthesia the intermittence was absent and the initial increase was more sustained temporarily. Simultaneous recordings of the CO_2 responses in two thalamic regions were usually synchronous and parallel; anesthesia by itself (Na pentabarbital) reversibly increased the flow in one and decreased it in the other. Light stimulus to eyes increased flow in the geniculate region. Signs of OHP (60psig) toxicity on the CNS were preceded by a gradual shift from a stable parallel flow relationship in the two regions to 90° out-of-phase flow cycles of increasing magnitude; a subsequent shift to an in-phase relationship of large flow changes occurred with the onset of O_2 convulsions and continued into decompression. Simultaneous recordings of regional changes in cerebral blood flow and pO_2 (O_2 electrode) were also made. The data substantiate earlier findings (Am. J. Physiol. 201:1192 1961; Physiologist 5:104, 1962) and their interpretation that asynchronous changes in regional pO_2 as recorded from multiple O_2 electrodes in the brain are associated with the O_2 convulsions and are due in large part to regional changes in brain blood flow (Oxygen in the Animal Organism, Pergamon Press, London, p496, 1963). These regional flow changes, frequently reciprocal, and the attendant changes in pO_2, CO_2, and pH, are important causal factors in CNS reactions induced by OHP but are masked in effluent brain blood. Supported by Natl. Inst. of Health Grant NB-01646.

THE COMPARATIVE HEMODYNAMIC EFFECTS OF TREADMILL AND SUPINE BICYCLE EXERCISE IN PATIENTS WITH CARDIAC IMPAIRMENT. G. David Beiser*, Stephen E. Epstein*, Morris Stampfer*, Eugene Braunwald. NIH, Bethesda, Md.

Although it is generally appreciated that the hemodynamic effects of exercise are influenced by changes in body position and the type of exercise performed, very little is known about the significance of these factors in patients with impaired cardiac function. Thus, data obtained from such patients during supine bicycle exercise, which is the method commonly in use, may not reflect accurately the circulatory responses occurring during ordinary upright activity. Accordingly, nine patients with moderate to severe cardiac impairment and eight subjects with normal cardiovascular systems were studied during both supine bicycle and upright treadmill exercise. At comparable levels of exertion, as determined by VO_2, there were no differences between the two modes of exercise in the response of cardiac index (CI) and stroke index (SI) in the patients. In normal subjects, however, CI was an average of 16% (0.83 L/min/M^2, $p<.005$) and SI 13% (7 ml/M^2, $p<.005$) lower during treadmill exercise. However, mean pulmonary arterial pressure (PAP) was lower in patients by an average of 17 mm Hg ($p<.005$) during upright exercise compared to a decrease of only 5 mm Hg ($p<.05$) in normals. In patients, heart rate (HR) was 10% (11 beats/min, $p<.05$) and arterial pressure was 22% (18 mm Hg, $p<.001$) higher during supine bicycle exercise, suggesting that in patients with cardiac impairment this form of exercise evokes greater sympathetic discharge to the heart and resistance vessels than a comparable level of treadmill exercise. In normals HR and AP were unchanged between the two forms of exercise. Thus, not only is the circulatory response to supine bicycle exercise quite different to that of upright treadmill exercise in both normal subjects and patients, but the changes that occur in the two groups from one mode of exercise to the other are dissimilar.

DEPRESSION OF PANCREATIC EXOCRINE FUNCTION BY ANESTHETIC AGENTS. Gur Ben-Ari*, Jack Rudick*, Allan E. Kark*, David A. Dreiling. The Mount Sinai School of Medicine, New York, N.Y.

Secretion of HCO_3, Cl, and amylase, stimulated by intravenous secretin (1 u/kg. and 5 u/kg.) and secretin (1 u/kg.) with pancreozymin (1 u/kg.) was studied in 11 dogs equipped with pancreatic fistulas during sodium pentobarbital (2%) anesthesia, chloralose-urethane (1:10) anesthesia, and also in the unanesthetized state. The addition of gastric fistulas prevented the release of endogenous secretin by acid contamination of the duodenal mucosa. Both anesthetic agents resulted in a 75% reduction of the resting rate of flow, with concomitant reductions of HCO_3 concentration and amylase concentration. The response to submaximal and maximal doses of secretin and secretin with pancreozymin was reduced by 30% -- rate of flow, HCO_3 concentration and amylase concentration were affected. No statistically significant difference was noted between the two anesthetics. Control experiments demonstrated no reduction in the response to repeated injections of secretin, irrespective of the time interval between injections. In a further 3 pancreatic fistula dogs subjected to truncal vagotomy, both anesthetic agents did not reduce the exocrine function either in the unstimulated state or in response to exogenous stimuli. These findings suggest a vagolytic effect of anesthetic agents on pancreatic exocrine function and may account for some discordance in physiologic observations and discrepancies in biological assays of secretin and pancreozymin recorded by different investigators utilizing anesthetic agents. (Supported by NIH Grant #AM-03889-07)

THE ROLE OF THE ANTERIOR LIMB OF THE ANTERIOR COMMISSURE IN OLFACTION.

Marvin H. Bennett (intr. by B. M. Wenzel). Department of Anatomy, Louisiana State University Medical Center, New Orleans, Louisiana

Behavioral measures were used to investigate the effects of lesions of olfactory system structures upon olfactory function in rats. Performance in odor discrimination and detection paradigms was not affected by unilateral bulb removal, or by unilateral or bilateral commissural lesions destroying less than 50% of both anterior limbs. A complete loss of discriminative performance followed bilateral commissural transection, though the habit was reestablished with retraining. Such loss also occurred in animals trained in the odor detection paradigms indicating that a loss of discriminative ability *per se* was not responsible for postoperative performance deficits. A successively increased threshold followed unilateral commissural transection, unilateral bulb removal, and bilateral commissural transection, whereas all three procedures produced the same decrease in adaptation rates. It was concluded that two anatomically and functionally discrete systems coursed through the anterior limb of the anterior commissure. The first, contained wholly within the anterior limb as commissural fibers, provides a component of the centrally originating olfactory adaptation. The second, contained in centrifugal decussating fibers, summate intensitive functions of each half of the olfactory system and perhaps provide a pathway for other centrally originating facilitative influences.

EFFECT OF BIOGENIC AMINES ON THE CHOLEDOCHUS OF DOGS. D. N. Benslay* and T. M. Lin. Lilly Research Labs, Indianapolis, Indiana.

In order to elucidate the actions of biogenic amines upon the choledochus, three cholecystectomized dogs with exteriorized fistulae of the common bile duct and, one dog similarly prepared but in addition provided with gastro-duodeno mucosal septum and gastro-jejunostomy were used. The hepatic and the choledochal ends of the common bile duct were connected to separate strain gauges which in turn were connected to each other. The hydrostatic pressure in the hepatic or choledochal system was each measured by an individual water manometer and strain gauge which in turn were connected to a Visicorder; the pressure in each recording system could be adjusted by infusion of sterile saline from a reservoir into each water manometer. Biogenic amines were given when (I) spontaneous hypertonicity (>200 mm H_2O) of the choledochus occurred, or (II) when experimental hypertonicity (>200 mm H_2O) was induced by infusing 1.5-2.0 ml/min of saline into the manometer. In either case, histamine 0.02--1.0 mg/kg, s.c. lowered the pressure in the choledocal system by approximately 100 mm H_2O in more than 80 tests. Serotonin, 0.04--0.6 mg/kg, s.c. had no effect in (I) but increased the pressure by about 100 mm H_2O in (II) in more than 12 tests. This effect of serotonin was either prevented or counteracted by histamine. Norepinephrine, 0.5--1.0 µg/kg, i.v. and epinephrine 20 µg/kg, s.c. had no effect upon the choledochus under either condition.

THE EFFECTS OF THYROTROPIN AND THYROXINE ON THE KINETICS OF I^{131} UPTAKE IN THE RAT THYROID GLAND

Samuel G. Benson (Intr. by A.L. Bennett)U. of Nebr Coll of Med. Omaha, Nebr.

The influence of various treatments on the rate of thyroidal uptake of injected I^{131} was studied in rats. They were first subjected to a seven day period either of control(no treatment) or of treatment designed to change the concentration of circulating thyroid-stimulating hormone(TSH). Three experimental groups were: T_4-daily injection of Thyroxine, 100 µg/Kg; TH-a single injection of Armour's Thytropar, 5 units/rat; Low I-on an iodine-deficient diet. Each rat(control and treated groups) then received 10 µc I^{131} intraperitoneally. Periodic scintillation counts were made over a limited area of the neck of the intact animal and also on the excised thyroid gland. A graphic representation of the rate of I^{131} uptake in situ was found to closely fit a curve expressing a rising exponential equation: $C=C_m(1-e^{-\frac{T}{\tau}})$, where C is the counts per minute(cpm) obtained at the time T after injection; C_m is the maximum cpm obtained; τ(hrs.) is the time at which 63.2% of C_m is reached, and e is the base for the natural logarithm.

Results:			
Control	-	C_m = 12,000;	τ = 2.1
T_4	-	5,100;	8.0
Low I	-	34,000;	0.8
TH	-	18,000;	1.4

A comparison was made between the in situ findings and the data obtained from excised glands. Correlation coefficients were calculated to be 0.91 for controls, 0.94 for the Low I group and -0.46 for the T_4 group.

THE EFFECT OF RESTRAINT STRESS AND FASTING ON ORGAN SIZE IN THE DOMESTIC FOWL [1]

E. L. Besch, A. H. Smith and R. R. Burton*, Institute for Environmental Research, Kansas State University, and Department of Animal Physiology, University of California, Davis.

Previous work has shown that restraint produces a state of acute stress in domestic fowl and results in a loss of body weight. This loss does not appear to be due to inanition per se, but little information is available on comparative organ weight loss in these animals. Accordingly, adult, male, domestic fowl were restrained, in series, in individual cages with feed and water ad libitum and comparisons of various organ weights made with tissue from control and fasted animals. Restraint and fasting caused a decrease in absolute organ weights in all organs. The loss of spleen tissue mass, superficial pectoral muscle mass, small intestine mass and pancreas mass was greater in the restrained than fasted groups. Loss of testes tissue mass was less in restrained than fasted. There were no apparent myocardial lesions in either group. The effects of both restraint and fasting appear to be directly proportional to the duration of treatment.

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[1] Supported by NASA:NGR:05-004-010.

SERUM INSULIN LEVELS IN SPONTANEOUSLY DIABETIC MICE OF THE KK STRAIN.

James H. Birnie, Peggy Pula* and Patricia Hammerle*, Smith Kline & French Laboratories, Philadelphia, Pa.

Hereditary diabetic mice of the KK strain have been reported as having elevated glucose tolerance curves and a higher than normal pancreatic insulin content (Nakamura and Yamada, Diabetologia 3:212, 1967). Studies in our laboratory indicated that mice of the KK strain had higher fasting insulin values than the CBA controls (42 μU/ml vs 26 μU/ml) when undiluted pooled serum samples were assayed by the rat hemidiaphragm method of Vallance-Owen and Hurlock, Lancet 1:68, 1954. An investigation of immunoreactive insulin levels in serum samples from individual mice, assayed by the method of Hales and Randle, Biochem. Jour. 88:137, 1963, showed that KK mice, fed ad lib., had significantly higher insulin levels than did the HaM/ICR controls (111 μU/ml vs 35 μU/ml). Following an 18-hour fast, the serum immunoreactive insulin of the KK and HaM/ICR strains were both reduced from the ad lib. level, but the KK remained higher than the controls (41 μU/ml vs 14 μU/ml). When animals were fasted for 18 hours and tested following an oral glucose load of 2 gm/kg, insulin levels were increased in both groups at one hour postglucose (50 μU/ml vs 32 μU/ml), but the percentage increase over the fasting level was smaller in the KK mice than in the controls. The basal in vitro glucose uptake of the epididymal fat pad and diaphragm muscle from KK mice was usually decreased when compared with tissues from the HaM/ICR controls.

DISCHARGE OF FRONTAL EYE FIELD (FEF) NEURONS DURING EYE AND HEAD MOVEMENT IN MONKEYS. E. Bizzi and P. H. Schiller (intro. by E. V. Evarts). Dept. of Psychology, MIT, Cambridge, Mass.

Previous investigations (Bizzi, Evarts 1967) indicated: 1) most FEF cells recorded in unanesthetized monkeys discharge in relation to eye position; 2) these cells do not change activity prior to initiation of an eye movement. The results were obtained in monkeys whose heads were restrained. In order to investigate the characteristic discharge of FEF neurons during coordinated eye-head turning, apparatus was constructed allowing spontaneous head rotations in the horizontal plane. It is known that during head movement the eyes begin to move first and are followed by the head. During head rotation the eyes display a backward compensatory movement with respect to the direction of the head movement. The firing pattern of FEF cells was examined with respect to both head and eye movement. Two populations of cells were observed: one related to eye movement, the other to head turning; cells responding to both were not found. The firing pattern of FEF neurons signaling eye movement or eye position was maintained irrespective of head movements or head position. Unitary discharge occurred also during the backward compensatory movement, provided that the eyes were moving across positions which would have associated with neuronal activity had the eyes come to rest there. In relation to head movement, two types of neurons were found: some discharged during any head movement, a few to head turning in a specific direction. Some of these units were identified by antidromic responses to stimulation of the cerebral peduncle.

Changes in Heart Rate Induced by Bacterial Endotoxin. Benjamin Blattberg and Matthew N. Levy. Research Div. St. Vincent Charity Hospital, Cleveland, Ohio 44115

In unanesthetized dogs, the intravenous injection of E. coli endotoxin results in an early triphasic change in heart rate; namely, a transient tachycardia, followed by bradycardia, and then a secondary tachycardia. In dogs anesthetized with pentobarbital, there is a similar initial tachycardia, followed by a more prolonged period of bradycardia. When morphine-chloralose-urethane anesthesia is employed, endotoxin also induces an initial tachycardia which is somewhat more prolonged than in the unanesthetized or pentobarbital anesthetized dogs. Heart rate then returns temporarily to the control level, but accelerates again secondarily. Most probably, the initial tachycardia observed in all three groups of animals is ascribable to reduced stimulation of the peripheral baroreceptors. The subsequent bradycardia is due principally to increased neural activity in the cardiac vagal fibers, despite the arterial hypotension. In the animals anesthetized with morphine-chloralose-urethane, this tendency for enhanced vagal activity is counteracted by the reflex response to arterial hypotension. When the arterial blood pressure is prevented from falling, then bradycardia appears after endotoxin with this combination of anesthetic agents, just as in the other two groups of animals.

MICROPHYSIOLOGICAL STUDIES ON A CENTRE MEDIAN (CM) RELAY SYSTEM.
Baruch Blum (Intro. by A. S. Marrazzi) Mt. Zion Neurological Institute, San Francisco, Calif.

Extracellular evoked unit-responses to single-pulse stimulation of the pyramidal tract, of the CM, and of the entopeduncular nucleus (Ent) were studied in areas 4 and 6 of the cat pre- and post-cruciate cortex. Utilizing known criteria neurons were classified as pyramidal tract neurons (Pt. n.) or as non Pt. n. Extending previous observations (Blum et al. 1966) it was shown that CM or Ent evoke units, which in many cases seemed to be of identical neurons, at latencies of 2 or 3 msec or more. These latencies showed great constancy from response to response of the same unit (S. D. practically 0.0). It is proposed that this temporal constancy reflects a characteristic of a specific system, rather than of a particular nucleus, i. e. of a system which has the capability to transmit digital signals to the sensori-motor cortex in a rather efficient and deterministic fashion. Projections from Ent to CM have been described by Nauta and Mehler (1961). However, the above unit responses were evoked at shorter latencies by Ent than by CM, the difference being a rather short delay accountable by two synapses. If however a working hypothesis is made that Ent in the cat is, at least in part, a homologue of the primate internal globus palidum (i. g. p.), the above units could be assumed to result from activation of a pathway equivalent to that shown by Nauta and Mehler (1966) in primates to link the CM to the putamen, the latter to the i. g. p. and hence via the thalamic ventrolateral nucleus to the sensori-motor cortex. Such a system seems to synapse widely in the sensori-motor cortex of the cat in area 4 and 6, of the pre- as well as the postcruciate gyri.
(Supported by USPHS Grant NB-05061).

REDUCED MYOCARDIAL NECROSIS WITH POST-SYSTOLIC AUGMENTATION.
A. J. Bocage*, L. A. Toth and A. S. Harris, Louisiana State University School of Medicine, New Orleans, Louisiana.

Post-systolic augmentation by arterio-arterial pumping with the Simas unit has significantly reduced myocardial damage judged by Na and K shifts in the dog heart following occlusion of the left anterior descending coronary artery at a standard high level. 8 control (not pumped) and 10 experimental (pumped) dogs were studied. Procedures were equal for control and experimental dogs except pumping. Under anesthesia, via thoracotomy, a dacron ligature was placed around the artery only, and threaded through a catheter which was buried subcutaneously. 4 to 8 days later the catheter was retrieved and the ligature tightened, occluding the artery. Just before making the occlusion the external iliac arteries were exposed and ligated. In the experimental series arterio-arterial pumping via catheters in the iliac arteries was begun 3 to 5 min before coronary occlusion and continued for periods of 5.5 to 12 hours. All dogs were sacrificed 24 hrs after coronary occlusion, and the ventricular myocardium was analyzed to determine Na gain and K loss in meq/100 g muscle. Differences between the means of the control and experimental groups were 0.643 (1.601-0.958) for Na, and 0.699 (1.527-0.828) for K. $P < 0.005$ for both Na and K. Aided by Grant Number HE-01109, USPHS.

SIMULTANEOUS SEKELJ AND GILFORD DENSITOMETER CURVES OF COOMASSIE BLUE. Clorinda S.-S. Bohler*, William A. Scoggin*, and Philip Dow. Depts. of Physiology and Obstetrics-Gynecology, Medical College of Georgia, Augusta.

Patients in the last trimester of pregnancy, whose sensitivity to norepinephrine and angiotensin was being studied, offered an opportunity for supplemental validation of the Sekelj absolute ear densitometer. With the patient lying on her side, appropriate doses of Coomassie Blue were injected into an antecubital vein and flushed in with the arm raised. The response of the Sekelj earpiece was led to a Sargent recorder. Simultaneously, blood was drawn from a femoral artery through a Gilford 103 IR densitometer and its response was led to a Texas dual Servoriter. The curves were calibrated, measured and analyzed independently and then compared. Similarity of form and area are shown in graphs of 20 curves from four patients. Since interest in the Dow "emergency formula" (1955) has recently been rekindled by the Sekelj group, comparisons were also made between this and the standard method for all curves and the favorable results are shown.
(Supported in part by a grant from the Life Insurance Medical Research Fund, a grant from the Georgia Heart Association, and HE 10158 from the U.S.P.H.S. Coomassie Blue, recently discontinued, was furnished by Ayerst Laboratories.)

ROLE OF SKIN VASCULATURE IN CONTROL OF ARTERIAL BLOOD PRESSURE. Robert F. Bond and Harold D. Green. Bowman Gray Sch. Med., Winston-Salem, N.C.

The role of the cutaneous vasculature in hemorrhagic hypotension was studied by measuring either venous outflow or arterial inflow with a square-wave flowmeter from functionally isolated cutaneous vascular beds during: 1) stepwise reduction in local perfusion pressure, 2) stepwise reduction in mean arterial pressure (MAP) induced by hemorrhage, 3) irreversible shock. In both innervated and denervated preparations the pressure/flow (P/F) curve for hemorrhage shifts towards the pressure axis; in irreversible shock it shifts even more, suggesting a progressively increasing vascular tone. To study the mechanism of increased tone, cardiac output and saphenous artery flows were monitored simultaneously during bilateral carotid occlusion (BCO) in: 1) normal, 2) bilaterally vagotomized, and 3) Dibenzyline treated vagotomized animals. Preliminary results indicate that BCO increased the total peripheral resistance (TPR) in all three preparations by approximately the same per cent as the MAP. Cutaneous vascular resistance decreased in all three, the greatest reduction occurred when the MAP response was highest, suggesting that in the pressure range utilized in this study, the cutaneous vascular beds 1) behave in a passive manner, and 2) do not contribute toward the increased MAP coincident with the BCO. The shift of the P/F curve to the right in the hemorrhage animals is probably the result of a higher output of catecholamines from the adrenal medulla than was obtained with BCO. (Supported by USPH grants 487, 5392, North Carolina and Forsyth County Heart Associations.)

TRANSMISSION OF ANTRAL SLOW WAVES ACROSS THE GASTRODUODENAL JUNCTION IN VIVO. Alex Bortoff and Robert S. Davis.* Upstate Med. Ctr., State University of New York, Syracuse, N. Y.

Although transmission of antral slow waves across the gastroduodenal junction has been demonstrated in isolated preparations of cat antral-duodenal segments (Bortoff and Weg, Amer. J. Physiol. 208: 531, 1965), recordings taken from this region in chronic dog preparations indicate that antral slow waves are interrupted at the junction by an "electric insulator" (Bass, Code and Lambert, Amer. J. Physiol. 201: 587, 1961). By using modified suction electrodes we have been able to record monophasic potentials, several mV in amplitude, from the gastroduodenal regions of both anesthetized cats and dogs. Although the electrical activity at the junction is attenuated, there is no evidence that it insulates the electrical activity of the antrum from that of the duodenum. On the contrary the attenuated antral slow waves appear to spread through the junction and into the proximal duodenum where they tend to increase the magnitude of depolarization of duodenal slow waves. Since spiking seems to be related to the level of slow wave depolarization, this could account for the correlation that has been noted between antral slow waves and duodenal spiking, especially when duodenal excitability is high as in postprandial animals (Allen, Poole and Code, Am. J. Physiol. 207: 906, 1965).

EFFECT OF AFTERLOADING ON PAPILLARY MUSCLE CONTRACTIONS. T. Earl Bowen, Jr., (intro. by T. J. Reeves). Dept. Of Physiol. Univ. of Ala. Birmingham, Alabama.

Anrep showed that an increase in contractility of the dog heart can result from elevation of aortic resistance; Sarnoff (Cir. Res. 8:1077, 1960) called this type of homeometric autoregulation. Treating afterload as the analog of aortic resistance an attempt has been made to show this phenomenon in cat papillary muscles. Muscles bathed in modified Krebs-Ringer solution (bubbled O_2 95%, CO_2 5%) were stimulated supramaximally with 5 msec pulses (15v) of 12-36/min at different initial lengths. Muscles ranged in length 2.3 - 5.85 mm; weights ranging 1.5-6.3 mg and temperatures 23 - 37^{0}C. Muscles worked against a low afterload (approx. 1/3 peak isometric tension) in an electromechanically loaded apparatus. Between two given beats the afterload was increased to approx. 2/3 peak tension and then returned to the lower load 10 beats later. The inotropic background was maintained constant. An increase in contractility could be detected if, after the initial decrease in shortening the higher load, there was an increase in the amount of shortening. Although the treppe phenomenon was readily demonstrated in all muscles, only two out of 10 muscles showed an increase in shortening (2-4 x 10^{-3}mm or 0.09%) in the response to an increase in load. These muscles also demonstrated an "overshoot" in shortening when the load was returned to the lower level. The 2 muscles showing the phenomenon had cross-sectional area<1.0mm^2; the others were>1.0mm^2. This would suggest that the degree of oxygenation may be important in demonstrating what is, in any case, a slight effect and can be compared to the changes observed in the intact ventricle. This work supported by grants HE 08922 and USPH-STIHTS-5148.

EXPERIMENTS ON TASTE BUD HOMOGRAFTS. Robert M. Bradley (intr. by L. M. Beidler.) Florida State University, Tallahassee, Florida.

It is possible to transplant tongue epithelium. Previous workers, however, were not primarily concerned with the fate of the taste buds in the grafts. The present series of experiments was to study the possibility of grafting taste buds. In preliminary experiments, pinch grafts were taken from the anterior third of rat tongue and transplanted to sites on the belly. The wound was dressed with tulle gras and a cast applied to prevent the animal from interfering with the graft. The grafts were removed, fixed and embedded in paraffin. They were sectioned at 10 microns and stained with H. and E. Although the grafts retained their tongue-like character, it was impossible to distinguish between filiform and fungiform papillae. A thick cuticle developed. No taste buds were seen in either the short term (10 day) or long term (20 day) grafts. In a second series of experiments the circumvallate papilla of the rat was grafted to the belly. These were examined histologically at 2, 4, 6, 8, and 10 days as described above. By the fourth day the taste buds have disappeared. The circumvallate papilla is still quite distinct. Thus, the taste buds are not maintained after grafting but the possibility of reinnervation after extended times is being investigated. This research has been supported in part by NIH Grant No. NB 5258-08 and NSF Grant No. GB-4068.

A MEASUREMENT OF THE ACTIVE STATE IN PAPILLARY MUSCLE. Allan J. Brady Department of Physiology, U.C.L.A., Los Angeles, California 90024.

The time course of tension development in cardiac muscle at constant contractile element length was recorded using a feedback system which continuously compensates for muscle series and parallel elasticity based on the three element model of muscle. The stress-strain characteristic of undamped series elasticity is first obtained by a series of quick releases to a light load at various times during successive contractions. The parallel elastic characteristic obtained by controlled stretch during diastole is then added to this relation. Using this combined tension-length curve as a mask for a oscillographic curve tracer (photoformer) a length correction signal is generated on the X-axis of the scope when the isometric tension signal drives the Y-axis of the scope. The length correction signal, properly scaled, then drives an ergometer attached to the muscle. Thus, as force development progresses in the muscle it is also stretched appropriately to compensate for the tendency of the contractile element to shorten against the series elastic element. Correction for the rise in resting tension accompanying the stretch is also accomplished. The resulting time course of tension development is the time course of the cardiac active state in terms of Hill's definition of active state intensity. Relative to an unstretched isometric contraction, the active state rises considerably faster and has a higher but only slightly earlier maximum. Relative to an unstretched isometric contraction at an initial length equal to the maximum length achieved during the active state measurement, the active state rises somewhat faster to the same level (but slightly earlier) and then decays somewhat ahead of it. (Supported by Grant #HE 09257 N.I.H.)

EFFECT OF SPLENIC SEQUESTRATION ON PULMONARY DIFFUSING CAPACITY. Richard E. Brashear* and Joseph C. Ross. Ind. Univ. School of Med., Indianapolis, Ind.

The function of the spleen as a reservoir in dogs has been well recognized for many years. It is also well established that changes in blood oxygen capacity alter pulmonary diffusing capacity for carbon monoxide (D_L) by changing the intracapillary component of D_L. Since investigations of the pulmonary circulation are being done by D_L measurements in dogs, this study was performed to determine the role which an intact spleen could have on the results. Breath holding D_L for carbon monoxide was determined in duplicate at 3 different oxygen tensions in 9 anesthetized mongrel dogs (20 - 30 kg). D_M and V_C were calculated. Oxygen uptake, oxygen capacity, hematocrit and red cell indices were also determined. The spleen was mobilized exteriorly and, with manual pressure, reduced to the smallest possible volume, then surgically removed. The wound was closed and all studies were repeated. The mean increase in D_L after splenic compression and removal was 4.2 ± 2.5 ml/min/mm Hg ($P<.002$). Mean increase in hematocrit was 10.7 ± 2.1 ($P<.001$) and in venous oxygen capacity, 4.7 ± 1.0 vol% ($P<.001$). Changes in the other parameters were not significant. Because of the variable reservoir function of the dog spleen, it is concluded that investigations of the pulmonary circulation or lung function in dogs using D_L measurements should ideally be done on splenectomized animals.

INHIBITION BY CYCLIC-AMP OF THE HEXOSE MONOPHOSPHATE PATHWAY IN ADIPOSE TISSUE, George A. Bray, New England Medical Center Hospitals, Boston, Massachusetts.

When adipose tissue is incubated with theophylline lipolysis is increased and the oxidation of glucose is inhibited. Theophylline was found to inhibit the oxidation of glucose-^{14}C and glucose-1-^{14}C, but it had no effect on the oxidation of glucose-6-^{14}C, fructose-^{14}C, pyruvate-1-^{14}C or pyruvate-3-^{14}C. The stimulation of glucose oxidation by epinephrine, corticotropin or thyrotropin was also inhibited by theophylline. The uptake of glucose was increased by epinephrine but inhibited by theophylline. When adipose tissue was incubated with dibutyryl-3', 5'-adenosine monophosphate (DBC) the oxidation of glucose-1-^{14}C was inhibited at concentrations of DBC below those required to stimulate lipolysis or to increase the oxidation of glucose-6-^{14}C. At high concentrations of DBC, the oxidation of glucose-1-^{14}C and glucose-6-^{14}C were equal. The stimulation of glucose-1-^{14}C oxidation by insulin was completely inhibited by theophylline but less strikingly inhibited by DBC. However, insulin plus DBC produced ratios of C-1, to C-6 oxidation that were closer to those of epinephrine than to control or insulin-treated tissues. When the enzyme of the hexose monophosphate shunt were assayed in homogenates of adipose tissue, dibutyryl cyclic-AMP was found to be a competitive inhibitor of 6-phosphogluconate dehydrogenase, but to have no effect on glucose-6-phosphate dehydrogenase.

EFFECT OF SULFONIMIDES ON ANION (CHLORIDE-SULPHATE) EXCHANGE IN RED CELLS. Michael O. Breitmeyer* and Warren H. Dennis. Department of Physiology, The University of Wisconsin, Madison, Wisconsin.

Human erythrocytes were collected in heparin, washed twice in saline (8 parts saline:1 part cells), then washed twice in balanced electrolyte (10:1) (Tyrode's with all anions replaced by chloride). Isotonic Na_2SO_4 (5 ml) was mixed with 3 ml of the washed, packed cells (hematocrit=90%). The exchange of intracellular Cl^- for external $SO_4^=$ was studied by measuring the time course of the external Cl^- concentration $[Cl_o]$ with a Ag/AgCl-calomel electrode system. The rate constant (k) of the exchange was calculated as the slope of $\ln([Cl_o]_{final}-[Cl_o]_{time})$ vs time plots. The mean k for the control exchange at 19°C (pH=7.0) was 0.0198±0.0044 min^{-1} (st. dev., n=65). The k was reduced to 51% of control (0.0101±0.0018 min^{-1}, n=13) by $2x10^{-4}$ M acetazolamide. Mean half times were 35.0 and 68.5 min. respectively. No reduction in k was evident until the acetazolamide was increased to 10^{-5} M; increasing the concentration from $5x10^{-5}$ to $5x10^{-4}$ did not significantly decrease k. Sulfanilamide and furosemide [$2x10^{-4}$ M] reduced k to 57% of control. The activation energy (E) for the exchange was determined by calculating k at various temperatures (10-30°C); E was 18.2 kcal/mole for the Cl^--$SO_4^=$ exchange and E was 20 kcal/mole with acetazolamide ($2x10^{-4}$ M). The Cl^--$SO_4^=$ exchange may depend on some interaction of the anions with the red cell membrane since the exchange rate was reduced by known carbonic anhydrase inhibitors and was more dependent on temperature than one expects for a purely diffusional process.

Micropuncture study of the primate nephron. B. M. Brenner*, C. M. Bennett*, and R. W. Berliner. Bethesda, Md.

Proximal (PT) and distal tubule (DT) function was studied in the rhesus monkey during hydropenia and furosemide diuresis (during which ECF was maintained). During hydropenia, proximal TF/P ratios for Na, K and osmolality approximated unity; about 30% of the filtered water remained at the end of the accessible portion of this segment (92% of length). Distal tubule fluid was always hypotonic to plasma [(TF/P)osm = 0.50 ± .16SD and (TF/P)Na = 0.43 ± .15SD] and did not change along this segment. Volume was reduced to 25% of filtered in the early DT; small but significant water reabsorption occurred in the remainder of DT. (TF/P)K ratios along the DT showed considerable scatter (range 0.26-3.43) but tended to increase. Ten out of twelve ratios in the early DT were less than one, whereas only seven of eighteen ratios in the late DT were less than one. The amount of K relative to the amount filtered increased from 13% in early DT to 26% in late DT. Following furosemide, animals excreted 1/3 of filtered Na and water. Electrolyte and water reabsorption along the PT did not differ from controls. DT osm and Na values approached plasma [(TF/P)osm = 0.89 ± .06SD and (TF/P)Na = 0.85 ± .08SD]. Na remaining at this site (22% of filtered) was twice controls (10%), but water remaining was only slightly increased (30% remaining), indicating that inhibition of Na reabsorption occurred in the water impermeable segment rather than the PT. Following furosemide, (TF/P)K ≥ one (range 0.98-3.43) suggesting inhibition of K reabsorption at or prior to this site. (TF/P)HCO_3 from the mid-portion of PT was 0.46 ± .14SD during hydropenia (mean pH = 7.04 ± .20SD); following recollection from the same site after acetazolamide (TF/P)HCO_3 rose to 1.32 ± .46SD (mean pH = 7.51 ± .12SD).

BRADYKININ INDUCING LEUKOCYTOSIS. THE ROLE OF VASOACTIVE NONAPEPTIDE IN INFLAMMATORY PROCESS. R.S. Bright and T.A. Balourdas (intr. by E.M.K. Geiling). Dept. of Pharmacology, Medical School, Howard University, Washington, D.C.

Functional and structural lesions in the microcirculation caused by Bradykinin, especially vasodilatation, increased capillary permeability, vascular hyperreactivity, venoconstriction, hemorrhages and hypotension were reported (Balourdas, T.A., Proc. III Internat. Pharmacological Congress, July 1966, Sao Paulo, Brazil, p.199 & Extra-Congress Symposium on Vaso-active Polypeptides, Ribeirao Preto, Brazil, Aug. 1966 (In press); Gonzalez, E.A. and Balourdas, T.A., The Pharmacologist, 8:174, 1966). The present investigations were undertaken to determine the role of participation of plasma kinins in the inflammatory and infectious processes. By in vivo microscopy of the rat mesoappendiceal microvessels using the masocaecum bioassay after I.V. injection or local application of synthetic Bradykinin (BRS) the same structural and functional changes were observed. In a group of normal rats the blood leukocytes were counted before and after the I.M. administration of BRS. Results: The treated animals with BRS (75 - 200 µg) exhibited a remarkable leukocytosis 22 to 24 hours after the injections. The leukocytes from the normal countings, found 8,000 to 16,550, were increased 2-3 fold. No increase was observed during the first 12 hours. Given the interrelationship of plasma kallikrein-kinin system and blood clotting mechanism, we observed by grosso modo determination of clotting time in the treated animals the development of hypercoagulability concomitant with leukocytosis. The microvascular findings and the developed leukocytosis with Bradykinin may indicate the aspect of participating role of plasma kinins in inflammatory and infectious processes with topical and systemic morbid manifestations.

VAGAL STIMULATION OF BILE FLOW IN CONSCIOUS DOGS. Frank P. Brooks and Morton I. Grossman. Veterans Adm. Center and UCLA School of Med., Los Angeles, Calif.

Present views of the mechanisms of stimulation of bile flow involve the secretion of bile salts by hepatic parenchymal cells and the addition of a bicarbonate rich fluid by the bile ducts. Bile salts themselves represent an example of stimulation of the first type while secretin is thought to act by the second. (Wheeler & Mancusi-Ungaro, Am. J. Physiol. 210: 1153, 1966) We have compared bile flow stimulated by 2-deoxy-d-glucose (2 DG), insulin and secretin in 9 conscious cholecystectomized dogs with duodenal fistulae permitting catheterization of the bile duct under direct vision. Bile flow doubled approximately after 1.5 U/Kg insulin I.V. whether given upon a background of I.V. saline or sodium taurocholate. 2 DG 100 mg/Kg I.V. was a much weaker choleretic, while secretin given by continuous I.V. infusion 2 U/Kg/hr upon a taurocholate background gave a flow about 90% that of insulin. Bicarbonate output was greatest with secretin. A characteristic feature of insulin induced choleresis was an increase in the biliary concentration of chloride by about 20 mEq/L. We suggest that vagal stimulation involves a third mechanism of bile secretion with the production of a chloride rich fluid. Histamine has previously been reported to have a similar effect. (Zaterka & Grossman, Gastroenterology 50: 500, 1966)

PULMONARY HYPERTENSION INDUCED BY HIGH PARTIAL PRESSURES OF OXYGEN. Gerald A. Brooksby, Boris Datnow and Daniel B. Menzel (intr. by H. A. Leon). National Aeronautics and Space Administration, Ames Research Center, Moffett Field, Calif., and Battelle Northwest, Richland, Wash.

The acute edematous response of the lung to elevated oxygen pressures has long been recognized. Chronically, oxygen damage consists of atelectasis, thickening of the inter-alveolar septa and a morphological picture bearing a strong resemblance to clinical emphysema in man. In this study 10 beagle dogs were exposed to 50% oxygen (at sea level pressure) for 35 days in an attempt to determine if changes occur in pulmonary hemodynamics at a level of oxygen pressure below that usually associated with histological changes in lung tissue. A chronic catheter inserted into the pulmonary artery of the dogs allowed us to obtain pulmonary angiograms and pulmonary artery pressures each week for the 5 weeks. Terminal measurements included pulmonary vascular resistance and macroradiography of the pulmonary vascular bed. Our findings indicated a progressive hypertension and hypertrophy in the right heart and hypertrophy and dilation of the pulmonary arterial system. In the pulmonary artery, mean systolic pressures increased from an initial value of 18±2.5 mm Hg. to 64±7.1 mm Hg. after 5 weeks of oxygen breathing. The oxygen exposed dogs showed about a 80% increase in cardiac output and a 140% increase in pulmonary vascular resistance. From radiographic evidence, the circulatory changes appeared to be attributable to destruction of the capillary bed in the lung with continuous breathing of a high P_{O_2}.

FURTHER STUDIES ON THE MODE OF ACTION OF THE TOXIN OF PASTEURELLA PSEUDOTUBERCULOSIS. James A. Brown, Jr.*, William L. West and William M. Banks*. Howard Univ., Depts. of Pharmacology and Zoology, Washington, D.C.

A previous report was concerned with certain physiological changes induced by the crude toxin, and the modifying effects of certain pharmacological agents of known mechanisms. The present study is concerned with pyrexia, blood dyscrasias and respiratory changes produced by the toxin. All experiments described were carried out in albino rabbits (2-3 kg). Toxin was isolated from Pasteurella pseudotuberculosis (PSTB 43/III by a method described by Schar and Thal, 1955). The following parameters were investigated on the same animals: rectal temperature, hematocrit, white cell count and differential leukocyte count. Standard methods were used throughout. Respiration was recorded directly from the trachea by attachment to a transducer and a Sanborn dual channel recorder. Toxin was given in doses of 0.5-250 ug/kg. At each dose level toxin produced an early leukopenia (1-3 hrs. after toxin). The fall persisted during the median interval (4-6 hrs. after toxin). During the late period (6-8 hrs. after toxin) the effects were variable. Associated with the leukopenia was a marked decreased in % polymorphonuclear blood elements and an increase in temperature. Hyperthermia was produced at all doses above 0.5 ug/kg. There was no evidence of hemoconcentration during the 5 hrs. of observation. The respiratory rate increased slowly with a range of 30-72/min. whereas the amplitude varied from 3-5 mm. The peak effect on rate and amplitude occurred at 30 min.

STIMULATION OF RENIN RELEASE BY INTRALUMINAL [Na]. Torrey C. Brown,* C. Robert Cooke* and W. Gordon Walker. Johns Hopkins School of Medicine, Baltimore, Maryland.

Intravenous administration of 50 mg of ethacrynic acid (EA) to anesthetized mongrel dogs produced an elevation of renal venous renin activity (RVRA) within 5 minutes (control value 1200, S.E. ± 303 ng angiotensin formed per 100 ml plasma, increasing to 3375, S.E. ± 975 ng ($p<.05$) following EA administration). When volume reduction was prevented by shunting urine flow into the femoral veins, this response to EA administration persisted (control value 1975, S.E. ± 196 ng, increasing to 4050, S.E. ± 399 ng ($p<.001$) following EA). This prompt rise in RVRA coincident with the appearance of drug-induced natriuresis suggests that increased intraluminal sodium concentration is a stimulus for renin release. Additional studies were performed in which both ureters were occluded for 40 minutes and EA was given at the mid-point of the occlusion. During the occlusion, RVRA before and after EA did not differ. When ureters were released and flow resumed, RVRA promptly rose.

Occlusion	4315, S.E. ± 588 ng	N.S.
Occlusion + EA	4754, S.E. ± 474 ng	
Release	7650, S.E. ± 705 ng	$p<.01$

[Na] changed abruptly from low to high values in post-release urine following the first 5 ml. These data show that stimulation of renin release occurs following administration of EA without Na and/or volume depletion. Under these conditions, increased intraluminal [Na] appears to be the principal stimulus for renin release.

GLUCOSE UTILIZATION IN SCHISTOSOMA MANSONI CERCARIAE. John Bruce*, Emilio Weiss, M. A. Stirewalt* and D. R. Lincicome. Howard University, Washington, D. C. and NMRI, Bethesda, Md.

Schistosome cercariae are non-feeding trematode larvae with an inherently limited brief free-living existence. Stored glycogen was assessed as a possible limiting mechanism of their life span. The stored glycogen of cercariae newly-emerged from their snail vector hosts was found to be reduced by 66% in 18-hour old free-swimming cercariae. In addition, glucose uptake was compared in newly-emerged and 18-hour old cercariae by measuring the evolution of $C^{14}O_2$ by cercariae of the two ages incubated with a uniformly-labeled glucose substrate. A three-fold increase in glucose uptake was demonstrated by 18-hour old as compared with newly-emerged cercariae. Thus it appears that these cercariae have a pronounced endogenous source of glycogen which plays a significant role in their energenic processes. The decrease in glycogen with increasing age and extended activity of cercariae may be an important life-limiting factor. These preliminary results which indicate that S. mansoni cercariae did not resynthesize glycogen from glucose suggest that these invasive larval parasites can utilize substrates for energy production but not for synthesis. The role of other substrates in cercarial metabolism is under investigation.
Supported in part by USPHS Research Training Grant 5T01-AI00040-09.

PRESENCE OF VILLIKININ, SECRETIN, AND CHOLECYSTOKININ IN THE DUODENAL CONTENT. W.D. Brunson, Jr.* and Eszter Kokas. Dept. of Physiology, Univ. of North Carolina School of Med., Chapel Hill, N.C.

In anesthetized dogs after intraduodenal administration of 0.4% HCl the presence of villikinin, secretin, and cholecystokinin was demonstrated in the withdrawn duodenal content. This withdrawn solution after neutralization, administered intravenously, increased manyfold villous motility, pancreatic juice secretion, and enhanced contractions of the gall bladder. Physiological saline and 1% bicarbonate, intraduodenally and after withdrawal, did not exhibit this effect. Neutralized stock solutions intravenously were also without effect. Histamine is present in all withdrawn solutions and is removed by treating the solutions with charcoal. Charcoal treatment also adsorbs secretin and cholecystokinin, but not villikinin. These observations demonstrate: a) the necessity of an acid medium for the release of these intestinal hormones and b) their presence in the duodenal content. This might indicate that these intestinal hormones pass through the mucosa into the duodenum and are absorbed from there into the blood stream. (Supported by NIH grant AM-04675).

MEASUREMENTS OF THE APPARENT PORE SIZE OF THE MEMBRANE OF SINGLE MUSCLE FIBERS. Wilton Bunch (intr. by C. Edwards), Dept. of Physiol., Univ. of Minn., Mpls., Minn.

In a study of the permeability of the membrane of the barnacle muscle fiber reported last year (Bunch, Physiologist, 9:3, 1966) Q_{10}'s up to 4.9 were found. One possible explanation for this high value could be an effect of temperature on the apparent pore size. To examine this, measurements have been made at two temperatures of the reflection coefficient of this membrane for several non-electrolytes. The temperature dependence of the pore size calculated from these measurements depends on the molecule used.

	Pore Size		Permeability (cm/sec x 10^{-5})		Q_{10}
	4°C	25°C	4°C	25°C	
Urea	3.5Å	3.5Å	.14 ± .03	1.05 ± .13	3.5
Glycerol	3.5Å	3.5Å		.80 ± .05	
DMSO	3.5Å	14. Å	.58 ± .03	7.43 ± .96	4.9

With urea or glycerol the reflection coefficients were equal at 4°C and at 25°C, which would imply no temperature effect on the pore size. However with DMSO, the reflection coefficient was smaller at 25°C than at 4°C, so that the pore radius was apparently increased four fold by the increase in temperature. Although the Q_{10} for urea is similar to that for DMSO, the above data suggest the existence of different mechanisms of permeability. Consistent with this suggestion is the finding that at 4°C the apparent pore sizes for DMSO and urea are identical, while the DMSO permeability is four times that of urea. (Aided by NIH Grant NB-02712).

CRITERIA FOR PHYSIOLOGICAL STRESS AND ADAPTATION. R. R. Burton* and A. H. Smith, Department of Animal Physiology, University of California, Davis, California.

Criteria for physiological status, relative to stress and adaptation, have been developed by comparing hematological observations with exercise capacity, survival, and sexual development in animals exposed to increased chronic acceleration. Such information is needed to interpret data from centrifugation experiments. Generally, results are quite variable, and this may arise from differences in "fitness" among the experimental animals. Exercise capacity of centrifuged animals was determined as the time necessary to exhaust adult male chickens on a treadmill (61 ft/min, at an incline angle of 4 degrees) immediately after being returned to normal gravity. Differential leucocyte counts were made, by standard methods and the lymphocyte frequency was correlated with their exercise capacity relative to pretreatment performance; which is best described by the equation: relative exercise capacity (%) = $2.5e^{0.055}$ lymphocyte (%). The mortality resulting from this "increased gravity" treatment was preceded by a reduction in the lymphocyte count. Generally, animals with a lymphopenia of 20% lymphocytes or less did not survive. The packed cell volumes (hematocrits) of birds living in an "increased gravity" environment for several months are quite variable. The hematocrit which is an index of sexual development in adult male chickens was also highly correlated with the relative lymphocyte number. These findings indicate that the "physiological fitness" of an individual with respect to exercise capacity, survival, and reproductive status, in a stressful environment can be estimated hematologically.
Supported by NASA (NGR 05-004-008).

TEMPERATURE SENSITIVE NEURONS IN A REPTILIAN BRAIN. M. Cabanac*, H. T. Hammel and J. D. Hardy. John B. Pierce Foundation Laboratory, Department of Physiology, Yale University, New Haven, Connecticut.

Temperature sensitive neurons have been described in the cat, dog and rabbit hypothalamus and arguments have been given suggesting their involvement in thermoregulation. Since a thermoregulatory behavioral response in the skink Tiliqua scincoides was recently shown to be partly dependent upon the brain temperature, we have explored the brain of this species for the existence of temperature sensitive neurons. The surgical preparation was performed under ether anesthesia or cold lethargia, then the animals were allowed to recover. In acute experiments on nonanesthetized animals, thermal stimulation of the brain was produced with a U shaped water perfused thermode. One to two millimeters away from the thermode a thermocouple was implanted, and extra cellular action potentials were recorded with a microelectrode and counted. In the range of the local brain temperature explored (20 to 36°C) insensitive neurons have been found with firing rates completely independent of temperature changes. However, sensitive neurons have also been found: cold neurons increased their activity with a decrease in temperature and warm neurons increased their activity with an increase in temperature. These neurons could conceivably be the basis for the temperature sensitivity previously shown to affect behavioral thermoregulation in this species.
(Supported by NIH Grant - NB-04655).

ANALYSIS OF BURSTS IN THE FIRING PATTERNS OF EPILEPTIC NEURONS.
William H. Calvin, George W. Sypert*, and Arthur A. Ward, Jr.*
Departments of Neurological Surgery and Physiology & Biophysics, University of Washington School of Medicine, Seattle, Washington 98105

The bursts seen during spontaneous firing are so labile that quantitative study of them is difficult in normal cortical neurons. Quite stereotyped bursts, however, may be seen recurring every 50-200 msec. in neurons near alumina foci in sensorimotor cortex of awake Rhesus monkeys. Since customary displays, e.g., interspike interval histograms, generally lose information about burst structure, more appropriate computer methods have been developed. Bursts were defined by a long interspike interval immediately followed by at least two short intervals. Raster displays lined up a burst beneath preceding bursts, with all of the first *(or second, or third)* spikes in a vertical line. Spike densities showed the probability of spike occurrence relative to the first *(or second, etc.)* spike of the burst. Scatter plots or histograms could be made of: all first *(or second, etc.)* intervals; spikes per burst; interval from the beginning *(or end)* of a burst to the beginning of the next burst; etc. A prominent feature of some epileptic neurons has been an unusually long first interval in the burst, e.g., a burst with intervals of 8.6, 1.3, 1.7, 2.2, 2.6,...msec. Thus the high frequency part of the burst does not begin until the second spike, with the first spike occupying a position analogous to a shock artifact. This long first interval may be variable, so that a display triggering on the second spike reveals the stereotyped structure of the bursts, whereas triggering on the first spike does not. In other units, this long first interval is remarkably fixed. Such behavior places some constraints upon theories about the mechanisms of burst generation. (Supported by NIH grants NB 04053 and NB 01752)

THE ROLE OF TOCOPHEROL IN REGULATING NAD DEPENDENT MITOCHONDRIAL OXIDATION. F.B. Carabello* and J.W.C. Bird. Rutgers University, Dept. Physiol. & Biochem., New Brunswick, New Jersey, 08903.

Acetoacetate (AcAc) formation was measured in liver mitochondria as an index of β-hydroxybutyrate oxidation. Significantly more AcAc was formed in tocopherol sufficient mitochondria (TSM) and menadione eliminated the tocopherol affect. Tocopherol appears to stimulate oxidation of NADH during β-hydroxybutyrate oxidation. Addition of succinate inhibited mitochondrial AcAc formation and tocopherol increased the affect of succinate. AcAc formation in the presence of succinate was linear in TSM for the full hour of incubation. In contrast, succinate became less inhibitory in tocopherol deficient mitochondria (TDM) during the second half hour of incubation. This effect may be attributable to oxaloacetate (OA) accumulation since this compound is a potent negative feedback inhibitor of succinic dehydrogenase. ATP and excess Mg^{++} render OA unavailable to inhibit succinic dehydrogenase and both agents partially increased the ability of succinate to inhibit AcAc formation in TDM. However, these agents did not completely reverse the affect of tocopherol on the succinate induced inhibition. Thus, the accumulation of OA is probably a secondary effect. Menadione and phosphate acceptor both decreased the ability of succinate to inhibit AcAc formation in TSM and these agents are known to oxidize NADH. Furthermore, menadione completely eliminated the affect of tocopherol on the succinate induced inhibition. Thus, the primary effect of tocopherol on this inhibition may be to prevent oxidation of NADH. This is in contrast to the previously mentioned ability of tocopherol to stimulate NADH oxidation in the absence of succinate.

SODIUM LOCALIZATION AND THE ROLE OF INTERCELLULAR CHANNELS IN SODIUM AND WATER TRANSFER ACROSS THE EPITHELIUM OF THE SMALL INTESTINE. M. M. Cassidy* and C. S. Tidball. Dept. of Physiol., George Washington University School of Medicine, Washington, D. C.

A general hypothesis concerning the route of water transport across epithelia implicates the intercellular channels between adjacent epithelial cells as the locus of osmotic equilibration of actively transported solute. Chelation depletion in vivo, has been shown to markedly alter both the passive permeability of intestinal tissue and the normal, tightly apposed appearance of these channels producing considerable distention of the intercellular areas. The ultrastructural appearance of these channels together with electron microscopic visualization of sodium has been studied in rat ileum under conditions of fasting, normal sodium and water transport, and elevated sodium and water transport. Both intracellular sodium and tissue labelling by C^{14} sugars have been found to increase during the period of elevated permeability, substantiating an increase in mucosal porosity as the basis for this phenomenon. Sodium was localized as sodium pyroantimonate by fixation in OsO_4 containing 8% $KSb(OH)_6$ in 0.1 M potassium borate buffer at pH 8.4. In control preparations the reaction product clearly outlined the lateral cell borders and basement membranes. In the chelated tissues, which could be presumed to have saturated Na^+ transport activity at the lateral borders, sodium pyroantimonate was densely precipitated at and within the highly distended intercellular spaces. Significantly, profuse sodium precipitate in these channels was observed chiefly in the apical third of the epithelial cells.

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STUDIES ON SEASONAL VARIATIONS IN ORGAN-TO-BODY WEIGHT RATIOS AND THERMOGENIC ENZYME SYSTEMS IN THE VOLE (MICROTUS OCHRAGASTER). R.R.J. Chaffee, C.H. Conaway*, and M.E. Richmond*. Dept. of Zool. and the SSRC, U. of Mo

Bimonthly comparisons of organ:body weights and oxidative enzyme activity levels were made between freshly caught wild animals and laboratory-grown-and-maintained Microtus. These studies started in September and continued to June. Animals were weighed and decapitated, and organ:body weight (ratio) regression curves and statistical comparisons were made. Kidney:body weight in wild animals increased in winter, but returned to control levels by June. Heart:body weight remained higher in wild animals. Brown fat:body weight was strikingly lower in wild animals regardless of the season, and became especially low during severe cold. Succinoxidase and glycerophosphate dehydrogenase activity of the brown fat of wild animals was strikingly higher during cold months than that of laboratory controls, but in June both dropped below control levels. Liver succinoxidase activity rapidly rose above control levels during cold spells, but didn't remain so. In conclusion, a number of changes seen in the wild rodents in the winter differ from those which are well known to be characteristic of changes seen in laboratory-cold-acclimated rodents. Supported by the SSRC of the U. of Mo.; U.S. Army Med. Res. and Dev. Command, Dept. of Army Contract DA-17-67-C0025; and USAF Aeromed. Res. Command, Contract F 29600-56-C-0009.

MYOFIBRILLAR ATPASE ACTIVITY IN EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY AND RIGHT VENTRICULAR FAILURE. B.M. Chandler*, E.H.Sonnenblick, J.F. Spann, Jr.*, and P.E. Pool*. Cardiology Branch, Natl. Heart Inst., Bethesda, Md.

While previous studies have suggested a depression of myofibrillar ATPase in the presence of heart failure, their interpretation has been limited by failure to exclude mitochondrial contamination and lack of information regarding the contractility of the tissue studied. To explore this fundamental question, myofibrils were prepared from the right and left ventricles of 15 normal cats, 10 cats with right ventricular hypertrophy (RVH) and 19 with RVH and right ventricular failure (RF), the latter groups following graded pulmonary artery stenosis. The contractility of these hearts was assessed using their right ventricular papillary muscles isolated in a myograph. Myofibrillar ATPase in all groups was maximally activated by 5 mM ATP, 5 mM $MgCl_2$ in the presence of 10^{-6} M Ca^{++} at pH 7.0 and 37°C, while mitochondrial contamination was eliminated by sodium azide. In RF, right ventricular myofibrillar ATPase was depressed by 39% from an average of 0.18 ± 0.01 in normal cats to 0.11 ± 0.01 μmoles inorganic phosphate/mg protein/min ($p<.001$). In RVH, right ventricular myofibrillar ATPase was not significantly depressed (0.16 ± 0.01 μmoles/mg/min). Of note, left ventricular myofibrillar ATPase was also significantly ($p<.05$) depressed in RF from 0.16 ± 0.01 to 0.13 ± 0.01 μmoles/mg/min. Contractility of the associated right ventricular papillary muscles, expressed as maximum rate of force development at the apex of the active length-tension curve, was directly correlated with myofibrillar ATPase activity ($r = 0.71$ $p<.001$). In summary, myofibrillar ATPase, devoid of mitochondrial contamination, was significantly reduced in experiment RF in both the right and left ventricles. In RVH alone, a significant depression was not found.

ATROPINE INDUCED PRANDIAL DRINKING. Harold W. Chapman* and Alan N. Epstein, Dept. of Biology, Univ. of Penna., Philadelphia, Penna.

All but one of 15 rats acquired the prandial style of drinking after one to four daily injections of atropine given immediately before feeding. They began to drink very small draughts of water just after each morsel of food was taken into the mouth. Atropine methyl nitrate (which has little central activity) as well as atropine sulphate were effective in intraperitoneal doses of 1-2 mg/kg. The rats ate for only one hour a day during which they pressed a bar for 45 mg pellets of dry food with water freely available. The drinking pattern was identical to that of surgically desalivate rats and, as in the desalivate, resulted in increases in water/food ratios and (except when the atropine caused severe anorexia) in increases in total water intakes. Atropine decreased the food intake of these rats, of the surgically desalivate, and of rats fed liquid food. The prandial style of drinking persisted in the feeding chamber, in six rats, without atropine injections (in two, for six months). In these six, appropriate doses of pilocarpine suppressed the prandial drinking. In two, suppression was also achieved by post-pellet oral infusions of water (0.14 ml/pellet) but not by 15 ml intragastric loads given 15 minutes before the session. This persistent prandial drinking disappeared when rats were left in the feeding chamber overnight (indicating that the glands were capable of functioning normally) and returned when the deprivation schedule was reimposed. This work shows that pharmacological as well as surgical drying of the mouth produces prandial drinking, supporting the idea that this style of drinking is generated by the necessity for lubrication when dry food must be swallowed from a dry mouth. (USPHS NB 03469-06)

VARIATIONS IN THE AMPLITUDE OF A BRAIN STEM REFLEX DURING SLEEP AND WAKEFULNESS. M.H. Chase, D.J. McGinty*, and M.B. Sterman, Depts. of Anatomy and Physiology, UCLA, and the Sepulveda VAH, Los Angeles, Calif.

Previous studies have reported systematic variations in the amplitude of spinal reflexes during sleep and wakefulness. Our interest was to determine the normative variations during these states for a brain stem reflex: the masseteric monosynaptic reflex. Electrodes to elicit and record the reflex response, along with others to monitor the EEG, eye movements, and neck activity were permanently fixed in place for chronic recording in the behaviorally awake cat. The reflex was induced by an electrical pulse delivered to the mesencephalic nucleus of the Vth nerve. The motor reflex response was recorded from the ipsilateral masseteric muscle. A liminally-induced reflex response was obtained and simultaneously recorded on paper with the other electrophysiologic activity during consecutive sleep cycles. As the cats passed from relaxed wakefulness to the drowsy state, the number of high amplitude potentials decreased. During quiet sleep there was a significant reduction in mean amplitude as compared with the drowsy state. Additionally, during quiet sleep a response sometimes failed to occur following the mesencephalic stimulus. During active sleep the reflex response was almost totally abolished. Thus, there was a gradual decrease in the reflex amplitude as the animal passed from the alert state, through the drowsy and quiet sleep states, and into active sleep. (Supported by U.S.P.H.S. Grant MH 10083.)

DISTRIBUTION OF BLOOD FLOW AND PHOSPHOLIPID SYNTHESIS IN THE FETAL LAMB LUNG. V. Chernick and D.E. Newman. (Intr. by J.A. Hildes) Dept. of Pediatrics and Physiology, University of Manitoba, Winnipeg, Man.

The upper lobe of the fetal lamb lung develops surfactant and a stable deflation pressure-volume relationship between 120-130 days gestation, a few days prior to the lower lobes. In several fetuses, this event correlated with a differential increase in disaturated lecithin. (Brumley et al, J. Clin. Invest. 46, 863, 1967) Is differential maturation dependent on an increased availability of substrate to the upper lobe, or is there a difference in the enzymatic capability of phospholipid synthesis? In 16 fetuses from 115 days to term (147 days), 50μc Cr^{51} labelled spheres (50 ± 10 microns) were injected into a forelimb vein while the rest of the fetus was in utero. The relative distribution of radioactivity (%) per mg DNA in the RU, RM, RL, LU and LL lobes was 19.6, 20.3, 21.3, 19.6 and 19.8 respectively, and did not change with gestational age. Samples of lung were minced and incubated in Krebs-Ringers at pH 7.4 for 2 hours with 0.5μc/10μM C^{14} labelled a) choline, b) methionine, and c) palmitate. Although incorporation into lecithin/mg DNA of a), b) and c) increased towards term, no upper-lower lobe differences were found. Therefore the difference in mechanical stability and surfactant is not related to a difference in substrate availability or phospholipid synthesis and must depend on other factors.
(Supported by the Medical Research Council of Canada.)

EFFECTS OF CATIONS ON HEPATIC VASCULAR RESISTANCES. C.C. Chou* and T.E. Emerson, Jr. Physiol. Dept., Mich. State Univ., E. Lansing, Mich.

Vessels of the forelimb, kidney, heart, stomach and small intestine are dilated by Mg^{++}. K^{+} dilates at low but constricts at high rates of infusion. Except in the stomach, Ca^{++} causes constriction. The present study describes the effects of these ions on 10 isolated dog livers from small dogs. The hepatic artery (HA) and portal vein (PV) were pump perfused at constant flow with femoral artery and portal venous blood from a large donor dog. Hepatic venous outflow was continuously returned to the donor after draining into a reservoir. Average HA and PV blood flow were 90 and 77 ml/min respectively. The perfusion pressure of HA and PV, and liver weight were recorded. Isosmotic solutions of NaCl, KCl, $CaCl_2$ and $MgCl_2$ were randomly infused into the HA or PV at 0.4, 1, 2, 4 and 7.8 ml/min in each liver. NaCl was used as a volume control. The percentage changes from control (cont.) for resistances in vessels supplied by the HA(HAR) and PV(PVR) at the infusion rate of 7.8 ml/min are shown below (cont. HAR and PVR in mmHg/ml/min):

	Infused to HA				Infused to PV			
	Cont. HAR	Changes in HAR	Cont. PVR	Changes in PVR	Cont. HAR	Changes in HAR	Cont. PVR	Changes in PVR
NaCl	0.99	- 9 %	0.12	-9 %	0.98	-2 %	0.11	-7 %
KCl	1.00	+30 %	0.13	-4 %	1.02	0 %	0.12	0 %
$CaCl_2$	1.09	- 8 %	0.11	+1 %	1.07	0 %	0.12	-1 %
$MgCl_2$	1.10	-21 %	0.11	-5 %	0.92	-9 %	0.10	-10%

KCl caused no significant change until the K^{+} concentration in HA was raised by about 7 mEq/L, when it raised HAR with a fall in liver weight. The findings show that in this preparation $CaCl_2$ does not increase resistance in vessels supplied by the HA or PV and KCl has no apparent dilator effect in these vessels. (Supported by NIH Grant HE 10899).

INTRACELLULAR MICROINJECTION OF ELECTROLYTES AND NON-ELECTROLYTES. Tushar K. Chowdhury* (intr. by H. S. Loukes) Dept. of Physiology, George Washington University, Washington, D. C.

A new technique for microinjection has been developed by which small quantities of electrolytes as well as non-electrolytes can be injected into the subcellular regions of a single cell. For this, specially drawn, fine-tipped, glass micropipettes are used whose cone angles are much larger than conventionally drawn micropipettes. When such a micropipette, filled with the solution to be injected, is vibrated at ultrasonic frequencies in the axial direction, with excursions of about 10 A, small but significant quantities of the filling solution are extruded due to hydrodynamic rectification. The extrusion is facilitated when few large spherical particles are present within the cone of the micropipette. Quantitation of extrusion has been made by introducing fluorescent materials into a carboxymethylcellulose gel system and determining the injected quantity by fluorescence microscopy. The microinjection technique is now being employed to inject various electrolytes and non-electrolytes into actively transporting single cells of various biological membranes. The injecting micropipette can itself serve as the potential measuring electrode in monitoring the intracellular electrical potential. Thus it becomes possible to detect simultaneously any transient electrical effects of the intracellular injection. The other major advantages of this technique are that (a) no extraneous pressure needs be applied on the micropipette and (b) unlike the ionophoretic technique, the injection is not restricted to electrolytes or other ionizable molecules.

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GASTROINTESTINAL ATPase FOLLOWING URETERAL LIGATION IN RATS. Dominick L. Cinti* and Donald B. Doemling. Dept. of Physiology, Jefferson Medical College, Philadelphia, Pa.

Total-ATPase and Na-K-dependent ATPase of the mucosa of the stomach, duodenum, jejunum, ileum, colon and cecum were measured in four groups of six rats each--24-hour fasting; 48-hour fasting; 24-hour fasting following bilateral ureteral ligation; and 48-hour fasting following bilateral ureteral ligation. Enzymatic activity was measured by the amount of inorganic phosphate released and was expressed as micromoles of ATP hydrolyzed/mg DNA/30 min. Fasting produced significant decreases in total ATPase activity in the ileum, colon and cecum. Twenty-four hours after ureteral ligation, there was a tendency toward increased activity in the upper gastrointestinal tract and decreased activity in the lower portions; however, the changes were significant only in the stomach. There was a significant increase in total ATPase activity in both the stomach and the colon 48 hours after ligation. Na-K-ATPase significantly decreased in the colon and cecum following fasting. The ligation tended to (1) counterbalance the decreased activity in the cecum, (2) reverse it in the colon, and (3) produce an increase in activity in the duodenum. In conclusion, fasting tends to reduce the levels of total ATPase and Na-K-ATPase in the gastrointestinal tract; the major effects are in the colon and cecum. Ureteral ligation counteracts the effects of fasting in the colon and the cecum. Ureteral ligation also produces an increase in total ATPase activity in the stomach and Na-K-ATPase activity in the duodenum. The effects of ligation are possibly related to increased blood levels of electrolytes.

THE EFFECT OF AORTIC PRESSURE INDUCED HOMEOMETRIC AUTOREGULATION ON MYOCARDIAL PERFORMANCE. Richard L. Clancy, Thomas P. Graham, Jr.*, Edmund H. Sonnenblick, John Ross, Jr., and Eugene Braunwald, Cardiology Branch, National Heart Institute, Bethesda, Md.

Homeometric autoregulation, characterized by an increase in contractility following aortic pressure (AP) elevation, has previously been analyzed by relating standard hemodynamic variables to the left ventricular end-diastolic pressure (LVEDP). However, with sizeable alterations in LVEDP, diastolic LV compliance has been shown to increase. This effect, as well as the Frank-Starling mechanism, may partially account for the steady-state increase in LV performance during an elevation of aortic pressure. Accordingly, the influence of homeometric autoregulation on LV performance at a known LV end-diastolic circumference (LVEDC) was compared with the effect of the Frank-Starling mechanism at the same LVEDC. Circumference was measured with a Hg-in-rubber gage, and the force-velocity (F-V) relations were analyzed during single isovolumic contractions, in the dog right heart bypass preparation. Mean values during homeometric autoregulation and during increased LV filling were, respectively: mean aortic pressure 113 and 78 mm Hg, LVEDC 20.2 and 20.2 cm, LVEDP 8.7 and 9.9 mm Hg, and stroke volume 11.3 and 18.9 ml. The steady-state level of LVEDP was always greater than control during both of these interventions. The isovolumic F-V curves were shifted to the right during homeometric autoregulation, maximum stress and contractile element velocity being 7.4 and 7.3% larger than during increased LV filling. These results suggest that the steady state increase in LV performance during pressure-induced homeometric autoregulation, within a physiologic range of aortic pressure, is associated with a small augmentation of LV contractility, but that the major effects result from the operation of the Frank-Starling mechanism, and from pressure-induced changes in ventricular compliance.

THE METABOLIC AND VENTILATORY RESPONSES TO SHORT DURATION HEAVY EXERCISE. Bernard Clarke (intr. by G. N. Bedell). Dept. Int. Medicine, University of Iowa, Iowa City.

The purpose of this paper was to stimulate anaerobic metabolism with a short period of heavy exercise and observe the metabolic and ventilatory responses to this stimulus. Five healthy but untrained subjects exercised by running upstairs at near top speed for about one minute. In the immediate succeeding hour each man had frequent measurements of minute ventilation ($\dot{V}E$), lactic acid, arterial PH, $PaCO_2$ and PaO_2. Standard bicarbonate was calculated from the direct measurements. An acute metabolic acidosis developed in all five subjects. During the first ten minutes of recovery mean PH decreased to 7.150, arterial PCO_2 tension decreased to a mean level of 30.8 mm. and the calculated standard bicarbonate decreased to a mean level of 11.5 meq/L. Lactic acid levels increased to a maximum mean level of 118.5 mgm.%. From 10 to 45 minutes after exercise there was a gradual return to resting level in all these measurements. Ventilation measured immediately after exercise had increased to a mean level of 61.6 L/min. From 3 to 10 minutes however, there was a rapid fall in $\dot{V}E$ and then a gradual decrease to resting levels over the next thirty minutes. The rapid decrease in ventilation in the first minutes after exercise is attributed to the withdrawal of non-chemical stimuli. The continued decrease in ventilation in the presence of a persistent and moderately severe acidosis is dissimilar to the ventilation response seen in chronic metabolic acidosis. This difference may be attributed to a presumed alkaline environment in the cerebrospinal fluid at the same time that arterial blood is acid.

PROLACTIN IMPLANT INTO THE MEDIAN EMINENCE INHIBITS PITUITARY PROLACTIN SECRETION, MAMMARY GROWTH AND LUTEAL FUNCTION. James A. Clemens* and Joseph Meites, Michigan State University, East Lansing, Mich.

Single stereotaxic implants of a prolactin-cocoa butter mixture were made in the median eminence of 10 mature and 6 ovariectomized female Sprague-Dawley rats. A similar number of control rats were implanted with cocoa butter alone. The animals were killed 6 days after implantation. The prolactin implanted rats showed marked mammary regression when compared with those of the control intact or control ovariectomized rats, nearly a 3 fold increase in hypothalamic content of prolactin inhibiting factor (PIF) in both intact and ovariectomized rats and a 40% decrease in pituitary prolactin concentration in the intact rats. The ovaries of intact prolactin-implanted rats were characterized by many well developed follicles and few corpora lutea while the ovaries from the corresponding controls showed mainly well developed corpora lutea. The former showed regular cycling while the latter appeared to be pseudopregnant, as judged by daily vaginal smears. These observations suggest that implanted prolactin inhibits pituitary prolactin synthesis and release by a direct feedback action on hypothalamic PIF, and this results in depressing pituitary prolactin concentration, mammary growth and luteal function (Supported by NIH grant No. AM-4784-07 and Michigan Cancer Foundation grant No. 66-149A).

VAGAL AND SYMPATHETIC CONTRIBUTIONS TO CLASSICALLY CONDITIONED TACHYCARDIA IN THE PIGEON. David H. Cohen and Lawrence H. Pitts (intr. by G. Sayers). Western Reserve Univ., School of Med., Cleveland, Ohio.

As part of an ongoing program to map the neural pathways mediating conditioned cardioacceleration, the present experiments were undertaken to assess the relative contributions of the vagi and cardiac sympathetics to this response. To establish the tachycardia, a Pavlovian paradigm was used in which a light was followed by foot-shock, a number of such pairings being presented. Birds with bilateral cervical vagotomy, beta-blockade (propanalol), or both were studied in this situation and their conditioning performances compared with those of conditioning and pseudoconditioning control animals. Conditioned responses of vagotomized birds were significantly below those of control animals, but substantial conditioning was still obtained. However, with beta-blockade conditioned rate responses were markedly reduced and were significantly below those of vagotomized animals. Functional denervation with combined vagotomy and propanalol entirely blocked the conditioned response. Although the form of the response for birds with either vagotomy or beta-blockade was similar to that of control animals, there was a significantly longer response latency in vagotomized birds. These results suggest the following conclusions: (a) Conditioned cardioacceleration is mediated entirely by the extrinsic cardiac nerves. (b) The shortest latency component of the response is vagally mediated. (c) The principal contribution is via the cardiac sympathetic nerves. Further evaluation of these and other conclusions is presently being undertaken with microelectrode recordings from cells of origin of the extrinsic cardiac nerves during cardiac conditioning. (Supported by NSF Grant No. GB 2767 and a grant from the Heart Association of Northeast Ohio).

CARDIAC OUTPUT, PERIPHERAL RESISTANCE, HEART RATE AND STROKE VOLUME IN THE INITIAL PHASES OF SALT INDUCED HYPERTENSION. Thomas G. Coleman* and Arthur C. Guyton. Dept. of Physiology & Biophysics, University of Mississippi School of Medicine, Jackson, Mississippi.

This experiment was designed to evaluate circulatory function during the initial phases of salt induced hypertension in subtotally nephrectomized dogs. Seven experiments consisting of near daily measurements were run on six mongrel dogs. Approximately 70% of the renal mass was removed at two operations and catheters were implanted in the aorta and right atrium. Baseline measurements were made over a period of 8 days following a surgical recovery period. The animals were then continuously infused with 310 mOs saline for 13 days. The daily average salt input per dog was 30.7 grams/day. Cardiac output was measured using dye-dilution techniques with Cardio-Green. Arterial pressure increased from 104.9 $\pm$ 2.0 mm Hg (Mean $\pm$ SEM) during the baseline period to a final value of 143.3 $\pm$ 3.5 mm Hg. All final values are averages of measurements from the last 4 days of the experiment. Cardiac output increased to a maximum of 129.1 $\pm$ 7.8% of baseline on the 3rd day and then decreased to a final value of 111.1 $\pm$ 4.5%. Peripheral resistance decreased to a value of 90.0 $\pm$ 4.3% of baseline on the 2nd day and then steadily increased to a final value of 122.0 $\pm$ 5.0%. Heart rate decreased to a minimum value of 69.0 $\pm$ 5.7% of baseline on the 6th day and then increased to a final value of 80.8 $\pm$ 4.1%. Stroke volume increased to a maximum of 166.6 $\pm$ 17.5% of baseline on the 6th day and then decreased to a final value of 132.4 $\pm$ 8.0%. This data supports the theory that an increase in cardiac output can alter peripheral resistance resulting in hypertension.

ACTION OF SCN ON NECTURUS GASTRIC MUCOSA R.C. Collier*, B.I. Hirschowitz, E.B. Carmichael and G. Sachs* Dept. of Medicine, U. of Alabama Medical Center, Birmingham, Alabama.

Thiocyanate has been regarded as a highly specific inhibitor of acid secretion in the in vitro amphibian mucosa. Thus in frog there is little effect on P.D. with a rise in resistance and a stated lack of effect on O_2 consumption. In the chambered Necturus gastric mucosa the addition of SCN^- (20mM) inhibits acid with a rise in resistance. In addition however there is a concomitant inhibition of O_2 consumption by 20%, a 50% depression of the P.D. and an apparent oxidation of NADH. Furthermore there is a significant reduction in the magnitude and rate of the P.D. change as a result of a K^+ change on the nutrient side with addition of SCN on the nutrient, but not the secretory side. With gastric mucosal strips preincubated in substrate free solutions, succinate and other Krebs cycle intermediates resulted in a rise of O_2 consumption and SCN had its maximal effect with succinate as a substrate, although there is inhibition of O_2 consumption with all substrates. Thus SCN, in addition to its effect on acid secretion, appears to act as a metabolic inhibitor, inhibits the P.D. and alters the passive permeability characteristics of the nutrient membrane. This latter effect rather than the inhibition of an electrogenic H^+ pump may account for the resistance changes observed with SCN^-. (NIH, NSF Support)

LACTIC DEHYDROGENASE ISOZYMES IN THE OVUM AND EMBRYO OF THE RAT. J. C. Cornette*, B. B. Pharriss*, and G. W. Duncan. Metabolic Diseases Research, The Upjohn Company, Kalamazoo, Michigan.

Lactic dehydrogenase (LDH) is one of the best known examples of an enzyme occurring in multiple molecular forms (isozymes). Within recent years, characteristic isozymal patterns for LDH have been described for many tissues including embryonic tissue (Markert and Ursprung, 1962; Goldberg and Cather, 1963; Kessel and Ellgaard, 1966). This report describes the previously unknown differences between LDH isozymes present in the mammalian ovum and in developing embryonic tissue. Ova and embryos at various stages of development were obtained from PMS-primed Sprague-Dawley rats. Homogenates of these tissues were electrophoretically separated on acrylamide gel using a disc apparatus. Resulting columns were stained for LDH activity using nitro-blue tetrazolium as the hydrogen ion acceptor and stain. Results show that there is a distinct difference in the LDH patterns obtained from the pre-implanted blastocyst and the implanted embryo. Unfertilized ova, fertilized ova and pre-implanted blastocysts were characterized by a single isozymal band corresponding to LDH-1, the isozyme predominant in cardiac tissue. In the 9 day-old implanted embryo LDH-1 becomes the least distinct band while LDH-5 and LDH-4 become the predominant forms of the enzyme.

ACTINOMYCIN D INHIBITION OF A VITAMIN D_3-INDUCED CALCIUM-BINDING PROTEIN (CaBP) IN CHICK DUODENAL MUCOSA. R. A. Corradino* and R. H. Wasserman, Department of Physical Biology, New York State Veterinary College, Cornell University, Ithaca, New York

The existence of a vitamin D_3-induced CaBP, the correlation between CaBP concentration and vitamin D_3-enhanced Ca^{++} absorption (Wasserman and Taylor. Science 152: 791, 1966) and the rapid stimulatory effect of vitamin D_3 on RNA synthesis (Norman. Biochem. Biophys. Res. Commun. 23: 335, 1966) in rachitic chick duodenal mucosa strongly suggest that vitamin D_3 function may be mediated through an interaction with the genetic system. To test this, a 2^2 factorial experiment was conducted in which rachitic chicks were injected I.V. with 0 or 100 μg actinomycin D (an inhibitor of DNA transcription) two hours prior to I.M. injection of 0 or 250 I.U. vitamin D_3. Sixteen hours later, duodenal mucosal supernatants were prepared, the concentration of CaBP assayed by an ion exchange method and protein electrophoretic patterns on acrylamide gel slabs were obtained, as previously described (Taylor and Wasserman. Arch. Biochem. Biophys. 119: 536, 1967). In two experiments the CaBP concentration was greater in the vitamin D_3-treated (250 I.U.) than in the rachitic (0 I.U.) chicks regardless of actinomycin D level. However, the CaBP concentration in vitamin D_3-treated chicks was significantly and preferentially reduced by prior actinomycin D injection. In a collateral experiment of similar protocol, actinomycin D was found to reduce $^{47}Ca^{++}$ absorption by ligated loops of duodenum in vitamin D_3-treated chicks. These results lend additional support to a possible vitamin D_3-gene interaction, either direct or indirect, in which CaBP may be the product. (NIH-AM-06271-05, NIH-AM-04652).

EFFECTS OF PARATHYROID EXTRACT INJECTION ON RESPIRATION AND PHOSPHORYLATION BY KIDNEY MITOCHONDRIA. **L. C. Costello and Lillian Darago*. University of Maryland School of Pharmacy, Baltimore, Md.**

Previous studies from this laboratory demonstrated an inhibition of citrate and isocitrate oxidation and phosphorylation with kidney mitochondria from rats injected with high doses of parathyroid extract (PTE). Under the same conditions, succinate oxidation was unaffected. The present report is concerned with the effects of PTE injection on the other reactions of the Kreb's cycle. In addition to the inhibitory effect on citrate and isocitrate oxidation, PTE injection resulted in an inhibition of the oxidation of alpha ketoglutarate, malate, and pyruvate by kidney mitochondria. In all cases, the coupled phosphorylation was also inhibited. These results indicated that all the oxidations involving nicotinamide nucleotide cofactors were inhibited as opposed to the lack of any effect on succinate oxidation which does not require a nucleotide cofactor. Supported by NIH grant AM-06442.

INFLUENCE OF BODY POSITION ON SUBCORTICAL AND RHINENCEPHALIC EEG IN THE CAT. A. Costin*, Z. Elazar*, D. O. Walter and W. R. Adey. Department of Anatomy and Space Biology Laboratory, University of California, Los Angeles, California.

Spectral analysis was applied to study the effect of body position on the EEG output from different subcortical and rhinencephalic structures. This study was performed on 10 cats with chronic implanted bipolar electrodes in dorsal and ventral hippocampus, amygdala, septum, midbrain reticular formation, anterior and posterior hypothalamus, caudate nucleus, putamen and globus pallidus. Each structure's activity was analyzed over a spectrum from 1 to 30 cycles per second; autospectra and "coherences" between pairs of channels were calculated. Sharpness of autospectral peaks varied in the different body positions with an increased concentration of power in the lower frequency bands (1-4), immediately following change of position. These augmented power densities were more marked by tilting the animal on the side contralateral to the location of the recording electrodes. (These studies were supported by NIH Grant NB-01883, US Air Force Contract 49-(638)-1387 and NASA Grant 237-62.

THE EFFECTS OF ACUTE AORTIC AND MITRAL REGURGITATION ON MYOCARDIAL OXYGEN CONSUMPTION AND THE MECHANICS OF LEFT VENTRICULAR CONTRACTION. James W. Covell*, Charles W. Urschel*, Thomas P. Graham, Jr.*, Richard L. Clancy, Edmund H. Sonnenblick, John Ross, Jr., and Eugene Braunwald. Cardiology Branch, Natl. Heart Inst., Bethesda, Md.

The energy costs of the alterations in the mechanics of left ventricular (LV) myocardial contraction produced by valvular cardiac lesions have not been defined. Accordingly, the effects of acute aortic (AI) and mitral insufficiency (MI) were examined in a canine right heart bypass preparation in which heart rate, aortic pressure, effective cardiac output, and peak tension could be controlled. AI was simulated with a shunt containing a ball valve and electromagnetic flow probe between the aorta and the apex of the LV, and MI by a shunt between the LV apex and the left atrium. When AI was induced (6 dogs), $M\dot{V}O_2$ (in ml/min/100 g LV) increased from 10.9 $\pm$ 1.0 to 12.7 $\pm$ 1.1 (SEM) ml/min/100 g LV. When MI was induced (7 dogs) $M\dot{V}O_2$ increased from 8.9 $\pm$ 0.9 to 10.1 to 0.9 ml/min/100 g LV. Wall tension increased, fiber and contractile element (CE) shortening were augmented, and the efficiencies of fiber shortening and CE work were increased by 64.8% and 38.5% respectively during AI, and by 39.6% and 22.2% during MI. When peak tensions in the control state were matched to those occurring during AI (6 experiments) and MI (8 experiments), $M\dot{V}O_2$ was not significantly altered from control, although CE and fiber shortening were significantly increased. It is concluded that the increase in LV wall tension usually observed in valvular regurgitation is responsible for the augmentation of $M\dot{V}O_2$ and that the relatively minor O_2 cost of the increased fiber shortening during AI and MI permits a more efficient contraction of the ventricular myocardium.

DEPTH LIMITS OF BREATH HOLD DIVING. Albert B. Craig, Jr. Univ. of Rochester School of Med., Rochester, New York.

It is generally accepted that the depth to which a breath hold diver can descend is determined by the ratio of the R.V.:T.L.C. If the diver descends farther, it is predicted that he would develop a "thoracic squeeze" as the intrathoracic pressure became less than the ambient pressure. Within the past 10 years a number of divers have proven their ability to go to depths at which the beginning gas volume must have been compressed to less than 20%. That such depths are possible indicates events other than simple compression of the thorax by the ambient pressure occur. The subject performed dives starting each after expiring to R.V. (2.0 l). Hyperventilation using 100% O_2 permitted the dive to last 30 sec. Pressure differences between an esophageal balloon and a balloon strapped to the chest wall were recorded. In dives to progressively deeper depths the pressure difference was the same whether the subject was just below the surface or as deep as 3.75 m. Pressure and volume relationships indicate that the air volume in the respiratory space must have decreased by at least 530 cc at the maximal depth. The finding that the difference of pressure is unrelated to the depth suggested that air compression can also be accomplished by a transfer of blood from the peripheral to the central reservoirs. If such events occurred in a breath hold diver whose R.V. was 1.5 l and whose T.L.C. was 7.0 l he could descend to 62.3 m which is about the present record but is considerably deeper than 36.7 m as would have been predicted previously.

INTRACELLULAR RECORDING FROM CAT INFERIOR OLIVE NUCLEUS. W.E. Crill (intr. by T.T. Kennedy). Dept. of Physiology and Biophysics, Univ. of Washington School of Medicine, Seattle.

Responses to cerebral, cutaneous, and cerebellar stimulation were recorded from inferior olive neurons of nembutal-anesthetized cats by means of extra- and intracellularly placed electrodes. Resting membrane potentials of -20 to -56 mv and spike potentials of 25 to 70 mv were measured. The rising phase of the action potential had an inflection and the spike was easily separated into A and B components by repetitive antidromic (cerebellum) or direct intracellular stimulation. The repolarization phase consistently had a prolonged depolarization (P-D), and the duration of successive action potentials evoked by a constant stimulus varied from 8 to 15 msec. Usually 1-3 smaller spikes with an interspike interval of 1.2 to 2.5 msec were superimposed on the P-D. The complex repolarization phase was always associated with the B spike and the entire response could be evoked by antidromic, orthodromic, or direct intracellular stimulation. Action potentials were both antidromically (2.5-4.5 msec latency) and orthodromically (9.5 msec latency) evoked from cerebellum. Spike potentials superimposed on EPSPs occurred following stimulation of ipsilateral cerebral cortex (12.8 msec latency) and contralateral forepaw (22 msec latency) and were followed by a hyperpolarizing potential lasting 75-85 msec. During this hyperpolarizing potential, other orthodromic input was inhibited or blocked and the threshold to direct intracellular stimulation was increased. (Supported by U.S. Public Health Service Grant NB 5082.)

THE EFFECT OF ALLOPURINOL ON HEMORRHAGIC SHOCK. Jack W. Crowell, Carl E. Jones*, and Elvin E. Smith. Dept. of Physiology & Biophysics, Univ. of Miss. School of Medicine, Jackson, Mississippi.

Twenty dogs were bled into reservoir bottles until their arterial pressure was 30 mm Hg. Ten dogs were given 50 mm/kg of allopurinol (Zyloprim) 20 minutes prior to hemorrhage. The remaining ten dogs served as control. After 20 per cent uptake of the shed blood, the remaining blood was reinfused. The oxygen consumption of the dogs was recorded continuously throughout the experiment. The results of the experiments are as follows. The total duration of hypotension in the control dogs averaged 73 minutes and the total duration of hypotension in the allopurinol treated dogs averaged 135 minutes. The average oxygen debt of the control dogs was 199 cc/kg and the average oxygen debt of the treated dogs was 285 cc/kg. Despite a hypotensive period which was 1.85 times that of the control dogs, and an oxygen debt 1.43 times that of the control dogs, the survival of the treated dogs was 6 times greater than the control group as 6 of 10 of the treated dogs survived, while only 1 of 10 of the control group lived.

Hypoxic cells lose their purine base which is subsequently catabolized to uric acid. The conversion of hypoxanthine to xanthine to uric acid by xanthine oxidase is irreversible. Thus, the blockage of this conversion by allopurinol retarded loss of the base chemical for resynthesis of ATP and prevented shock from becoming irreversible.

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ACTION OF ADENOSINE AND ATP ON ILEAL WALL TENSION AND BLOOD FLOW. J.M. Dabney, J.B. Scott, C.C. Chou*, Mich. State Univ., E. Lansing, Michigan.

Adenyl compounds have been implicated by several workers in the local mechanism for the regulation of blood flow in various organs. Adenyl compounds decrease coronary vascular resistance and have variable effects on the renal circulation. Their effects on intestinal vascular resistance (R in mm Hg/ml/gm/min) and visceral smooth muscle have not been studied extensively. We have studied the vascular effects of adenosine and ATP in ileal segments during natural (Nat) or constant flow (Const). Also, their effects on ileal wall compliance (C in ml/mm Hg), was studied in the constant flow preparation by measuring the changes in lumen pressure when lumen volume was increased. The results are summarized as follows:

			Pre-control		During		Post-control	
		N	C	R	C	R	C	R
Adenosine	Nat	7		173		127*		174
	Const	10	1.41	193	1.28*	127*	1.43	191
ATP	Nat	7		207		114*		207
	Const	10	1.45	187	1.21	124*	1.39	186

*Changes from either pre- or post-control values were statistically significant at p value less than 0.05.

At the dosages used, both adenosine and ATP decreased vascular resistance in the natural and constant flow experiments. No change in lumen pressure was seen with either agent during natural flow and only adenosine changed ileal wall compliance during the constant flow procedure. Our results indicate that these adenyl compounds are vasodilator in the ileum and that their dilator effect results from direct action on the vascular smooth muscle and the vasodilation is not much affected by an action on the visceral smooth muscle.

TRANSPORT OF URIC ACID AND PAH BY SNAKE KIDNEYS. William H. Dantzler (intr. by W. H. Sawyer). Department of Pharmacology, Columbia University, College of Physicians & Surgeons, New York, New York.

Ophidian reptiles excrete uric acid as end product of nitrogen metabolism. Clearance data demonstrate that uric acid is secreted by renal tubules. Present study compared transport of uric acid with PAH by snake (Natrix sipedon) kidney tissue in vitro. Some studies on effect of blood supply on transport were also undertaken in vivo. Uptake of C-14 uric acid and non-radioactive PAH by kidney slices was studied. A few comparisons of the kidney slice data with data obtained from separated renal tubules were also made. With about 3 X 10^{-4} mM uric acid/l in bicarbonate Ringer medium at 28 C, steady state slice/medium (S/M) ratio for uric acid only approached 2.0. With about 2 X 10^{-2} mM PAH/l in medium, steady state S/M ratio for PAH was about 7.0. Maximum S/M ratios for both uric acid and PAH decreased with increasing concentrations in the incubation medium. Steady state for S/M ratio was achieved in about 2 hours with uric acid and about 1 to 1 1/2 hours with PAH. Addition of various substrates (e.g., acetate) to medium, as possible energy sources, did not cause any increase in maximum S/M ratio for uric acid or PAH. No difference in rate or extent of uptake of either PAH or uric acid was observed when separated tubules rather than slices were studied. Maximum S/M ratio for either acid was not affected by the presence of the other acid in the medium, suggesting that the transport mechanisms differ. Reduction of renal portal blood flow in vivo appeared to reduce tubular secretion of PAH without affecting tubular secretion of uric acid, suggesting that sites as well as mechanisms for transport of these two acids may differ. (Supported by NSF GB-3309, NSF GB-6040, and a USPHS General Research Support Grant.)

EFFECTS OF IV AND IA ACETYLCHOLINE, BRADYKININ AND HISTAMINE ON DOG FORELIMB BLOOD FLOW AND WEIGHT. R.M. Daugherty, Jr.*, J.B. Scott, F.J. Haddy, and J. Schwinghamer*. Depts. of Physiol. and Med., Mich. State Univ., East Lansing, Michigan.

Aortic pressure, muscle and skin small and large vein pressures, brachial and cephalic venous outflows and limb weight were measured in the collateral free innervated dog forelimb during progressively faster intravenous (IV) and intrabrachial (IB) infusions of acetylcholine, bradykinin and histamine (N=20). IV acetylcholine (41-206 µg/min) and bradykinin (21-82 µg/min) did not affect brachial or cephalic outflows, venous pressures or weight. IV histamine at a rate of 21 µg/min increased brachial and cephalic outflows while 81 µg/min decreased both outflows, neither dose greatly affecting weight. IB acetylcholine (1-21 µg/min), bradykinin (5 and 10 µg/min) and histamine (10-41 µg/min) increased brachial and cephalic outflows and venous pressures. Limb weight rose progressively with each agent but to a much lesser extent with acetylcholine. With brachial arterial inflow held constant, IB acetylcholine (0.5-21 µg/min) and histamine (2-41 µg/min) failed to affect either brachial or cephalic outflows while bradykinin (0.5-10 µg/min) produced a slight shift of flow from cephalic to brachial vein (N=10). With each agent, limb weight rose much less than during natural inflow. At the above infusion rates, these agents produce little change in limb flow when given intravenously but large increases in flow when given intrabrachially and assuming brachial outflow is predominantly from muscle and cephalic outflow is from skin, acetylcholine and histamine appear to dilate muscle and skin arterioles proportionately while bradykinin dilates muscle more than skin. The enhanced filtration seen during natural inflow appears to result in part from an increase in capillary hydrostatic pressure secondary to increased capillary inflow.

Blood flow redistribution in the dog paw. D. L. Davis and Mary Hammond.* Medical College of Georgia, Augusta.

Redistribution of blood flow occurring in the dog paw in response to peripheral nerve stimulation was studied in mongrel dogs anesthetized with chloralose, treated with succinylcholine chloride, and maintained on positive pressure respiration. Arterial inflow was limited to the dorsalis pedis artery and maintained constant with a pump. Constancy of inflow was monitored with an electromagnetic square-wave flow meter. Digital artery blood flow was recorded with a drop-counter continuously and simultaneously with pressures from the dorsalis pedis artery, digital artery, and dorsal metatarsal vein. Small blood vessel responses were recorded during stimulation of either the sciatic, deep fibular, superficial fibular, or tibial nerve. Stimulation parameters included stimulation voltages of 15-70 volts, stimulation frequencies of 0.1 to 25/sec, stimulus duration of 5 msec, and total stimulation periods of 30 to 60 seconds. All stimulations produced evidence of an overall constrictor response with appreciable redistribution occurring as indicated by either an increase or decrease in the digital artery flow while inflow was maintained constant. The initial response to high frequency sciatic or tibial nerve stimulations was generally an increase in digital flow. During the latter portion of these stimulation periods flow was decreased. The response to low frequency stimulations of sciatic and tibial nerves was that of a maintained increase in digital flow throughout the stimulation period. Deep fibular and superficial fibular nerve stimulations also produced redistribution, but to a lesser extent than that occurring in response to sciatic and tibial nerve stimulations. Supported by grants from the Georgia Heart Assoc. and grants HE-00240, HE-05782-05, and 1-F1-GM, 133-01 from the USPHS.

BLOOD FRUCTOSE, GLUCOSE AND PLASMA INSULIN CONCENTRATIONS AFTER INTRAVENOUS FRUCTOSE INFUSIONS IN THE FETUSES OF CHRONIC UNANESTHETIZED SHEEP. J.R. Davis*, F.C. Battaglia*, P. Beck*, E.L. Makowski*, and G. Meschia, Univ. of Colo. Med. Center, Denver, Colorado.

Although fructose concentrations (concn.) are known to be higher in fetal sheep blood than in maternal, little is known about its metabolism in utero.

Fetal and maternal blood fructose, glucose and plasma insulin concn. were measured before, during and after 6 fructose infusions into the umbilical vein of 3 sheep fetuses of unanesthetized ewes. Chronic indwelling catheters in the fetal umbilical artery and vein, and maternal uterine vein and femoral artery were sampled at 1/2 hr. to 2 hr. intervals.

In 3 fetuses, baseline fetal blood fructose concn. ranged from 29-80 mg% at 120 days gestation, decreasing towards term. Consistently, maternal fructose concn. were lower and glucose higher than analagous fetal values with no apparent consistent maternal-fetal insulin concn. differences. Following fructose infusion, fetal blood fructose and plasma insulin concn. rose while blood glucose concn. fell, whereas mean maternal uterine vein fructose and glucose concn. did not change. The mean 1/2 life of fetal blood fructose concn. was 2 hrs.

The data indicate rapid fetal fructose concn. clearance as early as 120 days gestation, suggesting that the elevated fetal fructose concn. is not due to inadequate utilization of fructose but rather to specific regulatory mechanisms in the fetus.

INFLUENCE OF CORTICOSTEROIDS ON CARDIAC GLYCOGEN CONCENTRATION IN RATS. J. Charles Daw*, Allan M. Lefer, and Robert M. Berne, Department of Physiology, University of Virginia, Charlottesville, Virginia.

During a study on the glycogen metabolism of isolated papillary muscles, the initial glycogen concentration in papillary muscles from adrenalectomized rats was found to be consistently lower than that of control animals. Since adrenalectomy has previously been reported to be without effect on cardiac glycogen, this study was undertaken to reevaluate the influence of corticosteroids on the glycogen concentration of the heart. Rats were adrenalectomized and maintained on 0.9% NaCl as drinking water for 10-14 days prior to cardiac glycogen determination. Corticosteroid replacement therapy consisted of dexamethasone 200 μ g/day (intramuscularly) and 0.9% NaCl (orally) after adrenalectomy. Ventricles were collected from either pentobarbital or ether-anesthetized, non-fasted rats. Cardiac glycogen concentration was 6.0±0.4 mg/g for 6 intact rats and 3.8±0.2 mg/g for 7 adrenalectomized rats anesthetized with pentobarbital. Similar results were obtained for papillary muscles dissected from hearts immediately prior to freezing. Papillary muscles from intact rats showed a glycogen concentration of 4.7±0.4 compared with 4.8±0.6 for the donor hearts. The same relationship existed (papillary muscles to heart) for adrenalectomized rats (2.3±0.4 to 2.4±0.4). Steroid replacement therapy abolished the differences between hearts from intact and adrenalectomized rats. These results demonstrate that, contrary to prior reports, cardiac glycogen is decreased in the absence of corticosteroids, and that corticosteroids probably play a role in the maintenance of normal cardiac glycogen levels. (Supported by a grant from the NIH)

THE EFFECT OF SERUM INCUBATION ON HYALURONIC ACID AND ON ALGINIC ACID. J. DeFilippi*, A. Herp* and J. Fabianek, Dept. Biochem., N. Y. Medical College, New York, New York 10029.

A great number of various substances other than enzymes have been found to irreversibly degrade hyaluronic acid and several polysaccharides such as alginic acid. Hyaluronic acid incubated with serum at pH 3-5 also undergoes an irreversible degradation suspected to be an enzymic hydrolysis. In order to investigate the nature of this degradation, hyaluronic acid and alginic acid (at final concentration 0.112%) were incubated with serum at final concentration of 10% at pH 4.5 and 7.0 in a buffer of ionic strength of 0.3. The rate of degradation of these acids was determined by measurements of specific viscosity. At pH 4.5 a marked semi-logarithmic decrease in viscosity was observed in the hyaluronic acid system, while the viscosity of alginic acid remained unchanged. At pH 4.5 controls of both acids in the absence of serum showed no degradation. At pH 7.0 both hyaluronic acid and alginic acid were not degraded when incubated with or without serum. The results indicate the presence of hyaluronic acid specific enzyme in serum active at pH 3-5. (Supported by NIH grant AM-4619).

SOLUTE MOVEMENT ACROSS THE ALVEOLAR-CAPILLARY MEMBRANE OF THE TURTLE. D. Deitchman* and C. V. Paganelli. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

The object of the present study was to measure in vivo solute fluxes from pulmonary blood into liquid-filled alveoli of the turtle, Pseudemys scripta, and to calculate permeability constants of the membrane system which separates blood from alveolar space. The turtle was selected for this study because of its ability to withstand prolonged anoxia. Administration of radioactive solutes and collection of blood samples were carried out through a catheter in the left subclavian artery. Turtle Ringer's solution was placed in the lungs and sampled through a tracheal cannula. Under our experimental conditions passage of most solutes from pulmonary blood to alveolar liquid is not blood flow-limited. Permeability constants (P) for the solutes tested were calculated from unidirectional flux measurements and are shown in the table in units of 10^{-7}cm/sec. Our in vivo results, which are in agreement with the findings of Taylor et al. in the isolated lobe of the dog lung (Circ. Res. 15: 353, 1965), demonstrate the low permeability of the alveolar-capillary membrane system to small solutes when compared with other capillary beds. This low permeability may play an important role in preventing filtration of liquid into the alveoli from the pulmonary circulation.

Compound	P
3-0-methyl glucose	3.5
$SO_4^=$	4.4
Na^+	7.0
I^-	13.0
K^+	27.0
Thiourea	29.0
Antipyrine	40.0
Water	3000.0

(Supported in part by U.S.P.H.S. Training Grant 5 T1 GM 341.

A NEW VASOACTIVE SUBSTANCE FROM DOG KIDNEY CORTEX. Ignacio de la Riva* and David F. Bohr. Dept. Physiology, Univ. of Michigan, Ann Arbor, Mich.

Saline extract of kidney cortex causes contraction of isolated smooth muscle from renal resistance vessels (500μ o.d.). The active substance filters through dialysis tubing. It is partially inactivated when the protein-free filtrate is boiled (PFFB) for 15 minutes. Smooth muscle from renal vessels is more responsive to the PFFB than is that from coronary, skeletal muscle or mesenteric vessels of comparable size. The response to the PFFB can be differentiated from that to norepinephrine, serotonin, and angiotensin; response to the renal factor is not blocked by phentolamine and does not display tachyphylaxis. Fractionation with Sephadex G15 demonstrates that the molecular weights of the active components of the PFFB are below 1500. This fractionation indicates that there are at least two active fractions; the one that is most active on renal vascular smooth muscle causes negligible contraction of coronary smooth muscle. These results differentiate the renal factor from a vasoactive plasma factor (Circ. Res. 19:593, 1966) and from prostaglandins (Am. J. Physiol., in press), both of which cause contraction of coronary vascular smooth muscle. Saline extract of skeletal muscle also causes a contraction of isolated vascular smooth muscle which cannot be blocked by phentolamine. The active material from kidney cortex can be differentiated from that from skeletal muscle by Sephadex fractionation. (Dr. de la Riva is a fellow of the Consejo Nacional de Investigaciones Científicas y Técnicas de la República Argentina).

SEQUENCE OF HEMODYNAMIC EVENTS AFTER GRADUAL PROLONGED HEMORRHAGE.
J.M. Desai*, S.I. Kim*, J. Monks*, W.C. Shoemaker, Dept. of Surg. Res., Hektoen Institute, Cook County Hosp. and U. of Illinois. Chicago, Ill.

The sequence of cardiovascular events were studied in 19 dogs subjected to a gradual prolonged hemorrhagic shock. The animals were gradually bled to mean arterial pressure (MAP) of about 50 mm Hg over a period of several hrs. and maintained at that pressure until 1/3 of the shed blood was taken up or until 10 to 12 hrs. had elapsed. The remaining blood then was retransfused and the animal followed until its death 12-57 hrs. later. Events were divided into time periods: Control (Period A), Hemorrhage (B), Transfusion (C), Post-transfusion (D), Preterminal (E) and Terminal (F). The mean values and SE for each period for MAP, cardiac output (CO), systemic vascular resistance (SVR) pulmonary vascular resistance (PVR), mean pulmonary arterial pressure (MPAP), left (LVSW) and right (RVSW) ventricular stroke work are:

Stage	A	B	C	D	E	F
MAP	114±3	50±2	124±4	84±4	52±3	34±4
CO	3.62±0.2	1.47±0.2	4.21±0.3	5.92±0.4	7.15±0.4	1.36±0.2
SVR	1950±95	2900±220	1680±198	788±82	607±78	893±93
PVR	239±26	452±45	244±30	256±30	275±25	412±40
MPAP	14±1.3	9±2.0	18±3.1	15.5±3.0	14.5±3.4	13±4.5
LVSW	44±4.0	7±1.2	56±4.1	39±4.9	29±5.8	12±3.2
RVSW	6±0.2	1±0.2	9±0.8	8±1.5	8±1.6	7±1.5

In essence, high cardiac output occurred in stages C, D and E and fell precipitously in stage F. The SVR after an initial rise in stage B, dropped to control levels in stage C and continued to fall during stages D, E and F. By contrast, PVR remained elevated during stages C, D, E and F. The LVSW, in contrast to RVSW, fell in the late stages.

ORIGIN AND INHIBITORY RESTRICTION OF HIPPOCAMPAL EPILEPTIC SPIKES. **M. Dichter* and W.A. Spencer, NYU Med. Schl. NYC (Supp. USPHS NB-05980).**

Direct surface application of pencillin or strychnine crystals to cat hippocampus produces large surface negative-positive potentials at application sites, and positive potentials at a distance. Neither spontaneous action potentials, nor antidromic spikes, nor large recurrent IPSPs directly trigger paroxysmal discharges. However, discharges can be triggered at short (2-20 msec) latencies by stimulating the intact fornix, but only at longer (10-50 msec) latencies by stimulating the deafferented fornix. Since the difference between these preparations is the presence or absence of afferent excitatory pathways, these must trigger the short latency discharges in intact preparations. By inference, recurrent excitatory actions alone trigger discharges in deafferented preparations. Analysis of the discharge in the central focus in both preparations demonstrates a large amplitude intracellular depolarizing-hyperpolarizing sequence with action potentials appearing on the crest of the depolarization. At a distance only large intracellular hyperpolarizations are seen. The extracellular depth distribution of potentials associated with the hyperpolarizations closely mimics the known depth distribution of recurrent IPSPs, suggesting origin by recurrent inhibition. The following hypothesis is advanced: hippocampal neurons in these foci are postulated to have enhanced excitatory coupling over short distances but to retain widespread recurrent inhibition. Manipulation of formal models of small networks containing connections of this sort suggests that such inhibition could act to limit both the spread and duration of triggered paroxysmal discharges, and account for: (1) their "spike-like" gross configuration, (2) delayed onset, (3) failure to lead to sustained seizure, (4) surface potential distribution, and (5) the intracellular potentials recorded.

Hemodynamic Changes in the Left Ventricle Associated with the Injection of Angiocardiographic Contrast Medium. L.J.Dotmeier*, H.L. Falsetti*, Colin Grant*, I.L.Bunnell and D.G.Greene, Dept. of Medicine, S.U.N.Y. at Buffalo and Buffalo General Hospital, Buffalo, N.Y.

The radiological study of left ventricular function with contrast medium is limited by the distortions of function caused by the procedure itself. To define some of these limitations, left ventricular pressure was continuously recorded before, during and for at least 10 seconds following left atrial injection of 35 to 50 ml of 76% meglumine diatrizoate (Renografin) in 35 adult patients with valvular or muscular dysfunction. The usual response in peak systolic pressure was an immediate rise (30 of 35 subjects) followed by a fall below the control pressure (30 of 35 subjects) starting 7 seconds (range 4-11 sec.) after the beginning of injection. In only 2 of 35 subjects did the increase in left ventricular pressure exceed 10%. In 6 subjects left ventricular pressure was continuously recorded for five minutes after injection of contrast. The maximal drop in left ventricular pressure averaged 19% and occurred 24-33 seconds after injection (5 cases). A return to preinjection pressure levels occurred in an average of 53 seconds (range 40-76 seconds). At 3 minutes peak systolic pressure was within 10% of control in 5 of 6 subjects. In only 6 of 34 subjects was the injection of contrast medium followed by an increase in end-diastolic pressure greater than 3 mm of Hg. No correlation was found between the extent or duration of the pressure changes and the rate, volume or pressure of injection over the range studied. This study indicates that the major pressure changes associated with the injection of contrast medium occur after peak opacification and the usual time for volume measurements and have essentially disappeared by 3 minutes.

PHYSICAL CHARACTERISTICS OF ACTIVE AND PASSIVE COMPONENTS OF THE ARTERIAL WALL. Philip B. Dobrin* and Allen A. Rovick. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

Pressures, radii, tangential intramural stress (S_t) and incremental elastic moduli (E) were determined in isolated dog common carotid arteries under conditions of maximum (NEpi) and minimum (KCN) smooth muscle activation. Systematic stepwise alteration in transmural pressures from 250 to 25 mm Hg and back to 250 mm Hg in NEpi-treated vessels described a loop with the radius smaller on ascent than descent. Interruption of the ascent by pressure decreases resulted in minimal dimensional changes until identity with the descending limb was achieved. Failure to descend along the ascending curve suggests that muscle bond breakage occurs during increases in radius. In other experiments with NEpi, the stepwise pressure ascent was begun from progressively lower radii. This resulted in a group of curves, all of which coincided at about 225 mm Hg, further confirming bond breakage during ascent. At that point of confluence, the strain was less for the NEpi-treated state than with equivalent stress following KCN. The effective E was also greater at this point. This implies that following treatment with NEpi the highly elastic passive element encountered at large strains is accompanied by some remaining active muscle.

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WATER ABSORPTION FROM THE RUMEN. A. Dobson and A. F. Sellers. N.Y.S. Veterinary Col., Cornell Univ., Ithaca, N.Y.

The question of how closely the movement of water across rumen epithelium follows the osmotic gradient with different solutes in the rumen has so far not been examined. Solutions were confined within the washed ventral sac of the rumen of a conscious fistulated cow by a rubber dam, which floated beneath the cranial and caudal rumen pillars. By continuously labelling the saliva in the esophagus with creatinine and estimating this compound in the ruminal solutions, any small contamination of the ruminal solution with saliva could be determined. Water movements were observed by following the changes in concentration of a non-absorbed, soluble marker, the purple complex of chromium with ethylenediaminetetracetic acid. In eight experiments when the osmotic pressure was varied from 200 to 400 m-osmol/kg by the addition of KCl, the rate of absorption of water was linearly related to the osmotic pressure within the rumen. With NaCl or the sodium salts of the lower steam volatile fatty acids in the rumen, no net water flux took place when the osmotic pressure within the rumen was 6 m-osmol/kg above that of the plasma, i.e. nearly zero. Under more physiological circumstances, with 100% CO_2 in the rumen at pH 6.0-6.5, the intercept for the zero net water flux increased to 26 m-osmol/kg above that of the plasma in the absence, and 51 m-osmol/kg in the presence of fatty acid. This uptake of water from the lumen from hypertonic solutions could be due to the rapid absorption of carbon dioxide and the unionized fatty acids from the rumen. (Supported by NIH Grant No. AM 04679.)

CORONARY LYMPH: AN INDEX OF TRANSCAPILLARY EXCHANGE OF POTASSIUM. H. Fred Downey and Edward S. Kirk (intr. by F. R. Steggerda). Department of Physiology and Biophysics, University of Illinois, Urbana, Ill.

In 7 anesthetized dogs the coronary lymphatic duct was successfully cannulated and lymph was collected during intravenous infusions of K^{42}. A right thoracotomy was found to be more successful than the left-sided approach described by others. Intramyocardial and intrapulmonary injections of T-1824 dye located separate coronary and pulmonary lymphatic drainages. The infusions were adjusted to produce nearly constant levels of arterial K^{42} for a period of 1 hour. Specific activities of K^{42} were determined in arterial and coronary sinus plasma collected at 5 min intervals and in 5 min collections of lymph. Within 5 min K^{42} in the coronary sinus plasma rose to a value 30-50% of the arterial level; then gradually increased to 60-80% of arterial values. Throughout and after the K^{42} infusions, the specific activities in coronary lymph and coronary sinus plasma were nearly identical. These data indicate that potassium permeates capillaries with greater ease than it does myocardial cells. If lymph-tissue exchange reduces the specific activity in lymph below an average for interstitial fluid (ISF), the ISF levels are between arterial and venous levels. These results also support a model in which potassium freely permeates the capillary and mixes uniformly throughout the ISF (Conn, H. L., and J. S. Robertson, Am. J. Physiol. 181:319, 1955). The data are incompatible with models which place the major barrier for blood-tissue exchange of potassium at the capillary wall (Renkin, E. M., Am. J. Physiol. 197: 1205, 1959) or models which place no barrier for exchange of potassium between capillary blood and tissue (Friedman, J. J., Fed. Proc. 24:1099, 1965).

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RESPONSE OF CELLS TO RESTRICTED VISUAL STIMULI IN AN ASSOCIATION AREA OF CAT CEREBRAL CORTEX. R. Dubner and F.J. Brown* National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland.

Cellular responses to restricted light patterns (circular spots or vertical bars, 0.5-3.0° diam) were studied in the anterior part of middle suprasylvian gyrus of cats anesthetized with chloralose. "On", "off", or "on-off", phasic responses were observed over almost the entire visual field when stimulus intensities were two or more log units brighter than the background (approximately 0.1 cd/m^2). When near-threshold stimuli were employed, restricted receptive fields (3-30° diam) were located near the center of the visual field. The most extensive receptive field mapping was done near the horizontal meridian and the type of response often changed as the stimulus was moved to different parts of the field. Almost all cells were influenced by both eyes and summation was observed during binocular stimulation. Many of these cells also responded to auditory click stimuli. After surgical ablation or undercutting of ipsilateral primary visual cortical areas and section of the corpus callosum, cells rarely responded to restricted light stimuli although diffuse light stimuli were still effective. Functional ablation of primary visual areas by the application of KCl also eliminated cell responses to restricted spots of light; responses returned with recovery of the depressed cortical areas. The present data indicate that 1) sensory-specific visual input to this association or polysensory area is relayed from primary visual fields, and 2) this cortical locus may play a role in complex sensory mechanisms involving inter-modality, sensory-specific interactions.

DYNAMIC SCANNING OF OXYHEMOGLOBIN DISSOCIATION IN VITRO. M.A. Duvelleroy*, R.G. Buckles*, F.L. Rodkey*, S.W. Rosenkaimer* and M.B. Laver. Mass. Gen. Hosp. Boston, Mass. and Naval Med. Res. Inst., Bethesda, Md.

A method has been developed for drawing on an X-Y recorder a complete O_2 content versus Po_2 curve, using whole blood. A sample of stirred, deoxygenated whole blood, of known volume (V_{BLOOD}), maintained at 37C, is suddenly exposed to a gas compartment containing a known volume of oxygen (V_{GAS}). Changes in Po_2 are followed with membrane covered oxygen electrodes. O_2 content (ml/ml) plotted on Y-axis equals: $Po_2^{GAS} \cdot V_{GAS}/V_{BLOOD} \cdot .863$. Po_2 of blood is plotted on X axis. O_2 saturation is calculated from the curve with O_2 capacity as the point where extrapolation of the top, flat portion of the curve crosses the Y-axis. A curve from Po_2 = 0 to 400 mm Hg can be obtained with 6 ml blood in 60 minutes. Eleven curves from one non-smoker (SWR), over a 3 month period exhibited good reproducibility (Po_2^{50} = 27.12 ± 2.36 mm Hg at pH 7.4) and agreed closely with the Severinghaus slide rule (Po_2^{50} = 26.6 mm Hg). Blood of AVB was re-studied, a 43 year follow-up on the original curve. Po_2^{50} for AVB (1967) at pH 7.40 was 27.4 mm Hg and at P_{CO_2} = 40 mm Hg it was 28.4 mm Hg compared to 25 mm Hg reported for AVB (1924). The carbon monoxide conc. of AVB (1967) was 0.240 ml/100 ml. The device permits selective scanning of any desired portion of the dissociation curve, compares favorably with the gasometric method but holds the advantage of great speed when an entire dissociation curve is desired.

CHARACTERIZATION OF ARGININE-INITIATED INSULIN RELEASE FROM EXCISED RABBIT PANCREAS. P. Edgar,* E. Almogela,* T.J. Merimee,* and D. Rabinowitz. Johns Hopkins Hospital and University, Baltimore, Md.

The intravenous infusion of arginine monochloride is followed by a rise in plasma insulin concentration in man and in the rabbit. These in vivo experiments leave unresolved the question of whether or not the amino acid stimulates insulin release directly. It has been repeatedly demonstrated that glucose enhances insulin release from pancreas incubated in vitro. We have examined the influence of arginine and of glucose, singly and together, on insulin release by excised segments of rabbit pancreas, incubated in an enriched Krebs-bicarbonate buffer. We have confirmed that release of insulin into the bathing medium is increased four-to sixfold when the glucose concentration of the buffer is raised from 0.5 to 3.0mg/ml. This effect is inhibited by addition of epinephrine to the medium. Arginine monochloride, in concentrations up to 3mg/ml, failed to enhance insulin release when glucose was omitted from the medium, or was present in a concentration of 0.6mg/ml. However, the release of insulin which followed incubation of pancreas in a glucose concentration of 1.5mg/ml was enhanced by a factor of two when arginine was added to the medium. Arginine-dependent insulin release was not inhibited by addition of epinephrine to the medium. We conclude that the amino acid, l-arginine, directly enhances insulin release from excised rabbit pancreas. However, this effect of the amino acid appears to be dependent upon the presence in the medium of an enriched glucose concentration.

QUANTITATION OF ARTERIOVENOUS BLOOD FLOW IN THE CANINE STOMACH. R. F. Edlich*, R. J. Buchin*, M. V. Prevost*, Y. Tomiyama*, S. Tsung*, and O. H. Wangensteen. Dept. of Surgery, Univ. of Minnesota Med. School, Minneapolis, Minn.

Microscopic studies of the canine gastric microcirculation have provided evidence for arteriovenous shunts, but the functional significance of these vessels has not been adequately defined. The purpose of this study was to quantitate blood flow through arteriovenous shunts in the canine stomach. Prior to the flow determination, the gastric venous circulation of two groups of dogs was isolated. Nine days later, under chloralose anesthesia, a T-tube was tied in the portal vein. Carbonized $19.8 \pm 3.9\mu$ Yb^{169} microspheres were injected through a left intraventricular catheter into one group of dogs, while the other dogs received a ventricular injection $42.6 \pm 5.6\mu$ Yb^{169} microspheres. Fifteen seconds prior to the injection, the superior mesenteric artery and vein, pancreaticoduodenal vein, and portal vein cephalad to the T-tube were ligated. With the portal vein clamped, the isolated gastric venous outflow was collected. After the dog was sacrificed, the entire stomach, proximal 10 cm. of the duodenum, and the venous outflow were analyzed for radioactivity. The quantity of activity recovered in the venous outflow 30 seconds after injection is expressed as a fraction of the total amount of radioactivity entering the gastric microcirculation. The fraction of microspheres entering arteriovenous shunts larger than the 20μ and 45μ sphere diameter was $5.10 \pm 1.9\%$ and $1.36 \pm .91\%$ respectively.

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Pyrogen induced changes in thermo-responsiveness of septal,preoptic and hypothalamic neurons. J.S. Eisenman. Univ. of Penna., Phila., Pa.

Responses of single septal,preoptic and hypothalamic neurons to local brain temperature changes have been studied in Urethane anesthetized cats, before and after injection of pyrogenic bacterial polysaccharide suspension ("Piromen," 2-3 mcgm/kg,I.V.). Unit responses were recorded for control periods of 30-60 min and for up to 240 min post-injection. The units' thermosensitivities were determined every 15 min. Responses of thermally insensitive ($Q_{10}1$) units, and units with normal thermosensitivity ($Q_{10}2$) were unchanged by the pyrogen.The preoptic thermodetectors ($Q_{10}>2$) showed a marked decrease in thermosensitivity, usually becoming insensitive following pyrogen injection.This response was often, but not always, accompanied by a generalized decrease in firing rate. Latency of onset of the response was 30-45 min. The response was frequently double peaked, with the major component beginning 60-75 min after injection. The response maximum occurred 90-120 min after injection. A return toward control levels could be seen after 1-1/2 to 2-1/2 hrs. Units whose locations and response patterns characterized them as thermoregulatory interneurons responded to pyrogen with a shift of their operating range along the temperature axis. That is, the temperature at which the unit began firing was shifted, usually upward, as was the temperature at which the maximal firing rate was reached. The maximal firing rate was unchanged. While these results support the "shifting setpoint" hypothesis of fever production, it is not clear whether a direct action of the pyrogen on preoptic thermodetectors is responsible for the shift.

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The Effects of CNS Lesions on the Demonstration of Shock Avoidance Learning by the Roach, P. Americana. E. M. Eisenstein. State University of New York, Stony Brook.

The ability of the roach to demonstrate learning is being studied as a function of lesions made in various parts of the CNS. A training procedure similar to that previously employed was used on 108 animals. The left prothoracic legs of 2 animals were connected in series so when one member (P) of the pair extended its leg, a lead attached to its tarsus entered a saline bath to close a circuit and shock both. The shock terminated when P lifted its leg out of the saline. After a training period both animals were reconnected so each could shock itself independently of the other by extending its own leg. In addition, 48 single animals were used in which one prothoracic leg served as P & its genetically matched contralateral mate as R. With this preparation records were made of both P & R leg positions during training. No test period was run. The results with both these procedures indicate that P-R differences are greater when the prothoracic ganglion is isolated from the head (headless) or from the posterior ganglia (head attached but posterior connectives of the prothoracic ganglion are severed); however, the P-R difference is markedly reduced if both posterior & anterior influences on the prothoracic ganglion are left to operate simultaneously (intact animals). If the brain is removed & only the subesophageal & prothoracic ganglia are joined, the P-R difference is abolished due to flexion of P & R legs. It also has been observed that in headless animals P is more active than R during training while R is the more active during testing. This is a result of P becoming less & R becoming more active in the transition from training to testing. This latter result is interpreted as supporting the notion that in testing R first extinguishes competing responses before relearning that only leg flexion leads to avoidance. Supported by NIH Grant NB 05827-03 to the author.

CHANGES IN BLOOD FLOW AND RESISTANCE IN NEONATAL GOATS DURING HYPOXIA. D. Eitzman*, S. Cassin and J. Hessler*. Depts. Pediatrics, Physiol. and Comp. Med., Univ. of Fla., Coll. of Med., Gainesville, Fla.

Simultaneous measurements of blood flow, pressure, P_{O_2}, P_{CO_2} and pH were made in the carotid artery and thoracic aorta in 10 goats 1 to 42 days of age. Blood lactates were also determined. The goats were artificially ventilated with room air, 6-8% oxygen in N_2, or 3-4% oxygen in N_2. Resistance to flow was calculated while being ventilated with room air and at 2 minute intervals after the induction of hypoxia. Five animals 1-5 days of age demonstrated a decrease in carotid arterial resistance to blood flow during ventilation with the 3-4% and 6-8% oxygen mixture. Aortic resistance to flow remained at control level or showed an increase. The results obtained in three goats 15, 29, and 42 days of age, subjected to 3-4% and 6-8% oxygen usually showed no change or an increase in resistance to flow in the carotid artery. The occasional decrease in carotid resistance was relatively small. Thoracic aortic resistance to flow either did not change during the hypoxic episode or showed an increase. Arterial P_{CO_2} remained relatively constant. Generally, pH decreased while lactate increased during and following hypoxia. It is postulated that the changes observed in resistance to flow may be useful physiological adaptations for increasing the survival time of newborn goats subjected to hypoxia. These changes appear to diminish with increasing age. (Supported by Grants NIH FR-05003, NIH HE-10834-01 and Fla. Heart 67AG12).

AGING AND COHESION OF TENDON FIBRILS. H. R. Elden (introduced by N. W. Shock), Gerontology Research Center, NICHD, NIH, U. S. Department of Health, Education and Welfare, Bethesda, Md. and the Baltimore City Hospitals, Baltimore, Md.

The number of interchain attachments of collagen increases with aging, while there is also an increase in the number of fibrils and fibers. This study showed that cohesion of tendon fibers defined as W_Q, the ratio of weight/length, increased linearly with body weight of rats aged 1 to 12 months. The time (T_B) for tendons to rupture in 5M urea also increased linearly with low body weight, but it increased exponentially at high body weight. The standard deviation of both parameters, SD W_Q and SD T_B, increased linearly with their respective mean values. Deletion of pituitary, parathyroid, and adrenal glands followed by hormonal replacement changed W_Q, T_B, and body weight. Mean and SD values of W_Q and T_B remained congruently related even though body weight was less than controls in some cases. Linear dependence of SD W_Q on Mean W_Q showed that large fibers accrue with aging while retaining small ones. Parallel changes in T_B and between T_B and W_Q indicated that molecular interactions influence macroscopic cohesion of fibers. Since these relationships were influenced similarly by aging and certain endocrine disturbances, it is suggested that cohesion of fibers is regulated by hormones during aging.

EFFECT OF IV ACETYLCHOLINE INFUSION ON VENOUS RETURN. T.E. Emerson, Jr. and P.R. Dennis*. Physiol. Dept., Mich. State Univ., E. Lansing, Mich.

Transient and steady state effects of a 5 min acetylcholine (Ach) infusion (100ug/min) on venous return (VR) to the heart & other parameters were studied in dogs anesthetized with nembutal. VR was measured with a cylinder and stopwatch from the cannulated venae cavae; blood drained into a reservoir and was returned to the right atrium or aorta with a pump. Cardiac inflow was a) varied according to VR by adjusting a pump or b) maintained constant. Preparations used were a) intact (N=10), b) heart-lung bypassed (N=7) and c) abdominal eviscerated (N=5) dogs. When cardiac inflow was variable, infusion of Ach in intact dogs caused an immediate and sustained rise of VR and a fall of arterial blood pressure(ABP) and total peripheral resistance (TPR). Heart rate decreased and stroke volume rose. With cardiac inflow held constant,VR increased transiently and returned to near control by the 5th min of infusion. A total of 73 ml of blood accumulated in the venous reservoir, indicating the amount of blood moved centrally. ABP & TPR decreased throughout the infusion. When the cardiopulmonary system was bypassed and aortic inflow held constant, Ach caused similar changes of VR, ABP& TPR. A total of 106 ml of blood accumulated in the reservoir. However, when the abdominal viscera were removed and cardiac inflow held constant, Ach caused only a small increase or a slight fall of VR in the transient period & a sustained fall during the steady state. ABP & TPR fell less than in the other groups. The venous reservoir level decreased a total of 59 ml. These data show that IV Ach infusion at 100ug/min increases venous return to the heart and suggest that the increase is due to changes in the peripheral circulation, mainly in the hepatosplanchnic bed. (Supported by NIH Grant HE10899)

EFFECT OF INTRAVENOUS CHOLINE CHLORIDE ON BLOOD PRESSURE, ELECTROCARDIOGRAM, AND RESPIRATORY RATE OF DOGS. Richard L. Engen. College of Veterinary Medicine, Iowa State University, Ames, Iowa.

Ten anesthetized dogs were given intravenous injections of choline chloride. The dosages were distributed as follows; 0.5, 1, 2, 5, and 10 mg/kgm body weight. At the lower dosage level, a drop in carotid blood pressure occurred. However, at higher dosages, the initial drop was followed by elevated blood pressure. Both systolic and diastolic pressures were elevated. Respiratory rate increased briefly after injections of choline chloride. The heart rate remained relatively constant, but the amplitude of the QRS and T waves increased after the intravenous injections of choline chloride.

SUBSTRATE UPTAKE AND UTILIZATION IN NORMOTHERMIC AND HYPOTHERMIC PERFUSED RAT AND GROUND SQUIRREL HEARTS.
Beth Erasmus* and D. W. Rennie. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

The effect of temperature on myocardial substrate utilization patterns was studied by comparing the O_2 consumption, glucose uptake, lactate production, and glycogen content of perfused hearts of a representative hibernator and non-hibernator at 15 and 37 C. From these determinations, estimates were made of the proportions of exogenous and endogenous substrate used to satisfy total cardiac energy requirements at each temperature. O_2 consumption was reduced by hypothermia in all hearts; however, no species differences were observed at 37 C (in spontaneously beating hearts) or at 15 C in hearts driven at the same rate). At normal temperatures and when supplied with 20 mM glucose and insulin (40 mU/ml), rat and ground squirrels fulfilled their energy requirements from exogenous glucose. A similar metabolic pattern was maintained in rat hearts at 15 C but no glucose uptake and no significant breakdown of glycogen by ground squirrel hearts were observed. Furthermore, ground squirrel hearts were relatively unaffected by iodoacetate (0.004 M) at 15 C although O_2 consumption and contractility of rat hearts were severely depressed by this poison. These results indicate that ground squirrel hearts, adapted to function at low temperatures, utilized non-carbohydrate energy sources, probably lipids, in preference to exogenous and endogenous carbohydrates at low temperatures. Hypothermic rat hearts continued to utilize exogenous and endogenous carbohydrates and were apparently unable to shift to lipid oxidation when the glycolytic pathway was inhibited. (Supported in part by U.S.P.H.S. Training Grant 5 T1 GM 341.)

EFFECTS OF TETRODOTOXIN AND NOREPINEPHRINE ON FROG'S HEART ATRIUM.
D. Erlij and J. Aceves (intr. by A. Rosenblueth) Department of Physiology. Centro de Investigación y Estudios Avanzados del I.P.N., México 14, D.F. México.

We studied the effects of tetrodotoxin (TTX) on the isolated frog's atrial muscle and sinus venosus immersed in oxygenated Ringer's solution. TTX (10^{-8} to 10^{-6} g/ml) abolished the electrical activity of frog's atrial muscle. On the other hand these concentrations applied to the spontaneously beating sinus venosus only reduced its rate. Addition of norepinephrine ($5x10^{-6}$) to the TTX treated preparations increased the heart rate. This increase was of similar magnitude to that observed in control preparations. Norepinephrine also recovered the excitability of the atrial muscle paralyzed by TTX. The conduction velocity in the recovered tissue is much slower than before treatment. Intracellular records show that the rate of rise of the action potential of atrial muscle fibers is markedly slowed after treatment with TTX-norepinephrine.

In almost every tissue where action potentials are Na dependent, TTX abolishes propagation, while in those tissues where action currents are carried by alkaline earth ions TTX is without effect. Experiments are in progress to find whether or not the spikes observed in atria treated with TTX-norepinephrine are Na dependent. This work was supported by a Grant from the Life Insurance Research Fund.

RED BLOOD CELL AND WATER TRANSPORT BETWEEN GUT AND BLOOD. Edward A. Ernst*, Ralph A. Nelson and Hugh F. McCorkle*. Scott Research Laboratory and Departments of Anesthesiology and Pathology, Fairview General Hospital, Cleveland, O.

This study was undertaken to determine whether the red blood cell participates significantly in water transport between blood and gut. In five dogs, isotonic, hypotonic, or hypertonic tyrode solutions were instilled into an isolated jejunal loop with intact nerve and blood supply. These tests lasted 10 minutes each. In six additional dogs, one hour tests of hypotonic and one hour tests of hypertonic solutions were studied. Total venous drainage from the jejunal loop was collected at 15, 30 and 60 minute intervals. Blood was replaced from donor dogs to maintain normal blood volume. A constant sample of arterial blood was also withdrawn during each time interval (2 ml/min). Water content of RBC and plasma on both sides of the capillary bed were determined by dehydration. It was found that the RBC carried about half the water taken up by blood during gut absorption. The RBC contributed more than half the water appearing in the gut lumen when enterosorption occurred (net water gain by gut contents). It is concluded that the RBC is an important contributor to water movement between intestine and blood.

Supported by the Diabetes Association of Greater Cleveland.

GAS IN THE HEAD: ANESTHESIA WITH MIDBRAIN CHEMODES. F.R. Ervin, J. Folkman, V.H. Mark, A. Suematsu, & W.H. Sweet*. Massachusetts General Hospital, Boston, City Hospital, & Harvard Medical School, Boston, Mass.

The demonstration by Folkman, et al. that anesthetic gases will cross a Silastic membrane in therapeutic concentration has provided an important tool for pharmacological investigation. We have utilized chronic indwelling Silastic chemodes stereotactically placed in the mesencephalic formation of cats to deliver micro quantities of anesthetic gases. Observation of behavior and of EEG demonstrated the rapid onset of "natural" sleep in response to as little as 0.8 cc. of cyclopropane. Response to cyclopropane, tefluorane, nitrous oxide, CO_2, tenthrine, and ether has been studied. The similarity in response to the various agents place in question theories of anesthesia which differentiate cortical and midbrain loci of action. Movies will be shown.

EFFECT OF PHYSIOLOGICAL IMPERFECTIONS ON DIFFUSIONAL TRANSFER IN PLACENTAS. J. Job Faber. University of Oregon Medical School, Portland, Oregon.

A variety of hypothetical vascular patterns of fetal and maternal vessels in placentas served as models. Transfers were calculated on the basis of an assumed range of values of placental permeability and maternal and fetal blood flows in each of the models. The results were represented by a plot of a "maternal transport fraction", T^M, defined as $(C^{Ma}-C^{Mv})/(C^{Ma}-C^{Fa})$ versus a "fetal transport fraction", T^F, defined as $(C^{Fv}-C^{Fa})/(C^{Ma}-C^{Fa})$, as a function of a "permeability variable", d, defined as $P/\dot{Q}^M$. (C=concentration, a=arterial, v=venous, P=permeability, $\dot{Q}$=rate of blood flow). Subsequently, flows and / or permeability were assumed to be distributed unevenly. Calculations on these models showed that, within physiologically probable ranges, maldistribution of flow ratios grossly affects the effectiveness of exchange, but maldistribution of permeability does not. The transfer of relatively permeable substances ($d>1.0$) is particularly affected whereas the transfer of relatively impermeable substances ($d<0.1$) is not. Non-exchanging shunts in the maternal and fetal placental circulation affect the graphical representation of T^M and T^F by proportional reduction of the magnitudes of T^M and T^F respectively. Therefore, the line $d = \infty$ will intercept the axes at a T^M and a T^F equal to the non-shunted fraction of maternal and fetal blood flows respectively. Supported by NIH HD2313 and HE6336.

GAS-LIQUID CHROMATOGRAPHY WITH QUANTITATIVE ELECTRON CAPTURE DETECTION OF ALDOSTERONE AND CORTISOL FROM BLOOD. Louis F. Fabre, Jr.*, Robert E. Smith*, and Gordon Farrell. Texas Research Institute of Mental Sciences, Houston, Texas.

A comparatively rapid (48-hour) method for isolating and quantitating aldosterone and cortisol at submicrogram levels utilizing oxidation and thin layer chromatography coupled with gas chromatography with electron capture detection has been perfected. Quantitation is accomplished using a 4 ft. column of 2% SE-30 on gas chrome Q, at 250 C with electron capture detection. Aldosterone in the form of the γ-lactone exhibits a linear relationship with square centimeters peak area in the range 10-250 nanograms. Sensitivity for cortisol as the derivative adrenosterone is similar. Prior to gas chromatography, preparation of samples from blood involves addition of 10,000 DPM each aldosterone c-14 and cortisol c-14, to correct for losses incured in processing; $CHCl_3$ extraction; benzene: water partition; TLC (Etac:cyclohexane, 9:1), to separate aldosterone from cortisol; oxidation-HIO_4 for aldosterone, and CrO_3 for cortisol; and TLC (Etac:cyclohexane, 1:1), to separate the oxidized steroids from the reaction mixture. This process allows a 2-day simultaneous analysis of aldosterone and cortisol. It is possible to recover submicrogram quantities of steroids added to blood with 100%± 6% accuracy.

EFFECT OF ALTERED PO_2, P_{CO_2} AND pH ON RETRACTIVE FORCE AND SURFACE ACTIVITY OF DOG LUNG. Edmund E. Faridy. (Intr. by A. Naimark). Dept. of Physiology, University of Manitoba, Winnipeg, Manitoba.

The effect of acute alterations of pulmonary arterial blood gas tensions ($P\bar{v}CO_2$; $P\bar{v}O_2$) and alveolar gas tensions on the mechanical properties of lungs has been studied in left lower lobes of open chest dogs. After 4 hours the left lower lobes were excised, and static deflation pressure-volume curves and the stability ratio (S.R.) of bubbles expressed from the lung were measured. We have previously reported that a state of hypercapnia and hypoxia produced either through the pulmonary blood or through the ventilating gas mixture causes an increase in the retractive force of the lung. The decrease in the percent of maximum air volume remaining at 10 cm H_2O transpulmonary pressure ($V\%_{10}$) correlated with a decrease in S.R. In the present experiments, the effect of hypercapnia (pH kept normal with IV THAM or $NaHCO_3$) and hypoxia was compared with the effect of hypocapnia and hypoxia in the presence of acidosis (infusion of lactic acid or HCl). No correlation was found between $V\%_{10}$ and pulmonary arterial pH but a significant negative correlation was found between $V\%_{10}$ and $P\bar{v}CO_2$. The effect of $P\bar{v}CO_2$ (> 60 mm Hg) on the retractive force of the lung was prevented when $P\bar{v}O_2$ was greater than 60 mm Hg or when the lobe was ventilated with room air. However, the effect of inspired CO_2 (6 - 10%) on the retractive force of the lung was not prevented by $P\bar{v}O_2 > 250$ mm Hg or by O_2 (20 - 90%) in the inspired gas.

Supported by the Medical Research Council of Canada.

ALDOSTERONE SECRETION RATES IN 5-DAY POST-OPERATIVE NEPHRECTOMIZED DOGS Gordon Farrell and Louis F. Fabre, Jr.* Texas Research Institute of Mental Sciences, Houston, Texas.

A method has been devised for the separation of the endocrine and excretory functions of the kidney. Large male dogs were bilaterally nephrectomized by the ventral approach on day 1 and an AV shunt was performed on the femoral artery and vein to allow access to extracorporal hemodialysis. On days 3 and 5, the dogs underwent a 6-hour dialysis with a Skeggs-Leonards artificial kidney. During the procedure the dogs remain awake; no anesthetic is necessary. The dialysis solution was adjusted to allow normal ranges of plasma Na^+ and K^+ concentrations. BUN determinations were performed daily. On the 6th day, 5 days post-op the dogs were anesthetized with sodium pentobarbital and the left lumbo-adrenal vein was cannulated with the adrenal vein ligated. Two blood samples of ½ hour were collected. Aldosterone was quantitated as the derivative aldosterone γ lactone by gas chromatography and electron capture detection and aldosterone secretion rates (ASR) were calculated. The following results were obtained: control, BUN (at time of adrenal tap) 22 mg%, ASR 4.97, 17.82 µg/100 kg per hr (for 1st and 2cd ½ hour collection respectively); nephrectomized dog 1, BUN 112 mg%, ASR 48.3, 48.2 µg/100 kg per hr; nephrectomized dog 2, BUN 145 mg%, ASR 5.39, 17.89 µg/100 kg per hr; nephrectomized dog 3, BUN $>$ 250 mg%, ASR 1.37, 2.54 µg/100 kg per hr. These results indicate (1) that dogs can maintain aldosterone secretion rates as high or higher than controls in the absence of the renin-angiotensin system, (2) that high BUN levels are associated with low aldosterone secretion rates, and (3) that nephrectomized dogs can respond to hemorrhage with elevated aldosterone secretion rates. (With the assistance of Robert E. Smith, Jr. and Charles R. Turner).

EFFECT OF SUGARS AND SUGAR DERIVATIVES ON THE PREFERENTIAL BINDING OF D-GLUCOSE TO TRIS DISRUPTED MUCOSAL BRUSH BORDERS OF HAMSTER JEJUNUM. Robert G. Faust, Mary G. Leadbetter*, and Regina K. Plenge*. Dept. of Physiology, Univ. of North Carolina, School of Medicine, Chapel Hill, N. C.

Preferential binding of actively transported D-glucose (U.L.) C^{14} to disrupted brush borders (Faust, Wu and Faggard, Science, 155:1261, 1967) was studied in the presence of various unlabeled sugars and sugar derivatives at concentrations between 0.1 and 10 mM. Incubations were carried out at 37°C for 1 hr. in a phosphate buffer containing a radioactive sugar mixture of D-mannose-1-H^3 (10^{-5}mmole/l.) and D-glucose-C^{14} (10^{-3}mmole/l.). An increase in the ratio of the DPM for H^3 to that for C^{14} in the supernatant was indicative of preferential D-glucose binding to the disrupted brush borders. The non-actively transported sugars, L-sorbose, D-ribose, D-arabinose and L-arabinose did not affect the preferential binding of D-glucose. Experiments with actively transported sugars indicated that 3-O-methyl-D-glucose and D-xylose were more inhibitory than D-galactose. The most potent inhibitors of D-glucose binding, however, were unlabeled D-glucose, phlorizin and D-glucosamine. D-galactosamine, on the other hand, was not inhibitory. These results demonstrate that the mechanism of sugar transport can be studied with isolated and disrupted mucosal brush borders. (Supported by USPHS Grant AM 07998).

IN VITRO KIDNEY PRESERVATION WITH INTERMITTENT LOW FLOW HYPOTHERMIC PERFUSION. J. A. Feemster*, Y. Idezuki*, R. H. Dietzman* and R. C. Lillehei. Dept. of Surgery, Univ. of Minn. Med. School, Minneapolis, Minn.

We are able to preserve the in vitro viability of canine kidneys for 72 hours by hypothermia and hyperbaria, but function is impaired even at 24 hours. To preserve functional ability, new substrate for the nutrition of cells is needed. Thus, we have added an intermittent low flow perfusion technique to hypothermia and hyperbaria. With a balanced salt perfusate, kidneys preserved for 24 hours function immediately after autotransplantation and maintain a normal BUN creatinine and arterial blood pressure after contralateral nephrectomy. This is in contrast to elevations of these values in dogs supported by kidneys preserved only with hyperbaria and hypothermia. With blood perfusion, kidneys were preserved in a viable state for 5 days, but maintenance of a constant perfusion rate and pH was difficult. By diluting plasma with balanced salt solution, perfusion could be continused for 10 days. Tissue slices of all preserved kidneys were analyzed for sodium, potassium, glucose, lactic acid, alkaline and acid phosphatase, SGOT and SGPT. Elevation of potassium, alkaline and acid phosphatase were indicators of irreversible cellular damage. Biopsies examined by light and electron microscopy showed lysosomal disruption and mitochondrial swelling in kidneys perfused with only a balanced salt solution after 36 hours. These studies include observation of over 150 preserved kidneys.

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EYE MOVEMENT RESPONSES IN THE CALCARINE CORTEX AFTER RETINAL ABLATION. Martin Feldman* and Bernard Cohen. Department of Neurology, Mount Sinai School of Medicine, New York.

Prominent triphasic potentials are found in the calcarine cortex of the alert monkey which follow each rapid movement of the eyes in the light. These potentials have a latency of about 30 msec and are similar to the potentials evoked by light flash when the eyes are motionless. For the most part these potentials disappear in darkness. After retinal ablation a dramatic change takes place in calcarine activity. Prominent potentials which follow rapid eye movements are now widely distributed in the occipital cortex. These potentials appear 2 days after retinal ablation, reach maximum amplitude in 5 days, and persist for the life of the animal. They have a latency of about 50 msec and are particularly prominent after blinks. The waveform is complex and somewhat variable. Nevertheless, the initial portions are of opposite polarity to the eye movement response of the intact animal in the light. Calcarine potentials after retinal ablation are of greatest amplitude at stages of consciousness somewhere between maximum alertness and drowsiness and do not invariably occur after each eye movement. Similar potentials are also evoked in the calcarine cortex of these animals by somesthetic or auditory stimuli or by electric stimulation of the pontine or mesencephalic reticular formation.

Conclusion: These data suggest that calcarine cortex potentials accompanying eye movements after retinal ablation are related to ascending impulses from the brain stem reticular formation. They are probably transmitted through the lateral geniculate body. Similar projections from the brain stem to the calcarine cortex associated with rapid eye movements may be present in the intact animal as well.

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MEASUREMENT OF RESTING AND EXERCISE CARDIAC OUTPUT BY CO_2 REBREATHING AND DYE-DILUTION METHODS. R. J. Ferguson*, J. A. Faulkner*, S. Julius*, and J. Conway, University of Michigan, Ann Arbor, Michigan.

The cardiac output of 13 normal adult males ages 23 to 43 years was estimated by CO_2 rebreathing and dye-dilution methods. Reproducibility of the CO_2 method was assessed by duplicate determinations of cardiac output in sitting rest and at workloads of 600 and 900 kgm/min on a bicycle ergometer. Test-retest means for cardiac output were 5.4 - 5.1, 13.0 - 12.4, and 15.6 - 15.5 liters/min respectively. Correlations were .82, .93, and .86. Determinations of cardiac output were made by the CO_2 and dye-dilution methods at rest and during the 6th and 7th minute of exercise at 600 and 900 kgm/min and at maximum work. Maximum workloads ranged from 1200 to 1650 kgm/min corresponding to oxygen uptakes of 2.76 to 4.13 liters/min. For each experimental condition mean cardiac outputs for CO_2 and dye-dilution were 6.0 - 5.6, 12.6 - 13.5, 16.8 - 16.9, and 19.6 - 21.2 liters/min. Correlations were .22, .54, .64, and .87. The CO_2 method was reproducible at rest and during exercise. At rest, no significant difference was observed between the means for cardiac output as measured by the two methods, however, the low correlation indicates that comparable values for individual subjects were not obtained. The CO_2 rebreathing and the dye-dilution methods did provide comparable values for cardiac output in exercise. (Supported by NIH grants CD 00081 and GM 12554).

HEPARIN MODIFICATION OF ENDOTOXIN ACTIVATION OF RETICULOENDOTHELIAL FUNCTION AND SHOCK LETHALITY. James P. Filkins and N. R. Di Luzio, Dept. of Physiology & Biophysics, Univ. of Tenn. Med. Units, Memphis, Tennessee.

The reticuloendothelial system (RES) has often been ascribed a central role in host-defense against endotoxemia and the development of irreversible shock. Recent studies have indicated that heparin influences reticuloendothelial function both in vitro (Proc. Soc. Expt. Biol. & Med., v122, 548, 1966) and in vivo (J. Reticuloendothelial Soc., v3, 471, 1966). The present investigation evaluated the effects of heparin in rats on 1) the acute response of the RES to endotoxin, and 2) shock lethality induced by endotoxin. S. enteritidis lipopolysaccharide (0.5mg iv, 120 min. prior) markedly activated the RES as reflected in a ten-fold decrease in intravascular half-times for colloidal carbon. Heparin (1000 USP units) administered prior to endotoxin completely abolished the RES activation as evidenced in normal carbon clearing activity. Intravenous injection of either S. enteritidis or E. coli endotoxins (1mg/100gms iv) resulted in 67 - 73% shock mortality. Heparin administered prior to, simultaneously with, or shortly after the endotoxin reduced the mortality to 0 - 14%. These data suggest that heparin and the RES may interact in the prevention of endotoxin's actions on the circulatory system and thus deter the progression of endotoxin shock. (Supported by AEC).

RELATION BETWEEN DISPLACABLE AND TOTAL BLOOD VOLUME OF FOREARM. S. Finkielman*, E. Brown & M. R. Powell*, Cardiovasc. Res. Inst. and Depts of Med. & Radiol., UC School of Med. San Francisco, Cal. Knowledge of both the total blood content and its changes under various circumstances are needed for complete assessment of the capacity function of a regional circulation. Tissue displacement and movement artifacts interfere seriously with measurements of limb blood content by pressure plethysmography. With 2 Whitney gages on arm in rigid box we measured change of forearm volume (FV) during 3 min compressions at 200 mm Hg. In 22 expts on 10 healthy subjects (arm at heart level, comfortable conditions) the total volume expressed (tissue + blood) averaged 4.76 % FV (SE .33) and volume expressed from arm rendered "bloodless" by prior compression and arterial occlusion averaged 1.49 % FV (SE .23). Displacable blood volume (DBV), by subtraction, averaged 3.27 % FV (SE .21). By a refilling method (Litter and Wood, J. Clin. Invest. 33:798, 1954), DBV averaged 3.20 (SE .17). In 4 patients whose blood was tagged with CR^{51}, total blood content (TBC) was estimated by relating changes in external radioactivity to changes in FV and extrapolating to background radioactivity. In them, DBV and TBC averaged 2.67 and 4.80 % FV respectively. Residual blood after compression averaged 46% of TBC (range 32% to 52%). We have not yet determined whether residual volume is influenced by the functional status of the circulation at the time of compression. (Supported by USPHS Grant HE-06285.)

CHANGES IN CONTRACTILE PROPERTIES OF DISUSED MUSCLE. Gerald D. Fischbach* and Norman Robbins, Spinal Cord Sec., LNP, NINDB, Nat. Inst. of Health, Bethesda, Md.

A method was developed to record EMG's limited to individual muscles in unrestrained rats. Daily counts were made of distinct motor unit spikes over a period of several weeks during which recording conditions remained stable. Soleus muscles were more tonically active than fast muscles studied under similar conditions. Immobilization by pinning ankle and knee joints had an immediate and persistent effect on soleus activity. Total counts were reduced to 5-10% of control, and unit firing patterns were altered. Four weeks after pinning, the contractile properties of the soleus muscle studied in vitro under isometric conditions were significantly "faster" than controls. Twitch time to peak was shorter, maximum rate of tension development was increased, and both maximal and 5/sec. tetanus/twitch ratios were decreased. The maximal rate of tension development was greater than control at any given time or at any given %-maximum tension. Assuming unaltered compliance, the above findings imply a change in the force-velocity relation. In contrast to previous studies involving tenotomy, cross-innervation, or spinal cord section, activity and contractile properties were affected by a procedure which left all elements structurally intact The mechanism of the correlation between activity and contractile properties remains to be elucidated.

EFFECT OF ANGIOTENSIN AND NOREPINEPHRINE INFUSION ON RENIN PRODUCTION IN THE DOG. J. Fojas[x] and H. E. Schmid, Bowman Gray Sch. Med., Winston-Salem, N. C.

Calculations of plasma renin levels were made in the anesthetized dog with unilateral renal artery constriction, before, during and after angiotensin and norepinephrine infusion in low and high dose levels. Renal blood flow was measured continuously with the electromagnetic flowmeter (EMF) and renal plasma flow determined from the RBF and Hct. Glomerular filtration rate (GFR), cortical blood flow (CBF) and medullary blood flow (MBF) were determined from the extraction of creatinine and para-aminohippurate. Renin production was determined from the simultaneously drawn arterial and renal venous plasma levels which were prepared by the Helmer method and bioassayed in rats. Angiotensin infusion was followed by a decrease in plasma renin levels even under conditions of renal artery constriction that resulted in an initial decrease in GFR and RBF and a subsequent increase but not to as high as control levels, after termination of the infusion. Norepinephrine caused similar hemodynamic changes but resulted in little change in renin production. Frequent blood and urine samples during osmotic diuresis were obtained during renal artery constriction and infusion of angiotensin and norepinephrine in an attempt to better correlate the change in renin production with alterations in renal function. The findings are in agreement with the results reported by Vander that angiotensin may act in a specific manner to inhibit renin formation by the kidney. (This work supported by grant HE-7842, NIH and N. C. Heart Association.)

ACTION OF ACTH ON THE ANDROGENIC ACTIVITY OF THE REGENERATING ADRENAL CORTICES. G. Forester and M.J. Perrault (intr. by A. DesMarais). Department of National Health and Welfare and University of Ottawa, Ottawa, Canada.

Male Albino Wistar rats acclimated for 30 days at 2°C, are subjected to the following operations: adrenal demedullation, castration or castration-demedullation. The activity of the circulating androgens is assessed by the weight of the sexual accessory organs and by the $Zinc^{65}$ uptake by the dorsolateral prostate. The castrates display a massive but transient androgenic response on the 8th day of treatment. In the intact animals, an alternance of release and storage is indicated and the ACTH stimulation of androgenic production appears sustained. In spite of the regenerating adrenal cortex, the demedullated animals show a moderate transient stimulation followed by a decline probably due to pituitary feedback. The double-operated display a temporary elevation above untreated castrate level, associated with the regeneration of the adrenal cortex, but promptly cancelled by pituitary feedback. Thus, 1) the androgenic function of the adrenal cortex becomes visible in the absence of the testis, and 2) the circulating androgens resulting from the testis and/or the adrenal cortex, are capable of causing feedback depression of the pituitary gonadotropins.

VARIATION OF URINARY PRECESSION OF Na OVER INULIN WITH BLOOD PRESSURE. E.C. Foulkes, Depts.Env.Health & Physiol., Coll. of Med., Univ. of Cincinnati, Cincinnati, O.

Precession of Na over inulin in urine after simultaneous arterial injection is well documented. It has been attributed to an ion-permeable nephron segment in the renal medulla or papilla which permits complete exchange of Na between plasma and urine. On this view a factor limiting precession could be the plasma flow to the inner medulla (MPF). We have previously expressed the rate of Na precession in clearance terms (Proc. 3rd Int. Congr. Nephrol., 1966). The precession clearance, (CPR)Na, was of the same magnitude as that generally accepted for MPF. To test further the equation of (CPR)Na with MPF we have investigated its variation with blood pressure (BP). On the basis of the reported lack of autoregulation of MPF, (CPR)Na should vary directly with BP. The hypothesis was tested in mannitol and Na_2SO_4-loaded dogs treated with Furosemide to dissipate interstitial Na accumulation and to prevent Na reabsorption distal to the exchange site. In 12 studies on 6 dogs release of carotid clamps caused a mean drop in BP from 150 to 100 mm Hg, and simultaneously decreased (CPR)Na from 2.2 to 1.4 ml/min, corresponding to a fall from 4.1 to 3.0% of RPF (mean $\Delta = -1.1\% \pm 0.7$, SD, $P < .001$). By contrast, (CPR)Na changed from 3.3 to 3.4% of RPF in 8 studies on 4 dogs whose BP was kept constant at normal levels (mean $\Delta = -0.1\% \pm 0.2$). These results support the suggestion that Na precession is limited by MPF. (Supported by USPH.)

STATISTICAL INPUT-OUTPUT RELATIONS OF SINGLE CORTICAL NEURONS. Walter J. Freeman. Dept. Physiol., Univ. Calif, Berkeley.

The prepyriform excitatory and inhibitory neurons form a negative feedback loop requiring two transductions: synaptic currents control the rates of firing of the neurons, and the firing rates determine the synaptic currents. The input via the lateral olfactory tract is to the excitatory neurons, for which the synaptic currents produce the sinusoidal EEG and averaged evoked potentials (AEP) recorded extracellularly. AEP from single-shock stimulation of the tract have the shape of a damped sinusoid. The post-stimulus time (PST) histograms for the firing of single excitatory neurons approximate a damped sinusoid in phase with concomitantly averaged potentials. PST histograms for inhibitory neurons have the same generic form but lag the evoked potential by about 1/4 cycle. The EEG amplitude histogram is almost Gaussian. The probability density function of spontaneous inhibitory neuron firing conditional on amplitude (cpdf) has a maximum slope, when the unit train is lagged behind the EEG. The correlation is linear from maximum firing probability during maximum surface-positivity (hyperpolarization of the excitatory neurons) to zero at maximum surface-negativity. The cpdf for spontaneous excitatory neuron firing is maximally correlated with EEG amplitude at zero lag. Higher probabilities of firing are associated with depolarizing currents (surface-negativity), but the relationship is nonlinear. The cpdf for inhibitory units represents the input-output relation for pulse-to-wave transduction, whereas that for excitatory units represents the input-output relation for wave-to-pulse transduction. USPHS, NIMH06686.

WATER AND ELECTROLYTE EXCHANGE IN RATS EXPOSED TO COLD. Melvin J. Fregly. Dept. Physiol., Univ. Florida, College Medicine, Gainesville, Fla.

Twelve male Carworth rats weighing from 210 to 230 g were kept individually in metabolism cages in a thermoregulated (26° C.) room illuminated from 8 AM to 6 PM. During a 7 day control period, distilled water and food intakes as well as urine and fecal outputs were measured daily. At the end of the control period, 6 rats were exposed to cold (6° C.) for 10 days while 6 remained at 26° C. All rats were then kept at 26° C. for an additional 7 days. Urines were analyzed for sodium, potassium, chloride and osmolality. Feces were analyzed for sodium and potassium content. Comparison of water with food intake revealed a smaller water intake for a given food intake for cold-exposed than for control rats. The urine output at a given water intake was also greater for cold-exposed rats. These results suggest possible mechanisms for both the relative dehydration and increased plasma osmolality observed during cold in earlier studies (Canad. J. Physiol. Pharmacol. 44:651, 1966) and the "thirst" observed after removal of rats from cold air. Both fecal and urinary routes of sodium and potassium excretion were increased by cold exposure; however, fecal excretions of both potassium and sodium were greater fractions of the total output during cold exposure than prior to it. Although cold exposure in rats tends to induce a relative dehydration, an important factor limiting the extent of the dehydration may be increased fecal electrolyte loss. (Supported by Contract DA-49-193-MD-2549 with the Office of the Surgeon General).

COMPARATIVE CARDIOVASCULAR EFFECTS OF STOMACH DISTENTION AND WALL STRETCH. Jerome J. Freundlich* and M. H. F. Friedman. Dept. of Physiology, Jefferson Medical College of Philadelphia.

Distention of the stomach by overloading with food is known to lead to untoward effects on the heart and circulation but the mechanisms are not understood. Cardiovascular effects of gastric distention were studied in 26 dogs. Two methods of increasing stomach wall tension were compared. Inflation of a gastric balloon to pressures ranging from 10 to 25 mm Hg resulted in 80 per cent of the experiments in systemic arterial hypotension and bradycardia. Biphasic sequential effects were occasionally noted at the higher inflation pressures. The hypotensive effects of balloon distention were greater following vagectomy. A stretch force of 0.5 to 0.75 kg applied externally to the stomach wall to produce increases in stomach length of 0.5 to 2.0 cm always resulted in hypertension and usually in tachycardia. Effects of antrum stretch were more pronounced than those of corpus stretch. Afferent nerve fibers which mediate the hypertensive effects of stretching the antrum apparently occur in both vagus and sympathetics but those mediating the effects from the corpus appear confined to sympathetic routes. The cardiovascular effects were not due to simple physical redistribution of blood from the splanchnic area. No evidence for a humoral mechanism was found. The data are consistent with the view that baroreceptor sites for vasomotor depressor responses are distributed in the stomach at mucosal-submucosal levels, but not within the gastric musculature. This may comprise a homeostatic mechanism of clinical significance.

TRANSCAPILLARY EXCHANGE OF Rb-86 IN SKELETAL MUSCLE. J. J. Friedman. Indiana Univ. School of Med., Indianapolis, Ind.

The transcapillary exchange of a diffusible test, indicator (Rb-86) relative to a vascular reference indicator (Fe-59-Siderophillin) was determined in the isolated, autologous blood perfused dog gracilis muscle. Both indicators were simultaneously injected intraarterially and the venous indicator dilution curves obtained. The Rb curve differed from the reference curve by being consistently below it. This difference which represents extraction is more dramatically seen by examination of the ratio of test to reference indicators at each interval. A ratio of 0.00 would represent complete extraction of the test indicator, whereas a ratio of 1.0 would signify zero extraction. Intermediate ratios reflect fractional extractions. The resulting ratio curve is multiphasic signifying heterogeneity of extractability of muscle circulation; a heterogeneity which consists of a highly extracting circuit as well as an early, and a late, low extracting circuit. The level and form of the ratio curve is sensitive to blood flow. At elevated flows (8-10 ml/min/100gm) the initial samples exhibit a ratio of about 0.6 which decreases slightly to about 0.5 and then increases progressively to a ratio greater than 1.0, signifying back diffusion. At low flows (1.3 ml/min/100gm) the initial ratio is about 0.3 which decreased to a minimum of 0.15, then rises to a maximum of about 0.5 and then declines once more. Reactive hyperemia following arterial occlusion of 4 minutes duration, applied at various blood flows, changes the ratio pattern toward that of reduced blood flow. The data suggest that reduced flow or reactive hyperemia produce both an increase in exchange flow as well as an increased heterogeneity of blood flow distribution.

POSTURAL EFFECTS UPON DEGLUTITION. M. H. F. Friedman, L. Pierce,* R. Mackowiak,* H. Brenman and J. Breckenridge.* Dept. of Physiology, Jefferson Medical College, Philadelphia, Pa.

Previous work in this laboratory demonstrated that production of discrete acoustic bursts correlated with the process of deglutition. The present experiments investigated the effects of postural alterations upon these events. Studies were conducted on human adults with no evidence of bucco-pharyngeal or systemic disease. Swallowing sounds were detected with a miniature contact microphone placed on the neck lateral to the larynx. Arrival of the swallowed material at the cardio-esophageal junction was signaled by another microphone placed to the left of the xiphoid process. Heart sounds were eliminated by selective band pass filtration. Respiration was monitored with a special nasal thermistor. Rate and contour of peripheral pulse was detected with a digital photoelectric plethysmograph. Multichannel tape recordings were made of all variables for subsequent time expansion analysis. Position of the subject was altered with a tilt table. Swallows of tap water generally produced three discrete acoustic bursts. There was a progressive increase in the total duration of the sound profile as the subject was tilted from the upright to the head-down position. The average duration of the sound was 330 msec. in the upright position, 500 msec. in the horizontal position and 720 msec. in the inverted position. No portion of the acoustic profile obtained from the neck microphone reflected activity in the area of the cardio-esophageal sphincter. In all positions deglutition was initiated least frequently during inspiration.

LONG-TERM VARIATION OF CARDIAC OUTPUT IN NORMOTENSIVE AND HYPERTENSIVE MAN. Edward D. Frohlich, Robert C. Tarazi*, Milos Ilrych*, and Harriet P. Dustan*. Research Div., Cleveland Clinic, Cleveland, Ohio.

Although measurement of normal resting cardiac output varies little from one laboratory to another, information is meager concerning repeated determinations in the same individual, nor has this been documented in diastolic hypertension. Thus, repeated measurements of output (indocyanine green dye) were made 76 times in 6 normotensive and 24 hypertensive (14 essential, 6 renovascular, 2 renal parenchymal, 2 hyperaldosteronism) individuals. All patients had not taken antihypertensive drugs for at least one month and none had cardiac decompensation. Consecutive output measurements at one session varied by 7%; after 13 months (average; range: 1-37 months) variation was not significantly different (12%), and no more variable than mean arterial pressure (10%). Average cardiac indices were: normotensives 3.1 L./min./M.^{2}, essential and renovascular hypertensives, 2.6 and 3.2 L/min./M.^{2}, respectively. Thus, after as long as 37 months, cardiac output remained constant and significantly higher in renovascular than essential hypertension ($p < .001$). Moreover, variation in output was no greater than mean arterial pressure.

THE ROLE OF SH GROUPS IN CALCIUM CONTROL OF ACTOMYOSIN CONTRACTILITY. F. Fuchs*, B. Yasui*, and F. N. Briggs. Dept. Physiology, Univ. Pittsburgh, Sch. Medicine, Pittsburgh, Pa.

According to Ebashi a tropomyosin-troponin complex confers Ca sensitivity on actomyosin. The presence of SH groups is essential for this effect (Mueller, Biochem. Z. 345:300, 1966). To localize essential SH groups tropomyosin and troponin were prepared and reacted with $_{p}$CMB or NEM. Neither SH-tropomyosin nor SH-troponin alone had Ca sensitizing activity. A mixture of $_{p}$CMB-tropomyosin and SH-troponin had activity whereas a mixture of SH-tropomyosin and $_{p}$CMB-troponin had little activity. NEM treated proteins behaved similarly. We have shown that Ca ions which activate myofibrillar contraction bind to troponin (Fuchs and Briggs, Fed. Proc. 26:598, 1967). $_{p}$CMB and NEM had little influence on Ca binding to troponin. The data suggest that SH groups of troponin are essential for Ca activation but not Ca binding. (Supported by NIH grants HE-06782 and AM-10051).

THE ENDOGENOUS PRODUCTION OF THIOCYANATE, Cullie F. Funderburk* and L. Van Middlesworth, University of Tennessee Medical Units, Dept. of Physiology & Biophysics, Memphis, Tennessee.

To determine what portion of the thiocyanate normally present in plasma arises from endogenous metabolism and what portion arises exogenously from the diet, an experiment was designed to measure, during feeding and fasting, the rate of dilution of the specific activity of plasma thiocyanate after a single injection of 200 μg $S^{35}CN$ (14.6 μc). Eight 340-365 gram male albino rats were housed in individual metabolism cages and fed Purina Laboratory Chow; urine was collected daily, and frequent plasma samples were obtained. The rats were fasted for four days during the 17-day experiment. Chemical thiocyanate concentrations were measured by the method of Boxer and Rickards and radioactivity concentrations were measured using liquid scintillation. Chromatograms of plasma showed no appreciable changes in the chemical nature of the plasma $S^{35}CN$.

During the control periods, the rats excreted 100-125 μg SCN/day in the urine, and the plasma concentration of thiocyanate ranged around 600 μg/100 ml. The specific activity of plasma thiocyanate was diluted to one-half in 2.6 days, indicating a daily production of 350 μg SCN (assuming a SCN space of 40% of body weight). During fasting, the urinary excretion of thiocyanate decreased to one-half control values and the plasma concentration of thiocyanate rose to 800 μg/100 ml. The production of thiocyanate was decreased to 230 μg/day during the third and fourth day of fasting.

These data indicate that at least two-thirds the thiocyanate present in plasma arose from endogenous sources. The rise in the plasma thiocyanate concentration during fasting resulted from a continued, but decreased, production of thiocyanate, and from a decreased excretion of thiocyanate in the urine.

Red Cell Volume Regulation in Chronic Pulmonary Insufficiency with Hypoxemia and Hypercarbia. M. Galdston, J.H. Schwartz* and M.K. Ang*. New York University Medical Center, New York City.

Studies were carried out to investigate whether macrocytosis in patients with chronic pulmonary insufficiency is due to the adaptation of normocytic cells to a low O_2-high CO_2 environment. Washed red cells were suspended in a buffered Ringer's solution (Hct-1.5%) supplemented with glucose, adenosine, human serum albumin, streptomycin and penicillin and incubated at 37 C in a low pO_2 (60 mm Hg)-high pCO_2 (65 mm Hg), pH 7.25-7.21 environment and also in a normal pO_2 (100 mm Hg)-pCO_2 (40 mm Hg), pH 7.35-7.42 environment. Blood gas, pH measurements and cultures established the stability of the incubation medium which was changed at intervals of 6 up to 46 hours. Aliquots of cells were removed from both the normal and abnormal incubation environments at intervals of a few to 46 hours and suspended in tris-phosphate buffer (pH 7.42, isosmolar with the incubation medium) for measurements of cell counts, mean corpuscular volume (MCV) and cell size distribution curves, using a model B Coulter counter. In 7 patients with chronic pulmonary insufficiency (average MCV 100μ^3, range 98-104μ^3) and in 9 normals (average MCV 89μ^3, range 82-94μ^3), MCV and cell size distribution curves remained stable ($\pm$3 to 4% of control), with the curves of the macrocytic cells shifted to the right, and cell counts usually more than 90% of control (10,000-18,000/ml) for 48 to 72 hours, occasionally for 96 to 120 hours. Thereafter, MCV rose abruptly and cell counts generally fell below 80% of control. We conclude: macrocytic red cells of patients with chronic pulmonary insufficiency are natively large and not due to altered cell volume regulation of normocytic cells in a low O_2-high CO_2 environment. Supported by NIH Grant HE 09668-03.

INFORMATION TRANSMISSION AND AUDITORY EVOKED POTENTIALS. Martin F. Gardiner*, Dept. of Biophysics, Donald O. Walter, Dept. of Anatomy and Brain Research Institute, and George Moore, Dept. of Physiology and Brain Research Institute, University of California, Los Angeles.

An investigation of the transient changes in the human EEG evoked by sensory stimuli which carry information in forced decision tasks has shown consistent effects as the subject's attention is directed to different stimulus parameters by different decision tasks. Four gated sine-wave stimuli (loud-low pitched, loud-high pitched, soft-low pitched, soft-high pitched) are presented in random order over an earphone to the right ear of each subject. In some parts of the experiment the subject must report the pitch of each stimulus, while attempting to avoid distraction from loudness changes; in other parts of the experiment the same stimuli are presented again, with the subject reporting loudness and attempting to avoid distraction from pitch changes. EEG samples commencing with each stimulus are digitized and analyzed by inspection of averages (evoked potentials) for various stimulus and response conditions and by means of adaptive statistical classification techniques applied both to averaged and unaveraged data. The subject group is composed primarily of music students with highly developed auditory abilities, and the discriminations required during the experiments are made difficult to assure a high degree of concentration. Results are consistent with recent indications that EEG recordable from human scalp can contain components which are sensitively related to complex decision processes and suggest the possibility of parameter specific components which fluctuate in strength as a function of a subject's focus of attention. (Supported by Biophysics Training Grant USPHS 3-T1-GM-796-04S1 and Mental Health Training Grant USPHS 3-T1-MH-6415-10).

HEAT-INDUCED HYPERVENTILATION AND TETANY. Ralph Gaudio, Jr.* and Abbott T. Kissen. Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio.

The ability of heat to induce hyperventilation and tetany is well known. In order to precisely define the relation between heat, hyperventilation and tetany, 10 normal human volunteers were studied, sitting and at rest, in a 54.4°C - 49 mm Hg vapor pressure environment to tolerance (30-50 minutes). Study in a 26.7°F - 10 mm Hg vapor pressure or control environment for a duration equal to tolerance time at the higher temperature was carried out in a separate session. Minute volume (VE), respiratory rate (F), heart rate (HR), rectal (TR), skin (TS), body temperature (TB) were continuously determined. Venous blood was drawn before and after exposure for pH, pCO2, pO2 and lactic acid. Tidal volume (TV) was calculated using VE and F. Tetany was classed as either spontaneous or provocative with the occlusive cuff test. Mean HR rose 71 beats/min and mean TR rose 1.33°C during heat stress. Mean VE and TV rose significantly ($p < .05$) during heat stress, VE rising to a maximum of 4.8 L/M over control values at 80% of tolerance time. Mean (F) rose significantly ($p < .05$) only at 80% of tolerance and in the post-exposure period when it increased from 14 to 18 breaths/min. Mean pCO2 fell significantly ($p < .05$) from 44 to 33 mm Hg, mean pH rose from 7.38 to 7.46, mean lactic acid rose from 10 to 14 mg%. Two of the 10 subjects developed tetany but their VE, pH, pCO2 and lactic acid values did not differ significantly from those who did not. It is demonstrated that HV, resulting primarily from hypernea, is an invariable consequence of heat stress. The occurrence of tachypnea in the post-exposure period may well be an attempt at heat dissipation. Lactic acid rises during heat stress are probably related to HV.

THE HANDLING OF ADH BY THE KIDNEY OF THE ALCOHOL ANESTHETIZED RAT. O.H. Gauer and P.S. Tata*. Physiologisches Institut der Freien Universität Berlin.

1. In our modification of Jeffer's bioassay for ADH (Pflügers Arch. 290: 286, 1966) the volume of extra water reabsorbed (urine deficit UD) is related to the dose (0.2 - 20μU) of a single i.v. injection of Pitressin. The dose response curve apparently describes a saturation process. There is a linear relationship up to 1μU. At higher dosages the curve levels off. In the linear range 1μU ADH affords reabsorption of 4 - 5 ml water.
2. With an experimentally induced increase of control urine flow the duration of the antidiuretic period is reduced in such a way that the UD (cm^3) remains unchanged for a given dose.
3. When 5 - 6μU are injected 75% of the antidiuretic activity (ADA) is recovered from urine of the antidiuretic phase. With injection of 20μU 95% of the ADA are excreted in the urine. In the latter case determination of the time course of ADA excretion was possible. It followed an exponential curve (half life 5 minutes).

These observations are compatible with the following concept: Upon a single injection of ADH one μU suffices to react presumably with the proteins at tubular pore sites to open all available pores. The reversal of this process (closure of pores) is governed by the rate of water reabsorption. Vasopressin in excess of 1μU is excreted rapidly in the urine.

THE MECHANICS OF LEFT VENTRICULAR CONTRACTION IN MYOCARDIAL AND VALVULAR HEART DISEASE. James H. Gault*, John Ross, Jr., James W. Covell*, and Eugene Braunwald. Cardiology Branch, Nat'l Heart Inst., Bethesda, Md.

The mechanics of left ventricular (LV) myocardial contraction were examined in patients having no left heart disease, LV myocardial disease alone, or free aortic regurgitation (AI). The instantaneous velocity of fiber shortening (V_{CF}) was determined from high speed cineangiograms, and LV myocardial wall tension (LVT) was computed from LV radius and the simultaneously recorded LV pressure (Statham SF-1 micromanometer). In 7 patients without left heart disease, LVT reached a maximum level (T_{max}) soon after the onset of ejection, then declined rapidly while V_{CF} was sustained at high levels. In this group, maximum V_{CF} occurred after T_{max} and averaged 2.46 circumferences (circ)/sec; V_{CF} at T_{max} averaged 1.80 circ/sec. In 9 patients with myocardial disease alone, LVT reached a maximum level well after the onset of ejection, then declined slowly. Maximum V_{CF} occurred at or before T_{max}, averaging 0.76 circ/sec, and V_{CF} then fell while LVT remained at high levels. V_{CF} at T_{max} averaged 0.64 circ/sec. In 4 patients with AI, maximum V_{CF} and V_{CF}-T_{max} relations were markedly depressed (avg 0.63 circ/sec and 0.38 circ/sec, respectively). In these patients, maximum V_{CF} occurred early during ejection, well before T_{max}, and then declined as LVT increased. Of 6 additional patients with AI in whom LV end-diastolic pressures and cardiac indices were normal, 2 had normal tension-velocity relations while 4 exhibited slightly abnormal maximum V_{CF} and V_{CF}-T_{max} relations (avg 1.76 circ/sec and 1.10 circ/sec); however, in each of these patients high levels of V_{CF} were sustained throughout ejection and V_{CF} reached a maximum level after T_{max}. These findings indicate that distinctive abnormalities in the mechanics of LV contraction exist in patients with LV myocardial disease and that such abnormalities can be detected in the presence of valvular cardiac defects.

EFFECT OF CHANGES IN RENAL BLOOD OSMOLARITY ON RENAL VASCULAR RESISTANCE. S. Gazitua*, J.B. Scott and F.J. Haddy. Dept. of Physiol., Michigan State University, East Lansing, Michigan

The effects of 3 min. intra-arterial infusion of hypo, hyper and isosmotic solutions of NaCl, glucose and urea on renal perfusion pressure (P_{ra}) and renal vein osmolality (O_{rv}) were studied in the in situ dog kidney perfused at constant flow.

Solution	mO_{sm}/L	No. Exp.	P_{ra} mm Hg C	1	3	PI	C	O_{rv} mO_{sm}/L C	3	C	F ml/min	IR
NaCl	(300)	17	77	73*	76	80	79	303	302	300	128	5.1
	(1500)	17	77	63*	77	157*	74	301	344*	301	128	5.1
	(150)	8	73	65*	133*	159*	73	305	261*	300	112	29.3
Glucose	(300)	17	78	70*	71*	76	75	300	301	301	128	5.1
	(1500)	17	73	61*	65*	76	71	302	343*	304	128	5.1
	(150)	8	68	61*	129**	135**	68	300	260*	296	112	29.3
Urea	(300)	17	76	74	101**	113*	79	299	300	300	128	5.1
	(1500)	17	73	63*	79**	199*	73	303	343*	301	128	5.1
	(150)	8	68	62*	219*	219*	68	292	261*	292	112	29.3

*$p < 0.01$, **$p < 0.05$ when compared with the first control. IR=infusion rate of the solution; F=renal blood flow rate; C=control; 1=1st min. of infusion; 3=3rd min. of infusion; PI=immediately following infusion.

All solutions except isosmotic urea initially reduced renal vascular resistance (R_r). During the infusion the fall in R_r was maintained with hyper and isosmotic glucose, disappeared with isotonic and hypertonic NaCl and was replaced by a rise in R_r above control with the hyposmotic solutions. Dramatic increases in R_r were seen shortly after stopping the infusion of hyperosmotic NaCl and urea. Thus, changes in R_r seem to depend more on the agent than the osmolarity, except in the case of hyposmolarity.

SODIUM AND CALCIUM DEPENDENCY OF ACTION POTENTIAL OF AN APLYSIA NEURON. Donald Geduldig and Douglas Junge (intr. by T. H. Bullock).

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Substantial overshoot potentials can be obtained in solutions which are free of either Na or Ca ions substituted with tris or with sucrose. However, when both the normal Na and Ca are fully replaced with their equivalents of tris or sucrose, the giant cell soma of the visceral ganglion (with direct stimulation) is unable to produce any action potentials. Transmembrane potentials were measured and stimulating current pulses were applied by means of 3 M KCl-filled intracellular microelectrodes and sea-water-agar/AgCl electrodes in the bath. In Ca-free solutions (tris-substituted) the overshoot potential decreased with decreasing Na_o with a slope close to 58 mV / decade of Na_o. In Na-free solutions (tris-substituted) the overshoot potential decreased with decreasing Ca_o with a slope close to 29 mV / decade of Ca_o. (The extrapolated values of Ca_o and Na_o to give a zero-overshoot potential were about 3 mM and 90 mM respectively.) This strong agreement with the Nernst equation suggests that the membrane of this cell is selectively permeable to both Na and Ca during the time of the action potential, and that both ions play a part in the production of action potentials in the normal milieu.

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THE DENDRITIC TREE OF SPINAL NEURONS IN DOGS WITH EXPERIMENTAL HIND-LIMB RIGIDITY. Samuel Gelfan and Grace Kao.* New York Medical College, New York City.

About 25% of the normal neuron population at lumbosacral levels survives the temporary lumbosacral ischemia which produces the extensor rigidity of the hind limbs. The size of the dendritic tree of such spinal neurons in chronic preparations has been found to be considerably smaller than that of neurons at the same levels in normal dogs. Determinations on the size of the dendrite tree were carried out on all neurons observable in 150 μ thick transverse sections of spinal cords prepared by the Golgi-Kopsch technique. The mean number of primary dendrites per neuron in the unselected samples is only slightly smaller in the rigid animals. But the mean length of primary dendrites is reduced to some 65% of normal; the number of dendrite branches per neuron to 45%; the length of such branches to 40%; the longest uninterrupted extension from perikaryon in each neuron to 42%; the sum of the lengths of all dendrites per neuron is reduced to 33%. The changes, observed in both dorsal and ventral horn neurons, are most pronounced at the distal portions of the dendrite tree. The modifications of the relations between size of cell body and its dendrite number and lengths in the rigid animals merely reflect the reductions of dendrite number and lengths. The "atrophy", the reduction of total dendritic surface compounds the effect of the already demonstrated marked reduction of synaptic density in rigid preparations. This morphological evidence of altered lumbosacral neurons in such preparations parallels the electrophysiological evidence of altered postsynaptic characteristics.
(Supported by N I H grant NB 04417)

HISTAMINE INDUCED REDUCTION OF THE RENAL VASCULAR RESPONSE TO ANGIOTENSIN AND NOREPINEPHRINE. Ronald G. Geller* and J. E. Kendrick. Dept. of Physiology, University of Wisconsin, Madison, Wisconsin.

In an earlier paper (Circ. Res. 20:321, 1967) we reported that raising mean carotid sinus pressure in the dog from about 30 to about 200 mm Hg reduced the vasoconstrictor responses to angiotensin and norepinephrine in the perfused renal vascular bed. It was suggested that some substance was released when carotid sinus pressure was raised which reduced the sensitivity of this vascular bed to these agents. The experiments to be reported provide evidence that histamine release during carotid sinus stimulation may have been involved in our earlier results. In 6 dogs anesthetized with morphine-chloralose the innervated kidneys were perfused at a constant rate of flow. Histamine (10-50 γ/min) infused into the kidneys reduced the renal pressor response to angiotensin by 48% and to norepinephrine by 43%. Histamine at this rate had little or no effect on renal perfusion pressure. A histamine releasing agent, 48/80, produced an equal or greater reduction in the renal pressor response to these agents. A histamine blocking agent (tripelenamine) increased the sensitivity of renal vascular bed to angiotensin and norepinephrine and blocked reducing effect of infused histamine upon the pressor responses. Atropine also blocked the effect of histamine in this respect. In 5 other experiments, raising carotid sinus pressure reduced the average vasoconstrictor response to angiotensin and norepinephrine 70% and 63% respectively. Following tripelenamine only a 25% and 17% reduction in the responses was observed during carotid sinus stimulation. It is suggested that raising carotid sinus pressure causes the release of a substance which has an action similar to histamine, this substance in turn alters the responsiveness of the renal vascular bed to angiotensin and norepinephrine. (Support: USPHS HE04098, 5-T1-5540 and Wis. Heart Assoc.)

DISC GEL ELECTROPHORESIS PATTERNS OF SERUM ALKALINE PHOSPHATASE. John E. Gerich,* Gerald Morrow,* and J. V. Princiotto. Dept. of Physiology and Biophysics, Georgetown University Schools of Medicine and Dentistry, Washington, D. C.

Serum alkaline phosphatase represents a group of isoenzymes each of which may arise from a single organ. Several disease states such as ricketts and biliary obstruction have been correlated to some extent with alterations in individual fractions. Normal serum protein and alkaline phosphatase isoenzyme electrophoretic patterns were prepared using the method developed by Ornstein and Davis. Acrylamide gels were employed with a tris (hydroxymethyl) amino-methane buffer pH 9.5. Electrophoresis was carried out at 10 degrees C. using 3.5 milliamps per column. The gels were stained either for protein using amido-black or for enzyme activity using the Gomori lead conversion method. At present time, six enzyme bands have been noted in normal serum. This activity appears to be associated with bands corresponding to slow beta globulin, slow alpha globulin, haptoglobin 0.66, post-transferrin, transferrin and pre-transferrin. As many as nine fractions have been reported; however, no more than five in any one serum and no more than three in normal serum previous to our work. We are now attempting to correlate these six fractions with alkaline phosphatases extracted from various organs.

LESIONS BLOCKING ACTH SECRETION IN RESPONSE TO A NEURAL STRESS IN THE RAT. F.P. Gibbs (intr. by J.M. Brookhart), Department of Physiology, University of Oregon Medical School, Portland, Oregon.

Radio-frequency lesions approximately 1.5 mm in diameter were placed in the brains of 130-170 gm. female Sprague-Dawley rats. Twelve hours to sixty days later the rats were tested for their ability to respond to a tibial fracture with ACTH secretion. Thirty to forty-five minutes after injection of pentobarbital (3.5 - 4.5 mg/100 gm) their tibias were broken. Twenty minutes later the rats were decapitated and exsanguinated. Fluorescence in sulfuric acid and ethanol was used to measure plasma corticosterone as an indirect index of ACTH secretion. Unilateral lesions in the midbrain reticular formation two millimeters from the midline were found to depress the response to bilateral tibial fracture for up to twenty days. After periods longer than thirty days, unilateral midbrain lesions blocked only the response to contralateral tibial fracture.

The data imply that the unilateral midbrain lesion: 1) occupied a zone important for the facilitation of the stress-induced ACTH release under pentobarbital, and 2) interrupted a pathway essential for the response to contralateral tibial fracture. The facilitatory function could apparently be taken over by another area since the response to bilateral tibial fracture began to recover by twenty days and was 75% of control in thirty days. The discrete pathway from the contralateral leg apparently could not be rerouted, since the response to contralateral tibial fracture had not recovered at sixty days.
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RENAL TUBULAR TRANSPORT OF PHOSPHATE AND P^{32} EXCHANGE IN THE DOG. Jack M. Ginsburg, Univ. of Rochester School of Medicine, Rochester, N. Y.

Adenine nucleotides have been implicated as carriers in phosphate transport in some cells but their role in renal tubular reabsorption remains unresolved. Tubular transport of phosphate and renal accumulation of intra-arterially or intravenously infused P^{32} was determined. Urine, arterial and renal venous plasma radioactivity was measured during the infusion period. The distribution of P^{32} in acid soluble phosphate was measured by ion exchange chromatography of extracts of kidneys frozen in liquid N_2. The arteriovenous specific activity difference showed a rapid decrease in the first 50 to 70 seconds followed by a much slower decline. Calculation of the volume of distribution suggests that the rapid phase of renal P^{32} accumulation is a transcapillary event and that the slower phase represents mixing of P^{32} into intracellular phosphate pools. In 2.5 minutes 15 to 20% of the infused P^{32} was retained in the kidney, and 76% of this was present as barium insoluble phosphate. 85 to 90% of the barium insoluble P^{32} was present as inorganic orthophosphate and 7% as ADP and ATP. Less than 1 to 2% of the infused P^{32} was present in the combined sugar phosphate, phospholipid and phospho-protein fractions. The early labelling of the adenine nucleotides suggests a possible role of these compounds in tubular reabsorption of phosphate.

DIFFERENCES IN THE EFFECTS OF NICOTINE AND SUCCINYLCHOLINE ON THE MONOSYNAPTIC REFLEX. K. H. Ginzel*, Earl Eldred and Y. Sasaki*
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In cats anesthetized with pentobarbital or chloralose-urethane, a monosynaptic reflex (MSR) was elicited in the S_1 ventral root (VR) by stimulation of the cut left medial and lateral gastrocnemius nerves. Gamma unit activity was monitored from a filament of the same or an adjacent root. Unit or integrated spindle afferent activity originating from the gastrocnemius of the otherwise denervated right leg was recorded from the S_1 dorsal root. Depression of the MSR by iv succinylcholine (SCh) was always associated with enhanced spindle afferent activity. Nicotine, in doses of 20-40 μg/kg iv produced a just maximal block of the MSR without concomitant increase in spindle afferent discharge. Doses of 40-80 μg/kg first increased, then decreased gamma and spindle afferent activity. Ipsilateral section of L_6-S_2 VRs abolished these changes in afferent activity. Subsequently, 80-160 μg/kg of nicotine were needed to increase the firing of the de-efferented spindle organs. The accelerating effect of SCh on spindle discharge was unaffected by VR section. Gallamine abolished the SCh-induced increase in spindle afferent activity and MSR depression without altering the MSR blocking effect of nicotine. Mecamylamine, which inhibits the nicotinic cholinergic synapse at the Renshaw cell (Ueki, Koketsu & Domino,Exper.Neurol. 3:141,1961), abolished the MSR block produced by nicotine without affecting the MSR depression produced by SCh. Similar results were obtained in unanesthetized spinal preparations. Ipsi- or bilateral deafferentation from L_4 to S_2 abolished the MSR blocking effect of SCh, but preserved that of nicotine, although the duration of the latter was reduced. These findings provide further evidence that nicotine and SCh depress the monosynaptic reflex by different mechanisms.

SKELETAL MUSCLE METABOLISM IN DIBENZYLINE-TREATED DOGS IN HEMORRHAGIC SHOCK. V.V. Glaviano and M. Guerrero*. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

In anesthetized dogs, hemorrhagic shock was induced by bleeding to a pressure of 40 mm Hg which subsequently was maintained with an elevated blood reservoir for 4 hours. In two groups of experiments, arterial blood samples were analyzed for lactate, pyruvate, glucose, and FFA during a control period and after 3 and 4 hours of hypotension. In the control and hypotensive periods, skeletal muscle samples were excised from the forelimb and analyzed for glycogen, lactate, pyruvate and FFA. Dogs in Group I, untreated hemorrhagic shock, were compared to dogs in Group II, hemorrhagic shock treated with 2 mg/kg of dibenzyline after 3 hours of hypotension. In the untreated dogs, arterial lactate, pyruvate, glucose and FFA rose on the average of 600, 80, 30 and 20% respectively; skeletal muscle glycogen decreased by 10%, while pyruvate, lactate and FFA rose to 150, 180 and 20% above control respectively. In the treated dogs after 4 hours of hypotension, arterial lactate, pyruvate and glucose declined to an average of 11, 3 and 27% of the levels found after 3 hours of hypotension. FFA during this period rose to 15%. In skeletal muscle, lactate increased by 29%, while glycogen decreased by 20%. Although skeletal muscle blood flow in the hind limbs increased in shocked dogs treated with dibenzyline, the decrease encountered in metabolic substrates in arterial blood was found to be due to the uptake of blood from the reservoir rather than reflecting an improvement in tissue metabolism, since levels of FFA, lactate and pyruvate in skeletal muscle were not significantly different from muscle analyzed in the untreated dogs subjected to the same period of hemorrhagic hypotension. (Supported by ONR Contract 3502-01 and NIH HE 08682.)

MECHANISMS OF REFLEX VASODILATION: ASSESSMENT OF THE ROLE OF NEURAL REUPTAKE OF NOREPINEPHRINE AND RELEASE OF HISTAMINE. Gerald Glick, Andrew S. Wechsler* and Stephen E. Epstein*. Natl. Heart Inst., Bethesda, Md.

The mechanisms responsible for reflex vasodilation have been a source of controversy for many years. Recently, since vasodilation could largely be blocked by certain antihistamines, it has been attributed to the active release of histamine. Accordingly, the mechanisms of reflex vasodilation were studied in 28 innervated canine hindlimb preparations which were perfused at a constant flow rate and in which vasodilation was produced by suddenly increasing systemic pressure by the intravenous injection of norepinephrine. When the basal adrenergic tone exerted by the sympathetic nervous system on the systemic arterial bed was minimized, either by pretreatment with phenoxybenzamine, or with reserpine, reflex vasodilation was virtually abolished. Acute administration of cocaine, a drug which blocks reuptake of norepinephrine by the nerve terminals, significantly reduced reflex vasodilation, the response after cocaine averaging 47 (± SEM 1.4%) of the vasodilator response in the control period. Cocaine also potentiated the vasoconstriction caused by intra-arterially administered norepinephrine but attenuated the vasoconstriction induced by tyramine. The antihistamine, tripelennamine, had effects similar to those of cocaine. It is suggested, therefore, that reflex vasodilation results from a sudden decrease in the level of norepinephrine at the neuroeffector junction which is a consequence of the cessation of norepinephrine secretion, together with continued and possibly augmented uptake. When the uptake mechanism is impaired, either by the administration of cocaine or tripelennamine, the magnitude of reflex vasodilation is diminished. In conclusion, it does not appear necessary to postulate active secretion of a vasodilator substance to account for reflex vasodilation.

ENERGY EXPENDITURE OF NEGEV RESIDENTS DURING EXERCISE IN THE SUMMER AND WINTER. Armand J. Gold, Abraham Zornitzer* and Shlomo Samueloff*. Dept. of Environmental Physiology, Negev Institute for Arid Zone Research, Beersheva and Dept. of Physiology, Hadassah Medical School, Jerusalem, Israel.

The influence of season on the energy expenditure of residents of the Negev was examined at several levels of physical activity and experimental ambient temperatures. The Negev region of Israel, constituting the southern half of the country, has a semi-desert climate. Experiments were carried out on 17 male subjects (age range: 22-39) during August (mean t_{max}: 34°C; mean t_{min}: 18°C) and during January and February (mean t_{max}: 16°C; mean t_{min}: 5°C). Each subject was exposed in an environmental room to consecutive 30 min periods of (I) sitting-reading, (II) ascending and descending a 13 cm step 20 times/min and (III) ascending and descending a 26 cm step 20 times/min under the following conditions: (1) summer, 25°C; (2) summer, 40°C; (3) winter, 25°C; and (4) winter, 40°C. Results are summarized:

Conditions	Oxygen Consumption ($ml/m^2/min$)			Heart Rate (beats/min)		
	I	II	III	I	II	III
Summer, 25°C	158	431	652	66	89	110
Summer. 40°C	173	457	694	82	104	132
Winter, 25°C	166	465	712	69	98	123
Winter, 40°C	170	467	707	88	118	154

It is evident that oxygen demands were slightly, but consistently greater in the summer, 40°C and both winter series than in the summer, 25°C series at all levels of activity. Increases in heart rate were more exaggerated.

Rapid Decompression of Mice Breathing Fluorocarbon Liquid at 500 PSI

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In 1670 Robert Boyle noted the appearance of a gas bubble in the eye of a decompressed snake. Kylstra showed that mice could survive the breathing of aqueous liquid if its oxygen content were increased by increasing the oxygen pressure in equilibrium with it and suggested that liquid breathing may be a possible means of submarine escape. Clark and Gollan (Science 152:1755, 1966) discovered that certain organic liquids had such a high oxygen solubility that animals could survive breathing these liquids equilibrated with oxygen at normal atmospheric pressure. Hence it is possible to control the oxygen pressure in the lungs independently of the hydrostatic pressure. Mice were immersed in fluorocarbon liquid (FC-75, 3M Comp.) which had been fully oxygenated at atmospheric pressure and placed in a pressure chamber. A gas-impermeable Mylar membrane was used to prevent the entrance into the liquid of any significant amount of the air used for compression. The liquid was stirred to minimize the rebreathing of the exhaled liquid. The chamber was held under 500 lbs per sq. in. pressure for 10 minutes using air from a tank. After decompression which required about 5 seconds, the mouse was removed from the liquid, held head down to drain the fluid from the lungs, and placed in an atmosphere of gaseous oxygen. Twenty such liquid-breathing animals survived while twenty animals subjected to the same compression-decompression cycle in an air atmosphere died on removal from the chamber.

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EFFECT OF HYPOXIA AND GLYCOLYTIC BLOCKADE UPON ALVEOLO-CAPILLARY PERMEABILITY TO ALBUMIN IN THE DOG.

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The effect of hypoxia upon pulmonary capillary permeability was studied. Five isolated perfused canine lungs were tested under normal and hypoxic (pO_2 15 mm. Hg.) conditions. The tracheo-alveolar compartment was filled with Tyrode's solution containing dialyzed I^{131} labeled albumin. Permeability to albumin was computed from the uptake curve of I^{131} in the perfused vascular compartment. Under hypoxia the alveolo-capillary permeability did not increase significantly (from .037 to .043 cm. $min.^{-1} \times 10^{-5}$). In 4 additional experiments 2 mM/l iodoacetate was added to anoxic lungs. A 35 fold increase in permeability occurred. These experiments suggest that the integrity of the alveolo-capillary membrane is maintained at low pO_2 levels by anaerobic metabolism.

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NEURAL ACTIVITY FROM THE ISOLATED, PERFUSED MAMMALIAN EYE. P. Gouras
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Stable retinal responses can be obtained in the isolated, perfused cat eye maintained at 35° C for periods of 10 hours and longer. The technique involves removal of the eye from a cat whose body temperature has been reduced to 20° C, cannulation of the ophthalmic artery, which provides circulation for the entire eye, and subsequent perfusion by gravity of an oxygenated mammalian Ringer's solution containing glucose and dextran. Neural activity is recorded by introducing a fine micropipette electrode into the retina through a small scleral hole. At flow rates of 1-2 ml/min, electroretinogram (ERG), ganglion cell activity and S-potentials can be obtained following light stimulation. Spontaneous ganglion cell discharges are considerably reduced. Action spectra based on the amount of energy in a light pulse required to produce a specific criterion of response at 16 wavelengths extending from 419 to 672 nm have been determined for the former two responses. The overall sensitivity of the ERG is reduced although the spectral sensitivity reflects rod function predominantly. The a-wave of the ERG is of normal amplitude but the b-wave is reduced, being larger than the a-wave only with relatively dim stimuli. Ganglion cell responses also have higher than normal thresholds but the responses remain quite stable, have short latencies, ranging from 10 to 50 msec, and show spectral sensitivities which reflect cone activity. Longer latency rod responses can sometimes be detected at the ganglion cell but they are very weak. Although receptor function and synaptic transmission in both the inner and outer plexiform layers is present, the retina is abnormal and this abnormality involves rod much more than cone function. The defect appears to occur between the a-wave of the ERG and the ganglion cell layer, perhaps at the site of b-wave generation. Faster flow rates appear to reduce this defect.

COMPARATIVE INFLUENCE OF CONTRACTILE STATE AND TENSION DEVELOPMENT ON MYOCARDIAL OXYGEN CONSUMPTION. Thomas P. Graham, Jr.*, James W. Covell*, Edmund H. Sonnenblick, John Ross, Jr., and Eugene Braunwald. Cardiology Branch, National Heart Institute, Bethesda, Md.

Myocardial wall tension and inotropic state have both been demonstrated to affect myocardial oxygen consumption ($M\dot{V}O_2$); however, their relative effects on energy utilization are unknown. In order to compare the O_2 cost of these two variables in the same heart, $M\dot{V}O_2$ was measured in the isovolumically contracting left ventricles (LV) of 11 dogs over a range of peak developed tensions (PDT), but at a level of constant contractility; norepinephrine was then infused (0.76 to 7.6 μg/min) and $M\dot{V}O_2$ redetermined over a range of PDT comparable to those achieved prior to norepinephrine. Since at a given level of PDT series elastic extension was relatively constant, contractile element shortening and work were similar under the two conditions. Contractile element velocity at zero load (V_{max}) was used as the index of the level of inotropic (contractile) state. When PDT was increased from 49.7 ± 5.0 to 80.2 ± 5.7 g/cm^2 (+60%) at a constant V_{max}, $M\dot{V}O_2$ increased from 41.5 ± 2.2 to 49.0 ± 2.4 μl/beat/100 g LV (+18%). When V_{max} was increased from 41.8 ± 2.4 to 54.6 ± 2.9 cm/sec (+31%), at a constant PDT, $M\dot{V}O_2$ increased from 40.7 ± 2.7 to 57.0 ± 3.5 μl/beat/100 g LV (+40%). From multiple regression analysis the relative effects of PDT and V_{max} on the $M\dot{V}O_2$ could be expressed in the form of an equation: $M\dot{V}O_2$ (μl/beat/100gLV) = k + .25 PDT (g/cm^2) + 1.43 V_{max} (cm/sec). It is concluded that the O_2 cost of alterations in contractility is substantial, can be independent of changes in contractile element shortening and work, and is of an order of magnitude similar to that associated with alterations in wall tension.

THE EQUIVALENT STRAP MUSCLE OF THE LEFT VENTRICLE: A MODEL FOR DESCRIBING TOTAL MYOCARDIAL FORCE. Colin Grant*, D.G.Greene, I.L. Bunnell and H.L. Falsetti*. Department of Medicine, State Univ. of New York at Buffalo and Buffalo General Hospital, Buffalo, N.Y.

The left ventricle consists of myocardial fibers, each of which develops a finite tension during systole. In principle, the sum of tensions in all the fibers (total myocardial force) is an important physiological variable which could be used in describing myocardial contractility. The ventricle is treated as a thin-walled sphere made up from a very large number of circular loops of muscle, each of which forms a great circle around the cavity. These fiber loops are arranged randomly in all possible orientations, so that the surface is uniformly covered. It would be desirable in principle to consider the fibers as forming a network, and this more realistic arrangement can be shown to be equivalent to the simpler model formed of great circle fiber loops which is examined here. There are N loops, with tension T in each, so that the total myocardial force is NT. Each loop exerts a total inward force of $2\pi T$ and the sum of inward forces ($2\pi NT$) is equal to outward force from the pressure P, acting on the surface ($4\pi r^2$, where r is radius of the sphere).

$$2\pi NT = 4\pi r^2 P$$
$$NT = 2r^2 P$$

Each fiber loop has length $2\pi r$. If every loop is cut once, the fibers can be straightened out and arranged in parallel, to form a straight strap-shaped muscle $2\pi r$ long, generating a total myocardial force NT equal to $2r^2P$. Data on cavity volume and pressure in ten patients, obtained by one-plane cineangiocardiography, show that the adult human left ventricle is equivalent to a straight strap muscle 22 to 35 cm long initially, which generates a peak force of 3.5 to 9 kg.

RESPONSES TO LEUCOCYTIC PYROGEN (LP) IN HYPERTHERMIC AND HYPOTHALAMUS-HEATED RABBITS: A CHALLENGE TO "RESET" HYPOTHESES OF FEVER. Ronald Grant and Ronald D. Adler*, Stanford Univ., Stanford, Calif.

Unanesthetized rabbits with implanted thermocouples were exposed to hot dry environments (35-42°) to obtain characteristic curves for respiratory rate vs. hypothalamic temperature (RR/HT), then given moderate doses of LP at HT 42-43° and while still exposed to heat. Inhibitions of polypnea occurred, often as intense but usually of less duration than those seen in the same animals when normothermic. The low RR was like that in the non-febrile state at HT <39.5°. Ear vasoconstriction was seen in some animals and HT rose sharply. Other unanesthetized or urethane-anesthetized rabbits had received hypothalamic implants of 4 water-heated thermodes, 5 mm apart and bracketing the thermosensitive area, plus a midline thermocouple. Strong responses of RR and ear temperature were seen when H was heated moderately but neither responded during the chill phase (12-25') of LP fever, even when HT was raised to >46°. Responsiveness returned during defervescense. Similar results were obtained in endotoxin fever. Results are considered in terms of two "reset" hypotheses: (a) pyrogen raises the temperature threshold for activation of hypothalamic thermosensitive elements (TSE) without altering above-threshold sensitivity; (b) pyrogen excites thermally insensitive "set-poi nt" reference elements so that an "error signal" activating heat loss mechanisms is generated only when TSE become strongly activated by hyperthermia; also a "non-reset" viewpoint; (c) pyrogens depress or inhibit either the TSE or the effector neurons through which these operate in a way that is not adequately described as a temperature reset since heating does not reactivate heat loss mechanisms in the chill phase. Hypothesis (c) is favored. (Supported by Grant NB-04007 from NINDB.)

Prostaglandins and the Resistance, Capacitance, and Capillary Filtration Coefficient of the Hind Limb. Robert A. Greenberg, James R. Cant, and Harvey V. Sparks (intr. by John M. Weller). Department of Physiology, University of Michigan, Ann Arbor, Michigan.

The effects of prostaglandins (PG E_1 or $E_{1\ 217}$) on consecutive vascular sections of an isolated canine skin-muscle preparation have been studied. The total venous outflow of the leg and foot was measured from a cannula in the popliteal vein. The limb was enclosed in a water-filled plethysmograph, allowing estimation of vascular capacitance and capillary filtration coefficient (K_F, Mellander's CFC). Close arterial infusion of 0.01 to 0.1μg/min. of PG results in an increased blood flow within 30 seconds. Maximum increase, about two fold, results from an infusion of 10μg/min. A rapid increase in volume of the limb associated with the increased flow is interpreted to be increased vascular capacitance and averaged 0.5ml/100g tissue. Infusion of 0.01μg/min. of PG causes a slightly increased K_F and the maximum effect, a doubling of K_F, occurs with a dose of 1 to 10μg/min. Increased K_F may result from either increased capillary permeability or increased capillary surface area due to decreased precapillary sphincter tone. We believe the predominant effect of short infusions of PG to be a decrease in precapillary sphincter tone. Supporting this contention are: 1) a quick return of K_F to control values following cessation of infusion, 2) an absence of the net filtration usually associated with an increase in capillary permeability, and 3) a quick return of the filtered fluid to the vascular space following a period of net filtration. Supported by USPHS HE 09874.

The Effects of Nicotine upon the Cardiac Action Potential and Contractile State. Greenspan,K., Edmands,R.E.*, Knoebel,S.B.*, Fisch,C. From the Dept. of Med., Indiana Univ. School of Med., and the Krannert Inst. of Cardiology, Marion County General Hospital, Indpls., Ind.

A series of experiments was initiated to determine the effects of nicotine upon the inotropic state and action potential (AP) configuration of canine ventricular myocardium. Initially obtained in the control state, recordings were made of AP and isometric contractile responses at a fixed stimulus rate. Nicotine was then introduced at concentrations varying from 100-1000 μgms/cc. Contractile enhancement, without change in time-to-peak force development, was observed, and most strikingly with the higher concentrations of nicotine. In addition, a characteristic AP change was consistently observed in association with the inotropic enhancement; phase 2 abbreviation was noted, as was phase 3 prolongation with little or no change in total AP duration. A more prominent phase 2 abbreviation was observed with the more striking contractile enhancement produced by higher concentrations of nicotine. Comparable electrophysiological changes in canine Purkinje fibers were also observed, that is, phase 2 attenuation, unattended by any significant change in resting potential (R.P.). Less commonly observed changes included loss of R.P. and overshoot, decreased rate of rise, and development of a "step". The complex, thus altered, closely resembled that customarily recorded from AV nodal fibers. It is suggested, therefore, that both the inotropic response and the AP changes effected by nicotine may be associated with an increase in K+ efflux or membrane permeability to K+. (Supported in part by the Herman C. Krannert Fund, U.S.P.H.S. Grants HE-6308, HTS-5363 and HE-5749, Indiana Heart Association, and the AMA Committee for Research on Tobacco and Health.)

CORRELATION OF EXTRACELLULAR SPIKE POTENTIALS WITH NEURONAL SIZE IN BRAIN NUCLEI. Frances S. Grover* and Jennifer S. Buchwald. Dept. of Physiology and Brain Research Institute, UCLA, Los Angeles, Calif.

Recordings of multiple unit activity from brain nuclei (caudate nucleus, amygdaloid nucleus, medial geniculate body, and nucleus ventralis posterolateralis) have shown that amplitudes of neuronal discharge potentials vary markedly from one area to another. In an attempt to account for these differences, cell size of the neuronal populations surrounding the recording electrode tip have been correlated with the ongoing amplitude characteristic of that site. Ten μ sections were Kluver-stained and sampled every 30 μ through the electrode track. Neuronal measurements (mimimum and maximum diameters) extended 500 μ medially, laterally, and vertically from the electrode tip. Cell data were (1) analysed for homogeneity in the immediate vicinity of the recording tip (125 μ radius) as well as in the general surround (500 μ radius) and (2) correlated for relationship to amplitude recorded from that specific site. At all sites studied, a homogeneous cell population was found within the 125 μ radius of the electrode tip and within the 500 μ radius. A high correlation ($r=.85$) was shown between amplitude and maximum cell diameter. A linear relationship between amplitude and cell size can be stated as an equation from which amplitude can be predicted from cell size (maximum diameter) in a homogeneous population. It is concluded that cell size, while not the sole consideration, is an important factor in determining the amplitude of ongoing spike activity recorded extracellularly from a population of neurons. (Supported in part by USPHS Grant NB-21,935 and NB -05437.)

McARDLE SYNDROME: A STUDY OF A MYOPATHY WITH A SARCOLEMMA-FREE PREPARATION. Raphael P. Gruener* (intr. by B. C. Abbott)

Biopsies were obtained from a patient known to suffer from the McArdle syndrome (1) which relates to a severe deficiency of phosphorylase, pronounced accumulation of glycogen and silent electromyograms. Single fibers were separated under oil, and their sarcolemma partially stripped away permitting investigation of post membrane-excitation phenomena in live fibers. Calcium and caffeine were applied locally through micropipettes. One sample was electrically stimulated in-situ to simulate a state of post-exercise contracture. Control samples were obtained from skeletal muscles of two normal adults. An electrically stimulated mouse leg muscle served as a control for the stimulated biopsy. All samples were stored in oxygenated Krebs solution for 60 min at 19±3c° prior to use. Repeated focal applications of calcium or caffeine to control fibers resulted in reversible contractures indistinguishable from single applications. The affected fibers and most notably the stimulated fibers, however, showed residual contractures after the second application of calcium or caffeine. A few stimulated fibers in contracture were relaxed by the local application of a relaxing-medium containing ATP and EGTA. The results are interpreted as inability of the myopathic fibers to relax after even mild stress. This inability implicates more than the lack of an energy source in the relaxing machinery. The absence of a sarcolemma in such preparations precludes the possibility that the effects observed were due to a membrane abnormality.

Supported by USPH HE 08218 grant and by NATO fellowship. Thanks are extended to Dr. B. McArdle, present address: Marine Neurobiology Facility, Scripps Institution, La Jolla, California.

References: (1) McArdle, B., Clin. Sci. 10:13:1951.

HEMODYNAMIC EFFECTS OF BLOOD AND DEXTRAN INFUSIONS IN DIBENZYLINE TREATED DOGS IN HEMORRHAGIC SHOCK. M.J. Guerrero* and V.V. Glaviano. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

Anesthetized dogs subjected to hemorrhage at a constant pressure of 40 mm Hg using an elevated reservoir, were given dibenzyline (2 mg/Kg) after 3 hours. Cardiac output, systolic volume, heart rate, circulation time, venous pressure, TPR, and in the hind limbs, blood flow, resistance and blood pH, pO_2 and pCO_2 were monitored. Dibenzyline diminished circulation time, TPR and limb resistance markedly, while cardiac output, systolic volume and limb flow increased. No change was seen in heart rate. In another group of dogs, before giving dibenzyline, the blood in the reservoir was replaced by dextran. The changes were similar to those seen in the group of dogs treated with dibenzyline and blood replacement. Uptake of blood from the reservoir was markedly increased in dibenzyline-treated dogs (64%) and in dibenzyline plus dextran (57%) as compared with control animals (21%) subjected to 4 hours of hypotension. A direct correlation existed between the increased uptake of blood or oxygen from the reservoir and the increase in cardiac output and limb flow. Arterial pO_2 and pCO_2 didn't show significant changes after administration of dibenzyline, however, pCO_2 decreased in the treated dogs, whereas control dogs showed a continuous increase. After 4 hours the dogs were sacrificed. A significant post mortem finding was the intensity of subendocardial hemorrhages in the experimental animals as compared with the few petechiae found in the control dogs not treated with dibenzyline. The results indicate that despite the increase in oxygen carrying capacity of dogs treated with dibenzyline and blood replacement, no significant differences were noted when they were compared to treated dogs with dextran replacement. (Supported by ONR Contract 3502-01 and NIH Grant HE 08682.)

EPSILON AMINOCAPROIC ACID: VASODILATOR IN THE DOG. M. Mason Guest and Ted P. Bond* Department of Physiology, University of Texas Medical Branch, Galveston, Texas.

During an investigation, in which the monoamino carboxylic acid, epsilon aminocaproic acid (EACA) was used in an attempt to block fibrinolytic activation in the dog, a significant increase in pulse pressure was observed in all animals receiving 70 mg or more per kg body weight by vein. Larger amounts caused hemoconcentration and an increase in lymph flow. The skin regularly became reddish, indicating vasodilation; the mean blood pressure increased in some animals and decreased in others; cardiac rate and output increased; in the heart-lung preparation EACA had neither ionotropic nor chronotropic effects; the observed effects of EACA were not blocked by potent antihistamines; no vasodilation was evident by direct observation of mesenteric vessels. Lysine, when introduced in comparable amounts into the circulation of the dog, had no demonstrable effects on the pulse pressure. Evidence was also obtained that although fibrinolytic activation was blocked by EACA, large amounts of fibrinolytic activator were released from the intima of blood vessels. Since EACA is rapidly excreted via the kidneys, the possibility exists that fibrinolytic activation can become manifest following a single infusion of EACA. (Supported by USPHS Grant NIH 1P01-HE-10893-01).

ALVEOLAR-TO-MIXED VENOUS PCO_2 DIFFERENCE DURING REBREATHING. Gail H. Gurtner*, S. H. Song*, and L. E. Farhi. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Rebreathing into a bag initially containing a CO_2-N_2 mixture leads to PA_{O_2} and PA_{CO_2} plateaus which are maintained until recirculation occurs. Dog experiments show that the PCO_2 so obtained was consistently higher than $P\bar{v}_{CO_2}$ measured simultaneously, and that the difference increased as plasma pH was lowered. In order to investigate the reason for this discrepancy, part of the animal's lung was filled with a 10% sucrose solution. The PCO_2 of this solution rose rapidly above that of mixed venous blood, while in a steady state H^+, Na^+, and Cl^- concentrations appeared to be similar to those of mixed venous blood. The calculated HCO_3^- concentration was higher in the alveolar fluid than in the mixed venous blood. The difference between alveolar and mixed venous PCO_2 may be explained by the fact that alveolar gas comes into contact not with the blood but with the alveolar lining. It is possible that maintenance of H^+ and HCO_3^- levels within the epithelial cells leads to a cellular PCO_2 and hence an alveolar PCO_2 that is different from plasma PCO_2.

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BIOCHEMICAL AND HISTOCHEMICAL STUDIES ON REINNERVATED AND CROSS-REINNERVATED FAST AND SLOW MUSCLES. L. Guth, P.K. Watson* and W. C. Brown*. Lab. Neuroanat. Sciences, N.I.N.D.B., N.I.H., Bethesda, Md.

Fast (white) mammalian muscles have higher glycolytic and lower oxidative activity than slow (red) muscles. The present study was performed to test whether the innervation is responsible for these metabolic differences. Direct reinnervation or cross-reinnervation of medial gastrocnemius (fast) and soleus (slow) of adult rats and of rectus femoris (fast) and crureus (slow) of adult cats was obtained by nerve anastomosis. Six months postoperatively the muscles were examined (i) histochemically for phosphorylase (PPL) and succinic dehydrogenase (SDH); (ii) biochemically (quantitatively) for PPL, lactic dehydrogenase (LDH) and 6-phosphogluconic dehydrogenase (6-PGD) activity; (iii) electrophoretically for LDH isozymes and soluble protein patterns. Normal fast muscles showed greater PPL, LDH, and muscle-type LDH isozyme whereas normal slow muscles showed greater SDH, 6-PGD, and heart-type LDH isozyme. With respect to these parameters, the cross-innervated muscles came to resemble the opposite muscle type, but the enzymatic conversion was never complete. This is not surprising inasmuch as (i) the individual fibers that comprise these muscles normally exhibit diverse combinations of these enzymes (they do not fall uniformly into a high oxidative-low glycolytic or a high glycolytic-low oxidative class and (ii) because the size of the motor unit is not necessarily constant in normal and reinnervated muscle (e.g., a nerve that normally innervates many fibers of one class may innervate fewer such fibers in reinnervated muscle). The present experiment substantiates the conclusion of previous reports (Romanul and Van Der Meulen, 1966, Prewitt and Salafsky, 1967; Yellin, 1967) that the nerve is responsible for some of the distinctive enzyme characteristics of adult mammalian fast and slow muscle.

CHANGES IN MIXED VENOUS OXYGEN TENSION AND SATURATION AT REST AND MILD EXERCISE DURING EXPOSURE TO ALTITUDE. P. Haab*, A. Chinet*, M. Jaeger*, P. di Prampero*, D. W. Rennie, and L. E. Farhi. Depts. of Physiol., Univ. of Fribourg, Switzerland, Univ. of Milano, Italy, and State Univ. of New York at Buffalo, Buffalo, N. Y.

The present work was undertaken to study the course of O_2 tension in mixed venous blood ($P\bar{v}O_2$) during the early phase of exposure to altitude and to determine whether the observed variations were accompanied by concommitant changes in hemoglobin saturation. $P\bar{v}O_2$ was measured by a rebreathing technique and the arterial blood saturation was followed by an ear oximeter before and during the rebreathing maneuvers. Measurements on five healthy subjects were made at an altitude of 650 m, and, in the course of four subsequent days, at an altitude of 3450 m, at rest and during moderate exercise ($\dot{V}O_2$ = 1 l/min). Within a few hours after the ascent, the resting $P\bar{v}O_2$ dropped from a control level of 42 mm Hg to 27 mm Hg, while the exercise values fell from 38 mm Hg to 24 mm Hg. During the subsequent days the $P\bar{v}O_2$ increased, reaching 32 mm Hg and 28 mm Hg for rest and exercise, respectively. The measured mixed venous O_2 saturation followed a similar pattern. This drop and recovery process appears to depend upon changes in both ventilation and cardiac output in the course of the early adaptation to altitude.

IN VIVO MEASUREMENTS OF INTESTINAL ABSORPTION AND SECRETION IN UNANESTHETIZED RATS AND THEIR MORPHOLOGICAL CORRELATE. F.J. Haberich and R. Herzer (intr. by R. Thauer). Physiologisches Institut der Freien Universität Berlin.

With a specially devised technique a definite part of the intestine can be reversibly isolated and extracorporally perfused. Measuring changes in the volume and composition of the circulating fluid, transmucosal net-fluxes of water and solute can be determined. Afterwards the system is filled with Os O_4-solution (1%) for in vivo fixation. Between the rate of net-flux and the intraluminal osmolar concentration a different relationship can be obtained in the range of absorption and secretion, the turning point between them being slightly hypertonic (equivalent to about 1% NaCl). Net-fluxes of water and solutes under condition of more hypertonic or hypotonic solutions can be explained by imperfect osmosis. As demonstrated by electron-microscopy the intercellular spaces are markedly dilated during bulk flow of fluid according to transmucosal osmotic gradients. This indicates that these channels may be the route of transport. The tight junctions remain closed. Only isotonic and slightly hypertonic absorption needs the assumption of active transport processes for explanation.

EFFECTS OF GENERALIZED CHANGES IN PLASMA K^+, Ca^{++}, Mg^{++} AND H^+ CONCENTRATION ON BLOOD PRESSURE IN THE DOG. Francis J. Haddy, J.B. Scott and R.M. Daugherty*. Dept. of Physiol., Mich. State Univ., E.Lansing,Mich.

We have previously known that the acute local effects of hypercalcemia, hypokalemia, hypomagnesemia, and alkalosis on intact small blood vessels and heart muscle is constriction and stimulation, respectively (Am.J.Physiol. 204:202, 1963). On the other hand, local hypocalcemia, hyperkalemia, hypermagnesemia, and acidosis dilate small vessels and hypocalcemia depresses the heart. We now report the acute effects on blood pressure when these changes are generalized. A potent diuretic (furosemide, 20 mg/kg) was injected intravenously and plasma electrolyte concentration was altered 90 min. later by rapidly (5 min) and exactly replacing the lost water (ave=440 ml) with solutions containing excesses of some electrolytes and an absence of others. The replacement solutions were 1)476 mOs/l $NaHCO_3$ plus 30 ml 10% Ca gluconate and 2)477 mOs/l NaCl, KCl and $MgCl_2$(K^+21mEq/l,Mg^{++}6.4mEq/l). Average values for plasma electrolytes (mEq/l), hematocrit (%) and mean arterial pressure (mmHg) immediately before and after infusion of solutions (1) and (2) were:

	Before							After						
	n	Na	K	Ca	Mg	pH	Hct	Pa	Na	K	Ca	Mg	pH	Hct	Pa
1)	10	135	2.6	5.6	1.1	7.36	53	118	154	2.4	9.4	0.9	7.57	35	161
2)	6	140	3.1	4.6	1.2	7.41	48	134	149	4.0	3.8	2.2	7.36	34	118

The K^+, Ca^{++}, Mg^{++} and H^+ concentrations after solution (1) were significantly different from those after solution (2). The blood pressure rose significantly on infusion of solution (1) and fell significantly on infusion of solution (2). Thus combined changes in the concentrations of plasma K^+, Ca^{++}, Mg^{++} and H^+, when of proper direction, significantly influence blood pressure.

VORTEX TRAILS BEHIND A CYLINDER IN OX BLOOD. G. Halikas* and C. W. Sheppard. Univ. of Tenn. Med. Units, Memphis, Tenn.

It has long been known that a cylindrical obstacle placed in a moving fluid generates a wake consisting of a series of alternately detached vortices. The frequency, n, of detachment is given by $n=(v/d)f(Re)$, where v=velocity of fluid, d=obstacle diameter and f(Re)=Strouhal number, $St=dn/v$. Re, the Reynolds number=vd/ν, where ν=kinematic viscosity. For Newtonian fluids such as water or glycerin, $St\approx0.12$ at Re=60 and increases approximately exponentially with increasing Re, until at $Re\geq300$, $St\approx0.21$ and remains constant. The equivalent relationship of St to Re for blood has not been investigated. Accordingly, St's for blood at different Re's were determined by placing cylinders of 0.32, 0.48 and 0.64 cm. diameter in a flow channel through which blood flowed at velocities ranging from 3 to 6 cm/sec. (equivalent to Re of 38-220). St for blood showed a correlation with Re only when St's obtained with a given cylinder were considered. Furthermore, St's were almost 3 times greater than for water or glycerin at threshold Re (i.e., Re at which vortices begin to detach), and then decreased with increasing Re. Because of experimental limitations the range of Re's could not be extended far enough to determine if St=a constant. However, the lowest St's for blood clustered around the St-Re curve for Newtonian fluids. Moreover, the frequency of vortex detachment in blood, unlike that of water or glycerin which increased with increasing velocity, remained the same for a given cylinder. (Supported in part by USPHS Grant HE-09495.)

EFFECTS OF INSULIN ON OXIDATIVE PHOSPHORYLATION. James C. Hall and Bengt S. Liljeroot.* Dept. of Zoology and Physiology, Rutgers University, Newark, N.J. and Div. of Research Fac. and Res., Natl. Inst. of Health, Bethesda, Md.

Previously published data have indicated that oxidative phosphorylation is reduced in mitochondrial preparations from the livers of alloxan diabetic rats or depancreatized cats and that insulin, "in vivo" or "in vitro", can restore these P:O ratios to normal values. Because of conflicting reports by other investigators various parameters of the Warburg system used were reinvestigated. It was found that:

1. Insulin is effective in concentrations as low as 5×10^{-10} M. This is the physiological range and much lower than the 10^{-6} M concentration used originally.
2. No improvement is noted with inactivated insulin or with bovine serum albumin.
3. Mitochondria suspended in .25 M sucrose show the same response as those isolated in .25 M sucrose; .005 M EDTA.
4. A low concentration of Mg^{++} is essential for the insulin effect. High Mg^{++} (10^{-3} M) is tolerated in sucrose EDTA, but in sucrose the optimum concentration is 10^{-5} M or lower.
5. The use of ADP alone as the phosphate acceptor yields results similar to those obtained with ATP, or ADP, and a hexokinase glucose trap.
6. Preincubation with insulin is not necessary. The same stimulation of phosphorylation is obtained if insulin is added from the side arm after the period for temperature equilibration.
7. Mn-10^{-5} M can replace Mg^{++} in the system.

These experiments support the theory that insulin reacts with the mitochondrial membrane and thereby contributes to the efficiency of its function. A minimal concentration of Mg^{++} is necessary for this interaction.

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ELEVATED ESCAPE LATENCIES AFTER HINDBRAIN LESIONS. Bruce P. Halpern and John D. Halverson.* Cornell University, Ithaca, N.Y., and State University of New York Upstate Medical Center, Syracuse, N.Y.

Cats (F. catus) were trained to escape floor electric shock in a shuttle box. Training gave stable voltage-to-escape latency (Esc. La.) relationships. After training, electrolytic lesions were made, aimed at nucleus reticularis gigantocellularis (NGc), P 9, L 1.5, H -8 . At least six post-lesion days preceded re-measuring Esc. La. Animals without satisfactory results in post-lesion neurological exam., or without an Esc. La., at some voltage, equal to the lowest pre-lesion latency, were excluded. Three cats formed a preliminary study: One had a unilateral lesion of nucleus olivaris inferior but not NGc, and no Esc. La. changes. A second had a unilateral lesion in NGc and increased ($p < 0.005$, Wilcoxon Sign Rank) Esc. La. The third animal was studied for 5 months post lesion. Increased Esc. La. followed a unilateral lesion ($p < 0.025$). After a contralateral lesion, Esc. La. remained elevated for 131 days. Lesions were not located histologically. Five cats comprise the main study: All had the same training and testing sequence. Each animal had training voltages which gave Esc. La. from 20 sec. thru 1 sec. Three animals' lesions were unilateral (I); one, seriatim bilateral (I,II), and one, unilateral followed by sham (I,SII). Four animals had increased ($p \leq 0.05$) Esc. La. after I; the fifth, after II. The SII animal had no additional Esc. La. increases post-sham lesion. Histological study of two animals is completed. Lesions were localized in NGc. These observations implicate NGc as a functional transfer nucleus for responses to noxious stimuli in the cat. (Supported in part by Hendricks Fund Grant #37 and Upstate Medical Center Student Fellowships)

QUANTITATION OF EFFECTS OF LEFT AND RIGHT VAGAL STIMULATION ON S-A AND A-V NODES. Robert L. Hamlin and C. Roger Smith. Dept. Vet. Physiol. & Pharm.,Col. Vet. Med., Ohio State U., Columbus, Ohio

Peripheral ends of first left and then right vagus were stimulated at from 0 to 10 volts in dogs. Effects on P-P interval, on configurations of 3 intraatrial electrograms and on aVf ECG's were determined through analysis of high speed recordings during stimulation before and after beta adrenergic blockade with propranolol. Both left and right vagi had equal "gains" in prolonging P-P and P-Q intervals. Left vagal stimulation had greater "gain" in producing 2nd degree A-V block; while right vagal stimulation had greater "gain" in elevating Ta waves. In presence of 2nd degree block, pre-and post-blocked P-Q intervals may be normal. Stimulation of either vagus with low voltage caused slight decreases in P-P and P-Q intervals. Beta blockade caused a decrease in this acceleratory effect, and permitted a greater deceleratory effect for a given voltage to either vagus. These results suggest or confirm that both vagi have nearly equal physiologic effects on S-A and A-V nodes, that 2nd degree A-V block is not a pertrubation of 1st degree A-V block, that tachycardia resulting from vagal stimulation with low voltages is beta sympathetic mediated, and that sympathetic efferent activity moderates vagal effects. (Supported by Program Project, HE-09884-02 of the NIH.)

Innervation of dog paw veins. Mary Hammond* and D. L. Davis. Medical College of Georgia, Augusta.

Experiments were conducted to extend data published by Zimmerman (Circulation Res. 18:429, 1966) on the innervation of the vasculature of the dog hind paw, and to determine if it were possible to elicit by peripheral nerve stimulation a constrictor response restricted primarily to the venous segments of the paw. Mongrel dogs were anesthetized with chloralose, treated with succinylcholine chloride to permit electrical stimulation of peripheral nerves, and maintained on positive pressure respiration. Stimulations were made with a square-wave stimulator at voltages ranging from 15-70 volts, frequencies of 25/sec, a 5 msec pulse duration, and total stimulation periods of 30-60 seconds. Responses of a small vein segment, extending centrally from a dorsal metatarsal vein to the lateral saphenous vein at the ankle level, were interpreted from resistance changes in response to stimulation of the sciatic, tibial, superficial and deep fibular nerves. In some experiments the venous segment was perfused at a constant rate, and in other experiments at a constant pressure. Results were similar with both experimental procedures. Stimulation of both sciatic and superficial fibular nerves produced marked constrictor responses of the venous segment. Stimulation of the deep fibular and tibial nerves produced negligible resistance changes in the venous segment. It is concluded that a significant portion of the venous innervation of the paw vasculature is in the superficial fibular nerve, and that stimulation of this nerve produces marked constriction of the venous segments with little constriction of arterial segments of the paw. Supported by grants from the Georgia Heart Assoc. and grants HE-00240, HE-05782-05, and 1-FL-GM-01 from the USPHS.

FLOW LIMITING FACTORS IN LIQUID-FILLED LUNGS. Paul Hamosh, M. D. * and Peter C. Luchsinger, M. D. Georgetown University Medical School and Veterans Administration Hospital, Washington, D. C.

Isovolume-Pressure-Flow curves were recorded from isolated liquid-filled canine lungs suspended in a liquid-filled plethysmograph. Maximum flow was found to be reduced by a factor of 50 and the recoil pressures by a factor of 2 to 3 in comparison to air-filled lungs. Approaching maximum flow, the airways became unstable and intermittently collapse. This is probably due to the increased contribution of inertance to the flow resistive forces resulting in redistribution of resistance along the respiratory tree. If these observations in isolated lungs are applicable to the intact animal, even the vastly reduced maximum flow would be unatainable, since the intermittent collapse of the airways would limit breathing frequency.
It has been reported that ventilation of the lungs with hyperbarically oxygenated saline or fluorocarbon compounds might enable man to tolerate high G-acceleration or facilitate deep-sea diving. According to our observations and calculations, the decrease in maximum ventilation is the ultimate limitation which makes liquid breathing impractical.

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OCULOMOTOR DEFICITS AFTER LESIONS OF THE MESENCEPHALIC RETICULAR FORMATION IN MONKEYS. Henry E. Harris*, Atsushi Komatsuzaki*, and Bernard Cohen. Department of Neurology, Mount Sinai School of Medicine, New York

We have previously shown that lesions of the paramedian zone of the pontine reticular formation (PPRF) in the monkey are followed by a characteristic syndrome of oculomotor dysfunction. After PPRF lesions neither eye moves across the midline to the ipsilateral side, ipsilaterally-directed saccades are of low amplitude and velocity, ipsilateral quick phases and contralateral slow phases of induced caloric and optokinetic nystagmus are defective, and there is contralateral spontaneous nystagmus in darkness. In contrast, after mesencephalic reticular formation (MRF) lesions the eyes readily cross the midline to either side, and saccadic movements and vestibular nystagmus are normal. Spontaneous nystagmus is present to the ipsilateral side in the dark, and optokinetic nystagmus (OKN) with quick phases to the contralateral side is abnormal. The OKN abnormality is manifested primarily as a failure of the eyes to follow at the velocity of the stimulating drum during the slow phases to the ipsilateral side. The quick phases of this nystagmus are of normal amplitude and velocity. Failure of optokinetic following after MRF lesions is not associated with abnormal eye position, spasms of tonic deviation, or an increase in nystagmus frequency as is the case after PPRF lesions. Defects in OKN after MRF lesions persisted in some animals for more than a year. The data show that the primary oculomotor deficit after MRF lesions is in OKN slow phases to the ipsilateral side. This suggests that MRF lesions interrupted pathways carrying sensory information from the visual system to the pontine reticular formation. This is in contradistinction to PPRF lesions which appear to damage the motor apparatus for horizontal gaze itself.

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PLACENTAL TRANSFER OF SEVERAL MOLECULES. Frederick M. Hart* & J. Job Faber. Department of Physiology, Univ. of Oregon Medical School, Portland, Oregon.

The fetal circulations of rabbit placentas in situ were artificially perfused with rabbit blood. The rates of transfer were measured of acetylene and labelled water, Cl^-, Na^+, and urea diffusing from the fetal to the maternal circulation and of oxygen and labelled inulin and albumin diffusing in the opposite direction. The permeability, P, (ml/min) and "permeability variable",d, (dimensionless, see Circ. Res. 19:816, 1966) were calculated for steady state transfer of each of these substances in placentas of 27 - 29 out of 31 days gestation. These values and the coefficients of free diffusion in water ($10^{-5}cm^2/sec$) are:

Substance	D	P	d	experiments	rabbits
Acetylene	2	2000	1000	25	7
Oxygen	2	2000	10	63	20
Water	3	6	3	29	10
Urea	2	0.3	0.2	22	6
Cl^-	3	0.2	0.1	20	5
Na^+	2	0.1	0.1	17	7
Inulin	0.2	0.01	0.01	7	2
Albumin	0.09	0.003	0.002	7	2

We conclude that lipid insoluble molecules are transferred at rates proportional to the order of magnitude of their coefficients of free diffusion in water, regardless of any charge carried by the molecules. Supported by NIH HD 2313 & HE 6336.

PREVENTION OF THE CHRONIC ALCOHOL-INDUCED FATTY LIVER BY ANTIOXIDANTS. A. D. Hartman* and N. R. Di Luzio, Dept. of Physiology & Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

Our previous studies have demonstrated that lipid antioxidants can effectively inhibit acute ethanol-induced hepatic triglyceride accumulation and ethanol-corn oil induced hyperlipemia. In contrast to the inhibitory effect of antioxidants on the acute ethanol fatty liver, attempts to prevent the chronic alcohol induced fatty liver by oral antioxidant administration have been unsuccessful. The present investigation was undertaken to determine the effect of parental administration of the lipid antioxidant N,N'-diphenyl-p-phenylenediamine (DPPD) on the chronic alcohol steatosis. Female rats were maintained for 21 days on nutritionally adequate liquid formula diets containing either a "low" (13%) or "high" (23%) fat content and supplemented with either ethanol or sucrose as 35% of the calories. Ethanol ingestion in control and experimental groups approximated 14.3g/kg/day. Liver triglyceride concentrations in animals maintained on ethanol-supplemented diets were significantly elevated 114% and 193% on the "low" and "high" fat diets, respectively. The intraperitoneal administration of DPPD completely prevent the lipid accumulation in the low-fat ethanol group and significantly inhibited the ethanol-induced hepatic steatosis in the "high" fat group. Since ethanol-induced enhancement in lipid peroxidation has been implicated in the pathogenesis of the fatty liver in acute ethanol model, the present studies indicate that hepatic triglyceride accumulation resulting from prolonged alcohol ingestion may also involve this process. These studies also further accent the possible role of lipid antioxidants in the modification of hepatic injury. (Supported by USPHS AM-08084 and Licensed Beverage Industries).

ANTERIOR HYPOTHALAMIC BLOOD FLOW AS DETERMINED BY HEATED THERMISTOR FLOW PROBES. Craig R. Hassler* and Robert D. McCook. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

The hypothalamic blood flow has been measured by use of a commercially available 23-gauge heated thermistor probe. This probe allows for the measurement of both flow and temperature simultaneously. Constant power D.C. pulses of constant duration were applied to the heating element of the probe and the temperature rise was a hyperbolic function of velocity flow. In addition, temperatures were measured in associated areas with a second thermistor in order to determine the effective area of the probe. The probe was found to be adequately sensitive to record differences in velocity flow through the anterior hypothalamus of cats. The probe was stereotaxically inserted at either A 16.0, RL 1.0, H -2.4, or A 14.0, RL 1.5, H -4.0. Flow was measured under different conditions, i.e. nembutal and/or Sernylan anesthesia, 10% carbon-dioxide inhalation, bilateral carotid occlusion, death, etc. Bilateral carotid occlusion decreased the flow and increased hypothalamic temperature as expected, CO_2 inhalation increased the flow and decreased temperature, while the two anesthetic agents gave values between the above extremes. The dead animal value was used to establish a measure of zero flow. (Supported by NIH Grant HE 08682.)

HISTAMINE AND THE PULMONARY VASOCONSTRICTOR RESPONSE TO ALVEOLAR HYPOXIA. A. Hauge* and N. C. Staub. Cardiovasc. Res. Inst., Univ. Calif. San Francisco Med. Ctr., San Francisco, Calif.

We used two animal preparations to investigate the possible relation of histamine to the pulmonary vascular response to alveolar hypoxia. We perfused isolated rat lungs with fixed volume, pulsatile blood flow at 37°C while ventilating the lungs with positive pressure. In open-thorax, anesthetized cats, we ventilated the left lower lobe by positive pressure separately from the rest of the lung. We recorded pulmonary artery, left atrial, and femoral artery pressures and lobar artery blood flow with an electromagnetic flowmeter. A rise in pulmonary vascular resistance causes perfusion pressure increases (rat) or flow decreases (cat). We tested 3 min of 0-2% O_2 ventilation with intervals of 5 min of air ventilation. In rat lung, 5 antihistaminics blocked all or almost all of the hypoxic pressor response. Slow injection of 48/80 (50-200 µg) gave transient vaso- and bronchoconstriction. Afterwards, no pressor effect of hypoxia could be elicited. Constrictor effects of bradykinin and ATP were not affected. In the cat, slow infusion of 48/80 (100-400 µg) into the lobar artery gave transient decreases in flow and a fall in systemic pressure. Afterwards, hypoxia no longer elicited any decrease in lobe flow; in fact, it usually caused a small increase. The constrictor effects of ATP and histamine injection were not blocked. The data suggest a role for histamine in the mechanism of the pulmonary vasoconstrictor response to alveolar hypoxia. (Supported in part by USPHS grant HE-06285. A.H. is a USPHS International Postdoctoral Fellow.)

TEMPERATURE EFFECTS ON NEURONAL MEMBRANE POTENTIALS. H. Hayashi*, and G. Austin. Division of Neurosurgery, University of Oregon Medical School, Portland, Oregon.

Using intracellular microelectrodes we have measured the effects of temperature change ($\pm$ 3° - 5°C) on the membrane potentials and conductance of single neurons of Aplysia Californica. These neurons have both excitatory and inhibitory synaptic input, and are divided into D and H-types, depending on whether they depolarize or hyperpolarize in response to locally applied ACh.
I. Static Temperature Change: An increase of 3° - 5°C, normal (13°C), causes hyperpolarization, usually decreased conductance, and increase in spike height, rise time, fall time, and rate of slow depolarization. There is an increase in spike frequency of spontaneous firing (pace-maker) cells. A decrease in temperature causes the reverse.
II. Transient Temperature Change: Temperature increase (from 1°/sec. to 1°/min.) causes hyperpolarization. There was a decrease in rate of slow depolarization, decrease in spike frequency, and usually a transient increased conductance. Spike threshold showed a transient increase, thought to be due to smaller local potentials, whereas there was an increase in local potential with the static temperature increase. The reverse was observed in transient temperature decrease. No significant differences were found in D and H-type cells. The results can be interpreted with respect to metabolic influence on resting membrane plus the effects of synaptic activity.

POTASSIUM AND SODIUM ACCUMULATION IN SKELETAL MUSCLE OF DEVELOPING RATS. C. F. Hazlewood and B. L. Nichols*. Depts. of Physiology and Pediatrics, Baylor Univ. Col. of Medicine, Houston, Texas.

Remarkable changes in the muscle electrolyte content of developing rats have been reported: at birth the sodium (Na) content of the gastrocnemius is higher than the potassium (K) content, but by 8 days of age this pattern is reversed. These changes are seen regardless of the reference base used, and changes in extracellular space alone cannot account for them. That is, intracellular ion concentrations are also changing. The fat-free dry solids (FFDS) of a muscle increase with age (growth). In the work reported here FFDS are used as a reference base, and it is observed that the ratio of K to the FFDS is nearly constant from 0-65 days of age. A plot of the total quantity of K per gastrocnemius vs. the total FFDS per gastrocnemius reveals a highly significant linear relationship. That is, K content is increasing in proportion to the increase in muscle mass. The Na content of the muscle also increases with age (growth), but at a much slower rate. Thus, during early postnatal development, the K/FFDS ratio is nearly constant while the Na/FFDS ratio falls drastically. These data indicate an intimate relationship between cellular K and cellular protein. In support of this concept--growth was abated in rats, during the rapid growth phase, by protein free diet and net K accumulation was stopped.

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SENSORY ABNORMALITIES IN PATIENTS WITH TURNER'S SYNDROME. R.I.Henkin, M.S.Buchsbaum* and J.Silverman*. Natl.Insts. of Health, Bethesda, Md.

Taste, smell, hearing, oral and manual stereognosis, visual and kinesthetic perception and averaged visual evoked potentials (AVEP) were studied in 10 patients with Turner's Syndrome, the diagnosis confirmed by clinical observation and laboratory tests. Each of the patients was a phenotypic female and had a predominant 45 XO karyotype upon examination of peripheral leukocyte cultures. Median detection and/or recognition thresholds for sour and bitter were elevated above normal although thresholds for salt and sweet were normal. Median detection and recognition thresholds for the vapors of pyridine, thiophene and nitrobenzene were elevated above normal. Detection of sinusodial tones above 8000 cps and below 500 cps was impaired; word recognition and binaural loudness balancing of tones were also impaired. Identification of geometric forms in the mouth was impaired although identification of these forms in the hand was adequate. Differentiation of simple visual forms from complex patterns was also impaired. AVEP were measured at different light intensities; amplitude and latency of these responses were expressed as a function of light intensity. The shape of the intensity function for the patients was significantly different from that of normal females and resembled that of normal males. There were no significant latency differences between the patients and normal males or females. These results indicate that there are multiple sensory defects in patients with Turner's Syndrome. Some of these defects involve a specific sensory disability; others involve abnormalities of integration of sensory information not related to a specific sensory modality. The abnormalities seen in AVEP may refer to sensory disabilities derived from neuroendocrine changes which indicates that responses of these patients are inappropriate for their phenotypic sex.

EARLY SENESCING MICE: BONE & SKIN COLLAGEN BIOSYNTHESIS. Dorothy H. Henneman, M.D., L. Gaburo*, C. Neuwiesinger*, S. Thomas* Ortho Research Foundation, Raritan, N. J.

CBA/J mice show early senescense with obesity, arthritis, loss of hair and fertility, skin scaling, tumor formation in the female, and senile behavior. Changes are visible at 5 months in breeding females & advanced in both sexes at 9 months. Separation of mates accelerates senescence, particularly in males. Litters are small--with high incidence of teratology, stillbirth & neonatal death. Bone & skin hexosamine increase in both sexes but are higher in the female at all ages; ratios of skin hexosamine to collagen increase with age and are higher in the female. Skin collagen & proline are higher in the male and decrease with age despite increments in body weight; skin collagen in the female increases with age. In contrast, bone proline & OH-proline are higher in the female at all ages and increase with age in both sexes. Ratios of proline:OH-proline decrease with age in both sexes perhaps reflecting decreased collagen turnover in the aged. Correlation of ratio change with turnover has been demonstrated in this laboratory. (Fed. Proc. 26:667, 1967). In vivo incorporation of C^{14} proline into skin proline and OH-proline is greater in females despite higher collagen content in males. Incorporation into bone is the same in both sexes even though content is higher in the female. The greater content of collagen, proline, and hexosamine in female bone at all ages is unexpected since body weight is greater in the male & measurements are on decalcified bone matrix. These differences might reflect estrogenic effects on bone-remodeling and skin collagen since earlier studies indicated that estrogens stimulate collagen synthesis and turnover. Further study on aged females with estrogen deficiency should verify this possibility.

Splenic Contraction in Response to Non-Hypotensive Hemorrhage. Henry, J.P., Cabaud, H.E.† Hinderleider, C.D.* and Meehan, J.P., University of Southern California, School of Medicine, Department of Physiology, Los Angeles, California.

It has long been known that the dog's spleen contracts in response to hemorrhage (Barcroft et al, J.Physiol. 60:443, 1925). This report is concerned with the precise percentage of blood volume reduction needed to start the contraction and with the possible role of the splenic nerves in initiating the response. Using appropriate surgical techniques 8-10 twenty-four gauge stainless steel sutures were evenly spaced around the splenic margin. The splenic pedicle was stripped of its accompanying nerves in a control study. Two weeks later under chloralose anaesthesia the estimated blood volume (9% body wt.) was reduced in aliquots of 5% once every 2 minutes. Lateral Xrays were taken at each decrement. Contraction began in the normal animals prior to the loss of 10% and increased with progressive hemorrhage. Strong contraction was observed only after more than 25% volume loss. The denervated spleen did not respond significantly to minor blood loss. Since the contraction commences during the non-hypotensive phase of progressive blood loss it would appear that the receptors in the low pressure system (Gupta, et al, Am.J.Physiol. 211:1429, 1966) initiate this change as well as the increase in heart rate and in levels of antidiuretic hormone.

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STEADY-STATE RESPONSES OF HEART-LUNG COMPARTMENT OUTPUT TO VARIED PRE-LOAD AND AFTER-LOAD PRESSURES. Caleb Herndon* and Kiichi Sagawa. Univ. of Miss. Medical Center, Jackson, Mississippi.

In the previous studies*, the authors determined left ventricular net outflow (SF) as a function of mean aortic pressure (MAP) as well as mean left atrial pressure (MLAP) using a reflex-wise isolated dog heart preparation. This time, a similar relationship between the steady-state SF and loaded input and output pressures was studied of the entire heart-lung segment of the circulatory system. The preparations were similar to the previous ones except that mean right atrial pressure (MRAP) was controlled instead of MLAP and thereby MLAP was allowed to rise or fall as the left ventricular outflow varied. In 20 dogs MAP was controlled and altered from 30 to 300 mm Hg keeping MRAP at three different fixed levels. In another 11 dogs MRAP was increased from 0 to 22 mm Hg, specifying MAP at many different levels. When MRAP was within physiological range, the heart-lung compartment could pump an almost constant net outflow until MAP rose above 200 mm Hg. In contrast, when the MRAP was greater, the output decreased more significantly with increases in MAP. However, comparison of the pressure-load characteristics of the entire heart-lung compartment with that of merely the left ventricle clearly indicated that (1) the constancy of the outflow from the lumped compartment in the face of elevated MAP was definitely improved by virtue of the Starling mechanism and (2) SF decreased abruptly toward zero at the MAP of 240 to 250 mm Hg. This value of the maximum MAP is not significantly different from that found in the study of the left ventricle alone. When arterial baroreceptor reflex was left intact, the maximum MAP decreased to approximately 75% of the control.

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MODEL DESCRIBING THE STATIC HYSTERESIS COMPONENT OF LUNG PV LOOPS. Jacob Hildebrandt. Dept. of Physiol. & Biophys., West Virginia University Medical Center, Morgantown, W. Va.

It has been previously reported (Physiologist 8:193, 1965) that the area of PV loops obtained from excised cat lungs in a plethysmograph (where tracheal air flow is zero) is nearly constant in the frequency range from 0.01 to 2.0 Hz. This means that the energy losses are incompatible with those of a simple tissue viscous resistance. It was also shown (Physiologist 9:203, 1966) that only about one half the loop area could be accounted for by viscoelastic properties, i.e., "dynamic" hysteresis. The purpose of this paper is to present a model which can describe the remaining "static" hysteresis appearing in lung tissue. The experimental data with which the model should be consistent are the following: loop area is independent of breathing frequency; energy loss per cycle is proportional to the square of the tidal volume; "compliance" increases as tidal volume increases; when volume is forced sinusoidally, loops are non-elliptical. The model is an extension of configurations developed by others to explain properties of metal (Jaeger, 1956) and bone (Sedlin, 1965), and consists of a number of Prandtl bodies in series. The Prandtl body is composed of a Hookean body (spring) attached to a St. Venant body (rigid plastic). Neither a single Prandtl element nor the modified elements used in the science of solid materials meet the above requisite criteria. However, by increasing the number of elements in series, loops like those produced by the lung can be generated. The model suggests that (on a molecular level) as tissue is distorted some structural bonds rupture producing heat by a process that is not time of rate dependent. (The work upon which this publication is based was performed pursuant to Contract No. PH 86-67-80 with the USPHS, HEW.)

WHY pH 7.4? A. G. Hills, Dept. of Med., Univ. Miami Schl. Med.

The great stability of extracellular fluid reaction in the individual organism is obviously dictated (L. J. Henderson) by the profound effect of pH upon the velocity of the chemical reactions supporting life. Slight relative alkalinity of extracellular fluid (H. Rahn) appears, however, also to be uniform among most and perhaps all vertebrate species under normal circumstances. It is suggested that pressure may have been exerted throughout the course of vertebrate evolution upon extracellular fluid reaction by the dependence of effective renal acid-base regulation upon excretory buffering by CO_2 and NH_3. Hardly any other compounds available in the terrestrial biosphere possess the physicochemical properties -- especially the high volatility and diffusivity, low standard free energy of formation, and dissociability with differential water-lipid solubilities of gas and ion -- which collectively fit these compounds to serve volatile excretory buffering. Given the fundamental design of the acid-base-regulating mechanism of the vertebrate kidney, extracellular pH must be upwards of a pH unit above pK'_a for CO_2 in order to secure the highly effective regulatory fluctuations of plasma HCO_3^- which in turn appropriately govern the rate of elimination of excess alkali as HCO_3^-. Rising extracellular alkalinity would necessitate a rapidly increasing rate of energy expenditure (for H^+-secretion into the nephrons) to allow effective excretory buffering of excess acid as ammonium to come into play in HCO_3^--poor urine (pH roughly below 6.5). The faint alkalinity of vertebrate extracellular fluid may represent the most effective adaptation to the aqueous dissociation constants of CO_2 and NH_3, two compounds which may well be the fittest among the few compounds abundantly available in the environment which are at all adequately qualified by their properties to serve renal excretory buffering.

EFFECT OF COUNTERPULSATION ON LIMB RESISTANCE. L. J. Hirsch and S. Lluch (intr. by R. Pick). Cardiovascular Institute, Michael Reese Hosp. and Medical Center, Chicago, Illinois.

It has been observed by others that blood flow to various organs, such as the kidney, brain and limbs decreases during counterpulsation (CP). Since counterpulsation distorts the aortic pressure pulse and widens the pulse pressure, a series of ten experiments were undertaken in five normotensive dogs to determine whether the effects of diastolic augmentation on the peripheral circulation were reflexogenic in nature. CP produced a reduction in peripheral resistance in intact limbs or in innervated limbs which were perfused separately from the rest of the body by means of artificial circulation. On the other hand, in six experiments on three dogs, no decrease in resistance occurred when these limbs were denervated. In addition, in three animals ablation of both carotid and aortic arch baroreceptors effectively inhibited these vasomotor effects. Thus, in normotensive dogs, CP appears to activate baroreceptors to produce a reflex decrease in peripheral resistance. It remains to be seen however, whether this mechanism is also operative when shock or hypotension are present.

A PRECISE STATEMENT OF DOSE RESPONSIVE GASTRIC SECRETION OF WATER, H, Na, K, Cl. B.I. Hirschowitz. University of Alabama Medical Center, Birmingham, Alabama.

If the rate of secretion (V) of any component of gastric juice, due to a stimulant infused at a certain rate (S), represents the rate of the reaction (V) of the reversible combination of S with cell substrate (R), and furthermore if S or some function of S, (e.g. s') represents the combination SR or substrate concentration responsible for secretion (V), then the kinetics can be described by the well-known linear equation $1/V = b\ 1/S + a$ (eq. 1). Ten gastric fistula dogs were each studied with 8 dogs were each studied with 8 doses of histamine base (2-125 µg/kg/hr), each given separately I.V. for 4 1/2 hr. I was transposed to $S/V = b + aS$ (eq. 2). s' was determined experimentally from low dose studies to be 2.5 µg/kg/hr lower than s for all parameters except Na and this corresponds to a threshold dose for histamine. With eq. 2, s' correlated well with s'/V for water, H, Cl or K ($r = +.9997$). Implicit in eq. 2 is the calculation (b/a) of s'_{50} or the dose of s' required for 50% of max. rate of secretion (V^{max}) which can be calculated from 1/a. Thus s'_{50} values calculated for each parameter were: K^+ = 11.72, H_2O = 11.76, Cl^- = 12.35, H^+ = 12.89 µg/kg/hr (6 to 6 x 10^{-8}M) and V^{max} values were about 10% above those observed with 125 µg/kg/hr. No threshold was apparent for Na^+, for which S_{50} was 19.45 µg i.e. much lower than for other electrolytes. Eq. 2 was equally valid for total and peak outputs. In 6 dogs gastrin pentapeptide (0.1 = 6.0 µg/kg/hr) (M.W. 770) had an S_{50} of 0.5 µg/kg/hr (6.5 x 10^{-10}M) (i.e. 100 x as potent as histamine), showed no threshold and showed the same kinetics for pepsin as for electrolytes in contrast to histamine, which inhibited pepsin secretion.

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METABOLISM OF FATTY ACIDS AND GLUCOSE IN ISOLATED MAST CELLS. R. J. Ho*, M. S. Cabut* and H. C. Meng, Vanderbilt Univ., Med. Sch., Nashville, Tenn.

Pure peritoneal mast cells (mcs) were isolated from normal fed male rats according to the method of Uvnas and Thon. The oxidation of glucose (g), 2.5 mM, to CO_2 was linear with respect to the concentration of msc in the incubation medium. The time curves for the oxidation of g and palmitic acid (pa), 0.02 mM, were linear up to 4 and 1 hr of incubation, respectively. The substrate concentration curves of g (up to 10 mM), pa (up to 1.5 mM) and oleic acid (up to 1.5 mM) were obtained; under the experimental conditions, the CO_2 production had approached the maximum at the higher concentrations of these substrates. The studies of the metabolism of g-1-^{14}C, g-6-^{14}C and g-u-^{14}C suggest that mcs have an active pentose-phosphate pathway for g metabolism. The oxidation of g-1-^{14}C was 5-7 times greater than that of g-6-^{14}C, and 3-4 times greater than that of g-u-^{14}C. The oxidation of g was inhibited by pa and vice versa. The oxidation of pa was a function of both free fatty acid (FFA) concentration and FFA to albumin molar ratio. At a constant albumin concentration, the oxidation of pa to CO_2 was increased with increasing substrate concentration On the other hand, at a given concentration of pa (0.414 mM or 0.114 mM), the CO_2 formation from pa-1-^{14}C was decreased by increasing the albumin concentration. It is concluded that glucose and fatty acids are utilized for energy by the isolated peritoneal mast cells of the rat. The metabolism of glucose is predominately by the pentose-phosphate pathway. (Supported by grant from NIH).

REWARDING HYPOTHALAMIC STIMULATION MADE AVERSIVE BY EXCESSIVE FEEDING OR OBESITY. Bartley G. Hoebel (intr. by John R. Brobeck). Princeton University, Princeton, New Jersey.

In rats electrodes implanted in the lateral hypothalamus elicited three behavioral effects, self-stimulation (reward), stimulation-escape (aversion), and stimulation-bound feeding (hunger). Hypothalamic reward and aversion were measured immediately before and after tube-feeding 10 cc. of liquid diet to seven rats at a normal body weight. Four others were made experimentally obese by a new technique using self-induced stimulation-bound eating which increased body weight 200 gms. The basic results were similar in both groups. The rate of hypothalamic self-stimulation decreased, whereas the rate of stimulation-escape increased. In the normal rats this shift occured within the 10 min. after tube-feeding. The obese rats displayed the shift in daily 1 hour tests for several weeks. When their food intake was restricted, hypothalamic escape continued at the augmented level until body weight declined to near normal levels. When body weight returned to normal, so did the rate of self-stimulation and escape. This demonstrated: (1) that the reward of lateral hypothalamic stimulation can shift to aversion, and (2) that the shift can occur as a function of physiological states which exert short and long term inhibitory control over food intake.

A SPECIALIZED FIBER TYPE IN THE CANINE RIGHT ATRIUM. P. M. Hogan and L. D. Davis (intr. by W. B. Youmans). Department of Physiology, University of Wisconsin, Madison, Wisconsin.

Fibers which have an action potential (AP) similar to that of Purkinje fibers have been described in the canine right atrium (Cir. Res. 18:692, 1966). Further investigation of these fibers has been made in the present study. Right atria were excised, immersed in Tyrode solution and the endocardial surface exposed. Microelectrodes were used to impale fibers in different areas of the atrium and appendage. At the auriculo-caval angle and in the crista terminalis fibers were found which had an AP like that of Purkinje fibers. Prominent features were a large sharp spike, long plateau phase and usually a small amount of diastolic depolarization. In 10 experiments the maximum upstroke velocity of these fibers and of simultaneously recorded non-plateau fibers was determined electronically. The difference in mean upstroke velocities of the two fiber types (126.3 V/sec) was significant ($P<.005$). Epinephrine increased the rate of diastolic depolarization of plateau fibers while simultaneously recorded non-plateau fibers were unchanged. Acetylcholine caused loss of the plateau and the AP then resembled that of non-plateau fibers. It is demonstrated that plateau fibers in the right atrium possess several characteristics exhibited by specialized conducting and impulse generating fibers. (Supported by grants from the Wis. Heart Assoc. and USPHS No. 5-T1-5540-05 and No. 5-T1-5375-07.)

Metabolism of the Excised, Vascularly Perfused Whole Small Intestine. Frank J. Hohenleitner and John R. Senior (intr. by T.G. Schnabel, Jr.) Philadelphia General Hospital, Philadelphia, Pennsylvania.

Studies of O_2 and glucose consumption, lactate and CO_2 production were carried out in small gut perfused vascularly through the superior mesenteric artery. The entire jejuno-ileal segment of canine small intestine was perfused up to five hours in vitro with Ringer's solution containing 6% dextran alone or with added sheep erythrocytes. Under hyperglycemic or normoglycemic conditions glucose uptake from the perfusate varied from 0.31-1.63 mmoles/hr/100 g and lactate output 0.17-3.73 mmoles/hr/100 g. Intestinal O_2 consumption and CO_2 output were a function of perfusate flow. Sympathetic nervous activity within the perfused tissue limited maximum flow at physiological pressures to 63 ml/100 g/min (average 40 ml/100 g/min) and a maximum O_2 consumption of 1.30 ml/100 g/min (average 0.87 ml/100 g/min). The use of the adrenergic blocking agent phenoxybenzamine reduced resistance and increased flow rates to an average of 61 and 91 ml/100 g/min with and without red blood cells respectively. Maximal O_2 consumption with red cells was 2.34 ml/100 g/min (average 1.49 ml/100 g/min). Atropine, a vagal inhibitor, or cyproheptadine, an antagonist of both histamine and serotonin, when administered together greatly reduced motility, and decreased O_2 consumption and CO_2 output. Under conditions of minimal motility the intestine could be perfused without erythrocytes, with similar O_2 consumption and CO_2 output (both ca 0.80 ml/100 g/min), glucose uptake (ca 0.80 mmoles/hr/100 g) and lactate output (ca 1.0 mmoles/hr/100 g). The preparation described here may be useful in studying the absorptive, metabolic or synthetic capacity of the small intestine free of the influence of other organs.

TRANSIENT VENTILATORY RESPONSES TO STEPS OF LOW O_2 WITH FIXED ALVEOLAR CO_2. Garland H. Holloman, Jr. and Howard T. Milhorn, Jr. (intr. by William A. Neely), Dept. of Physiology & Biophysics, Univ. Medical Center, Jackson, Mississippi.

An experimental system has been developed to study the isolated effects of positive and negative steps of inspired O_2 on alveolar ventilation. This system consists of (1) an analog computer program for the calculation of tidal volume, minute ventilation, alveolar ventilation, and respiratory frequency, and (2) a servomechanism for the automatic regulation of alveolar CO_2 concentration. The air flow signal is corrected to body temperature and standard pressure, and the inspiratory signal is integrated to obtain tidal volume. The integrator is reset at the end of inspiration by a trigger circuit operated by the air flow signal. Respiratory period is obtained by generating a ramp function which is also reset at the end of each inspiration. Respiratory frequency is the reciprocal of this time ramp. Tidal volume and respiratory period are used to compute breath-by-breath minute ventilation and, with corrections for dead space, alveolar ventilation. By triggering at the end of expiration, end tidal CO_2 is sampled and held until the next sampling. This signal is compared to a reference value, and the resulting error is used to drive a servo driven valve which regulates the concentration of inspired CO_2. Thus, alveolar CO_2 is regulated by negative feedback. By maintaining CO_2 at a constant value the "braking" effect of hypocapnia is eliminated. Therefore, the observed respiratory response is due only to the low oxygen stimulus.

ELECTRICAL ACTIVITY OF THE SUPERIOR MESENTERIC VEIN OF THE GUINEA PIG. L. Horn and A. Nakajima*. New York Medical College, New York.

We have previously reported on intracellular recording of spontaneous and drug-induced electrical changes of smooth muscle from the longitudinal layer of guinea pig superior mesenteric vein (Fed. Proc. 26:330, 1967, Am. J. Physiol. 213: July, 1967). Further data on changes in membrane activity in response to catecholamines and acetylcholine will be reported. Adrenaline and noradrenaline have an excitatory effect brought about by depolarization or increase in spike activity. Adrenaline has an additional positive inotropic effect not associated with detectable change in membrane potential when the muscle has been extensively depolarized by increased external potassium. Isoproterenol abolishes spike activity and hyperpolarizes the membrane. We have previously reported that acetylcholine may briefly hyperpolarize the membrane before the depolarization to about 40 mV associated with the excitatory effects of the drug. The depolarizing effects of acetylcholine reverses when the membrane has been depolarized by KCl to about 30 mV prior to drug application. It is suggested that acetylcholine has an equilibrium potential of about 40 mV in this muscle. (Supported by Contract DA-49-193-MD-2843 with the U. S. Army R & D Command and a Grant from the American Heart Association.)

K^+ Loss During Graded Degrees of Cardiac Edema. Jan Hornbuckle*, John M. Ginski. University of Tennessee School of Basic Medical Sciences. Memphis, Tennessee.

As previously reported, addition of homologous erythrocytes to a colloid containing perfusion fluid reduced edema formation in the isolated guinea pig heart. This study examined the loss of myocardial K^+ in graded states of cardiac edema. The edema was induced by 15 minute exposures to perfusion fluids of different composition and measured by comparing the alteration of ventricular dry-wet weight ratios (D/W %). Four series of experiments were conducted. The composition of the perfusion fluid varied as follows: Group I, a modified Ringer-Locke (R-L) solution; Group II, R-L containing 11.0 x 10^7 RBC/cc; Group III, 1.2% dextran in R-L; and Group IV, 1.2% dextran in R-L containing 11.0 x 10^7 RBC/cc. The mean changes are summarized as follows:

	D/W % ± S.E.	mEq K^+/Kg Wet Wt. ± S.E.
Group I	17.17 ± 0.23	69.4 ± 2.8
Group II	17.53 ± 0.21	70.4 ± 1.2
Group III	18.16 ± 0.21	73.6 ± 1.2
Group IV	18.40 ± 0.19	81.2 ± 1.8

Addition of RBC to R-L will neither prevent tissue water (H_2O_t) accumulation nor prevent K^+ loss. 1.2% dextran decreases H_2O_t ($P < 0.01$) but does not alter K^+ loss. Addition of both dextran and RBC decreases H_2O_t ($P < 0.001$) and K^+ loss ($P < 0.01$). The reduction of K^+ loss cannot be effected by merely decreasing H_2O_t, and the H_2O_t must be reduced before the effect of RBC can be observed.

ESTIMATED THERMAL CONTRIBUTION OF BROWN FAT DURING AROUSAL OF THE GROUND SQUIRREL, C. LATERALIS. B. A. Horwitz,* R. E. Smith, and E. T. Pengelley*. Univ. Calif.: Dept. Physiol., UCLA; Dept. Physiol. Sci., UC Davis; and Dept. Life Sci., UC Riverside, California.

In an attempt to evaluate the thermogenic contribution of brown fat relative to that of the intact ground squirrel during arousal from hibernation, the tissue oxygen consumption *in vivo* was approximated from *in vitro* rates of oxygen uptake obtained in the presence of catecholamines. Equations describing the tissue heat production as a function of arousal time were derived from direct temperature recordings of the brown fat by assuming that the time course of the tissue's oxygen uptake during arousal parallels that of the brown fat temperature. From these equations, the amount of oxygen consumed by the brown fat over a given time interval was calculated. Comparing these values with the measured heat production of the animal, estimates of the heat attributable to brown fat metabolism ranged from 10-15% initially to 5-7% as the squirrels approached normothermic body temperatures. Since these estimates are directly related to the *in vitro* qO_2's employed, the possibility that these rates are lower than those occurring *in vivo* was considered, and on the basis of the differences observed between the magnitude of the *in vitro* and *in vivo* stimulatory effects of catecholamines on rabbit brown fat metabolism, the estimated contributions of brown fat were recalculated to values of 41% initially and 20% near the time when the posterior circulation opened. Thus, the average contribution of 8-11% of the total caloric cost is considered a minimal estimate of the tissue's heat production in support of arousal from deep hibernation at low ambient temperatures. (Supported by NASA Res. Gr. NSG 721, USPHS Res. Gr. HD-01826, NSF Res. Gr. GB-6179, a Riverside Cty. (Calif.) Heart Assoc. Res. Gr., and USPHS Postdoctoral Fellowship, 1-F2-GM-13,445.)

CARDIOVASCULAR EFFECTS OF REVERSIBLE VAGAL BLOCKAGE IN CONSCIOUS DOGS. L.D. Horwitz,* H.F. Stegall,* V.S. Bishop, H.L. Stone, and B. Wiggins, Jr.,* USAF School of Aerospace Medicine, Brooks Air Force Base, Texas, 78235.

Repeated, reversible acute vagal blockage was obtained in 8 mongrel dogs with chronically implanted vagal cooling coils. A hollow stainless steel coil was placed around the right cervical vagus nerve. Silicone rubber tubing was connected to each end of the coil and brought outside the skin at the neck. The left cervical vagus nerve was cut. An electromagnetic or Doppler ultrasonic flowmeter probe was affixed to the ascending aorta and catheters were inserted into the left and right atria. After a two-week recovery period acute vagal blockage was achieved by pumping refrigerated alcohol through the vagal cooling coil while recording heart rate, aortic flow, left and right atrial pressures and femoral artery pressure. Upon blockage of the vagus nerve the heart rate increased to an average plateau value of 203 beats/min. This was an average increase of 87 beats/min. which was significant. The cardiac output increased from an average resting value of 158 cc/min.-kg to 182 cc/min.-kg during the blockage. This average increase of 24 cc/min.-kg was statistically significant ($P = .02$). Thus a significant decrease in stroke volume of 0.81 cc/b-kg was observed. The arterial pressure and right atrial pressure did not change significantly during the cooling although increasing 12 mm Hg and 0.5 mm Hg, respectively. The left atrial pressure decreased an average of 2 mm Hg; this, too, was not significant. Thus increasing the heart rate to extreme levels by acute blockage of the right vagus results in a small but significant increased cardiac output.

REST, ACTIVITY, AND ANTICOAGULANT THERAPY IN THE TREATMENT OF VENOUS THROMBOSIS. Orville Horwitz, Thorne Sparkman, Jr., Heatly D. Sebring and H. Edward Holling. University of Pennsylvania, School of Medicine, Philadelphia, Pa.

Our studies have shown the incidence of venous thrombosis in patients suffering from catatonia and severe cerebral arteriosclerosis to be at least 21%. In corresponding age groups in general hospitals it is 11% and in ambulatory patients less than 3%. Strain gauge plethysmographic measurements showed a decreased blood flow to the calves of catatonic patients. This is further confirmation that bed rest, and inactivity are precipitating if not etiologic factors in venous thrombosis. In patients suffering from post-phlebitis ulcers polarographic measurements of oxygen tension by us have shown a sluggish blood flow to the skin of the leg. Histological studies of the skin near stasis ulcers show lumen obliteration by thrombi and endothelial proliferation in arterioles, venules and capillaries. These microscopic thrombi may be more responsible for ulceration, pain, and edema than is damage to larger vessels. This provides further rationale for the use of anticoagulants. Considering these facts we believe that patients with acute venous thrombosis should be treated with strict bed rest and leg elevation only until pain and edema have subsided, usually two or three days. After this a daily increase of activity should be encouraged. These measurements must be accompanied by prompt and satisfactory anticoagulation.

RESPONSES OF ISOLATED VASCULAR STRIPS TO INCREASING ELECTRIC FIELD STIMULI. J. D. Huff*, C. M. Olmsted*, and R. L. Sandberg. Dept. Physiol., Univ. Ark., Little Rock, Ark.

Neither canine nor rat vascular muscle exhibit a double-peaked response to electrical stimuli. Previously reported results by others using uterine and ileal muscle typically show such a response. An inhibitory process somewhere in the excitation-contraction sequence has been postulated to account for declining responses after the first peak. Using helical strips of dog mesenteric artery and vein, dog saphenous vein, and rat portal vein in Kreb's P. P. S. with sine or square wave stimuli of ten seconds duration, a smooth sigmoid wave of tension resulted from increasing field strengths up to 9 volts rms/cm. In some preparations, isometric contractile force fell off above 5 volts/cm, but responses at lower voltages similarly declined, and were time-irreversable. The monotonic relationship of stimulus strength to contractile force held in increasing concentrations of external K^+ up to 120 meq/liter, at temperatures down to 4° C, and with decreased CA^{++}

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INFLUENCE OF RELEASE OF ADRENERGIC VASOCONSTRICTOR TONE ON EXCHANGE CIRCULATION IN SKELETAL MUSCLE. C. Hyman and W.H. Wong * Depts. of Physiology and Medicine (Section of Dermatology) U.S.C. School of Med., Los Angeles, California

It has been shown that when total blood flow through either skin or skeletal muscle is increased by activation of cholinergic autonomic fibers there is no demonstrable increase in the exchange function. A corresponding unilateral effect on shunt circulation after reduction of adrenergic tone has not been clearly established. Simultaneous plethysmographic measurements of total and cutaneous blood flow and determinations of NaI^{131} clearance from intra-muscular injection sites were made in supine normal subjects before, during and after elevation of the legs and lower trunk. It has been shown that this procedure increases blood flow through the skeletal muscle of the extremities by release of pre-existing adrenergic tone. In every case, during the elevation of the legs blood flow through the skin remained unaltered, total blood flow through muscle, however, increased by at least 150%. In no case did the clearance of I^{131} from muscle increase significantly. We conclude that withdrawal of adrenergic tone, like imposition of cholinergic stimulii, is without influence on the exchange function in peripheral tissues. Supported by the U.S.P.H.S.

EFFECT OF SPREADING DEPRESSION ON THE N WAVE DCR AND ON BETZ CELLS. M. Ichijo* and S. Ochs. (Introduced by K. Knoebel). Dept. of Physiol., Ind. Univ. Med. Ctr., Indianapolis, Ind.

Propagation of spreading depression (SD) in the 1st layer of the cerebral cortex was earlier shown by the means of cuts made from below up to the molecular (1st) layer (Ochs and Hunt, J. Neurophysiol. 23: 432, 1960). Transmission of the negative wave DCR (N wave DCR) takes place in the 1st layer also as shown by such cuts (Ochs and Suzuki, EEG. clin. Neurophysiol. 19: 230, 1965). The conducting elements are axonal as indicated by the lack of effect of GABA on them. Stimulating electrodes S_1 on one side of a cut excite these axons which then synapse on apical dendrites to give rise to the N wave DCR recorded on the other side. A second set of stimulating electrodes S_2 on the opposite side was used to also excite N wave DCRs. SD elicited on the S_1 stimulated side depressed excitation of the N wave DCR and when SD propagated over the line of the cut, the responses to stimulation of S_2 were depressed. These both recovered within 3-10 min as expected. GABA placed over the line of the cut had no effect on N wave DCR transmission, but it reversibly blocked SD transmission. The depression of axonal excitation of the N wave DCR by SD is consistent with an extracellular release of some neuronal depressive agent. A depressive agent is also indicated by the reversible block of Betz cells during SD. These units were extracellularly recorded by microelectrodes at levels in the cortex between 1000-2000 μ. The units showed a short latency on pes peduncular stimulation and a refractoriness with paired responses expected of an antidromic response. SD blocked Betz cell responses soon after the N wave DCR recorded at the surface was depressed.

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IN VITRO INSULIN PRODUCTION OF THE PANCREAS. Y. Idezuki*, J.A. Feemster*, R.H. Dietzman*, F.C. Goetz*, and R.C. Lillehei. University of Minnesota Medical School, Minneapolis, Minnesota.

In the preserved pancreas, in vitro secretion of insulin was studied using a modified perfusion technique developed by Long. In 30 dogs the pancreas and attached duodenum were resected with the celiac axis and portal vein. After washout with Ringer's solution, the pancreaticoduodenal (P-D) grafts were stored at 2°C and 3 atmospheres of O_2 for up to 48 hours. At varying times P-D grafts were removed and perfused with a blood-Ringer's mixture (38°C, Ht, 26-32%, Flow Rate, 12-40 ml per minute). The islet cells were stimulated by adding 500 mg/l of glucose to the perfusate. Samples taken from the portal venous drainage were used for insulin determinations by radio-immunoassay (Goetz-Greenberg), and for oxygen consumption. All P-D grafts preserved up to 6 hours responded to this stimulation by an average increase of insulin of 46% (range, 152% to 720%); four of the six 24 hour preserved P-D grafts also responded, but none of the 48-hour preserved P-D grafts responded. These in vitro results correspond with the fact that a pancreatectomized dog which received a 22-hour preserved P-D allograft is still alive with a good functioning of the graft after 3 months. Rejection is being suppressed by azathioprene. In vitro productivity of insulin in response to glucose stimulation is a reliable means to predict the functional ability of preserved pancreas.

(Supported by United States Public Health Service.)

ATP-ADP EXCHANGE AND FRAGMENTED SARCOPLASMIC RETICULUM. G. Inesi*, J. Almendares* and S. Watanabe. University of California, San Francisco Medical Center, San Francisco, Calif.

A very rapid (4-5μmoles/min/mg/prot) ^{14}C, ADP-ATP exchange is catalyzed by fragmented sarcoplasmic reticulum. The activity is retained by the membrane fragments after several washings with water or ATP-Mg(mM). The exchange reaction is calcium dependent and the calcium concentration required for half maximal activities of exchange reaction, calcium uptake and "extra" ATP splitting are very close. Aging of the preparation produces a parallel decay in the three forementioned activities, while calcium independent ATPase is more stable. Treatment of the membranes with diethylether produces a slight decrease in the exchange rate, while calcium uptake is completely inhibited and calcium dependent ATP hydrolysis greatly enhanced. In the presence of oxalate, the initial rates (30 sec. speed) of calcium uptake and "extra" ATP splitting are markedly increased, while the initial rate of exchange is not significantly changed. In the absence of oxalate, however, the exchange proceeds for a longer time due to a slower reduction of the calcium concentration in the medium. The results suggest a transphosphorylation occurring on the outer surface of the membrane as the first step in the process of calcium uptake. (AHA 66 742, NSF GB 4754, USPHS HE 09878, USPHS GM 14076)

DUAL EFFECT OF ACETYLCHOLINE ON BIVALVE HEART. Hiroshi Irisawa, Norikazu Shigeto and Issei Seyama (intr. by Y. Kuno). Dept. of Physiology, School of Med., Hiroshima Univ., Hiroshima, JAPAN.

Since the classical studies of Prosser and Welsh, it is well known that most molluscan hearts are inhibited by acetylcholine but some are excitated especially at higher concentrations. An example of such excitatory effect of acetylcholine on the molluscan heart was found in mytilidae, while that of inhibitory effect was observed in oysters. The mechanism responsible for this pharmacological difference of acetylcholine on the heart of these two closely related bivalves was studied by the ultramicroelectrode technique. No significant difference in resting potential was observed between these two heart muscles. Both myocardiums continue to excite within sodium free artificial sea water. When acetylcholine was administered, the membrane potential of the mytilus heart was depolarized and the frequency of the spontaneous cardiac cycles was increased. On the contrary, in the oyster heart the membrane resting potential was hyperpolarized and spontaneous activity ceased. In sodium free solutions, the mytilus heart was inhibited by acetylcholine, while in the oyster heart inhibition was observed as in normal sea water solution. Inhibition in the oyster heart was blocked when Cl^- ions of artificial sea water were removed and replaced by Na_2SO_4. Excitation in the mytilus heart is probably caused by increased permeability of Na ions, while inhibition in the oyster heart may due to increased permeability of Cl^- ions. (Supported by PHS grant HE 06968).

A FASTER METHOD FOR DETERMINING PLASMA LIPOPROTEINS BY PAPER ELECTROPHORESIS. Ericson J. Isles* and Harry Y. C. Wong. Dept. of Physiol., Howard Univ. Col. of Med., Washington, D. C.

According to the Oil Red O method by Beckman Tech. Bull.RC-TB-001B (1965) using the Spinco Model R electrophoresis system, it takes almost two days to determine plasma or serum lipoproteins. Since we had to analyze as many as 100-150 blood samples weekly for total cholesterol and other blood lipids as well as the lipoprotein fractions, a study was undertaken to determine whether a faster and reliable method could be developed. In the course of our study, it was found that the time could be reduced by almost 17-19 hours with reliable results when compared to the method by Beckman. Our modification of this method is to allow the separation in the electrophoresis cells to proceed for 3 hours and staining of the strips in the Oil Red O dye solution overnight. The method according to Beckman is to allow separation in the electrophoresis cell for 16 hours and placing of strips in the dye for 18-20 hours. Data will be presented showing the results obtained by our method as compared to Beckman's method.

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ELECTRICAL ACTIVITY IN THE NERVOUS SYSTEM OF APLYSIA MEDIATED BY THE EYE. Jon W. Jacklet (intr. by Felix Strumwasser). California Institute of Technology, Pasadena, California.

The study of identifiable neurons in the nervous system of Aplysia has contributed to our knowledge of the system and the interactions between neurons. It is of importance to relate the animal's behavior to our knowledge of the nervous system. One approach is to study the influence of light, mediated by the eye, on the nervous system. It is known that light influences the general locomotory activity of the animal and that prior photoperiod is important in modulating the endogenous activity of specific neurons (Strumwasser, 1965). The eye is situated anterior to the rhinophore and connected to the cerebral ganglion by the optic nerve. Silver stained sections show the cup-shaped eye is 600 μ in diameter and has a receptor density of about 7000/mm^2. Electrical recording with suction electrodes on the isolated eye and optic nerve show a corneal negative ERG followed by an "on" response in the optic nerve. The train of action potentials in the optic nerve is sustained until cessation of illumination. The latency of the ERG is 0.4 sec at 10°C, varies inversely with temperature and has a Q_{10} of 2 over 10-20°C. A preparation of the eye and optic nerve intact to the central ganglia (cerebral, pedals, pleurals, and parieto-visceral) enables intracellular recording of potentials in specific neurons while stimulating the eye with light. Such recording indicates that the paired anterior giant cells of the cerebral ganglion and the giant cells of the left pleural and parieto-visceral ganglia do not receive synaptic input as a consequence of light stimulation of the eye. Preliminary recording from cell 3 (parabolic burster) of the parieto-visceral ganglion suggests that light modulates the spontaneous synaptic input impinging on cell 3 from the right connective. Supported by PHS Fellowship 1F2NB35,411-01 NSRB and U.S. Air Force Contract 49(638)-1447.

CONSTRICTION OF NASAL BLOOD VESSELS BY PROSTAGLANDINS. Richard T. Jackson and Russell Stovall*. Emory Univ. Med. School, Atlanta, Ga.

A rhinometric technique was used to measure the changes in the blood flow in the dog's nasal mucosa. Four forms of prostaglandin (PGE_1, PGE_2, PGA and $PGF_{1\alpha}$) were compared to epinephrine, norepinephrine and papaverine. The drugs were introduced into the carotid artery in pentobarbital-anesthetized dogs. All the PG's induced a constriction of the blood vessels of the nasal mucosa. The two PGE forms were equipotent to epinephrine but their duration of action was more than seven times as long. The response to PG seemed to have little effect on subsequent responses to epinephrine. Also, the response to PG seemed little affected by prior treatment with vasodilators such as papaverine or aminophylline. The threshold dose of PGE was near $1x10^{-6}$ mg/kg; within the limits of sensitivity to PGE in other preparations. Commonly, the lower doses of PGE induced a nasal response without a corresponding change in blood pressure.

REACTION OF THE GUINEA PIG'S ILEUM TO BLOOD OF PATIENTS WITH DUODENAL ULCER. N.C. Jefferson, A. Geisel*, and H. Necheles. Michael Reese Hospital and Medical Center, Chicago, Ill.

We have investigated the effect of small amounts of heparinized blood (1 ml) from patients with active duodenal ulcer on the isolated conventional strip of guinea pig ileum. The criteria for positive results were the length of the latent period and the height of contraction of the ileum. Blood from normal controls and from patients with other diseases was also used. The results indicate that there is a distinct shift to the left in cases with active duodenal ulcer, namely, a shorter latent period and a greater height of contraction of the strip of guinea pig ileum.

Supported by U.S.P.H. AM6078-05.

RESPIRATORY PATTERNS IN THE UNANAESTHETIZED DOG BREATHING VARIOUS MIXTURES OF OXYGEN AND CARBON DIOXIDE IN COOL AND WARM ROOMS. Donald B. Jennings and David Macklin*, Department of Physiology, Queen's University, Kingston, Ontario, Canada.

Seven dogs were prepared with chronic tracheostomies for placement of endotracheal tubes and with carotid loops for placement of arterial catheters. Studies were carried out both at rest and while exercising at one mile per hour on the treadmill in either a cool room (19-23°C) or a warm room (27-32°C). The dogs breathed through a high resistance Ambu two-way valve. In resting dogs breathing room air in a cool room, repeated measurements showed that the relation between respiratory frequency and ventilation was sigmoidal with a mean respiratory frequency of 15 breaths per minute when the mean ventilation was 2.9 litres per minute and with a mean frequency of 276 breaths per minute when the mean ventilation was 27.5 litres per minute. This fundamental relation was shifted to the right slightly by breathing low oxygen or by exercising, and more markedly by breathing 5% carbon dioxide. In a warm room the patterns established in the cool room were shifted to the left. Respiratory frequency at rest when breathing room air was related to the rectal temperature. Thus the respiratory frequency response of the animal to a change in the inspired oxygen or carbon dioxide mixture depended upon the initial frequency-ventilation relation. Physiological dead space in the dog breathing room air was related not only to the tidal volume but increased to a maximum for any given tidal volume when the dog changed from a low respiratory frequency to a frequency greater than 50-60 breaths per minute.

(Supported by the Defence Research Board of Canada and the Ontario Heart Foundation)

THE RELATIONSHIP BETWEEN LEFT ATRIAL PRESSURE AND PLASMA ADH LEVELS IN THE DOG. J. A. Johnson*, W. W. Moore and W. E. Segar*. Depts. of Physiol. and Peds., Ind. Univ. Med. Ctr., Indianapolis, Ind.

Acute studies were conducted on thirteen pentobarbital-anesthetized dogs to determine the effect of small changes in left atrial pressure (LAP) on plasma ADH levels. LAP was increased by inflating a balloon inserted into the left atrial appendage three hours after completion of surgery. Peripheral arterial plasma ADH concentrations were determined by bioassay in the ethanol-anesthetized rat after extraction and concentration of the hormone. No significant changes in P_{osm}, C_{cr}, C_{pah}, C_{osm}, or mean arterial blood pressure were observed following balloon inflation. The plasma ADH level (% control) decreased linearly ($b = -5.46 \pm 1.09$) with increasing LAP between zero and 7 cm of H_2O. As the plasma ADH levels decreased significant increases (% control) in urine volume and CH_2O and a decrease (% control) in U_{osm}/P_{osm} were observed. These findings lend strong support to the concept that the left atrial "volume-sensitive" stretch receptors play a substantial functional role in the regulation of ADH secretion and the control of water balance.

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A Study of the Development of Fatigue and Pain in Working, Ischemic Muscles of the Human Forearm. D.S. Jones and J.M. Colletti (intr. by A.C. Higginbotham) Loyola U., Chicago and W. Va. University.

The ischemia was produced by a sphygmomanometer on the arm inflated to a pressure of 240 mm of mercury. Work was performed by squeezing an ergometer once persecond and was recorded with an ink writing Grass polygraph. It was considered to be the beginning of fatigue when the person could no longer displace the ink writer 2 cm against a standard resistance. Complete fatigue was the inability to move the ink-writer. Each of one hundred persons tested worked until completely fatigued or until pain was severe. Each person was tested without vascular compression, with compression immediately before work, and with compression seven minutes before work began. Beginning fatigue in the normal developed in about two minutes, average, with a range between 18 and 620 seconds. Fatigue with compression developed in about 40 seconds, average, with a range between 7 and 100 seconds. Pain in the ischemic muscle developed in about one minute, average, with a range between 30 and 123 seconds. Pain almost always followed fatigue. The most interesting aspect was that nine of the hundred individuals progressed to complete fatigue with no pain. Vascular compression seven minutes prior to working caused no significant difference in the occurrence of fatigue or pain.

EFFECTS OF VMH LESIONS IN NEWBORN GUINEA PIGS. Shirley A. Joseph* and Karl M. Knigge. Univ. of Rochester School of Med., Rochester, New York.

Lesions were placed in the ventromedial nucleus of the hypothalamus (VMH) in both male and female guinea pigs at 1-2 days of age and the animals sacrificed between the 72nd and 75th post-operative day. No significant deficit in the rate of growth or differences in body weight were observed in the lesioned pigs, when compared to controls. Organ weights and histology of pituitary, thyroid and testes were unaffected by VMH lesions. The pituitary-adrenal response to ether stress of the lesioned males, as measured by plasma cortisol levels, was significantly greater than that of controls. This finding may suggest that VMH normally participates in a dampening or restraining action on acute ACTH release. On the basis of ovarian histology, control female pigs had ovulated at least once by the 75th day. The ovaries of lesioned females were however devoid of corpora lutea and exhibited a notable shift in follicular population; the ovaries contained vesicular follicles normally seen prior to the ovulating surge of LH release. From these observations it is suggested that early VMH destruction in the guinea pig may either impair the maturation or produce a permanent deficit in the neural mechanism for release of the pituitary LH associated with ovulation.

SENSITIVITY OF SPIKE OVERSHOOT IN APLYSIA GIANT NEURONS TO TETRODOTOXIN, COBALT, AND TEA. Douglas Junge and Donald Geduldig (intr. by Theodore Enns). Scripps Institution of Oceanography, U.C.S.D., La Jolla, Calif.

Action potentials evoked by direct intracellular stimulation were studied in the exposed giant (R_2) cell in the visceral ganglion of Aplysia californica. The spike overshoot was reduced about the same amount (20 mV) by application of 3×10^{-5} M tetrodotoxin (TTX) as by complete replacement of external sodium with tris or sucrose. (In the "Na-free" or "Ca-free" solutions tested, all other ions were present in normal concentrations.) In Na-free solution, 3×10^{-5} M TTX did not significantly affect the reduced spike, which has been shown to depend on calcium. In Ca-free solution, however, 3×10^{-5} M TTX reduced the spike to a small transient depolarization. These results indicate that TTX blocks only the Na^+ component of the spike. Application of 30 mM $CoCl_2$ in normal saline caused little or no reduction in overshoot, as was the case with complete replacement of external Ca^{++}. Cobalt had no effect on the spike in Ca-free solution, which is known to be Na-dependent. However, 30 mM $CoCl_2$ applied in Na-free solution resulted in complete blockage. Apparently, cobalt blocks only the Ca^{++} component of the spike. The ability to selectively interfere with the Na^+ and Ca^{++} components of the spike suggests that these ions may pass through functionally separate channels in the membrane. In 4/5 x normal Na and in Na-free solution, 100 mM TEA prolonged the spike up to 200 msec, but had very little effect on overshoot. The effects of all agents tested were reversible upon washing with normal saline.

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GUANINE NUCLEOTIDE PROTECTION AGAINST ISOPROTERENOL TOXICITY. John Kabal* and E. R. Ramey. Department of Physiology and Biophysics, Georgetown Medical Center, Washington, D.C.

Isoproterenol (40 mg/Kg S.C.) produces cardiac edema in rats. The cardiac index (heart weight/gm body weight) is elevated from 362 ± 18 in controls to 526 ± 29 in drug treated rats. Seven days pretreatment with 15 mg/Kg guanylic acid daily significantly reduced the damaging effect of Isoproterenol on the myocardium (cardiac index was 465 ± 21). Adenylic acid did not have this protective effect. Bilateral tourniquet application results in 100% mortality with a survival time to 3.2 ± 0.6 hrs. Pretreatment with guanylic acid plus Isoproterenol and tourniquet extended survival to 5.8 ± 0.9 hrs. Adenylic acid had no effect. It is suggested that guanine nucleotides play a role in maintaining homeostasis during a stress. They may be released normally from involuting lymphatic tissues resulting from the stress induced cortical steroid production. It has been shown that there is increased nucleotide synthesis in the liver during a stress and that blood levels of nucleotides are elevated. Previous work from this laboratory has also shown that guanine nucleotides act to maintain liver glycogen and blood NEFA levels at non-stressed levels even when exogenous adrenaline is administered. It is possible that the mechanism of this action is related to increased RNA and protein synthesis due to increased guanine nucleotides.

CYCLIC CHANGES IN THE INTRACELLULAR REDOX STATE IN THE TURTLE HEART. K.J. Kako and M. Chapman*. Department of Physiology, University of Ottawa, Ottawa, Ontario, Canada.

A minute change in the phosphate potential that is produced by the contractile activity of the heart muscle results in changes in the redox state of NAD in the cell compartments. The free $(NAD^+)/(NADH)$ ratios of cytoplasma and mitochondria were determined by the fluorometric assays of several pairs of metabolites of the NAD-linked dehydrogenase systems. The tissue extract was prepared from the heart of turtles, chrysemys picta, frozen in situ during various phases of the cardiac cycle. The ratio of the total $(NAD^+)/(NADH)$ changed cyclically, showing its peak at the R wave (ECG) and its lowest value at around 0.6 sec after the R(cardiac cycle=2 sec). The cytoplasmic $(NAD^+)/(NADH)$, as indicated by the (pyruvate)/(lactate) ratio, was out of phase by 180-270 degrees, compared to the above change. The change in the ratio, (dihydroxyacetone phosphate(P))/(glycerol-1-P) was also 180 degrees out of phase. A similar but less marked cycle, out of phase 90-180 degrees in comparison to the $(NAD^+)/(NADH)$ cycle, existed with regard to the levels of malate, glucose-6-P and ATP, and the ratios (glutamate)/(oxoglutarate) and (ATP)(creatine)/(ADP)(creatine P). In contrast, no noticeable difference was observed in the ratio $(NADP^+)/(NADPH)$ and in the level of ADP and AMP among the samples taken at various points of the cardiac cycle. The results of this study indicate that the redox potential of the myocardium fluctuates cyclically together with the contractile activity and that the redox states in the cytoplasmic and mitochondrial spaces do not necessarily move in parallel during the cardiac cycle.

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THE EFFECT OF PROTEOLYTIC ENZYMES AND SOME PROTEIN DENATURING AGENTS ON MYOSINS OF NORMAL AND DYSTROPHIC EXPERIMENTAL ANIMALS.[1] G. Kaldor[2], L. Kuo* and M. DiGiovanni*. Dept. of Physiology & Biophysics, Woman's Med. Coll. of Pa., Philadelphia, Pa.

Myosin A and myosin B extracted from chickens afflicted with genetically controlled muscular dystrophy and also from rats two weeks after the dissection of the ischiadic nerve were investigated. The number of peptide bonds hydrolyzed in the neutral pH range by trypsin, pronase and carboxypeptidase A was studied by pH-stat measurements. The results showed no significant difference between the dystrophic myosins and their normal controls. 1 M urea increased, 30-40% ethylene glycol decreased the speed of trypsin digestion with dystrophic and normal myosins almost equally. Superprecipitation was studied by the turbidity increase method. Five out of seven dystrophic chicken myosin B preparations and the two myofibrillar suspensions studied showed a slower and smaller turbidity increase than their respective controls under otherwise identical conditions. Forty percent of the rat myosin B preparations investigated gave similar results. Mg^{++} and Ca^{++} gave qualitatively similar effects with both myosin B-s. Interaction inhibitors like EDTA, polyethylene sulphonate and also low concentrations of urea exerted similar depressing effects on the superprecipitation of both normal and dystrophic myosin B.

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2 NIH Research Career Awardee 1-K3-NB-33

POTASSIUM EXCRETION BY TOAD BLADDER IN VIVO. F.T. Kallus* and John C. Vanatta. Univ. Tex. Southwestern Med. Sch., Dallas, Texas.

Leaf (J. Gen. Physiol., 41:661, 1958) reported urine K concentrations greater than plasma K concentrations in Bufo marinus. Studies to determine the role of the bladder in this concentration of K have been undertaken. In vivo studies of toads subjected to a KCl load sufficient to yield plasma K levels of 4.5 meq/l or greater have been done by isolating the bladder surgically in 1 of 3 basic techniques: ligating a portion of the bladder to create a blind sac; creating a blind sac with an indwelling catheter; or suturing the bladder orifice creating a closed bladder. Measured volumes of regular Ringer's solution (3.0 meq/l K) were instilled into the bladder preparation after prior rinsing and emptying. Samples were taken after 24 to 120 hr and K concentrations determined. In 36 experiments, the range of final concentrations was 0.9 to 62.2 meq/l. Only 2 samples were below 3.0 meq/l, and 10 were above 12.0 meq/l. These concentrations could not be explained by observed volume changes. Subsequently 12 experiments using C^{14}-inulin to evaluate water movements were done. All 12 showed K concentration increases greater than could be explained by water movements. Six of these showed K concentrations in the bladder sample to be higher than plasma K concentration at the time of sampling. Whether this K concentration is due to Na-K exchange or a primary K pump is not apparent at this time. Preliminary data indicate that it is dependent on the presence of Na in the bladder lumen. (Supported by PHS grant HE-01574-13 and GM-34 243-01.)

EVALUATION OF MYOCARDIAL FUNCTION IN ATRIAL FIBRILLATION. M. H. Keelan*, J. T. Botticelli* and R. L. Lange, Dept. of Med., Marquette Univ. Sch. of Med., Milwaukee, Wisc.

The irregular rhythm of atrial fibrillation (AF) precludes steady state observation of rate of tension or pressure generation, duration of contraction and heterometric response. The arterial pressure in AF constantly displays left ventricular output as diastolic filling and aortic diastolic pressure is varied. If the increase in stroke volume (and pulse pressure) with prolongation of previous R-R interval implies normal left ventricular function as in AF due to valvular heart disease (VHD-AF), then primary myocardial dysfunction (PMD-AF) may be deduced from a reduced augmentation of stroke volume as R-R interval is increased. Two variables were plotted against the previous R-R interval: 1) pulse pressure (PP); 2) systolic pressure change from previous systolic pressure (ΔSP). The latter is a function of the previous pressure generation, rate of diastolic pressure drop and PP. Aortic femoral or brachial artery pulses (20 to 50) were examined consecutively during prolonged expiratory pauses in 11 patients with VHD-AF and eight patients with PMD-AF, diagnosed by cardiac catheterization, surgery or necropsy. The mean regression of PP with R-R interval (0.5 to 1.2 sec.) was +54.4 mm Hg/sec. in VHD-AF but was significantly lower in PMD-AF (+27.1), $p < 0.01$, inferring reduced heterometric response. With R-R intervals from 0.5 to 1.2 sec., regression ΔSP was +26.8 mm Hg/sec. in VHD-AF. In striking contrast, regression ΔSP became negative with increasing R-R interval in PMD-AF. The mean ΔSP regression in PMD-AF was -3.8 mm Hg/sec., $p < 0.001$, because ventricular ejection was inadequate to overcome the lower diastolic pressure of long diastole. Heart rate, cardiac output and peripheral vascular resistance were similar in both groups. We suggest that this analysis allows evaluation of myocardial function in AF when other methods are not applicable.

PRODUCTION OF ANTIBODIES AGAINST ERYTHROPOIETIN. G. Keighley, P.H. Lowy°, J.C. McCune°, N.S. Magnuson°, M. Rouklove°, M.G. Keighley°, and B.G. Sanders°. California Institute of Technology, Pasadena, Calif.

Antibodies against human urinary erythropoietin can be produced in rabbits (J.C. Schooley and J.F. Garcia, Proc. Exp. Biol. Med. 109, 325. 1962) but many of the injected rabbits produce no detectable antibody. Precipitin tests are unreliable, antibodies have to be detected by inhibition of exogenous erythropoietin or suppression of erythropoiesis. As these tests take several days it is difficult to bleed an animal at the right time. We sought an indirect but quick way of deciding which few of the many rabbits injected are producing antibodies. We have injected initially 150-300 units of erythropoietin, S.Q. with Freund's complete adjuvant in 5 doses on alternate days, and at intervals of 4-5 weeks 50 unit boosters I.V. in 4 doses. While injecting and after we make daily reticulocyte counts. The normal range is 1.0-2.5%. A count less than 1.0% in a rabbit is a reliable sign that it is producing antibodies. Out of 25 sets of initial or booster injections, in 18, reticulocyte counts were normal with no antibody detected, in 6 counts were low and antibody was high. In only one case was there a normal count with antibody production (the count fell 3 days later). The hematocrit is not a reliable indicator. It is possible to maintain productive rabbits and bleed them repeatedly. At times such rabbits may develop high (5% or over) reticulocyte counts and the antibody titre drops. It may be that the rabbits' erythropoietin cross reacts to the antibody and the incipient anemia initiates a wave of erythropoietin production. We are investigating this and other possibilities. Antibodies produced are of the γG variety. Supported by PHS HE 07683 and AEC AT(04-3)-642.

MYO-ELECTRIC POTENTIALS OF THE STOMACH. Keith A. Kelly* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The objective of this experiment was to define the patterns of electric activity in the smooth muscle of the stomach by simultaneously recording from sites over the entire organ during fasting, feeding, distention with a balloon, and stimulation by insulin hypoglycemia in healthy, unanesthetized dogs. Eight detecting electrodes were implanted on the anterior serosal surface of the stomach of 6 dogs at regular intervals from the fundus to the pylorus. With the animals lying quietly, recordings were made 2 weeks after operation and periodically during 3 or more months. Simultaneous intraluminal pressure determinations and cinefluorographic observations also were sometimes accomplished. A regular, rhythmic, triphasic, electric complex (BER) originated in the orad corpus and was propagated from there to the pylorus. Velocity of propagation and amplitude increased as the electric wave approached the pylorus. A burst of spike or action potentials was superimposed on the BER when contractions were recorded. In fasting animals, the mean frequency of the BER was 5.4/min. The frequency decreased after meals of water and after balloon distention but remained the same after fatty meals and after insulin hypoglycemia. Propagation of the BER between corporeal electrodes during fasting required 7.6 sec (mean). This period lengthened after distention and meals of water and fat, but shortened after insulin hypoglycemia. The mean ratio of spikes to BER for fasting animals was 0.32. This ratio increased after hydrous meals, distention, and insulin hypoglycemia, but was smaller after fatty meals. (Supported in part by NIH Grant AM-2015.)

PRESSURE-INDUCED HOMEOMETRIC AUTOREGULATION OF THE HYPOTHERMIC HEART. Kenneth M. Kent,* E.C. Peirce II, W.E. Goetter,* and S.H. Sinclair.* Depts. of Physiology and Surgery, Emory Univ. Sch. Med., Atlanta, Ga.

Cardiac deterioration of large non-hibernating mammals in hypothermia is well documented. To elucidate this deterioration, the control mechanisms of the hypothermic heart have been studied. Small increases in heart rate, by pacing, improve ventricular function in hypothermia (S.H.Sinclair, E.C.Peirce II, K.M. Kent. Fed. Proc. 26:664,1967), suggesting that rate-induced homeometric autoregulation persists at low temperatures. To further investigate the autoregulatory phenomena, cardiovascular studies have been carried out in 20 intact closed-chest dogs at average body temperatures ranging from 25 to 15°C. Uniform cooling was accomplished by a combined immersion and perfusion technique. A partial veno-arterial bypass with a membrane lung and a heat exchanger was used for perfusion cooling. A water spray was used for surface cooling. The arterial pumps for the perfusion circuit were operated as pressure-controlled servo systems and the arterial pressure and carotid sinus pressure of the animal were controlled independently. Aortic flow was measured with a chronically implanted aortic flow probe. The function of the heart was evaluated by ventricular function curves at different afterloads. Increases in aortic pressure shift the ventricular function curves of hypothermic hearts to the left. The control of cardiac function is generally considered to be a balance between neural, hormonal, and autoregulatory. It is postulated that the reduction of neural and hormonal control of the heart in hypothermia increases the importance of the autoregulatory control. The persistance of the autoregulation of the hypothermic heart allows the use of left ventricular outflow resistance to improve cardiac function.

DEPENDENCE OF AMNESTIC EFFECTS UPON LOCUS OF ELECTROCONVULSIVE STIMULATION. Raymond P. Kesner* and Robert W. Doty, Center for Brain Research, University of Rochester, Rochester, New York.

Cats were trained for several days to enter a small compartment for food. They then received a punishing 10-mA mouth-shock while eating in the compartment. All 10 cats used as controls showed great hesitation and increased latency for entering the compartment when tested 24 hr subsequent to such punishment. Through electrodes implanted over temporal cortex 6 other cats were subjected to tonic-clonic convulsions within 4 sec after punishment. None showed hesitation nor change in latency for entering the compartment 24 hr later. Convulsions per se, however, are insufficient to produce amnesia for the punishment, since all cats subjected to tonic-clonic seizures initiated from stimulation of frontal cortex (4 cats), or clonic seizures following mesencephalic stimulation (3 cats), had the same hesitancy and increase in latency as did control animals. On the other hand, amnesia was produced if within 4 sec after punishment electrical seizure activity, recorded in the limbic system, was initiated by stimulation of dorsal hippocampus (8 of 12 cats) or amygdala (4 of 4 cats); but not if initiated from septum (4 of 4 cats) or ventral hippocampus (3 of 3 cats). The electrical seizure activity in the limbic system was in all cases accompanied by various behavioral signs, but never by motor convulsions. Present interpretation is that near normal function in amygdala and perhaps dorsal hippocampus is necessary for fixation of an aversive experience and that seizure activity must engage these areas fully to produce amnesia of punishment. (Supported by USPHS Grants NB 5395 and NB 03606.)

SEPARATION OF LABELLED PROTEIN AND PEPTIDE COMPONENTS IN MOTOR AXONS FOLLOWING INTRACORD INJECTION OF ^{3}H-LEUCINE AND AXOPLASMIC FLOW. A. M. Kidwai* and S. Ochs. Dept. of Physiology, Ind. Univ. Med. Ctr., Indianapolis, Ind.

Following injection of ^{3}H-leucine into cat spinal cords near the motoneurons supplying the lumbar 7 and sacral 1st roots, radioactivity was found in their corresponding ventral roots consistent with an axoplasmic flow. The labelled material was identified as soluble protein by hydrolysis of the TCA precipitate and paper chromatography (Ochs, Johnson and Ng, J. Neurochem. 14: 317, 1967). The same general procedure of injection was followed in the present experiments. Ventral roots were homogenized and centrifuged at 100,000 g for 60 minutes. The supernatant was placed on Sephadex G-100 column. A flow rate of 0.2 ml/min was used and 1 ml fractions collected. The radioactivity was found to be associated with fractions containing protein as shown by the Lowry technique. Ninhydrin color was found associated with the protein containing fractions with a later appearing peak identified as peptide. A small amount of radioactivity was found associated with the peptide fractions. This was the case at times between injection of precursor and removal of the roots of three days or longer. At earlier times there was a relative increase in the activity found present in the peptide fractions. There was evidence of a downflow of incorporated material as early as 6 hours after injection. This is in line with recent studies showing the presence in these fibers of a fast axoplasmic flow, at a rate estimated to be greater than 100 mm per day (Ochs and Johnson, in preparation).

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EFFECT OF α HYDRAZION-HISTIDINE ON THE HISTAMINE FORMING CAPACITY OF THE RAT STOMACH. K. S. Kim, (Intr. by D. F. Magee). Dept. of Pharmacol. George Washington Univ., Washington, D. C.

Alpha-hydrazino-histidine (αHH, MK-785) has been shown to inhibit fetal specific histidine decarboxylase in vitro and to reduce tissue histamine content and urinary histamine excretion in vivo in rats (Levine et al. Biochem. Pharmacol. 14:139, 1965). In view of the possible relationship between histamine and gastric acid secretion, effects of αHH on the histamine forming capacity of the rat stomach (RS-HFC) were studied. Contrary to one's expectation, αHH (100 mg/Kg i.p.) increased RS-HFC approximately 5 times over that of the control (saline i.p. in fasting rats (2 1/2 hr. after treatment). Increased RS-HFC induced by refeeding was not affected by αHH treatment. Increased RS-HFC induced by insulin (5 U/Kg i.p.) was only slightly reduced by αHH administration. These findings suggest that gastric histidine decarboxylase is not inhibited by αHH (100 mg/Kg). This dose of αHH was shown by Levine et al. to decrease histamine content of the stomach and urinary histamine excretion. Further work is required to resolve this discrepancy. αHH also decreased gastric emptying time judging by the gastric content after similar food intake. Rats treated with αHH became very sensitive to insulin, showing prompt hypoglycemic symptoms and died often without convulsions if glucose was withheld. (Supported by USPHS Grant 1 PO1 GM 13749).

SEQUENCE OF PULMONARY FUNCTIONAL CHANGES AFTER GRADUAL PROLONGED HEMORRHAGE. S.I. Kim*, J.M. Desai* and W.C. Shoemaker, Dept. of Surg. Research, Hektoen Institute, Cook County Hospital, Chicago, Illinois.

Sequential changes in arterial (PaO_2) and venous (PvO_2) oxygen tension, CO_2 tension ($PaCO_2$ and $PvCO_2$), Arterial and Venous pH, O_2 consumption ($\dot{V}O_2$) and pulmonary shunting (Qs) were observed on the same series of unanesthetized dogs with the protocol and definition of stages during prolonged hemorrhagic shock described in the companion abstract. The pulmonary changes were measured on a background of hemodynamic measurements. The data expressed as mean and S.E. are:

Stage	A	B	C	D	E	F
PaO_2	73.0±3.4	77.7±4.6	74.3±4.6	64.4±6.2	58.2±19.7	450±21.0*
PvO_2	40.7±2.0	26.2±2.6	35.2±4.2	26.6±3.8	27.6±5.4	52.0±10.1*
$PaCO_2$	35.8±2.6	26.8±3.4	31.5±4.6	25.3±4.7	22.0±1.5	28.0±5.2
$PvCO_2$	41.5±2.7	36.2±3.0	39.1±5.7	32.1±4.7	29.7±5.2	67.1±8.2
Art.pH	7.41±.02	7.22±.02	7.29±.04	7.26±.06	7.30±.04	6.99±.08
Ven.pH	7.35±.02	7.13±.04	7.20±.03	7.29±.06	7.26±.04	6.85±.07
VO_2	162±13	135±18	212±32	265±42	158±23	82±24
O_2Ext.Ratio	23±4	83±7	35±7	42±6	32±9	18±3
Qs(%CO)	16±4	12±3	32±6	28±5	26±5	32±7

* on 100% O_2 ventilation

After an initial increase in $\dot{V}O_2$, there was gradual decrease; the latter was associated with increased CO and low SVR, suggesting peripheral A-V shunting in the late stages. High PVR was associated with low pH and not with high PCO_2. Pulmonary shunting increased markedly in the late stages of half of the experiments. There was also gradual decrease in PaO_2 in stage D and E despite hyperventilation and low $PaCO_2$. During hemorrhage, sighing frequency increased greater than % increase of respiratory rate. The increase of sighing was associated with low venous pH and PvO_2, but not PCO_2.

INTERRELATIONSHIPS BETWEEN RIGHT VENTRICULAR VOLUMES, HEART RATE, STROKE VOLUME, CARDIAC OUTPUT, HEART WEIGHT, BODY WEIGHT, BODY SURFACE AND METABOLIC RATE IN MAMMALS. H. Kines*, E. A. Rhode* and J. P. Holt. Heart Research Lab., Dept. Med., Univ. of Louisville, and Univ. of Calif., Sch. of Vet. Med., Davis, Calif.

Heart rate, R, cardiac output, CO, heart weight, HW, and body weight BW, were determined and right ventricular end-diastolic, EDV, end-systolic, ESV, and stroke volume, S, measured by the indicator-dilution technique in the control state in anesthetized swine, dogs, horses and cattle; and S, R, CO, HW and BW were measured in rabbits. Body surface, BS, and metabolic rate, MR, were calculated from BW. HW, expressed as percent of body weight, varied from 0.19 (rabbit) to 0.83 (dog), and the relationships between the various cardiovascular parameters to HW showed less scatter than the relationships to BW. In the following relationships the correlation coefficient, r, was better than 0.96: $S = 0.22\ HW^{0.99}$; $R = 379\ HW^{-0.27}$; $CO = 158\ BW^{0.81} = 84\ HW^{0.72}$; $CO = 1.6\ MR^{1.08}$; $EDV = 0.88\ HW^{0.91}$. The relationship between ESV and EDV was described by the equation: ESV = 0.57 EDV, with one standard error of the slope of ± 4%. BW is in kg; MR is in Kcal/day; other dimensions are ml, gm, ml/min, and beats/min. Our results in mammals varying 364 fold in BW were in good agreement with data from the literature relating HW and R to BW over a much larger range of mammals. From the data in the literature and the results of our studies it is suggested that for all mammals the relationships of the following cardiovascular parameters to body weight are described by the equations: $MR = 70\ BW^{0.75}$, $HW = 4.4\ BW^{1.0}$, $S = 1.1\ BW^{1.0}$, $R = 203\ BW^{-0.25}$, $CO = 223\ BW^{0.75}$, $EDV = 2.3\ BW^{1.0}$, $ESV = 1.2\ BW^{1.0}$.

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CHRONIC MONITORING OF CHANGES IN MYOCARDIAL FORCE-VELOCITY RELATIONSHIPS IN AWAKE DOGS. Rose M. King* and Eleanor Ison-Franklin, College of Medicine, Howard University, Washington, D. C.

Semi-continuous observations were made on the simultaneous changes in aortic and ventricular pressures, heart rate, left ventricular circumference (LVC) and left ventricular force-velocity (FV) relations in 16 normal, awake dogs. Average heart rates (105 + 30) and mean aortic pressures (92.4 + 17.5 mmHg) were similar to those reported for trained dogs. Changes in FV relations of the ventricular myocardium were measured by determining the initial velocity of shortening of the LVC during ejection and the simultaneous left ventricular pressure as an index of myocardial force. According to criteria already established for changes in FV relations, predictable responses to steady-state infusions of known inotropic (nor-epinephrine or NE, isoproterenol) and pressor (methoxamine HCl, angiotensin) drugs were observed (Hefner et al, Circ. Res. 11:654, 1962; Fry et al, Circ. Res. 14: 73, 1964; Sonnenblick, Circ. Res. 16: 441, 1965; Glick et al, J. Clin. Invest. 44: 978, 1965). Shifts in the FV relations in response to NE, isoproterenol and methoxamine were found to agree with those reported by others using cinefluorographic and dilution techniques. FV responses to angiotensin indicate that this substance has no apparent inotropic effect upon the heart. Experiments of this type provide the opportunity to study progressive adjustments in cardiac performance during the course of long term effects of experimental interventions. (Supported in part by NHI grant #H-01015-14 and in part by NIH GRS grant #FR5361-05)

CAPILLARY DENSITY: EFFECT ON EXTRACTION OF POTASSIUM - 42 (K^{42}) FROM CORONARY BLOOD. Edward S. Kirk (intr. by J. S. Willis). Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

The role of changing numbers of open capillaries has been well established for skeletal muscle, both by functional and histological criteria. This report presents similar evidence for myocardial capillaries. In anesthetized dogs variations in K^{42} extraction by the coronary circulation perfused at constant flow was used to indicate changes in the functional capillary bed. Vasoconstriction caused by coronary arterial injections of vasopressin reduced K^{42} extraction while vasodilation caused by hypoxia or by injections of nitroglycerine or papaverine increased K^{42} extraction. The fact that K^{42} extraction by the heart can be altered with coronary flow held constant casts serious doubts on measurements of coronary blood flow based on the myocardial clearance of rubidium isotopes. These changes in blood-tissue exchange of K^{42} probably correspond to changes in the number of open capillaries which are caused by opening and closing of precapillary sphinctors. This interpretation is supported by counts of stained red blood cells in sections of rat myocardium. Hearts removed and rapidly fixed immediately after injecting vasopressin showed a decreased number of red blood cells in the terminal vasculature compared to controls. Hypoxia and nitroglycerine caused increases. A picture of a dynamic coronary microcirculation is suggested in which the number of open capillaries varies in response to the same stimuli which modify resistance to flow. (Supported by NIH Grants HE-08658 and HE-10788)

DESCRIPTION AND EVALUATION OF AN ON-LINE OXYGEN UPTAKE COMPUTER. Abbott T. Kissen and Donald W. McGuire.* Biomed. Lab., Aerospace Med. Res. Labs., AMD, AFSC, Wright-Patterson AFB, Ohio.

Research programs conducted at our laboratory evoke variable degrees of test subject isolation relative to monitoring equipment and personnel. Difficulties pertaining to test subject accessibility generally preclude determinations of oxygen uptake by conventional techniques. These circumstances have stimulated efforts leading to the development of the OCC-2500, an on-line, remotely monitored oxygen uptake computer. The OCC-2500 is an electronic instrument which includes a mask-sensor assembly and a special purpose analog computer. Intended for the analysis of respiratory gases in human subjects, the device produces a real-time analog voltage proportional to the oxygen uptake in one minute or other time periods as determined by the operator. It utilizes two pO_2 polarographic sensors (to obtain the ambient-exhaled air pO_2 differential) and a mass gas flowmeter. For the evaluation study described, the mask-sensor assembly was modified so that the output of the OCC-2500 computer was synchronous with the collection of expired air samples in a gasometer. Samples drawn from the gasometer were analyzed by gas chromatography. Appropriate statistical correlation analysis procedures were then applied to the OCC-2500 computer output and date derived from the conventional oxygen consumption determination technique. Oxygen uptake values (200-3200 cc/min) obtained from 15 subjects (297 observations) during rest and exercise, produced a sample correlation coefficient of 0.998. Subject mobility is virtually unrestrained since the only attachments to monitoring equipment consists of electrical leads. Personnel support requirements are significantly reduced. The compactness of the sensor package and recently demonstrated signal telemetry feasibility permit its application in unusual experimental situations such as pressure suit and underwater studies.

Pulmonary Hypertension and Left Ventricular Atrophy in Dogs with Spontaneous Cor Pulmonale. **D.H. Knight (intr. by D.K. Detweiler). Compara. Cardiovasc. Studies Unit, Sch.Vet.Med., Univ. Penn., Phila., Pa.**

Pathological reports of biventricular hypertrophy in human patients with various forms of cor pulmonale have challenged the traditional concept of isolated right ventricular (RV) hypertrophy in response to pulmonary hypertension. Chronic heartworm infestation produces severe obstructive pulmonary endarteritis (OPE) in the dog leading to pulmonary hypertension, RV hypertrophy and eventually right-sided congestive heart failure (R-CHF). Four dogs with various degrees of OPE but not in R-CHF were exercised on a horizontal treadmill. Left atrial pressure was measured in 3 dogs and did not change remarkably. Exercise was accompanied by the greatest increase in pulmonary arterial pressure (PAP) in the dogs with the highest PAP at rest. In one, the PAP rose from 30 to 75 mm Hg during exercise sufficient to induce a 3-fold increase in pulmonary blood flow (dye dilution technique). Other dogs in R-CHF had PAP's of 60-80 mm Hg under anesthesia. From gross morphologic studies of 21 dogs in various clinical stages of infestation, the left ventricles (LV) were on the average lighter ($P < 0.001$) and in 6 cases fell below the 95% standard error of estimate limits for the relationship of LV weight to body weight in 299 normal dogs. Five of the 6 were in clinical R-CHF. These findings suggest that in this disease increased pulmonary vascular resistance becomes an important factor limiting the increase in RV output during exercise and in the most hypertensive cases even preventing the RV from consistently sustaining a normal output at rest. The LV output is diminished correspondingly, thereby reducing its customary workload. The observation of LV atrophy in the more severely affected dogs further supports this concept.
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DYNAMIC PROPERTIES OF BARNACLE MUSCLE FIBERS DURING SINUSOIDAL STRETCH
M. Kobayashi* and G. Hoyle. Dept. of Biology, Univ. of Oregon, Eugene.

The viscosity and elasticity of single giant muscle fibers of the barnacle, B. nubilus, were studied by recording the length-tension and the velocity-tension figures simultaneously during sinusoidal stretching. In contrast with fast frog muscles the barnacle fibers show graded contractions, not all-or-nothing ones. The work done by the muscle fiber, which is represented by the area of the length-tension figure, could be gradually increased by increasing either frequency or voltage of stimulation at constant pulse duration. When the duration was increased the work rose steeply and reached a plateau at about 3 msec. No further work was done even at stimulus durations beyond 10 msec, which gave rise to further increase in the maximum tension. Viscous and elastic resistance of the muscle changed nearly exactly in parallel at durations up to 10 msec, but only elastic resistance increased beyond that duration. The effect of stretch frequencies of 0.1-10 c/s on the muscle properties was considerably different between passive and tetanized muscles. With passive muscle, both viscous and elastic resistance increased remarkably at the higher frequencies. In tetanized muscle, however, there were no significant changes in elasticity and viscosity with increasing frequency of stretch. These results suggest that the passive muscle fiber is partially activated by stretch. Muscle fibers stretched to twice their original length could still contract vigorously. At this length the elastic resistance increased much more than the viscous resistance, so that the phase difference between length and tension became smaller. This could be explained by an effectively long series elastic component within the sarcomeres which changes with stimulation. Supported by PHS NB 03819-05 to G. Hoyle.

ESTIMATION OF EXTRACELLULAR FLUID VOLUME BY USE OF SUCROSE IN PIG-TAILED MONKEYS.
A. M. Kodama*, N. Pace and R. S. Gilfillan*, Department of Physiology, University of California, Berkeley.

A study was undertaken to determine the feasibility of using the distribution volume of sucrose following intravenous injection of a single dose of sucrose-C^{14} as a measure of extracellular fluid volume in the pig-tailed monkey *(Macaca nemestrina)*. A problem associated with the use of sucrose to estimate the extracellular fluid compartment is its rapid excretion from the animal by way of the kidneys, and the positive identification of this loss component in the plasma disappearance curve of injected sucrose. It has been possible to follow the plasma disappearance and urinary excretion of sucrose-C^{14} simultaneously in several monkeys with permanently implanted vascular and ureteral catheters. Typically, the plasma disappearance curves showed a fast mixing component with half-times of 15-25 minutes and a major component with half-times which ranged from 70-155 minutes. The urinary excretion curves showed a single component with half-times which agreed within 10% of that found for the major component of the corresponding plasma disappearance curves. The results indicate that extrapolation of the major component of the plasma disappearance curve should provide a reasonable zero time or "equilibrium" concentration of sucrose for use in the calculation of extracellular fluid volume by the usual dilution method. In 6 animals the extrapolation of the logarithm of plasma concentrations obtained at 1, 2, 3, and 4 hours after injection of sucrose-C^{14} yielded extracellular fluid volumes which ranged from 20-25% of body weight. (Supported by NASA Grant NsG-513.)

FURTHER STUDIES ON THE DIURETIC ACTIVITY OF THE ANTIDIURETIC HORMONE. Jenö L. Kramár, Edward H. Grinnell*, Willard M. Duff* and Thomas E. Lydon*. Creighton Medical School, Omaha, Nebraska.

Studies on the diuretic activity of vasopressin, recently observed in the alcoholized rat, has been extended to dogs as the experimental animal. Female dogs were used with previously prepared bladder fistula which permitted direct collection of urine while eliminating surgical stress factors during the experiments. Under Pentobarbital anesthesia first a normal solution (dextrose, NaCl and $NaHCO_3$) was infused at constant low rate until urine flow became even, then infusion was changed to normal solution containing Pitressin or synthetic arginine-vasopressin. In several experiments these two periods were repeatedly alternated. In control experiments periods of similar length were compared using only normal solution without vasopressin. Significant diuresis was observed during vasopressin periods in 17 of 21 experiments. The diuresis, as a rule, was accompanied by marked increase in the output and concentration of urinary chlorides. In a second group of experiments trained dogs were used without anesthesia. The results were similar: diuresis was seen in 10 of 12 experiments. The previous finding on the alcoholized rat that vasopressin, under certain conditions, may cause diuresis as well as antidiuresis, was thus confirmed in another species. In addition, anesthesia was ruled out as a decisive factor in this phenomenon. (Supported by USPHS Grant HE 01151 and by the John Hartford Foundation).

A HEAT IMPULSE METHOD FOR STUDYING THERMAL PROPERTIES OF SKIN. K.K. Kraning, J.M. Short,* and R.F. Rushmer. University of Washington, Department of Physiology and Biophysics, Sch. of Med., Seattle, Wash.

Studies of cutaneous thermal properties are complicated by reactivity of skin to temperature and trauma. Physiologic disturbance can be minimized by a measurement technique utilizing transient heating and surface temperature measurements. Various solutions of the heat conduction equation can be applied to known changes in surface temperature ($T(o,t)$) to determine thermal inertia (μ) (thermal conductivity x density x heat capacity). We have obtained the solution corresponding to an impulse of radiant energy which instantaneously increases the temperature of a very thin surface layer of a semi-infinite solid. Following the impulse, $T(o,t)$ decreases as $Q/\sqrt{\pi\mu t}$, where Q is the energy absorbed. While a true impulse cannot be generated experimentally, the solution is still valid for a short heat pulse if the time of measurement of $T(o,t)$ is sufficiently long. We have used the impulse technique on the skin of extremities in normal men. Impulses were generated by a flashbulb mounted behind a camera shutter which limited pulse width. Surface temperature was measured with a small thermocouple wrapped around the extremity. Thermocouples and skin were blackened while together. Typically, the temperature peak reached 6 degrees ($dT/dt \geq 300$ deg C/sec). Our results indicate μ is uniform in the forearm from 50 msec to 2 sec. after the flash. Further, μ is not significantly altered by up to 10 minutes of arterial or venous occlusion or reactive hyperemia. Since time of measurement of $T(o,t)$ is indicative of depth to which μ is measured, the impulse technique is most useful for measurements of the superficial tissues, and is complementary to the low intensity heating techniques, which are more useful after several seconds of heating. (Supported by N.I.H. Grant HTS-5147).

EFFECT OF FREQUENCY OF EXPOSURE TO SEVERE COLD ON COLD TOLERANCE. M. Kreider (intr. by M. Landowne) US Army Rsch Inst of Env Med, Natick, Mass.

Cold acclimatization in the rat has been customarily produced experimentally by continuous exposure to 5°C for 4-8 weeks. This study was designed to determine if discontinuous exposures to more severe cold would influence cold tolerance (C.T.). Clipped white rats of 250 gm weight were fasted for 10 hrs prior to exposure in air at -10°C (range ± 2.5°C). Rectal temperatures were measured at intervals, more frequently as temperature fell below 35°C and animals were removed when readings were 32.2°C or less. C.T. was measured as the time for rectal temperature to fall to 32.2°C. Thirty-three rats were divided into 3 groups and exposed as follows:

	Cold Tolerance, minutes (mean ± S.E.)				No.**
Exposure Schedule	1st Expo.	2nd Expo.	Diff.	Final	>8 hr.
"Daily" (9X/12 days)	81 ±5	105 ±10	24 ± 7*	>1060	9
"Biweekly"(7X/21 days)	71 ±3	116 ± 5	44 ± 5*	> 465	8
"Weekly" (4X/22 days)	82 ±6	139 ±15	57 ±11*	> 255	1

*p< .01; **Number of rats with C.T. >8 hrs.

O_2 consumption ($\dot{V}O_2$) was measured at 5-10 min. intervals in 6 additional rats, and mean peak values showed a progressive rise with repeated daily exposure. Conclusions: Discontinuous severe exposure results in an increase in C.T. This was most rapid on daily exposure and still manifest 1 week after a single exposure. This increase in cold tolerance is accompanied by increased $\dot{V}O_2$ as is observed in rats cold acclimatized by customary methods. Although piloerection probably does not contribute to increased C.T. in this study, other means of reducing heat loss cannot be excluded.

CINEFLUOROGRAPHIC DEMONSTRATION OF NICOTINE ACCELERATION OF URETERAL PERISTALSIS AND ITS ANTAGONISM BY ISOPROTERENOL, A BETA-ADRENERGIC STIMULATOR. Peregrina Labay*, C. June Pfautz*, and Saul Boyarsky, Duke Univ. Med. Ctr., and Durham V.A. Hospital Durham, North Carolina.

Ureteral peristaltic activity demonstrated cinefluorographically by a slow infusion, 6 drops/min, of 25% sodium diatrizoate shows a frequency of 6-10 contractions per minute. Nicotinic stimulation increases this frequency to 30/min whether from inhalation of cigar smoke or intravenous injection of 200 mg/kg. The effect lasts up to ten minutes in the intact, anesthetized animal and is followed by a similar period of fatigue before the normal pattern of activity returns. Both spontaneous and stimulated activity are stopped by Isoproterenol, 3 mg/kg I. V. These demonstrations are presumptive evidence for the presence of alpha-adrenergic and beta-adrenergic receptors in the ureter; supporting evidence will be cited. Nicotine does not induce diuresis. These findings are interpreted as evidence for functional ureteral innervation. (Aided by NIH, VA and AMA grants).

NORMAL CANINE MYOCARDIAL CELL & SARCOMERE LENGTHS. M.M. Laks*, and H.J. Swan. Cedars-Sinai Research Institute, Los Angeles, California.

The purpose of this study was to measure myocardial cell and sarcomere lengths at the bases & apices of the right (RV) and left ventricle (LV) of 4 normal canine hearts. The RV and LV were simultaneously fixed with gluteraldehyde at zero transmural pressure. Sections of trabeculae carneae were taken from the 1 cm cut at the bases (free wall) of the RV & LV. They were further fixed with oxmium tetroxide, embedded in Epon 812, sectioned at ½ - 1μ and stained with Azure II - Methylene blue. From photomicrographs (X 1,000) taken with the phase microscope, cell length measurements averaged 70.9μ + 1.49**; no statistical difference existed between the cell lengths at the bases & apices of the RV & LV. From adjacent tissue, the measurements of sarcomere lengths made from photomicrographs (X 4,000), taken under oil immersion with the phase microscope, were not statistically different from those made with the electron microscope (P> 0.9). The sarcomere lengths at the LV base were the shortest - 2.16μ + 0.002**, followed by the LV apex - 2.28μ + 0.005**, RV base - 2.41μ + 0.006**, and RV apex 2.46μ + 0.003**. The sarcomere lengths were related inversely to the thickness of the ventricular wall. The data suggests that the smallest sarcomere length at the LV base may be considered the ultrastructural reflection of its least distensibility and is the result of it containing the largest number of muscle fibers. ** - S.E.M.

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EXCITATORY-INHIBITORY INTERACTION AT THE CORTICAL INPUT LEVEL OF THE VISUAL SYSTEM. Yves Lamarre* and Gian F. Poggio, The Johns Hopkins University, Baltimore, Maryland

In light adapted unanesthetized cats, center and surround regions of concentric receptive fields of geniculate neurons were independently stimulated with stationary patterns of light (spots and annuli). Time histograms of the impulse sequences generally were used for analysis. At near threshold intensities the responses evoked by stimulation of either center or surround regions appeared to have similar latencies (60-70 msec). At higher intensities the response to center stimulation, whether excitatory or inhibitory in nature, usually started earlier than that evoked by surround stimulation, a phenomenon which may be ascribed to the greater sensitivity of the center portion of the receptive field. In several instances illumination of surround inhibitory regions had little or no influence on the spontaneous activity of geniculate neurons, but effectively reduced the response evoked by center stimulation. For ON-center neurons evidence was found that illumination of the center region itself may be responsible for part of the inhibition observed when the surround was simultaneously illuminated. The temporal evolution of this "ON-center inhibitory effect" follows closely the time course of the excitatory response evoked by illumination of the center alone. It is suggested that the two opponent mechanisms which compose the receptive field are operationally co-extensive, at least over the center region and that they have similar intrinsic characteristics with respect to time course of action and dependency on stimulus intensity and duration.

(Supported by a USPHS grant).

VENTILATORY RESPONSES OF ANESTHETIZED CATS TO SCIATIC NERVE STIMULATION. T.W. Lamb. Department of Physiology, University of Virginia School of Medicine, Charlottesville, Virginia.

Periodic stimulation of the sciatic nerves was used as a means for studying ventilatory responses to increased metabolism in four pentobarbital-anesthetized cats. Changes in total body oxygen consumption occurred which were related to the amount of stimulation and were distributed over a range of values from the resting level to twice that amount. In response to a particular rate of stimulation, ventilation became steady after 1 to 2 minutes. Measurements were made after four minutes. The increases in alveolar ventilation associated with these altered levels of metabolism were such that no significant changes were observed in the arterial P_{O_2}, P_{CO_2} or pH from that seen at rest.

In four cats in whom the spinal cord was transected at the second lumbar vertebra, both metabolism and ventilation increased in a manner similar to that seen in the intact animals. Although the spinal cord was cut, arterial blood gas partial pressures again remained constant. Furthermore, in two additional animals, the ventilatory responses to skeletal muscle activity were the same after spinal cord transection as had been observed in the same animal before this denervation procedure.

During the increased metabolism of skeletal muscle activity, arterial blood gas homeostasis persists in the anesthetized cat in the absence of direct afferent impulses from muscles, joints or limbs. Such neural inputs are not, therefore, obligatory components of the complex regulatory mechanism which effects the close relationship between metabolism and alveolar ventilation.

Vascular Perfusion of Rat Jejunum Permitting Simultaneous Measurement of Intestinal Absorption, Arterial Inflow, Venous Outflow and Lymph Flow. J. S. Lee and Kathryn Duncan*. University of Minnesota Minneapolis, Minnesota

This report describes a technique for vascular perfusion of jejunum with heparinized blood via the mesenteric artery. The mesenteric artery, portal vein and main lymphatic duct were cannulated. Mucosal fluid was bicarbonate Ringer with glucose. The perfused segment absorbed fluid for more than 1 hr. The V-A volume difference (venous outflow—arterial inflow) measured net fluid absorption into the venous system and lymph flow measured that into the lymphatic system. The sum of V-A difference and lymph flow was approximately equal to fluid disappearance rate from the lumen. Fluid transported across serosal surface as "serosal sweat" was negligible. With increased venous pressure, absorption of fluid into the lymphatic system increased and absorption into the venous system decreased. At a venous pressure of 10 mm Hg and arterial pressure of 70 mm Hg, lymph flow accounted for 22-47% of the total absorbed fluid. At higher venous pressures (20-25 mm Hg), fluid absorption rate was markedly reduced; and fluid transport was entirely by way of the lymphatic system. Supported by USPHS Grant AM 05073 and Research Fund of the Graduate School of the University of Minnesota.

SIMULTANEOUS STIMULATION OF MULTIPLE CORTICAL POINTS. Richard A.Lende, Dennis A. Poulos*, and Clarence Davis*. Subdept. Neurosurgery, Albany Medical College, Albany, New York.

Cortical stimulation of single points, multiple points simultaneously, and areas was carried out in 11 Macaca mulatta under pentobarbital. Unipolar 60 cycle stimuli for 3 seconds, measured in milliamperes, were delivered through one to 10 electrodes in a variety of spatial configurations. Initially, threshold movements were established at individual points in an array. Simultaneous stimulation of combinations of 2 to 10 of these points showed that surprisingly little current was required at each electrode to achieve threshold. As the number of electrodes stimulated increased, the current required per electrode decreased. For instance, in one study the average threshold on single stimulations of electrodes 2 mm. apart was 0.90 ma.; threshold current per electrode on simultaneous stimulation of 2 points was 0.60 ma., of 5 was 0.20 ma., of 10 was 0.1 ma. This finding was less pronounced with wider electrode spacing. Threshold movements induced on multiple and single point stimulation were similar in nature. Stimulation in one precentral subdivision lowered the threshold in another subdivision, e.g., face and forelimb areas. Similar observations on thresholds were made on multiple point stimulation of white matter after precentral ablation, and of intact postcentral cortex. Precentral thresholds were lowered moderately by simultaneous stimulation of postcentral points and slightly by "silent" frontal points. Areal stimulation with a large gold-leaf pad electrode of 150 $mm.^2$ on the precentral strip produced single movements at thresholds as low as 2.0 ma.
(Supported by NIH Research Grant NB59-76.)

DIFFUSION COEFFICIENT: A MATHEMATICAL MODEL. Eugene A. Lentini and Sam Ketner*. Department of Physiology and Biometry, Medical College of Virginia, Richmond, Virginia

The determination of the myocardial diffusion coefficient of O_2 ($D'O_2$) has been calculated by utilizing the mechanical activity of elliptical tissue preparations as an index of adequate tissue oxygenation. Previous calculations based on the available geometrical model of a cylinder revealed an approximate value. Consequently, a specific elliptical mathematical model was developed for the tissue. The $D'O_2$ value obtained is in agreement with the value derived by Krogh for skeletal muscle. Some of the limitations of the model are those of Fick's law when applied to multicompartmental biological systems and preferential channels for the diffusion of molecules. In general, the model may be applied for the determination of diffusion into many elliptical in vivo and in vitro preparations.

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CHANGES IN PLASMA PROTEIN BOUND IODINE OF THE RAT DURING EXPOSURE TO OXYGEN: EFFECT OF FOOD CONSUMPTION. H. A. Leon, G. A. Brooksby* and M. J. Chackerian*. National Aeronautics and Space Administration, Biotechnology Div., Ames Research Center, Moffett Field, Calif.

It is reported that in rats exposed to 100% oxygen at 1 atm, a significant decrease in plasma PBI is observed within 48 hrs. It was suggested that this change is attributable to the oxygen per se. We have observed that during this period, food consumption is greatly reduced. In view of the known effect of food intake on plasma PBI, experiments were performed to determine if nutrition was a factor in the above changes. In one series of experiments O_2 exposed male rats showed the expected decrease in PBI after 72 hrs of exposure. Pair-fed control values were also decreased but not to the same extent (Table 1). In fasted rats exposed to O_2 for 24 or 44 hrs, decreases in PBI occurred; however, in air-exposed animals fasted for the same period, similar decreases were also noted. Thus, it is concluded that an altered food consumption is a major determinant in the decreased plasma PBI seen as a result of exposure to O_2 at 1 atm. The intermediate decrements seen in pair-fed rats is attributed to the mode of feeding in that they consume their limited ration within a short period of time.

Table 1 - Terminal PBI Values, μg/100 ml in Fed and Faste Exposed Rats

Ad Libitum control (220 gm)	3.5±.1	Control, fasted 24 hrs	2.1±.1	NS
	$p < .05$	O_2 exposed 24 hrs, fas ed	2.2±.1	
Pair-fed control	2.8±.2	Control, fasted 44 hrs	1.5±.1	NS
	$p < .001$	O_2 exposed 44 hrs, fasted	1.4±.1	
O_2 exposed, 72 hrs	0.7±.1			

LEAST SQUARES SPECTRAL ANALYSES ON CORE TEMPERATURE AND BLOOD PRESSURE OF A COMATOSE GIRL. H. Levine*, W. A. Ramshaw* and F. Halberg. Dept. of Pathology, Univ. of Minnesota, Minneapolis, and New Britain General Hospital, New Britain, Connecticut.

Conventional statistical and spectral (Acta Endocr. Suppl. 103, 1965) analyses were carried out on time series from a 4-year-old girl studied in an air-conditioned room following (an ≈10') cardiac arrest resulting in diffuse cerebral cortical impairment revealed by "bilateral symmetrical slowing" in electroencephalograms. Eyelids were sutured during 3rd week of study. For 2 weeks subject was fed i.v.; thereafter by stomach tube at equal intervals (of 1 h or 4 h). During first 3 weeks hypothermia was induced: mean (± standard deviation) esophageal temperature was 96.2 °F ± 3.5 (N = 1277). During subsequent 2 months mean rectal temperature was 99.7 ± .8 (N = 392). Systolic pressure averaged 143 ± 13 (N = 1284) during hypothermia and 154 ± 14 mm Hg (N = 611) thereafter. Diastolic pressure was 95 ± 12 (N = 1266) before hypothermia and 102 ± 13 (N = 601) mm Hg thereafter. Least squares spectra and temporal amplitude (C) and phase diagrams of systolic blood pressure during hypothermia revealed a desynchronized circadian component, corresponding to a trial period (τ) of ≈24.6 h, with C = 4.3 ± .5 mm Hg; circadian pressure rhythms also were found after hypothermia. Rhythms with a longer-than-circadian τ were more prominent than the C's of circadian τ's for systolic, diastolic or temperature variation. After hypothermia the C of the core-temperature rhythm with a τ of ≈68 h increased as C's for circadian τ's decreased. Results indicate "metabolic slowing"--a partial variance transposition into lower-than-circadian spectral regions, with some persisting circadian rhythmicity--in a case of human coma.

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UNIT ACTIVITY IN VESTIBULAR NERVE DURING CONTINUOUSLY VARYING TILT. H. Levitan, J. Rosenberg and J. Vidal (intr. by J. P. Segundo). Depts. Anatomy, Engineering and Brain Research Inst., UCLA, Los Angeles, Calif.

Single unit records were obtained from the vestibular nerve of cerebellectomized cats under pentobarbital anesthesia while the animals were submitted to continuous oscillation about a rostro-caudal axis. Only units which were non-adapting at a fixed tilt position, and thus presumably "utricular", were considered. Statistics of the spike train were related to tilt angle (within 10^{o} of the horizontal) and frequency (1 to 30 cycles/min) through analog and digital processing techniques. Under these conditions the firing rate was modulated at the tilt frequency, and over the range of frequencies used, there was little change in gain or phase. The dynamic limitations of the receptor were therefore not revealed. In addition to persistent "random" irregularities in the mean firing rate several specific non-linearities were superimposed on the dominant sinusoidal modulation. i) The modulation was generally asymetric with respect to the rate at the horizontal position, indicating preferential sensitivity to lateral tilt in one direction; ii) there was sometimes a small, high frequency modulation at specific points in the tilting cycle; and iii) following abrupt changes in the tilting frequency there was a transitory perturbation in the modulation lasting several minutes in some cases. The range of mean rates corresponding to each position was much less than that observed in static experiments (Rosenberg and Jeannerod, 1966). These experiments are part of an effort to understand how the utricle responds to natural stimuli and generates particular afferent discharge patterns. A relatively simple model involving certain mechanical (plastic) properties is suggested. (Supported by NIH, NASA, and United Cerebral Palsy Foundation.)

REDISTRIBUTION OF ALVEOLAR VENTILATION FOLLOWING PULMONARY THROMBOEMBOLISM. S.E. Levy* and D.H. Simmons. Cedars-Sinai Med. Res. Inst., Depts. of Med., C-S Med. Ctr. and UCLA Sch. of Med., Los Angeles, California.

The purpose of this study was to determine whether or not there is any redistribution of alveolar ventilation following pulmonary thromboembolism in dogs, with a shift away from unperfused, embolized segments to perfused, unembolized segments. Mongrel dogs were anesthetized, paralyzed with succinylcholine, and ventilated at a constant tidal volume and frequency before and after embolization with autologous in-vivo thrombi. Assuming uniform distribution of ventilation and perfusion prior to embolization, loss of perfusion to a segment of lung following embolization should, in the absence of redistribution of ventilation, result in a comparable decrease in effective alveolar ventilation (V_{Aeff}). In the absence of compensatory hyperventilation a shift of ventilation away from non-perfused to perfused lung segments (air-shift) would be the only mechanism that would minimize the expected decrease in V_{Aeff}. The percentage of non-perfused lung following embolization was determined using an India Ink infusion technique and the % decrease in V_{Aeff} was calculated using a modification of the Bohr equation which required the measurement of $PaCO_2$ and $PECO_2$ before and after embolization. Following embolization the decrease in V_{Aeff} was significantly less than the amount of non-perfused lung in 16 of 21 dogs, indicating that air-shift had taken place. Inhalation of 3% CO_2 in air completely prevented air-shift in another 10 dogs. Thus embolization resulting in cessation of perfusion to a lung segment is usually accompanied by a variable decrease in ventilation to that segment. The mechanism of the observed air-shift is most likely related to hypocapneic induced bronchoconstriction and airway closure, in the non-perfused lung segments. (Supported by NIH Grant HE 10525.)

DISTRIBUTION OF BLOOD FLOW IN A RETICULUM CELL LYMPHOSARCOMA AND AN AMELANOTIC MELANOMA. D.V. Lewis*, N.A. Staley*, R.F. Edlich*, and W. Rogers*. (intr. by: R.C. Lillehei) Dept. of Surgery, Univ. of Minnesota Med. School, Minneapolis, Minn.

The distribution of intravenously administered triphenylmethane dye and Rb^{86} and intra-arterially infused Yb^{169} microspheres (18.6± 2.3μ) within the amelanotic melanoma and reticulum cell lymphosarcoma changes as these tumors enlarge. With advancing age, the center of the tumor becomes unstained and has an uptake per gram of tissue which is 1.4 to 15.3 fold less than that of the intensely stained periphery of the tumor. This reduction in isotopic untake by the center of the tumor corresponds with the development of central tumor necrosis. The extent of central necrosis within these tumors is markedly different. In the small tumors (2.9 gm.), the central unstained portion constitutes 57.6% of the total weight of the amelanotic melanoma, while as unstained region in the reticulum cell lymphosarcoma is detected in only 5.5% of the total tumor. With increase in size of amelanotic melanoma (7.2 gm.), the central unstained region comprises 82.5% of the total tumor weight. Unstained areas of large reticulum cell lymphosarcomas of equal size account for only 12.7% of the total tumor weight.

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FURTHER STUDIES OF A CIRCADIAN RHYTHM IN A SINGLE NEURON: SEASONAL MODULATIONS AND ADIURNAL ENTRAINMENT. Marvin E. Lickey (intr. by A. Van Harreveld). Calif. Inst. of Technol., Pasadena, California.

Strumwasser has shown that the PB neuron in the isolated parieto-visceral ganglion of Aplysia has an endogenous circadian rhythm such that the frequency of spontaneous spikes passes through a maximum at or near the projected time of dawn. Further studies have now shown that the behavior of PB corresponds to environmental events in at least two additional ways. 1) The phase relation between the cellular rhythm and L/D:12/12 light cycles is dependent upon the season of the year. In the winter the peak occurs near the projected dawn but in the summer near the projected noon. In mid-autumn and again in mid-spring some preparations show a dawn peak and others show a noon peak. 2) The period (or phase) of the cellular rhythm is partially controlled by the period of environmental light cycles. By measuring the elapsed time between the last experienced dawn and the recorded cellular peak in animals previously exposed to a variety of photoperiods, it has been found that: i) In winter runs entrainment is equally precise to both 24 and 27 hr photoperiods, the peak being well synchronized with the projected dawn. ii) In summer runs the cellular rhythm is clearly modulated by 21, 24, and 27 hr photoperiods, but both the phase and the period appear to be affected. Cells entrained to 21 hr typically peak at about 2 hr post dawn (morning peak); cells entrained to 24 hr peak at about 6 hr post dawn (noon peak); and cells entrained to 27 hr peak at about 10 hr post dawn (evening peak). Entrainment is generally less precise in summer than in winter especially in the case of 27 hr photoperiods. These environmental modulations of neuronal activity lend support to the view that the Aplysia nervous system should provide a favorable model system for studies of learning and memory.

THE EFFECT OF VIBRATION ON TOTAL VASCULAR RESISTANCE IN THE FORELIMB OF THE DOG. A. J. Liedtke,* P. G. Schmid,* and J. W. Heim. Environmental Medicine Division, Aerospace Medical Research Laboratories, Wright-Patterson AFB, Ohio.

Vibration has been reported previously to have a significant effect on total peripheral vascular resistance. To further delineate this relationship, total forelimb vascular resistance changes in response to various levels of vibration were observed in 6 dogs. The animals were anesthetized with chloralose-urethane, treated with decamethonium bromide, intubated, and ventilated by a respirator. Each brachial artery was partially transected, and the distal segment perfused with blood from the ipsilateral femoral artery through independent cannulae and tubing. Flow rate was held constant using a dual pumping system. One forelimb was left neurally intact; the other forelimb was denervated. Perfusion pressure was measured from a sidearm of the brachial artery cannula with Statham pressure transducers. Resistance was calculated as the ratio of perfusion pressure to flow. Data were evaluated using analysis of variance. Vertical vibration, directed perpendicular to the long axis of the supine, restrained animal, was varied to include peak accelerations of 0.9, 1.2 and 1.6 G at frequencies of 9, 12 and 16 cycles/sec. The 9 combinations of acceleration and frequency were randomized for each dog and applied for 1 minute periods followed by 4 minutes of rest. Vasodilation occurred universally during every vibration in the intact limb and was greater with increases in peak acceleration ($P<0.05$) or decreases in frequency ($P<0.025$). The maximum dilation occurred at 1.6 G and 9 cycles/sec. Responses in the denervated forelimb were absent or markedly attenuated which suggests that optimal responsivity requires intact nervous pathways.

INHIBITION OF GASTRIC HCl SECRETION BY GLUCAGON IN DOGS. T. M. Lin and G. F. Spray,* Lilly Res. Labs. Indianapolis, Indiana

Steady state HCl secretion in dogs with vagally innervated or denervated gastric pouch and in dogs with both a Heidenhain(H) pouch and stomach(S) fistula was maintained by repeated injections of histamine, "gastrin," or gastrin tetra- or pentapeptide subcutaneously. A single dose of glucagon(G), 0.05-0.1 mg/kg s.c., or secretin, 75-100 u i.v., inhibited volume and acid outputs from both H&S in two dogs; the inhibitory effect of 1 mg of G was greater than that of 100 u of secretin. Reduction of HCl secretion by G was preceeded by sudden hyperkalemia, diuresis, and loss of Na and K from the urine, and was accompanied by hyperglycemia and an almost equal rise of [Na] in the gastric juice. The N terminal fragment of G(21-22 amino acids) caused only hyperglycemia but none of the other effects whereas the C terminal fragment (11-12 amino acids) did not even have the hyperglycemic activity. The inhibitory action of G on gastric HCl probably requires the integrity of the whole molecule. The mechanism of inhibition by G is different from that by insulin because the effect of G was not antagonized by pre-injection of KCl, 1 meq/kg i.v.

EFFECTS OF ENVIRONMENTAL TEMPERATURES ON THE CATECHOLAMINE CONCENTRATION OF PLASMA, HEART AND ADRENALS OF ADULT MALE CHICKENS. Y. C. Lin° and P. D. Sturkie, Rutgers-The State University, New Brunswick, N. J.

Adult White Leghorn males were exposed to high temperatures (32°C, 12 hrs; 25°C, 12 hrs), intermediate temperatures (control - 23-25°C), and to low temperatures (0°C, 12 hrs; 25°C, 12 hrs) for 4-20 weeks and the effects upon catecholamine levels of plasma, heart and adrenal tissue were determined spectrophotofluorometrically. Plasma Norepinephrine (N) of the cold-treated group rose sharply during the first 4 weeks and then declined slowly, but it was still 60% higher than that of the control group after 20 weeks of exposure. Plasma Epinephrine (E) of the cold-treated birds also rose initially, but then it declined rapidly to near control levels. Plasma N and E of the heat-treated group rose initially, then fell below the control level after 4 weeks; however, only E was statistically below the control level at the 8th week. Adrenal levels of N and E at the 12th week were significantly increased in the heat-treated birds, but were not significantly changed in the cold-treated group. The accumulation of N and E in the adrenal gland, and the low plasma concentration of the same amines in the heat-treated group suggest that the adrenomedullary releasing mechanism was inhibited. The elevation of plasma levels of N and E with no change in adrenal catecholamines of the cold-treated group suggests that the biosynthesis of these amines was increased. After 12 and 20 weeks exposure to cold, N of right atrium was higher than control group, but in the heat-treated birds at 12 weeks it was below control level. E level of heart was not affected by cold treatments, but was depressed by heat. Under all conditions, E level was higher than N in heart, adrenals and blood.

Effect of Posture on Circulatory and Respiratory Changes in the Hemorrhagic Dog. C.T. Liu*, R.A. Huggins, and H.E. Hoff, Department of Physiology, Baylor University College of Medicine, Houston, Texas.

Although the use of Trendelenburg's technique has long been suggested in the treatment of shock in man, this position was not successful in preventing death following massive hemorrhage in rats. The purpose of this study was to reevaluate the circulatory and respiratory changes produced by different postures in the dog before and after hemorrhage. The morphine-pentobarbital anesthetized dogs were bled to a mean blood pressure of 60-70 mm Hg and maintained at that level for 30 min. They were tilted head-up or head-down to positions from horizontal before and after hemorrhage. Prior to hemorrhage and during head-down tilts, a respiratory-heart rate response was clearly shown. Also, prior to hemorrhage, apnea was induced when the dog was tilted to a head-up position or back to 0° from a head-down position. Following hemorrhage, little change was observed in blood pressure, heart rate, and respiration during a head-down tilt. However, during a head-up tilt severe hypotension and marked hyperpnea were observed. Neither head-up nor head-down positions benefitted the circulation after hemorrhage; the head-up position was particularly deleterious.

THE EFFECT OF NOREPINEPHRINE INFUSIONS AND ADRENERGIC BLOCKING AGENTS ON SERUM GLUTAMIC-OXALACETIC TRANSAMINASE IN DOGS. Daniel J. Loegering and Jerry B. Critz (intr. by D. K. Meyer) Univ. of Western Ontario, London, Ontario.

Mongrel dogs were infused with 6, 96, or 384 µg/kg of norepinephrine at a constant rate for one hour. SGOT, blood pressure, and heart rate were recorded during and for 10 hours following the infusion. The 6 µg/kg dose caused no change in blood pressure or SGOT activity. The infusion of 96 µg/kg resulted in a rise in SGOT activity at the end of the infusion only. SGOT activity more than doubled by the end of the infusion of the 384 µg/kg dose and more than tripled by 10 hours after the infusion. Animals infused with 384 µg/kg of norepinephrine and pre-treated with either Dibenzyline (5.0 mg/kg) or Propranolol (0.5 mg/kg) showed a delayed rise in SGOT activity. Neither of these drugs alone blocked increases in SGOT activity for more than two hours following the infusion of norepinephrine. The group pre-treated with both blocking agents showed no increase in SGOT activity. The hypertension due to the vasoconstriction produced by norepinephrine may be accompanied by hypoxic conditions in the tissues. This hypoxia, in turn, may cause membrane permeability changes of sufficient magnitude to allow release of the GOT enzyme into the blood. The effect of the adrenergic blocking agents may be due to the reduction or elimination of the pressor response to norepinephrine.

THE IN VITRO UPTAKE OF 6-METHYLTHIOPURINE RIBOSIDE BY HUMAN ERYTHROCYTES. Ti Li Loo and Donald R. Blossom (intr. by Edwin L. Smith). The University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Texas

Clinical pharmacological studies on 6-methylthiopurine riboside (MMPR) revealed that it was preferentially taken up by human RBC. In vitro work with MMPR-S^{35} showed the uptake was against a concentration gradient. Within a concentration range of 0.05 mM to 0.3 mM of MMPR in whole blood, the uptake followed Michaelis-Menton kinetics. Preloading the RBC with MMPR lowered both the rate and extent of the uptake. Once inside, the efflux of radioactivity from the cell was negligible. Adenosine was a competitive inhibitor of the uptake whilst 6-thioinosine, inosine, deoxyadenosine, iodoacetic acid, and p-chloromercuribenzoic acid were noncompetitive inhibitors. 6-Mercaptopurine, 2,4-dinitrophenol, sodium fluoride, sodium arsenite, phloridzin, phloretin, persantin, reserpin and ouabain were all without effect. Intracellularly, MMPR was completely phosphorylated. Apparently, the uptake was by passive diffusion followed by conversion into the ribonucleotide which persisted in RBC. (Supported by contract PH 43-66-1156 with the National Cancer Institute).

SECRETORY ACTIVITY OF THE SPERM-HOST GLANDS OF THE DOMESTIC FOWL.
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Sperm-host glands are present in the uterovaginal junction and in the infundibulum of the hen's oviduct. The functional life span of spermatozoa is greatly prolonged in glands of both regions, but spermatozoa stored in infundibular glands have produced abnormally large numbers of defective embryos. The sperm environment in lumena of the uterovaginal glands, as estimated by histochemical techniques, is richly supplied with glycogen and a complex lipid. Glycogen is absent from infundibular glands, and lipid granules in the cytoplasm are less abundant and smaller than in uterovaginal gland cells. Qualitative differences appear to exist in the lipid content of the granules in the two regions. These differences may be related to differences in the subsequent performance of spermatozoa from the two sets of glands.
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TIME OF MATING BEHAVIOR IN THE 4 DAY AND 5 DAY CYCLIC RAT.
Lynn Lorenzen-Nequin* and Neena B. Schwartz. Univ. Ill. Col. Med., Chicago, Ill.

In rats exhibiting 4 vs 5 day estrous cycles, estrogen secretion and vaginal cornification appear to be initiated at the same time with respect to the last ovulation, and the "critical period" for LH release appears to begin at the same time on the day of proestrus in both. However, the duration of the estrogen secretion, the vaginal cornification and the "critical period" are prolonged in the 5 day rat. Previous work concerning mating behavior did not attempt to differentiate the 4 day from the 5 day rat with respect to the time at which mating behavior begins on proestrus. In the present study (lights on 5AM - 7PM), intact females were placed with males beginning at 8AM on proestrus, and were observed for the time at which lordosis began. A significant difference ($P=0.001$) was found in the time at which the first lordosis response was seen in the 4 and 5 day rat. In the 4 day rat, lordosis was first seen at 5PM (SD$\pm$ 1 hr, 19min); and in the 5 day at 2PM (SD$\pm$ 2 hrs,52min). Since the early mating behavior seen in the 5 day rat cannot presumably be due to progesterone secretion resulting from the ovulatory surge of LH, several alternative hypotheses may be offered: (1) progesterone may be released from the ovary prior to the LH surge; (2) progestins may be secreted from non-LH dependent tissue (adrenals ?); progesterone may not be as necessary for mating behavior in the intact rat as it is in the ovariectomized rat. (Supported in part by PHS Research Grants HD 00440-05 and 2 T01 GM 00738-05 and -06)

CENTRAL VAGUS STIMULATION AND GASTRIC SECRETION. P. Lott Jr.*, A. Geisel*, N.C. Jefferson, and H. Necheles. Michael Reese Hospital and Medical Center, Chicago, Ill.

We have reported here previously that central vagus stimulation in the dog is followed by active contractions of the stomach. A group in Philadelphia then reported that central vagus stimulation is followed by increased mucoid secretion of the stomach but with no increase in acid secretion. We have pursued this question further and have used dogs with total gastric fistulas anesthetized with nembutal, primed with s.c. histamine and with a constant injection of .35 mg of histamine base per hour i.v. Controls were performed on dogs with vagi intact, dogs with vagi cut but without stimulation, and dogs with vagi cut and stimulation of the central ends of the vagus nerves in the neck. It was found that vagotomy per se did not affect the secretion either of acid nor of volume to an appreciable degree as compared to dogs with intact vagus nerves. However, in a similar series of animals with vagi cut and constant injection of histamine, stimulation of the central ends of the vagus nerves produced a distinct increase in volume and total acid secretion. It is believed that in a stomach stimulated with subthreshold doses of histamine central vagus stimulation may effect increased secretion of acid, while basal secretion is not affected.

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MECHANICAL WORK OUTPUT IN HUMAN LOCOMOTION. L. Lukin. Biomechanics Lab., Univ. Calif. School of Med., San Francisco, California 94122

Vertical and horizontal oscillations of the trunk were measured in subjects walking on a treadmill at 3 different speeds. The potential energy (PE) and the kinetic energy (KE) levels for time intervals of 0.02 sec were calculated. Delta PE per step ranged between 0.030 and 0.128 cal/kg, and delta KE per step ranged between 0.061 and 0.188 cal/kg. Kinetic work was always greater than gravitational work; the ratio KE/PE averaged 1.6 for all speeds of level walking. Efficiency calculated from gravitational work was thus smaller than that calculated from kinetic work. The sum of delta PE and delta KE per step provides an overestimation of the work output because in most cases the KE and PE curves were approximately 180 degrees out of phase, almost forming a mirror image of each other, and suggesting an exchange of energy analogous to that observed in a conservative system such as a pendulum. However, the system under consideration is not truly conservative, and a 100% conversion of energy between potential and kinetic forms therefore cannot be assumed. Vertical addition of the PE and KE values for each time interval, although correctly yielding the change in the mechanical energy level of the trunk, does not necessarily represent the actual work performed to produce this change. Of particular importance in connection with energy exchange is the shift in the phase relations between the PE and the KE curves. The best condition for energy exchange is obtained when the two curves form a mirror image of each other; the most unfavorable condition is when the two curves are exactly in phase. (Supported by NASA Grant NsG722 and NIH Grant AM-08605)

EFFECT OF PITUITARY OCTAPEPTIDES ON THE ISOLATED MUSCLE STRIPS OF THE URINARY BLADDER. Thomas E. Lydon*, Edward H. Grinnell* and Jenő L. Kramár. Creighton Medical School, Omaha, Nebraska.

In the few studies of the action of vasopressin upon the bladder muscle, made during 1926-37, extracts of the whole gland or the posterior lobe were used. Various changes in tonus and in frequency and amplitude of contractions were observed. No such study was found in the literature since isolation and synthesis of the pituitary octapeptides. Synthetic arginine-vasopressin, lysine-vasopressin and oxytocin were, therefore, investigated for this activity. Longitudinal bladder strips of mouse, rat, rabbit and guinea pig were suspended in 2.5 ml. Rademaker solution and attached to isotonic myograph. Recording was done with the E & M Physiograph. Observations were made on 133 muscle samples of 109 animals. (1) In general, the bladder muscle was found to be very sensitive to the octapeptides. One microunit of arginine-vasopressin, e.g., when added to the muscle bath still caused a well demonstrable effect.(2) The bladder sensitivity may vary with the animal species. Following is the sequence (in declining order): rabbit, rat, mouse, guinea pig. (3) The response was also qualitatively variable: increase or decrease of tonus and (in the guinea pig) changes in the amplitude and frequency of contractions. (4) Even though the response, as a rule, increased with increasing doses there was no correlation between dose and degree of response. (5) The sensitivity was the greatest to arginine-vasopressin and less to lysine-vasopressin and oxytocin. (6) No evidence of tachyphylaxis was observed. (Supported by USPHS Grant HE 01151 and by the John Hartford Foundation).

SPECIES DIFFERENCES IN GLUTAMINE SYNTHESIS. Mary Lou Lyon* and Robert F. Pitts. Cornell University Medical College, New York, New York.

Glutamine synthesis is endergonic and is catalyzed by glutamine synthetase. The enzyme has been demonstrated in the kidney of the rat, guinea pig and rabbit in vitro. It has not been uniformily demonstrated in the dog or cat. In no species has it been demonstrated in vivo. The amide nitrogen of glutamine has been postulated by some to be the ultimate source of all ammonia produced by the kidney regardless of the species or the original source of nitrogen. If glutamine is the final common pathway for production of ammonia, the kidney of the dog and cat as well as that of the rat, rabbit and guinea pig must synthesize glutamine. To assess this hypothesis we studied glutamine synthesis in the intact anesthetized dog, cat, rat and guinea pig. C^{14} labeled α-ketoglutarate, infused into the left renal artery of each animal, resulted in the incorporation of the isotope into the glutamic acid of the infused kidney of each species probably by transamination. The synthesis of labeled glutamine from this glutamic acid was assessed in the following manner. The concentrations of renal glutamic acid and glutamine were determined by automatic amino acid analysis and the C^{14} content of each was measured by flow scintillation counting. Our results show that the glutamine of the dog and the cat is not significantly labeled. Hence these animals do not synthesize glutamine and all nitrogen appearing as ammonia is not obligatorily funneled through glutamine. The glutamine of the rat and guinea pig is highly labeled supporting the in vitro evidence of glutamine synthesis. Glutamine may be a common pathway for ammonia secretion in these latter animals though not proven by these experiments.

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MASS EXCURSION PARAMETERS OF FIRST HEART SOUND ENERGY. D.M. MacCanon, D.W. Bruce*, P.R. Lynch and J.L. Nickerson. Div. of Cardiovascular Research and Dept. of Physiology, The Chicago Medical School, Chicago, Ill., and the Dept. of Physiology of Temple University School of Medicine, Phila., Pa.

Attempts to relate first heart sound energy to the vibration of heart structures were carried out in anesthetized dogs. Measurements of the first heart sound using a calibrated microphone gave values of 50,000 dynes/cm^2 at a basic frequency of 34 H_z at the epicardial surface. A mitral participation of approximately 150,000 dynes, a half wave forcing function of 75,000 dynes and an average energy content of 37,000a gm-cm. (where a equals the half wave amplitude in centimeters) for center-to-peak motion were calculated. Substituting this last figure in the formula for the inertial energy content of a transducer gave values of 1.74 gm cm. for the mitral interface. Rapid (540 frames/sec.) cineangiographic studies show mitral excursion to be less than 0.5 cm. at the time of the first heart sound. Leaflets plus chordae weigh less than 0.5 gm. This accounts for less than 0.2 gm cm. or only about one tenth of the first heart sound energy. The participation of 50 gm of heart muscle and 50 gm of blood in the oscillation moving approximately 0.016 cm. could easily account for the rest of the first sound energy. These results suggest that it is unlikely that the mitral valve and attached chordae alone could account for the first heart sound. Supported by Grants HE-09350 and HE-08886 U.S.P.H.S.

INTERPRETATION OF UNIDIRECTIONAL FLUX MEASUREMENTS IN EPITHELIAL TISSUE. **R.I. Macey and J.G. Forte, Department of Physiology, University of California, Berkeley, California.**

The interpretation of unidirectional flux measurements through isolated epithelial tissue is often obscured by complex tissue geometry. Extracellular spaces and tubular lumina form pockets of unstirred media and if diffusion through these regions is sufficiently slow, the specific activity of solute at cell membranes is not necessarily identical with the specific activity in the bathing medium. This problem is exacerbated by bulk flow which accompanies the secretions of most epithelia. To evaluate the magnitude of these effects, a one-dimensional steady state model is proposed which superimposes bulk flow and diffusion. The tissue is assumed to be infiltrated with a number of non-interacting invaginations and it is further assumed that: 1) The tissue secretes an isotonic solution, 2) the water flow per unit surface area of membrane is constant, 3) local unidirectional flux through the membrane is proportional to the local concentration. The system is described by a confluent hypergeometric differential equation which is solved subject to boundary conditions imposed on the concentration in bathing medium and on the flux at the bottom of each invagination. Using parameters characteristic of gastric mucosa, where the invaginations consist of relatively long gastric glands, it is shown that the apparent back flux is frequently about 60% of the actual back flux. At the serosal surface of the small intestine where the invaginations consist of the relatively short spaces between cells, this distinction diminishes. **Supported by NSF GB 1928 and USPHS AM10141.**

TECHNIQUES FOR THE ESTIMATION OF CRANIAL BLOOD FLOW.

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The following procedures were devised in an attempt to measure and indicate changes in cranial blood flow - particularly those of a transient nature. Venous occlusion was applied to the neck at 50mm Hg. in the methods described below.

INTRACRANIAL FLOW. Orbital vascular volume changes were recorded from swimming goggles. Exenterated orbits provided no flow record. Subject sitting or supine. Calibrated volumetrically.

EXTRACRANIAL FLOW. Vascular volume changes were recorded from a nylon covered cuff (28 cms x 4 cms) inflated to 5 cms. H_2O and bound lightly against the forehead. Subject supine or sitting. Calibrated volumetrically.

TOTAL CRANIAL FLOW was recorded from the incremental weight changes of the head during venous occlusion. The head and neck were supported on a semi-inflated rubber bladder to reduce neck muscle tension and to allow head movement with weight changes. The head was placed in an elastic sling attached to a Grass Force Displacement Transducer (F T 10.) Subject supine 20° head-up. Calibration gravimetric.

The most marked effect on the "Blood Flow" records was that induced by hyperventilation, here, the resistance of the orbital vessels was increased two to threefold. Supported by P.H.S. Grant No. HE 07722 and Puerto Rican Heart Assoc.

PARTITIONING OF PULMONARY RESISTANCE IN THE DOG.

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Royal Victoria Hospital, McGill University, Montreal, and Cardiovascular Research Institute, U.C. Medical School, San Francisco.

The retrograde catheter technique (Macklem & Mead, J.A.P. 22: 395, 1967) was modified to partition pulmonary resistance, R_L, in dogs at known sites along the airway before and after vagotomy. Airway diameter and generation at each site where R_L was partitioned was estimated by fixing the lungs in inflation and dissecting to the points of measurement. Before vagotomy R_L increased considerably as volume diminished primarily as a result of an increase in resistance of 3-8 mm i.d. bronchi which made up ca 60% of R_L at FRC. At higher lung volumes the contribution of these airways to R_L was much less. Vagotomy decreased the resistance of 3-8 mm i.d. bronchi much more than it decreased resistance at other levels of the tracheo bronchial tree, with the result that R_L changed very little with lung volume. We conclude that in the dog, bronchomotor tone is responsible for much of the increase in R_L as volume diminishes and that its effect is primarily on 3-8 mm i.d. bronchi. (Supported by the John A. Hartford Foundation and the Defense Research Board of Canada.

REGIONAL CHANGES IN PULSE WAVE VELOCITY

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The purpose of the investigation was to determine rate of pulse wave propagation in the peripheral circulation of man using externally applied sensors. Studies were conducted on normotensive adults with no evidence of peripheral vascular disease. Special piezoelectric transducers were positioned over the distal ends of the brachial and radial arteries. Digital pulsation was detected by a transilluminated photoresistor. Scalar ECG and phonocardiogram were obtained in the usual manner. A multichannel FM tape recorder was used for storage of obtained data. Subsequent time-expansion analysis was performed on the pulse waveforms. Elapsed transmission time was computed from the onset of the first heart sound to the time of arrival of the propagated wave at the peripheral sensor. Pulse wave velocity from the aorta to terminal brachial artery had an average value of 4.60 mm/msec. Velocity in the radial artery was 7.80 mm/msec. Pulse velocity from the wrist to the distal end of the index finger was 5.30 mm/msec. There was a tendency for females to have a somewhat lower velocity than males in more peripheral vessels. Age related changes in pulse wave velocity were more frequently noted in smaller branches of the arterial tree than in vessels of larger calibre. These changes tended to correlate with other age-related alterations in the peripheral pulse waveform such as reduction in amplitude of the digital dicrotic notch and prolongation of the rise time of the anacrotic limb.

Thermoregulation of the Canine Brain by Alar Fold and Intervening Arteriovenous Heat Exchange Systems. J. H. Magilton and C. S. Swift (introduced by N. R. Cholvin). Iowa State University, Ames, Iowa. Eleven experiments were conducted on six dogs. Thermistors were employed to detect temperature changes. The alar folds of the maxilloturbinates were irrigated with water ranging from 12.0° C to 52.0° C (dry ice was also used in experiment 8). The temperature curves of brain probes followed those of the angularis oculi vein but to varying degrees. In the region of the posterior communicating artery it began its downward trend six seconds after it occurred in the angularis oculi vein. The configurations of the two curves were very similar. With the water at 15.0° the thalamus was 1.6° cooler than the cortex, but when the water was at 51.0° the thalamus was 1.4° warmer than the cortex. The cortical change lagged behind that of the thalamus by about one minute. The maximum temperature achievable in the brain was 38.9° while the minimum temperature was 24.6°. Assumptions made are: 1. Normally heat must be transported away from the brain; 2. Circulating blood would be the most efficient means by which to transport heat; 3. Efficiency in transporting heat increases as blood temperature decreases and flow increases; 4. Body core blood temperature is too high for optimum efficiency. Thermoregulation (brain cooling) is attained by heat being picked up by blood after leaving the circle of Willis. Blood in the circle of Willis is cooled by heat passing from arterial blood to venous blood in the cavernous sinus. Flow rate in the cavernous sinus is changed by differential regulation between the angularis oculi and facial veins. Temperature of venous blood in the cavernous sinus is lowered by a heat exchanger in the alar fold of the maxilloturbinate. Blood from the alar fold reaches the cavernous sinus via the dorsal nasal, angularis oculi and ophthalmic veins.

ROLE OF PHOSPHOLIPIDS IN Rb^+ TRANSPORT BY RENAL CORTICAL TUBULES. Amra Malila*, E. J. Masoro and F. D. DeMartinis*, Dept. of Physiology and Biophysics, Woman's Medical Coll. of Pa., Philadelphia, Pa.

It has been postulated that phospholipids are involved in ion transport across cell membranes but unequivocal proof for such a function is lacking. Experiments were designed to gain direct information on the importance of the phospholipid structure of renal cortical tubules on the ability of these tubules to actively take up Rb^+ Treatment of isolated cortical tubules with low levels of commercial phospholipase C from Clostridium Welchii caused very little destruction of the phospholipid structure but markedly curtailed the ability of the tubules to actively sequester Rb^+. That these results relate to the phospholipase C activity of this enzyme preparation is supported by the following evidence: 1) the Rb^+ sequestering activity was protected when the phospholipase C treatment was carried out in the absence of Ca^{++} or in the presence of a large quantity of micellar phospholipid or in the presence of Clostridium Welchii antitoxin; 2) purification of the phospholipase C, which increased the specific activity two fold, did not alter its influence on Rb^+ uptake per unit of activity; 3) the phospholipase C preparations showed no proteolytic activity. Preliminary evidence indicates that the diminished net Rb^+ sequestration caused by the phospholipase treatment is the result of a reduced rate of active uptake and not of an increased rate of efflux. It is therefore concluded that the phospholipid structure of renal tubules functions significantly in Rb^+ uptake and that minor changes in that structure diminish transport of the monovalent cation. (Supported by Public Health Grant AM-09458.)

EFFECTS OF POLYLYSINE ON WATER AND SODIUM TRANSPORT BY THE URINARY BLADDER OF THE TOAD. M. Mamelak* and P. F. Gulyassy. C.V.R.I., Univ. of California School of Medicine, San Francisco.

Different transport properties have been attributed to the mucosal and serosal surfaces of the epithelial cells of the toad urinary bladder. To investigate the consequences on water and Na^+ transport of altering selectively one of these surfaces, use has been made of polylysine (PL)- a polypeptide of lysine with a m.w. of 100,000-150,000. At physiological pH's PL is strongly cationic, whereas the mucosal face of the urinary bladder has a net negative charge. Because of its large size it is expected that the PL will not penetrate the cell. In 10 paired experiments 80 µg/ml PL added to the mucosal face resulted in a drop in transepithelial potential difference (PD) to 21% ± 3% of the baseline value in a 2 hr period. The short-circuit current (scc), a measure of Na^+ transport, fell to 54% ± 4% of its baseline value in the same period. Osmotic water flow totaled 176 ± 16.2 µl during the 2 hr period compared to 35 ± 11.09 µl in controls. Slight effects on PD and scc were seen with concentrations as low as 4 µg/ml. PL added to the serosal face was ineffective. Following 2 hrs of mucosal exposure to 80 µg/ml PL, vasopressin stimulated osmotic water flow was irreversibly inhibited. The effects of vasopressin on scc and PD were still seen; as in controls the rise after vasopressin being proportional to the baseline. Similarly, PL 80 µg/ml for 2 hrs did not inhibit the response of the bladder to amphotericin. Aldosterone, followed in 1 hr by 80 µg/ml of PL, still produced an increase in scc although the effect was masked by a simultaneous fall in baseline. Radioautographic studies are in progress to determine if any PL enters the cell.

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ACID-BASE STATUS OF THE TWO-TOED SLOTH (Choloepus hoffmanni) IN ACUTE HYPOTHERMIA. Jacob Marder* and Robert B. Reeves. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Our interest has been aroused in the control of mammalian blood pH (pH_B) when body temperature changes; in cold-blooded vertebrates pH_B has been found to decrease .019 units per °C body temperature rise. We have therefore investigated the acid-base metabolism of the two-toed sloth, a well known non-hibernating heterotherm. Normal arterial values at body temperature (T_B) of 34.5°C (ambient 25°C) were as follows: pH - 7.441 ± .038; PCO_2 - 36.1 ± 3.2 mm Hg; calculated (HCO_3^-) - 25.3 ± 2.9 mM. Six cycles of acute (circa 12 hr) cold exposure, carried out on 3 animals, each resulting in an average drop of 10°C in T_B, typically showed no significant change in pH_B and a decreased PCO_2. One such experiment gave values of pH_B 7.39, pCO_2 27.0, and (HCO_3^-) 19.5 at reduced T_B (25.4°C). The salient result of these experiments was the finding of a stable regulated arterial pH as body temperature was altered. Total oxygen content (15.4 ± 1.66 vol%) and arterial blood pressure (110 ± 10.2 mm Hg) were normal and stable during hypothermia. Heart rate, however, dropped from 80 ± 4.6 beats/min to 40 ± 2.1 after the body temperature reached 25°C.

EFFECT OF AGE ON THE VENTRAL PROSTATE GLAND RESPONSE TO THYMECTOMY. Constance R. Martin, Betty Rosoff* and Lorraine K. Miller.* Hunter College, C.U.N.Y., New York, New York.

Studies in this laboratory have shown that the thymus gland influence on growth of the ventral prostate gland varies with the age of the animal. Hooded male rats thymectomized (T) at 30-33 days of age and autopsied 21 days later had heavier ventral prostates than sham thymectomized (S) or unoperated (U) controls. When surgery was performed at 42-45 days and autopsy 21 days later, T rats had significantly heavier ventral prostates than S (but not U) rats. No significant differences in prostate weights for T, S and U rats were found when autopsy was performed 7, 14, 18 or 28 days after surgery at 42-45 days. To determine whether gonadotrophins can modify the age dependent thymectomy effect, 42-45 day operated rats were injected with FSH, LH, Prolactin or HCG during the 2 weeks prior to autopsy at 28 days. LH, Prolactin and HCG did not elicit thymectomy effects on ventral prostate weight. However, a total dose of 2 mg FSH produced a pattern in 28 day rats similar to that observed in uninjected 21 day rats. A 4 mg dose of FSH was ineffective in 28 day rats. In another study, a total of 2 mg of FSH given during the 2nd and 3rd weeks after surgery abolished the described differences observed in uninjected rats 21 days after surgery. To determine the long range effects of thymectomy, rats operated at 42-45 days were autopsied 4-6 months after surgery. Ventral prostate glands of T rats were markedly hypertrophied, as compared with S and U controls. (Supported by American Cancer Society Grant # P-382A; Gonadotrophins donated by National Institutes of Health)

MICROPERFUSION STUDIES OF EXCRETORY DUCT FUNCTION IN THE RAT SUBMANDIBULAR GLAND. J. Ricardo Martinez* and William E. Lassiter, Dept. of Medicine, Univ. of N.C. School of Medicine, Chapel Hill, N.C.

This study was designed to investigate the effects of intraluminal Na concentration and osmolality on transfer of Na, K, and water across the main excretory duct of the rat submandibular gland. Solutions of differing Na concentrations or osmolalities, containing NaCl and/or mannitol and tracer quantities of Na-22 and inulin-methoxy-H-3, were instilled by micropuncture into the duct, isolated between droplets of mineral oil. After varying time intervals each sample was aspirated, and its osmolality and Na and K content determined. Net water movement was estimated from the change in inulin concentration, and unidirectional Na flux from the loss of Na-22. Regardless of initial composition, aspirated samples were invariably hypotonic to plasma, and concentrations of Na were lower, and K higher, than plasma. The results indicate that the excretory duct epithelium has a relatively low osmotic permeability to water, and that it is capable of reabsorbing Na and secreting K against large concentration gradients. The main excretory duct appears to play a major role in determining the osmolality and electrolyte composition of submandibular gland saliva in the rat.

EMBEDDING OF 5-FLUOROURACIL IN NORMOTHERMIC TUMORS OF HYPOTHERMIC ANIMALS. Roberto Masironi* and Vojin Popovic. Dept. Physiol., Emory Univ. School of Medicine, Atlanta, Ga.

In experiments reported earlier Popovic and Masironi have shown that subsequent to cooling of the whole body of golden hamsters their normothermically kept tumors disappear (Popovic, V. and Masironi, R. Disappearance of euthermic tumors after 10-hour generalized hypothermia, Life Sci. 4: 533-43, 1965; Popovic, V. and Masironi, R. Effect of generalized hypothermia on normothermic tumors, Am. J. Physiol. 211: 462-466, 1966). In order to induce tumor disappearance the differential hypothermia (warm tumor - cold body) had to last at least 10 hours (Popovic, V. and Masironi, R. Disappearance of normothermic tumors in shallow (30°C) hypothermia, Cancer Res. 26: 863-864, 1966). Much shorter differential hypothermia is also effective when it is combined with one single administration of 5-fluorouracil (FU), an anticancer drug (Popovic, V. and Masironi, R.: Enhancement of 5-fluorouracil action on normothermic tumors induced by generalized hypothermia, Cancer Res. 26: 2353-2356, 1966). As the first step in understanding the mechanisms of tumor disappearance after the treatment with differential hypothermia and with 5-fluorouracil, the distribution of C^{14} labelled 5-fluorouracil was studied in this work in profoundly cooled hamsters whose tumors were kept normothermic (differential hypothermia). While the radioactivity of blood in normothermic animals fell quickly after the administration of FU, the radioactivity of blood in hypothermic animals stayed constantly at a high level. The differential hypothermia acted thus as a long-term 5-fluorouracil perfusion of the whole body affecting preferentially warm tumors due to their much higher blood circulation and a much higher metabolism as compared to the rest of the hypothermically kept body.

ELECTROPHYSIOLOGICAL ACTIVITY DURING AND FOLLOWING COMPLETE ISOLATION OF THE MONKEY BRAIN. L. C. Massopust, Jr., R. J. White, M. S. Albin*, L. R. Wolin*, R. Meder* and D. Yashon*. Neurophysiol. Lab., Cleveland Psychiatric Inst.; Neurosurg. Sect., Metropolitan Gen. Hosp.; Western Reserve Univ. Med. School, Cleveland, Ohio.

Chronically implanted bilateral silver ball electrodes in the motor and somesthetic cortex and deep needle electrodes in the anterior reticular formation were used to record spontaneous electrical activity from the White isolated monkey brain during the following phases: 1] during dissection of the soft tissue from the skull, 2] during cannulation of the carotid arteries, 3] during ligation of the vertebral arteries, 4] during ligation and severance of the spinal cord, 5] for approximately two hours of donor perfusion of the completely isolated monkey brain. Spontaneous activity indicated an essentially viable brain and normally functioning cortex under the conditions of the experiment with desynchronized medium voltage fast activity. This indicated an intact ARAS with a normal internal automaticity without the major cranial nerve inputs (8th nerve intact) and without the spinal cord connections. Visually evoked responses recorded from the visual cortex (right eye and orbital structures left intact) after isolation and during donor perfusion were similar to those obtained in the intact monkey. "On" and "off" responses were observed with afterpotentials and latencies were essentially normal. (Supported by grants NB03859 and NB06552 from the National Institutes of Health.)

THE EFFECTS OF PROPANOLOL ON MYOCARDIAL CARBOHYDRATE AND FATTY ACID METABOLISM. T.N. Masters* and V.V. Glaviano. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

The myocardial metabolic effects of the beta adrenergic blocking drug, propranolol, were studied in 16 open-chest anesthetized mongrel dogs in which mean blood pressure and left ventricular pressure was recorded. The coronary sinus was cannulated from which the effluent blood was returned to the right atrium. A "T" tube in this circuit allowed for measuring coronary blood flow and also for the collection of coronary sinus blood samples. The myocardial uptake (A-V difference x flow) of glucose, lactate, pyruvate and total fatty acids was measured in arterial and coronary sinus blood taken during control and ten minutes after the intravenous administration of propranolol (1 mg/kg). A significant decrease in the uptake of lactate (33%), pyruvate (35%), and total fatty acids (68%) occurred while glucose remained unchanged. In addition, a decrease in heart rate from 175 beats/min to 123 beats/min and dp/dt from 2600 mm Hg/sec to 2000 mm Hg/sec was noted. In order to determine whether the decreased substrate uptake after propranolol was associated with a decrease in cardiac performance or metabolic blockade, pacing electrodes were attached to the left atrial appendage to stimulate the heart rate to near control levels. In the propranolol-treated dogs, pacing caused a significant increase in the uptake of lactate and pyruvate. However, glucose during pacing rose while total fatty acids remained essentially unchanged. These results indicate a relationship between fatty acid uptake and beta adrenergic receptor activity. (Supported by ONR Contract 3502-01 and NIH Grant HE 08682.)

ACCURACY OF OXYGEN CONSUMPTION CONTINUOUSLY DETERMINED DURING FITNESS TESTS TO MAXIMUM. J. A. Mastropaolo, W. E. Jackson and I. T. Whipple (intr. by D. B. Dill). Douglas Aircraft Co., Long Beach, California.

The outputs of an infrared CO_2 analyzer, a rapid response Pauling meter, and a pneumotachograph were recorded on a photographic oscillograph. During fitness tests at sub-maximum and maximum oxygen consumptions on a bicycle ergometer, the electronic recordings were compared to the Haldane-Douglas bag method: this was our standard. In 100 experiments on 16 men the electronic analyzers differed from the standard by 0.02 ± 0.21 volume percent (%) CO_2 (mean and standard deviation), by 0.03 ± 0.10 % O_2, 0.5 ± 2.0 L/min STPD expired volume (V_E), by 54 ± 123 ml/min STPD oxygen consumption (V_{O_2}), by 10 ± 196 ml/min STPD carbon dioxide production (V_{CO_2}), and by 0.02 ± 0.08 respiratory exchange ratio (R) over a range of 0.71 to 3.75 L/min V_{O_2} (mean: 2.08). In 20 determinations of maximum V_{O_2}, the electronic recordings gave 2 false positive and 5 false negative values. These data suggest that further refinements in technique may permit quick, convenient, continuous measurement of metabolic rate to maximum within the technical error of the Haldane-Douglas bag method.

NOREPINEPHRINE CONTENT OF VARIOUS VASCULAR SEGMENTS. Howard E. Mayer*, Francois M. Abboud and John W. Eckstein. CV Res. Labs., U. of Iowa Coll. of Med., Iowa City, Iowa.

In previous experiments large and small arteries and veins in the foreleg of the dog reacted differently in response to nerve stimulation. Sodium and potassium content of these segments also differed. In the present experiments norepinephrine was measured in vessels of the foreleg by a fluorometric method (29 vascular segments from 5 animals) and also by bioassay (28 segments from 3 dogs). The bioassay was done on saline extracts of pulverized frozen tissue. The pressor responses of the rat to intravenous injections of aliquots of the extracts were measured before and after administration of phentolamine and propranolol. The results indicate that the average concentration of norepinephrine in the brachial artery (0.14 µg/gm of wet tissue) was significantly lower than that in the ulnar (0.70 µg/gm) and metacarpal arteries (0.66 µg/gm) by the fluorometric method. A similar difference in concentration between the arterial segments was found by the assay method. The norepinephrine content of cephalic and metacarpal veins did not appear to differ significantly from that of the ulnar and metacarpal arteries. It is of interest that the brachial artery which had the lowest concentration of norepinephrine did not appear to constrict in response to nerve stimulation.
(Supported by USPHS grants HE-09835 and HE-02644.)

ANTIDIURETIC HORMONE RESPONSE TO SELECTIVE CARDIAC VAGOTOMY. E. A. Mazzei* and V. L. Willman. Dept. of Surg., St. Louis University, St. Louis, Missouri. (Aided by Grants HE0-6312, USPHS and HE-5299)

The contribution of the cardiac vagal efferent innervation to urine control has been studied in five mongrel dogs with selective cardiac vagotomy before operation and for twenty-one days postoperative. Blood volumes were determined during the second postoperative week. Preoperative antidiuretic hormone levels averaged 3.2 μU/ml plasma. Postoperative values remained elevated for five days with the first postoperative day average level of 7.1 μU/ml plasma. From day 6 through day 21 antidiuretic hormone levels were below preoperative levels which is common for many intrathoracic operations not involving neural interruption. Blood volume of the five cardiac vagotomy dogs averaged 98.8 ml/Kg while nine normal dogs had an average blood volume of 78.0 ml/Kg. Although the cardiac vagotomy dogs have relatively normal antidiuretic hormone levels following operation, they have blood volumes which are 20.8 ml/Kg higher than controls. This may be due to the lack of afferent volume receptor impulses from the left atrium following cardiac vagotomy while osmoreceptors may dominate in the regulation of antidiuretic hormone secretion.

EFFECTS OF HEAD OUT WATER IMMERSION ON URINE FLOW, PLASMA VOLUME, CATECHOLAMINE EXCRETION AND TILT TABLE TOLERANCE. Michael McCally (intr. by J.F. Hall). Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio.

Head out neutral temperature (34°C) water immersion of human subjects produces diuresis, plasma volume contraction, decreased urinary norepinephrine excretion and subsequent orthostatic intolerance as previously reported (New England J. Med. 269:508, 1963). Similar responses have been reported after prolonged manned space flight. Six protective techniques or countermeasures, including: 1) four extremity venous tourniquets or cuffs, 2) an elastic leotard, 3) antidiuretic hormone (ADH) injection, and 4) cold immersion (30-31°C), were assayed for their ability to alter or prevent these immersion responses. Chair rest, bed rest and bed rest with lower body negative pressure (LBNP) were studied as non-immersion controls. Venous blood and urine were collected in six subjects every two hours during each eight hour exposure. The elastic leotard donned after immersion, just prior to tilt, was the most effective measure tested and restored tilt table responses to control level ($p<0.01$). Four extremity venous tourniquets, inflated two minutes on and four minutes off, offered no protection but in a one minute on and one minute off cycle, significantly ($p<0.05$) increased urinary norepinephrine excretion and decreased the maximum heart rate response to the post-immersion tilt. Cold significantly increased urinary norepinephrine excretion during immersion but did not prevent post-immersion orthostatic tachycardia. Anti-diuretic hormone administration prevented the immersion diuresis but was without effect on subsequent tilt table tolerance. These observations may be pertinent to the prevention of the orthostatic intolerance seen after prolonged manned space flight.

FUNCTIONAL ADAPTATION OF MYOCARDIAL TISSUE IN HIGH ALTITUDE EXPOSURE. James McGrath* and Robert W. Bullard. Indiana University, Bloomington, Indiana.

Experiments have been continued to functionally test the extent of tissue level adaptation in exposure to simulated high altitude. Laboratory rats were exposed to 22,500 feet in a barometric chamber for 20 hours/day for 15 days. Right ventricular strips were removed, isolated in a Krebs-Ringers solution, attached to a force transducer and stimulating electrodes, and stimulated at a frequency of six contractions per minute. Aeration with 95% O_2 and 5% CO_2 was continued until the developed tension was stabilized. Testing for function under anoxic conditions was made by switching the aerating gas mixture to 95% N_2 and 5% O_2. The time interval then required for the contracting myocardium to reach one-half of the preanoxic tension in preparations from high altitude exposed rats was approximately twice as great as that of controls. A positive correlation was found between the hemoglobin concentration levels attained and the tissue resistance to anoxia. As the adaptive response was blocked by iodoacetate an alteration in glycolytic capacity is involved in the high altitude change.
Supported by NSF grant GB-11.

PULMONARY STRETCH RECEPTORS IN THE GRASS FROG. T. McKean (intro. by B.B. Ross). Department of Physiology, University of Oregon Medical School, Portland, Oregon.

Unitary discharge of stretch receptors of the isolated frog lung was recorded in order to correlate discharge frequency with lung volume. Action potentials from single fibers were amplified and recorded either on photographic film or on magnetic tape and were used to trigger counting devices. The volume of the lung was controlled by a syringe pump system filled with Ringer's solution. The experimental input waveform was a ramp of controlled slope terminated by a stable plateau of controlled amplitude and duration. The slope of the ramp ranged from 0.12 ml/sec. to 0.50 ml/sec. in increments of 0.125 ml/sec.. The volume of the lung was increased in 0.2 ml increments from resting lung volume to 1.0 ml above resting lung volume.

Approximately 70% of the receptors exhibited discharge in the uninflated state. The threshold for the remaining 30% ranged from 0.15 ml - 0.8 ml above resting lung volume. Approximately 25% of the receptors showed discharge only during inflation and appeared to respond to time rate of change of lung volume. 30% responded only to level of lung inflation. The remaining 45% showed a response to both rate of lung inflation and level of lung inflation.

Pressure-volume curves for the frog lung were comparable to those found in previous investigations.

It is concluded that the frog lung is capable of providing the C.N.S. with information pertaining to both lung volume and time rate of change of lung volume.
Supported by USPHS G:538.

Influence of Exercise and Emotion on the Telemetered Blood Pressure of Dogs During Obedience Training. Meehan,J.P., Sears,W.,* Reid,D.,* and Henry,J.P.,Univ.So.Calif.,Sch.of Med.,Dept.Physiol. Los Angeles, Calif.

Muller (Tierarztliche Umschau, 18:296, 1963) has shown that with careful habituation during sphygmomanometry, a "casual" pressure will fall by 40 mmHg to "basal" values on the order of 110/60 mmHg. Solid state transducers 6.5 mm diameter were implanted in the abdominal aorta of healthy young (50 lb.) German Shepherds. Leads were exteriorized over the lumbar region. The miniature FM/FM telemetry system employed is described elsewhere. (Meehan and Rader, I.S.A. Aerospace Symposium, 1967, in press). Calibration of pressure readings was against a direct measurement by a femoral needle. An obedience training course provided emotional arousal, and for physiological stimuli the animals exercised on a treadmill at various grades and speeds up to exhaustion. Responses of a subject implanted for five months were as follows: When sleeping the pressure averaged 103/52 mmHg (H.R.68) and on the treadmill was 144/78 (H.R.184) for moderate and 172/97 (H.R.282) for peak exertion. With exhaustion the pressure fell to 90/50 (H.R.300) and an irregularity of rhythm developed. As the table shows, pressures during obedience training were highest when the command was new to the animal. The heart rate remained persistently elevated at 150 to 200/min as compared with the sleeping average of 68/min.

Days	1-10		10-20		20-28	
	BP	HR	BP	HR	BP	HR
Sit	181/106	169	144/76	159	131/69	156
Heel	172/96	198	133/69	178	125/64	176
Stand	172/92	167	148/85	157	127/69	149

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TISSUE BLOOD FLOW AND ISOTOPE CLEARANCE. M. Meyer & M. Path*, Dept. of Physiol. and Sch. of Dent., Univ. of Minn., Mpls.

The clearance rate of a minute amount of isotope placed into a tissue may be an index of local blood flow. This study related this isotope disappearance rate in masseter muscle and oral mucosa to their blood flow. A minute amount of I^{131} (0.5-1.μl, 2-3μc) is injected into the mucosa and exposed muscle of anethetized dogs stablized in a head holder. Isotope activity is detected with a collimated probe connected to a ratemeter and recorded on a servo recorder. Following sacrifice, disappearance rate is re-examined. Calculation of tissue flow involved the application of the K^{42} isotope dilution and fractionation technique by which cardiac output (CO) and the fraction of the CO going to the tissue are determined. With circulation intact, disappearance was monitored for 30-50 minutes. Without circulation, about 80% of original activity injected was detected at 50 minutes in the mucosa, whereas about 90% was still detected in the muscle. Initial slope of a semi-logarithmic plot of the clearance curve corrected for background, disappearance under no flow conditions and normalized was essentially linear. Time for 63.2% to disappear averaged about 4 1/2 minutes for the mucosa and 7.0 minutes for the muscle. Tissue flow averaged about 0.36cc/min-gm in mucosa and about 0.24 cc/min-gm in muscle. Mean ratio of the recipocal time constant of muscle to mucosa and ratio of their blood flow were between 0.6 and 0.7. There appears to be a direct relationship between the amount of tissue flow and the rate of isotope disappearance. Supported by NIDR Grant #DE 02212.

MECHANISM OF CHANGES IN ACTIVE TENSION IN BRONCHIAL SMOOTH MUSCLE. J. L. Meyers*, N. L. Stephens*, and R. M. Cherniack. Departments of Medicine and Physiology, University of Manitoba, Winnipeg, Canada.

It has been demonstrated that increases in muscle length and stimulus voltage increase maximum isometric tetanic tension (AP_{max}) in bronchial smooth muscle, while changes in the gas tensions of the surrounding media reduce AP_{max}. The purpose of this study was to analyze the mechanism of changes in AP_{max}. The active state of the contractile element is an index of mechanical energy derived from chemical reactions, and is a measure of the force generating process of the contractile element. Changes in AP_{max} can be brought about by a change in the intensity of the active state, which may be reflected by the maximum rate of tension development (dP/dt_{max}), or by a change in the duration of the active state, which may be reflected by the time taken to reach peak tension development ($t_{AP_{max}}$). The increase in AP_{max} with increased muscle length and stimulus voltage was associated with an increase in dP/dt_{max}, $t_{AP_{max}}$ remaining constant. The decrease in AP_{max} with hypoxia and metabolic acidosis was associated with a decrease in dP/dt_{max}. $t_{AP_{max}}$ was unchanged with hypoxia but increased with metabolic acidosis. It is concluded that the observed changes in AP_{max} with muscle length, stimulus voltage, and hypoxia are probably due to changes in the intensity of the active state of the contractile element. Changes in AP_{max} with metabolic acidosis are likely due to changes in both intensity and duration of the active state.

EFFECT OF HYPOTHALAMIC LESIONS ON THE EXCITABILITY OF SPINAL MOTONEURONS. P. R. Miles and W. E. Gladfelter (intr. by E. J. Van Liere). Dept. of Physiology and Biophysics, West Virginia University Medical Center, Morgantown, West Virginia.

Damage to the lateral hypothalamus at the level of the tuber cinereum will cause a decrease in the spontaneous locomotor activity of rats. Experiments were performed to determine if a decrease in the excitability of spinal motoneurons is the mechanism by which these lesions cause hypoactivity. A supramaximal afferent volley was delivered to the third lumbar dorsal root, and the electrical reflex discharge was recorded from the corresponding ventral root in control animals and in rats with lateral hypothalamic lesions. It was found that the amplitudes and the areas of the monosynaptic and polysynaptic responses were decreased from the control level in rats with hypothalamic lesions. This indicates that the number of cells firing in response to the dorsal root volley was decreased in animals with hypothalamic destruction. In addition, lesions slightly increased central delay. When spinal reflexes were recorded during stimulation of the lateral hypothalamus, there was an increase in the number of cells firing in response to the dorsal root volley and a decrease in central delay. (Supported by NIH grants GM-437 and 5S01FR-05433-06).

REGIONAL DISTRIBUTION OF PULMONARY VENTILATION AND PERFUSION IN ELDERLY SUBJECTS. J. Milic-Emili, J. Holland* P.T. Macklem, and D.V. Bates. Joint Cardio-Respiratory Service, Royal Victoria Hospital, McGill University, Montreal, Canada.

Using ^{133}Xe, the regional distribution of pulmonary ventilation and perfusion have been measured at rest in 6 upright normal men, whose age averaged 69 years (range: 65-75). In 5 subjects, ventilation was distributed preferentially to the upper and middle lung zones instead of to the lower zones as it is in normal young men. This difference is consistent with airway closure in the dependent lung zones resulting from loss of elastic recoil of the lungs that occurs with age. In the other old subject ventilation distribution was normal. In all 6 elderly subjects perfusion distribution was preferential to the lower lung zones. Thus, in 5 of the elderly subjects there was a significant $\dot{V}/\dot{Q}$ abnormality on a regional basis which may explain at least in part the reported increase in A - a differences for oxygen in aged subjects.

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POSITIVE CHRONOTROPIC EFFECTS OF DOPAMINE. **R. W. Millard*** **and E. T. Angelakos.** **Dept. of Physiology, Boston Univ. Sch of Medicine, Boston, Mass.**

The chronotropic effects of dopamine (DA) and norepinephrine (NE) were examined by direct perfusion of the sinus node artery of the dog at a rate of 0.75 to 4 ml/min. DA produced a dose dependent tachycardia in amounts of 0.1 to 1.0 μg (total) comparable to that produced by 0.01 to 0.1 μg of NE, corresponding to a dose ratio of roughly 10:1. By contrast intravenous injections of 20 to 40 μg/Kg of DA caused an increase in heart rate (and cardiac contractility) comparable to that produced by 0.1 to 0.5 μg/Kg of NE or a dose ratio of 200:1. The submaximal effect of intranodal DA persisted much longer (10 min) than that of equipotent doses of NE (1 min). Beta adrenergic blocking agents (DCI 100 μg, prenethalol 500 μg, intranodally) prevented the positive chronotropic effects of intranodal NE and DA. Cocaine (100 μg intranodally) potentiated the tachycardic effect of NE (ca 2x) while it abolished completely the effect of DA up to doses of 50 μg. It is concluded that the positive inotropic effect of intranodal DA is dependent upon NE release. (Supported by USPHS grants HE 05680 and HE 09616 and Career Development Award K3-15,457.)

PERMEABILITY OF RAT TONGUE EPITHELIUM. Charlotte M. Mistretta* and L. M. Beidler. Florida State University, Tallahassee, Florida.

How well can taste substances penetrate the surface of the rat tongue? The tongue is covered with a coating of stratified squamous epithelium containing taste buds and free nerve endings. With this in mind, experiments were undertaken to compare the permeability of areas of the tongue with and without taste buds and to compare the permeability to that of epidermis from other body areas. After injecting a 1.0% solution of collagenase under the surface of rat tongue, one can easily slip off the epithelium, including taste buds. Histology on control tissue shows that full thickness epithelium is being removed. An area of tissue 0.49 cm^2 is placed in a diffusion cell and the movement of radioisotope through the epithelium is studied. Constant temperature and a constant volume flow of collecting solution beneath the tissue is maintained throughout experiments. A series of chemicals were investigated to determine the contributions of lipid solubility, molecular size, and electrical charge to penetration. Present results indicate that the epithelium is generally less permeable than epidermis from areas of the body previously studied. Passive diffusion accounts for the penetration of all substances studied. This work was supported in part by a contract with the Division of Biology and Medicine, U. S. Atomic Energy Commission.

EVIDENCE FOR A MONOSYNAPTIC INPUT TO BULBAR RETICULAR FORMATION FROM CAROTID SINUS NERVE IN CAT. M. Miura* and D.J. Reis, Cornell University Medical College, New York, New York.

Evoked responses elicited by electrical stimulation of the carotid sinus nerve (CSN) were recorded with capillary microelectrodes (20-30μ) in the medulla oblongata of cats anesthetized with chloralose and immobilized with Flaxedil. Among other responses a short latency negative wave, the early response (ER), was identified. Its onset latency ranged from 0.7 to 1.2 msec, the average peak latency was 1.4 msec, it fell to 50% peak amplitude at stimulus frequencies near 200 c/s and reached maximum size with stimulus intensities less than 5 times threshold. In contrast, the onset latency of the antidromic CSN response elicited from the reticular formation ranges from 0.3 to 0.9 msec and 50% fall-off occurs above 900 c/s (Crill & Reis), thus indicating the monosynaptic origin of ER. Calculated conduction velocities and intensity/response characteristics indicate ER is triggered by myelinated fibers. The ER covered a vertical field up to 2.2 mm but peaked to 80% of its size only over 300μ. Peak amplitudes reached 18 mV. Approaching the maxima, the rising slope steepened and the peak latency shortened consistent with propagation of the response into dendrites at 1 m/sec. 80% of maximum responses were located in the reticular formation, mostly medial, and 20% in the nucleus solitarius. Myelinated fibers of the CSN, probably baroreceptor in origin, therefore, make monosynaptic connection with neurons of the medullary reticular formation in cat. (Supported by N.I.H. grants NB-04876 and NB-06911.)

ANTRAL DEPLETION OF GASTRIN BY ELECTRIC STIMULATION OF THE VAGUS NERVE. E. Molina*, R. F. Edlich*, Y. Tomiyama*, W. P. Ritchie*, and O. H. Wangensteen. Dept. of Surgery, Univ. of Minnesota Med. School, Minneapolis, Minn.

In dogs with intact stomach, under light chloralose anesthesia, the vagus nerves were divided in the chest and an electric stimulus of 0.5 to 100 mV was applied for a single 15 minute period to the distal end of either nerve. A gastric secretory cycle was obtained which lasted 3 to 4 hours. Following this response, stimulation of the same or opposite vagus nerve did not elicit further acid production. In another group of dogs, the vagus was stimulated at various intervals either before, during or after a S. C. dose of 0.1 to 0.4 mg/kg weight of histamine base. In each instance, vagal stimulation either provoked acid production or enhanced acid secretion induced by histamine. In a third group of dogs with denervated fundic and innervated antral pouches, the acid secretory response of the intact stomach and denervated fundic pouch to the perfusion of the antral pouch with acetylcholine 0.5% sol., and to the administration of exogenous gastrin was studied before and after electric stimulation of the vagus. Acid secretion could not be elicited by acetycholine perfusion following electric stimulation, even though the denervated fundic pouch and intact stomach had a normal response to lyophilized exogenous gastrin. The results suggest that failure of a second stimulus to provoke acid secretion in this preparation is a result of depletion of antral gastrin.

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

THE EFFECT OF +Gz AND +Gx ACCELERATION ON BLOOD ADH LEVELS IN THE HUMAN. **W. W. Moore, J. D. Rogge*, W. E. Segar*, and A. F. Fasola*. Depts. of Physiol. and Peds., Ind. Univ. Med. Ctr., Indianapolis, Ind., Sch. of Aerospace Med., Brooks AFB, Tex., and Lilly Lab. Clin. Res., Indianapolis, Ind.**

The effect of +2 Gz and +2 Gx acceleration for 30 minutes on the peripheral venous ADH levels in human subjects was studied on the USAF-SAM Human Centrifuge. A mean rise in the blood ADH level of 2.97 uU/ml ($p < 0.05$) was found at the termination of the +Gz runs, and this rise could be inhibited by having the subjects wear an anti-G suit inflated to 60 mm of Hg. A mean decrease in the blood ADH level of 0.89 uU/ml ($p < 0.05$) was found following Gx acceleration. The changes in blood ADH level observed are probably secondary to shifts in distribution of blood volume into and out of the thorax during acceleration. Volume-sensitive stretch receptors in the left atrium are suggested to be the loci through which impulses are transmitted to the hypothalamo-neurohypophysial system and alter ADH secretion. Changes in urine volume previously reported by others during +Gz and +Gx acceleration are probably a result of changes in ADH secretion.

(Supported by USPHS Grants HE-10401 and H-6308).

A TECHNIQUE FOR THE CHRONIC IMPLANTATION OF MULTIPLE MOVABLE MICROELECTRODES. Pilar Morgades* and E. Roy John (intr. by). Brain Res. Laboratory. New York Medical College.

A simple, cheap technique will be described which permits long term recording of unit activity in unrestrained animals. This method utilizes a chronically implanted base which carries two metal microelectrodes located 125 microns apart inside a ceramic insulator. The ceramic is within a stainless steel tube, normally held motionless by an undersized Teflon bushing. The electrode assembly can be advanced smoothly and precisely by a micrometer which attaches to the base when necessary.

Examples will be shown of unit recordings, post-stimulus frequency histograms and averaged evoked potentials obtained under different conditions from a cat over a period of two months. (This work was supported by a grant number 08579 - 04 from the National Institute of Mental Health)

Effect of A.D.H. on osmotic equilibration in collecting ducts of an isolated rat papilla. Trefor Morgan†, and Fuminori Sakai (Intro. by J. Handler). N.I.H., Bethesda, Md.

Mechanism of osmotic equilibration was studied by stopflow and freeflow perfusion. Net water flow was calculated from the change in inulin concentration. Diffusional permeability to urea and water was measured by isotopic techniques. Net water and solute movement occurred only when osmolar or solute concentration gradients were present. The diffusional water permeability coefficient was 53 ± 4.3 cms sec^{-1} x 10^{-5} and increased to 95 ± 8.5 after A.D.H. The corresponding figures for urea were 13.8 ± 0.79 and 20.2 ± 1.3. Net water flux was 4.1 ± 0.92 $\mu l\ cm^{-2}\ min^{-1}\ mOsm^{-1}$ x 10^{-3} and increased to 21.0 ± 2.3. If the gradient was reversed an equal degree of water movement occurred in the opposite direction. Only when there was net water movement were intercellular spaces seen by electron microscopy. The difference in permeability to urea between the cortical and medullary collecting ducts and the residual permeability to water in the absence of A.D.H. are important for the functioning of the countercurrent concentrating mechanism.

†Supported by the Post Graduate Committee of the University of Sydney.

DELAY TIMES IN POSTURAL CONTROL. Shigemi Mori* and John M. Brookhart. Dept. of Physiology, Univ. of Oregon Medical School, Portland, Oregon.

The posture of quietly standing trained dogs has been perturbed by moving the supporting surface 20 mm in 100, 84, and 58 msec. approximating a step function of displacement in order to estimate delay time in the control system. Weight on posterior feet and EMG patterns from hind limb muscles have been correlated with onset of movement. Records from sets of muscles in each of 10 dogs have been obtained. The oscillatory pattern of weight change in response to forward displacement is bilaterally symmetrical uniform between trials and between animals, and consists of two major peaks of increase at 40-60 msec and 130-160 msec followed by smaller oscillations complete in approximately 300 msec. Tonically active muscles (e.g.M. biceps femoris anterior and medialis) exhibit cessation of discharge starting at 50-60 msec and enduring for 70-80 msec. Phasically active muscles (e.g.M. biceps femoris posterior and M. semitendinosus) exhibit a sharp burst of activity at 50-60 msec enduring for variable periods sometimes followed by a second burst at approximately 170 msec. M. adductor magnus and M. semimembranosus exhibit two modes of behavior, their reactions resembling those of tonically active muscles at some times and phasically active muscles at other times. The delay times may be slightly sensitive to changes of velocity in the range tested (0.2 to 0.35 M/sec.) The magnitude and probability of occurrence of specific change in some muscle activity patterns appear to increase with increases in velocity over the range tested. The delay times, their narrow range of variation, and their uniformity among muscles of various functions suggest the operation of an integrative mechanism involving supraspinal structures.
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SOME ELECTROPHYSIOLOGICAL PHENOMENA DEPENDENT UPON CHLORALOSE ANESTHESIA. J. B. Munson (intr. by E. B. Wright). Dept. of Physiol., Coll. of Med., Univ. of Fla., Gainesville, Fla.

Auditory and visual input to the cerebellar tuber vermis is modulated by primary sensory cerebral cortex in acute, chloralose-anesthetized cats (Munson and Snider, Fed. Proc. 1965). Specifically, KCl depression or surgical ablation of auditory cortex reduces (whereas strychnine application increases) the amplitude of both auditory and visual cerebellar evoked responses (CERs). Such treatment of visual cortex affects only visually elicited CERs.

Chloralose augments (2-4x) evoked response amplitudes in cats with chronically implanted electrodes. Ablation of auditory cortex in such cats under chloralose acutely depresses CERs as before, but postoperatively (24 hr) the CERs recover their full pre-operative unanesthetized amplitude. Reanesthetization with chloralose again augments CERs, but less so than in intact cats. Cats ablated under pentobarbital similarly show no residual deficit unanesthetized.

Tonic cortico-tectal facilitation of tecto-cerebellar transmission, hypothesized as the mechanism underlying our earlier observations, is apparently operative only in the case of chloralose anesthesia. Alternatively, it may be present in the unanesthetized state, but balanced by cortico-tectal inhibition of tecto-cerebellar transmission.

Electrical stimulation of inferior colliculus was observed to produce only ipsilateral cortical evoked responses without anesthesia, whereas under chloralose the responses appeared bilaterally.
(Supported by NSF Research Grant G 24013).

INFLUENCE OF THE AMYGDALA UPON SINGLE HYPOTHALAMIC NEURONS

J.T. Murphy [1], J.J. Dreifuss, P. Gloor, (intr. by Dr. F.C. MacIntosh), Montreal Neurological Institute, Montreal, Canada.

Extracellular records from single neurons in the tuberal hypothalamus of the cat were analyzed using computer summation techniques. Medial hypothalamic neurons were found to differ from lateral neurons both in spontaneous firing and in their response patterns to amygdaloid stimulation. Basal and cortico-medial amygdaloid stimulation influenced a greater number of these neurons than did lateral amygdaloid stimulation. Two amygdaloid efferent systems, the stria terminalis and the ventral amygdalo-fugal pathway, were studied anatomically and electrophysiologically. These two pathways differed in the slow potentials evoked by each, and in the effects of each upon the firing of single neurons. Convergence of these two pathways upon the same neurons was demonstrated. Stimulus locked periods of activation and/or inhibition were observed. Short latency activation was regularly seen with ventral amygdalo-fugal stimulation. There was evidence that the inhibition was mediated by local short-axon interneurons, except in the case of stria terminalis stimulation which probably produced its inhibitory effects directly. The effects of repetitive amygdaloid stimulation were dependent upon the post-stimulus firing patterns obtained with single-shock stimulation.

[1] Supported by U.S.P.H.S. Fellowship 2 F2 NB 28, 505-02

TEMPERATURE-RELATED CHANGE IN CALCIUM ION DEPENDENCE OF MYOFIBRILLAR ATPase ACTIVITY. R. A. Murphy and W. Hasselbach*. Univ. of Mich., Ann Arbor, Mich. and Max-Planck-Institut für Physiologie, Heidelberg.

Myofibrillar ATPase activity is increased by a rise in temperature or in [Ca^{++}]. Mühlrad and Hegyi (Biochim. Biophys. Acta, 105, 341, 1965) report that an increase in temperature decreases the [Ca^{++}] required for any given degree of activation. We have explored the effect of temperature on the [Ca^{++}] dependence of myofibrillar ATPase activity by measuring the inorganic phosphate liberated under the following conditions: myofibrils, 0.15 mg/ml; Ca^{++} determined by the ratio of EGTA/CaEGTA with total EGTA, 1 mM; ATP, 5 mM; $MgCl_2$, 5 mM; histidine, 20 mM (adjusted to give pH 7.0 upon addition of ATP at each temperature employed); KCl, 40 mM (μ = 0.1). The "initial rate" of ATPase activity was found to be a function of [Ca^{++}] from 20 to 40 C. However, as the temperature is increased from 20 to 40 C, the "basic rate" of ATPase activity becomes progressively independent of the [Ca^{++}]. At 40 C, almost no Ca is required for maximal ATPase activity. The loss of Ca^{++} sensitivity occurs under conditions when the rates of syneresis and ATPase activity are high: in the presence of ATP and Ca, and at physiological temperatures. Myofibrils which have lost sensitivity to Ca^{++} at 40 C no longer exhibit Ca^{++} dependent ATPase activity when retested at 20 C. This is also true of actomyosin extracted from myofibrils which were preincubated in the presence of ATP and Ca^{++} at 40 C. Thus, the loss of Ca^{++} sensitivity persists following additional purification of the contractile proteins. In contrast to myofibrils, natural actomyosin extracted from rabbit skeletal muscle shows no change in the normal [Ca^{++}] requirement between 20 and 40 C. (Supported by a Public Health Service Fellowship 2 F2 NB 11, 747 and a Grant from the Life Insurance Medical Research Fund.)

HELIUM-COLD INDUCED HYPOTHERMIA IN THE HAMSTER AND RADIO-RESISTANCE. X.J. Musacchia and R.E. Barr*. Departments of Physiology and Radiology, and Space Sciences Research Center, University of Missouri, Columbia, Missouri.

Hamsters, Mesocricetus auratus, placed in an ambient atmosphere of 80% helium and 20% oxygen at temperatures of from 5°C to 15°C, become hypothermic. Depending upon body size and ambient temperature, it takes from 6 to 12 hours for body temperature to fall to approximately ambient levels. The hypothermic hamster is relaxed and limp. These animals revive from hypothermia by exposure to room temperature. Comparison of radio-sensitivity between active and hypothermic hamsters were made. In a typical series, whole body exposure to ^{60}Co at 1000, 1250, 1500, and 2000R showed higher mean survival times in hypothermic irradiated animals at all dose levels. The LD 50/30 for the hypothermic animals is approximately 1100R, whereas for the active hamsters the LD 50/30 is approximately 800R. (Supported by NASA NGR 26-004-021).

THE EFFECT OF VISUAL DEPRIVATION ON RAPID EYE MOVEMENTS OF DESYNCHRONIZED SLEEP IN THE CAT. G. E. Myers and A. R. Morrison (intr. by J. M. Sprague). School of Vet. Med., Univ. of Penna., Philadelphia.

The result of impaired development of visual function on the rapid eye movements (REM) of the cat is still an unsettled question. As part of a study designed to examine the effects of visual deprivation of varying degrees of severity, the eyelids of each of ten kittens were closed with sutures at six to nine days of age, prior to the time of normal eye opening. In two cats complete eye closure was accomplished; while partial eye closure was obtained in four others. At least seven months later electrodes were implanted for chronic recording of the electro-oculogram, electroencephalogram, and electromyographic activity of the dorsal cervical muscles in two cats of each group. The records obtained from both groups did not differ from those of normal cats studied. The sleep-wakefulness cycle was not altered. During desynchronized sleep REM were present in all animals. The frequency of occurrence of REM, the rates of ocular movements within bursts of REM and the amplitudes of the EOG tracings appeared normal. These data, therefore, support the concept that REM result from central neural discharges which do not depend on normal patterned visual input for their occurrence. (Supported by USPHS Grants 5T5 GM-1604-10 and 2 T1 NB-5273).

ISOPROTERENOL - A POSSIBLE MEDIATOR OF SYMPATHETIC VASODILATION. Helen A. Myers* and Carl R. Honig. Univ. of Rochester, Sch. of Med., Roch., N.Y.

It is currently held that acetylcholine is the mediator released by sympathetic vasodilator nerves to skeletal muscle. The possibility that isoproterenol is the mediator instead is suggested by reports that isoproterenol occurs *in vivo*, and by the similar characteristics of vasodilations produced by isoproterenol, acetylcholine, and sympathetic nerves. Evidence that the mediator is acetylcholine is entirely pharmacological, and suffers from lack of specificity of drug action and uncertainty as to the locus of drug effects. In dogs anesthetized with chloralose sympathetic vasodilator areas in hypothalamus, described by Lindgren *et al* (J. Comp. Neurol. 105:95,1956), were stimulated at 70 cps, 2 msec pulse duration, 0.2 mamp constant current. Resistance across the hind limb exclusive of paw was calculated from continuous measurements of pressure and femoral flow. Statistical methods were devised for evaluating, for various values of control resistance, the degree of blockade of vasodilation produced by antiadrenergic and anticholinergic drugs. Dichloroisoproterenol (2.5 - 10 mg/kg), propranolol (2.5 - 7.5 mg/kg), and methoxamine (0.8 mg/kg) inhibited vasodilation. Inhibition was dose dependent and within the range required for cardiac effects. Cardiovascular effects of injected acetylcholine and vagal stimulation were unaltered. Inhibition of sympathetic vasodilation by atropine was dose dependent over the range 0.03 - 3.0 mg/kg, whereas vagal effects on heart rate were completely blocked by 0.1 mg/kg. Atropine given after dichloroisoproterenol usually enhanced the response to hypothalamic stimulation. A distal site of action of dichloroisoproterenol was demonstrated on isolated, innervated gracilis muscles perfused from a reservoir. We conclude that it is as reasonable to interpret the data to mean that the mediator is isoproterenol as it is to believe that it is acetylcholine.

RESPONSE OF SKELETAL MUSCLE VEINS IN LOCAL REGULATION OF BLOOD FLOW. F. J. Nagle,* J. B. Scott, and F. J. Haddy. Depts. of Physiol. Univ. of Wisconsin, Madison, Wisconsin and Michigan State University, E. Lansing, Michigan.

An examination of the resistance to flow through veins in skeletal muscle during active hyperemia, reactive hyperemia, autoregulation and the venous arteriolar response has been made in the dog. The gracilis muscle was isolated so that blood entered via the gracilis artery and left via the gracilis vein. The gracilis vein was cannulated for blood flow measurements. Pressures were measured in side branches of the gracilis artery and vein and in a small vein extending directly from the muscle belly. Flows and pressures were measured before, during and immediately after electrical stimulation (4V, 0.02ms, 4/sec.) of the gracilis nerve, partial occlusion of the gracilis artery and partial occlusion of the gracilis vein.

Venous resistance fell during active hyperemia and remained low for a short period following termination of the exercise. It rose during partial arterial occlusion and then fell below the control level on release of occlusion. Partial venous occlusion lowered venous resistance. Total resistance fell during and after nerve stimulation; it did not change significantly during partial arterial occlusion but fell on release of occlusion, and rose during partial venous occlusion. In each case the change in venous resistance was in the direction of the change in venous transmural pressure.

RADIATION OF LUNG: EFFECT ON PHOSPHOLIPIDS, SURFACE ACTIVITY AND MORPHOLOGY. Arnold Naimark, Donald Newman*, Drummond H. Bowden*. Depts. of Physiology and Pathology, Univ. of Manitoba.

The nature of radiation injury to the lung was studied in rats. At intervals of 1-4 months after radiation of the right hemithorax (3000r, single dose) exposed lungs were compared to contralateral shielded lungs and the right lungs of non-radiated control rats. The DNA and total lipid phosphorus (P) content of radiated lungs did not differ from controls but the ratio - lipid P / DNA - increased, suggesting qualitative change in the cell population. Tissue slices from radiated lungs exhibited markedly depressed incorporation of palmitate-C^{14} into various phospholipids in vitro. The stability of bubbles expressed from the cut surface of radiated lungs decreased progressively after radiation, indicating impaired surface activity of the lung lining layer. Electron microscopy revealed no qualitative changes in the alveolar epithelial cells. Morphologic evidence of injury was limited to the capillaries. They showed endothelial swelling, mast cell and plasma cell infiltration and collagenous lumenal occlusion. The changes were focal in nature and unevenly distributed throughout the affected lung. It is postulated that a small, but metabolically highly active, population of lung cells is depleted following radiation, perhaps as a consequence of capillary damage. The pronounced effect on surface activity suggests that these cells may be involved in the elaboration or maintenance of the lung lining layer.

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EFFECTS OF LABYRINTHINE AND VISUAL DEPRIVATION ON POSTURAL STABILITY. Calvin Nakao* and John M. Brookhart. Dept. of Physiology, Univ. of Oregon Medical School, Portland, Oregon

Spontaneous variations in distribution of weight of quietly standing dogs has been used as an index of postural stability. Five dogs have been studied in the normal condition (C), blindfolded (B), after chronic labyrinthine deprivation (L), and with the combined deprivation (LB). Caloric stimulation was used to test completeness of labyrinth destruction. Movements of the center of weight distribution in the longitudinal and transverse directions were recorded in ten consecutive 5 min. trials for each condition in each dog. No significant changes were noted in lateral movements of the center of weight distribution. The mean standard deviation (within--trial variability) of longitudinal movements did not change significantly in any condition. When the LB condition was compared with the L and B conditions, the mean of means and the standard error of longitudinal variations indicated that the doubly-deprived dogs shifted their centers of weight distribution slightly (0 to 15 mm) forward ($p < 0.05$). The results suggest that the control system in the doubly-deprived animal reflects a distortion of feedback information related to position but no alteration of information related to change of position. The small magnitude of the deviation from normal may imply 1) the overwhelming importance of information from somesthetic sources to the operation of the control system or 2) that the perturbations encountered during quiet standing do not test the control system severely enough to reveal the deficits resulting from these deprivations.

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GLYCOGEN CONTENT IN THE INTESTINE OF THE FETAL AND NEONATAL RAT. Paul Nathan. Shriner's Burns Unit and the Depts. of Physiology and Surgery, Univ. of Cincinnati Coll. of Med., Cincinnati, Ohio.

Studies of everted pouches of intestine obtained from neonatal rats showed active transport of glucose. Some experiments demonstrated a net gain in sugar in the solutions bathing the intestines. This net accumulation of sugar was not observed with similar preparations from mature rats. In the present work, glycogen levels were measured in segments of the jejunum and ileum as a potential source of the extra sugar seen in the experiments with young rats. Intestines were removed from young albino rats one day prior to their birth and at 1, 12, 21 and 28 days of age. Six animals were studied in each group. Four cm lengths of tissue were weighed and then analyzed for their glycogen content by the anthrone method. All the results are expressed as mg glycogen/100 gm wet weight of intestine. In the fetal rat glycogen varied from a level of 60 mg in the duodenum to 250 mg in the ileum. The newly born rat had approximately 100 mg in the proximal intestinal segments increasing to 160 mg in the distal ileum. In the 12-day old rat, the glycogen values varied between 50 and 100 mg in the proximal 2/3 of the small intestine, and attained values of 150 mg in the distal 1/3. By contrast, in the more mature rats at 21 or 28 days of age, the duodenal portion of the intestine contained less than 50 mg of glycogen /100 gm wet weight, and the ileal segments demonstrated a level of 40 mg. Thus, the intestine of the younger rats showed a consistently higher glycogen concentration than that seen in the older animals. It appears likely that some of the sugar transported by everted sacs of neonatal rat intestine may arise from glycogen stores in the tissues.

EFFECT OF ALTERATIONS IN URETERAL PRESSURE ON RENAL AUTOREGULATORY CAPACITY. L. Gabriel Navar*, Philip G. Baer*, and A. C. Guyton (intro. by Ben H. Douglas). Univ. of Miss. Medical Center, Jackson, Miss.

This study was undertaken to determine the effect of increased ureteral pressure (UP) on renal blood flow (RBF) and renal autoregulatory capacity. Dogs anesthetized with Na pentobarbital were given an intravenous isotonic saline drip of 0.5 to 1 ml/min. Arterial pressure was elevated by constriction of the carotid arteries. Through a left flank incision, an electromagnetic flow probe and an adjustable plastic clamp, used to vary renal arterial pressure (RAP), were placed around the renal artery. RAP was measured through a teflon needle inserted distal to the clamp. The ureter was connected to a pressure transducer and a drop recorder. UP was elevated by raising the drop recorder and allowing the kidney to excrete urine against the increased hydrostatic pressure. Control pressure-flow relationships at zero UP exhibited typical autoregulation. Moderate increases in UP (up to 20 mm Hg) caused a slight increase in RBF and a minimal elevation of the plateau in the pressure flow curve. RBF increased as much as 100% with greater increases in UP up to 50-80 mm Hg. The pressure-flow relationship showed a progressively elevated plateau with the breakpoint between the plateau and the linear portion of the curve occurring at a higher RAP. The RAP at zero RBF and the slope of the linear portion of the pressure-flow relationship were not noticably influenced by increases in UP. Elevation of UP to the extent that urine flow ceased resulted in a passive pressure-flow relationship with no further increment in RBF. Upon re-establishment of zero UP, RBF showed a variable degree of recovery from complete to 50% but the pressure-flow curves demonstrated adequate autoregulatory capacity. Prolonged polyuria occurred after UP was returned to control levels.

THE FATE OF ^{14}C HISTAMINE DURING GASTRIC SECRETION. Henri Navert,* Eunice V. Flock,* Gertrude M. Tyce,* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Histamine (2-ring-^{14}C) di-HCl (H) (0.05 mg/kg/hr) was injected i.v. continuously for 140 min in conscious, adult dogs with Heidenhain pouches until the levels of concentration of radioactive H in plasma, gastric mucosa, and juice were constant (steady state). To determine rates of disappearance of H and its catabolites, the same quantity of nonradioactive H was given for 100 min. Mucosa of the corpus was serially biopsied at 10 or 20 min intervals; venous plasma and gastric juice were collected simultaneously. Radioactive H and catabolites were extracted and identified by TLC or HVPE or both. Mean values during the steady state in two experiments were:

Compounds	% Total activity		
	Mucosa	Plasma	Juice
I histamine (H)	9.1	15.1	3.6
II 1,4 methyl-histamine	53.0	13.6	32.5
III 1,4 methyl-imidazole acetic acid	17.2	42.0	4.9
IV imidazole acetic acid	6.4	14.6	2.4
V imidazole acetic acid riboside	6.5	5.9	0
VI acetyl histamine (?)	3.2	3.8	53.5
Undetermined	4.6	5.0	3.1
Relative ratios of total activity	10	5	1

Thus, relatively little radioactive H could be identified in plasma, gastric mucosa, and gastric juice. The data suggest that I is rapidly metabolized; of the catabolites, II accumulates in mucosa, III predominates in plasma, and VI in gastric juice. (Supported in part by grants from the Louis W. and Maud Hill Family Foundation, NIH Grant NB-4004, and the Foundation of Jean-Louis Lévesque, Montreal.)

SODIUM AND POTASSIUM LEVELS IN SERUM AND URINE OF COLD-EXPOSED CHIPMUNKS. William H. Neff* and Adam Anthony. Department of Biology, Pennsylvania State University.

Urinary and serum sodium and potassium levels were measured in chipmunks exposed to cold (3±2 C) for 1, 4, 8 and 30 day periods. Cold induced diuresis caused a net increase in the excretion rate of both sodium (+45%) and potassium (+42%) over the entire exposure interval despite a reduced concentration of sodium and potassium per unit volume of urine. However, serum levels of sodium and potassium were maintained within normal limits except on day 4 when the Na/K ratio was reduced due to increased serum potassium (+22%) and decreased serum sodium (-10%) concentrations. The overall findings are in keeping with the belief that rapid homeostatic restoration of serum ionic balance during cold exposure probably results from an increased renal reabsorption of sodium. This could occur through an increased secretion of aldosterone triggered by relatively high circulating levels of potassium during the first few days of exposure. (Supported in part by NASA Grant NGR-39-009-015 and Public Health Research Grant GM 07678 from the Institute of General Medical Sciences.)

NON-LINEAR ELECTRICAL PROPERTIES OF THE MOTONEURON MEMBRANE. P.G. Nelson, R.E. Burke and H.D. Lux, Natl Inst.of Health, Bethesda, Md., and Max Planck Inst., Munich, Germany.

Complex responses of the cat motoneuron membrane to pulses of current have been described in terms of 3 exponential processes by Ito and Oshima (J.Physiol.1965). They also showed that the motoneuron membrane may exhibit anomalous rectification. The present experiments indicate that polarizing currents produce complex time and voltage dependent alterations in membrane conductance and e.m.f. When small pulses of current are superimposed on long pulses or steady currents, both the time course and steady value of the voltage produced by the short pulses indicate that a change in membrane resistance may be produced by the long-lasting currents. Overshoots of the membrane potential following the longer currents suggest that a change in membrane e.m.f. has occurred. A complete description of the motoneuron membrane must incorporate these complex non-linearities. Nevertheless, some of the membrane electrical characteristics at a given membrane potential can be determined assuming linear behavior. Dendritic spread of current and membrane non-linearities must be distinguished and taken into account in analyzing the transient response of the membrane to current pulses. Both membrane non-linearity and accommodative properties are membrane potential dependent (Koizumi,et al, J.Neurophysiol. 1966). Accommodation does not necessarily accompany the membrane non-linearity.

INTESTINAL TRANSPORT, COENZYME A CONTENT AND ULCERATIVE COLITIS IN SWINE DEFICIENT IN PANTOTHENIC ACID. Ralph A. Nelson and Howard S. Teague.* Scott Research Laboratories, Fairview General Hospital, Cleveland, O. and Ohio Agricultural Research and Development Center, Wooster, O. and Ohio State University.

Studies of the effect of pantothenic acid deficiency on transport of water, sodium, potassium and glucose were carried out in jejunal and colonic segments of 22 pigs. Assays of coenzyme A activity of the colonic mucosa were performed in 16 animals. In the jejunum, deficiency produced an equal reduction in the bidirectional flux rates of sodium and mild reductions in net potassium and glucose transport. Net water and sodium movement were unaffected. In the cecum, enterosorption of body water and sodium was produced or accentuated in deficient pigs or in pigs weaned from gilts fed a diet low in this vitamin. In long term chronic studies in two animals, exsorption of sodium declined as well as net water, sodium and potassium transport. Early in the development of deficiency large quantities of water, sodium and potassium were lost into the gut lumen of two of four pigs with chronic jejunal segments. Also early in deficiency, cecal transport demonstrated a sudden increase in K enterosorption accompanied by an increase in Na absorption. Both of these effects disappeared as the deficiency state progressed. Coenzyme A activity of the colonic mucosa was reduced by more than 75 per cent in pantothenic acid deficient pigs with bloody diarrhea and ulcerative mucosal lesions which appeared similar to ulcerative colitis of humans. It was concluded that pantothenic acid deficiency affects gut transport and produces reduced levels of coenzyme A content in colonic mucosa.
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ADENOSINETRIPHOSPHATASE ACTIVITY OF ARTERIAL WALL ACTOMYOSIN: MAGNESIUM ION DEPENDENCE. D. L. Newman*, R. A. Murphy and D. F. Bohr. Univ. of Mich., Ann Arbor, Mich.

The $[Mg^{++}]$ requirement of glycerinated hog carotid artery strips for tension development is much greater than that of glycerinated rabbit psoas (Filo, et.al., Science, 147, 1581, 1965). The following results show that this relationship is also characteristic of the ATPase activity of actomyosin extracted from hog carotid arteries (VSM-AM) compared with that from rabbit skeletal muscle (SK-AM). Technique for isolation of VSM-AM was similar to that of Filo, et.al. for the "purified preparation" (Am. J. Physiol., 205, 1247, 1963). ATPase activity was measured under the following conditions: VSM-AM, 0.3 mg/ml (37 C) or SK-AM, 0.15 mg/ml (20 C); ATP, 1 mM; histidine, 20 mM (pH 7.0); KCl, 40 mM (μ, 0.1); $[Ca^{++}]$, 10^{-5} M; $[Mg^{++}]$, 10^{-8} to 10^{-2}M. $[Mg^{++}]$ and $[Ca^{++}]$ were calculated using a MgUDA--UDA--CaUDA buffer system where total uramil-N,N-diacetic acid (UDA) was 1 mM. The basic rate of VSM-AM ATPase activity was very low at $[Mg^{++}]$ up to 10^{-4} M. With higher $[Mg^{++}]$ there was a progressive increase in ATPase activity to a maximum of 0.05 μM P_i/mg protein per min at 10^{-2}M Mg^{++}. SK-AM ATPase activity increased with $[Mg^{++}]$ from 10^{-8} to 10^{-4} M to a maximum of 0.23 μM P_i/mg protein per min whereas greater $[Mg^{++}]$ decreased ATPase activity. The $[Mg^{++}]$ dependence of the VSM-AM preparation is significantly different from that of SK-AM, and is consistent with the effects of $[Mg^{++}]$ on tension development of glycerinated strips in the two types of muscles. (Supported by a Grant from the Life Insurance Medical Research Fund.)

THE PRESSURE GRADIENT BETWEEN LEFT VENTRICLE AND ASCENDING AORTA DURING SYSTOLE. M. I. M. Noble (intr. by M. B. McIlroy). Cardiovascular Research Institute, Univ. Calif. Med. Ctr., San Francisco, Calif.

The pressure difference between left ventricle (LV) and ascending aorta was studied in conscious and closed chest, anesthetized dogs. A Microsystems 1017 pressure transducer was implanted through the anterior wall of the LV and the transducer of a Statham M-4000 electromagnetic flowmeter was placed around the root of the aorta. Subsequently, a Statham SF1 catheter tip manometer with side hole was advanced retrograde into the LV and its pressure signal matched in gain and zero level with that of the 1017 transducer. The SF1 was then withdrawn into the ascending aorta. LV pressure exceeded aortic pressure in early systole and was less than aortic pressure in late systole; the maximum differences were 6-11 mm Hg in each case. The early systolic positive gradient was greater than the late systolic negative gradient but of shorter duration; it had no large peak. Pressures equalized just after the peak of aortic flow. Injection of calcium gluconate into left atrium or coronary artery increased both positive and negative gradients as well as acceleration and deceleration of LV outflow. Similar systolic pressure gradients were found in the LV outflow tract and have been reported for the ascending aorta. The results confirm in the conscious dog that the longitudinal impedance is largely inertial at these sites and suggest that the same LV pressures in early and late systole do not imply equal potential energy production by the LV muscle. (Supported in part by USPHS grant HE-06285, and a Senior Fellowship from the San Francisco Heart Assoc.)

THE ACTIVITY OF NEURONS IN CAT GLOBUS PALLIDUS FOLLOWING CORTICAL AND SUBCORTICAL STIMULATION[1]. H. Noda*, S. Manohar*, and W. R. Adey. Space Biology Laboratory, University of California, Los Angeles.

The response patterns of neurons in globus pallidus to single or repetitive stimulation of caudate, sensorimotor cortex, non-specific thalamic nuclei, midbrain reticular formation, amygdala and subthalamic areas were investigated with steel microelectrodes in locally anesthetized and immobilized cats. Three general patterns of spontaneous activities were observed. The first group of neurons showed high frequency discharges, the second low frequency discharges and the third repetitive bursts. The effects of stimulation were analyzed by digital computation. Caudate stimulation caused inhibition and sometimes this was preceded by oligo-synaptic activation. Less frequently inhibition was observed on stimulation of sensorimotor cortex. Non-specific thalamic and midbrain reticular stimulation usually caused marked facilitation. Stimulation of amygdaloid complex and subthalamic areas commonly produced facilitation; rarely, initial facilitation was followed by inhibition. The effects of stimulations and the response patterns were variable in different units. A large number of units was responsive to reticular stimulation. However, others responded exclusively to amygdala, caudate, non-specific thalamic nuclei or subthalamic areas. These units were scattered through the pallidum. Some units responded to stimulation of more than two structures. This was commonly observed in the first group of neurons. Sometimes it was difficult to elicit responses to stimulation of any structures examined from the second and third group of neurons. The data suggest that one class of pallidal neurons shows responses only to a single stimulus site, whereas convergent pathways exist to closely adjacent pallidal neurons from caudate, amygdala, non-specific thalamic nuclei, and midbrain reticular formation.

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BSP CLEARANCE AND FATTY INFILTRATION OF THE LIVER IN THE DOMESTIC FOWL. J. O. Nordstrom* and A. H. Smith, Department of Animal Physiology, University of California, Davis, California.

Fatty infiltration of the liver in the female bird during reproductive activity (egg formation) is a natural phenomenon. Under these conditions, one might anticipate the rate of disappearance of BSP from the plasma (BSP disappearance constant, "k") following a single injection of the dye to be decreased. Fatty infiltration of the liver in the domestic fowl (chicken), however, does not appear to impede the removal of BSP from the plasma by the liver, and in general, k tends to increase as the liver fat content increases. In the laying hen, there appear to be two separate relationships between k and liver fat content, one at liver fat levels below 75 mg fat/gm fresh liver ($k = 0.0080$ (mg fat/gm fresh liver) $- 0.18$), and the other at liver fat levels above 75 mg fat/gm fresh liver ($k = 0.0021$ (mg fat/gm fresh liver) $+ 0.016$). During a progesterone-induced molt, in which the liver fat content is considerably reduced, k will systematically increase or decrease depending upon the value of k in a given animal during the laying state (k during molt = 0.69 - 1.13 (k during laying)). The response of k in transition from the laying to the molting state can be explained from the relationship between k and liver fat content in the laying hen. The results suggest that the rate of hepatic removal of BSP from the plasma in the female chicken is closely related to and enhanced in some way by the amount of liver fat present.

VENTILATION STUDIES WITH SYNTHETIC FLUIDS. R.H. Norton*, L. Malone*, B. Yates* and D.M. Long. Dept. of Surg. Research, Hektoen Institute and University of Illinois. Chicago, Illinois

Polyfluorocarbon and polysiloxane fluids are of physiological interest because of their high O_2 solubility, low viscosity, low surface tension and low toxicity. The properties are such that animals can be ventilated with these fluids at ambient pressure with survival. Diseased lungs can be inflated with synthetic fluids with no losses into the lung tissue. Thus it has been possible to differentiate between mechanical abnormalities due to interfacial forces and abnormalities in tissue elasticity. Toxicity is associated with acute emphysematous and hemorrhagic lesions and rapidly developing (<5 minutes) CO_2 retention. However, sequential experiments with a given quantity of the fluid indicate that there is decreased toxicity through use.

MEASUREMENTS OF UMBILICAL BLOOD FLOW AND VASCULAR VOLUME BY DYE DILUTION. Miles J. Novy* and James Metcalfe. Heart Research Laboratory, University of Oregon Medical School, Portland, Oregon.

Measurements of umbilical blood flow, using indocyanine green dye, were made in 8 fetal goats (128-140 days gestational age) while the fetuses were in utero and the mothers were under halothane and barbiturate anesthesia. Placental arteriovenous shunting was not detected by this method. Circulation time in the umbilical circuit averaged 7.2 seconds. Each umbilical artery and its accompanying vein represent a virtually separate circulation prior to intra-abdominal fusion of the umbilical veins. Mean umbilical blood flow was 143 (± 62 S.D.) ml/kg/min. Umbilical C_vO_2-C_aO_2 was 3.6 (± 0.2 S.D.) ml/100 ml. Fetal oxygen consumption was 5.1 (± 1.9 S.D.) ml O_2/kg/min, and fetal pH ranged from 7.00-7.44. Total fetal blood volume was 143 ml/kg of fetus. Placental blood volume averaged 39.2 ml/kg of fetus. In 3 experiments injection of norepinephrine into the umbilical artery increased arterial blood pressure and placental vascular resistance. This was associated with a fall in umbilical flow rate, an increase in mean placental transit time, and an increase in blood volume in the umbilical circuit. (Supported in part by grants from NICHD and NHI.)

A COMPARISON OF PYRAMIDAL TRACT ORGANIZATION IN PRE- AND POSTCRUCIATE CORTEX OF THE CAT. Judith K. Nyquist*, David Whitehorn* and Arnold L. Towe. Dept. of Physiology and Biophysics, Univ. of Washington, Seattle, Washington 98105.

In the forelimb region of postcruciate cortex of the cat under chloralose anesthesia, the order in which the PT cells are brought into activity is similar following stimulation of ipsilateral forepaw and both hindpaws. However, the pattern displayed in response to stimulation of the contralateral forepaw is unique. We have previously suggested (Fed. Proc. 26:491, 1967) that an interaction of small-field non-PT cells and wide-field PT cells is involved in production of this unique pattern. In the precruciate cortex, which contains very few small-field cells, a comparison of the PT population response following input from each of the four extremities yields a different picture. A strong correlation (r=0.7) is found between the sequences of activation when stimulation of the two forepaws or the two hindpaws are compared. A weaker, but significant correlation (r=0.4) exists between the orders of discharge following stimulation of the two contralateral paws or the two ipsilateral paws. Comparison of the responses to inputs from a forepaw and the opposite hindpaw yields a poor correlation (r=0.2). Previous work has shown the pattern of activation to differ in the pre- and postcruciate PT populations when the same peripheral site is stimulated. The present results indicate that the manner in which these patterns change with a change in the site of peripheral stimulation also differs. The implications of this finding with respect to the organization of the afferent input to the two cortices will be discussed. (Supported by research grants NB 396 and NB 5136 from USPHS.)

QUANTITATIVE STIMULATION OF SINGLE OLFACTORY RECEPTORS. R. O'Connell* and M. Mozell. State University of New York Upstate Med. Ctr., Syracuse, N.Y.

The electrical activity of single receptors was recorded extracellularly with metal filled microelectrodes from the exposed ventral olfactory mucosa of the frog. The purity of the four chemicals used as stimuli was assured chromatographically. The olfactometer was calibrated with a gas chromatograph. Approximately 50% of the observed cells were unaffected by all four chemicals. Of the 48 cells whose activity could be modulated 47 were excited and one was inhibited. The mean spontaneous level of the excited cells was 3 spikes/min. The frequency of response increased with concentration; its latency decreased. For any one chemical the slope of the response function (frequency or latency vs. concentration) varied from cell to cell. It also varied from chemical to chemical for any one cell. As a consequence of this variance in slope a given cell ranked the four chemicals, according to frequency or latency, in a reproducible but concentration dependent order. A comparison of 23 cells revealed that there are several different rank orders although some are more common than others. In 14 cells the simultaneous presentation of two different chemicals elicited a response which was greater than the sum of the responses obtained with each chemical given alone; in 11 cells it was less. Increases in response were most often seen in those cells which fired at a low rate to individual stimuli. Decreases were noted for those cells that fired at a high rate. These data suggest that the receptor sites involved are not homogenous. Supported by NIH Grant NB 03904.

THE LOCALIZATION OF RELAXIN IN THE REPRODUCTIVE ORGANS OF THE PREGNANT MAMMAL. W. B. O'Connor* and M. X. Zarrow. Dept. of Biological Sciences, Purdue University, Lafayette, Ind.

An antibody to relaxin was developed in the rabbit. The specificity and potency of this antibody was demonstrated by both in vivo and in vitro assay techniques. The antibody to relaxin was labelled with Iodine-125 and a specific activity of 20-40 $\mu C/\mu g$ was obtained. Amounts ranging from 0.5 to 6.0 μg of this antibody preparation were injected into pregnant mice, rats and rabbits in the last week of their respective gestation periods. Tissue sections of various reproductive organs were cut on the cryostat at 6-10 μ, dipped in Kodak NTB-2 emulsion and prepared for autoradiographic examination. The iodinated relaxin antibody was found in the ovary, uterus, vagina and placenta of the mouse, rat and rabbit. It was also localized in the cervix of the rat and rabbit. Control studies with iodinated normal rabbit gamma globulin, Iodine-125 alone, and non-pregnant animals failed to show any definite localization in any of the above organs. This study demonstrates the specific localization of relaxin in the reproductive tract of the rat and rabbit during pregnancy and substantiates the concept that relaxin is a hormone of pregnancy. The localization of relaxin in the uterine endometrium could indicate either a site of action, a site of degradation, or a site of relaxin synthesis. The latter concept has been suggested from other studies. (Aided in part by Grant HD-02068 from NIH.)

Effects of hypercapnia on airways and ventilation in the pilot whale. C. R. Olsen, F. C. Hale*, R. W. Elsner and D. W. Kenney*. V. A. Center, Los Angeles, Depts of Medicine and Physiology, UCLA School of Medicine and Scripps Institution of Oceanography, UCSD.

Scholander suggested that compression of alveolar gas into bronchi protects diving whales from bends. This implies that the airways must withstand narrowing under compression. Hypercapnia, which occurs in diving, induces bronchoconstriction in the dog and cat; this in turn helps cat trachae and bronchi to withstand compressive narrowing. To determine cetacean airway responses to hypercapnia we measured esophageal and blowhole pressures and simultaneous volume and flow at the blowhole of a 400 kg whale. Lung volumes were measured by helium dilution and alveolar gases by volumetric analysis. End-expired lung volume averaged 5.56 L, and tidal volume (V_T) ranged from 9 to 29 L. V_T and respiratory rate increased in response to both hypercapnia and rebreathing. Average pulmonary resistance (R_L), calculated from inspiratory and expiratory pressures and flows at the same lung volumes, was 0.12 cm H_2O/L/sec. R_L did not increase in response to rebreathing or to added CO_2 to alveolar Pco_2's as high as 159 mm Hg. Pressure-volume hysteresis with large tidal volumes and Bernoulli effect in the blowhole probably subjected the R_L measurement to error. However, isovolume expiratory flows also did not change in response to CO_2, and all expirations were passive. This does not exclude a response in the diving whale, where average Pco_2 (urine) is reported as high as 500 mm Hg (A. H. Laurie. Discov. Rep. 7: 363, 1933).

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MICROCIRCULATORY LESIONS INDUCED BY WHOLE BODY X-IRRADIATION. EFFECTS OF CORTICOSTEROIDS. N.A. On'gele, T.A. Balourdas, Noralean Williams and F.D. Drew (intr. by E.M.K. Geiling). Depts. of Pharmacology and Radiology, Medical School, Howard University, Washington, D.C.

The harmful effects of the X-rays irradiation on the peripheral vascular system and especially the microvessels of the rat mesentery were studied. The animals were subjected to whole body irradiation (200r), and the mesocaecum bioassay was used for direct visualization of the mesoappendiceal vessels by in vivo microscopy, given that the most toxic and potential lethal effects of radiation are exerted on the minute blood vessels with visceral hemorrhages and on the bone marrow with aplastic anaemia and other blood dyscrasias. Microangiopathy with functional and structural findings we had observed using higher doses of 400r, 600r and 1200r. (Balourdas, T.A., Proceedings XX Internat. Physiological Congress, Brussels, Belgium, 1956, p. 58). In the present investigations three groups were experimented (1) untreated; (2) treated with cortisone before and after irradiation; and (3) treated with cortisone immediately after irradiation. Results: Microvascular hyperreactivity, slowing flow, stases, petechial hemorrhages, increased capillary permeability, vasodilatation, abnormal vasomotion were observed in the untreated animals. Cortisone had a beneficial effect on the capillary permeability and fragility but none on the hyperreactivity. No hemorrhage appeared in the last two groups. The selective effects of cortisone suggest the disassociation of the capillary permeability and the sympathetic tonus.

FACILITATION OF HEART MUSCLE CONTRACTION AND ITS DEPENDENCE ON EXTERNAL CALCIUM AND SODIUM. R. K. Orkand (intr. by A. M. Brown) Univ. of Utah College of Medicine, Salt Lake City, Utah.

The magnitude and timecourse of the facilitation of contraction following previous stimulation have been studied in quiescent strips of frog ventricle when the external concentrations of Na and Ca were varied. The maximum tension and the maximum rate of rise of tension have been used as indices of activation of the contractile element. Under the experimental conditions these two parameters changed similarly. At low stimulus frequencies (3-12 beats/min), and moderate concentrations of external Ca, (2-5mM), the facilitation of contraction with repetitive stimulation can be predicted by assuming each contraction to produce an amount of facilitation which sums linearly with that remaining from previous stimuli. Thus, the staircase can be constructed from the decay of facilitation following a single contraction. The decay of facilitation appears to consist of two components. The first has a half-time of about 3 sec; the second about 50 sec. The decay of the second component is slowed and its magnitude increased by raising the external Ca from 2-5mM. Reducing the external Na concentration increases both the strength of contraction and the amount of facilitation. When the ratio Ca/Na^2 is constant, the first contraction in a series is the same, but facilitation is less at low concentrations of Ca and Na. Facilitation, therefore, does not depend solely on the amount of initial activation of the contractile system. The results are consistent with the tentative hypothesis that facilitation depends on the amount of calcium retained in some cellular store. (Supported by USPHS Grant NB 06698).

PRESSURE RECORDING FOR VASCULAR IMPEDANCE DETERMINATION. M.F.O'Rourke* (intr. by W.R.Milnor), Johns Hopkins University, Baltimore, Maryland, and Sydney University, Sydney, Australia.

Calculation of aortic or pulmonary arterial input impedance from blood flow and lateral pressures rather than impact (end) pressures, omits the kinetic energy associated with flow and thereby underestimates the load presented to the ventricles. To determine the differences between impedances calculated from these two kinds of pressure measurement, impact and lateral pressures were measured simultaneously with flow (electromagnetic flowmeter) in the ascending aorta and pulmonary artery of 12 anesthetized dogs.

The difference between impact and lateral pressure was greatest during forward flow, approximating the theoretic value (i.e., 3.75 mmHg at 100 cm/sec, 15 mmHg at 200 cm/sec). Under control conditions peak forward flow in the aorta averaged 130 cm/sec and in the pulmonary artery, 70 cm/sec. Impedance modulus calculated from lateral pressure was always smaller than that calculated from impact pressure and the difference was more marked at the second and higher harmonics; impedance modulus from lateral pressure averaged 0.74 of modulus from impact pressure between 1 and 10 cycles/sec, and impedance phase was more negative (average difference 0.12 radian). Coherency (a measure of the linear interdependence of pressure and flow as a function of frequency) of lateral pressure/flow relationships decreased markedly above 4 cycles/sec while a high (>0.9) coherency of impact pressure /flow relationships was usually maintained up to 10 cycles/sec.

EFFECT OF PROCAINAMIDE ON VENTRICULAR FUNCTION IN THE INTACT CONSCIOUS DOG. R.A. O'Rourke*, V.S. Bishop, H.L. Stone, and E. Rapaport. USAF School of Aerospace Medicine, Brooks AFB, Texas, and Univ. of California, San Francisco Med. Center, San Francisco, Calif.

The effect of continuous intravenous infusion of 1 mg./kg./min. of procainamide for 30 minutes on ventricular function was studied in five conscious dogs. An electromagnetic flowmeter probe was placed around the pulmonary artery and catheters were positioned in both atria and in the superior vena cava. Two weeks later, ventricular function curves were determined by the rapid infusion of Tyrodes solution in the superior vena cava catheter while recording right and left atrial pressure, heart rate, mean artefial pressure, mean cardiac output and pulsatile pulmonary artery flow. Ten control ventricular function curves were obtained. A total of eleven ventricular function curves were obtained following 25 minutes of procainamide infusion. There was no significant change in the average resting mean arterial pressure, heart rate, ventricular output, or stroke volume prior to or following the procainamide. The average plateau of the ventricular output curve was 296 cc/min./kg. [± 14.9] during the control studies and 299 cc/min./kg. [± 13.1] during the infusion of procainamide. Thus there were no significant changes observed in either resting hemodynamics or the ventricular function curves resulting from the continuous intravenous administration of procainamide.

FORELIMB VASCULAR RESPONSES IN RENAL HYPERTENSIVE DOGS. H.W. Overbeck* and F.J. Haddy. Depts. of Physiol. and Med., Univ. of Okla. Med. Cent., Okla. City, Okla., and Mich. State Univ., E. Lansing, Mich.

Various abnormalities in the metabolism of potassium, magnesium and calcium occur in chronic arterial hypertension. The present work was designed to determine if forelimb vascular responses to these cations are normal in renal hypertensive dogs. Isotonic solutions of magnesium chloride at two dose levels (3 and 5 ml./min.), potassium chloride at two dose levels (1.2 and 2.0 ml./min.) and calcium chloride at one dose level (1.5 ml./min.) were infused in turn into the pump perfused (100 ml./min.) brachial arteries of 33 male mongrel dogs. Tourniquets were applied to the limb to reduce collateral blood flow. In 19 of these dogs (Hypertensive Group) sustained hypertension was created by cellophane perinephritis. Fourteen dogs (Control Group) underwent only unilateral nephrectomy. Nine weeks later vascular responses to these vasoactive solutions were studied in the opposite forelimb. Changes in response within each group were tested by the paired Student's t test. Resting forelimb flow in normotension and hypertension was determined by measuring pump flow with perfusion pressure set to equal aortic pressure. Forelimb blood flow and vascular resistance were normal and significantly elevated, respectively, in the hypertensive dogs. In normotensive dogs there was a significant linear correlation between magnitude of response to each cation tested and initial level of limb vascular resistance. Considering this covariance relationship, there was a significantly decreased response ($P = < .05$) to potassium in the Hypertensive Group. In contrast there was no significant difference in response to potassium in the Control Group, nor to magnesium or calcium in either Hypertensive or Control Groups. The results suggest that limb vascular responses to either potassium or to both calcium and magnesium are altered in renal hypertensive dogs.

HEMODYNAMIC DETERMINANTS OF THE PRESSURE GRADIENT ACROSS THE AORTIC VALVE. John B. Pace* (introduced by Walter C. Randall). Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

Utilizing a right heart bypass preparation, it was possible to measure the pressure difference from the left ventricular outflow tract to the ascending aorta, together with pulsatile blood flow, for differing cardiac outputs and aortic mean pressures. Observations on the pressure differential throughout the cardiac cycle revealed that left ventricular pressure (LVP) exceeded aortic pressure (AP) only in the initial phases of ejection. After the attainment of peak flow, the differential (LVP-AP) was reversed indicating that throughout the remainder of ejection AP exceeded LVP. In situations in which aortic mean pressure was held constant the pressure difference (LVP-AP) was found to increase as a function of left ventricular end diastolic pressure (LVEDP). At a given left ventricular end diastolic pressure, increases in afterload resulted in increased pressure differences (LVP-AP). Over the range of values presented, peak pulsatile flow velocity was found to increase linearly with the peak pressure differential (LVP-AP). Both mean flow and the first derivative of the flow pulse were also found to be linear functions of the peak pressure difference. Cardiac sympathetic nerve stimulation produced marked increases in the pressure difference across the aortic valve. In addition, the duration of the positive phase of the pressure difference (LVP greater than AP) increased markedly over control and usually persisted throughout the entire ejection period. Similar results were obtained with the beta adrenergic drug, isoproterenol. (Supported by NIH Grant HE 08682.)

EFFECT OF Ba^{++} IN THE NUTRIENT FLUID ON THE K^+ PERMEABILITY OF THE FROG'S GASTRIC MUCOSA. A. D. Pacifico,* and W. S. Rehm. Department of Physiology and Biophysics, Medical Center, University of Alabama, Birmingham, Ala.

It has been shown (Schwartz, M. T., et al., Physiologist 9:284, 1966) that addition of Ba^{++} (0.1 mM to 2.0 mM) to the nutrient fluid results in a marked increase in transmucosal resistance and relatively little change in either the H^+ secretory rate or potential difference (PD). Using an in vitro technique we have studied the effects of moderate and large elevations of nutrient $[K^+]$ on the Ba^{++} effect. The resistance was determined as the ΔPD per unit of applied current (ΔPD/I), and in previous work no rectification occurred. In the presence of Ba^{++}, a definite rectification was observed, with a smaller ΔPD/I when current was sent from the secretory to nutrient side. Results to be considered here are applicable with either resistance value, and the average was used. It was found that increasing the $[K^+]$ from 4 to 79 mM results in a rapid decline in resistance to control values and also a ΔPD response essentially the same as in controls without Ba^{++}. Normalized plots show that the change in resistance (half time < 1 min) was definitely faster than the change in PD. A tentative hypothesis is that the elevated resistance with Ba^{++} is due to diminished K^+ permeability of the nutrient membrane and that high K^+ reverses this effect. This was tested by studying the effect on the PD of changing $[K^+]$ from 4 to 10 mM. Results predicted by the hypothesis were obtained, i.e., ΔPD in controls averaged 10 mv (range 8-12) while in the presence of Ba^{++} the average ΔPD was < 1.0 mv (range 0 to 2), and the change in resistance was < 20%. (NIH and NSF support.)

EFFECTS OF EXERCISE ON PLASMA LACTIC DEHYDROGENASE (LDH) AND ISOENZYME LEVELS IN TRAINED AND UNTRAINED RATS. Nicholas M. Papadopoulos*, Arthur S. Leon* and Colin M. Bloor. Walter Reed Army Institute of Research, Washington, D. C. 20012.

Previous studies in rats have stated that exercise training prevents the rise of serum LDH due to organ damage observed in untrained rats subjected to acute exercise. However, the methods for LDH determination used in these studies give extremely variable results and high LDH values even in controls. In our study it was shown that contributing factors to this discrepancy include the variable release of LDH from the heart during cardiac puncture for collection of blood and from red blood cells and platelets during the preparation of serum. When blood was collected from the vena cava in plastic tubes, heparinized and plasma, instead of serum, immediately prepared for analysis, these extraneous factors were eliminated. Control LDH values of less than 100 units/ml/min were consistently obtained. These modifications were then employed for the determination of plasma LDH and isoenzyme levels in 10 untrained rats subjected to 4 hours of swimming, and in 10 unexercised controls. A mean level of 196 $\pm$ 6 (SEM) units/ml/min was present in the exercised group as compared to 62 $\pm$ 3 (SEM) units/ml/min in the controls. LDH isoenzyme determinations and histological examination indicated that the probable sources of the increased plasma LDH were the heart, liver and skeletal muscle. In other rats, trained by swimming one hour daily for periods of 2 weeks to one year, when subsequently subjected to 4 hours of swimming, plasma LDH levels ranged from 110 - 180 units/ml/min, more than twice the level obtained in unexercised controls.

KIDNEY EXCLUSION AND CATECHOLAMINE CONTENT OF ADRENAL GLAND IN RATS. J. Papayoanou*, D. Zagury*, O. Steinsland* and G. G. Nahas, Dept. of Anesth., College of Physicians and Surgeons, Columbia Univ., New York, N.Y.

During acute hypercapnia, there is an increased rate of catecholamine (CA) synthesis in the rat, and CA adrenal stores remain normal. The possible participation of the kidney in this mechanism was studied in view of the report that the renin angiotensin system might sustain CA production during hypercapnia. (Fed. Proc. 26: 492, 1967). In a group of 23 rats, breathing room air, ligation of the renal pedicle did not alter adrenal CA content as compared to a control group. A second group of 20 rats similarly prepared and exposed to 20% CO_2, 25% O_2, balance N_2 for 5 hours, presented a 38% decrease in adrenal CA content. A third group, only laparotomized and exposed to similar hypercapnia, presented a 15% decrease in adrenal CA content. Electron photomicrographs of adrenals of hypercapnic laparotomized rats showed groups of chromaffin cells filled with granulations adjacent to cells with degranulated areas, but there were far more extensive areas of degranulation of the chromaffin cells of the adrenal of hypercapnic rats with kidney exclusion. The addition of surgical stress to hypercapnic acidosis has some effect in depleting the adrenal. However, the significantly greater decrease in adrenal CA content ($P < 0.001$) and the extensive degranulation of the chromaffin cells in hypercapnic rats with kidneys excluded, seem to indicate that the kidney may play a role in the maintenance of normal CA levels in the adrenal during hypercapnic acidosis. (This work was supported, in part, by Army Contract DA-49-193MD-2265 and N.I.H. Grant GM-09069-05).

RENAL EFFECTS OF ACETYLCHOLINE IN THE CHICKEN. Marian Parmelee and M. Kathleen Carter (intr. by Roberta M. O'Dell). Tulane University School of Medicine, Depts. of Physiology and Pharmacology, New Orleans, La.

Acetylcholine (2.5 - 7.5 mcg/kg/min) infused unilaterally into the renal portal system of unanesthetized hens, according to the technique originally developed by Sperber, produced a significant unilateral natriuresis and diuresis (UV_{Na} increased 300-400%; urine volume increased 200-400%). The ATEF of PAH increased simultaneously, probably as a result of better closure of the valve which controls blood flow to the peritubular area of the kidney. The natriuresis and diuresis was a dose-dependent response and was blocked by atropine. Butyrylcholine infused at comparable levels (9.6 - 14.4 mcg/kg/min) did not result in natriuresis or diuresis. This finding seems consistent with the unpublished observation of M. Kathleen Carter that, while acetylcholine increased the uptake of sodium and oxygen consumption in incubated rat kidney slices, butyrylcholine had no effect. The results support the idea that cholinergic agents produce a natriuresis and diuresis by a direct tubular effect in addition to the effects resulting from vasodilation observed in mammalian species. (Supported by NASA fellowship through Tulane University and a grant from the Louisiana Heart Association.)

PYRIDINE NUCLEOTIDE CONCENTRATIONS IN HUMAN ERYTHROCYTES IN DIFFERENT METABOLIC STATES. T. E. Parry*, C. B. Scott*, and A. Omachi. Univ. of Illinois Coll. of Medicine, Chicago, Ill.

NAD^+, NADH, $NADP^+$, and NADPH concentrations were determined in human red cells after incubation in Tris-buffered Ringer's solution at 37°. Acid and alkaline extracts were prepared by the procedure of Lowry, et al (J. Biol. Chem. 236:2746, 1961). NAD was analyzed by the method of Gupta, et al (Abstr.III Internat.Pharmacol.Congr., Sao Paulo, 1966). NADP was determined after conversion to NAD with alkaline phosphatase. Compared to controls without added substrate, increased NADH levels were noted in the presence of 10 mM glucose, 10 mM lactate, or 0.005 M fluoride. In contrast to controls with glucose, decreased NADH concentrations were observed in the presence of 10 mM pyruvate, 0.0005 M iodoacetate, or in acid medium. These results are consistent with conventional metabolic concepts based largely on studies with broken cell preparations. A change in NADH was often reflected in a similar change in NADPH, e.g., increases were noted with lactate and decreases were observed with pyruvate in the presence of glucose. Another unexpected observation was the lower level of $NAD^+ + NADH$ whenever glycolysis was inhibited and NADH was decreased, i.e., with iodoacetate, substrate lack, and acid pH. This result did not occur at 22° suggesting that enzymatic degradation of NAD may be responsible for the change at 37° although this could be due also to a permeability difference at the two temperatures. It seems possible that there could be a constant turnover of these compounds in intact cells which may have functional significance. 10^{-4} M ouabain, however, had no influence on the levels of the pyridine nucleotides.
(Supported by USPHS grant, GM-11430.)

ELECTROENCEPHALOGRAPHIC SLEEP PATTERNS OF UNRESTRAINED RATS FOLLOWING EXPERIMENTAL CONCUSSION. L. Claire Parsons and F. Hermann Rudenberg (intr. by S. N. Kolmen). Department of Physiology, The University of Texas Medical Branch, Galveston, Texas, 77550.

We have continued previous studies (Fed.Proc. 20:329,1961) with the addition of stereotactically placed electrodes in the hippocampus and reticular formation as well as electrodes in neck muscles to permit recognition of sleep stages. Following recovery from surgery and conditioning to a sound-attenuating chamber, daily 4-hour recordings were made until control sleep patterns were established. Acceleration concussion results in immediate unconsciousness and prompt flattening of cortical activity, followed by diminution of hippocampal and reticular amplitude about 5 seconds later. Apnea is very brief and the EKG is irregular, as reported previously. At approximately 30 seconds following concussion, reticular formation recordings show 50 to 100 μV, 4 to 6 cycles per second, activity which disappears as faster activity reappears. Consciousness returns within 5 minutes. Paradoxical sleep (PS) is not seen for several hours. Preliminary indications are that on subsequent days post-traumatic sleep records reveal altered patterns of wakefulness, slow wave sleep, and PS, including altered cycling and total time in PS. One of the factors being considered as affecting this alteration is the effect of PS deprivation as a result of the concussive blow.

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DYNAMICS OF VESTIBULO-MOTOR RESPONSES

Lloyd D. Partridge J. H. Kim* U. of Tenn., Memphis

Dynamics signal handling capabilities and limitation were tested for the path from vestibular apparatus to triceps sura in decerebrate cats. Input to individual vestibular nerve branches was a sinusoidally modulated rate of supramaximal stimulus pulses. Output was muscle tension. Phase and amplitude ratio vs frequency response graphs were obtained. A first order lag system with time constant of about 0.18 sec. added to a 15 m second conduction delay fits the data. The muscle alone shows a first order lag with similar time constant. These dynamics are compatable with vestibular correction of physiological range whole body movements. A non canal-specific mechanism of interaction with the stretch reflex appears to determine the motor corrective program. Vestibular excitation to any canal nerve has a multiplying action on adapting stretch reflexes. Thus canal stimulus results in augmented contraction of whatever muscle was simultaneously stretched. This produces suitable corrective contraction inspite of varied body position. (Supported by a grant from Easter Seal Research Foundation.)

INTESTINAL ABSORPTION OF RADIOIODIDE IN RATS EXPOSED TO HYPOXIA (380 mm Hg) AND FOOD DEPRIVATION. Peter F. Pearson* and Adam Anthony. Department of Biology, The Pennsylvania State University.

Effects of exposing rats to hypoxia (380 mm Hg) and food deprivation on absorption of parenterally administered radioiodide and on circulating and thyroidal iodide levels were studied. Forty-eight adult male Holtzman rats were used. In one experiment, 12 rats were placed in a decompression chamber for 24 hours with 12 controls kept at ambient pressures. Both groups were fed ad libitum. In experiment two, 12 rats were food deprived for 24 hours and subsequently subjected to hypoxia for 24 hours. In all instances 0.2μc NaI-131 was given parenterally 24 hours prior to sacrifice.

It was found that hypoxia causes a marked delay in movement of food and iodide to the small intestine which is the major absorption site of iodide. Food deprivation alone had no effect. Second, hypoxic rats exhibited higher circulating levels of radioiodide than controls despite lowered intestinal iodide absorption. This was due in part to delayed urinary and fecal radioiodide excretion. Hypoxic rats also had smaller thyroids and a reduced 24 hour radioiodide uptake relative to controls.

These findings indicate that a decreased intestinal absorption of iodide may be responsible for lowered thyroid function which is observed during the very onset of hypoxia acclimation. (Supported by grants GM-05112 from the Institute of General Medical Sciences and NASA NGR-39-009-015.)

RESPIRATORY SINUS ARRHYTHMIA IN DOGS WITH CHRONIC BILATERAL CERVICAL VAGOTOMIES. Jorge Perez-Cruet. Pavlovian Lab., Johns Hopkins Univ. Sch. of Med., Baltimore, Md.

Sinus arrhythmia is usually, but not always, influenced by respiration. Sinus arrhythmia in dogs has been shown to be independent of respiration during severe panting as reported elsewhere by Perez-Cruet and Gantt (Fed. Proc. 20:89, 1961) and also during apnea as observed by Vallbona, et al. (Amer. J. Cardiol. 16:386, 1965). Vagal Influences are undoubtedly of importance in the mediation of respiratory sinus arrhythmia in intact dogs. In a study designed to investigate cardiovascular conditioning in vagotomized dogs (Fed. Proc. 26:328, 1967) we made a series of observations of changes in heart rate accompanying respiration similar to those observed during respiratory sinus arrhythmia. A total of 7 dogs in whom the vagosympathetic nerve has been cut bilaterally at the level of the third cervical vertebrae were studied. In 4 dogs there was definite evidence of sinus arrhythmia synchronous with respiration. All dogs that showed sinus arrhythmia developed the accelerative phase of sinus arrhythmia during expiration whereas in normal dogs the accelerative phase usually occurs during inspiration. The changes in heart rate from the trough to the crest of the accelerative phase varied between 10 to 20 beats above the lowest heart rate level. This study shows that sinus arrhythmia can occur even after the vagi nerves are cut and that under these conditions the accelerative phase paradoxically occurs during expiration rather than during inspiration indicating a shift in the cycling of sinus arrhythmia.

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Reactions of Retinene with Amines

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Retinene, the aldehyde derivative of vitamin A, can form Schiff bases with the free primary amine groups of amines or amino acids. It also can form a mercaptan by reaction with a free sulfhydryl group. When both primary amine and sulfhydryl groups are present on a molecule in proper juxtaposition a ring structure, thiozolidine carboxylic acid, is formed. All of these compounds involve covalent bonding. This type of reaction does not occur when the amine group is substituted, a primary amine is required. However, if the substituted amine group is on an aromatic residue a reaction with retinene will occur and a colored complex results. The conditions of formation, high local concentration, and the stability to dissociating reagents suggest that the product formed in this case is a charge transfer or similar complex, in which the bonding is considerably weaker than in the covalent bonded Schiff bases and rhodopsin.

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Tissue catecholamines content in the ground squirrel during activity and hibernation. V.M. Petrovic and V. Davidovic (Spon: O. Héroux), Biological Institute, Beograd.

Variations in total catecholamine content and adrenaline /noradrenaline ratio of the hypothalamus, heart and adrenal glands, during summer activity and hibernation are reported Catecholamines were determined using von Euler and Lishajko's method. In the period prior to hibernation, catecholamine content in hypothalamus of the ground squirrel is 0.982 µg/gr of which noradrenaline is 80 per cent. In the hibernating animal the amount of catecholamine is 0.874 µg/gr of which noradrenaline represents 88 per cent. In the heart there is no significant change in the total catecholamine content in hibernating animals (0.698 µg/gr) compared with active ones (0.566 µg/gr); the proportion of noradrenaline changes from 85 per cent in active animals to 97 per cent in hibernating ones. Catecholamine content in the adrenal gland is lower in hibernating animals (281 µg/gr) than in active ones (805 µg/gr); the proportion of noradrenaline being 20 per cent and 53 per cent respectively. Data will be discussed in term of the activity of the sympatho-adrenal system in hibernators.

Effect of Protein Intake on Maximum Urine and Renal Tissue Solute Concentrations in the Muskrat. E. W. Pfeiffer* and T. Zahn (intr. by James R. Templeton). Univ. of Montana, Missoula, Montana.

Muskrats were fed high and low protein diets for at least two weeks and were then dehydrated until approximately 7% of body weight was lost. They were then killed 30 minutes after spontaneous emptying of the bladder, and the kidneys were removed and immediately frozen in dry ice and acetone. Terminal urine and plasma samples and slices of renal cortex and medulla were analyzed for urea, sodium, and potassium. Urine and plasma osmolalties were also determined. The mean urine osmotic ceiling of muskrats on a high protein diet (1063 mOsm/l.: U/Posm = 3.3) was not much higher than that of muskrats on a low protein diet (934 mOsm/l : U/P 2.9). All animals were able to establish high solute gradients in the renal medulla. Urea concentration in the renal papilla was about 460 mM/l and sodium concentration was approximately 250 mEq/l. A potassium gradient was not present in the renal tissue. Although sodium concentrations are similar to those in renal tissues of the beaver and Aplodontia, rodents with similar aquatic habitat and food requirements, urea concentrations in muskrat renal medullary tissue and the urine osmotic ceiling are much higher than those in the beaver and Aplodontia. Because the two latter species lack an inner zone of the medulla and the muskrat possesses such a zone, it is hypothesized that an inner zone is needed for urea accumulation in the medulla. (Supported by Montana Heart Assn. grant and USPHS grant No. AM 11342-01.)

THE EFFECTS OF RESTRAINT AND SHORT LIGHT CYCLING ON THE NORMAL TEMPERATURE PATTERN OF THE RHESUS MONKEY (MACACA MULATTA). J.M. Phillips* and H. L. Stone, USAF School of Aerospace Medicine, Brooks AFB Tex 78235.

A temperature transmitter was implanted between the abdominal muscles in 9 monkeys to establish the normal temperature pattern using condition of lights from 0800 to 1700 hrs. Temperature sampling was performed every 5 min. following a 1-week recovery period. The data for the last 5 days of each week of any experimental period were averaged by using all data 30 min. prior to and 30 min. following each hour. An additional 3 animals were instrumented in the same manner but following the recovery period were placed in restraint chairs and exposed to the same lighting conditions as above for 1 week. For the next 3 weeks the lights were cycled in continuous periods of 60 min. light followed by 30 min. darkness to observe alteration in the diurnal pattern. In the 9 controls with lights on from 0800 to 1700 hrs a diurnal cycle was observed with an average high temperature of 101.44° F. occurring at 1700 hrs and a low of 98.75° F. occurring at 0200 hrs while the 3 monkeys placed in restraint chairs with similar lighting conditions cycled with an average temperature of 101.47° F. at 1600 hrs and an average low temperature of 98.82° at 0500 hrs. The short light cycling period of 60 min. light and 30 min. darkness disturbed the diurnal pattern observed in these animals. During the third week of this experimental period the monkeys demonstrated an average high temperature of 101.88° F. at 1600 and 1700 hrs and average low of 99.87° F. at 0300 hrs. From these studies it can be concluded that restraint alone does not alter the normal temperature pattern of the rhesus monkey but in the presence of short light cycling periods restraint does effect the normal pattern.

INFLUENCE OF VASOACTIVE SUBSTANCES ON FOURIER ANALYSIS OF THE AORTIC PRESSURE PULSE IN DOGS. T. E. Piemme, R. W. Baloh, and E. L. Williamson (intr. by J.D. Myers). Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.

Fourier analysis has been applied to the aortic pressure pulse of both animals and man by various workers. In most instances this has been done with standard catheter-transducer systems which do not allow resolution of the higher harmonics. The present analyses were done on analog tape records obtained from the Dallons-Telco microtransducer. Conversion was achieved on a computer of average transients with a digitization rate of 2000 samples/sec. Analysis of data was performed on the IBM 7090. Estimate of the error reveals significance out to 90 cycles/sec. The amplitudes of the harmonic moduli in control animals were seen to drop off rapidly by the third or fourth harmonic, and then oscillate with clear maxima and minima while dropping slowly through the harmonic spectrum. Administration of methoxamine raised mean aortic pressure, shifting the low frequency maxima toward higher harmonics, a direction compatible with an attendant increase in pulse wave velocity and wave length. Bradykinin lowered mean pressure, decreasing both wave velocity and length, resulting in a shift of the low frequency maxima toward the lower harmonics. This is consistent with the concept of augmentation of the lower harmonics by reflected waves. This influence is not seen in the higher harmonics. Intropic drugs such as isoproterenol resulted in an increase in the amplitude of the moduli of all harmonics with accentuation of the maxima and minima. Significant shift in location of the maxima was not seen. The results imply that the maxima and minima of higher frequencies, and their accentuation by intropic stimulation of the heart, are generated de novo in the central aorta, probably by an augmentation of vibration of the heart attendant upon increased ejection velocity, and consequent increase in accelerative forces within the system.

EXPERIMENTS ON THE DISTENSIBILITY OF THE AORTA IN INTACT ANESTHETIZED DOGS. Heinz P. Pieper and Arnold M. Epstein*. Dept. of Physiol. and Div. of Thoracic Surg., The Ohio State Univ. Coll. of Med., Columbus, Ohio.

A catheter-tip instrument has been developed for measuring the aortic and other large vessel diameters. This instrument is a modification of the catheter-tip gauge for measuring left ventricular diameter [J. Appl. Physiol. 21:1412-1416 (1966)]. The frequency response is flat to at least 30 Hz (tested by subjecting the instrument to forced sinusoidal oscillations). In the experiments reported here, the diameter gauge and a catheter-tip manometer were placed in the same cross section of the descending aorta using fluoroscopy. A sinusoidal piston pump was connected by catheter to the abdominal aorta. In operation this pump caused slow oscillations of both the aortic pressure and diameter (cycle period 4 to 5 seconds). The normal (cardiogenic) pulsations were superimposed on these slow oscillations. From recordings of 2 to 3 pump cycles, pulse-by-pulse values of pressure and diameter were obtained. These values were taken at the end of diastole. A plot of these pressure vs. diameter values yielded a straight line relationship. The slope of this line describes the distensibility of the aorta for a given set of cardiovascular conditions. There is no hysteresis loop indicated in the plot. The effect of various drugs, hemorrhage and other manipulations on this relationship has been studied.

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CHANGES OF HEART RATE, BLOOD PRESSURE AND INTRATHORACIC PRESSURE IN PROLONGED BREATH HOLDING. James O. Pinkston and Mark L. Engel*. Department of Physiology, School of Medicine, Downstate Medical Center, State University of New York, Brooklyn, New York.

With prolonged breath holding, following maximum inspiration, in 7 young male subjects, there was an increase of intrathoracic pressure (ITP) (esophageal balloon method) in 21 of 23 observations: The average increase was 91.6 mm H_2O. Accompanying this increased ITP, there was a consistent decrease in heart rate (Waters cardiotachometer) of about 10 beats per minute: The range of this decrease was 2 to 25. In all cases, but to varying degrees, there was an increase in arterial blood pressure (sphygmomanometer method) during the breath hold. This increase usually was greater in diastolic pressure than in systolic, and frequently amounted to 20 mm Hg: The average of 12 determinations of diastolic pressure was 21.7 mm Hg, with a range of 8 to 36 mm Hg. In the case of a similar breath hold, preceded by hyperventilation, the bradycardia and rise of blood pressure were more marked, but it should be noted that hyperventilation itself, although having little effect on blood pressure, resulted in an elevated heart rate prior to the onset of the breath hold. In our subjects, the so-called Valsalva maneuver caused an increase in ITP, as did the other breath holding procedures; however, as was to be expected, the increase was considerably greater. Furthermore, there was cardiac acceleration with the Valsalva maneuver, whereas bradycardia occurred with ordinary breath holding. The cardiac acceleration was apparent immediately after the start of the Valsalva maneuver, and steadily became more pronounced until the conclusion of the maneuver.

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CONTINGENT MODIFICATION OF AN ENDOGENOUS BURSTING RHYTHM BY MONOSYNAPTIC INHIBITION. H. Pinsker* and E. Kandel, NYU Med. School, NYC

Cell L3 in the isolated abdominal ganglion of Aplysia has an endogenous bursting rhythm. The quiet period between bursts is a summated hyperpol. afterpotential whose duration is a function of the number of spikes per burst (Waziri, et al. 1965). Frazier et al. (1965) showed that the bursting rhythm can be modified by nerve stimulation. Nerve stim. given at burst onset (contingency A) decreased the number of spikes per burst and shortened the burst onset interval (BOI); nerve stim. presented later in the burst cycle (cont. B) lengthened the BOI. In the present study we simplified the synaptic input by intracellularly stimulating an identified interneuron that produces an elementary monosynaptic IPSP in L3. Cont. A and B stim. of the interneuron produces opposite effects on the BOI: stim. at the beginning of the burst is most effective in reducing spikes per burst and therefore produces maximal shortening of the BOI (up to 60%), whereas stimulation at the end of the quiet period produces maximal lengthening (up to 70%). Intermediate placements of the stim. produce intermediate effects on the BOI which suggest that the stim. produces opposite effects on two independent overlapping processes: one process limited to the burst itself, and the other occurring throughout the entire oscillatory burst cycle. With repetitive trials of cont. A stim. the immediate effects tend to build up and, in many cases, these effects persist for periods from 1 to 30 min. after stimulation is discontinued. Preliminary experiments indicate that both the immediate build up and the persistence of the effect can be enhanced by repeated blocks of trials. These data support the suggestion (Strumwasser, 1965) that endogenous properties of nerve cells may undergo plastic change, in this case produced by contingent synaptic stimulation.

BEHAVIORAL RESPONSES TO ANTERIOR HYPOTHALAMIC COOLING IN UNANESTHETIZED BABOON J. D. Pister† M. Jobin† and C. C. Gale Dept. Physiol. & Biophysics and Regional Primate Research Ctr., U. of Wash., Seattle

Experiments were performed to determine whether local cooling in the anterior hypothalamus (AH) induces a subjective sensation of cold and elicits cold defense behavior in unanesthetized baboons. Theoretically, if central cooling (CC) induces cold sensation, S will work for heat reinforcement. A chaired baboon with a water perfused thermode in the AH and thermocouples in the AH and posterior hypothalamus (PH) was trained to bar press for heat reinforcement from 4 infrared lamps. When room temperature (T) was lowered from neutrality (25 ° C) to cool (17 °), S increased bar pressing rate markedly and maintained the high rate as room T fell step-wise to 12 °. Core (PH) T rose 0.2° during 2½ hours of this peripheral cooling. When CC was performed at neutral room T, S showed a great increase in bar pressing rate, shivering, and core T rose 1 ° in 30 minutes. Upon cessation of CC, S stopped bar pressing and core T fell to pre-cooling level within 30 minutes. This sequence was observed during repeated periods of CC. A ganglionic blocker (Arfonad) was infused i.v. to S maintained at neutral room T to cause peripheral vasodilatation and to prevent stimulation of peripheral cold receptors. When CC was performed during such infusion, S showed a great increase in bar pressing rate in association with a fall in core T of 1.7 ° (presumably secondary to vasodilatation). These data demonstrate that S will work for heat reinforcement when cooled centrally in the absence of stimulatory inflow from peripheral cold receptors. It is suggested that local hypothalamic cooling per se elicits a subjective sensation of cold. (Supported by NIH Grants FR 00166 and NB 06622, and Washington State Grant I 171).

EFFECT OF REACTIVE HYPEREMIA ON THE CLEARANCE OF INTRAMYOCARDIAL INJECTION OF Xe^{133}. Bertram Pitt*, Gottlieb C. Friesinger, H. Leon Greene*, and C. Richard Conti*. The Johns Hopkins University School of Medicine and Hospital, Baltimore, Maryland.

In 5 pentobarbital anesthetized open chest dogs (35-40 lbs) Xe^{133}(0.05-0.1 ml) was injected locally into the epi- or endocardial layer of the left ventricle. Three paired injections were made and a semilogarithmic replot of the initial slope of the curve used to calculate the clearance, expressed as half time (T 1/2). During the control period the average epicardial T 1/2 was 0.53 seconds and endocardial 0.60 seconds (endocardial Xe^{133}clearance 13% less than epicardial). The left coronary artery was occluded for 30 seconds and Xe^{133}injected during the period of occlusion. After release of the occlusion epicardial T 1/2 fell to 0.47 seconds and endocardial to 0.39 seconds(endocardial Xe^{133}clearance 17% faster than epicardial). This finding of a relatively decreased endocardial clearance of Xe^{133} in the control state agrees with the findings of others. Several explanations for this finding have been offered including the greater intramyocardial pressure in the subendocardial layer. Artifacts due to methodology could be responsible for the gradient and cannot be excluded. However, the finding of a reversal of the Xe^{133} clearance gradient during reactive hyperemia, using the same method, must indicate a redistribution of blood flow. It is postulated that coronary occlusion results in relatively greater endocardial than epicardial ischemia. During the reactive hyperemic phase this results in a relatively greater endocardial coronary blood flow in an attempt to repay the oxygen debt incurred during the period of ischemia.

ARTERIAL BLOOD PRESSURE DURING SLEEP. V. P. Popovic and R. B. Addlestone*. Dept. Physiol., Emory Univ. School of Medicine, Atlanta, Ga.

Mean arterial blood pressure of twenty-four unanesthetized and unrestrained adult white rats was recorded continuously in experiments lasting 120 hours. The blood pressure was recorded through polyethylene cannulas implanted in the aorta one month earlier. During recording each rat was placed in a sound-proof chamber with a 12/12 hour light/dark cycle. The activity of the animal was monitored by a high frequency transmitter and a receiver located in the chamber. During the phase of complete inactivity (sleep period, 11:00 a. m. to 5:00 p.m.) the mean arterial pressure of all rats had a low value of 83-85 mm Hg. During the activity periods the arterial blood pressure of rats was appreciably higher, 95-120 mm Hg. However, these patterns were observed only after an initial "adaptation period" lasting between 12 and 72 hours during which the arterial blood pressure as well as the activity of the animals fluctuated without any regularity.

ROLE OF A SAMPLING SITE MIXER IN INDICATOR CONCENTRATION STUDIES OF $\bar{T}$, $\dot{Q}$ and Q. C.I.Porciuncula*, C.E.Rapela and H.D.Green. Bowman Gray Sch. Med., Winston-Salem, North Carolina.

Previous studies using Cardio-Green as indicator, showed that flow ($\dot{Q}$), mean transit time ($\bar{T}$), and volume of the model ($Q = \dot{Q} \times \bar{T}$) were incorrectly indicated if laminar flow existed at the injection site; correct data were obtained if turbulence were induced by a mixer (Fed. Proc. 22: 523, 1963). Mixing at the sampling site did not appear to be as important. However, when dye was used, turbulence was probably induced at the sampling site during the continuous withdrawal of an aliquot of flow for determination of dye concentration. Present studies were carried out, therefore, to determine the influence of mixing per se at the sampling site. $RIHSA^{131}$ was injected into a mixer which disperses the indicator in proportion to the flow of each lamina within the flowing blood. Indicator concentration curves were obtained by means of a collimated scintillation detector placed directly over the model vessel. Mean velocities = 0.6 to 3.0 tube diameters per second and model length = 175 diameters. When there was no mixing at the sampling site, the indicator particles traveled under the detector at the velocities of the lamina which they tagged. This resulted in marked underestimation of $\dot{Q}$ and marked overestimation of $\bar{T}$ and Q. When the flowing blood was mixed at the sampling site, all particles of indicator traveled under the detector at the same velocity regardless of their respective velocities upstream. Under this condition, the calculated values of $\dot{Q}$, $\bar{T}$ and Q differed $< 10\%$ from the actual value. It is concluded that appropriate mixing of the indicator and blood at both injection and sampling sites is necessary to obtain correct measurements of $\dot{Q}$, $\bar{T}$ and Q. These are in accord with the postulations in an earlier publication (IRE Trans. Med. Electronics 6: 277, 1959). Supported by NIH grant HE-487.

ALTERING CEREBROSPINAL FLUID pH DOES NOT CHANGE CEREBRAL BLOOD FLOW. J.B. Posner*, F. Plum and D. Zee*, Cornell University Medical College, New York, New York.

Hypercapnia increases cerebral blood flow (CBF) and hypocapnia decreases CBF but whether the CO_2 affects cerebral vessels directly or indirectly by altering the pH of the brain's extracellular fluid is unknown. We perfused artificial cerebrospinal fluid (CSF) at various pH values from cerebral ventricle to cisterna magna and measured the effect of the altered CSF pH (and, presumably, brain extracellular pH) on CBF. Eight anesthetized, paralyzed dogs were ventilated at constant P_ECO_2 levels while cerebral venous outflow (CBF) was measured by an electromagnetic flowmeter connected to a torcular-jugular shunt. Blood pressure, EEG and ventricular pressure were monitored. Artificial CSF containing HCO_3^- concentrations of 10, 23 or 50 mM was perfused at 1 cc/min for 20-120 min. At normocapnia, varying the cisternal pH from 7.10 to 7.59 failed to change the CBF, EEG, ventricular or blood pressure. However, hypercapnia significantly increased CBF and hypocapnia decreased it no matter which artificial CSF solution was being perfused. The effect of altering blood CO_2 on CBF was marked even when the blood CO_2 alteration changed the cisternal pH less than did changing the perfusion solution. It would appear that CSF pH (brain extracellular pH) per se does not control CBF. (Supported by N.I.H. grant NB-04928.)

MATERNAL-FETAL OXYGEN TENSION DIFFERENCE DUE TO UNEVEN PLACENTAL BLOOD FLOWS. Gordon G. Power and Lawrence D. Longo (Introduced by Robert E. Forster, II). Grad. Div. Sch. of Med., Univ. of Pa., Phila., Pa.

We have calculated the contribution of uneven distribution of maternal placental to fetal placental blood flow ($\dot{Q}_M/\dot{Q}_F$), to the observed uterine vein-umbilical vein oxygen tension difference. The basic data were derived from measurements of the distribution of $\dot{Q}_M/\dot{Q}_F$ in 8 sheep placentas using macroaggregates of albumin labeled with ^{125}I and ^{131}I. The placenta was arbitrarily divided into 24 compartments, one for each 0.1 increment of $\dot{Q}_M/\dot{Q}_F$ over the range of $\dot{Q}_M/\dot{Q}_F$ from 0 to 2.4. Total maternal-fetal O_2 exchange and total uterine and umbilical flows were obtained from observed values. Changes in oxygen content were calculated for each compartment on the basis of its $\dot{Q}_M/\dot{Q}_F$, arterial O_2 contents and dissociation curves. The O_2 contents and tensions of the mixed uterine and umbilical venous bloods were calculated from the blood flow and O_2 content change in each of the compartments. The method assumes that diffusion does not limit O_2 exchange significantly so that the end-capillary oxygen tensions are equilibrated in each maternal-fetal placental capillary unit. The normal uterine vein-umbilical vein P_{O_2} gradient is about 15 mm Hg. Our results indicate an average P_{O_2} difference of 10 mm Hg (range 6 to 15 mm Hg) between uterine and umbilical veins due to uneven $\dot{Q}_M/\dot{Q}_F$ in 5 ewes breathing air. In 3 ewes breathing 10 to 12% O_2, in which $\dot{Q}_M/\dot{Q}_F$ has been found experimentally to become more uniform, the calculated P_{O_2} difference decreased to about 5 mm Hg. We conclude that uneven $\dot{Q}_M/\dot{Q}_F$ is the principle limitation to placental O_2 exchange during normal oxygenation and accounts for more than one-half of the total uterine vein-umbilical vein oxygen tension gradient. During hypoxia uneven $\dot{Q}_M/\dot{Q}_F$ accounts for only a third of the total gradient.

CARDIOVASCULAR EFFECTS OF EXPOSURE TO ATMOSPHERIC PRESSURES OF 4 MM HG AND 55 MM HG. A. J. Pratt*, H. L. Stone, H. F. Stegall and W. C. Kaufman. Aeromedical Res. Lab., Holloman AFB, and USAF Sch. of Aerospace Med., Brooks AFB.

Exposure of animals to both 4 and 55 mm Hg pressure on air causes complete anoxia. Additionally, body water vaporizes at 4 mm Hg. Aortic and postcaval pressures, ECG and aortic blood velocity were measured in 5 anesthetized dogs. Standard methods were used except for aortic blood velocity where a catheter-tip doppler flowmeter was employed. During exposure to 4 mm Hg for 1 min, aortic and postcaval pressures tended to equalize and aortic blood velocity decreased to negligible levels. During exposure to 55 mm Hg for 1 min, aortic pressure was sustained, postcaval pressure increased slightly, and aortic blood velocity was maintained. When a chimpanzee was identically exposed to either condition, aortic and postcaval pressures tended to equalize and aortic blood velocity decreased to negligible levels. All animals survived these experiments. Evidently the dog can maintain cardiovascular function during exposure to anoxia but the mechanical effects of vaporizing water within the thorax prevent it. Anoxia in the chimpanzee appears to terminate cardiovascular function even when uncomplicated by the formation of water vapor. Observation showed that the chimpanzee torso did not expand at 4 mm Hg to the massive size exhibited by the dog. The physical characteristics of the torso in these two species are probably involved in this difference.

ALTERED PLASMA PROTEIN BINDING OF THYROXINE IN THYROGLOBULIN IMMUNITY. B. N. Premachandra, Ph.D., F.R.I.C. and S. Lang, Ph.D. V.A. Hospital, Jefferson Barracks and Washington University, St. Louis, Missouri.

Adult rabbits were immunized with bovine thyroglobulin (1%) and the antibody titer was measured by radioelectrophoretic techniques at weekly intervals. Even 7 months after the initial immunization there was a high level of antibody titer. At and during this period normal and immune sera were equilibrated with ^{125}I-T_4 at 37° C and subjected to paper electrophoresis (barbital buffer, pH 8.6). Radioactivity in the normal serum was entirely at or near the albumin region. Radioactivity in the immune sera was avidly bound to proteins in the gamma globulin region. Addition of excess T_4 displaced gamma bound radioactivity to the binding sites in the albumin area. Such avid gamma globulin binding of ^{125}I-T_4 was also seen in vertical acrylamide gel electrophoresis in Tris-borate buffer at pH 9.0. In the results so far observed the binding capacity of the immune globulin varied between 12 to 50 μg of thyroxine/100 ml in individual animals. These studies also show that immune globulin binding is many times stronger than the normal T_4 binding proteins of the rabbit. (Supported in part by N.I.H. grant AM07676).

EFFECTS OF ACUTE pH CHANGES ON AMMONIA PRODUCTION IN VITRO. H.G. Preuss D.P. Ponder and M.S. Campbell, (intr. by H.V. Murdaugh). University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

Isolated cortical tubules of dogs incubated in a phosphate buffered medium at pH 7.1 produce more ammonia and glucose from mono sodium glutamate than do tubules incubated at pH 7.7. To determine if this increase in the production of ammonia was secondary to the increased gluconeogenesis, various substances which interfere with gluconeogenesis were added to the medium.

		Ammonia Production **			Glucose Production **		
Substrate	M	pH 7.1	pH 7.7	p	pH 7.1	pH 7.7	p
None (20)	0	6.43	3.71	<.001	2.12	1.11	<.001
Arsenite (8)	10^{-4}	5.95	4.01	<.02	0	0	NS
Malonate (8)	10^{-3}	10.25	8.40	<.001	.36	.37	NS
Iodoacetate (8)	10^{-4}	7.03	5.20	<.01	.41	.37	NS
Maleic Acid (8)	10^{-4}	6.83	5.65	>.1	.27	.38	NS
DNP (6)	10^{-4}	8.16	7.72	>.6	.47	.56	NS

**(μM/gm/hr)

In the presence of the substances listed in the table, glucose production dropped and no stimulation of gluconeogenesis at the lower pH was noted. However, in the presence of arsenite, malonate, and iodoacetate, a significant increase in ammonia production still was noted at the lower pH. In the presence of DNP, gluconeogenesis decreased while ammonia production and oxygen consumption increased. Since the increase in ammonia production was relatively greater in the medium at pH 7.7, no significant difference in the pH effect on ammonia production in the presence of DNP was noted. These data suggest that the stimulation in ammonia production seen at pH 7.1 as compared to pH 7.7 may be due in part to factors other than increased gluconeogenesis.

ELECTRICAL ACTIVITY OF THE MITRAL VALVE. D. V. Priola*, T. Cooper, and L. M. Napolitano*, Univ. of New Mexico, Albuquerque, N.M.

Previous experiments have shown that muscle found in the mitral valve leaflets behaves in vitro like cardiac muscle in its reaction to drugs and its inherent contractile characteristics. The following experiments were designed in order to evaluate the electrical characteristics of the mitral valve muscle in situ. In 10 dogs, during total cardiopulmonary by-pass, a Hoffman-type electrode was sutured to the atrial surface of the septal leaflet of the mitral valve through a left atriotomy. Additional electrodes were sutured to endocardial or epicardial surfaces of the left ventricle and to either the epicardial or endocardial surface of the left atrium. A standard limb lead ECG was recorded to provide a common reference for the electrograms. Depolarization of the mitral valve consistently occurred simultaneously with or 5-10 msec. prior to the earliest deflection of the QRS complex of the ECG. The amplitude of the mitral potential is always less than that recorded from ventricular epicardial surfaces. The electrical activity of the valve was dissociated from left atrial electrical activity during complete A-V block. Section of the His bundle did not alter the temporal relationship of the mitral potential with ventricular electrical activity. The results show that the mitral valve musculature is electrically active in situ and indicate that activation takes place very early in the period of ventricular depolarization. While these experiments do not elucidate the role of the mitral valve muscle in cardiac mechanical performance, they support the notion that contraction of the mitral valve muscle might assist in apposition of the valve leaflets early in systole, and in minimizing bulging of the valve into the atrium during isovolumetric ventricular contraction.

IONIC BASIS OF TWO-COMPONENT SLOW WAVES IN GASTRIC SMOOTH MUSCLE. C. L. Prosser, M. P. Papasova*, and T. Nagai*. Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

Cat stomach in vitro shows spontaneous slow waves and spikes. The slow waves are of two components. The first is a rapid component which is propagated, is not associated with contraction and which is lost when sodium is replaced by Tris or sucrose. The second slow wave component is not propagated, is associated with contraction, is abolished when calcium is absent from the medium and is abolished by manganese. Spikes may appear on the second component and enhance contraction. Tetrodotoxin has no effect on either component. Frequency of spontaneous waves is reduced in low Ca_o and enhanced by high Ca_o. The first component slow wave is analogous to the slow waves of small intestine and the second to prepotentials and spikes of taenia coli.

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INFLUENCE OF CARDIOVASCULAR DRUGS ON THE FORCE-VELOCITY RELATION OF THE INTACT HEART. Pritpal S. Puri* and Richard J. Bing. Wayne State Univ. School of Med., Detroit, Michigan

Rapid changes in the contractile state of the left ventricle were investigated in 45 close-chest dogs employing a new technique to study instantaneous force-velocity relation at a constant muscle length (isolength). A newly devised strain-gauge catheter assembly was used to register curve of fiber shortening on beat to beat basis. At an isolength point on the curve of shortening, velocity was measured by drawing a tangent to the curve; the intraventricular pressure, related in time to the isolength point, provided a measure of force. It was found that drugs like isoproterenol increased velocity of shortening without producing significant changes in force. Norepinephrine and metaraminol, on the other hand, increased both force and velocity. In contrast, methoxamine led to a fall in velocity as the force increased. Of other drugs tested, nitroglycerin and propranolol led to a fall of both force and velocity, while nicotine increased both of these parameters. It is concluded that with this new technique (strain gauge assembly), it is possible to evaluate the contractile state of the intact heart as reflected in its force-velocity relation.

EFFECTS OF HYPERPOLARIZING CURRENTS ON MEMBRANE AND SYNAPTIC POTENTIALS OF HIPPOCAMPAL NEURONS. D.P. Purpura, A. Malliani*, S. Prelevic* and M. Santini*. Albert Einstein College of Medicine, Yeshiva University, New York.

Fimbrial stimulation elicits IPSP's in hippocampal neurons which are frequently compounded with early EPSP's as revealed by latencies of responses during induced membrane hyperpolarization. IPSP's are occasionally observed as the only synaptic event evoked by subiculum stimulation. The vast majority of hippocampal neurons exhibit EPSP-IPSP sequences during subiculum stimulation. Strong hyperpolarizing currents attenuate early EPSP's and augment late EPSP's which summate with inverted IPSP's and trigger spike potentials. Cells with high resting potentials and 60-70 mV spikes exhibit early peaks in membrane potential and reduced plateau phases during application of strong hyperpolarizing currents. The plateau is reached in 30-40msec. Superposed brief testing hyperpolarizing pulses are attenuated and their time constant is decreased during prolonged conditioning hyperpolarizing currents. The data suggest that anomalous rectification or hyperpolarizing activation occurs in hippocampal neurons and may explain in part the attenuation of early subiculum evoked EPSP's. Hyperpolarizing activation serves to complicate analysis of PSP components generated at different sites on the soma-dendritic membrane of hippocampal neurons.

IONIC FLUXES IN ISOLATED BULLFROG INTESTINE. J.F.Quay* and W.McD. Armstrong. Dept. of Physiology, Indiana University School of Medicine, Indianapolis, Indiana.

Isolated bullfrog intestine mounted in a conventional Ussing chamber maintains a stable transmural p.d. (serosal side positive) and short circuit current for 3-4 hours at 26°C. When intestinal segments were mounted between identical normal chloride Ringers, transmural p.d's ranged from 0.8-4 mV. The short circuit current was 3-30 $\mu A/cm^2$. Measurement of unidirectional Na fluxes under these conditions, using Na^{22} and Na^{24}, showed that the average net mucosal to serosal Na flux (24.6 ± 13.2 $nM/min.cm^2$) was significantly greater ($P<.001$) than the corresponding short circuit current (6.9 ± 5.4 $nM/min.cm^2$). Determination under the same conditions of unidirectional chloride fluxes using Cl^{36} revealed a marked asymmetry between the m → s and s → m fluxes of this ion, the m → s flux being significantly greater ($P<.01$). The net m → s chloride flux accounted satisfactorily for the difference between net Na flux and short circuit current. In sulfate media both the transmural p.d. and the short circuit current were considerably higher than in chloride media. Further, the average net Na flux (16.8 ± 13.2 $mN/min.cm^2$) and short circuit current (15.0 ± 6.6 $nM/min.cm^2$ were not significantly different ($P>0.2$) under these conditions, indicating that the increased short circuit current in sulfate media is due to the absence of a large net anion flux. In sulfate media addition of alanine to the mucosal fluid causes a rapid increase of short circuit current. The magnitude of this increase is saturable with respect to alanine concentration. Preliminary results give a K_m value of about 6 mM. Addition of alanine to the serosal fluid does not change the short circuit current. (Supported by USPHS grants GM 10971, HE 6308, and by NIH Fellowship 1-F1-GM 29, 918).

LACK OF DAY-NIGHT RHYTHM AND EFFECT OF DARKNESS IN RAT PINEAL CONTENT OF N-ACETYLSEROTONIN O-METHYLTRANSFERASE. W. B. Quay. Dept. of Zoology, University of California, Berkeley, California.

An earlier study suggested a higher nocturnal than diurnal content of melatonin in the rat's pineal gland, but could not show a consistent difference in "melatonin-forming activity" in vitro (Quay, Proc. Soc. Exptl. Biol. & Med. 1964 115: 710-713). However, subsequent use of a more specific and sensitive method of measuring the activity of the enzyme (N-acetylserotonin O-methyltransferase, or hydroxyindole O-methyl transferase, or ASMT) responsible in the final biosynthetic step for melatonin was claimed to show a significantly greater enzyme activity at mid-night than during the day, marked rise in constant darkness and decrease in continuous light (Axelrod, Wurtman & Snyder, J. Biol. Chem. 1965 240: 949-954). In ten experiments utilizing the latter technique and 450 adult rats I have been able to confirm the inhibitory effect of continuous light (4, 20 or 85 ft. candles for one week) and to extend it to long daily photoperiods (23 hours/day) as well. But in rats in a daily photoperiod of 14 hours no day-night rhythm in ASMT could be demonstrated at any season or under any of the conditions investigated, nor could any differences be shown in relation to those animals in continuous darkness or dim red light. Other findings also support the belief that possible daily rhythmic changes in effective in vivo rat pineal ASMT activity may be due to factor(s) other than local concentration of enzyme (ASMT) protein. The effect of continuous light on the adult rat pineal is of a broadly inhibitory, and possibly nonspecific stressful, nature; it can be mediated by the central nervous system and the pineal's sympathetic innervation. (Supported by NIH research grant GM-05219 and The Miller Institute for Basic Research in Science, University of California, Berkeley.)

PLACENTAL EXCHANGE. John H. G. Rankin*, Edward N. Peterson*, J. Job Faber and James Metcalfe. Departments of Physiology and Medicine, University of Oregon Medical School, Portland, Oregon.

Placental perfusions were performed on 20 adult goats that were 120-135 days pregnant. Cannulae were placed in all umbilical vessels and both common maternal uterine veins. Blood was equilibrated with a mixture of gases (25% C_2H_2, 0.5% O_2, 6% CO_2 and 68.5% N_2), filtered, warmed to 39° C and infused into the umbilical arteries. The ratio of placental to uterine blood flows could be varied over the range 0.1-10. Under steady state conditions samples of blood were drawn at various perfusion ratios from all vessels, and analyzed for N_2O and C_2H_2 by gas chromatography. These data when analyzed graphically resulted in a line compatible with that of a concurrent exchanger with moderate maldistribution of flow ratios or a more efficient exchanger with greater maldistribution of flow ratios. The extrapolation of the line to flow ratios of infinity and zero indicated a non-exchanging fetal shunt of the order of 20% and a non-exchanging maternal shunt of the order of 35%. Five percent Dextran in Krebs solution saturated with carbon monoxide (CO) was infused into the umbilical arteries of 4 placentas, and in 6 other pregnant goats the abdominal aorta was occluded and the femoral arteries were infused with CO-Dextran-Krebs solution. Maternal and fetal samples were analyzed for CO by gas chromatography. These data yielded values of 23% (S. D. 2.2%) for the fetal shunt and 36% (S. D. 3.9%) for the maternal shunt. (Supported in part by NIH grants #HD 2313 and HE 5499.)

METABOLIC RESPONSE OF MAN TO HYPERBARIC HELIUM. Lawrence W. Raymond* (Introd. by Esther Hardenbergh). Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md. 20014.

Increased transfer of body heat by convection occurs in helium-rich atmospheres. We studied this effect in 5 men at pressures of 4.3 to 14.6 atmospheres absolute (ATA), maintaining oxygen and nitrogen partial pressures of 0.3 and 1.1 ATA, respectively. In these pressure chamber studies, ambient temperature averaged 28.4 to 29.3 C., water vapor pressure 21.5 to 23.4 mm Hg, and velocity 0 to 1.6 meters/min. No change in overall metabolic rate (M) was observed, but changes in the relative amounts of heat loss by evaporation (E), radiation (R) and convection (C) were striking. Mean skin temperature ($\bar{T}_s$) was decreased in helium, especially at higher pressures, but shivering did not occur. Rectal temperature (T_r) was reduced slightly. Mean values were as follows:

	AIR	HELIUM WITH 0.3 ATA O_2 AND 1.1 ATA N_2		
	1 ATA	4.3 ATA	9.1 ATA	14.6 ATA
E, kcal/m^2 hr	16.5	13.5	9.3	9.6
R " "	18.3	12.4	8.8	5.9
C " "	13.0	21.2	30.1	36.1
M " "	47.8	47.1	48.2	51.6
$\bar{T}_s$, °C.	32.7	31.8	31.6	30.5
T_r "	36.9	36.8	36.6	36.5

Higher pressure or atmospheric velocity, and cooler ambient or radiant temperatures, would likely elicit greater skin cooling with shivering.

EFFECT OF GRAVITATIONAL AND INERTIAL FORCES ON REGIONAL DISTRIBUTION OF PULMONARY BLOOD FLOW. J. H. Reed, Jr.*, R. A. Vandenberg*, and E. H. Wood, Mayo Clinic and Mayo Graduate School of Medicine, Rochester, Minnesota.

The distribution of pulmonary blood flow (DPBF) in 10 mongrel dogs in the right lateral position was determined by an embolization technic utilizing radioactive plastic 35 ±5 microspheres. Injections were made into the right ventricular outflow tract while recording femoral and pulmonary arterial, left atrial, and airway pressures. Cardiac output (CO) was determined by dye dilution. The lungs were air dried under 30 cm H_2O pressure for 4 days, embedded in urethane foam, cut coronally in 15 to 18 one-cm slices, the fraction of total lung volume in each slice determined by planimetry and multiple one-cubic-centimeter sections from each slice counted in a scintillation well counter. DPBF to the dependent lung at rest varied from 50 to 73% of the total CO. The lower values were associated with higher left atrial pressure and vice versa. Under increased acceleration, the superior regions showed a progressive decrease in the fraction of the cardiac output passing through it as compared to 1G (0.2 to 6.1 at 2G, 4.5 to 8.0 at 4G, and 7.5 to 18.4 at 6G). In the mid-lung region, the fraction of CO increased similarly to the loss in superior region whereas the most dependent region of the lung showed little change in spite of the fact that the greatest change in hydrostatic pressures occurred here. DPBF plus oxygen saturation data from superior and dependent pulmonary veins suggest that redistribution away from the most dependent region occurred toward the end of the 60-second exposure. (Supported in part by Research Grants NASA NsG-327 and NIH HE-03532.)

FREE FATTY ACID RELEASE FROM TISSUE STORES DURING CHYLE INFUSION. T.J. Regan, H.A. Oldewurtel*, A. Passanante*, W.M. Burke*, and S. Asokan*. Department of Medicine, New Jersey College of Medicine and Dentistry, Jersey City, New Jersey.

While studying lipid metabolism in the myocardium of intact anesthetized dogs a rapid (3 min) rise of free fatty acid (FFA) in arterial blood was observed early in the course of a 30 min chyle infusion into a systemic vein of recipient animals. Since this response preceded the rise of arterial triglyceride concentration, the possibility of mobilization of FFA from tissue stores was explored. Chyle from corn oil-fed donor animals was infused and serial arterial samples from the recipient animals were analyzed by Gas Liquid Chromatography to assess the time course of individual FFA responses. Oleic acid was predominant in the early plasma FFA increments. After 25 min linoleic acid became predominant, presumably from hydrolysis of the corn oil chyle. In addition the early FFA rise was greater in venous effluent from an adipose tissue area than in arterial blood. To evaluate the contribution of the sympathetic nervous system, a group of animals were pre-treated with butoxamine. Chyle infusion failed to elicit an FFA rise until after 25 min. Hence the early increment of plasma FFA during chyle infusion appears to be related to mobilization of peripheral stores and to be mediated by the adrenergic system.

^{14}C AMINO ACID AND ^{3}HOH RETENTION BY PROLACTIN STIMULATED PIGEON CROPS. James A. Rillema* and William L. Frantz. Dept. of Physiol., Michigan State Univ., East Lansing, Michigan.

The initial response of pigeon crop mucosa to prolactin is poorly understood, although the later stages are well defined and form the basis of a commonly used prolactin bioassay. To better describe some of the early effects, prolactin was injected subdermally over one lateral aspect of the crop sac of 4 to 6 week-old White King pigeons. As a control distilled water was injected over the other half. At 6,12 and 24 hours subsequent to this injection 2.5 μc of ^{14}C-amino acids mixed with 2.5μc of ^{3}HOH were injected IV. At intervals from 1 to 6 hours, crop mucosa immediately next to the prolactin and water treated areas was excised, blotted, weighed and counted; the data is reported as the ratio of treated mucosa (prolactin) vs control mucosa (water).

Prolactin

Dose	Incubation	1	2	4	6
25μg	6 hrs.	.98±.06°	1.08±.08	.90±.05	.83±.12
25μg	12 hrs.			1.05±.17	.80±.06
0.0μg	24 hrs.	.89±.05	.84±.03	1.10±.15	.94±.10
1.25μg	24 hrs.	1.19±.05*		1.22±.11	
12.5μg	24 hrs.	1.34±.12*	1.33±.15*	1.46±.22*	1.49±.20*
25μg	24 hrs.	1.10±.17	1.35±.21	1.74±.29*	1.75±.17*

°=T/C ± SE (N = 5) *=T/C > 1.0, P < .05

The data indicate an initial increased amino acid uptake (T/C > 1.0) after 18 to 24 hours of prolactin exposure. T/C is not greater than 1.0 for prolactin exposure time of less than 18 hours. T/C ratios vs time for ^{3}HOH are similar to those of the ^{14}C amino acids, but closer to 1.0 with less variability. (Supported in part by NSF Grant GB 6024).

DISTRIBUTION OF PULMONARY BLOOD FLOW IN ACUTE EDEMA IN ISOLATED DOG LUNG. B. C. Ritchie,* G. Schauberger,* and N. C. Staub. Cardiovasc. Res. Inst. & Dept. Physiol., Univ. Calif. Med. Ctr., San Francisco, Calif.

West et al. (Circ. Res. 17:191, 1965) found inversion of the hydrostatic pulmonary blood flow distribution per unit lung volume ($\dot{Q}/V$) under very special conditions in acute edema induced by high pulmonary venous pressure (HVP). We repeated their experiments in isolated, perfused dog lungs, determining $\dot{Q}/V$ by the xenon-133 scanning procedure and weighing the lungs continuously to determine the rate of edema formation. We perfused 18 lungs for 1½–2 hours each (6 controls, 6 with increased capillary permeability by alloxan, and 6 HVP). We also rapidly froze 2 more lungs in each class. Control lungs [artery pressure (Pa)>alveolar pressure (Palv)>venous pressure (Pv)] developed edema slowly. They did not show $\dot{Q}/V$ inversion. Alloxan lungs (Pa>Palv>Pv) showed rapid edema formation but no $\dot{Q}/V$ inversion. HVP lungs (Pa>Pv>Palv) showed the expected re-distribution but no inversion of $\dot{Q}/V$ unless Pa−Pv < 2.5 Torr and $\dot{Q}$ < 100 ml/min. All frozen lungs showed interstitial perivascular edema decreasing from bottom to top of lung. HVP lungs showed perivascular hemorrhage at the hilum. Alveolar walls were more congested and extra-alveolar vessels more distended at comparable levels in HVP lungs than controls or alloxan lungs. We have not found any vascular compression, kinking, or nipping in lungs with $\dot{Q}/V$ inversion. The data confirm the inversion of $\dot{Q}/V$ found under the special conditions of HVP, very low Pa-Pv, and low flow. The phenomenon does not appear to be related to pulmonary edema in general. (Supported in part by USPHS grant HE-06285. B.C.R. is a Senior Fellow of the San Francisco Heart Association. G.S. is a Volkswagon Grant Scholar.)

INFLUENCE OF DESOXYCORTICOSTERONE ACETATE ON RENIN RELEASE IN DOGS. C. A. Robb*, J. O. Davis, C. I. Johnston*, and P. M. Hartroft*, University of Missouri School of Medicine, Columbia, Missouri, and Washington University School of Medicine, St. Louis, Missouri.

The comparative responses in plasma renin to the intravenous injection of 2 ml. of Mercuhydrin were studied in 5 dogs before and after 2 weeks of the daily intramuscular injection of 15 mg. of desoxycorticosterone acetate (DOCA). The experiments were conducted on conscious female mongrel dogs weighing 18-25 kg.; the animals were given a constant sodium intake of 60 mEq/day. Plasma renin and renal sodium excretion were measured before and for 3½ hours following the intravenous injection of Mercuhydrin. Before DOCA administration plasma renin increased 3-6 fold within 90 minutes following Mercuhydrin injection. In striking contrast, after 2 weeks of DOCA injection, the initial plasma levels of renin were markedly depressed and the response in plasma renin to Mercuhydrin was negligible or absent. The natriuresis induced by Mercuhydrin was essentially the same before and after DOCA administration. Histological examination of the kidneys revealed hyaline deposits between the juxtaglomerular cells of the renal afferent arterioles after treatment with DOCA. Thus, attention is called to the association of hyaline deposits in the renal afferent arterioles with the failure of plasma renin to increase in response to Mercuhydrin injection during chronic DOCA administration.

THE EFFECT OF INSPIRATORY FLOW RATE ON REGIONAL DISTRIBUTION OF INSPIRED GAS. P.C. Robertson*, W.R.D. Ross* & N.R. Anthonisen, McGill University Clinic, Royal Victoria Hospital, Montreal.

One millicurie (2-4ml) boluses of ^{133}xenon were rapidly injected at the mouthpiece at selected lung volumes during vital-capacity inspirations of varied flow rate in standing normal subjects. After 15 seconds breath-hold regional chest concentrations at TLC were measured by ten scintillation counters. The xenon concentration of the subsequent vital-capacity expiration was followed by a counter in the mouthpiece. For boluses injected at RV rapid inspiration (5L per sec.) markedly flattened the slope of the xenon alveolar plateau due to a striking reduction in the 6:1 top to bottom regional concentration gradient produced by slow inspiration (0.2 L per sec.). A curvilinear relationship appears to exist for intermediate flow rates. The slope of the alveolar plateau and regional concentrations were much less dependent upon inspiratory flow rate when boluses were injected above 40% VC. Fast inspiration slightly reduced the 2:1 bottom to top regional concentration gradient of slow inspiration chiefly by increasing apical concentrations. It is likely that closure of lower airways occurs at low lung volumes and that they can be reopened much earlier by a rapid inspiration resulting in more even regional distribution of ventilation. At high lung volumes, distribution is governed by airways resistance which appears to be lower in the upper part of the lung. (Supp. by M.R.C. of Canada and the John A. Hartford Found.)

ROENTGENOGRAPHIC EVIDENCE FOR THE FLITTER MECHANISM OF MURMUR PRODUCTION. Simon Rodbard and Hyman Gildenhorn.* City of Hope Medical Center, Duarte, California.

Ejection through stenotic aortic or pulmonary valves generates oscillations in pressure as evidenced by a saw-tooth anacrotic pressure wave and a coarse systolic murmur. Ejection at critical velocities through soft-walled tubes or valves also produces a saw-tooth pressure upstroke and a coarse systolic murmur-like sound. Direct observations of the mechanism in the model system show that these effects result from recurrent closure and reopening (flitter) of the leaflets resulting from recurrent interchange of pressure and velocity at the region of the narrowing. We have therefore suggested that murmurs in stenotic lesions are also produced by flitter (Am. Heart J. 46:715-725, 1953). Roentgenkymographic recordings of the movements of the aortic or pulmonary roots during ejection provide further support for the flitter concept. Early in the ejection phase in organic or relative aortic stenosis, the aortic root exhibits several abrupt lateral movements. Each discrete aortic movement can be associated with the ejection of a discrete bolus of blood into the aorta during the open phase of the valve leaflets of each flitter cycle. A succession of such closings and reopenings of the aortic valves is believed to generate the brusque aortic movements in the manner of a Bourdon tube. Similar oscillations are observed in the pulmonary artery root in stenosis of the outflow tract of the right ventricle. These discrete movements of the aorta or pulmonary artery cannot be attributed to turbulence or vortices. The timing of discrete acoustic impulses recorded in these patients by conventional phonocardiographic means or with the heart sound analyzer developed in this laboratory supports the thesis that the murmurs are produced by flitter.

FLUORESCENCE LEVELS IN DORSAL ROOT GANGLION FOLLOWING PERIPHERAL NERVE STIMULATION AND AFTER AMYTAL AND IODOACETATE TREATMENT. C. Rodriguez-Estrada (intr. by L. M. N. Bach). I.V.I.C., Caracas, Venezuela.

Fluorescence in dorsal root ganglion (Rana Palmipes Spix) was induced by a 361 nm excitation wavelength. Fluorescence emission at 447 nm was measured and attributed to $NADH_2$ (Chance et al. Science 137: 499-508, 1962). An attempt is made to correlate bioelectrical and biochemical changes. Fluorescence was measured on in vitro preparations kept in pure oxygen at 15°C. Under these experimental conditions a change of the reference fluorescence level was observed following (5 sec) peripheral nerve stimulation. This fluorescence change was named "the aerobic fluorescence response". The aerobic fluorescence response is characterized by 2 successive deflections from the reference fluorescence level. These 2 deflections correspond to a decrease and an increase of the fluorescence respectively. The first deflection of the aerobic fluorescence response, a decrease of fluorescence, is selectively blocked by (5 mM) Amytal treatment. The second deflection of the aerobic fluorescence response, an increase of fluorescence, is selectively blocked by (5 mM) Iodoacetate treatment. The effects of these inhibitors, under aerobic conditions, suggest that the respiratory chain and glycolysis play a role in energy restoration and these metabolic pathways are triggered simultaneously following excitation.

THERMOREGULATORY RESPONSES TO LOCAL WARMING OF SKIN OVER THE SPINAL COLUMN. C. F. Roe*, J. D. Hardy and J.A.J. Stolwijk. John B. Pierce Foundation Laboratory, Department of Physiology, Yale University, New Haven, Connecticut, and Department of Surgery, Columbia University, New York, N.Y.

Radiant heating was applied to a skin area measuring 7 cm x 43 cm overlying the dorsal spine of human volunteers. The thermal input was approximately 4 Kcal/hr, and the temperature of the heated skin rose to 39-41°C. As the irradiated area was only about 1/100 of the total surface area, the mean weighted skin temperature was almost unchanged. At an ambient temperature of 20°C, the irradiation produced sweating at a rate which exceeded the radiant heat input. This sweating was maintained in spite of the falling core and mean skin temperatures. At ambient temperatures around 30°C where slight sweating was already occurring, heating of the back caused a marked increase in evaporative heat loss, again considerably in excess of the heat gain, and more than the amount which could be produced by the heated skin alone. In the control experiments, a surface area of the back five times as large was heated with the same intensity. The thermal input varied between 24 and 28 Kcals/hr, and the mean skin temperature was raised by an average of 0.2°C. The increase in heat loss stimulated by the thermal radiation was almost the same whether the whole back or only the center strip overlying the spine was heated. Heating of the skin over the spine reflects either a sensory importance to this area which is out of proportion to its surface area, or else signifies the presence of deeper temperature sensors possibly in the spinal cord. This necessitates some re-evaluation of the formula previously used to predict the onset and amount of sweating in response to thermal stimuli.

A BIOCHEMICAL DEFINITION OF BLOOD VISCOSITY: ITS POSSIBLE SIGNIFICANCE IN THE PATHOPHYSIOLOGY OF SHOCK. F. E. ROSATO, M.D., L. D. Miller, M.D., M. Behar, Ph.D. and John Zapp, B.S. (intr. by J. E. Rhoads, M.D.), School of Med., Univ. of Penna., Phila., Pa.

We have demonstrated, for the first time, that viscosity is directly related to the negatively charged N-Acetyl Neuraminic Acid moiety of glycoprotein. The sole and specific action of the enzyme Neuraminidase is to cleave N-Acetyl Neuraminic Acid. In serum samples from four adult dogs, approximately 90% of the protein bound N-Acetyl Neuraminic Acid was released to the free form, as determined by the method of Warren, after incubation with Neuraminidase. In six samples from healthy adult human males, the addition of 500 units Neuraminidase to 1.5 cc. heparinized whole blood resulted in uniform elevation of blood viscosity, without significant change in hematocrit. In this in vitro system, then, an increase in viscosity was effected by liberation of negatively charged N-Acetyl Neuraminic Acid. Finally, in three dogs subjected to hemorrhagic shock, a progressive decrease in serum total N-Acetyl Neuraminic Acid was documented. Since bacterially produced Neuraminidase is present in the intestine, the loss of a mucosal barrier function in shock with liberation of the enzyme into the peripheral circulation may be the determining factor in the maladaptive increase in viscosity seen in advanced shock.

PASSIVE FLUXES OF ^{22}Na, ^{36}Cl AND HTO PREDICTED FROM P.D./J_{sc}. Richard C. Rose* and William L. Frantz. Dept. of Physiol., Michigan State Univ., East Lansing, Michigan.

The ratio of PD/J_{sc} is found to correlate with the passive movement of ions and HOH in a perfused membrane. Since J_{sc} is a measure of the current generated by the Na pump when PD is clamped at 0, the calculated resistance (R_c=PD/J_{sc}) will differ from the measured resistance in the proportion that the movement of the other ions reduces the open circuit P.D. Using the Ussing technique muscle-free pigeon crop mucosae and grass frog skins were perfused with isotonic Ringer solutions at both surfaces. The short-circuiting current was continuously monitored except during brief periods when the P.D. was recorded. Fluxes of ^{22}Na, ^{36}Cl and ^{3}HOH were measured in each direction. The passive fluxes of ions are high when the PD/J_{sc} is low and approaches zero when the PD/J_{sc} is high. This relationship is expressed in the exponential equation of the general form: $\emptyset(\mu eq/cm^2/hr)=R_1 - R_c^x$, where R_1 is the PD/J_{sc} when $\emptyset$ is minimal, R_c is calculated from the measured PD/J_{sc} and x is an exponent $0 < x < 1.0$. These constants R_1 and x differ with the diffusing particle and with the source of the membrane. Higher flux rates of water fit the above equation for pigeon crop mucosa but not for frog skin. Moreover, at the limiting ratio the flux of HOH is not zero, but about 2 mmole/cm^2/hr. This correlation of fluxes with PD/J_{sc} affords a possible means of evaluating the effect of therapeutic agents on the passive permeability of membranes in the presence of the sodium pump. Likewise, the application of this concept can serve as a method of estimating the variability of passive fluxes in the untreated membranes. (Supported in part by NSF Grant GB 6024).

HEMODYNAMICS OF COLLATERAL CIRCULATION DILATATION FOLLOWING OCCLUSION OF THE FEMORAL ARTERY. Stanley L. Rosenthal* and Arthur C. Guyton (intr. by Elvin E. Smith), Dept. of Physiology & Biophysics, Univ. of Miss. School of Medicine, Jackson, Mississippi.

The progressive dilatation of collateral vessels around an acute femoral artery occlusion was studied in anesthetized dogs. Femoral artery pressure proximal to the occlusion and anterior tibial artery pressure and flow distal to the occlusion were recorded while a clamp was applied to the femoral artery. Immediately following occlusion, the anterior tibial artery pressure and flow dropped in 14 seconds to an average of 28% and 21% of the preocclusion levels respectively, and then rose during the first minute to 53% and 58% of control levels. Tibial pressure and flow rose approximately another 5% during the ensuing hour, while femoral pressure did not change significantly during the entire period. The increase in anterior tibial pressure and flow was used as a measure of dilatation of collateral vessels around the occlusion. The dilatation was not affected by sympathectomy, spinal anesthesia, reserpine or hexamethonium; however, the collateral dilatation occurred prior to occlusion during systemic hypotension. Following removal of the occlusion, the collateral vessels constricted, the time required for complete constriction depended on the duration of the occlusion. When the clamp was removed after a 2 minute occlusion, the collateral vessels began to constrict in about 4 minutes and constriction was maximal by 11 minutes. Collateral constriction was slower following longer periods of occlusion. The data supports the concept that peripheral ischemia is one of the factors responsible for initation of collateral circulation development.

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SYMPATHETIC VASOCONSTRICTOR RESPONSES IN THE DOG HIND LIMB DURING SIMULATED EXERCISE: A TIME-DEPENDENT CHANGE IN MAGNITUDE.
D. J. Rowlands* and D. E. Donald, Mayo Clinic, Rochester, Minnesota.

Anesthetized atropinized dogs were studied at rest and during simulated exercise of the hind limb, using constant flow perfusion. Stimulation of the lumbar sympathetic trunk (0.2 to 16 cps) gave vasoconstrictor responses appreciably smaller during the first 10 minutes of exercise than in the resting state, at all but the higher frequencies. During continued steady exercise there was an increase in the magnitude of the constrictor responses over 10-20 minutes, after which no further systematic change occurred. The increase in response was not uniform at all frequencies, thus frequency-response curves taken in the first 10 minutes of exercise differed in shape from those taken after the sensitivity change. Similar time-dependent changes were seen (i) in the skinned limb and (ii) with the vasoconstrictor response to carotid sinus stimulation. The changes were not seen in the contralateral resting limb, and could not be reproduced by changing the pH, Pco_2 or temperature of blood perfusing a resting limb to match values found in the effluent venous blood of exercising limbs. Similar but smaller time-dependent changes were seen during drug induced vasodilatation. A time-dependent change was not seen when norepinephrine was used as the vasoconstrictor stimulus and at equivalent blood concentrations of norepinephrine a greater response occurred in the exercising than in the resting state. It is suggested that the constrictor response of vascular smooth muscle is related to its initial length or tension and that following dilatation there is a time dependent change in the efficacy of the vasoconstrictor system. The site of this change appears to be distal to the lumbar sympathetic trunk and proximal to the smooth muscle receptor site for norepinephrine.

Supported in part by NIH grant HE06143.

ELECTROLYTE SECRETION OF THE CANINE PANCREAS IN RESPONSE TO GASTRIN-PENTAPEPTIDE. Jack Rudick*, Miguel J. Zerpa*, Allan E. Kark*, David A. Dreiling. The Mount Sinai School of Medicine, New York, N.Y.

Effects of gastrin-pentapeptide (GP) on electrolyte composition of pancreatic secretion was studied in four dogs equipped with a chronic pancreatic and a gastric fistula, a gastroenterostomy and mucosal septum between antrum and duodenum. Increasing doses of GP were administered intravenously to the conscious, fasting dog with and without a background of continuous secretin infusion. Ten-minute samples of pancreatic secretion were analyzed individually for volume, HCO_3, Cl, K, Na, amylase and osmolality. GP produced a mild stimulation of flow with an increase in HCO_3 concentration in the resting gland. When a secretory plateau (volume, HCO_3, and Cl concentration) had been reached with secretin infusion, GP produced an increase in Cl and decrease in HCO_3 concentration despite a constant or increasing flow rate. The ratio of HCO_3:Cl output diminished with increasing doses of GP, decreasing the inverse relationship between these two ions. Na, K and osmolality were unchanged while amylase output was increased. Control experiments with saline showed constant HCO_3 and Cl concentrations with constant ratios of HCO_3:Cl output. Exhaustion of the gland or suppression of secretion with supramaximal doses of GP was not noted. These findings indicate that gastrin-pentapeptide is capable of increasing Cl concentration in pancreatic juice, suggesting the possibility of an active, rather than a passive, mechanism for the secretion of Cl ions. Alternatively, it may enhance the diffusion of HCO_3 across pancreatic duct epithelium. (Supported by NIH Grant #AM-03889-07)

THE EFFECTS OF AFFERENT VOLLEYS ON THE EXCITABILITY FLUCTUATIONS OF Ia MUSCLE AFFERENT TERMINALS. P. Rudomín and H. Dutton (intr. by R. Hernández-Peón). Centro de Investigación y de Estudios Avanzados del IPN. México 14, D. F.

In non anesthetized immobilized spinal cats successive antidromic responses of Ia afferent fibers of lateral gastrocnemius, produced by constant direct stimulation of the motoneuronal nucleus, showed considerable fluctuations. These fluctuations were reduced after the intravenous injection of Nembutal (3 to 10 mg/kg) or by preceding conditioning stimulation (3 shocks at 300 cps) of posterior biceps semitendinosus, or of the peronei, tibialis anterior and extensor digitorum longus or plantaris flexor digitorum and hallucis longus Ia and Ib afferent fibers. The time course of this effect closely resembled that of the hyperexcitability of Ia afferent terminals : onset at 3 to 7 msec, peak at 20 to 40 msec and gradual decay up to 100 msec. The effects on variability produced by the conditioning afferent volleys were greatly impaired after 1 to 2 mg/kg picrotoxin. We suggest that the polysynaptic paths leading to depolarization of Ia afferent terminals are continuously active and highly correlated in their fluctuations and that variability reduction results from synchronous activation and subsequent depression of these paths. Since similar conditioning stimulations also reduced variability of the gastrocnemius monosynaptic reflex, we conclude that membrane potential fluctuations of Ia afferent terminals play an important role in variability of transmission from Ia afferents to motoneurons.

EFFECT OF COMBINED SYMPATHETIC AND VAGAL STIMULATION ON HEART RATE. R. O. Russell, Jr.* and H. R. Warner, Dept. of Biophysics & Bioengg., Univ. of Utah, Salt Lake City, Utah. Supported by a grant and a special fellowship from NIH, nos. HE-03607 and HE-32,441.

The model of Cox and Warner (JAP 17: 349, 1962) will predict the time-course of heart rate resulting from stimulation of sympathetic or vagus nerves to the heart. This model has been extended to permit prediction of heart rate resulting from stimulation of cardiac sympathetic and vagus nerves (HR_{SV}) at all combinations of stimulus frequencies:

$$HR_{SV}=HR_V+(HR_S-HR_0)\times(HR_V-HR_{MIN})/(HR_0-HR_{MIN})$$

where HR_V is the heart rate predicted for vagal stimulation at frequency (V), HR_S is heart rate predicted for sympathetic stimulation at frequency (S), HR_0 is heart rate with no stimulation and HR_{MIN} is the minimum heart rate achievable by vagal stimulation short of complete arrest (usually 25-30/min). Data used to test the theory were obtained from dogs in whom both vagus nerves and all accessible cardiac sympathetic nerves were cut and the distal ends of the nerves stimulated supramaximally at frequencies generated from a digital computer. The time-course of heart rate and frequency of stimulation of vagus (V) and sympathetic (S) nerves was stored for later testing against the model. In each experiment the parameters of the model were first determined using the response to sympathetic stimulation alone and vagus alone and then tested against data obtained by simultaneous stimulation of both nerves at various frequency combinations.

OPSONIN INVOLVEMENT IN RETICULOENDOTHELIAL PHAGOCYTIC "BLOCKADE" AND RECOVERY. Thomas M. Saba* and N. R. Di Luzio, Department of Physiology and Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

The importance of plasma or serum factors called "opsonins" as a major determinant of phagocytosis has been demonstrated. Furthermore, opsonins have been implicated in the development of RE "blockade". In the present study, the role of opsonins in "blockade" induction and recovery was evaluated with the use of a gelatinized "RE test lipid emulsion". The intravenous administration of the emulsion to rats (50mg/100g) induced a state of phagocytic depression as evaluated by the subsequent intravascular clearance and tissue distribution of a test dose (50mg/100g) of the same emulsion. "Blockade", which was apparent at 30 min. post-injection, was only temporary, as complete recovery was observed by 2 hr. Opsonic activity evaluated before, during and following "blockade" revealed that a 92.3% depression in circulating opsonin levels existed during RE "blockade" which was restored to normal within 2 hrs. The injection of the emulsion in an opsonized form during RE "blockade" completely eliminated the manifestations of "blockade" as determined by clearance and distribution of the colloid. The excellent temporal relationship between RE "blockade" and opsonic depression, as well as the correlation between phagocytic recovery and elevation of circulating opsonin levels demonstrates that 1) RE "blockade" is the result of a depletion of circulating opsonins, and 2) that recovery from "blockade" is due to a restoration of opsonin concentration and/or activity. The compensatory response of the opsonic system after RE "blockade" as revealed by the rapid elevation, overshoot, and eventual return to normal of opsonin levels suggests the existence of a physiological control of blood opsonin levels. (Supported by USPHS and AEC).

THE RELATIONSHIP OF THE PHOSPHORYLATED INTERMEDIATE TO BRAIN TRANSPORT ATPase G. Sachs*, M.M. Long* and B.I. Hirschowitz, Dept. of Medicine, U. of Alabama Medical Center, Birmingham, Alabama.

A subcellular fraction prepared from pig brain by a sucrose EDTA technique shows a Mg + Na + K:Mg ratio for ATPase activity of 2 to 3, characteristic of transport ATPase. Furthermore incubation of this fraction with ATP^{32} and Mg^{2+} at pH 7.4, 0°C for 15 secs. results in labelling of the PCA precipitable protein, stimulated several fold by 100mM NaCl, characteristic of the 'phosphorylated intermediate' in the ATPase reaction. The Na^+ labelling increment on the basis of its NH_2OH sensitivity is due to a carboxyl phosphate. Since 0.8M NH_2OH does not inhibit the overall ATPase reactions, it has been suggested that a hydroxamate is not formed from the carboxyl phosphate when the enzyme is in its native configuration. However if the enzyme is preincubated with Na + ATP + NH_2OH, washed and assayed for transport ATPase activity, no effect is observed, but the Na stimulated P^{32} incorporation into PCA precipitable protein is inhibited, only if all 3 substances are present in the preincubation. It is concluded therefore, that a hydroxamate is formed during the preincubation, irreversibly inhibiting the formation of the carboxyl phosphate but not enzyme activity. Thus the carboxyl phosphate is not a true intermediate of the transport reaction, but is probably formed from the actual intermediate which is not detected by current techniques. (NIH, NSF Support)

COMPLIANCE OF THE PULMONARY ARTERIAL TREE. Marvin A. Sackner and Jack J Greenberg*, Mt. Sinai Hosp., Miami Beach and Univ.of Miami Sch. Med., Coral Gables, Fla.

Previous estimates of pulmonary arterial compliance in closed chest subjects have been indirect. The purpose of the present study is to describe a direct method for estimation of the pressure volume curve of the pulmonary arterial tree. The method hinges upon increasing the volume of the pulmonary arterial tree by applying negative pressures to the body surface of an anesthetized, paralyzed dog enclosed within a body plethysmograph while maintaining tracheal pressure at atmospheric pressure. This maneuver produces a rise in "effective pulmonary arterial pressure", the difference between mean pulmonary arterial and pleural pressures. Pulmonary arterial blood volume is measured by an ether plethysmographic method (Feisal, Soni and DuBois, J.C.I. 41:390, 1962). The slope of the pressure volume curve is roughly linear on raising mean effective pulmonary arterial pressure up to 12mmHg above control values; preliminary data suggest hysteresis is present on deflation. The compliance of the pulmonary arterial tree in 4 normal dogs weighing between 11 and 16Kg. was respectively, 1.0,1.2,1.4 and 1.7ml per mm Hg; in 1 dog with pulmonary hypertension, the value was 0.5ml per mm Hg. Minimal changes occur in pulmonary blood flow and pulmonary vascular resistance when up to 15mm Hg of negative transthoracic pressure is produced. Total pulmonary blood volume (measured by indicator dilution methods) was plotted against effective pulmonary vascular pressure (average of effective pulmonary arterial and effective left atrial pressures).These data showed considerable scatter and the estimate of total compliance can only be considered a gross approximation. It appears as if pulmonary arterial compliance ranges from 11 to 34% of the total compliance of the pulmonary vascular bed (supported by NIH grant HE 10622-01).

OLFACTORY NERVE SECTION OR BULB ABLATION AND BEHAVIOR OF PIGEONS IN NON-OLFACTORY LEARNING. A. Salzman* and B.M. Wenzel. Dept. of Physiol. and Brain Res. Inst., UCLA Med. Sch., Los Angeles, Calif.

The olfactory bulbs of mammals have long been known to originate extensive connecting pathways with other brain structures, the majority of which are usually identified with the limbic system. Although little is known about olfactory bulb efferents in birds, it seems reasonable to assume an analogous distribution. As part of a study of avian olfaction, it was asked whether sectioning of the primary olfactory pathway in pigeons would affect behavior in a non-olfactory learning situation. The task required pecking on the left of two translucent discs when both discs were lighted with Color 1, and pecking on the right disc when both were lighted with Color 2. Correct responses were reinforced with grain on a VR 3 schedule. Four groups of 5 birds were trained, viz., birds with olfactory nerve section, with olfactory bulb removal, with a comparable amount of hyperstriatal ablation, and sham operates. All lesions were bilateral. Results showed that the groups with olfactory pathway damage were significantly slower in learning to eat from the hopper, in learning to peck the discs, and in transferring responses from the disc on which they were first trained to the other disc. The hyperstriatal group did not differ from the sham operates in these characteristics. A replication yielded the same trends. The similarity between birds with nerve section or bulb ablation indicates that activity in the primary olfactory pathway was a critical factor. Because the affected behavior seems independent of olfactory cues and because similar effects have been reported after limbic lesions in mammals, the suggestion is that the olfactory system is an integral limbic component. (Supported by NSF grant GB 4596)

DEPENDENCE OF THE MAGNITUDE OF THE K^+ PERMEABILITY OF THE MEMBRANES OF THE FROG'S GASTRIC MUCOSA ON AEROBIC METABOLISM. S. S. Sanders,* and W. S. Rehm. Department of Physiology and Biophysics, Medical Center, University of Alabama, Birmingham, Alabama.

With an in vitro technique the relative ionic permeability to K^+ of the limiting membranes of the mucosal cell layer of the frog's gastric mucosa was assessed by determining the response of the transmucosal potential difference (PD) to unilateral changes in $[K^+]$ of the bathing media. The half time for the response is from 15 to 90 sec. Under aerobic conditions the ΔPD per ten fold change in $[K^+]$ ($\Delta PD/10K^+$) with $SO_4^=$ media (Cl^--free) was about |25 mv| for both the nutrient and secretory membranes while with Cl^- media it was about |35 mv| for the nutrient membrane (the response of the secretory membrane in Cl^- media is complex and will not be considered further). With either anoxia or 2,4-dinitrophenol the $\Delta PD/10K^+$ decreases markedly and the decrease is apparent within 7 min. The decrease is reversible (readily so with anoxia, less so with the DNP). The time course of the change in PD was studied during readmission of O_2. The $[K^+]$ on a given side was changed during anoxia from 4 to 79 mM K^+ and then, with 79 mM K^+ still present, O_2 was readmitted and this changed the PD to a new level with a half time for the response of from 1 to 3 min. For the nutrient membrane in Cl^- and $SO_4^=$ the level upon readmission of O_2 was about that predicted on the basis of the previous controls with 79 mM K^+ in O_2; in $SO_4^=$ the PD changed from about -7 mv (nutrient negative) to -56 mv while in Cl^- it changed from about -5 to -20 mv. We conclude that the magnitude of the K^+ permeability is dependent on aerobic metabolism and rapidly changes with changes in the metabolic state. (NIH and NSF support.)

PURIFICATION OF ANGIOTENSIN II ON SEPHADEX LH-20. Armando Sandoval,* David J. Miletich,* and J. V. Princiotto (intr. by L. S. Lilienfield). Dept. of Physiology and Biophysics, Georgetown University Schools of Medicine and Dentistry, Washington, D. C.

A clean-up procedure is described whereby the vasopressor peptide angiotensin II (M.W. 1031) can be rid of small molecular weight contaminants such as arginine (M.W. 174) on a Sephadex LH-20 column. This particular separation is instrumental towards the development of a radioactive derivative assay based on quantitation of its arginine residue. The alcohol solubility of the peptide coupled with Sephadex LH-20's organic solvent compatibility allows a convenient volatile solvent mixture to be employed. Efficacy of separation has been shown with near milligram loads as well as with nanogram loads within limits of detection by ninhydrin staining, angiotensin II bioassay and liquid scintillation radiation counting. Needless to say, this clean-up technique can be extended to removal of other small molecular weight contaminants as well.

A READILY ACCESSIBLE COMPARTMENT OF LYMPHOCYTES IN CHRONIC LYMPHOCYTIC LEUKEMIA: EXAMINATION BY THREE METHODS. L.M. Schiffer*, A.D. Chanana*, E.P. Cronkite, M.L. Greenberg*, P.A. Stryckmans*, and P.C. Vincent*. Medical Research Center, Brookhaven National Laboratory, Upton, N. Y.

The pattern of response of blood lymphocytes (BLy) in patients with chronic lymphocytic leukemia, when treated by extracorporeal irradiation of the blood (ECIB), is an abrupt exponential decline followed by a steady state. Since ECIB involves irradiation of BLy, without any known effects on lymphopoiesis, we postulate that attainment of a steady state during ECIB signifies the depletion, not only of BLy, but an easily mobilized, readily accessible compartment (RAC) of lymphocytes (Ly). RAC size may be computed from measured values and assumed variables. The known values are blood volume, number of BLy irradiated daily, and dose of irradiation to BLy. The assumed variables are the dose necessary to destroy BLy (500+ rads) and blood T1/2 of lethally irradiated BLy (0.75 days). Experimental evidence for these statements will be presented. Our results, in 9 patients with widely varying initial BLy counts, indicate a RAC 0.67 to 5.3X the total BLy. The anatomic relationships of RAC are not known and probably vary from patient-to-patient. This is shown in patients with similar RAC's, only a few of whom have marked decreases in lymph node and/or spleen size after ECIB. Other methods of evaluating analogous, but not necessary identical, RAC's of Ly involve removal of BLy, labeling with ^{3}H-cytidine (Cyt) or ^{75}Se-methionine (Met), infusion, and measurement of dilution of label. There are potential errors in these techniques but the overall results are similar to that found by ECIB. Values for $RAC_{(Cyt)}$ varied from 0.33 to 4.5X and $RAC_{(Met)}$ between 1.9 and 7.3X the total BLy. In all instances where multiple studies were performed the $RAC_{(Cyt)}$ results were consistently lower than, and the $RAC_{(Met)}$ results consistently higher than, the corresponding RAC(ECIB) values.

THE STIMULATION OF HEPATIC GLUCONEOGENESIS DURING FASTING; THE ROLE OF FREE FATTY ACIDS. R.J. Schimmel* and E. Knobil, Dept. Physiology, University of Pittsburgh School of Med., Pittsburgh, Pa.

The conversion of lactate, pyruvate, glycerol, fructose, α ketoglutarate, and oxaloacetate to glucose by liver slices in vitro was measured in the course of 90 min. incubation at 37 C. in Krebs-Ringer buffer containing 80 mg% glucose and 5% bovine serum albumin. A 24 hr. fast increased gluconeogenesis from all the substrates examined. Increasing the FFA concentration from .35 eq/L. to 1.15 eq/L. stimulated gluconeogenesis from lactate and pyruvate, inhibited gluconeogenesis from glycerol and α ketoglutarate and had no effect on gluconeogenesis from fructose and oxaloacetate. These data suggest that the enhanced hepatic glucose production seen during fasting cannot be accounted for by the increased availability of FFA consequent to food deprivation. Nevertheless, the results are consonant with the view that FFA stimulates pyruvate carboxylase activity and elevates the NADH/NAD ratio in the liver cell. (Supported by an NIH predoctoral research fellowship, GM-25,909, and by a grant, AM 05655 from the USPHS.)

THE CONTINUOUS DETERMINATION OF THE EXTRACTION AND CLEARANCE OF 131 IODINE LABELLED DIATRIZOATE AN INULIN SUBSTITUTE BY THE KIDNEY. Herman E. Schmid, Bowman Gray Sch. Med., Winston-Salem, N. C.

Diatrizoate has been shown to be an adequate substitute for inulin in clearance and extraction studies in dogs and man. The extraction of this compound labelled with 131 Iodine (131 I-Renografin, Squibb) can be determined continuously from arterial and renal venous blood samples pumped through polyethylene coils (Radicoil, Abbott) inserted into a dual well-type scintillation, ratemeter, recorder system. The left kidney of anesthetized dogs was exposed via a flank incision and the renal vein cannulated. Renal blood flow was measured or drugs infused via a needle inserted into the artery distal to the flowmeter probe. Glomerular filtration rate (GFR) was calculated from the extraction of 131 I-Renografin, renal blood flow, and the Hct values. Extractions were obtained during alterations in renal perfusion pressure, and during infusion of vasoactive drugs, acetylcholine and angiotensin, by the continuous method described and compared to the standard inulin. The use of an analogue computer will enable a continuous line recording of extraction, clearance (GFR), total renal vascular resistance and pre- and postglomerular vascular resistances. (Supported by a grant from NIH, NIH, HE-7842.)

EFFECT OF VIBRATION ON VASCULAR SMOOTH MUSCLE RESPONSIVENESS TO NOREPINEPHRINE (NE) AND TYRAMINE (TY). P.G. Schmid*, A.J. Liedtke* and A.S. Hyde. Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio.

Forelimb vascular resistance changes in response to injected NE, 0.5, 1.0 and 2.0 μg base and TY, 128, 256 and 512 μg base, were observed in 7 control dogs before and after a rest period of one hour and in 7 test dogs before and after vibration for one hour. Vertical vibration, directed perpendicular to the long axis of the supine, restrained dog, was maintained at one G peak acceleration and ten cycles/second. Each brachial artery was cannulated and perfused separately from the ipsilateral femoral artery. Flow in the two independent circuits was kept equal and constant. Responses to NE and TY before rest or vibration were evaluated in one forelimb; responses after rest or vibration were evaluated in the other forelimb. Each limb was denervated 20 minutes before drug injections. Resistance (calculated as the ratio perfusion pressure/flow) was expressed in arbitrary units. Δ R, the increase in resistance with NE or TY was tabulated; results were analyzed using a parallel line bioassay as a statistical test. In control dogs, average Δ R in response to NE increased significantly ($P < 0.05$) from 1.21 $\pm$ 0.12 (mean $\pm$ SE) before to 1.61 $\pm$ 0.15 units after rest. Average Δ R in response to TY also increased significantly ($P < 0.05$) from 0.70 $\pm$ 0.05 before to 1.17 $\pm$ 0.14 units after rest. In test dogs, the average Δ R in response to NE was 1.27 $\pm$ 0.19 before and 1.30 $\pm$ 0.18 units after vibration. Average Δ R in response to TY was 1.03 $\pm$ 0.22 before and 1.26 $\pm$ 0.23 units after vibration. Vibration did not depress responsiveness to NE or TY in test dogs. Vibration may have inhibited mechanisms which, in control dogs, acted to augment the responsiveness of vascular smooth muscle to NE and TY.

DIURETIC, ANTIDIURETIC AND VASOPRESSOR EFFECTS OF ARGININE-VASOPRESSIN (VA) POTENTIATED BY MINIMAL DOSES OF ANGIOTENSIN II (AN). G.H.Schmitt. (intr. by K.L.Sydnor) Univ. of Ky. Med. Cntr., Lexington.

Non-pressor doses of VA are diuretic and natriuretic during isotonic NaCl infusions, and antidiuretic during water loading or in presence of exogenous mineralocorticoid in pentobarbitalized dogs.(Schmitt, Aerospace Med. in press) Arterial BP and renal water and Na excretion were measured during intravenous infusion of (1) isotonic NaCl (0.17ml/Kg/min. for 2-3 hours), (2) same saline infusion plus 0.04U VA/Kg/hour, (3) saline infusion plus 5 or 10 nanogm AN/Kg/hour, and (4) saline infusion plus the same doses of both VA and AN together. VA alone (2) caused diuresis and natriuresis and no rise in BP. AN alone (3) had no effect on BP or renal H_2O and Na excretion. VA and AN together (4) caused a rise in arterial BP in some expts. and a greater diuretic and natriuretic effect than VA alone in every expt. The doses used represent about one 50th minimal pressor dose (MPD) of AN and one third (or less) MPD of VA under these exptl. conditions. On the other hand, the same dose AN increased BP and diuresis and natriuresis during intravenous infusion of hypertonic (2.5%) NaCl (presumably effect of endogenous VA, potentiated by exogenous AN). However, during water diuresis in dogs, AN potentiated the antidiuretic effect of VA. Since water loading stimulates (Acta physiol. Acad.Sci.Hung.31:141,1967) and saline loading inhibits aldosterone secretion, it is suggested that renal effects of both VA and AN depend on the existing level of mineralocorticoid activity.

DOG RENIN ASSAY USING A ZERO ORDER KINETIC SYSTEM.
Edward G. Schneider* and H.H. Rostorfer, Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana.

The quantification of renin release depends on the use of exact methods. The endogenous substrate bioassay for dog renin is substrate dependent. The variance (CV) for substrate in normal anesthetized dogs is 29% (CV) which contributes to a variance for the zero order constant, Ko, of 24% and the first order constant, K_1, of 19% calculated from data obtained by the endogenous method. In order to avoid the effect of substrate variations between animals and to measure renin in plasma with very low substrate concentrations, a zero order kinetic method has been developed using partially purified dog substrate for the addition to unknown plasma samples. Zero order constants (Ko) of $3.27\pm6.1\%$ (CV) and $3.25\pm8.6\%$ (CV) were found for substrate concentration ranges of 4.2-5.6 AU/ml and 7.0-8.7 AU/ml, respectively. Angiotensinase activity was completely inhibited by incubation in the presence of EDTA+DFP at pH 5.3. The Ko of $3.24\pm 4.1\%$ (CV) for the addition of 1 part plasma to 3 parts substrate concentrate indicated that the addition of normal plasma did not effect the kinetic relationship. The substrate independence, the lack of interference by normal plasma, and the small coefficient of variation for Ko indicated that the kinetic condition was zero order above a substrate concentration of 4.2 AU/ml. To guarantee a zero order kinetic condition, the substrate concentration for the assay should be maintained higher than 5.5 AU/ml. The overall accuracy of the zero order assay compared with the endogenous assay greatly supports the use of the zero order assay method for measuring plasma renin concentrations.
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SYNERGISM AND ANTAGONISM OF VARIOUS PROCEDURES IN THE PRESTONALIZED DOG. Robert T. Schopp and Raymond R. Walsh, Dept. of Physiol., Univ. of Colo. Med. Ctr., Denver, Colorado.

Curariform drugs are classified on the basis of their mechanisms of action, i.e.: Type I - depolarizers (e.g. decamethonium /C-10) or Type II - competitors (e.g. d-tubocurarine /d-TC). Some investigators identify another type of curariform drug which exerts its effect by non-competitive antagonism of acetylcholine: Type III - e.g. Prestonal. This comparative study involves the effects of a number of chemicals and procedures on transmission in canine peroneal-tibialis anticus nerve-muscle preparations, which have been partially paralyzed with Prestonal or C-10 or d-TC. The table below summarizes some of these responses:

Procedure	Type I (C-10)	Type II (d-TC)	Type III (Prestonal)
Epinephrine (i.a.)	No effect	Antagonism	Antagonism
Epinephrine (i.a.) after Dibenzyline		No effect	Synergism
Isotonic KCl (i.a.)	No effect	Antagonism	Antagonism
Isotonic $MgCl_2$ (i.a.)	Synergism	Synergism	Synergism
5-HT	No effect	Antagonism	Antagonism
Anti-ChE (i.a.)	Synergism	Antagonism	Synergism
Tetanic Stimulation	Well-sustained contraction	Poorly-sustained contraction	Poorly-sustained contraction
Post-tetanic potentiation	None	Very prominent	Very prominent

REBOUND AND AFTER-INHIBITION OF A SINGLE INHIBITOR-TO-PACEMAKER SYNAPSE. Joseph H. Schulman (intr. by W.F.H. Mommaerts), University of California, Dept. of Zoology.

Rebound and after-inhibition were measured as a function of inhibitory frequency at the inhibitory synapse of the crayfish stretch receptor. It was found that a low frequency inhibitory burst produced rebound, while a high frequency inhibitory burst with the same number of ipsp's (inhibitory post synaptic potentials) caused after-inhibition. The time constant for recovery from rebound is about four times greater than that of after-inhibition for the same number of ipsp's. It was also observed that the overshoot in the recovery phase of after-inhibition coincides with the recovery of rebound. It may be deduced from these findings that both phenomena are caused by the interaction of two opposing membrane parameters. One is initially dominant, has a short recovery time and causes the after-inhibition. Due to its brief recovery time this parameter soon gives way to the second parameter which has a longer recovery time and causes the rebound. By injecting the ipsp's in rapid succession there is only a short time for recovery during the inhibition, and after-inhibition is produced. By spreading the ipsp's out in time, the recovery occurs during the inhibition, allowing the rebound phenomenon to be expressed. By selecting the correct ipsp frequency the two phenomena cancel out.

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PERIPHERAL VASCULAR RESPONSES TO ACUTE COLD EXPOSURE IN THE ANESTHETIZED CAT. James M. Schwinghamer*, Thomas Adams and Larry R. Klevans*. Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

Vascular responses accompanying extremity local cold exposure, usually indexed by skin surface or intradermal temperatures, have been used to identify general peripheral vascular reactivity and tone set by central neural activity. Skin surface temperatures of the pinna of the ear and the foot and toe pads of anesthetized ("Diabutal", 36 mg./Kg., I.P.), adult, male and female cats were measured by 36 g. copper-constantan thermocouples in 32 experiments on 17 animals during an acute, local cold exposure (immersion of the extremity in a stirred ice water bath). Rectal temperatures were maintained between 37.5-39.5°C by a heating pad. From an initial level of 32-34°C skin temperature in all tests fell abruptly to 2-3°C. For the foot and toe pads, initial cooling was interrupted by periods of spontaneous rewarming within 2-3 minutes after immersion. These phases were characterized by an initial warming rate of 6-8°C/min. to bring the skin surface to nominally 5-8°C before secondary cooling. These oscillations were maintained unchanged or damped within a few cycles. Foot and toe pads did not necessarily respond in phase. In contrast, the response of the ear was qualitatively similar to that of the human digital pad subjected to similar exposure conditions; initial cooling was followed by a single, maintained vasodilation phase. Chronic denervation of the foot (tested 60 days after section of the Sciatic and Tibial nerves) did not modify the response, compared either to the contralateral, normally innervated limb or to the same extremity before neurotomy. The extremities of the anesthetized cat are suggested to represent promising test sites for the study of local and reflexly regulated circulation especially cold induced vasodilating mechanisms.

INFLUENCE OF RESPIRATION ON PULMONARY CAPILLARY BLOOD FLOW ($\dot{Q}c$) AND PULSATILITY IN DIFFERENT POSTURES IN MAN. N. Segel* and M.B. McIlroy. Cardiovasc. Res. Inst., Univ. Calif. Med. Ctr., San Francisco, Calif.

$\dot{Q}c$ was measured in 10 normal subjects during a slow expiration starting at total lung capacity and during a slow inspiration starting at the resting lung volume. Measurements were made sitting, tilted to 45°, and supine in a body plethysmograph. $\dot{Q}c$, peak systolic and diastolic flow, and capillary pulse amplitude (CPA) were calculated from the rate of uptake and alveolar concentration of N_2O measured after 0.5, 1.0, 1.5 and 2.0 L of the breath in or out. Measurements were also made during quiet breathing in the sitting position. $\dot{Q}c$, stroke volume, peak systolic flow and CPA were all greater and diastolic flow less during inspiration in the sitting and 45° tilt positions. These differences were less marked in the supine position. CPA was greatest at the beginning of a slow expiration while the converse was true during a slow inspiration. During quiet breathing, $\dot{Q}c$ and heart rate were greater towards the end of inspiration but stroke volume did not change. CPA was greatest at the time of changeover from inspiration to expiration and least at the changeover from expiration to inspiration. The greater pulmonary capillary pulsatility during inspiration in the upright and 45° positions may in part be due to the increase in stroke volume; however, the fall in diastolic flow suggests a simultaneous fall in pulmonary vascular resistance. This might be due to the opening up of vessels in the upper zones of the lung which were closed during expiration. In the supine position these differences may be less marked, presumably because the vessels are all open. During quiet breathing, with small changes in lung volume, it seems that the increase in flow and pulsatility during inspiration carries over into expiration so that, at normal respiratory rates, blood flow tends to be pulsatile during both phases of respiration.

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LAMINAR SPINAL CORD ORGANIZATION OF VISCERAL AND CUTANEOUS AFFERENT ACTIONS, AND VISCERAL FACILITATION OF CUTANEOUS UNITARY RESPONSES. M. Selzer* and W.A. Spencer, NYU Med. Schl. NYC (Supp. USPHS NB-05980).

In a previous communication (Fed Proc. 1967) convergence and reciprocal inhibition of visceral and cutaneous afferent actions in the lumbar spinal cord of anesthetized spinal cats were described. In the present experiments, we compared the distribution of focal potentials generated at the L4 level by visceral and cutaneous afferent volleys. Microelectrode recordings showed that lateral femoral cutaneous nerve volleys generated an early maximum focal negativity (N_1 wave) associated with short latency unitary responses in Rexed's lamina IV, but lumbar sympathetic chain visceral afferent volleys did not. However, in lamina V, visceral afferent volleys did generate a maximum focal negativity, associated with unitary responses, which corresponded to similar potentials of the second cutaneous (N_2) response component. Convergence of these two pathways onto common interneurons at this level was often seen. In addition, instances of visceral facilitation of cutaneous unitary responses in ascending white matter was noted, but no mechanism for this effect can yet be proposed. Stimulation of primary afferent terminals with microelectrodes located in the dorsal horn produced a compound antidromic action potential in afferents of these visceral and cutaneous nerves. Conditioning supramaximal cutaneous afferent volleys increased the excitability of the A delta but not A beta afferents of the sympathetic chain, indicating depolarization of the central terminals of the A delta visceral afferent fibers. Conditioning stimuli to sympathetic chain afferents increased the excitability of both A beta and A delta cutaneous afferent terminals. A detailed anatomical scheme is proposed to explain both the primary afferent depolarizing actions, which presumably mediate presynaptic inhibition, and the convergence of visceral and cutaneous pathways.

FURTHER OBSERVATIONS ON SPINO-BULBO-SPINAL REFLEXES IN VARIOUS VERTEBRATES. Muneo Shimamura (intr. by Robert B. Livingston). Univ. of Calif. School of Med., La Jolla, Calif.

Spino-bulbo-spinal (SBS) reflexes are transmitted by impulses which ascend from spinal (mainly cutaneous) afferents to bulbar reticular formation, and recurrent relayed impulses which descend the spinal cord to induce ventral root discharges along all spinal segments in descending order from the bulb (J. Neurophysiol. 26:258-272, 1963). SBS reflexes are to be contrasted with propriospinal reflexes which cause discharges in all ventral roots in an order which radiates upward and downward from the point of stimulated dorsal root entry. SBS reflexes have been demonstrated in the cat, dog, monkey, rat and man (Jap. J. Physiol., 14:411-421, 1964). The present study extends investigation of SBS reflexes to several additional species of animals which manifest different locomotor behavior, e.g., frogs, toads, lizards, turtles, fishes, birds, kangaroo-rats, bats, among others. The experiments were performed under chloralose anesthesia and both SBS and propriospinal interlimb reflexes were evoked from both upper and lower extremities. Comparative physiology of interlimb reflexes reveal significant differences between remote species.

INTRACELLULAR POTENTIALS IN ARTERIOLAR SMOOTH MUSCLE. George R. Siggins* and Herbert J. Berman, Boston University, Department of Biology, Boston, Massachusetts.

Electrophysiological studies on the smooth muscle of terminal arterioles are confined to only one published report (Funaki, Nature 191: 1102, 1961). Intracellular potentials were recorded in vivo from the vascular smooth muscle of pre-capillary arterioles in the thin retrolingual membrane of the frog (Rana pipiens). Each frog was lightly anesthetized with MS-222 (tricaine methanesulfonate), the membrane then exposed, and arterioles of 15 to 60 μ diameter and associated terminal vasomotor nerves visualized at 200 or 400 X. 103 readily visible arteriolar smooth muscle cells were impaled with 3 M KCl-filled ultramicropipettes of 20 to 80 MΩ resistance and the membrane potentials recorded on a Tektronix 564 storage oscilloscope. The range of the resting potentials were -18 to -59 mV. The arithmetic mean ($\pm$ S. D.) was -34 ($\pm$ 11) mV. The vasomotor nerves accompanying the arterioles were stimulated by a microelectrode with single rectangular pulses of 0.25 to 1.00 ma intensity and .01 msec duration. All arterioles constricted, but only 25 intracellular "action potentials" were recorded. Two distinct types of action potentials were observed. "Slow waves" with an average duration of 140 msec and amplitude of 12 mV were recorded in 18 cases. In 7 cases, faster "spikes" with an average duration of 74 msec and amplitude of 30 mV were observed. The latent periods averaged 11 msec for the first type and 12 msec for the second. Prepotentials, overshoots, and spontaneous action potentials were not observed . The nerve-induced action potentials recorded here were of a form similar to those found in amphibian cutaneous arterioles by Funaki. (Supported by Grant HE-902 from NIH and Contract DA-49-MD-2696.)

GLUCOSE TRANSPORT ACROSS THE ANTILUMINAL SURFACE OF THE RENAL TUBULES OF THE DOG. M. Silverman* and F.P. Chinard. Goldwater Mem. Hosp. and New York Univ. School of Med., New York, N.Y.

The multiple indicator dilution technique has been used to investigate the renal transport of glucose in anesthetized dogs. Phlorizin solutions of varied concentration were infused systemically at a constant rate of 4ml/min. After 30-40 min., a solution containing T-1824, creatinine, D-Glucose-C^{14} and THO was injected into the left renal artery. Outflow patterns of all indicators were determined in renal venous blood and urine. The blood glucose concentration varied between 50-70mg/100ml whole blood. Previous studies have shown that: (1) creatinine is a valid marker of the extracellular volume of the kidney; (2) glucose is transported with the 6 carbon chain intact; (3) less than 0.2% of the injected glucose is converted to CO_2. In the present studies glucose exit from the tubular lumen is found to be almost completely blocked by cumulative systemic phlorizin doses as low as 200 μg/Kg wt. Under these conditions simultaneously obtained renal vein outflow patterns indicate that glucose has a greater distribution volume than creatinine. This excess volume may reflect glucose penetration of the antiluminal surface of the proximal tubule. The penetration shows certain characteristics of "active transport": (i)stereospecificity (L-glucose-C^{14} has the same renal vein outflow pattern as creatinine); (ii) competitive inhibition (with high doses of phlorizin, of the order of 1000 x the dose necessary to block the luminal surface, the renal vein patterns of D-glucose-C^{14} and creatinine coincide). No evidence was obtained for the existence of a pathway for glucose across the tubule cells from peritubular fluid to urine. We propose that the transport mechanism at the antiluminal surface is an integral part of the process of glucose transfer from urine to blood.

FACTORS AFFECTING SURVIVAL AND DEVELOPMENT OF NIPPOSTRONGYLUS BRASILIENSIS IN INFECTED RATS. J.O.Simaren* and J.Fabianek, Department of Life Sciences,New-York Institute of Technology, New-York,N.Y.10023.

Four groups of 6-week-old rats were infected with Nippostrongylus larvae subcutaneously,intravenously,intraperitoneally and orally. The eggs were counted daily in feces from 5th to 14th day after infection and the number of adult worms was determined in intestines of rats sacrificed on the tenth day. The number of egg production relative to the various routes of infection were in good agreement with the corresponding number of adult worms found in intestine. The routes of infection did not affect the size of the adult parasites. When induced per os and into the peritoneum,only 15 percent and 50 percent respectively of larvae developed into adult worms. Fifty five percent and seventy percent larvae developed into adult worms when induced intravenously and subcutaneously. Enzymes,toxic compounds or a possible defficiency of oxygen in gastrointestinal tract,intraperitoneal cavity and blood vessels appear to be limiting factors for survival and development of larvae into adulthood.

ROLE OF pH AND ALPHA RECEPTORS ON THE HEMODYNAMIC RESPONSE OF THE DOG HIND LIMB TO ACIDOSIS. D.H. SIMMONS. UCLA School of Medicine, Los Angeles, California.

Previous studies showed that increasingly severe respiratory acidosis causes progressive vasoconstriction in muscle and vasodilatation in skin and paw of the femoral artery circulation of the anesthetized dog. In this study during respiratory acidosis, conductance of the femoral circulation decreased approximately 15% of control values at extreme pH's in the region of 6.85 while during metabolic acidosis it decreased approximately 40%, suggesting the possibility that a local dilating effect of hypercapnia may partially obscure a constrictor response to acidosis. The partitioning of blood flow and conductance to muscle, skin, and paw in the femoral circulation was essentially the same during both types of acidosis as determined by a modification of the K^{42} method of Sapirstein. Muscle conductance was markedly decreased in both cases, while skin and paw conductance increased during respiratory acidosis and was constant or increased during metabolic acidosis. Injection of dibenzyline locally into the femoral circulation resulted in approximately doubling flow and conductance of the total femoral circulation and the circulations to individual tissues during the most severe acidosis, but had only minor or no effect during moderate or mild acidosis. It also had essentially no effect on the distribution of flow and conductance to the three tissues. These results suggest that: 1) there is both pH- and P_{CO_2}-dependence of vasomotion in muscle, skin, and paw in the femoral circulation; 2) alpha-adrenergic receptor stimulation causes decreased conductance only during extreme decreases in pH and this vasoconstriction may occur in large vessels.

THE CARDIAC SINUS RESPONSE IN HYPOTHERMIA. S.H. Sinclair,* Kenneth M. Kent,* W.E. Goetter,* and E.C.Peirce II. Depts. of Surgery and Physiology, Emory University School of Medicine, Atlanta, Georgia.

The cardiac function of large non-hibernating mammals becomes unpredictable in deep hypothermia as cooling changes the balance of the various neural, hormonal, and autoregulatory mechanisms of the heart. To investigate the neural control, studies were made on closed-chest dogs uniformly cooled to average body temperatures, ranging from 25 to 15°C. Uniform cooling was accomplished with a partial veno-arterial bypass circuit including a membrane lung and a heat exchanger, combined with a 10°C water spray for surface cooling. Aortic pressure (AP) and carotid sinus pressure (CSP) were controlled independently by means of separate pressure-controlled servo pumps. Aortic flow was determined using implanted ascending aortic flow probes. Left ventricular volumes were estimated by a thermal dilution technique. Myocardial function was assessed by ventricular function curves (stroke work vs end diastolic volume) at a constant AP. The carotid sinus response including the control of cardiac rate and contractile force and the control of systemic arteriolar resistance was present at 25°C however, the sensitivity of this negative feedback control mechanism was reduced at this temperature when compared to 37°C. Increases in the CSP caused a decrease in heart rate and vasodilation. Vagotomy abolished the decrease in heart rate which accompanied an increase in CSP, but the vasodilation persisted. The depression of the carotid sinus response at low temperatures demonstrates the reduction of neural control of the hypothermic heart.

ABOLITION OF SYMPATHETIC VASOCONSTRICTION IN DOG SKELETAL MUSCLE: ROLE OF K^+ AND REDUCED O_2 TENSION. N.S. Skinner, Jr. U. Tex. Southwestern Medical School, Dallas, Texas.

The effects of O_2 deficient blood of different K^+ concentrations on vascular resistance during lumbar sympathetic chain stimulation were studied in the isolated, perfused gracilis muscle of the dog. Reservoirs containing blood of identical reduced O_2 tension (pO_2 9-25 mm Hg), pH and hematocrit were used. One contained K^+ in a concentration of 2.0-2.5 mEq/L while in the other the concentration of K^+ was 6.0-8.0 mEq/L. Blood of normal O_2 content and K^+ concentration was used to obtain control vascular resistance values before perfusion of O_2 deficient blood. In all experiments (14 animals) vascular resistance was increased 30 to 100% by lumbar sympathetic stimulation. In each experiment resistance to blood flow fell less during perfusion with low O_2, low K^+ blood than during perfusion with low O_2, high K^+ blood even though venous pO_2 was reduced to the same degree. In a second type of experiment (4 animals) the gracilis muscle was perfused with hypoxic blood before initiation of sympathetic stimulation. In these, a given intensity of sympathetic stimulation produced greater vasoconstriction during perfusion with low O_2, low K^+ blood than during perfusion with low O_2, high K^+ blood. These data suggest that O_2 deficiency and the concentration of K^+ may function importantly in the established abolition of sympathetic vasoconstriction during contraction of skeletal muscle. (These studies were supported by USPHS grant HE 10614 and a grant from the Dallas Heart Association.)

FEEDING RESPONSES TO DECREASED GLUCOSE UTILIZATION IN MONKEYS.
G. P. Smith* (intr. by A.N. Epstein). Dept. of Physiology, Univ. of Pennsylvania, Philadelphia, Pa.

Although injections of the glucose analogue, 2-deoxy-D-glucose (2-DG), into human subjects are known to produce decreased glucose utilization, hyperglycemia and hunger sensations (Landau et al, J. Nat. Cancer Inst. 21:485, 1958), food intake after 2-DG has not been studied in humans or other animals. Food intake was measured hourly in 3 male, rhesus monkeys (Macaca mulatta) in the 2 hours following the intravenous injection of 2-DG (300 mg/kg). All 3 monkeys ate more plain monkey pellets in the first hour (2-DG: 61.5 ± 5.5 g, n=9; Control: 25.6 ± 3.0 g, n=14; $p < 0.005$). The response was reproducible and usually ended within 2 hours after the injection. These data are strong evidence that decreased glucose utilization, not low blood sugar, drives the monkey to eat more. This result is consistent with the idea that decreased glucose utilization is an important short-term factor in the normal control of food intake. (Supported by USPHS NB 06073-02)

A SHEET-FLOW CONCEPT OF THE PULMONARY ALVEOLAR MICROCIRCULATION.
S.S. Sobin, Dept. Physiology, Univ. Southern Calif., Los Angeles, and Y.C. Fung,* AMES Dept., Univ. Calif. San Diego, La Jolla, Calif.

Structurally, the microvasculature of the alveolar wall may be described as 2 membranes separated and interconnected by a number of regularly spaced posts. Correspondingly, blood flow may be described as sheet-flow with regularly spaced obstructions. Compared with the classical concept of the alveolar capillary system as a network, this terminology offers a more realistic description of blood flow. Histological materials were prepared from the cat lung perfused in situ from the pulmonary artery with an appropriate silicone elastomer by methods previously described (Sobin, et al., 1966). Photomicrographs were made of optical sections and the projected image analyzed. In each plane section the vascular and non-vascular spaces were demarcated and the respective areas determined by planimetry. The results are expressed as a solidity-ratio of the vascular to total space of the alveolar wall, which quantitatively describes the proposed geometric model. In addition, other geometric characteristics such as curvature of the alveolar wall are determined. The sheet-flow description of the alveolar microcirculation provides a new approach to lung mechanics and dissociates analysis of blood flow resistance from the Poiseuille's formula for the cylinder. With a more accurate description of geometry a more realistic boundary value problem is formulated for the blood flow in the alveolus which is attacked both mathematically and by model experiment.

METABOLISM OF GLUCOSE THROUGHOUT THE REPRODUCTIVE CYCLE OF THE GOAT. Donna Sooby and Robert W. Phillips (intr. by William J. Tietz). Colorado State University, Fort Collins, Colorado

The degree of participation by the pentose phosphate pathway in glucose metabolism in ruminants was investigated using glucose-1-^{14}C and glucose-6-^{14}C. Fourteen experiments were conducted on female goats in the normal, the pregnant and the lactating states. In each case approximately 150 μc of the radioactive glucose was administered intravenously by single injection technique. The rate and extent of conversion of carbon atoms 1 and 6 to respiratory CO_2 was determined. In the normal goat there was no significant difference in either the rate or the extent of conversion of the two labels. The mid or late pregnant animal showed a slightly greater conversion of carbon 1 than carbon 6. However, in the lactating goat both the rate and the extent of glucose-1-^{14}C conversion to respiratory CO_2 was much greater. The $^{14}CO_2$ production from carbon atom 1 appeared in less than one-third of the time and was 3 times higher than the peak from carbon atom 6. This suggests that the pentose phosphate pathway is inactive in the normal state, only slightly active during pregnancy and highly active during lactation. The total transfer of glucose carbon to CO_2 was greatest in the non-pregnant animal, decreased somewhat in pregnancy and declined sharply in lactation, indicating that the demand for non-oxidative glucose utilization is greatly enhanced by the carbohydrate demands of lactation.

Respiratory Insensitivity to Hypoxia Persisting After Correction of Fallot's Tetralogy S.C. Sørensen* and J.W. Severinghaus. Univ. of California Medical Center, Cardiovascular Research Institute, San Francisco, California.

We have previously reported (Fed. Proc. 26:665, 1967) that high altitude natives have a lower respiratory response to hypoxia than sea level natives. High altitude natives still have a low response to hypoxia after staying at sea level for several years. We were not able to detect any decrease in hypoxia sensitivity at altitude in sea level natives who had been exposed to hypoxia for years during their adult life. This study was undertaken to determine the respiratory response to hypoxia in a group of subjects born with Fallot's tetralogy who, therefore, had been exposed to a low Pao_2 for the first years of life. Five subjects, 15 to 31 years of age, were examined. Four of the subjects had palliative anastomotic operations performed in the first years of life. All five subjects had the cardiac malformation corrected, 1 to 7 years, before this study. Pao_2 breathing air was 80.6±13.8 (SD) mm Hg at the time of the study (P_B = 750 mm Hg). The respiratory response to CO_2 was determined at two levels of oxygenation: Pao_2 = 200 mm Hg and Pao_2 = 40 mm Hg. The respiratory response to a reduction of arterial Po_2 from 200 to 40 mm Hg was computed in two ways. (1) At their normal $Paco_2$, hypoxia increased ventilation 0.3±2.0 (SD) L/min/M^2, compared to the average response of 9.7±7.0 (SD) L/min/M^2 in normal man at sea level. (2) Hypoxia increased the slope of the CO_2 response curve from 1.4 to 1.5 L/min/M^2/mm Hg Pco_2, a 7% increase, which compares with a 114% increase in our normal subjects. We conclude that the respiratory sensitivity to hypoxia is irreversibly decreased by prolonged hypoxia during childhood. Since the response of these subjects is similar to high altitude natives who have moved to sea level, there is no need to invoke a genetic factor in the response of the Peruvian Andean native. (Research supported in part by USPHS HE 06285).

MYOCARDIAL CONTRACTILITY IN HYPERTROPHY AND HEART FAILURE. James F. Spann, Jr.*, James W. Covell†, Dwain L. Eckberg*, Edmund H. Sonnenblick, John Ross, Jr., and Eugene Braunwald. Cardiology Branch, National Heart Institute, Bethesda, Maryland.

The contractility of intact right ventricles (RV) and isolated RV papillary muscles of seven cats with chronic RV hypertrophy and heart failure (CHF) due to pulmonary artery constriction were compared with those of ten normal (N) cats. In CHF, peak isovolumic pressure increased from 64 ± 3 to 111 ± 16 mm Hg (74%), RV end-diastolic pressure from 3.0 ± 0.5 to 13.3 cm. H_2O, RV end-diastolic volume from 1.0 ± 0.1 to 1.9 ± 0.1 ml/kg (90%) and RV weight from 0.5 ± 0.1 to 1.2 ± 0.1 g/kg (140%). Maximum contractile element velocity (V_{max}) of intact ventricles was reduced from 2.7 ± 0.1 (N) to 1.5 ± 0.1 (CHF) muscle lengths/sec ($p < .001$) while isometric tension was not altered strikingly. In papillary muscles isolated from these CHF hearts V_{max} was similarly decreased from 0.95 ± 0.08 to 0.32 ± 0.08 muscle lengths/sec and isometric tension at the apex of the length tension curve was also reduced, from 8.2 ± 1.4 to 3.1 ± 0.6 g/mm^2. Thus in CHF, both force and velocity were depressed in the isolated muscle. In the failing ventricle the increased fiber length maintained the force developed per muscle unit, while the reduced ventricular V_{max}, a property which is unchanged by muscle length, accurately reflected the depressed myocardial contractile state that was evident in the papillary muscles from these hearts. These findings indicate that the intrinsic rate of interaction of contractile sites is reduced in the intact hypertrophied and failing heart and demonstrate that in the intact heart augmentation of end-diastolic volume and increased muscle mass compensate for this basic contractile defect, thus maintaining total ventricular force and pressure.

HUMAN VISUAL EVOKED RESPONSE AND FREQUENCY DENSITY SPECTRA. Louise B. Speck, Natl. Inst. of Mental Health, Chevy Chase, Md. and Dorothy S. Dobbs,* St. Elizabeths Hos., Washington, D.C.

Techniques for recording the visual evoked response (VER), standard error, and frequency density spectra were developed for use on a LINC computer. Relationships between human VER and spectra variables and their interrelationships were investigated. Comparison of energy contents of occipital and temporal recordings from the same subject showed that delta, theta, and $fast_2$ activity was greater in the temporal area, while alpha and $fast_1$ was greater in the occipital area. When the autospectrograms were compared under resting conditions and during stimulation, the total energy contents remained constant but were redistributed. Latency, amplitude, and recovery variables were calculated for three VER deflections. Amplitudes of the early components were associated; the late component was independent. Latencies showed correlation; none was associated with amplitudes. Of 160 intercorrelations of VER with spectra variables, seven were significant at $P < .01$ level; three indicated a relationship of alpha with latency. The latency of the vertex wave was found to be twice alpha period. Ringing was never seen without alpha. A linear relationship with period of ringing was seen. No relationship of recovery function was found with any frequency. Alpha period was the only frequency variable significantly associated with any VER variable.

COLOR CODED COMPONENTS OF THE INTRARETINAL ACTION POTENTIAL. H. Spekreijse*, H. G. Wagner, M. L. Wolbarsht, and D. K. Heffner*. Naval Medical Research Institute, Bethesda, Md.

The intraretinal action potential is an electroretinogram (ERG) from within the retina (T. Tomita, Jap. J. Physiol. 1-110, 1950: also designated "Local Electroretinogram or LERG", by K. Brown, Jap. J. Ophthal., 10, suppl. 130, 1966). In the isolated goldfish retina, intraretinal electrodes record an intraretinal action potential which can be shown to be composed of two components, a slow potential and oscillations, both generated by the light stimulus. The frequency of the oscillations is approximately fifteen per second. In some recording locations the spectral sensitivity of the two components is not the same. One component (the slow process) had the same action spectrum as the green process of the ganglion cell response (Wagner, et al, J. Gen. Physiol., 43, suppl. 2, 45, 1960). The action spectrum of the oscillatory process was the same as that of the red ganglion cell process. The sensitivity of either process could be depressed relative to the other by appropriate chromatic adaptation. This demonstrated the independence of the two components of this LERG. Oscillatory phenomena have also been seen in the ERG of the cephalopod, birds, and humans. The hypothesis that the oscillations may result from activity fed back from the brain is not tenable, at least in our preparation, since the retina was not connected to the brain. (From the Bureau of Medicine and Surgery, Navy Department, Research Task MR005.04-0013.)

EFFECT OF STABLE CALCIUM ON Sr^{90} ABSORPTION IN MAN. Herta Spencer, Joseph Samachson*, Edward P. Hardy, Jr.*, and Joseph Rivera*. Metabolic Section, Veterans Administration Hospital, Hines, Illinois and Health and Safety Laboratories, U.S. Atomic Energy Commission, New York City.

In order to investigate whether stable calcium decreases the absorption of Sr^{90}, balances of Sr^{90} and of calcium were performed under constant dietary conditions during low and high calcium intake. The average low calcium intake was 213 mg/day, the average high calcium intake was 1718 mg/day. The high calcium intake was attained by adding calcium gluconate tablets to the constant low calcium diet, thereby keeping the Sr^{90} intake similar during the low and high calcium intake, 4.6 and 5.7 pCi/day, respectively. The average Sr^{90} balance was +0.01 pCi/day during low calcium intake and was slightly more negative during high calcium intake, -0.36 pCi/day. Although the net absorption of Sr^{90} during the addition of calcium to the diet was lower, on the average 6.3%, than during low calcium intake, 12.3%, these differences were not significant. There was no correlation between Sr^{90} and calcium balances, while there was a correlation between the urinary excretion of Sr^{90} and of calcium and between the urinary excretion of Sr^{90} and Sr^{90} intake. The Sr^{90}/Ca ratios of urine were more variable than the Sr^{90}/Ca ratios of stool during the intake of the low and high calcium intake. The Sr^{90}/Ca ratios of stool were similar to the Sr^{90}/Ca ratios of the diet during the intake of either calcium level. (This research was supported by Contract AT(11-1)-1231-35 from the U.S. Atomic Energy Commission.)

TRANSPORT OF A SUBSTRATE BY TWO OR MORE INTESTINAL SYSTEMS: A POSSIBLE EVOLUTIONARY REMNANT. Richard P. Spencer. Department of Radiology, Yale University School of Medicine, New Haven, Connecticut.

While most materials enter the small gut wall by a single mechanism, there is evidence that some are transported by 2 or more systems. If the systems are not cross-coupled, total entry or velocity can be treated as the linear sum of the individual components. When 2 transport systems are operative on a substrate, possibilities are: 2 passive systems (urea passage across the gut by diffusion and convection), one passive system and one active system (pyrimidine movement in the insect small gut, and amino acid transport in Ehrlich ascites cells), or 2 active systems (basic amino acid transport by the kidney). Equations for each type of dual transport have been written for processing by analogue and digital computers. The presence of multiple systems for transporting a substrate may represent an evolutionary remnant or diversification (such as isoenzymes). This is particularly true when 2 active transport systems are present. Each is likely under genetic control, and may be absent in mutants. If both of the active systems can be described by Michaelis-Menten formulations, they cannot kinetically be readily separated if $K_1 = K_2$ (that is, if the Michaelis constants are the same). If $K_1 \neq K_2$, a distinct bend appears in Lineweaver-Burk plots. (Supported by USPHS Grants CA6519 and AM09429).

THROMBOSIS ON METAL SURFACES-RELATIONSHIP TO POSITION OF METAL IN THE ELECTROMOTIVE SERIES+ AND METAL BLOOD INTERFACE POTENTIAL. S.Srinivasan P.S.Chopra*, T.Lucas* (intr.by P.N.Sawyer)
Electrochemical and Biophysical Laboratories of the Vascular Surgical Services, Department of Surgery and Surgical Research,State University of New York, Downstate Medical Center,Brooklyn

Recent interest in the electrochemical nature of thrombosis (Biophysical Mechanisms in Intravascular Thrombosis,P.N. Sawyer,Ed.,Appelton, Century,Crofts 1965) prompted a study of rate of thrombus deposition on metal wires(electrodes) inserted through side branches into the carotid and femoral arteries of mongrel dogs. Mg,Al,Cd,Ni,Cu,Au, and Pt which cover a wide range in the electromotive series were chosen for the present investigation. Four electrodes of the same metal were inserted through side branches into both carotid and femoral arteries in healthy anaesthetised mongrel dogs for 30-40 minute periods. Care was taken to prevent injury to the intimal surface. The spontaneous potential of each of these electrodes in contact with flowing blood was measured.At termination, the vessels were clamped above and below the electrodes. The dogs were sacrificed, after injection of formalin into the vessels for fixation of thrombus deposits. The vessels were slit open and the electrodes examined. The results were striking. Electrodes of metals establishing a negative interfacial potential $<$ 0.mv/NHE (Mg,Al,Cd) were antithrombotic, whereas metals with a positively charge surface $>$ 0.0 mv/NHE (Cu,Ni,Au,Pt) were thrombotic. These findings are of considerable fundamental importance and provide scientific assistance in the search for suitable non-thrombogenic surfaces to incorporate into various artificial internal organs.

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ARTERIAL AND VENOUS RESPONSES DURING VASOVAGAL SYNCOPE. M.Stampfer, S.F.Epstein, G.D. Beiser (intr. by E. Braunwald). NIH, Bethesda, Md.

The circulatory changes which cause vasovagal syncope are not thoroughly understood. Several studies have shown that the fall in mean arterial pressure (AP) that occurs is associated with a decrease in cardiac output (CO), and it has been suggested that withdrawal of sympathetic tone to the veins, by promoting peripheral pooling of blood, contributes significantly to the decrease in CO. Conflicting results have been reported concerning changes in CO, forearm blood flow (FBF), and forearm vascular resistance (FVR), and no measurements of venous tone (VT) during syncope have been reported. In the course of other studies on the circulatory effects of lower body negative pressure and 80^{o} head-up tilt, vasovagal reactions occurred in 10 subjects. Heart rate (HR), central venous pressure (CVP), AP, FBF, FVR, and forearm VT were measured. The typical vasovagal reaction could be divided into 2 phases. A gradual fall in AP and occasionally HR signified the onset of Phase 1, during which FVR did not change significantly. The duration of Phase 1 was highly variable. The onset of Phase 2 was denoted by an abrupt fall in AP and HR and a decrease of 62% in FVR, from 36 to 14 mm Hg/ml/100 g/min. However, in none of the subjects did forearm or hand VT decrease. Venodilation probably did not occur in other vascular beds, since CVP did not change prior to or during the onset of the reaction. It is concluded that there are 2 stages in the development of vasovagal syncope. Initially AP and occasionally HR fall gradually, followed by a precipitous reduction in sympathetic tone, reflected by the fall in FVR, and accompanied by marked hypotension and bradycardia. The venous bed of the limbs does not appear to participate in these changes. It is also probable that the conflicting results obtained previously may be explained in part by the lack of recognition of these 2 distinct phases and the omission of observations during Phase 2.

CHANGES IN HUMAN BODY COMPOSITION AND OXYGEN CONSUMPTION WITH AGE. J. M. Steele, G. T. Lesser* and S. Deutsch*. New York Univ. Research Service, Goldwater Memorial Hospital, Welfare Island, New York, N. Y.

Independent measurement of total body fat (by uptake of inert gas) in 45 human subjects aged 16 to 90 has permitted study of the composition of and changes in the fat-free body (FFB = body weight - body fat) during aging. Body water (TBW = vol. of dilution of tritiated water) remains a constant proportion (71%) of the FFB. However, the proportion of "extracellular" water (ECW = vol. of dilution of $Na_2S^{35}O_4$) is increased, and that of intracellular water (ICW = TBW - ECW) decreased. With the evidence that cell hydration remains constant, these changes indicate a loss of cell mass with age. In older subjects, basal oxygen consumption was decreased with respect to S.A., remained constant with respect to TBW or FFB mass, but rose with respect to intracellular water. The long-held concept that oxygen consumption of tissues diminishes with age is not consistent with these observations. There is evidence that, with aging, cell mass is lost primarily in muscle, and only negligibly in other tissues. The present observations on oxygen consumption can be quantitatively explained by these changes in body composition, suggesting that basal O_2 uptake of remaining cells is unchanged.

INCREASED RATE OF CATECHOLAMINE SYNTHESIS IN RATS DURING HYPERCAPNIA. Odd Steinsland*, James Papayoanou*, Mariagnes Verosky* and Gabriel G. Nahas. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, N.Y.

During hypercapnic acidosis there is a significant rise in circulating plasma catecholamines which can be attributed to an increased release from peripheral nerve endings and adrenal gland. This increase was not accompanied in the rat by significant depletion of catecholamine stores. In a group of 20 rats exposed to 20% CO_2, 25% O_2, balance N_2, for periods of up to 5 hours, there were no significant changes in norepinephrine (NE) content of the heart and epinephrine (E) content of the adrenal gland as compared to a control group breathing air. NE in heart increased by 4.5% and E in adrenal gland decreased by 1.3%. Another group of rats was given intraperitoneally 300 mg/kg of alpha-methyl-para-tyrosine (a-MT) in 3 divided dosages before and during a similar period of hypercapnia. They presented a 35.8% decrease in myocardial NE content and a 38.6% decrease in adrenal E content. Rats treated with a-MT and breathing room air did not present significant changes in catecholamine content of heart or adrenal gland. During hypercapnia, inhibition of catecholamine synthesis results in significant depletion of catecholamine stores. These results indicate that, since catecholamine stores remain normal during hypercapnic acidosis, an increased rate of catecholamine synthesis should also occur in hypercapnia. (This work was supported, in part, by Army Contract DA-49-193MD-2265 and N.I.H. Grant GM-09069-05).

RELATIONSHIP BETWEEN STIMULUS STRENGTH, LENGTH AND PULMONARY ARTERIAL (PA) ISOMETRIC ACTIVE TETANIC TENSION (AP) DEVELOPMENT. N. L. Stephens, J. L. Meyers (intr. by R. M. Cherniack). Departments of Physiology and Medicine, University of Manitoba, Winnipeg, Canada.

Previously we reported (Physiologist 9:296, 1966) that with electrical stimulation at a given PA length, AP first increased curvilinearly and then achieved a maximum steady state value (AP_{max}). AP_{max} increased with stimulating voltage and qualitatively resembled striated muscle. The time taken to achieve AP_{max}--(tAP_{max}), was unaffected by changes in voltage. While the maximum rate of AP development, (dP/dt_{max}), increased with increasing voltage the time taken to reach dP/dt_{max}--($t_{dP/dt_{max}}$), was constant. We have now assessed the effect of muscle length on these parameters using supramaximal voltage stimulation. The length-tension curves resembled those of other smooth muscle preparations and revealed a stretched length (L_{max}) at which maximum AP_{max} developed. tAP_{max} was the same at all lengths. dP/dt_{max} increased with stretched length up to L_{max} and then decreased. $t_{dP/dt_{max}}$ was the same at all lengths. Thus stimulating voltage and muscle length affect these parameters in identical ways. It is tentatively proposed that the influences of stimulus strength and muscle length in releasing energy for AP development in vascular smooth muscle are similar.

NEW APPROACH TO RETINAL OSCILLATORY POTENTIALS IN MAN AND ANIMALS. H. Lee Stewart and William W. Dawson. College of Med., Univ. Fla., Gainesville, Fla.

Electrical oscillations reported in research on animals may be selectively recorded from the human cornea if the customary ERG is rejected by active passband filtering. Species differences in the response are distinct. Latency ranged from 6 mscc in mangabey to 55 mscc in bullfrog. Cat, chicken, rabbit and man gave intermediate values. Response amplitude and stimulus intensity vary directly to a point where high intensity produces increasing wave complexity. Control procedures which include isolation of the eye from the ocular musculature and retrobulbar anesethesia suggest that the response is retinal in origin. In agreement with direct recordings, the results indicate that electrical events may be recorded which occur before the B wave and in some cases before the A wave. Supported by Department of Army contract DADA17-67-C-7118 and aided by UHPHS grant NB-06654.

MUSCLE STRENGTH AND ELECTRICITY ACTIVITY, HEART RATE AND ENERGY COST DURING ISOMETRIC CONTRACTIONS IN DISABLED AND NON-DISABLED. Hans Stoboy, Frieda Trainor, Bryan Wilson-Rich, Michael Dacso (intr. by X. Sandow), New York University Medical Center, Dept. Rehabilitation Medicine, Goldwater Memorial Hospital.

The electrical activity of muscle is lineraly correlated to strength (Lippold; Sommer; Bergstroem). With increasing maximal strength during training, the same load can be held though the electrical activity is less (Stoboy, Friedebold and Nuessgen; Stoboy und Duentsch; Fischer). Ergometric investigations have shown that heart rate and oxygen consumption depend on the physical fitness (Balke; Hallman; Reindell; Mellerowicz). The aim of the investigation was to determine the degree of disabled subjects who are wheelchair bound. The following values were measured or calculated: strength of the m. biceps femoris, the integrated electrical activity, heart rate, O_2 consumption, CO_2 output and energy expenditure. It has been shown that the disabled subjects who propel a wheelchair several miles daily have lower values for the measured parameters than the nondisabled. From a comparison of the subjects, it is concluded that the disabled individual is physically well adapted to his disability.

MICROPERFUSION STUDIES OF RENAL TUBULAR REABSORPTION OF 3-O-METHYL-D-GLUCOSE, D-FRUCTOSE AND D-GLUCOSE IN THE RAT. Hilmar Stolte*, J. B. Van Liew* and John W. Boylan. Departments of Physiology and Medicine, State University of New York at Buffalo.

In single perfused surface segments of proximal tubules of the rat kidney in vivo we measured the rate of reabsorption of 3-O-methyl-D-glucose (3MG), D-fructose and D-glucose. Perfusion fluid, isosmotic Ringer's solution containing 4.5 or 18 mM/L of the C-14 labeled sugar and 100 mg% tritiated inulin, was delivered at 20 x 10^{-6} ml min^{-1}. Comparative reabsorptive rates, given as percentage of load per mm perfused tubule, ranged from 17-32% for D-glucose and 5-15% for 3MG. There was no reabsorption of D-fructose. Clearance experiments in the intact rat confirm reabsorption of 3MG at approximately 50% the rate of D-glucose. Results with D-glucose and 3MG are compatible with the hypothesis that the process of sugar reabsorption may be accelerated by metabolic reduction of its intracellular concentration (J. Gen. Physiol. 50: 113, 1966). The data for fructose confirm that metabolic utilization of a sugar does not necessarily imply its reabsorption. Secretion of 3MG, reported in dog kidney (Proc. Soc. Exp. Biol. and Med. 124: 20, 1967), could not be demonstrated in the rat. (Supported by Buswell Fellowship and NIH Grant AM-10779-01.)

EFFECTS OF ESTRADIOL BENZOATE (EB) ON CORPORA LUTEA IN RATS BEARING PITUITARY AUTOGRAFTS. S. J. Stolzenberg*, R. G. Eggert* and W. H. Linkenheimer. American Cyanamid Company, Agricultural Division, Princeton, New Jersey.

Female rats received pituitary autotransplants beneath the kidney capsule at 11 to 12 weeks of age. Subcutaneous injections of EB were started 30 to 40 days following surgery in the first 3 experiments. In Experiments 1 and 2, Series 1 injections consisted of 50, 50 and 25 mcg of EB given subcutaneously on days 0, 3 and 5. Series 2 injections were the same as series 1 but given on days 16, 19 and 21. Pituitary grafts were removed from half of the rats on day 15 in Experiment 1. Ovarian weights were obtained on day 28. In Experiment 3, the dose of EB was raised to 100 mcg per injection giving a total of 300 mcg for each series. In Experiment 4, subcutaneous injections of EB were started 5 to 7 days following pituitary autotransplant. Rats were injected daily for 5, 10, 20, 40 and 80 days, with autopsies following 4 or 5 days after the last injection. The immediate effect of EB injections into rats bearing pituitary autografts was a significant ($P < 0.01$) increase in ovarian weight. Long term treatment with EB (>40 days) caused a significant ($P < 0.05$) decrease in ovarian weight. Short term treatment followed by a 23 or 35 day period of no treatment gave an even greater decrease in ovarian weight ($P < 0.01$). Hypophysectomized rats showed no effect on ovarian weights with similar EB treatments, indicating the importance of the pituitary in this response. Removal of the autotransplanted pituitary 10 days after the first series of EB was completed, however, had no apparent effect on subsequent regression of the corpora lutea.

MUSCLE ACTION POTENTIALS AND CONTRACTIONS DURING FATIGUE, STRESS AND CHLORPROMAZINE ADMINISTRATION. F. L. Strand, V. Lange* and Hans Stoboy*
Biology Dept. New York University and Goldwater Memorial Hospital.

The influence of hormones on the peripheral nervous system has been demonstrated mainly in isolated systems. These experiments correlate electrical and mechanical changes with hormonal variations in the intact rat. Only the Achilles tendon is freed to permit recording of muscle contractions. The sciatic nerve is stimulated without being severed (freq.5/sec;duration 0.1msec;slightly supermaximal strength). Simultaneous recordings of gastrocnemius contractions and APs were made on 35 rats during 30 min stimulation. The effects of rest,post rest stimulation, cold-stress (4°C for 4 hr) and cold-stress preceded by chlorpromazine (50mg/kg) 1 hr prior to cold, were investigated. In normal rats there is a sharp decline in the amplitude of contraction and of the AP during the first 5 min of stimulation. Contraction decreased 50%, APs decreased 45% in this time, to fall only another 10% each during the next 20 min of stimulation. 10 min rest had little effect on contraction height but AP amplitude recovered to 70% initial values. Neither stress nor chlorpromazine+ stress affected contraction height significantly but both diminished the signs of early AP fatigue (stress causing a 30% decrease and chlorpromazine+stress a 40% decrease vs the normal fall of 45%). In all groups a marked treppe was seen in the first min of stimulation but there was no corresponding AP peak. These results indicate that rapid stimulation decreased the amplitude of muscle APs and contractions and that changes in hormonal environment, presumably due to alterations in ACTH levels, affect mainly the electrical parameters in the intact animal. (Supported by the N.I.H. Biomedical Sciences Support Grant to New York University).

MODIFICATION OF MONOSYNAPTIC REFLEX BY VISUAL STIMULUS. Wilford P. Stratten* and Charles D. Barnes. Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana.

Visual conditioning of a monosynaptic reflex recorded at L7 has been demonstrated in cats lightly anesthetized with chloralose (75 mg./kg.). The conditioning stimulus, consisting of a 100 msec. light pulse, produces a modification of the monosynaptic reflex which though quantitatively different from animal to animal is qualitatively stable. This pattern is first a period of facilitation lasting about 25 msec. with a maximum 92 msec. after the onset of the light, followed by 70 msec. of inhibition with its maximum at 140 msec. The effect is equal for ipsilateral or contralateral light stimulus.
(Supported in part by USPHS research grant NB 05949)

THE EFFECTS OF FECAL BULK ON THYROID FUNCTION IN COLD-EXPOSED RATS. James A. Straw (intr. by Fred B. Benjamin) . George Washington Univ. Dept. of Pharmacology, Washington, D. C.

It has been postulated (Intoccia and Van Middlesworth, Endocrinol. 64: 462, 1959) that the enhanced thyroid function in cold-exposed rats is caused by the increased fecal loss of thyroxine which accompanies the greater food consumption and fecal bulk. This hypothesis was tested by feeding control and cold-exposed rats a low-bulk diet and supplementing the diet of the control rats with sufficient non-nutritive bulk (purified cellulose) to produce a daily fecal weight equal to that of the cold-exposed group. After 30 days of cold exposure (2 ± 2°C) the rats were injected with carrier-free NaI^{131}. Fecal and urinary losses of I^{131} were the same in both groups. However, uptakes by the thyroid glands as well as release rates of I^{131} from the glands were greater in the cold-exposed group. The increases in these indices of thyroid function were of the same magnitude as those seen in comparably treated rats fed a normal diet during cold exposure. It would thus appear that increased fecal loss of thyroxine does not make a significant contribution to the hyperactivity of the thyroid gland during cold acclimation. (Supported by USPHS grant 1-S0-1-FR-5359-04-5)

TETRODOTOXIN REVEALS TWO STABLE STATES OF THE RESTING POTENTIAL IN A NEURON GENERATING ENDOGENOUS BURSTS. Felix Strumwasser. California Institute of Technology, Pasadena, California.

Previous work from this laboratory has shown that cell 3 (PB) of the isolated parieto-visceral ganglion of Aplysia californica produces bursts of impulses followed by a period of relative hyperpolarization (post-burst hyperpolarization, POBH) through an endogenous mechanism. It had been postulated, from Cl injection experiments, that the POBH was a chloride potential triggered by some products accumulating during the burst of spikes. In the present experiments, tetrodotoxin (TTX) was used to block the sodium channel mediating spike electrogenesis (Narahashi et al.,1964). Exposure of PB, free of overlying connective tissue,to TTX ($<10^{-5}$ M) results in block of impulses but not necessarily the slow oscillations giving rise to the prior bursting rhythm. Such oscillations generally move from -65 to -30 mV. If oscillations stop, the membrane is at rest at one of these two levels. When at -30 mV (upper state a small hyperpolarizing current will reset the membrane potential to -65 mV (lower state) where it will stay after current termination. When in the lower state, a small depolarizing current will set the membrane to -30 mV where it also remains after current ceases. A depolarization can also reset the membrane from the upper to the lower state but only at the termination of current flow. Since replacement of chloride by acetate in the bathing fluid abolishes the two stable state system, it is clear that chloride participates in the mechanism. The normal burst generating mechanism involves a shift from the lower-state to the upper state where impulses occur. Probably as K ions build up in the immediate extracellular space, during the burst of impulses, a Cl channel is opened or/and a K channel is closed resulting in the termination of a burst due to the hyperpolarizing shift toward a chloride equilibrium. [Supported by U.S. Air Force contract AF 49(638-1447) and NIH grant NB 07071.]

EFFECTS OF ACTINOMYCIN AND PUROMYCIN ON THE INDUCTION OF L-GULONOLACTONE HYDROLASE BY SOMATOTROPHIC HORMONE. Don W. Stubbs and Dale B. Haufrect (intr. by R. D. Baker). The University of Texas Medical Branch, Galveston, Texas 77550.

We have previously shown somatotrophic hormone (STH) to influence biosynthesis of ascorbic acid in male rats by its effect on gulonolactone hydrolase (GLH)(Fed. Proc. 22:422). In the present study the earliest significant increase in GLH activity in both male and female hypophysectomized rats following daily injections of STH (3mg/kg) was 3 days. Actinomycin D in a total dose of 750µg/kg over five days failed to inhibit induction, whereas puromycin in a total dose of 90mg/kg as 3 injections on the third day of STH administration effectively did so. This suggests that STH may act at the level of enzyme synthesis (translation) rather than by increasing mRNA (transcription). Complete inhibition of protein synthesis by a single large dose of puromycin (150mg/kg) has permitted calculation of the half-life of GLH which was found to be 7 hours in both male and female intact rats. It is proposed that the specificity of hypophysectomy and STH in altering GLH activity to the exclusion of other enzymes in ascorbate synthesis may be the result of the enzyme's rapid turnover in the face of generalized changes in protein anabolism. (This work was supported by NIH Grant AM 09669.)

MICROCIRCULATION IN THE INNER EAR OF THE GUINEA PIG: AN IMPEDANCE PLETHYSMOGRAPHIC STUDY. Fumiro Suga and James B. Snow, Jr. (intr. by W. H. Massion). University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

The inner ear is one of the most difficult organs in which to measure the blood flow because of the anatomical features, and findings in the blood circulation in the inner ear are limited. An electrical impedance plethysmograph was applied to record blood circulation in the cochlea of guinea pigs which were anesthetized by pentobarbital sodium. This method is based on a principle that changes in blood volume in the tissue cause changes in electrical impedance. The plethysmograph used in this study consists of an oscillator, bridge circuit, amplifiers and pen-recorder. The cochlea was exposed through the auditory bulla. Under a binocular operating microscope four steel wire electrodes, approximately 0.2mm in diameter and insulated except at the tip, were implanted in the cochlea. A 25 KC current of low voltage was continuously presented between two of the electrodes, and the impedance changes between the two other electrodes were recorded as pulse waves on a pen-recorder. Blood pressure was recorded from the carotid artery with a strain gauge manometer. Hypoventilation increased the cochlear blood flow and hyperventilation decreased it. Intravenous injections of epinephrine(0.01mg/Kg) and norepinephrine(0.2mg/Kg) increased the cochlear blood flow after a temporary, slight decrease. The increase in cochlear blood flow was accompanied by an increase in blood pressure. An infusion of a 50% glucose solution greatly increased cochlear blood flow. Papaverine(1mg/Kg) increased cochlear blood flow without great change in blood pressure. Several other drugs were also presented intravenously, and for each of these drugs the functional relationship between cochlear blood flow and the systemic blood pressure was studied.

PROJECTIONS OF THE AMYGDALOID COMPLEX TO THE RETICULAR FORMATION STUDIED BY "TEGMENTAL TREMOR". E.G. Szekely, D. Zivanovic* and J.J. Egyed*. Temple University Health Sciences Center, Philadelphia, Penna.

Investigations in cats (Szekely and Zivanovic) showed that large lesions in the amygdaloid complex in 75% of the cases increased the amplitude of the tremor elicited by electrical stimulation of the midbrain reticular formation. Excitation of the amygdala and/or of the pyriform cortex decreased, even abolished the tremor especially on chemical stimulation using 10-30 µg carbachol powder. Salivation accompanied the tremor inhibition apparently independently of the tremor alteration. Changes of the characteristics of the phasic movements were recorded on a Grass EEG and also averaged by a Mnemotron Computer. In an effort to analyze the efferent amygdaloid pathways responsible for these effects the following experiments were carried out. Large septal lesions or bilateral elimination of the stria terminalis or extensive bilateral electrolytic destruction of the hypothalamus did not prevent the amygdaloid inhibition of the tegmental tremor. No salivation accompanied the amygdala stimulation following hypothalamic destruction. Electrolytic lesions in the stria medullaris just in front of the habenula prevented the suppression of the tremor on chemical stimulation of the amygdaloid nucleus or the pyriform cortex. These lesions did not hinder the appearance of salivation.

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CARCINOGENIC EFFECT OF HENS' EGGS AND OF CHOLESTEROL UPON CASTRATED MICE. J. Szepsenwol and H. J. Cestero-Aguilar,* Dept. of Anatomy, University of Puerto Rico School of Medicine.

On the basis of previous results it was thought that hens' eggs influence carcinogenesis in mice, at least in part, through the endocrine system. Mice of the T.M. strain maintained from the day of birth on the Rockland rat diet (Group 1 control) supplemented with egg yolk (Group 2), hard boiled egg white (Group 3), cholesterol and lard (Group 4) or cholesterol alone (Group 5) were castrated at the age of 4 to 5 weeks and placed back on the above diets. The incidence of malignant tumors in these mice were more or less the same as in the corresponding non-castrated animals: Group 1 had an incidence of 22%, while in the experimental 4 groups it was 78 to 93%. Moreover, lung tumors were the most frequent neoplasms, lymphosarcomas and mammary cancer, the incidence of which varied, occurred in groups 1 to 4, none in the mice on the diet supplemented with cholesterol. One outstanding feature of the castrated mice, particularly of groups 2 to 5, is the enlargment of the adrenals, many of which were tumorous. Moreover, one of the mice of group 2 developed a tumor of the pituitary gland originating from the intermediate lobe. These results support the point of view expressed above. (Supported by General Research Grant FR-5419-04.)

DISTRIBUTION OF CORONARY INFLOW AND OUTFLOW IN POSTMORTEM CANINE HEART. K. Tamura*, M.M. Laks*, D. Garner*, and H.J. Swan. Cedars-Sinai Research Institute, Los Angeles, Calif.

The purpose of this study was to measure simultaneously the coronary inflow and the coronary outflow distribution of Ringer solution at 23° C. In ten fresh postmortem canine hearts the right, left anterior descending and left circumflex coronary arteries were infused continuously at a pressure of 100 mm Hg. The inflow rates were measured separately with three glass ball flowmeters. The outflow was collected separately from the right atrium, anterior cardiac veins, coronary sinus, right ventricle, and combined left atrium and ventricle. The measurements were performed 40 min. after death and completed within 10 min. Associated with the development of rigor mortis, the flow decreased 15% to 20% every hour after the initial measurements. The total inflow was 142 + 21** ml/100 Gm of total heart weight/min. The inflow distribution was 23.4 + 4.9%** in the right coronary, 36.7 + 5.9%** in the left anterior descending and 40.0 + 6.4%** in the left circumflex coronary artery. The outflow distribution was 9.4 + 3.8%** from the anterior cardiac veins, 58.4 + 4.9%** from the coronary sinus, 9.4 + 2.2%** from the right atrium, 20.4 + 6.1%** from the right ventricle and 2.5 + 1.5%** from the left atrium and ventricle.

** - Mean and S.D.

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EFFECT OF SUGARS ON ION TRANSPORT IN INTESTINE. A. E. Taylor*, E. M. Wright*, S. G. Schultz, and P. F. Curran, Harvard Medical School, Boston, Mass.

The relations between short-circuit current and net sodium transport across rat and rabbit small intestine in the presence of 25 mM glucose or galactose have been investigated. In all instances both short-circuit current and net sodium transport are increased by the addition of these sugars. Short-circuit current was approximately equal to sodium transport across both rat and rabbit ileum in the presence of glucose or galactose. In jejunum, this equality was found only in the presence of glucose; short-circuit current in the presence of galactose was approximately twice the net sodium flux. In rat jejunum, this difference between short-circuit current and net sodium transport is due to active secretion of chloride into the mucosal solution. Short-circuit current and net sodium transport across rat jejunum were identical when sulfate replaced chloride in the bathing medium. These findings together with observations on the electrical responses of the tissue appear to be compatible with the neutral NaCl pump that results in secretion of NaCl. The possible origin of the differences between the responses of jejunal and ileal tissue to galactose stimulation of short-circuit current may be related to the different metabolic requirements of these tissues. (This work was supported by USPHS Grant AM-06540, the American Heart Association, and Atomic Energy Commission.)

PERMEABILITY AND TRANSPORT PROPERTIES OF DEVELOPING FROG SKIN. R.E. Taylor, Jr. and S.B. Barker, Univ. of Ala. Med. Ctr., Birmingham, Ala.

Ohmic resistance and isotopically determined unidirectional sodium fluxes measured in Rana catesbeiana tadpole skin bathed on both sides by amphibian Ringer's solution are high before metamorphosis and decline markedly, concurrent with or just prior to the appearance of previously absent skin potentials and active sodium transport. These observations suggest rates of sodium loss from tadpole to pond water which should lead to hyponatremia and death within a few days. However, tadpoles fasted in distilled water changed every 24 hr did not die, and plasma sodium concentrations and total body sodium declined only during the first day of an 8-day period, suggesting that sodium efflux might be reduced when sodium concentration of the external bathing solution is low. Evidence in support of this possibility has been obtained with both isolated tadpole skin and intact tadpoles; sodium efflux decreased systematically with decreasing external sodium concentration even when osmolarity was maintained constant by added sucrose. In contrast, the efflux of sodium thru isolated adult frog skin was not significantly influenced by external sodium concentration. This trans effect of sodium in tadpole skin, which is not predicted by the laws governing simple diffusion, suggests exchange diffusion mediated by a mobile carrier localized in a critical cell membrane. The changes occuring at the time of transition from larval to adult skin may result from the development of energy-requiring mechanisms which alter the carrier at the membrane-body fluid interface reducing its affinity for sodium, thus decreasing exchange diffusion and providing a mechanism for active transport.

Support in part by Grant AM 10436 from the NIH.

A COMPARISON OF THE LEFT VENTRICULAR ISOVOLUMIC AND AUXOTONIC VOLUME-TENSION DIAGRAMS IN THE INTACT DOG. Roger R. Taylor*, and John Ross, Jr. Cardiology Branch, National Heart Institute, Bethesda, Md.

In skeletal muscle stimulated tetanically, the relations between fiber length and tension at the termination of isotonic shortening coincide with points on the length-tension curve obtained from isometric contractions. Isovolumic and auxotonic left ventricular volume-tension relations were compared in 9 closed-chest, sedated dogs. Transmural left ventricular (LV) pressure was obtained by percutaneous puncture and an intrapleural catheter, ventricular end-diastolic volume was determined from end-diastolic pressure and the pressure-volume relation of arrested ventricle, and instantaneous volume during auxotonic contractions from the time integral of aortic flow (electromagnetic flowmeter). Heart rate was controlled. The volume-tension relation of isovolumic beats was determined from contractions induced by sudden balloon occlusion of the ascending aorta, and a wide range of ventricular filling was produced by transfusion and bleeding. In 6 of 9 animals the end-systolic volume-tension relations of auxotonic contractions corresponded closely with points on the volume-tension relation of isovolumic contractions. In 3 animals ejection fell short of the isovolumic relation by 20 to 38% of stroke volume, although when all animals were considered this discrepancy was not significant ($p>0.1$), averaging 1.9 ± 3.8 (SD) ml or 8% of stroke volume. It is concluded that the limit to fiber shortening and ejection in the intact left ventricle is determined by the volume-tension relation of isovolumic beats and that fiber shortening frequently proceeds to equilibrium with this relation. Therefore, although tension development in isovolumic ventricular contractions is known to be affected to some degree by active state duration, this factor usually does not appear to impose an additional limitation upon fiber shortening in auxotonic contractions.

THE EFFECT OF AEROBACTER AEROGENES ON URETERAL MOTILITY. N. Teague*, S. Boyarsky, and J. F. Glenn*, Duke Univ. Med. Ctr., Durham, North Carolina

Coliform organisms and E. coli endotoxin administered intraluminally into the dog renal pelvis produced suppression of ureteral peristalsis, while intraaortic injections resulted in acceleration. Similar experiments have now been performed employing Aerobacter aerogenes. Cultures were administered intraaortically, intravenously and intraluminally into the canine renal pelvis. Ureteral activity was monitored by peristaltic pressure recordings and cinefluorographic examinations. Eighteen of 23 procedures performed in 16 dogs showed significant changes: Initial response in 16 instances was acceleration of ureteral activity, a 2 to 7 fold increase in ureteral peristaltic frequency was noted within 10 seconds. These effects were corroborated by cinefluorography. Depression of ureteral activity followed the hyperactivity in six experiments; In two procedures the only response was suppression of activity. The ureteral effects produced by Aerobacter resembled those of histamine in part. It is concluded that Aerobacter can alter ureteral activity. (Supported by NIH and VA grants).

CARDIOVASCULAR RESPONSES TO ACETYLCHOLINE: EFFECTS OF PENTOBARBITAL AND AUTONOMIC BLOCKING AGENTS. H. A. Teitelbaum*, J.E.O. Newton, and W.H. Gantt, Pavlovian Lab, Johns Hopkins Sch. of Medicine, Baltimore, Md.

Earlier studies showed that acetylcholine (ACh) in awake dogs causes slowing of heart rate (HR) followed by HR increase. Pentobarbital anesthesia accentuated the slowing without affecting the HR increase. Studies by others have shown that atropine blocks the HR decrease due to ACh, and that nicotine and curare inhibit the acceleration. The present studies confirm in 4 dogs the above observations, except that the ACh cardiac acceleration is inhibited by the B-adrenergic blocking agent propranolol rather than by curare.

Blood pressure (BP) measured from intraaortic catheters showed initial prompt fall and then a more precipitous decrease related to the maximal cardiac inhibition (cardiac standstill) due to ACh. Gradual return of BP to baseline followed. Pentobarbital and curare did not affect the BP response to ACh. Under atropine ACh caused a more gradual fall in BP followed by a striking rise above the baseline. Propranolol caused a diminution in pulse pressure, but no change in the BP response to ACh.

The action of atropine on the HR response to ACh indicates a muscarinic effect of ACh, while the response to propranolol indicates epinephrine release as basis for the acceleration. Correlations between the above and the cardiac orienting and conditional reflexes suggest the possibility that the above mechanisms may play a role in these reflexes. (Supported by NIH Grant HE-06945).

DISCHARGE PATTERNS OF PURKINJE AND CEREBELLAR NUCLEAR NEURONS DURING RAPIDLY ALTERNATING ARM MOVEMENTS IN THE AWAKE MONKEY. W. T. Thach, Jr. (intr. by E. V. Evarts). Natl. Inst. Mental Health, Bethesda, Md.

The activity of single units was recorded extracellularly with platinum-glass microelectrodes in the cerebellum of the awake monkey at rest and during learned arm movements. The movements consisted of rapidly alternating flexion-extension of the wrist and of the shoulder of either arm. Units were presumptively identified as Purkinje or as nuclear cells by occasionally marking the recording sites with electrolytic lesions made with the recording electrode, and reconstructing the penetration from subsequent histological sections. A Purkinje cell generated spikes of two distinct shapes: a "simple" spike resembled the parallel fiber response, and a "complex" spike the climbing fiber response that Eccles and colleagues have recorded intracellularly from the Purkinje cell. With the monkey still, the simple spike of most Purkinje cells occurred at high maintained frequencies (up to around 100/sec), occasionally interrupted by the complex spike (up to several/sec). When the activity of a Purkinje cell was related to movement, frequency of the simple spike alternated between rates higher and lower than the resting rate, with a consistent temporal relationship to the different phases of each successive movement cycle. The complex spike, even in those cells whose simple spike was strongly related to a movement, was itself unrelated to the movement: it discharged during the movement in the same sporadic manner as during rest, and showed no consistent temporal relation to phases of the movement cycle. Nuclear cells also had high resting discharge frequencies; for a cell related to movement, the discharge frequency also alternated between rates higher and lower than the resting rate. Purkinje and nuclear cells were related to ipsilateral movements only.

HYPOXIC PULMONARY VASOCONSTRICTION IN UNANESTHETIZED DOGS WITH CONSTANT ARTERIAL P_{CO_2} AND pH. Otto G. Thilenius. Univ. of Chicago, Chicago, Ill.

Awake dogs with chronically implanted intravascular catheters (pulmonary artery, left atrium, aorta) and electromagnetic flowprobes (pulmonary blood flow) were repeatedly exposed to 45 minutes of acute hypoxia (9.5% O_2). After this "control response" was established, the dogs were challenged with the same degree of hypoxia, but arterial P_{CO_2} and pH were kept constant by adding CO_2 to the inspired gas, monitoring end-tidal CO_2. Intravascular pressures, pulmonary vascular resistance (PVR), O_2 consumption, CO_2 production, alveolar and arterial gas tensions, and pH were studied. During hypoxia the rise in pulmonary artery pressure (40%), cardiac output (7%), PVR (50%), and $\dot{V}_{CO_2}$ (18%), and the decrease in $\dot{V}_{O_2}$ (40%) were NOT different in the two series of experiments. Only the rise in respiratory minute volume during hypoxia was markedly larger in the iso-P_{CO_2} series (85%) than in the control series (20%). It is concluded that respiratory alkalosis and hypocapnia which accompany acute hypoxia do not contribute to hypoxic pulmonary vasoconstriction of unanesthetized dogs.

AUDITORY CONDITIONING OF MONOSYNAPTIC REFLEX. J. Steven Thomas* and Charles D. Barnes. Department of Anatomy and Physiology, Indiana University, Bloomington, Indiana.

Using decerebrate cats it has been possible to demonstrate auditory conditioning of the monosynaptic reflex recorded at L-7. The conditioning stimulus was a brief tone (BEEP) from an auditory tone generator. With the test shock gated to be given at varying intervals after the initiation of the sound stimulus it has been possible to profile the effects of a sudden tone on the amplitude of the monosynaptic reflex. Although the quantitative variation in response from cat to cat is considerable, the qualitative pattern is relatively constant. It consists of an initial period of facilitation beginning approximately 15 msec after the start of the tone, reaching a maximum at 25-30 msec, and declining to control values at 45 msec for a total facilitation period of some 30 msec. The slope of the declining action potentials continues smoothly into a period of inhibition which reaches a maximum at 60-70 msec and returns to control at approximately 120-140 msec giving an inhibitory response of some 90 msec. Provided that the sound was audible as a distinct tone, the duration of the conditioning stimulus has no effect on the pattern of the response. Occasionally a slight (15% of control) ventral root discharge to the sound alone has been recorded lasting approximately 5 msec and corresponding to the facilitation maximum. (Supported in part by USPHS research grant NB 05949.)

OXYGEN CONSUMPTION AND MEMBRANE PERMEABILITY OF IN VITRO SAC PREPARATIONS OF RAT SMALL INTESTINE. C. S. Tidball, T. R. Liebross*, S. Thomas* and M. M. Cassidy*. Dept. of Physiology, George Washington University, Washington, D. C.

The oxygen consumption of intestinal sacs in both normal and everted orientation was studied by standard manometric techniques as a function of intestinal location and sac distention. The oxygen utilization of normally oriented segments (15 μl O_2/gm dry wt/min) did not differ significantly from that for everted segments (20 μl O_2/gm dry wt/min). Oxygen utilization decreased aborally in both orientations. The decrease was enhanced by increasing sac distention and may be related to wall thickness which also decreases from duodenum to ileum. Net water transfer, bulk water movement, and transepithelial fluxes of a series of C^{14} labeled solutes were studied as a function of segment orientation, location, and sac distention. From the above, permeability coefficients and estimates of the equivalent pore radius were derived. In the everted orientation, the permeation of a passively transported solute is greater than that obtained with normally oriented sacs. Net water absorption and bulk water movement for a given osmotic gradient increases aborally. Net water absorption in the everted preparation decreases with increased filling pressure whereas the permeability coefficient for C^{14} mannitol increases with sac distention. The failure of eversion to increase oxygen utilization and the demonstrated elevation in passive permeability of this preparation coupled with the non-ideal permeability characteristics of normally oriented sacs from rat intestine lead one to conclude that this particular tissue is best studied in vivo. (Supported by NSF GB-4769)

THE MECHANICAL WORK OF BREATHING IN METABOLIC ACIDOSIS
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The mechanical work of ventilating the lung was measured in artificially ventilated dogs under the following conditions: (a) normal acid-base balance, (b) metabolic acidosis induced by lactic acid infusion (c) induced metabolic acidosis and hyperventilation. The findings indicate that metabolic acidosis (pH 7.126) causes a moderate decrease in lung compliance (-10%), and an increase in elastic work (11%), resistive work (6%), and total pulmonary work (11%). Hyperventilation causes a decrease in lung compliance (-18%), and an increase in elastic work (21%), resistive work (70%), and total pulmonary work (35%). Hyperventilation during induced metabolic acidosis causes a decrease in compliance (-22%), and an increase in elastic work (29%), resistive work (90%), and total pulmonary work (52%). These results suggest that although pure metabolic acidosis has a moderately detrimental effect on pulmonary function, the major increase in pulmonary work in the course of metabolic acidosis stems from the attempt to compensate by respiratory means (hyperventilation) for the low pH caused by the excess "fixed" acidity.

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LIGAMENTOUS STRENGTH MEASUREMENTS FROM HYPOPHYSECTOMIZED RATS. C. M. Tipton, D. D. Sandage*, and F. W. Booth*. Exercise Physiology Lab., Univ. of Iowa, Iowa City, Ia.

Results from dogs indicate that the force (SF) required to separate an intact or repaired medial collateral ligament of the knee is significantly higher in animals that have been exercised for six weeks. However, in no group, trained or nontrained, does the repaired strength equal the SF value obtained from the non-lesioned leg. To acquire more information on the responsible mechanisms, 150 male hypophysectomized rats were assigned to one of the following groups: nontrained, trained, nontrained + TSH, trained + TSH, nontrained + GH, immobilized, sham operated, lesion + repair + immobilization, lesion + repair, and lesion + repair + GH. The minimal experimental period was six weeks. Since SF is significantly correlated with body weight, results were expressed on a SF/BW ratio or SFR. As with the dog results, the lowest value 4.78 ± 0.58 (12) was obtained from the lesion + repair + immobilization group. The lesion group without immobilization had a mean of 7.72 ± 0.49 (23). The nontrained animals had a SFR result of 8.31 ± 0.34 (28) whereas the trained group had a value of 9.73 ± 0.57 (13). Although the presence of GH decreased the incidence of tearing at the lesion site, it had no appreciable influence on ligamentous strength at the point of its osseous attachment. Mean for nontrained + GH was 6.21 ± 0.39 (13) and 5.45 ± 0.36 (13) for the lesion + exogenous GH. Administration of TSH was associated with a higher SFR for the nontrained 9.37 ± 0.49 (15) as well as for the trained 12.49 ± 0.69 (10). These findings provide additional support to the concept that exercise has an effect on ligamentous tissue that is independent of hypophyseal influences. (Supported by PHS Grant AM-08893-3).

EFFECT OF VAGUS AND SYMPATHETIC STIMULATION ON STROKE VOLUME. W. S. Topham and D. K. Johnson (intr. by H. R. Warner), Dept. of Biophysics & Bioengg., Univ. of Utah, Salt Lake City, Utah. Supported by grant no. HE-03607 and special fellowship no. GM-33,694 from NIH.

Using the method described by Williams (Fed Proc 23: 413, 1964) to produce atrioventricular block without thoracotomy, the relationship of vagus and sympathetic stimulation to stroke volume was studied at constant ventricular rate. The atrial rate was not controlled. Stroke volume was calculated from the central pressure pulse (Warner, JAMA 196: 944, 1966) and verified with the dye dilution method. The vagus nerves were cut bilaterally in the neck and the sympathetic nerves were cut as they emerged from both the right and left stellate ganglia. A stimulation of 8 per sec. was generally used although frequencies of 2 to 10 per sec. were tried. Stimulation of the left sympathetic produced the greatest change in the central pressure pulse with the pulse pressure increasing 30%, duration of systole shortening and the rate of contraction of the left ventricle increasing. Stimulation of the right sympathetic produced similar but less dramatic changes. Although the effects of stimulus caused large changes in ventricular contraction, the stroke volume changes averaged only 12%. The same change occurred in stroke volume regardless of the frequency of stimulus but the mean pressure increased 23% as the stimulus frequency was increased from 2 to 10 per sec. During vagus stimulation stroke volume was unaffected and no changes were observed in the central pressure waveform.

CONTRIBUTION TO THE SEROTONIN THEORY OF SLEEP,PARADOXICAL SLEEP, AND DREAMING(LSD INFUSION). Clara Torda*(intr.by Gabor Kaley). Downstate Med.Col.,State Univ. of New York,Brooklyn,N.Y.

Since increased brain serotonin(SE) has hypnogenic effects (Koella &Czieman,Amer.J.Physiol.,211:926,1966),and brain SE depletion induces complete insomnia(Torda,Pharmacologist,1967),brain SE is assumed to be essential for sleep initiation.Attempts to ascertain the role of brain SE on paradoxical(REM)sleep are here presented.Chronic brain SE increase is known to prolong dreamtime(Hartmann,et al.).Since blood-brain barrier passage of SE is negligible,acute experiments required to study the effect of SE on the latency of REM sleep have not yet been performed. LSD, in low concentrations, has a SE-like effect in man and readily passes the blood-brain barrier.Starting at various phases of stage 4 sleep, LSD has been intravenously infused into man in conc. of 5 gamma/min. until the onset of the next REM period. In all instances,LSD infusion significantly shortened the latency of the next REM period and induced vivid dreams. LSD infusion during wakefulness induced visual hallucinations.--In another group of experiments EEG arousal patterns have been observed in animals receiving through an implanted micropipette norepinephrine(NE) injection into the hypothalamus during stage 4 sleep.Combination of NE injection and LSD infusion induced REM sleep.These results support a previously described cybernetic mechanism capable of interchanging stage 4 and REM sleep(Torda,Proc.APSS,1967;Lancet, 1967,p.1011),i.e.an intracerebral release of biogenic amines(with approximately 90 min. periodocoty)initiates both a threatened arousal and a SE-dependent chain reaction counteracting arousal. REM sleep(& its symptomatology) are physiological manifestations of the combination of these two opposing processes.

EFFECT OF ACUTE VAGOTOMY ON LEFT VENTRICULAR HEMODYNAMICS IN INTACT DOGS
A. G. Tsakiris*, R. A. Vandenberg*, D. E. Donald, and E. H. Wood, Mayo Clinic and Mayo Graduate School of Medicine, Rochester, Minnesota.

The response of the left ventricle to comparable increases in aortic pressure, caused by intra-aortic infusion of angiotensin II before and after acute vagotomy was studied in 10 intact anesthetized dogs which had been previously sympathectomized. Experiments were done with constant heart rates (driving the atria and ventricles with coupled pacemakers) and repeated in 6 dogs with spontaneous sinus rhythm. Control values for left ventricular end-diastolic pressure (LVEDP) at constant heart rates (125-160 beats/minute) were higher before (average 8, range 2-12, cm H_2O) than after vagotomy (average 4, 1-8, cm H_2O) while stroke volume and aortic pressure were similar. The average LVEDP of 18 (10-21) cm H_2O associated with an increased level of aortic pressure before vagotomy was significantly greater than the value of 8 (2-12) obtained at comparable aortic pressures after vagotomy, while stroke volumes were unchanged or slightly increased. Similarly under spontaneous sinus rhythm, end-diastolic pressures were lower after vagotomy than before. Left ventricular end-diastolic volumes, as estimated from repeated video angiograms in 6 dogs were closely similar before and after vagotomy. These data are compatible with the interpretation that the reflex increase in vagal tone presumably associated with increased levels of aortic pressure decreased the distensibility of the left ventricular myocardium. (Supported in part by Research Grants NIH HE-03532 and AHA CI-10.

The relationship between oscillating slow waves and single unit activity in the subthalamic nucleus.

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Under barbiturate anesthesia spontaneous 8-12/sec. slow wave activity which is abolished by stimulation of the globus pallidus occurs in the subthalamic nucleus. In an effort to identify the cellular mechanism underlying these changes, the discharge patterns of subthalamic neurons have been classified according to their response to pallidal stimulation in both barbiturate and locally anesthesized cats. In the locally anesthesized animals, post stimulus latency histogram show two peaks, at 8 and 14 msec. These neurons respond to each pallidal stimulus by discharging 5 or 6 action potentials, and constitute 32% of the sample. Another 23% respond with a mean of 8 msec. latency, but show only 1 or 2 spikes per stimulus. A third group (45%) discharges a single action potential which is followed by a 50-150 msec. silent period in spontaneous discharge pattern. Under barbiturate anesthesia, 83% of the cells sampled show only a post stimulus silent period of 70-200 msec. following pallidal stimulation. This corresponds to the period during which slow wave activity is suppressed. 15% not spontaneously active, but respond to pallidal stimulation after a latency of 20-40 msec. with a burst of high frequency spikes. The temporal relation of the 'bursting' cells to the silent period in subthalamic nucleus neurons suggest they may be involved in pallidal inhibition of activity in this nucleus.

MYOGENIC BASAL TONE IN ISOLATED PERFUSED RESISTANCE VESSELS. Eiichi Uchida*, David F. Bohr and Sibley W. Hoobler. Depts. Physiol. and Med. Univ. of Michigan, Ann Arbor, Mich.

Single, isolated resistance vessels, 100 to 250μ o.d., were perfused at a constant flow rate with physiological salt solution containing 1.6 mM Ca^{++}. Vessels from rat skeletal muscle showed an unusually high resistance to flow which was reduced by approximately 50% by using Ca-free perfusate, as well as by using 1 mg/ml sodium nitrite. The basal tone was not eliminated by a dose of phentolamine sufficient to block a norepinephrine response, indicating that the muscle tone is of intrinsic myogenic origin. Vessels from rat mesentery and from rabbit mesentery, brain, kidney, subcutaneous tissue and skeletal muscle did not show such basal tone. These vessels constricted in response to small doses of norepinephrine. In a calcium-free solution these responses to norepinephrine usually did not decline to zero within 30 minutes, whereas the intrinsic myogenic tone of the rat skeletal muscle vessel was lost within 3 minutes. This contrast suggests that basic differences exist between the contractile machinery responsible for intrinsic myogenic tone and that causing the response to norepinephrine. (This study was supported by USPHS Grants HE-03756 and FR-05383.)

BILIARY EXCRETION OF BILIRUBIN IN SHEEP. Dan W. Upson*, Ronald Gronwall* and Charles E. Cornelius. Dept. of Physiol., College of Vet. Med., Kansas State University, Manhattan, Kansas. Endogenous bilirubin excretion in sheep was independent of bile flow at rates between 7.4 and 35 μl/min/Kg during depletion of the taurocholic acid pool following the quantitative collection of bile for periods up to 4 hours. The rate of endogenous bilirubin excretion into bile was increased by returning taurocholic acid either by intravenous infusion of the bile acid or intraduodenal infusion of the collected bile. Following the quantitative collection of bile for 90 minutes, the average flow rate was 7.4 μl/min/Kg which was approximately 20% of the average initial flow rate (35 μl/min/Kg). Unconjugated bilirubin was infused intravenously at four different rates. Bile flow was maintained at initial rates by continuous intravenous infusion of 1.3 mg of taurocholic acid /min/Kg. The proportion of the infused bilirubin excreted into the bile was 70% at the infusion rate of 0.2 mg/min/Kg, 74% at 0.4 mg/min/Kg, 75% at 0.6 mg/min/Kg, but decreased markedly to 23% at 0.8 mg/min/Kg. Maximum biliary excretory rates of bilirubin at the 0.6 mg/min/Kg infusion rate averaged 0.45 mg/min/Kg. The highest concentration of bilirubin in bile was observed at the 0.6 mg/min/Kg infusion rate and averaged 18 mg/ml.

THE MODIFICATION OF VENTRICULAR PERFORMANCE BY CHANGES IN THE INSTANTANEOUS RESISTANCE TO EJECTION. Charles W. Urschel*, James W. Covell*, John Ross, Jr., Edmund H. Sonnenblick, and Eugene Braunwald. Cardiology Branch, National Heart Institute, Bethesda, Md.

The effects of altering the instantaneous resistance to ejection on the mechanics of contraction during the steady state in the intact dog heart were analyzed. Resistance was lowered by the simulation of aortic or mitral valvular regurgitation. With either lesion the instantaneous impedance to ejection (LV pressure/flow) was decreased throughout ejection. When left ventricular end-diastolic pressure (LVEDP) was held constant, total stroke volume and peak ejection velocity increased when valvular regurgitation was induced, although contractility was unchanged, as shown by the isovolumic force-velocity relation. The rate of tension decline during ejection was accelerated, due to the more rapid diminution of LV size during ejection. The reduction in instantaneous resistance to ejection therefore allowed the ventricular muscle to shorten faster and further, increasing external energy output. Calculated instantaneous resistance to ejection was increased in 8 other dogs by the use of a noncompliant bypass shunt in place of the aorta. When LVEDP was held constant, peak aortic systolic pressure and wall tension rose, ejection was prolonged and stroke volume fell. It is concluded that the performance of the intact heart can be modified substantially by changes in the instantaneous resistance to ejection, independent of altered myocardial contractility and resting fiber length. Assessment of the effects on ventricular performance of lesions producing valvular regurgitation or changes in aortic compliance must include a consideration of instantaneous myocardial length, tension, velocity, and the resistance to ejection.

EFFECT OF GASTRIN ON MOTILITY OF GALLBLADDER. Monique Vagne* and Morton I. Grossman. Veterans Administration Center, Los Angeles, California.

Mutt and Jorpes (Biochem. Biophys. Res. Comm. 26: 392, 1967) showed that the C-terminal tetrapeptide amide of cholecystokinin-pancreozymin (CCK) was similar to or identical with that of gastrin. Previous studies had shown no effect of gastrin on motility of the gallbladder but in light of this recent finding, we reexamined the question. In 3 dogs with cystic duct ligated and a permanent cannula in the fundus of the gallbladder, the effects of CCK (GI Hormone Lab., Karolinska Institutes, Stockholm) and of pure porcine gastrin II (gift of Prof. R.A. Gregory) were compared by measuring changes in pressure (cannula connected to strain gauge) produced by rapid intravenous injection. The doses used were 0.05 to 0.4 unit/kg for CCK and 0.25 to 2.0 μg/kg for gastrin. The increase in pressure with 0.1 u/kg CCK was about the same as with 0.5 μg/kg of gastrin. Assuming that pure CCK has 6 u/μg, the potency of gastrin is about 1/30th that of CCK on a weight basis. This low potency suggests that endogenous gastrin probably does not participate significantly in regulation of contraction of the gallbladder.

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POTASSIUM FLUX IN THE TOAD BLADDER. John C. Vanatta and F.T. Kallus*. Univ. Tex. Southwestern Med. Sch., Dallas, Texas.

Kallus (The Physiologist, this issue) reports that K is concentrated in the urinary bladder of Bufo marinus under conditions of K loading In view of this, K fluxes were measured in isolated bladders from K loaded toads. Oxygenated plasma from K loaded toads was the bath on both sides of the bladder. K-42 in K_2CO_3 was added to the plasma on one side, and an equivalent amount of unlabeled K_2CO_3 was added to the plasma on the opposite side. The unidirectional fluxes of hemibladders were compared, one half bladder being used for serosal to mucosal (S-M) flux and the other for the reverse (M-S) flux. In four pairs of half-bladders the fluxes were measured and after one hour of washing, the reverse flux was measured in each half-bladder using plasma with a 60 fold increase in specific activity. This diminished errors due to residual K in the bladder. However, the flux in either direction increased with time making comparisons of the same half-bladders insensitive. A total of 13 paired determinations were done on 9 pairs of half-bladders. The flux was greater in the S-M direction in 10 of the 13 ($p = 0.046$). This was true whether the flux was expressed per unit area, or per unit weight of the bladder. In six experiments the S-M flux was more than double M-S flux of the paired half-bladder. These findings are consistant with the theory that the urinary bladder of the toad functions as an excretory organ for K under conditions of K loading. (Supported in part by PHS grant HE 01574-13 and GM 34243-01 from Natl. Inst. of Health.)

MESENTERIC FLOW RESPONSES OF AMBULATORY CHIMPANZEES. R.L Van Citters and D Franklin. Regional Primate Research Center and Department of Physiology and Biophysics, University of Washington, Seattle and Scripps Clinic Research Foundation, La Jolla, California.

The Doppler telemetry flowmeter was used to monitor blood flow through the superior mesenteric artery of adult chimpanzees moving freely in a large outdoor enclosure at the San Diego Zoo. The transducer was chronically implanted around the artery proximal to its subdivision into intestinal radicles, and lead wires were brought out through the skin of the back for attachment to a flow-meter telemetry system which the animal carried in a backpack. The telemetered flow responses were tape recorded along with a hidden observer's description of the animal's activity. Phasic wave forms of mesenteric flow were identical with those recorded in baboons and dogs; peak velocity reached 60 cm/sec and reverse flow did not occur. Mesenteric flow calculated by integrating flow velocity with respect to the fixed lumen diameter, averaged about 600 cm^3/min (12 cm^3/kg/min) at rest. Only slight changes occurred during spontaneous activity; when the animal was startled flow dropped for only a few seconds. Flow was essentially constant during sleep, but a sustained increase occurred during excitement. The greatest decrease occurred during defecation when flow was transiently interrupted, apparently due to venous compression rather than vasomotor activity. The general patterns of mesenteric flow in the chimpanzee were similar to those recorded in active baboons. (Supported by the Washington State Heart Association, and USPHS Grants HE 08433, HE 08337 and FR 00166-06.)

ROLE OF DIFFUSION AND CAPILLARY PERFUSION IN EXIT OF OXYGEN FROM GAS POCKETS. Hugh D. Van Liew. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Measured exit rate of oxygen ($\dot{V}O_2$) from subcutaneous gas pockets in rats is approximately proportional to the square root of the tension of oxygen in the pocket (PO_2). This is evidence that the system is neither perfectly diffusion limited (in which $\dot{V}O_2$ would be directly proportional to PO_2) nor perfectly perfusion limited in the conventional sense (in which $\dot{V}O_2$ would level off when PO_2 was high enough to saturate all the hemoglobin of the blood supply.) The data can be explained by a theory based on the assumption that the amount of blood which participates in O_2 removal increases as the PO_2 of the pocket gas increases. It is assumed that capillaries are homogeneously distributed throughout the tissue, and when pocket PO_2 is high, O_2 diffuses farther into the tissue and therefore meets more capillaries. An equation (analogous to Warburg's classical equation for penetration of O_2 into a thick tissue slice in a respirometer) predicts that $\dot{V}O_2$ is proportional to the square root of PO_2, as observed. The equation also predicts that $\dot{V}O_2$ is proportional to the square root of blood flow through the tissue (ml of blood per ml of tissue per min) and to the square root of the normal arteriovenous O_2 difference of the tissue. (Supported in part by the U. S. Air Force.)

THE EFFECTS OF BODY THERMAL STATE ON MANUAL PERFORMANCE. J. A. Vaughan, E. A. Higgins and G. E. Funkhouser (intr. by P. F. Iampietro). Physiology Laboratory, CAMI, FAA, Oklahoma City, Oklahoma.

Thirty-six young men were exposed for two hours to environmental temperatures of either 10 C, 26.7 C or 46 C. Experiments at these conditions were conducted both in the early morning, (Low T_r), and in mid-afternoon, (High T_r). Measurements of rectal and skin temperature, heart rate and respiratory rate were made, and average skin and average body temperatures were calculated. Peripheral vasomotor changes were indexed by cold-induced vasodilatation (CIVD). Manual performance consisted of standardized peg tests for hand and finger dexterity, and a paper and pencil motor coordination test. Converted scores showed no significant differences in peg placing at any of the thermal states studied, nor in any of the tests comparing AM with PM results at either the cold or hot exposures. Scores for motor coordination and peg turning at 26.7 C were better in the PM than in the AM. Men exposed to the neutral environment scored highest in the finger dexterity tests, and values for motor coordination were greater in the heat than in the other two conditions. These data suggest that coarse hand movements are independent of body thermal state, but that more discrete tasks involving hand and finger dexterity, and motor coordination, can be most efficiently performed in warmer environments which promote at least thermally neutral values of skin and deep body temperature. Analysis of the temperature curves on the finger immersed in ice water showed no rise in finger temperature due to vasodilatation for subjects exposed to 10 C, but revealed increasing spontaneous rewarming rates and rewarming finger temperatures together with decreasing cycle times at 26.7 C and at 46 C, the responses being more pronounced at the higher ambient temperature. These findings support the manual performance responses to differences in body thermal state.

EFFECTS OF ESTRADIOL-17β-AND PROGESTERONE-PROGRAMMING ON UTERINE GROWTH IN RATS. Joseph Thomas Velardo, Barbara A. Kasprow*, Wayne A. Krueger*, Thomas E. Durica*, Henry T. Cerha*, Roger R. Abood*, and Hardy P. Funk*. Inst. For Study Of Human Reproduction, Saint Ann Hospital and John Carroll University, Cleveland.

Utilizing an experimental model system (EMS), est.-17β (E_2) - programming effects on uterine growth have been assessed by a simultaneity of cyto-, histo- and biochemical analyses in rats (Velardo, J.T., 1964, Am.Zool. 4(4): 418). The current report adds progesterone (P) to the EMS. Albino rats, 50 days old, were ♂, and 1 wk later were given s.c. inj'ns of a) 0.2 cc sesame oil, b) 0.1 μg E_2, c) 1.5 mg P, or d) E_2 + P at separate sites, for specific times. The EMS involves following protocols 1 wk after ♂: 1st wk, 4 inj'ns; 2nd thru 4th wks, 5 inj'ns/wk; thereafter, treatments a, b, c or d every other day for given experiments. Necropsies were begun 24-72 hrs after last inj'n(s) depending upon duration of experiment. Results reveal uterine growth is a) not stimulated in sesame oil controls (SOC): uterine weight decreases from 40 mgms% (wk 1) to 18 (wk 23); b) physiologically induced with E_2-programming: increasing from SOC of 40 mgms% to 60 (wk 1), to 80 (3rd wk), thence to 74(4th wk), 60 (5th wk), and to 48-52 during weeks 6-23; c) slightly (inconstantly) elicited during weeks 1-5 with P, i.e. >2<5 mgm% increases over SOC; thereafter, 2 mgm% increases over SOC; and d) not significantly modified by addition of P to EMS: curves for E_2 alone and with P appear identical. Morphological studies are in progress. The EMS accommodates physiological amounts of P for multi-assessments of hormonal-programming in uterine growth. (Supported by U.S.P.H.S. Grant HD00147-05).

CARDIAC PERFORMANCE DURING EXPERIMENTAL ADRENAL INSUFFICIENCY IN THE CAT. Richard L. Verrier* and Allan M. Lefer., University of Virginia, School of Medicine, Charlottesville, Virginia.

Although peripheral vascular failure has been suggested as the major mechanism leading to the circulatory collapse seen in adrenal insufficiency, the cardiac component of the collapse has not been clearly studied. The purpose of this study was to evaluate cardiac performance after acute and chronic adrenalectomy. Left ventricular function curve analysis was selected as the means to evaluate cardiac performance. Mean arterial blood pressure (MABP) declines to 50 mmHg and cardiac output (CO) decreases by 58.3% within 3-4 hours after adrenalectomy. Total peripheral resistance is not significantly changed at this time. Submaximal volume infusion (50 ml infused at a rate of 72 ml/min from a baseline MABP of 50 mmHg) resulted in a 19.6% reduction of peak work two hours after adrenalectomy and a 34.1% reduction two hours later. This was reflected by equal impairments of maximal MABP and CO. Maximal infusion (70 to 90 ml infused at a rate of 50 ml/min from a non-bled baseline MABP) to a ventricular output plateau resulted in a 50.4% decrease in peak left ventricular work in acutely adrenalectomized cats compared with a 15.0% decrease in sham adrenalectomized cats. Approximately equal reductions in maximal CO (-28.1%) and in peak MABP (-28.3%) contributed to the 50.4% decrease in peak work. In both infusion methods, peak left ventricular filling pressure was not significantly different between adrenalectomized and control animals. The data indicate that acutely adrenalectomized cats show a progressive decrease in left ventricular work capacity indicative of cardiac impairment. Thus, the heart appears to be an important site of the circulatory collapse in adrenal insufficiency. (Supported by a grant from the NIH)

RELATION BETWEEN HYPOXIA AND pH IN THE PULMONARY VASCULAR BED OF THE CAT. P. H. Viles* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The influence of the hydrogen ion concentration of the perfusate on the response of the pulmonary vascular bed to acute hypoxia was studied in the intact adult cat (pentobarbital anesthesia) and in the isolated perfused cat lung. Hydrogen ion concentration was altered by infusion of 0.3 N HCl or 7.5% $NaHCO_3$. In the intact animal, cardiac output was determined by the thermodilution method and left atrial pressure was measured by transseptal puncture. The pulmonary vasoconstriction to ventilation with 10% O_2 (arterial pO_2 = 40 mm Hg) was abolished or greatly reduced at pH 7.5. Isolated lung perfusions were performed on cats anesthetized with chloralose. After exsanguination, the chest was opened and cannulas were placed in the main pulmonary artery and left atrium. The lungs and rib cage were removed and suspended horizontally by a pin through the vertebral canal. The lungs were rhythmically inflated (+2 to +15 cm H_2O) and perfused at constant flow (75 ml/min/kg) with autologous blood at 37 C by a roller pump. Pulmonary artery pressure was measured and left atrial pressure was kept constant. A curvilinear relation existed between the increase in PA pressure and the decrease in pO_2 of the perfusate. Increasing hydrogen ion concentration alone caused vasoconstriction, and the pressor response to any given degree of hypoxia increased progressively with a fall in pH from 7.5 to 7.0. The pressor response to hypoxia was reduced (pO_2 = 20 mm Hg) or abolished ($pO_2 \geq 40$ mm Hg) at pH 7.5-7.6. The role of hydrogen ion must be considered in any mechanism for hypoxic pulmonary vasoconstriction. (Supported by NIH Grant HE 05883.)

LOCAL NEURONAL EFFECTS OF THALAMIC STIMULATION. Jaime Villablanca* and John Schlag. Department of Anatomy, University of California, Los Angeles.

It is not known exactly what happens when complex nervous structures are electrically stimulated yet it is currently assumed that synchronous volleys of nerve impulses are thus generated. This problem was investigated in 24 Flaxedilized, locally anesthetized cats; a concentric electrode was implanted in nucleus ventralis lateralis of the thalamus, square pulses (0.5 msec, 120-200 μA) were delivered and responses of surrounding neurons were recorded with a micropipette. In 145 cells within a 4-mm radius from the stimulated point, 3 types of behavior were distinguished: A. no response (39%); B. initial burst (41%) of 1-15 spikes at 1.5-18 msec latency followed by silence and a discharge at 120-200 msec; C. initial silence (20%) in which spontaneous activity stopped for 100-600 msec and restarted with a rebound-like burst. Thus between 20-120 msec after the stimulus most cells were silent. Firing in less than 1 msec was found only in few neurons. Topographically, most initially silenced cells were between 2-3 mm from the stimulating electrode whereas non-responding cells were encountered everywhere. With pulse repetition (100 msec interval), most previously unaffected and initially silenced neurons responded with initial burst; initial burst cells discharged more profusely at longer latencies in augmenting-like fashion. Comparable results were obtained in the medial geniculate body but no evidence of initial inhibition was found in midbrain cells. It is concluded that depression of neuronal activity is a major, intrinsic (since basically the same findings were repeated in 73 thalamic neurons in completely decorticate preparations) effect of thalamic stimulation; a consideration of these patterns of responses may be helpful in understanding local interactions and cortical incrementation due to thalamic stimulation. (Supported by USPHS Grants NB 04955, NB 02501 and Training Grant 1 F05TW998.)

INHIBITION OF HISTAMINE SYNTHESIS IN VIVO. P. C. Voukydis* and E. T. Angelakos. Dept. of Physiology, Boston Univ. Sch of Medicine, Boston, Mass.

The ability of α-hydrazino histidine (HH) (a potent inhibitor of histidine decarboxylase in vitro) to inhibit the in vivo formation of "non-mast cell histamine" (NMCH) was tested in rats pretreated with compound 48/80. Heart histamine (H) was determined fluorometrically in rats injected intraperitoneally daily for 10 days with: (A) 48/80 alone, in increasing doses from 0.2 mg/rat to 1.0 mg/rat; (B) 48/80 as above, plus HH 100 mg/rat daily from the 5th to 10th day; (C) HH only as above; and (D) saline. No statistically significant differences in cardiac H were observed between C and D. However mean cardiac H was significantly lower in A and B as compared to D. Furthermore, cardiac H in B was significantly lower than in A or C. The combination treatment (B) resulted in over 70% depletion of cardiac H compared to controls (D), and about 50% greater depletion compared to 48/80 treatment alone (A). These results suggest that continued treatment with HH can produce a partial inhibition of NMCH synthesis. (Supported by USPHS grant HE 09616 and Career Development Award K3-15,457.)

A DIRECT SYNAPTIC CONNECTION MEDIATING BOTH INHIBITION AND EXCITATION. H. Wachtel* and E. Kandel, Dept. of Physiology, N.Y.U. Med. School, NYC

A multibranched, presumably cholinergic, interneuron located in the abdominal ganglion of Aplysia californica mediates synaptic inhibition to certain identified follower cells and excitation to others (Kandel et al. 1967). We have found one follower cell (L7) which receives both synaptic excitation and inhibition from this interneuron.

When the interneuron is fired directly at <1 per sec. it generates EPSPs in L7. When the firing rate is increased to >3 per sec. the EPSPs gradually diminish in size and finally invert to IPSPs. The EPSPs can summate to depolarize and fire the follower cell and the IPSPs summate to hyperpolarize and inhibit it. When the interneuron undergoes a burst the summated PSP in L7 is diphasic with the early component depolarizing and the later component hyperpolarizing. The short and equal latency of both EPSP and IPSP , and their ability to follow high firing rates, indicates a monosynaptic connection.

When acetylcholine is added to the bathing solution or is injected iontophoretically onto the cell body of L7, it produces a diphasic response which parallels the synaptic effects produced by a burst of spikes from the interneuron. Repeated injections of ACh lead to rapid desensitization of the excitatory component of the response. Curare blocks both components of the synaptic and of the ACh responses. These results support the hypothesis that the synaptic connection is cholinergic and that the dual action results from two post synaptic receptors with different desensitization thresholds.

L7 appears to combine in one cell the receptor properties of cells receiving either pure E or I branches from the interneuron. As a consequence of its dual action this synaptic connection is highly sensitive to the temporal pattern of impulses in the interneuron.

SITE OF EDEMA IN TISSUES OF THE FOREARM IN MAN. J.A. Walsh *, W. J. LaJoie *, C. Hyman and W.H. Wong *. Depts. Physiol. and Physical Med., U.S.C. School of Med., Los Angeles, California.

It is assumed, but not proven, that the loose areolar part of subcutaneous tissue is the principal site for accumulation of fluid, whereas the tight investing fascia of muscle significantly restricts edema in this tissue. This study was designed to establish which forearm tissues are involved in the accumulation of extracellular fluid. Capillary filtration, i.e., controlled edema formation, was measured by an electrocapacitance plethysmograph. Blood flow through the superficial tissues in a 10 cm forearm segment was abolished by epinephrine iontophoresis (1/2000 epinephrine chloride at 20 mA for 20 min). Capillary filtration rate was measured during 8-10 min of proximal venous occlusion at 40, 50 and 60 mm Hg. From these rates the capillary filtration coefficient (CFC), i.e., volume increment (ml) /100 ml forearm tissue/min/mm Hg was calculated. Control CFC was measured on the ipsilateral arm prior to iontophoresis or on the contralateral forearm simultaneously with CFC on the treated forearm. A gross reduction in CFC in the epinephrine-treated limbs was found. Control values of CFC agreed with those obtained in earlier experiments. Since the skin and subcutaneous tissue comprise approximately 16-18% of the total forearm volume, yet the CFC was reduced by some 75% when circulation in these areas was presumably eliminated, it is concluded that edema in the forearm of man occurs primarily in the tissues accessible to epinephrine iontophoresis, i.e., the skin and subcutaneous tissues. (Supported by L.A. County Heart Assoc. and U.S.P.H.S.)

POSTEXTRASYSTOLIC POTENTIATION AND PROCAINE AMIDE. Kenneth E. Walter and Robert A. Horvath (intr. by J.C. McGiff). V.A. Hosp. and St. Louis Univ. School of Med., St. Louis, Mo.

The clinical application of postextrasystolic potentiation (PESP) raises the question of the influence of antiarrhythmic agents on the hemodynamic consequences of this intervention. In eight open-chest mongrel dogs, anesthetized with chloralose, the following parameters were measured; mean arterial blood pressure (MABP), heart rate (HR), myocardial contractile force (MCF), left ventricular end diastolic pressure and its derivative (LVED pr. & dp/dt), venous pressure (VP), and corrected QT interval (QTc). A 3 min. bout of PESP, at a rate of 100/min., was induced every 15 min. during a 2 hr. constant infusion of procaine amide (1.42 mg/kg/min.). The results were calculated as % of the initial observations (100%) and the mean values were:

Min.		MABP	HR	MCF	LVED pr.	LV dp/dt	VP	QTc
0	Con	100	100	100	100	100	100	100
	PESP	88	-	141	103	153	120	-
60	Con	56	73	67	79	60	86	116
	PESP	50	-	117	53	100	98	-
120	Con	47	61	66	120	59	80	121
	PESP	47	-	113	105	72	91	-

Within 60 min., the QTc lengthened. Except for LVED pr., all the baseline parameters fell significantly ($p < 0.01$). PESP resulted in a rise in MCF ($p = 0.001$) and LVED dp/dt. LVED pr. fell and VP rose but remained within normal limits. MABP fell with PESP. It is concluded that PESP continues to exert its hemodynamic effects during the administration of procaine amide. It is postulated that the desireable results of PESP can be expected in those situations in which procaine amide has been administered.

ELECTRORETINOGRAM DURING +Gz ACCELERATION IN DOGS. Brian Ward (intr.by R.H.Murray). Indiana U.Cardiopulmonary Lab,Wright-Patterson AFB, Ohio.

To study the effects of +Gz acceleration on the electroretinogram (ERG) 6 anesthetized Beagles were exposed to graded +Gz stress on a short-radius centrifuge as follows: onset 1-3 G/minute, duration of steady state G was 20 min at 1.5 G and 4 min at 2,2.5 and 3 G; a minimum of 15 minutes rest was allowed between tests. The ERG was the response to the flash of a strobe light (1 cps) recorded with an intracorneal electrode. ERG,ECG and aortic blood pressure (BP) were telemetered to a recorder. The ERG a-wave (receptor potential) was not found to change except at the higher G levels, when it decreased slightly.The amplitude of the b-wave fell by some 40,80,95 and 100% (with decreasing time to full effect) at 1.5,2.0,2.5 and 3.0 G respectively. Small transient increases in the b-wave were noted in the very early stages of the stress. Mean BP fell by up to 40% of control values followed by compensatory recovery, while the heart rate rose to some 40% above control. The ERG recovery after the test was prolonged and frequently incomplete 15 minutes after a 3-4 minute run at the higher G levels. It is concluded that the amplitude of the b-wave of the ERG provides a useful index of +Gz acceleration stress, the change being due to retinal ischemia. The b-wave provides a correlate of perfusion of the bipolar layers of the retina,but gives no information on the responsivity of the ganglion cells and so does not necessarily indicate the site of primary retinal failure in "blackout".

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PURIFICATION AND SOME PROPERTIES OF A VITAMIN D_3-INDUCED INTESTINAL CALCIUM BINDING PROTEIN, A POSSIBLE TRANSPORT CARRIER. R. H. Wasserman and R. A. Corradino*, Department of Physical Biology, New York State Veterinary College, Cornell University, Ithaca, New York.

A vitamin D-induced calcium-binding protein (CaBP) has recently been identified in chick intestinal mucosa (Wasserman and Taylor. Science 152: 791, 1966; Taylor and Wasserman. Arch. Biochem. Biophys. 119: 536, 1967). Physiological and nutritional studies have suggested that CaBP is intimately associated with Ca translocation across the intestine. This protein has been isolated in high purity, using gel filtration (Sephadex G-100) and preparative discontinuous acrylamide gel electrophoresis. The purified material gave a single Schlieren peak in an analytical ultracentrifuge, and a single band on acrylamide gels run under different conditions. The molecular weight, as determined by calibrated gel filtration, averaged about 28,000, and by sedimentation equilibrium, about 26,000. The sedimentation constant is 2.32 Svedberg units (20°C). Automatic amino acid analysis of a 6N HCl hydrolysate of the purified product showed that glutamic acid, aspartic acid, leucine and lysine (in decreasing order) were the most abundant amino acids. Little or no lipid or phosphate appears to be associated with CaBP. The association constants between CaBP and Ca^{++}, Ba^{++}, and Sr^{++}, measured by the procedure of Schubert et al.(J.B.C. 185: 387, 1950), were observed to be 2.6×10^{6}, 3.9×10^{4} and 5.8×10^{3} M^{-1}, respectively. (NIH-AM-04652, NIH-AM-06271-MTN, AEC-AT(30-1)-2147).

EFFECTS OF LOW EXTRACELLULAR SODIUM CONCENTRATION ON ATRIOVENTRICULAR CONDUCTION. Yoshio Watanabe* and Leonard S. Dreifus.
Hahnemann Medical College, Philadelphia, Pa.

Electrophysiologic effects of low extracellular sodium (Na) concentrations on atrioventricular (A-V) transmission were studied in isolated, perfused rabbit hearts driven at a constant rate. Timing of activation in various A-V junctional fibers was determined utilizing ultramicroelectrodes as well as bipolar atrial and ventricular electrograms. Following the control perfusion, Na concentration was lowered from 144.8 mEq/L to either 108.6 or 77.4 mEq/L, by replacing NaCl with isosmotic amount of sucrose. The following observations were made: (1) Lowering of Na to 108.6 mEq/L invariably caused a prolongation of the A-V interval (first degree A-V block), with subsequent development of transmission failure (second degree A-V block) in some instances. Lowering of Na to 77.4 mEq/L caused second degree A-V block usually within 10 minutes. (2) First degree A-V block resulted from prolongation of conduction time in every portion of the A-V transmission system. However, the degree of prolongation was greatest within the A-V node, moderate within the atrial tissue, and least in the subnodal (His-Purkinje) conduction. (3) In the presence of second degree A-V block, failure of impulse propagation commonly occurred within the A-V node (Nregion). (4) The amplitude and duration of action potentials were decreased in all the A-V junctional fibers. It is concluded that low sodium, similar to low potassium, depresses conduction in the crucial N region of the A-V junction.

(Supported by a USPHS Grant)

LINEARITY OF THE ELECTRICAL IMPEDANCE OF FROG SKIN. Don W. Watkins* and Warren H. Dennis. Department of Physiology, University of Wisconsin, Madison, Wisconsin.

We have determined the electrical impedance of the abdominal skin of the frog (Rana pipiens) using a four electrode system. Five levels of alternating current from 16 to 245 microamperes peak-to-peak per sq. cm. at 50 Hz were repeatedly applied in groups. Each group consisted of the five current levels arranged in random sequence. After an analysis of variance on the data we concluded that the system was linear within the range of current specified. In other experiments current levels up to 2050 microamperes peak-to-peak per sq. cm. were used. At such high current levels a markedly reduced impedance is observed. Measurements made with low current, immediately after an application of high current, indicate that the impedance rises sharply to reach a maximum within 10 seconds considerably higher than before the high current. The impedance decays from this maximum toward the original level. The potential difference after a high current increases rapidly and then decays toward its previous level, following a time course similar to that seen for the impedance. The alterations in impedance, both the low values at high current and the rapid increase and decay after high current, may be interpretable by a simple equivalent circuit composed of a stable polarization element in parallel with a changing pure resistance.

INDEPENDENCE OF ALDOSTERONE-INCREASED SODIUM REABSORPTION AND SUBSTRATE-INCREASED PHOSPHATE REABSORPTION IN ISOLATED DOG KIDNEYS. William H. Waugh and Tadashi Kubo*, Dept. of Med., Univ. of Ky., Lexington, Ky.

In the pump-oxygenator-dog kidney preparation at essentially normal filtered loads, progressive natruresis and phosphaturia result over 4½ hr. blood perfusions when only glucose is supplied as exogenous substrate. When lactate & pyruvate are also infused at constant rate, the natruresis & phosphaturia are both minimized. Aldosterone addition then significantly increases the % F_{Na} resorbed to about 98.5% but does not influence the % F_{PO_4} excreted (about 6-9%). This progressive phosphaturia is, however, prevented by L-proline infusion (about 1-4% of F_{PO_4} excreted, at equal PO_4 loads) with only slight further increase in the % F_{Na} resorbed (to 99%). Thus, aldosterone augments Na resorption in isolated kidneys supplied with lactate & pyruvate without influencing PO_4 resorption and exogenous metabolizable substrates can augment PO_4 resorption disporportionate to their augmentation of Na resorption. These results suggest for the dog kidney that 1) the aldosterone effect on Na transport is mediated by a Na permease-like action (Sharp & Leaf) rather than by making more energy or ATP available for transport (Edelman)--hypotheses from toad bladder studies -- and 2) tubular PO_4 resorption may be rate-limited by a high-energy carrier system. (Supported by NIH grant HE 06092 & Ky. Heart Assoc. Chair Cardiovascular Research).

RESPONSE OF LARGE HINDLIMB VEINS OF THE DOG TO CHANGES IN TEMPERATURE. M. M. Webb-Peploe* and J. T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

In anesthetized dogs respired with oxygen, the lateral saphenous vein was cannulated at the ankle and perfused at constant flow with autologous arterial blood. Inflow and popliteal vein pressures were measured; alterations in the difference between these pressures were due to changes in venomotor activity. The venoconstrictor responses to electric stimulation of the lumbar sympathetic trunk (8-10 volts; 0 delay; 1 msec duration; 2, 6, and 10 cps) and to norepinephrine infusions (5, 10, and 20 μg base/min) were determined with perfusate temperatures of 42, 37, 27, and 17 C. Compared to 37 C, the venoconstriction with stimulation and drug infusion was slightly increased at 27 C and greatly reduced at 42 and 17 C. With sympathetic nerves intact, cooling the perfusate from 37 to 17 C caused the perfusion pressure to increase from 28 to 77 mm Hg; warming it from 37 to 47 C decreased the pressure from 28 to 8 mm Hg. Most of the venoconstriction occurred in cooling from 37 to 27 C, and most of the dilatation on warming from 37 to 42 C. The venoconstriction with cooling is reflex, in part, since lumbar sympathectomy reduced the response by 60%. The reflex may be initiated by receptors in the leg and is abolished by pentobarbital but not by chloralose anesthesia. (Supported by NIH Grant HE 05883.)

PERIPHERAL AUTONOMIC PATHWAYS TO THE HEART OF THE DOG: LOCALIZATION AND SYNAPTIC CONNECTIONS. James S. Wechsler*, John B. Pace* and Walter C. Randall. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

Sympathetic innervation pathways to the heart of the dog are known to include diffuse projections from the upper thoracic and stellate, caudal cervical and superior cervical ganglia. Also, evidence is accumulating for sympathetic outflows from cervical segments of the spinal cord. In this study myocardial force changes caused by electrical stimulation of selected cardiomotor nerves are monitored by multiple strain gauge arches sutured to the epicardial surface. Atropine and nicotine or hexamethonium are used to produce ganglionic blockade since these agents alone do not consistently produce complete interruption of ganglionic transmission. Electrical stimulation of cardiac nerves, central and distal to visible ganglia, before and after administration of blocking agents, permits localization of specific synapses. Motor responses include both positive and negative inotropic alterations in individual chamber performance, accompanied by either positive or negative chronotropic effects. This work shows the presence of synaptic connections in each of the stellate, caudal cervical and superior cervical ganglia. Before ganglionic blockade, stimulation of the vagosympathetic trunk distal to the caudal cervical ganglion elicits combinations of positive and negative inotropic responses from the atria and ventricles with either cardiac slowing or acceleration. Responses may differ from area to area on the same chamber as well as from chamber to chamber. (Supported by NIH Grant HE 08682.)

RED CELL MASS-ARTERIAL OXYGEN RELATIONSHIP IN NORMAL MAN. J.V. Weil,* G. Jamieson,* D.W. Brown* and R.F. Grover. Cardiovascular Research Lab., University of Colorado Medical School, Denver, Colorado.

The relationships between arterial blood oxygenation and red cell mass (RCM), plasma volume (PV), and hematocrit (Hct) were examined in 73 normal men residing at three altitudes: sea level (n=16), 1600 m (n=19) and 3100 m (n=39). RCM was measured with autologous Cr^{51}-labeled red cells, PV was calculated from the peripheral Hct, and arterial oxygen saturation (SaO_2) and tension (PaO_2) were measured directly. Ranges in data were: SaO_2 97.3 - 83.4%, PaO_2 96.0 - 46.5 mmHg, RCM 22.4 - 41.8 ml/kg, PV 24.4 - 47.4 ml/kg, and Hct 41.3 - 59.5%.

Hematocrit was inversely related to SaO_2 (r=-.61). However, since Hct is the ratio RCM/(RCM + PV), it is an insensitive indicator of changes in RCM. For example, at Hct 50% and constant PV, doubling RCM would increase Hct by only one third. PV was variable and bore no significant relationship to SaO_2 (r=-.10).

RCM was highly correlated with SaO_2 (r=-.75, $p < .001$) and increased in a simple linear fashion with decreasing SaO_2; RCM (ml/kg) = 125 - 1.04 SaO_2. In contrast, RCM remained unchanged over the range of PaO_2 from 96 to 67 mmHg. Only at lower values of PaO_2, from 67 to 46 mmHg, did RCM increase with a high degree of correlation with PaO_2 (r=-.77). Thus, only those reductions in PaO_2 which lowered SaO_2 produced an increase in RCM. This suggests that erythropoiesis is influenced more by oxygen transport (SaO_2) and tissue oxygenation than by PaO_2.

INTRACELLULAR OXYGEN TENSION (pO_2) OF SKELETAL MUSCLE DURING VASCULAR REFLEXES. Gerald K. Weiss and Edward S. Kirk (intr. by C. L. Prosser). Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

Vasodilation, caused by release of sympathetic tone, is associated with stimulation of oxygen consumption in resting skeletal muscle. The increase in blood-tissue exchange of Rb^{86} that occurs during the dilation suggests that increased metabolism is caused by increased oxygen delivery rather than by direct stimulation of the metabolism (Acta Physiol. Scand. 54: 241, 1962). If this is so, pO_2 in the tissue must increase during the dilation. To test this hypothesis we measured changes in intracellular pO_2 with a modification of Millikan's spectrophotometric method (Proc. Roy. Soc. 123: 218, 1937). Two photoresistors with appropriate filters measured shifts in the transmission spectra of intact muscle. These shifts indicate changes in the saturation of myoglobin which is responsive to intracellular pO_2. In anesthetized dogs the circulation to a gracilis muscle was isolated and blood flow was maintained constant with a pump. Varying the pressure in an isolated carotid sinus caused reflex changes in vascular tone: vasodilations were accompanied by increases in muscle pO_2, while vasoconstrictions resulted in a decrease. Corresponding results were obtained during acetylcholine dilations and norepinephrine constrictions. Our data support the hypothesis that changes in blood-tissue diffusion of oxygen cause changes in metabolism. In at least some parts of resting muscle, metabolism appears to be limited by the availability of oxygen.

EFFECTS OF MANNITOL ON THE RENAL CIRCULATION DURING HEMORRHAGIC HYPOTENSION. Michael G. Wendling*, John W. Eckstein and Francois M. Abboud. CV Res. Labs., U. of Iowa Coll. of Med., Iowa City, Iowa.

Observations on mean arterial pressure, blood flow (electromagnetic flowmeter) through the left renal artery and urine flow from the left ureter were made on eight dogs anesthetized with pentobarbital. Four dogs received continuous intravenous infusions of 18% mannitol at a rate of 7.6 ml/min; the others received normal saline at the same rate. All dogs were bled slowly until urine output stopped. Arterial pressure averaged 70 mm Hg and renal blood flow averaged 135 ml/min when anuria occurred in dogs given saline. Anuria in dogs given mannitol occurred at an average arterial pressure of 30 mm Hg and an average renal blood flow of 20 ml/min. Plasma proteins and hematocrit averaged 5.1 gm % and 39.3% respectively in the saline group; corresponding averages in the mannitol group were 4.3 gm % and 27.0%. It was possible to lower arterial pressure to 20 mm Hg in one animal in the mannitol group before anuria occurred. In this dog the calculated osmotic pressure of the plasma proteins was 9 mm Hg; renal interstitial pressure was 4 mm Hg. Glomerular capillary pressure must have been less than 20 mm Hg. It appears that urine can be formed when the net pressure favoring glomerular filtration is in the vicinity of 7 mm Hg and renal blood flow is about 20 ml/min. (Supported by USPHS grants HE-02644 and HE-09835.)

Experimental Hypoxic Pulmonary Edema in the Rat. T.F. Whayne, Jr.* and J.W. Severinghaus. Cardiovasc.Res.Inst.,Univ.of Calif.Med.Ctr.,San Francisco, Ca.

An experimental animal model is needed to study the mechanism and site of formation of hypoxic pulmonary edema seen at high altitude in man. Long Evans rats were sacrificed after 10 minutes of exercise induced by swimming in water at 36°C while breathing 8-10% O_2. 8.5% O_2 appeared optimal. At 8% O_2, 20 of 40 rats were unable to swim 10 minutes, and were sacrificed when they remained under the surface for 5-10 seconds. A high concentration of methylene blue in the water disclosed no aspiration except in rats allowed to drown. Microscopic interstitial pulmonary edema formed in the majority of hypoxic rats and in a few air breathing exercised controls. The predominant form was patchy eosinophilic cuffing around medium sized arteries and veins. The eosinophilia suggests the presence of protein. Peribronchial, lymphatic and alveolar edema were uncommon. Perivascular edema formation was recorded only when it was clearly present, as follows: Weight 150-225 gms: air, 2/16 (2 of 16 rats had edema); 10% O_2, 1/6; 8.5% O_2, 6/8; 8% O_2, 16/26. Weight over 225 gms: air, 0/4; 8% O_2, 5/14. Hemorrhages were frequently noted under the visceral pleural and occasionally on the cut lung surfaces: air, 3/21; 10% O_2, 3/6; 8.5% O_2, 3/8; 8% O_2, 18/40. Erythrocytes were also noted in the perivascular edema fluid of 3 rats. In hypoxic rats, wet lung weight, whether related to dry weight or total body weight, was slightly but not significantly higher than controls. Dyes and tracers are being used to determine whether hypoxic pulmonary edema formation is trans-arterial or trans-capillary. Neither india ink nor a stainable protein of MW 40,000 (horseradish peroxidase) has been found traversing arterial walls. (Research supported in part by USPHS HE 06285).

RAPID BRAIN COOLING AFTER CARDIAC ARREST WITH A SIMPLIFIED CAROTID PERFUSION SYSTEM. Robert J. White, M.D., Ph.D., M. S. Albin, M.D.*, G. E. Locke, M.D.* and David Yashon, M.D.*, Brain Research Laboratory, Division of Neurosurgery, Western Reserve University School of Medicine at Cleveland Metropolitan General Hospital, Cleveland, Ohio 44109.

Emergency measures (e.g., external cardiac massage) to restore circulation following cardiac arrest result in only a small patient salvage because of the sensitivity of brain to anoxia. Temperature reduction is known to exert a protective effect on cerebral tissue during circulatory deprivation. Toward designing a simple in-hospital technique of intravascular perfusion for rapidly cooling the brain during resuscitation, the cerebral cooling characteristics of arterialized blood, 6% Dextran and Saline (all at 1°C) administered intracarotidly were studied. In 19 heparinized, cardiac arrested dogs (av. wt. 11 kg.) the carotid arteries were punctured with #15 Rochester needles connected by plastic tubing to I.V. bottles containing the cooled perfusate. Fluids were delivered (av. pressure 75 mmHg.) by an attached standard sphygmomanometer bulb.

		AVERAGE INTRACEREBRAL TEMPERATURES °C.						Total Vol.
#Dogs	Fluid(1°C)	5	10	20	25	30	Time(min.)	cc Perfusate
5	Blood	32.5	29.0	23.0	21.7	20.6		1,600
7	Dextran	31.9	26.4	18.7	17.3	14.6		2,100
7	Saline	33.4	27.2	19.6	17.5	16.5		3,450

With large perfusate volumes, brain cooling is evidenced with this simple method; however, the canine cephalic vasculature is an inefficient hydraulic system for differential brain hypothermia. In a human case of cardiac arrest, intracerebral temperature of 42°C was reduced to 32°C in ten minutes with an intracarotid perfusion of 1°C Dextran.

THE INFLUENCE OF MAGNESIUM ON THE ESTROGEN-HISTAMINE RELATIONSHIP. C. F. Whitfield* and M. E. Tidball. George Washington University School of Medicine, Washington, D. C.

Histamine has been reported to be a mediator in the action of estrogen on the uterus. Histamine metabolism has also been reported to be altered in magnesium deficiency in rats. Therefore histamine and magnesium were measured in the uterus and skeletal muscle of intact and ovariectomized female Sprague-Dawley rats fed diets containing 650 ppm magnesium (control) or < 20 ppm magnesium (deficient). Ovariectomy resulted in progressively increasing uterine histamine from 7 μg to 30 μg/gm dry weight at 65 days. Muscle histamine was unaltered by ovariectomy (mean = 7 μg/gm). Magnesium deficiency in both intact and ovariectomized animals resulted in decreased uterine and muscle histamine to < 2 μg/gm. All animals fed the magnesium deficient diet also exhibited decreases of 25-50% of the magnesium content of both tissues. Thus decreased tissue magnesium was always associated with decreased tissue histamine, whereas estrogen deficiency was associated with either an increase or no change in tissue histamine. These results suggest that magnesium is a primary determinant of the level of tissue histamine and is thus more important than estrogen in the regulation of uterine histamine content.

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EFFECTS OF RESERPINE ON DIET INDUCED CALCIFIC ATHEROMATOUS AORTIC LESIONS. Peggy J. Whittington,* Ben R. Clower* and Oliver Carrier, Jr. Univ. Miss. Med. Ctr., Depts. of Anatomy and Pharmacology, Jackson, Miss.

Twenty rabbits weighing 2-3 kg were fed a standard pellet diet to which was added a cholesterol supplement of 2% by weight for 11 weeks with 10 receiving injections of vasopressin and 10 receiving injections of vasopressin and reserpine. Ten rabbits weighing 2-3 kg were fed a standard pellet diet while ten rabbits were fed a standard pellet diet and were additionally treated with vasopressin. The calcium content of rabbit aortae receiving vasopressin and cholesterol [8.57±0.73 mEq Ca^{++}/kg fat free dry wt.] was significantly higher ($P < 0.001$) than that of the aortae of rabbits receiving reserpine [4.07 mEq Ca^{++}/kg fat free dry wt.]. The aortae of normal rabbits contained 6.68±0.38 mEq Ca^{++}/kg fat free dry wt. while the aortae of rabbits on a standard pellet diet and receiving vasopressin contained 6.69± 0.39 mEq Ca^{++}/kg fat free dry wt. Both of these values were significantly higher than those of the reserpine treated group. Histological results showed organized atheromatous plaques within the intimal layer of the aortae in the vasopressin and cholesterol group. These atheromatous lesions contained large deposits of lipid material and traces of calcium. Reserpine treated animals, rabbits on a normal diet, and rabbits on a normal diet receiving vasopressin showed no aortic lesions. These results indicate that reserpine has a vascular action in vivo affecting fat and calcium. Supported by USPHS Grant HE 09031, and CIBA Pharmac. Co.

RECEPTIVE FIELDS IN CAT SUPERIOR COLLICULUS. B.Wickelgren & P.Sterling (Intr.by D.H. Hubel & T.N.Wiesel). Harvard Medical School, Boston.

Using natural stimuli we have studied the visual receptive fields of 100 single units in the superior colliculus of cats lightly anesthetised with pentothal and paralyzed with succinylcholine. Electrolytic lesions and subsequent histology showed that all of the units were located in the 2 most superficial cellular laminae. Most receptive fields lay in the contralateral half of the visual field and ranged from a few degrees in diameter in the area centralis to 20° or more in the periphery; a few receptive fields lay in the ipsilateral half of the visual field. The majority of the units could be driven about equally from either eye,though often the contralateral eye was somewhat dominant. Most responded poorly or not at all to changes in background illumination or to stimuli turned on or off within their receptive fields. The best responses were elicited with moving stimuli,which for most units could be either brighter or darker than background. The sizes, shapes, rates and directions of movement of the stimuli were critical. An optimal stimulus orientation could be demonstrated for many units but this requirement was less stringent than it is in the visual cortex. More than half of the units responded best to movement in only one direction and of these,87% preferred movement from the center of gaze toward the contralateral visual field. Thirty-nine collicular units in 3 cats whose visual cortex had been removed 1-3 weeks previously showed no directional or orientational preferences and most responded briskly to "on" and/or "off" of stationary light spots. These units could not be driven equally from either eye but exhibited strong preferences for one eye or the other. The results suggest that the orientational and directional preferences and the binocular interactions exhibited by units in the normal colliculus are dependent on a cortico-collicular pathway.

EFFECT OF MOVEMENT AND LEVEL OF AROUSAL ON CLICK-EVOKED RESPONSES IN CATS. Warren O. Wickelgren (intr. by Robert Galambos) Dept. of Psychology, Yale University, New Haven, Conn. 06510

The effects of movement and level of arousal on click-evoked responses were studied in 2 experiments. Responses from cochlear nucleus (CN), superior olive (SO), inferior colliculus (IC), medial geniculate (MG), auditory cortex (AC), and cerebellar vermis (CV) were recorded from cats whose middle ear muscles had been bilaterally cut. The clicks were presented by earphones in order to hold acoustic input constant. The effect of quiet movement on click-evoked responses was tested by forcing cats to walk on a motor-driven treadmill. Computer-summed responses during walking were compared with responses during resting on a platform above the moving treadmill. There were no differences between the responses recorded along the classical auditory system (CN, SO, IC, MG, and AC) in the 2 conditions. Responses from CV, however, were greatly attenuated during walking. Click-evoked responses were also recorded during various states of arousal (wakefulness, drowsiness, slow-wave (SW) sleep, and rapid-eye-movement (REM) sleep). Level of arousal had no effect on responses from CN, SO, and IC. Responses from MG and AC were of larger amplitude and different waveform during drowsiness and SW sleep than during wakefulness and REM sleep. Responses from CV were largest during wakefulness and smallest during SW sleep. During the drowsy and SW sleep states click rates over 6/sec produced large "augmenting" responses at MG and AC. These "augmenting" responses, unlike normal click-evoked responses at MG and AC, could be abolished by any slight movement by the animal or by novel visual stimuli. (Supported by NSF G 23584.)

COLLOID SHOCK IN THE DOG. V.T. Wiedmeier*, J.M. Lubitz* and J.J. Smith. Departments of Physiology and Pathology, Marquette University School of Medicine, Milwaukee, Wisconsin.

It is commonly held that reticuloendothelial system (RES) blockade is importantly concerned with the mechanism of irreversible shock, although how it contributes to the circulatory failure is unknown. On the possibility that 'artificial' blockade might be useful in studying this problem, the circulatory and hematologic effects of large doses of various-sized colloids were determined in the Nembutalized (30 mg/kg) dog. Intravenous injection (over exactly 5 min) of polystyrene latex (PSL, 880Å, 188 mg/kg), ThO_2 (Thorotrast, 80Å, 8 ml/kg) and saline-in-gel usually caused a sudden but transitory hypotension, a moderate, temporary hemodilution and an abrupt leukopenia with rebound within 2 to 4 hours; PSL, ThO_2 and saline-gel caused no serious hemodynamic effects or fatalities. However, about 90 minutes after injection of SiO_2 (Syton, 450Å, 350 mg/kg) or colloidal carbon-in-gel (CCG, 250Å, 160 mg/kg), there usually began a tachycardia and tachypnea with a pronounced progressive hypotension, usually fatal (mortality--100% with Syton, 71% with CCG). After Syton and CCG there was a typical leukopenia but with delayed recovery and often lymphocytosis, a progressive hemoconcentration, an accumulation of the colloid within the leukocytes and phagocytic cells of liver, spleen and lung with consequent autolysis of some cells. The findings suggest that circulatory failure may be associated with a toxic action of the colloid on the leukocytes and RES cellular elements with subsequent leukocytic sequestration and disintegration.

The influence of hypercapnia and vagal inactivation on the ventilatory effects of sinus nerve stimulation. W. Wiemer* and P. Kiwull (intr. by P. Kezdi), Ruhr-University, Bochum, Germany.

In rabbits rebreathing oxygen one carotid sinus nerve was stimulated repeatedly by electrical stimuli of constant intensity, both before and after inactivation of vagi by cold blocking or sectioning. Respiration, end-tidal P_{CO2} and arterial blood pressure were recorded. In animals with intact vagi the reflex hyperpnea elicited by the nerve stimulation decreased only slightly with increasing hypercapnia. After inactivation of the vagi the stimulatory effect was, at normal P_{CO2}, mostly greater than in the intact condition. With increasing hypercapnia the decrease of the reflex hyperpnea was generally steeper than in the intact preparation, sometimes reaching even lower values than before inactivation. It is concluded that the ventilatory effect of chemoreceptor afferents is modified both by blood P_{CO2} and by vagal afferents, probably originating in stretch receptors in the lungs.

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CARDIOVASCULAR-VENTILATORY REFLEXES FROM THE ISOLATED LEG: EFFECTS OF INTRA-ARTERIAL INFUSIONS OF POTASSIUM. K. Wildenthal*, D.S. Mierzwiak*, N.S. Skinner, Jr. and J.H. Mitchell. U. Tex. Southwestern Med. Sch., Dallas, Texas.

In 7 chloralose-anesthetized, closed-chest dogs, the right hind limb was vascularly isolated, leaving femoral and sciatic nerves intact. While venous outflow was clamped for 60 seconds, KCl (0.3-1.0 mMole) was infused close arterially during the first 15 seconds of the period of venous occlusion. In addition to increasing minute ventilation, these KCl infusions caused significant elevations of blood pressure (BP) and heart rate (HR). Femoral venous blood K^+ following infusion of KCl ranged from 4.7 to 10.7 mEq/L (1.2 to 6.7 mEq/L above control levels). Results from 31 infusions were as follows: mean increases of 7.2 $\pm$ 1.1 (SE) beats/min in HR ($p < 0.001$), 13.3 $\pm$ 1.7 mm Hg in mean arterial BP ($p < 0.001$), 785 $\pm$ 140 ml/min in ventilation ($p < 0.001$), 1.7 $\pm$ 0.5 breaths/min ($p < 0.005$), and 45 $\pm$ 13 ml in tidal volume ($p < 0.005$). Magnitude of the changes appeared to be dose related. No changes in HR, BP, and ventilation were seen after intracutaneous, subcutaneous and intramuscular injections of similar amounts, nor after other painful stimuli. When ventilation was controlled with a respirator and the dogs anesthetized to the point of apnea, BP and HR responses to intra-arterial K^+ persisted, indicating that these changes were not consequent to hemodynamic alterations resulting from augmented ventilatory activity. Cutting the nerves from the leg abolished the changes with KCl infusion. (Supported by USPHS HE 06296 and HE 07717 and the Dallas Heart Association.)

A PHYSIOLOGICAL APPROACH TO ASSIST THE CIRCULATION. C. Wildevuur, S.D. Moulopoulos, J. Kolff, and M.J. Crosby (intr. by P.A. Khairallah). The Cleveland Clinic Foundation, Cleveland, Ohio.

Assisted circulation is an approach to sustain life of a patient who otherwise will die from an insufficient circulation caused by a failing heart. Two problems have to be considered: (1) How to restore a normal circulation. In these cases an insufficient circulation is manifest by a high atrial pressure and a low cardiac output. In this sense, assisted circulation should reduce atrial pressure and increase cardiac output. This can be done by placing in parallel with the heart, a bypass pump from atrium to artery. In order to restore a normal atrial pressure and cardiac output, a normal Starling's Law curve (function curve) has to be obtained by the sum of the function curves of both "hearts". In acute experiments of left heart bypass on sheep, this principle was tested. A diaphragm pump was used which during diastole was driven by air pressure, regulated by atrial pressure and that could have any desirable function curve by setting bias and amplitude in a TR-10 computer (NASA driving system). A failing heart was induced by ligating the anterior descending branch of the left coronary artery. When the left atrial pressure rose in the failing heart, the bypass pump was automatically activated so that atrial pressure and cardiac output returned to and were maintained at normal levels. (2) The effect of this type of assisted circulation on the failing heart. When the assisted circulation is not proportional to the failing circulation, we encountered reversible arrythmia occasionally leading to ventricular fibrillation. Recovery of the failing heart can be indicated when the function curve of this heart returns to normal. In these short-term experiments we have been unable to detect improvement in the function curve of the failing heart during bypass pumping. (Supported by N.I.H. grant HE04448 and The Cleveland Clinic Foundation)

CARDIORESPIRATORY RESPONSES OF TWO "GENETIC" TYPES OF CATTLE TO HYPOBARIA. D. H. Will, C. S. Card*, G. D. Vandlandingham* and A. F. Alexander. Colorado State U., Fort Collins, Colo.

Cattle exposed to high altitude are known to develop a pulmonary hypertension varying from moderate to marked and in some cases, congestive right heart failure i.e. high mountain or Brisket disease. In an effort to explain these variations, two different "genetic" groups of fifteen adult female cattle, native to 10,000 ft. were selected based on the presence or absence of high mountain disease in their history and were mated to males of similar background. Their offspring, designated "susceptible" and "resistant" were the two experimental groups studied. Cardiorespiratory measurements were made on both groups at 10, 30, 60 and 90 days of age at 5,000 ft. (Ft. Collins altitude), and also restudied at 10 and 90 days of age after two hours at a chamber altitude of 15,000 ft. The most striking data were the significantly lower levels of pulmonary arterial pressure observed in the resistant group, at all measurement times. At 5,000 ft., the average group mean pressures were 9, 8, 9 and 6 mm Hg below that of the susceptible animals. At 15,000 ft., the increase in pressure and final level of pulmonary hypertension were also less in the resistant group. Resistance to pulmonary blood flow was the main reason for these differences. At both altitudes, the susceptible calves showed greater lung ventilation; however, they consistently had a greater decrease in oxygen content and saturation of both arterial and venous blood at 15,000 ft. The susceptible group showed a greater reduction in the tissue a-v oxygen gradient at 15,000 ft. Blood pH changes related closely to the different respiratory responses. The results suggest that variations in functional characteristics obtained by studying prepotent, homogeneous populations may explain individual responses to high altitude.

ELECTRICAL PROPERTIES OF THYROID FOLLICLES. J.A. Williams (intr. by J.W. Woodbury). Dept. of Physiol. and Biophys., Univ. of Wash. Seattle, Wash.

Electrical properties of the thyroid follicle were studied in the perfused rabbit thyroid. Current pulses of a few nanoamp were passed through the microelectrode as it was advanced into the gland. Three regions were found: (i) A nonpolarizable compartment with a steady potential of 0 mV is assumed to be extracellular space; (ii) a polarizable compartment at 0 to -10 mV is attributed to lumina; and (iii) a polarizable compartment at -25 to -50 mV is attributed to cells. Mean input resistances of cells and lumina are 9.4 and 5.6 mΩ respectively; both have a capacitance of .07 nF. A histologically measured follicular diameter of 50 μ gives specific membrane capacitance of 1.8 $\mu F/cm^2$. Follicular wall resistance is 440 Ω - cm^2. If intercellular resistance is assumed negligible the specific membrane resistance of follicular membrane is about 220 Ω - cm^2. The cellular measurements are consistent with the hypothesis that follicular cells are connected by low resistance bridges, as shown for other types of epithelia. Removal of Ca^{++} from the perfusate had no effect, but removal of Ca^{++} with addition of 3 mM EDTA caused input resistance to drop to 3 M Ω in lumina and increase to 15 to 20 M Ω in cells. This is consistent with a decreased specific membrane resistance and a partial uncoupling of cellular junctions. Cellular potentials also decreased to 0 to -20 mV in 40 min. These effects were at least partially reversible when Ca^{++} was replaced. (Supported in part by USPHS Grant NB 01752.)

COLD RESISTANCE OF Na,K STIMULATED ATPase IN KIDNEY CORTEX OF HIBERNATING RODENTS. J. S. Willis and Nancy Ma*. Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

Cells of kidney cortex of hibernating rodents (hamsters and ground squirrels) accumulate K at 5°C at a rate greater than do those of non-hibernating rodents (rats and guinea pigs). The present study sought to determine the activity of Na,K-stimulated ATPase at various temperatures in kidney cortex of rats and hamsters. The total ATPase activity of the nuclear-mitochondrial fraction of homogenates of kidney cortex was determined by release of P^{32} from γ-labelled ATP^{32} in a reaction mixture containing 100 mM-Na, 10 mM-K, 4 mM-Mg, 4 mM-ATP and 40-mM Tris (pH 8 at all temperatures). The Na stimulated portion of this total was determined by subtracting the rate of ATP hydrolysis in a Na-free reaction mixture (containing 140 mM Tris).

The net Na-stimulated activity of rat kidney decreased from 9.55 m-moles Pi/mg protein/hr. at 37° to 0.20 at 15°C, while that of hamster decreased from 19.76 to 1.39 over the same range. The fraction of total activity represented by this Na,K-stimulated portion was 37 per cent at 37° and 6 per cent at 15° in the rat, and it was 61 per cent and 46 per cent respectively in the hamster. At 10°C there was no significant Na, K stimulated activity in rat kidney ($P>0.4$ for 7 cases) whereas in hamster kidney that activity was highly significant at 10°C (0.42 ± 0.07, $P<0.001$ for 7 cases) and still possibly significant at 5°C (0.09 ± 0.04, $P<0.05$ for 13 cases). While it appears that Na,K ATPase activity of kidney cortex of hamsters is less affected by low temperature than that of rat, it is also true that in hamster the fourteen-fold decrease in ATP hydrolysis between 15° and 5° is much greater than the four-fold decrease in rate of K transport observed under comparable conditions. Disruption of the cell may, therefore, lead to some loss of apparent cold resistance at the enzymatic level. (Supported by USPH GM11494).

DISSOCIATION OF ERYTHROPOIETIN-PROTEIN COMPLEXES WITH ACID. J. Winkert and E. Winkert*. Meharry Med. Col. Sch. of Med., Nashville, Tenn. and State Univ. of N.Y. Sch. of Med., Buffalo, N.Y.

Erythropoietin (ESF) is generally regarded as the principal hormone involved in the physiological control of erythropoiesis and which, after being synthesized at least partly by renal tissue in response to hypoxic stimuli circulates to erythroid organs where it initiates red cell development at an early stage. How ESF achieves its effects is not clear but early actions on RNA synthesis (Goldwasser 1964) and on the priming of RNA synthesis by DNA-protein (Winkert 1966) suggest that the process of inducing erythropoiesis may involve alterations in gene activity. The nature of ESF is not yet clear although it is generally conceded to be a glycoprotein. Estimates of its molecular size have ranged from 5500 (Goldwasser, 1962) based on tryptophane residues, to 28,000 (Rosse, 1962) based on radiation target theory, to 39,900(White, 1959) based on its ultracentrifugal behavior. The fact that ESF readily appears in many protein peaks or bands, eg. five from a DEAE-cellulose column and two in a Sephadex G-200 column (Winkert 1964) and in both the albumin and post-albumin bands separated by acrylamide gel electrophoresis suggests that discrepancies in molecular size estimates may be due to erythropoietin-protein aggregations. An attempt was made to use a strong hydrogen ion concentration in order to rupture some of the bonds which may contribute to protein-protein interactions. Although acid labile at 37°C it was found possible to dissociate human urinary ESF at a pH of 2.5 on a Sephadex G-200 column run at 4°C for 3 hours. The biological activity shifted from a 50,000 molecular weight fraction into one which was completely included by the gel which has a limit for complete inclusion of molecules with a molecular weight of 5,000. Supported by N.I.H. grant HE-09540-01.

THE CAUSE OF HYPERTENSION IN PHEOCHROMOCYTOMA. Robert L. Wolf, Milton Mendlowitz, Julia Roboz*, Eric Naftchi* and Gordon Bautz*. The Mount Sinai School of Medicine and The Mount Sinai Hospital, New York, N.Y.

Hypertension in pheochromocytoma has been related to increased secretion of the catecholamine, norepinephrine (NE), from the tumor. In order to test this hypothesis we administered a daily, oral dose of 50 mg of guanethidine for 1 week to a patient with a solitary, benign pheochromocytoma and performed separate assays for urinary, diurnal normetanephrine (NM), metanephrine (M) and 3-methoxy-4-hydroxymandelic acid (VMA). NM and M were separately assayed by high-voltage electrophoresis after (a) hydrolysis at pH 1.0, (b) adjustment of the pH of the hydrolysate to 6.5, (c) absorption on an Amberlite CG-50 resin column, (d) elution with 4N NH_4OH, (e) evaporation of the eluates *in vacuo* and, (f) extraction with ethyl acetate at pH 11.0. The concentrations of NM, M and VMA (ug per mg of creatinine) in the pheochromocytoma urine, before the administration of guanethidine were 0.20 (normal mean value: 0.11), 0.51 (normal mean value: 0.12) and 11.0 (normal mean value: 1.8), respectively. Following the administration of guanethidine, there was a reduction in urinary excretions of NM, M and VMA of at least 50 per cent concurrent with a sustained blood pressure rise from normal to hypertensive levels. These results indicate that the hypertension associated with pheochromocytoma may not be caused by the increased secretion of NE by the tumor.

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IN VITRO STUDIES OF HUMAN ECCRINE SWEAT GLANDS. Sidney M. Wolfe*, Gary W. Cage*, Ronald H. Thompson, Lois W. Tice*, and Robert S. Gordon, Jr. Natl. Inst. Arth. & Metabol. Dis., Bethesda, Md.

Human eccrine sweat glands were obtained by microdissection from surgical or biopsy specimens of skin. Vital staining with methylene blue or toluidine blue facilitated the dissection. The glands were incubated in a small volume of Krebs buffer and the effects of compounds known to affect sweating were studied. The production of lactate, a compound known to be a major constituent of sweat, was followed as an index of glandular activity. Acetyl-β-methylcholine (Mecholyl) in concentrations as low as 10^{-6} M stimulated lactate production, usually by more than two-fold, and this effect could be inhibited by atropine. Epinephrine, at similar concentrations, was also found to stimulate lactate production. The amount of lactate produced (5-10 nM/gland/hour for up to 3 hours) is more than might be expected were stored glycogen the only source. Accordingly, experiments were performed with and without glucose and these demonstrated that glucose was necessary for optimal lactate production. In addition to being metabolically active, the sweat glands were shown by electron microscopy to have an intact ultrastructure. This system appears promising for further study of the relationship between the stimulatory effects of various neurohumors and metabolic activity in sweat glands. Studies are now in progress to determine whether the stimulation of lactate production by Mecholyl is mediated by activation of phosphorylase with increased glycogenolysis.

Development of a Dye Dilution Technique for Continuous Measurement of Regional Blood Flow. R.A. Wolthuis*, H.W. Overbeck*, and W.D. Collings, Depts. of Physiology and Medicine, Mich. State Univ., E. Lansing, Mich.

A dye dilution technique providing continuous measurement of human upper extremity blood flow would increase the flexibility of previously reported techniques (Physiologist 8:247, 1965). A dye cuvette is required which responds accurately at low blood withdrawal rates. It is also desirable that the recirculating dye concentration remain constant. Preliminary studies were made in 8 dogs and 2 men. In dogs the forelimb was completely isolated from the body. A blood pump was interposed between the femoral and brachial arteries so that limb blood flow was supplied solely by pump. Pump flow was varied over the range 20-200 ml./min. Total venous outflow from the limb flowed from cephalic and brachial veins into a reservoir and was returned to the dog by a second pump. Venous outflow rate was measured by graduated cylinders. Limb venous blood was sampled by withdrawing it from each vein in turn through a Gilson dye cuvette at 1.5 ml./min. At each forelimb perfusion rate indocyanine green (0.4 mg/min) was continuously infused into the arterial tubing upstream to a mixing chamber until a dye concentration plateau was achieved in downstream venous blood. Changes in recirculating dye concentration were calculated on the basis of the slope of the plateau. Flow values calculated from mean dye concentration in the two veins were compared to total venous outflow. In human subjects dye was infused at 0.4 mg/min. into an antecubital vein and sampled continuously from the contralateral antecubital vein. In 68 measurements in dogs the mean percent difference between actual and calculated flows was -0.54 ± 10.3(S.D.) %. In the two humans the recirculating dye level remained essentially constant and at very low concentrations (< 2 mg/l) over a two hour infusion period. Continuous recording of human upper extremity blood flow by this technique appears promising.

INFLUENCE OF THE AUTONOMIC NERVOUS SYSTEM ON AIRWAY CALIBRE AND ELASTIC RECOIL. A. Woolcock*, P. Macklem, J. Hogg*, & N. Wilson*. Joint Cardiorespiratory Service, Royal Victoria Hospital, Montreal, Canada.

We used the retrograde catheter technique in dogs to partition pulmonary resistance into peripheral, Rp, and central Rc, components in the following experiments. 1. During vagal stimulation. 2 After β-adrenergic block. 3. During vagal stimulation after β-adrenergic block. 4. Following vagotomy after β-adrenergic block. In expt. 1, Rc increased more than Rp in some dogs whereas in others the opposite was true. In dogs with an increase in Rp there was a proportionate increase in elastic recoil during vagal stimulation. In expt. 2, both Rp and elastic recoil increased in all dogs. In expt. 3, Rp increased more than Rc in all dogs, even those whose central airways constricted more during expt. 1. Expt. 4 reversed the increase in Rp and elastic recoil seen in expt. 2. These results indicate that vagal tone operates at all levels of the airway. Its effect on peripheral airways is masked by adrenergic mechanisms, which permit vagal tone to act without affecting elastic properties of lungs. (Supported by the John A. Hartford Foundation and the Defense Research Board of Canada.)

EFFECT OF HYPERLIPEMIC SERUM AND CORTICOIDS ON LIPID METABOLISM IN THE PERFUSED RAT LIVER. C.H. Wu,* A. Lemberg* J. Daunas,* B. Brodoff,* R. Levine and J.C. Penhos. Res. Found. Washington Hosp. Ctr.; Dept. of Med., G. W. Univ., Washington, D. C. and Dept. of Med., New York Med. Col., New York.

Livers obtained from "fed" or "fasted" rats were perfused with blood from "fasted" rats with and without the addition of corticoids (triamcinolone) and/or hyperlipemic serum (HLS).

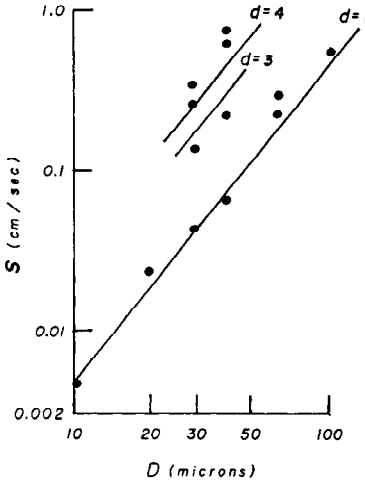
The addition of the hormone alone or with HLS to the perfusate in perfusions of "fasted" or "fed" livers reduced the levels of blood sugar and increased the levels of non-esterified fatty acids in the perfusate.

The output of triglycerides, phospholipids and cholesterol was reduced when the hormone was added to the perfusate. When HLS was added with triamcinolone the uptake of triglycerides, phospholipids and cholesterol was also reduced.

The levels of urea and ketone bodies in perfusions of "fed" and "fasted" livers with or without the addition of HLS were not affected when triamcinolone was added.

The magnitude of the effects noted were greater when a "fed" liver was used during the perfusion.

HYDRAULIC PROPERTIES OF THE PLEURAL SPACE SUGGESTED BY SEDIMENTATION OF THE TYPE ANTICIPATED FOR AN OPEN FLUID CHANNEL BY MICROSPHERES IN DOGS WITHOUT THORACOTOMY. C. C. Wunder, J. H. Reed, Jr.*, W. M. McConahey, III*, and B. H. Wood, Mayo Clinic and Mayo Graduate School of Medicine, Rochester, Minnesota.



In an attempt to partially resolve the different concepts concerning the nature of the pleural space (J. Appl. Physiol. 21:1500, 1966; Handbook of Physiol. III, Vol. 1, p. 403, 1964) spheres of varying density (d) were injected through narrow percutaneously inserted catheters and the sedimentation rates (S) observed by gamma emission of Yb^{169} or by roentgen videometry. Up to a sphere diameter (D) of 100 microns in the prone position, values for S complied with those predicted by Stokes' Law (solid lines) but not for D in excess of 1000 microns which preliminary optical measurements suggest may be the extreme limiting width of the space at mid-lung. (Supported in part by Research Grants NASA NsG-327 and NIH 1-F3-GM-4756.)

REVERSAL OF SWEAT RECRUITMENT PATTERNS. R.D. Wurster, C.R. Hassler*, R.D. McCook and W.C. Randall. Loyola University, Stritch School of Medicine, Department of Physiology, Chicago, Illinois.

In previous papers this laboratory has reported patterns of sweat recruitment in which sweating consistently first appeared on the lower extremities, proceeding in a rostral direction until sweating is present on all cutaneous surfaces. The appearance of local sweating appeared to be independent of local skin temperature. This phenomenon of differential sweat recruitment has obvious importance to the concept of setpoint determination of sweating. The problem is further complicated by alterations in recruitment patterns under conditions of different central and skin temperatures. Experiments were designed to test the influence of exposure of the upper half of the body to high ambient temperatures (60°C) while the lower half of the body was exposed to cool environments (20°C) and vice versa. Sweating was measured on seven cutaneous areas while oral, tympanic membrane, and rectal temperatures were recorded. Skin temperatures also were recorded, from which total, upper, and lower body mean skin temperatures were calculated. Heating the upper cutaneous areas (while cooling the lower) reversed the pattern of sweat recruitment. Heating of the lower half while cooling the upper half produced the usual caudal to rostral recruitment pattern. The interval between initial appearance of sweating on the lower and upper extremities could be extended by as much as 90 minutes. Theoretical explanation of the varying recruitment patterns and their relationship to set point control theory are discussed. (Supported by NIH Grant HE 08682.)

VISUAL RECEPTIVE FIELDS IN STRIATE CORTEX NEURONS OF AWAKE MONKEYS. Robert H. Wurtz, NIMH, Bethesda, Md.

Monkeys were trained to fixate a point on a screen for several seconds; this fixation minimized large voluntary eye movements while leaving the physiological nystagmus of normal vision unaltered. Deviations of the eyes from the fixation point were indicated by an electro-oculogram. Single unit activity was then recorded from striate cortex while the monkey sat in a primate chair with its head rigidly held. The receptive field of each unit was located during successive fixations by projecting white light stimuli onto the screen in various parts of the visual field Receptive fields studied were within 15 degrees of the fixation point; eyes were in the light adapted state. Many units responded vigorously to non-moving stimuli in the receptive field, and the responses continued without adaptation for the several seconds of the stimulus presentation, presumably in part because of the retinal movement produced by physiological nystagmus. Narrow rectangles of light, dark bars on a light background or the edge between light and dark areas were effective stimuli, being most effective in a particular orientation (vertical, horizontal, etc.) Receptive field centers as small as 2.0 by 0.5 degrees of arc have been found. Other units responded best to moving stimuli of a particular shape and orientation. The response of these units was frequently directionally specific, with excitation for stimulus movement in one direction and inhibition for movement in the other direction.

MUSCULAR CONTRACTION AND ELASTICITY OF ARTERIAL WALL. M. Wurzel and G.R. Cowper.*Dept.Physiology,University of Ottawa, and National Research Council, Ottawa, Canada.

Viscoelasticity of spirally-cut rabbit aortic strips suspended at 37°C in Ringer's solution was examined in the fully relaxed and in the contracted state. The results were interpreted with reference to a mechanical model consisting of a spring (of modulus E_1) and a dashpot (of viscosity V) in series,acting in parallel with a second spring of modulus E_2.Upon contraction E_2 was found to decrease to half of its value, E_1 to increase from zero to a maximum, and viscosity, likewise, to increase gradually from a negligeable value to a maximum at the fully contracted state.The effect of contraction on E_1, E_2,and V persisted even when the initial tension on the arterial wall was varied from 5 to 40 g/cm, i.e. up to physiological values of wall tension in vivo. Fibers contained in the arterial wall can be described as being built in twp ways: 1) contractile and non-contractile fibers connected in series,and 2) non-contractile fibers arranged independently of contractile fibers. Upon gradual stretch, an increasing number of elastic fibers are recruited, and therefore participate in the build up of resistance to an imposed external stretch; thus E_2 gradually increases. Upon contraction a part of the elastic fibers become more slack, and therefore, E_2 values become smaller. The increase of modulus E_1, upon contraction, from a negligeable level to a value comparable to E_2 can be attributed to stiffening of the contractile fibers. Gradual increase of viscosity observed with increasing contraction could be attributed to structural changes in the contractile matter itself, or to closer packing of fibers, i.e. to altered interfiber relations. Arterial wall contracted with norepinephrine cannot maintain its shorter length when submitted to rhythmic stretching, but it maintains it well when contracted with serotonin and histamine.Grants from MRC and Ontario Heart Foundation.

BLOOD GLUCOSE OXIDATION AND REPLACEMENT DURING PROLONGED EXERCISE IN MAN. D. R. Young. National Aeronautics and Space Administration, Ames Research Center, Moffett Field, Calif.

Experiments were performed in order to develop quantitative information with regard to glucose production and oxidation in the post-absorptive state. Male subjects were required either to walk on a treadmill at a workload approximately 1/3rd of the maximal work capacity, or to rest on a reclining couch for a period of 13-1/2 hr. Water and salt were provided regularly in order to avoid important dehydration. The level of blood lactate was low and uniform (10-12 mg/100 ml) during both test conditions. After 9 hr of rest or exercise, a steady state level of the blood glucose, glycerol, and free-fatty acids was maintained. Uniformly labelled ^{14}C-glucose was then administered as a single injection, and observations were made during the subsequent 4-1/2 hr period. In 10 resting subjects, the blood glucose level was 72 mg/100 ml, the glucose pool was 26.2±4.2 g, glucose turnover rate was 140±38.6 mg/kg/hr, glucose oxidation was 79.0±28.3 mg/kg/hr. During exercise, the blood glucose level was 69 mg/100 ml, the glucose pool was 28.3±5.9 g, glucose turnover was 206±55.8 mg/kg/hr, and glucose oxidation was 175±62.7 mg/kg/hr. These experiments demonstrate that during "alactic" work, the blood glucose is maintained at a constant level as a consequence of a brisk replacement rate commensurate with the elevated rate of glucose oxidation. The oxidation of at least 8-20 g of glucose per hour did not prevent a minor ketonuria in exercising subjects.

DEUTERIUM ISOTOPE RATE EFFECTS WITH IN SITU ACETYLCHOLINESTERASE IN THE VAGAL HEART SYSTEM. Wei Young. Bio-Medical Division, Lawrence Radiation Laboratory, University of California, Livermore, California.

The recognition of the central role of acetylcholinesterase (AChE) in the action of important synaptic transmitter, namely, acetylcholine (ACh), has stimulated much research. Our recent demonstration of the in situ AChE kinetics (Biochim. Biophys. Acta, 64:60-64, 1962) may have contributed to a better understanding of some aspects of cholinergic mechanisms (Physiologist 9:324, 1966). The utilization of deuterium either replacing H_2O with D_2O or by replacing hydrogen on the substrate with deuterium, has been especially useful for probing the mechanism of enzyme action. The magnitude of the isotope rate effect when a hydrogen atom is removed or added in a rate determining step can be as large as 6-7. The ratio of K_H/K_D in the vagal heart system was found to be 5.7, when all the hydrogens in the ACh molecules were replaced by deuterium atoms. A lower K_H/K_D value was observed when the hydrogens were partially replaced. When 25%, 50% or 75% of the H_2O was replaced by D_2O, K_H/K_D was found to be 1.72, 2.63 and 3.12 respectively. Higher concentrations of D_2O inhibited the contracting system. These results suggest that transfer of a proton seems to be the rate limiting step. (Supported by U.S.A.E.C.)

COLD SURVIVAL OF SURGICALLY- AND RADIO-THYROIDECTOMIZED HAMSTERS. M.K. Yousef*, R.R.J. Chaffee, W.D. Robertson* and H.D. Johnson. Depts. Dairy Husb., Zool. and the SSRC, Univ. Mo., Columbia, Mo.

Earlier studies (Chaffee et al, Am. Zool. 3, 538) showed that surgically thyroidectomized (Thx) hamsters unlike rats (You and Sellers, Endocrinology 49:374) are highly resistant to prolonged cold. These studies were made to see if there is evidence for the presence of any ectopic thyroid tissue in the Thx hamsters. Three groups of hamsters were exposed to 8°C below zero. Group I were controls, Group II were surgically Thx, and Group III were Thx using I^{131}. O_2 consumption (MR) and body weights (BW) were measured before and after exposure. Plasma protein-bound-Iodine (PBI) was determined in all groups. The PBI in Group II was significantly lower than in Group I and higher than in Group III. These studies indicate that hamsters may have ectopic thyroid tissue. Cold caused a significant increase in MR and a decrease in BW in all 3 groups, indicating that increased MR can occur sans an increase in thyroid activity. Animals in Group I and II survived for more than 9 days; however, 68% of the animals in Group III died within the first 72 hours of exposure. The survival data suggests that increased thyroid activity in cold exposure has no significant effect upon survival. The non-resistance of radio-Thx hamsters to cold may be due to quicker failure of thermogenic mechanisms. Supported in part by the SSRC of the U of Mo.; U.S. Army Med. Res. and Dev. Command, Dept. of the Army Contract No. DA-17-67-C0025; and USAF Aeromed. Res. Command, Contract F 29600-56-C-0009.

SITE OF FORMATION AND LACK OF SPECIES SPECIFICITY OF THE RENAL ERYTHROPOIETIC FACTOR (REF). Esmail D. Zanjani*, George W. Cooper*, Albert S. Gordon, Keith K. Wong* and Joseph F. Contrera*. Lab. Exp. Hematol., Dept. Biol., Grad. School of Arts and Sci., New York University, New York.

The REF, an enzyme capable of generating erythropoietin (ESF) when incubated with normal serum, was prepared from light mitochondrial extracts of kidneys from normal and hypoxic rats and rabbits, normal and renal artery-ligated dogs, normal pigs and humans. These tissues were first separated into cortical, medullary and cortico-medullary regions. Contamination of cortical and medullary regions with each other was prevented by removing the cortico-medullary portion. The ESF-generating capacity of the REF from each of these regions was assayed after incubation with normal EDTA-dialyzed serum in polycythemic mice. REF activity was found to be present in all fractions tested. Further division of cortical tissue into glomeruli and tubules revealed that the REF was distributed throughout the nephron. In addition, REF from any one of the above species was capable of generating ESF when incubated with serum of the other species. These findings provide evidence that the REF is produced in both the renal cortex and medulla and also that the ESF-generating system is similar and non-species specific within the mammalian group. (Supported by a grant from the NIH, HE03357-10).

Effect of hypothermia on renal function of the marmot, Marmota flaviventris. Marvin L. Zataman*, Esther P. Thompson*, and Frank E. South. Department of Physiology, University of Missouri School of Medicine and Space Sciences Research Center, Columbia, Missouri.

Hypothermia is known to depress renal function in mammals, but little is known of the effects of cooling hibernants. Clearances of Polyethylene Glycol (m.w. 3700), inulin, creatinine, and para-aminohippurate were determined prior to, during and following hypothermia (20°C rectal temperature). All clearances were reduced during hypothermia and increased toward initial values after the animal was rewarmed. Glucosuria resulted from hypothermia in all animals, while a diuretic response was not uniformly elicited. When diuresis occurred during hypothermia, urine osmotic pressures were reduced, but returned toward initial values when animals were rewarmed. (Supported by NIH grant: GM 13960).

ELECTRICAL ACTIVITY IN THE CAT NEUROHYPOPHYSIS. Guillermo Zeballos* and Alan B. Rothballer. Department of Physiology, New York Medical College, New York.

Electrical recording of the neurohypophysis was done to characterize its bioelectrically active elements and to use electrical activity as an indicator of the hypothalamico-hypophysial system's response to various influences. In cats anesthetized with chloralose, the pituitary gland and ventral hypothalamus were exposed transpharyngeally, the dura opened, and stainless steel micro-electrodes (tip diameter, 2μ; 50,000 Ohms) introduced directly into various portions of the neurohypophysis under visual control. Spontaneous activity was recorded, and that following electrical stimulation of the radial nerve and injection of hypertonic solutions into the carotid circulation. Continuous recordings of electrical activity within the neurohypophysis disclosed some relatively larger potentials (0.3 to 0.5 mV) of 2 to 4 msec duration, and others of lower amplitude and longer duration. Analysis of 10 sec. periods showed spontaneous discharge rates of 1-3/sec. at certain sites in the gland and frequencies of 0-0.7/sec. at others. These rates of discharge are within the range reported by others for hypothalamic units. Stimulation of the radial nerve increased the rate of discharge 3 to 10 fold, with varying latent periods, some very short, others from 2 to 8 seconds. Stimulation with hypertonic solutions produced a similar response but of a longer latency (around 1 minute) and duration (around 30 minutes), affecting principally the frequency of the larger potentials. Thus recordable electrical neurohypophysial activity can be related to stimuli known to cause vasopressin release and may prove a useful indicator of neurohypophysial function. (Supported by Public Health Service Research Grant Number NB-06624, NINDB.)

EFFECT OF LOW CERVICAL SPINAL CORD LESIONS ON DETECTION OF INCREASED AIRFLOW RESISTANCE IN MAN. F. W. Zechman, Jr., R. O'Neill* & R. Shannon* Department of Physiology & Biophysics and Department of Medicine University of Kentucky Medical Center, Lexington, Kentucky.

Two patients with low cervical cord lesions have been studied to determine the extent to which information from the chest wall contributes to perception of increased inspiratory airflow resistance. Both are young male adults without previous histories of cardiopulmonary disease. Their V.C.'s and C_L's were reduced and pulmonary resistances elevated. E.R.V.'s were zero. $Paco_2$'s were normal and Pao_2's slightly reduced. Strain gauges indicated upper chest circumferences decreased with each inspiration. Threshold for detection of added resistance was carried out as recently described (Resp. Physiol. 2: 73-87, 1966). Instead of pressing a button however, the guadriplegics closed their eyes to signal detection of added resistance. The relationship between detection scores and the proportionate changes in resistance were plotted for each patient & compared with similar data for 5 control subjects. The patients detected added inspiratory resistance as well as the control subjects. In view of the strain gauge findings cited above, it is unlikely that residual sensory function of the upper chest could be responsible for detection. It is concluded that the trunk is not the sole or unique information source necessary for perception of resistance. Guz et al (Clin. Sci. 30: 161-170, 1966) recently reported ability to detect elastic loading unaffected by blocking IX & X cranial nerves. Perhaps the nonspecific sensations which lead a subject to indicate he detects loading originates from multiple sources (trunk, lungs, airways, diaphragm). Redundancy of the sensory input system could explain why disruption of various individual segments of input has not altered the ability to detect loading. (Supported by NIH Grants HE 10628-01 and HE 08932-03).

PARTITION OF BLOOD FLOW TO THE CUTANEOUS AND MUSCULAR BEDS OF THE FOREARM, AT REST AND DURING LEG EXERCISE IN NORMAL SUBJECTS AND PATIENTS WITH HEART FAILURE. Robert Zelis*, Dean T. Mason, and Eugene Braunwald, Cardiology Branch, Natl. Heart Inst., Bethesda, Md.

Although major adjustments of the regional vascular beds accompany the circulatory response to physiologic and pathologic stress, it has been thought that blood flow to resting muscle is normally not altered during exercise and that flow to this area is maintained at normal levels in resting patients with congestive heart failure (CHF). The blood flow in the cutaneous and muscle circulations of the forearm was determined at rest and during supine leg exercise in 11 normal subjects and in 9 patients with CHF. Forearm blood flow (FBF) was determined plethysmographically in an untreated forearm and simultaneously in the opposite forearm in which the skin circulation had been arrested by epinephrine iontophoresis. In normal resting subjects, FBF averaged 5.5 ml/100 g/min, 61% partitioned to muscle and 39% to skin. In patients with CHF, FBF averaged 2.5 ml/100 g/min with 49% to muscle and 51% to skin; each component was significantly lower than in normal subjects. In normal subjects performing mild exercise, forearm muscle flow was not significantly changed, but during strenuous activity it was reduced significantly (-28%). Cutaneous blood flow, however, declined at both levels of exertion by 49% and 74% respectively. In normal subjects cutaneous hyperemia occurred late during mild exercise and with strenuous exercise was delayed until after exercise was discontinued. In contrast, in CHF, muscle blood flow decreased strikingly during both mild (-45%) and strenuous exercise (-51%); cutaneous flow diminished by 75% and 82% respectively and no postexercise hyperemia occurred. Thus, in CHF both the cutaneous and muscle beds of the forearm are abnormally constricted at rest, there is excessive vasoconstriction in both beds during leg exercise and postexercise hyperemia is abolished.

THE EFFECTS OF LOCAL AND CENTRAL BODY HEATING ON VENOMOTOR REACTIONS R.S. Zitnik, R.E. Hyatt and J.T. Shepherd. Mayo Grad. School of Med. Rochester, Minn.

Changes in venous pressure (VP) distal to a pneumatic cuff inflated to arrest the circulation reflect changes in tension in the venous wall if no blood enters or leaves the occluded distal limb (ODL). In 7 normal male subjects (age 22-35) forearm and/or hand VP was measured simultaneously with forearm and/or hand volume (water filled or strain gauge plethysmographs). During the venomotor response to a deep breath or mental stress (increased wall tension resulting in increased VP) (VMR), no change in forearm and/or hand volume was noted. Arterial inflow or infusion of heparinized blood into the ODL sufficient to raise the VP to levels observed after a deep breath, resulted in clearly measurable increases in volume.

In 4 subjects, both hands were placed in water-filled plethysmographs and hand VP measured in the ODL. Water bath temperature (t) regulating kept skin t at 35-36° C in the one hand (control) and 41-44.2°C in the other. VMR were depressed but never completely absent in the heated hand and always present in the control hand. In 7 subjects central body t was raised to 100.5°-102° F (oral) by placing the feet in water at 44° C and the use of thermal blankets. VMR were depressed or absent at the height of heating, but returned immediately on cooling the subject. VMR were equally depressed in the control hand (skin t 35-36° C) and cool hand (32-33° C). These results indicate that blood does not enter or leave the distal limb after complete occlusion during the VMR to a deep breath. A VP rise must therefore reflect changes in venous wall tension. Local heating depresses but does not abolish VMR. Central body heating may abolish VMR and local cooling does not restore it, suggesting that the impairment of VMR by central heating is a central and not a local effect.