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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.

PROJECTIONS FROM VESTIBULAR NUCLEAR COMPLEX TO MEDIAL PONTO-MEDULLARY RETICULAR FORMATION IN THE CAT. Charles Abzug and Barry W. Peterson (intro. by Victor J. Wilson). Rockefeller University, New York 10021.

Electrical stimulation was applied at several points within the vestibular nuclear complex, and PSPs(minimum latency 0.9 msec) were observed in some neurons of the contralateral reticular formation, located in nuclei reticulares gigantocellularis and pontis caudalis. In other experiments we recorded extracellularly the action potentials of neurons in the vestibular nuclei that were evoked by direct electrical stimulation of their axons or collateral processes situated in the same regions of the contralateral reticular formation from which intracellular recordings had been made. Each neuron found within the vestibular nuclei was tested to determine whether it was activated directly rather than synaptically by the electrical stimulus. Criteria were: latency shift of less than 0.15 msec with either (i) increase of stimulus intensity, or (ii) change of stimulus frequency; and (iii) threshold to single-shock stimulation within 10% of threshold to 3- or 5-shock high-frequency stimulation. 56 neurons responding at latencies of less than three milliseconds were adequately tested by these criteria. 55 of these neurons were found to be directly driven, and only one was driven synaptically. Minimum latency for direct activation(0.6 msec) is 0.3 msec shorter than the minimum latency for PSPs evoked in reticular formation neurons by electrical stimulation of the vestibular nuclei. Thus there are neurons in the vestibular nuclei with slowly conducting axonal or collateral processes which cross the midline and travel through the reticular formation. We suggest that at least some of these fibers may synapse with the local neuronal population, and may therefore be responsible for the PSPs evoked by electrical stimulation of the vestibular nuclear complex. (Supported by grants NSF P2B2590 and NS 02619. C.A. was an NIH Postdoctoral Fellow.)

THE EFFECT OF FLOW ON THE UPTAKE OF SOLUBLE VAPORS BY THE NOSE. E.F. Aharonson*, H.A. Menkes, G.H. Gurtner, and D.L. Swift*, Johns Hopkins Sch Hyg & Pub Health, Baltimore, Maryland.

Removal of soluble vapors from the inhaled air takes place in the nose at the same time as the air is heated to body temperature and saturated with water vapor. As a result, air reaching the trachea may contain only a fraction of the soluble compounds being inhaled. We examined the effect of flow on the uptake of soluble vapors in the nose. Tracheotomies were performed on anesthetized dogs, and their nasal passage used for the measurements. Mixtures of soluble vapor (S) and an insoluble inert gas (I) in air were driven through the nose at constant flow rates and the resulting changes in composition measured by a mass-spectrometer. Concentrations of S, relative to I, measured above the tracheotomy (C_{out}) were compared with those inspired (C_{in}) under various flow conditions. At physiological flow-rates, the ratio C_{out}/C_{in} increased rapidly during the first few seconds of exposure and leveled off later, presumably when the tissues immediately adjacent to the nasal passage were saturated. The value of this ratio at the plateau for highly soluble vapors, was considerably less than 1, and remained steady for relatively long periods of time. The average transfer factor in the nose (i.e. the amount of vapor removed per unit time and partial pressure of vapor in the gas phase - δ) went up when the flow was increased. With acetone we found that increasing flow from 1 to 5 lpm caused δ to increase at least two fold. Improved transfer at higher flow-rates may be due to a bigger contact area between air and tissue, to a thinner boundary layer at the nasal walls, or to better perfusion of the nose. (Supported in part by PHS grants HL 14153, HL 13721, and HL 10342.)

TEMPORAL CHARACTERISTICS OF THE SIMPLE MUSCLE TWITCH UNDER HYPERBARIC O_2, N_2, He, AND Ar CONDITIONS. T. K. Akers. Department of Physiology and Pharmacology, University of North Dakota, Grand Forks, N.D. 58201

The purpose of these experiments was to measure the effect of non-narcotic gases on the temporal characteristics of compound action potentials, synaptic delay, muscle membrane potentials, and contraction of the frog sciatic nerve-gastrocnemius muscle preparation. The sciatic nerve, including spinal cell bodies and associated gastrocnemius muscles, was carefully dissected out from pithed Rana Pipiens and mounted in a plastic moist chamber with appropriate stimulating and pick-up electrodes in place. A Statham U-2 universal transducer was used for muscle tension recordings. The preparation was placed at 25°C into a Bethlehem pressure chamber and appropriate mixtures of gases added. Pressurizing with N_2 to 10 ATA above room air decreased synaptic delay and coupling time. He and O_2 to 10 ATA also decreased these times significantly. Argon produced a slight increase in these times. Increased pressure and substitution of other gases for N_2 produced a reduction in contraction time. These results point towards the interaction of these gas mixtures with the physico-dynamics of the membrane.

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EFFECTS OF DRUGS OF ABUSE ON EXTREMITY BLOOD FLOW. Ernest C. Alix, Creighton B. Wright, (intr. by Kenneth G. Swan). Walter Reed Army Institute of Research, Washington, D. C.

Accidental arterial injection of several drugs of abuse has resulted in gangrene of extremities. These drugs have included stimulants, hypnotics and analgesics. One proposed explanation for this effect has been "the vasoconstrictive properties" of these agents. This hypothesis was tested in anesthetized dogs. Femoral arterial flow (FAF) was measured electromagnetically during femoral arterial injection of amphetamines, barbiturates, propoxyphene, methadone, and morphine in a wide dose range to include the usual "abuse" dose. Drug and dose administration was randomized and both pure and commercial preparations were compared. Arterial and venous pressures were recorded. Control flow was 124 $\pm$ 18 (SE) ml/min. Dextroamphetamine (5×10^{-5} to 5×10^{-3} mg (base)/kg) caused dose dependent reductions of FAF. The decrease following 5×10^{-3} mg/kg was 60 $\pm$ 5 ml/min ($p<.01$). Methamphetamine produced similar responses. Barbiturates (10^{-2} to 10^{0} mg/kg) caused dose dependent increases of FAF. Secobarbital sodium (1.0 mg/kg) increased flow by 302 $\pm$ 34 ml/min ($p<.01$). Propoxyphene (10^{-2} to 10^{0} mg/kg) increased flow. The highest dose increased flow 262 $\pm$ 47 ml/min ($p<.01$) and decreased arterial pressure by 35 $\pm$ 4 mm Hg ($p<.01$). Methadone and morphine produced dose dependent increases in FAF. Methadone (0.1 mg/kg) increased flow by 278 $\pm$ 8 ml/min and morphine (0.1 mg/kg) increased flow by 246 $\pm$ 92 ml/min. Excipients and pH of solutions occasionally altered the magnitude, but not the direction of the responses. Of the drugs tested, amphetamines were the only group which reduced extremity blood flow. All the remaining drugs increased flow. These data suggest that the syndrome of vascular insufficiency after intraarterial drug administration may not always be precipitated by vasoconstrictive properties of the drug. Other etiologic mechanisms should be sought.

MECHANISMS OF INTERACTION FOR NERVE AND CORTICAL INPUTS TO THE PARS INTERMEDIA OF THE CEREBELLUM. Gary I. Allen and Tadao Ohno*. Lab. of Neurobiology, Dept. of Physiology, State Univ. of N. Y. at Buffalo, N. Y. 14226.

Single Purkyně cells of the pars intermedia receive converging inputs from cerebral cortex and peripheral nerves representing the same limb. Several hypotheses have been presented by which these two inputs may cooperate in the initiation and control of movement. This study was performed to examine the ways in which the cortical and nerve inputs interact in influencing the Purkyně cell output. In experiments performed on cats anesthetized with nitrous oxide, nerves and sensorimotor cortex were stimulated. Since each Purkyně cell receives only one climbing fiber, but both nerve and cortical inputs via the climbing system, these two inputs must converge onto the inferior olive neuron projecting to the Purkyně cell. Two properties of the inferior olive neurons and their network determine the nerve-cortical interactions via the climbing fiber system: (1) a single shock to either nerve or cortex evokes a weak response, but by pairing the two inputs to arrive coincidentally, the response is facilitated, (2) if one input arrives before the other, transmission of the second input through the inferior olive is depressed. The fastest mossy fiber inputs from the periphery and cortex travel separately to the cerebellum. In the cerebellar cortex, each granule cell appears to integrate only nerve or cortical information, with these two inputs finally interacting at the Purkyně cell level. Consideration of the relative timing for the arrival of cortical and peripheral inputs during a volitional movement suggests that the Purkyně cell probably does not operate on nerve and cortical inputs representing the same phase of the movement, but rather different phases of the movement.

A 5 PARAMETER CURVE: THE BEST FIT FOR THE FORCE:VELOCITY RELATIONSHIP OF IN SITU DOG SKELETAL MUSCLE. P. D. Allen*, and W. N. Stainsby. Dept. of Physiology, Coll. of Med., Univ. of Fla., Gainesville, Florida, 32601.

The present study was undertaken to examine the relationship between force and velocity of in situ perfused dog skeletal muscle. Two muscles were used in the study: the parallel fibered semitendinosis and the pennate-spiral gastrocnemius plantaris. The muscles were stimulated via their motor nerves using brief tetanic stimuli(50/sec. for 200msec.) Force:velocity curves were obtained by a stepwise alteration of the afterload from the smallest load possible to maximal isometric tension. This was done at several different initial lengths and using both supramaximal and submaximal stimulation voltage. The data obtained was fit to the three parameter Hill equation for a rectangular hyperbola, $V=b(c-P)/(P+a)$. The correlation between this model and the observed data was statistically very good. The bottom 1/3 of the curve, however, did not fit the data as well as the top 2/3. Velocity,at high loads, decreased more than would be predicted by this model. This is evidenced by the fact that c, predicted P_o, was larger in every case than observed P_o. This observation has been seen previously, especially in cardiac muscle. In an attempt to describe more closely all of the observed data a second equation was derived which adds a descending exponential to the three parameter curve yielding the five parameter equation, $V=b(c-P)/(P+a)+d(1-e^{(f(P-c))})$. The correlation between this model and the observed data was not only statistically better, but also predicted P_o was nearly the same as the observed value. Whereas the data from this study might only be suggestive of the need for a new force:velocity model, the five parameter model is required when the force:lengthening curves of Mashima are considered(Jap. H. J. 12:545-561,1971).

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TEMPORAL DISPERSION OF UNIT DISCHARGES IN VISUAL CORTEX DUE TO MRF-LGB INTERACTION. I. Alter* and W.S. Battersby. Queens Coll., CUNY, N.Y.

Tetanization (300 cps) of mesencephalic reticular formation (MRF) in analgesic (N_2O/O_2) flaxedilized cats produced a temporally dependent effect on the extracellularly recorded unit response elicited in visual cortex by a single test shock to lateral geniculate body (LGB). The test response typically consisted of a short initial burst, succeeded by a period of marked suppression (100-250 msec in duration) in unit discharges, followed by a return to the spontaneous or higher level. MRF tetanization had 3 effects: (1) In most cases, it markedly enhanced the level of spontaneous discharge for several hundred msec. (2) When MRF tetanization preceded the LGB test shock at short time intervals (0-50 msec), the suppression duration in the test response was decreased (down to 20% of control). (3) With longer MRF-LGB intervals (100-250 msec), however, suppression duration was increased (up to 200% of control). When either a train or a single conditioning pulse was delivered, as a control, to LGB in lieu of MRF, the opposite effect was observed; i.e., at short LGB-LGB intervals, suppression duration was extended, while at longer intervals it was decreased. The above findings indicate that MRF activation produces an initial decrease and a subsequent increase in the cortical inhibitory processes initiated by a test stimulus in the geniculo-calcarine pathways. (Work supported by USPHS Grants EN00575 and MH 10395.)

MECHANISMS MEDIATING VAGALLY INDUCED CARDIOACCELERATION. Alter, W.A.*, Priola, D.V. and G.K. Weiss. University of New Mexico School of Medicine, Albuquerque, New Mexico 87131.

Previous investigations have shown that the canine vagasympathetic trunk,(VST) contains at least two cardioaccelerator pathways which are revealed after atropine blockade. One pathway is responsible for a short latency (3 ± 1 sec) and fast rate of rise tachycardia and is mediated by cardiac sympathetic nerves in the VST. After this sympathetic component is eliminated with bretylium, 6-OHDA or practolol, the "slow component" is maintained. It has a characteristically long latency (12-15 sec) and long recovery time (138 ± 13 sec to 80% recovery). Because this "slow component" is blocked neither by treatment with 6-OHDA nor practolol it is probably not mediated by catecholamines released either from neuronal or extra-neuronal stores. These experiments were performed to evaluate the possibility that the slow-component acceleration is mediated via a diffuse effect of released acetylcholine on the pacemaker cell membrane. In five dogs, intracoronary injection of 4-8 mg lidocaine (L) did not effect the magnitude of cardioacceleration produced by stellate ganglion stimulation before β-blockade. However, L eliminated the "slow component" acceleration produced by vagal stimulation after β-blockade. In some experiments in which both "fast" and "slow" vagal tachycardias were present after atropine blockade, L eliminated the "slow" without affecting the "fast". This blockade lasted from 5-7 min which is consistent with the duration of action of i.v. lidocaine on cardiac excitable membranes. The results of these studies support the hypothesis that ACH released by vagal stimulation can produce increases in heart rate by a direct membrane effect which does not involve a classical drug receptor. (Supported by NHLI Grants 10869, 13783 and 15912 and American Heart Association Grant 71-836).

SYSTOLIC TIME INTERVALS IN INDUCED ATRIAL FIBRILLATION IN THE DOG. James F. Amend and Mark B. Knudson*, Veterinary Physiology and Pharmacology, College of Veterinary Medicine, Wash. State Univ., Pullman, Wa.

The diagnostic utility of ventricular systolic time intervals, obtained by atraumatic means, has been established for a number of heart diseases. The study reported here examined changes in systolic time intervals in dogs in which atrial fibrillation was induced by enhancement of vagal tone with morphine sulfate and direct mechanical stimulation of the right atrium. Dogs received 15 mg/kg morphine sulfate subcutaneously, followed by 3 mg/kg sodium pentobarbital. Electrocardiogram, atrial electrogram, phonocardiogram, and direct aortic pressure were recorded during periods of sinus rhythm and during periods of fibrillation. Data were analyzed by selecting cardiac cycles from periods of each condition, determining time intervals, and comparing by paired "t" test. Cycles were selected so that the broadest spectrum of rates were examined for each animal. One hundred cycles were examined from five dogs for each condition, or 200 total cycles. Heart rate and end diastolic pressure (aortic) showed no significant difference between the two groups. Significant increases ($p > 0.01$) were observed in length of preejection period, externally obtained isovolumic contraction period, and electrical cycle (QT). Left ventricular ejection time was unchanged. Increases in duration of pre-ejection phenomena were seen in S1-S2 and Q-S2, which were increased even though ejection time was unchanged. The prolongation of QT, together with increased duration of pre-ejection related intervals, suggest that altered electrical activation may affect mechanical efficiency of the developing contraction, leading to reduced rate of development of ventricular pressure prior to ejection.

(This study was supported by the Wash. State Heart Assn.)

EFFECTS OF AVERSIVE PAVLOVIAN CONDITIONING UPON RENAL BLOOD FLOW IN THE DOG. D.E. Anderson*, D.C. Randall*, L.P. Schramm, & J.V. Brady*, The Johns Hopkins University School of Medicine, Baltimore, Maryland.

This study was designed to confirm and extend previous research using indirect measurement techniques indicating that renal blood flow may decrease under conditions of behavioral stress. Electromagnetic flow transducers were chronically implanted around the left renal artery, and indwelling cannulae inserted into the aorta via a carotid artery in each of four adult male mongrel dogs. After recovery from surgery and extinction of orienting reflexes, a 10-second auditory stimulus (CS) was paired 10 times at offset with a 0.5 sec., 3-8 ma. electric shock (US), delivered via electrodes to the dog's rear leg. Intertrial intervals averaged 4 minutes. Within 5 pairings, conditioned cardiovascular reflexes developed in each dog, including changes in renal blood flow. During conditioning trials 6-10, increases in mean arterial pressure averaging more than 25% and increases in renal artery resistance averaging more than 100% were observed during the CS-US interval, together with conditioned decreases in renal artery blood flow, averaging more than 35% for this group of dogs. These effects were consistent between subjects. Within 10 seconds of shock occurrence, however, renal flow returned to within 5% of pre-CS baseline levels, renal resistance to within 20% of pre-CS levels, and arterial pressure remained elevated at 20% above baseline levels. These results may be relevant to the role of behavioral factors in the pathogenesis of hypertensive disorders. (Supported by NHLI Grant #HE-06945)

MECHANICAL PROPERTIES OF MUSCLE FIBERS IN AQUEOUS AND DEUTERIUM OXIDE SOLUTIONS. Julia T. Apter and Stephen Berman*. Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois.

Mechanical properties of tissues probably reflect the composition, structure, and orientation of the constituent macromolecules. Muscular tissues have variable properties since they depend on whether the muscle is relaxed or contracted. Relaxed viable muscle, for example, is longer and more extensible than contracted muscle. Previous attempts to use deuterium oxide (D_2O) to clarify the molecular basis of muscular contraction have failed to distinguish among the effects of D_2O on unstrained length ℓ_o and on elastic modulus $|E|$ and to investigate its effects on resting viable muscle. They showed only that D_2O reduces the tension increase brought on either by stimulation of a viable muscle or by adding Ca-ATP to glycerinated muscle fibers. But the tension exerted by a stretched material can decrease if ℓ_o lengthens or if $|E|$ decreases or both. A "contractile" material would lengthen and become more extensible when "relaxed"; therefore a decrease in tension does not give unique information about $|E|$ and ℓ_o since a tension drop could be effected either by a decrease in $|E|$ or an increase in ℓ_o or both. D_2O reduced the tension exerted by both resting viable muscle and glycerol extracted muscle fibers, calling attention to a hitherto unsuspected dichotomy between $|E|$ and ℓ_o. When the medium changed from H_2O to D_2O, $|E|$ of resting muscle and of glycerinated fibers did not increase, so that all tension reduction resulted from an increase in ℓ_o. Any agent affecting ℓ_o and $|E|$ in such differing ways holds promise of becoming a tool for clarifying the molecular basis of muscular "force production" and helps re-evaluate the sliding filament hypothesis now less favored also because of electron microscopy evidence that myosin filaments shorten in contraction. (Supported in part by NIH grants GM-14659 and RR-05477.)

EFFECTS OF AFFERENT CARDIAC NERVE STIMULATION IN CONSCIOUS DOGS. J.A. Armour and J.B. Pace. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Eighteen mongrel dogs weighing from 14 to 21 kg were chronically instrumented with Walton-Brodie strain gauges sutured to an atrium and a ventricle; blood pressure was measured via a cannula in the internal mammary artery and EKG wires were implanted subcutaneously. Stimulating electrodes were placed around the central end of a sectioned cardiac nerve. On the second post-operative day and on subsequent days the nerve was stimulated (4 volts, 3 msec, and 1 to 50 cps) while the dog was quietly resting. Afferent stimulation of the recurrent cardiac, ventromedial, or innominate nerves consistently elicited reflex cardiovascular responses; in three animals no cardiovascular responses were elicited by stimulation of the craniovagal, dorsal, or ventrolateral cardiac nerves. Stimulations elicited a variety of cardiovascular responses which included bradycardia, tachycardia, hypotension or hypertension, as well as positive or negative atrial and ventricular inotropism. Frequently hypertensive responses were elicited by elevations in total peripheral resistance. By utilizing atropine, propranolol, or dibenzylene it was concluded that cardiac responses elicited by afferent stimulations were mediated via parasympathetic and β-adrenergic mechanisms; the peripheral vascular resistance changes were mediated by α-adrenergic mechanisms. The afferents travelled centrally primarily in the ipsilateral vagus as demonstrated by vagotomy on terminal day, and were either depressed or abolished by pentothal (30 mg/kg). Sometimes respiratory rate and depth were increased during stimulations of higher voltages; generalized excitement of the dogs was frequently associated with hypertensive responses. Thus, in conscious dogs, activation of thoracic afferents profoundly modifies cardiovascular dynamics. (Supported by NIH Grant HL 08682.)

On the Number of Fiber Types in Skeletal Muscle of Humans and Other Species. **C. R. Ashmore and L. Doerr (intr. by H. H. Cole). University of California, Davis, California**

Lack of agreement between investigators concerning an acceptable system of nomenclature continues to provide confusion when attempting to correlate biochemical and physiological features of muscle fibers of different species. It is commonly reported that human muscles contain only two types of fibers, whereas other species have three or more. Muscles from adult humans, dogs, elk, sheep, pigs, and mice were examined cytochemically and analyzed for fiber type patterns. In each of these species β fibers (slow-twitch) exhibited a dependence upon aerobic metabolism for energy production and a negative reaction for myofibrillar ATPase activity. Within a given muscle the β fibers were generally of uniform phenotype. The α fibers (fast-twitch) most often exhibited a continuum of activities of metabolic enzymes ranging from those fibers dependent upon aerobic metabolism (αR) to those dependent upon anaerobic metabolism (αW). In each of these species biopsies were also observed to contain α fibers which exhibited a continuum of myofibrillar ATPase activity. In normal muscles of mammalian species it appears that β and α fibers are "static" and "dynamic" with regard to their relative phenotypes. The metabolic spectrum of the α fiber population within a muscle likely reflects the functional activity pattern of the muscle. In this regard human muscles do not appear to differ significantly from other mammalian species.

INTERACTION OF TWO CIRCADIAN OSCILLATORS IN THE ISOLATED CENTRAL NERVOUS SYSTEM OF APLYSIA. Gerald Audesirk (intr. by F. Strumwasser) Div. of Biology, Calif. Inst. of Technology, Pasadena, Calif. 91109

A circadian rhythm of spiking has been shown for the identified neuron R15, in the isolated abdominal ganglion of Aplysia californica (Strumwasser, 1965). This rhythm usually takes the form of a single major peak of activity near projected dawn or dusk. The isolated eyes also show a circadian rhythm of impulse activity, recorded in constant darkness (Jacklet, 1969), consisting of a period of activity during projected day, with a peak near dawn. If the entire central nervous system is isolated intact, with the eyes, both R15 and the eyes produce clear rhythms for three or more days, in constant darkness. The R15 rhythm is different in such a preparation than in the isolated abdominal ganglion. Usually two, but up to four distinct activity peaks occur daily. These peaks are correlated with an increased frequency of a large monosynaptic EPSP from an unidentified neuron in the right pleural ganglion. Periodogram analyses of R15 spiking show major energy peaks at periods of 21 to 33 hours. The eye rhythm is more irregular than that of a isolated eye, with the timing of the peak more variable but later than projected dawn. R15 peaks seldom occur during the period of high eye activity. When this does happen, however, R15 peaks usually coincide with relative troughs of eye activity. Electrical stimulation of the optic nerve, which includes centrifugal fibers as well as afferent fibers from the eye, causes an increase in the frequency of the monosynaptic EPSP in R15, but spontaneous afferent eye impulses do not. Implications for the role of the eye in the entrainment of R15 will be discussed. Supported by a predoctoral fellowship from NSF and by grants from NIH and the Sloan Foundation to F. Strumwasser.

DEPENDENCE OF AORTIC BLOOD FLOW ACCELERATION ON VENTRICULAR PRE-LOAD. David B. Averill,* Robert C. Tarazi* and Carlos M. Ferrario. Research Division, Cleveland Clinic Foundation, Cleveland, Ohio 44106.

Particular attention has been focused recently on the maximum acceleration of blood in the ascending aorta as an apparently ideal index of the inotropic state of the cardiac muscle and hence contractility. The concept implies that changes in aortic blood flow acceleration are insensitive to variations in end-diastolic pressure or volume. In the course of cardiac function studies using an electromagnetic flow probe placed around the ascending aorta in 21 open chest Wistar rats [body weight: 351 ± 9 (M ± SE) gm] anesthetized with ether, it was observed that blood flow acceleration paralleled changes in right atrial pressure. Hence it was felt necessary to reevaluate to what extent left ventricular end-diastolic pressure correlated with maximum blood flow acceleration. Left ventricular function was assessed by simultaneous measurements of peak aortic blood flow (5.9 ± 0.5 ml/sec), maximum aortic blood flow acceleration (14 ± 1.3 g), stroke volume (0.25 ± 0.02 ml), cardiac output (92 ± 3 ml/min), mean arterial pressure (62 ± mm Hg), and right atrial and left ventricular pressures. When cardiac output was altered by rapid withdrawal and re-infusion of blood (4 ml/min) via a femoral catheter, a highly significant correlation was obtained between maximum blood flow acceleration and stroke volume [correlation coefficient: 0.96 ± 0.02 ($p < 0.02$)], left ventricular end-diastolic pressure [$R = 0.96 \pm 0.02$ ($p < 0.02$)] and maximum left ventricular dp/dt [$R = 0.94 \pm 0.03$ ($p < 0.02$)]. Thus, since any change in left ventricular end-diastolic pressure or stroke volume always caused an equivalent change in maximum blood flow acceleration, this factor should be taken into account when maximum blood flow acceleration is used to estimate the inotropic function of the cardiac muscle. (Supported in part by Grants HL-15357 and HL-15837 from the N.H.L.I).

BREATH-BY-BREATH ANALYSIS OF EXERCISE HYPERPNEA EMPLOYING COMPUTER TECHNIQUES. Anthony M. Babich*, Sarah S. Mei* and Frederick F. Kao. Depts. of Medical Computer Science and Physiology, Downstate Medical Center, State University of New York, Brooklyn, N.Y. 11203.

Previous studies have established that by treating the respiratory chemostat with a three-compartment analysis and with ten fundamental equations to describe the functions of these compartments, a loop existed when $\dot{V}$ was plotted as a function of P_Aco_2 during CO_2 inhalation (Acta Neurobiol. Exp., 33:163-175, 1971; Bulletin de Physio-Pathologie Respiratoire, 1972; Fed. Proc., 31:361, 1972). Four distinctive components of this $\dot{V}$-P_Aco_2 loop could be identified to describe the on-CO_2 effects and the off-CO_2 effects. The shape of this $\dot{V}$-P_Aco_2 loop, obtained by means of experimental CO_2 inhalation as carried out in man, agreed well with that of theoretical analysis. After studying the $\dot{V}$-P_Aco_2 loop behaviors in emphysema patients, we extended this investigation to exercise hyperpnea. Theoretical analysis employing the known functions including the neurogenic hypothesis for exercise hyperpnea and the metabolic hyperbolae for the feedback pathway revealed a vertical response on the $\dot{V}$-P_Aco_2 plot with additional loops when exercise was performed in addition to CO_2 inhalation. Experimental results agreed well with the theoretical analysis (Supported in part by a NHLI grant(HE-04032) and a NIH grant(RR00291).

ELECTRICAL ACTIVITY IN THE PHRENIC NERVE AND DIAPHRAGM OF THE FETAL LAMB IN-UTERO. A. Bahoric* and V. Chernick, Depts. Physiol. & Pediat., University of Manitoba, Winnipeg, Canada.

Dawes et al (J. Physiol. 220: 110, 1972)monitored tracheal pressure and volume change of fetal lambs in-utero and described respiratory movements with a frequency of 1 to 4 Hz associated with periods of REM sleep. The present study was undertaken to more directly monitor fetal respiratory center output in-utero by chronic recordings of phrenic & diaphragmatic electrical activity. Pregnant ewes (105 to 125 days gestation) were anesthetized and following hysterotomy a fetal thoracotomy performed on the marsupialized fetus. Bipolar recording electrodes were implanted on either the right or left phrenic nerve and diaphragm and shielded leads tunneled to the dorsum of the ewe. Intrapleural or intratracheal pressures were monitored through liquid filled catheters. One week was allowed for recovery from surgery and recordings were obtained from awake preparations for as long as three weeks. In contrast to phrenic nerve activity in newborn and adult animals, fetal phrenic nerve activity was not phasic but consisted of episodic bursts interspersed by quiescent periods lasting up to 30 minutes. Activity was present as early as 112 days gestation. These bursts were present in all fetuses and were coupled with diaphragmatic activity and changes in intrapleural or intratracheal pressure. Fetal asphyxia was associated with continuous phrenic nerve activity and intrapleural pressure changes. This study indicates the presence of phrenic nerve discharges during the latter third of fetal life in the sheep. It is suggested that the fetal respiratory center is active in-utero but this activity is minimal when compared to that present during extra-uterine life. (Supported by the Medical Research Council of Canada & The Children's Hospital Research Foundation, Inc.).

ISOLATED SKELETAL MUSCLE BLOOD FLOW AND VOLUME CHANGES DURING CONTRACTILE ACTIVITY. Carleton H. Baker and Darrell L. Davis. Dept. of Physiol., Col. of Med., Univ. of So. Fla., Tampa, Fla. 33620

Dog gracilis muscles were removed, enclosed in a plethysmograph and perfused at an inflow pressure of 110 mm Hg. Venous pressure was 5 mm Hg. Circulating blood volumes were measured by the constant infusion technique using RBC $-^{51}Cr$ (8 Muscles) or albumin $-^{131}I$ (8 Muscles). Volumes were calculated from the infusion of the indicator and also from the washout of the indicator. The skeletal muscle contraction was produced by stimulation of the gracilis nerve stump with maximal stimuli at rates from 0.5 to 20 Herz for periods ranging from 0.25 to 1.0 min. Volume changes during and following the stimulations were measured by plethysmography and by changes in total muscle radioactivity. Inflow and outflow were also measured. Changes in interstitial fluid volume were calculated as the difference between total tissue volume change and vascular volume change. There was increased blood volume at all contraction rates. Total tissue volume decreased during the initial time of contractions and then increased continuing into the post-stimulation period and then returning to control. Interstitial fluid volume decreased markedly during the time of contraction and then increased above control or returned to the control level post-stimulation. The data indicates the tissue pressure is markedly increased during contraction causing fluid movement into the vascular system. Loss of labeled albumin during the contraction time indicates increased capillary permeability. (Supported by USPHS Grant 2-R01-HL 14541-02 and Suncoast Heart Association.)

EFFECT OF PRESSURE, GAS DENSITY AND P_{O_2} ON THE WORK CAPACITY OF THE RAT D.G. Baker* and Y.C. Lin. Univ. of Hawaii Sch. of Med. Honolulu, HI.

Various factors affecting the work capacity of the rat were studied by factorial-design to partition the effects of pressure, gas density, and partial pressure of oxygen. The water temperature was kept constant at 37 $\pm$ 1°C in these experiments. The oxygen consumption was measured with a ventilated hyperbaric chamber which also served as swimming chamber. The appropriate comparison of periods before, during, and after swimming were achieved by a stage which can be lowered or raised above water level by compression or decompression of the space within the telescopically arranged pneumatic jack. The resting $\dot{V}_{O_2}$ was the same regardless of pressure (1 or 3 ATA), gas density(0.33, 1 or 3 relative to air at 1 ATA), or P_{O_2} (150 or 450 mm Hg). Resting oxygen pulse was increased at 3 ATA air as compared to 1 ATA air. This is inconsistent with the findings in man during chamber dive. The heart rate was obtained using an AM telemetry system. Rest, peak, and average $\dot{V}_{O_2}$ (ml/kg/min, mean $\pm$ S.E.) were respectively, 27 $\pm$ 1.6 (10), 64 $\pm$ 2.7 (4) and 45 $\pm$ 0.7 (8) at 1 ATA air, and were not affected by breathing 1 ATA $He-O_2$ mixture (80-20%). The rats were not able to complete 30 min assigned swimming period under 3 ATA while breathing $He-O_2$ (80-20%, P_{O_2} = 450 mm Hg) and N_2-O_2 (93-7%, P_{O_2} = 150 mm Hg). Time to exhaustion for these two conditions were 19.8 $\pm$ 2.5 (9) and 19.3 $\pm$ 4.6 (6) min. However the rats were able to complete 30 min swimming period at 3 ATA while breathing air. Both peak and average $\dot{V}_{O_2}$ were depressed similarly at 3 ATA, regardless of P_{O_2}, or gas density. Since the reduction in work capacity cannot be attributed to increased P_{O_2} or gas density, it is concluded that pressure per se exerts an adversive effect on the work capacity in the rat. (Supported by ONR contract N00014-67-A-0387-0014).

CARDIOVASCULAR RESPONSES OF SQUIRREL MONKEYS EXPOSED TO ACUTE HYPOXIA: METHODOLOGICAL EFFECTS. L. E. Banderet, P. W. Phair, and R. L. Jackson (intr. by Sumner Robinson), Military Stress Laboratory, U. S. Army Research Institute of Environmental Medicine, Natick, MA.

Previous research reported at APS (1970) demonstrated that Squirrel Monkeys (SM) with chronically implanted catheters exhibited bradycardia and reduced blood pressures when exposed to acute hypoxia. Our objective was to determine why cardiovascular responses of SMs to acute hypoxia were dissimilar to that of man. The heart rate responses of 6 cage-roving (low level restraint) or chair-restrained (intermediate & high level restraint) SMs were determined over a 4-6 hour interval with 21 and 11% O_2 gas mixtures. The SMs were seated in plastic chairs and restricted with waist stocks in the intermediate level of restraint; in the high level of restraint the SMs were restricted in chairs with both neck & waist stocks. Measures of heart rate were obtained with external electrodes coupled to a telemeter; the telemeter was attached to a fabric vest worn by the monkeys. Results: Cage-roving SMs exposed to acute hypoxia (11% O_2) have a mean heart rate of 250 bpm which is 70 bpm greater than the normoxic (21% O_2) value. Chair-restrained SMs (intermediate level restraint) either show an increased or decreased heart rate in response to 11% O_2; exposure to hypoxia resulted in a consistent bradycardia for the high level of restraint. Thus, we have demonstrated that the cardiovascular response of the SM to acute hypoxia is dependent upon the degree of restraint, i.e., SMs minimally restrained exhibit tachycardia which is in agreement with data for man.

PHYSIOLOGY CURRICULUM CONTENT SELECTION FOR MEDICAL STUDENTS. Neal R. Bandick* and David F. Bohr. Oregon College of Education, Monmouth, and Dept. of Physiol., U.of Mich., Ann Arbor.

Because of the stringent constraints on teaching time imposed by medical school curriculum revisions, an orderly plan must be available for interdepartmental selection of curriculum content. Such a plan should meet the following objectives: 1) provide an outline of the upper level of principles and concepts that should be taught in the premedical curriculum, 2) furnish outlined content and logical sequences of instruction, 3) show the forms of clinical experience that require physiology as a pre-clinical science and the forms that can be learned concurrently with physiological instruction, 4) provide a reference for correction and change. Robert Gagné has devised a series of procedures that can be used to identify the curriculum content needed by a medical student. These procedures are based on the principle that once the learning objectives are defined the subordinate information needed for the understanding of these objectives can then be identified and arranged in the form of a content hierarchy. This is a curriculum map which outlines the information needed before the next learning step. The major advantage in the stepwise preparation of a hierarchy map lies in reduction of the possibility of omitting essential material from the curriculum. Content hierarchies show students how seemingly useless bits of information will be applied later to medical problems; they also save teaching time by eliminating non-relevant information.

PROPERTIES OF ARTERIAL WALL FROM RATS AFTER REVERSAL OF RENAL HYPERTENSION. Neal R. Bandick* and Harvey V. Sparks. Oregon College of Education, Monmouth, and Dept. of Physiology, University of Michigan, Ann Arbor.

Previously (Am. J. Physiol. 219:348, 1970) we have demonstrated that helical strips from femoral arteries of renal hypertensive rats exhibit autorhythmic contractions more frequently, develop less active tension, have a lower threshold to norepinephrine and less extensible walls than comparable strips from normotensive rats. In the current study renal hypertension was reversed by removing the renal artery clamp from unilaterally nephrectomized renal hypertensive rats. Paired helical strips from femoral arteries of normotensive controls and from rats after reversal of renal hypertension were mounted in a common bath for comparison. 1) Autorhythmicity was equivalent in the two types of strips. 2) Active tension in response to norepinephrine (10^{-6}g/ml) was greater in strips from rats that had recovered from hypertension in 7 of 8 exps. 3) Threshold concentration for norepinephrine response was the same for the two. 4) In passive length-tension studies, strips from rats recovered from hypertension remained less extensible (5 of 6 exps.). These results show that after removal of the femoral artery clamp from the renal hypertensive rat, the performance of its vascular smooth muscle returns to that of the controls (autorhythmicity and threshold) or the muscle develops a greater norepinephrine response. There is no such recovery or reversal in the passive characteristics of the vessel walls. (Supported by NIH HL-14874 and the H.R. Kaiser Foundation.)

PALMITATE METABOLISM IN RAT RENAL CORTEX. Mario Barac-Nieto intr. by Julius J. Cohen. Univ. del Valle, Cali, Colombia. Rat renal cortical slices were incubated with 1-^{14}C-palmitate bound to 2.5% albumin. As medium palmitate concentration increased from .5 to 1.5mM, oxidation and esterification of palmitate increased but progressively, a larger fraction of the total utilized was esterified. With respect to controls with 1mM palmitate alone the following effects of lactate and glutamine were found: at increasing medium lactate (.8, 3.2, 8 and 16mM) palmitate utilization increased up to 8mM lactate with an optimal at 3.2 mM. At 16mM, palmitate utilization decreased. Palmitate oxidation was stimulated at .8 and 3.2mM lactate; slight inhibition of oxidation was noticed only at 16mM lactate. Esterification was significantly stimulated at 3.2mM lactate but inhibited at 16mM lactate. Medium glutamine (.1 and 1mM) stimulated palmitate utilization and oxidation but inhibited esterification. High medium glutamine (10mM) inhibited palmitate utilization, esterification and oxidation to CO_2 but increased its incorporation into incomplete oxidation products. In sum, only at high medium concentrations, lactate or glutamine inhibit the complete oxidation of palmitate to CO_2; kidney cortex seems to prefer palmitate to lactate or glutamine as an energy substrate. Stimulation of palmitate oxidation by low lactate or glutamine levels might relate to provision of oxaloacetate for citrate synthesis with acetylCoA derived from fatty acid oxidation. Inhibition of utilization, oxidation and esterification at high lactate or glutamine levels might relate to competition for CoA by acyl groups derived from lactate or glutamine with those derived from fatty acids. Finally the increase in esterification at low lactate levels might relate to provision of glycerophosphate from lactate through the gluconeogenic pathway. Supported by ICMRT and FORGE Foundation.

LOCALIZATION OF VASOMOTOR FIBERS OF THE DESCENDING SPINAL SYMPATHETIC PATHWAYS OF DOGS. S.M. Barman* and R.D. Wurster. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Previously, this laboratory has reported the localization of descending vasopressor fibers in cats (Foreman and Wurster, Physiologist 14: 143, 1971). Presently, the study of the organization of this tract as to its distribution to various vascular beds is being initiated. Vasomotor activity to the vascular bed supplied by the femoral artery has been investigated in dogs anesthetized with sernylan and chloralose during stimulation of descending sympathetic pathways in the cervical spinal cord. Femoral flow, systemic blood pressure, and central venous pressure were recorded during ipsilateral stimulation (50 Hz, 1 msec, 4 v) on the surface of the cord between the dorsal lateral sulcus (DLS) and the dentate ligament. Resistance changes could then be calculated. Maximum vasoconstriction results from stimulations 3-4 mm ventrolateral to the DLS, with resistance increasing to 250% above control levels and flow decreasing to 40% below control. This corresponds to the region of maximum systemic pressure change, with pressure increasing to 80% above control. The constrictor response is abolished by cutting the ipsilateral sciatic nerve, with resistance now decreasing to 50% below control levels and flow increasing to 250% above control. Pressure changes were not effected by cutting this nerve. Vasodilatation results from stimulations 1-2 mm below the DLS, with the maximum dilatation at 2 mm. Here flow increases to 180% above control and resistance decreases to 40% below control. The carotid resistance is also being studied to determine the localization of descending vasomotor fibers to the vascular bed supplied by the carotid artery. (Supported by NIH Grant HL 08682.)

HEMODYNAMIC DETERMINANTS OF THE MAXIMUM RATE OF CHANGE OF LEFT VENTRICULAR PRESSURE AND INTERNAL DIAMETER DURING VENTRICULAR RELAXATION. George E. Barnes* and Vernon S. Bishop. The University of Texas Medical School at San Antonio, San Antonio, Texas.

The hemodynamic determinants of the maximum rate of change of left ventricular pressure (-dP/dt max) and internal diameter (-dD/dt max) during relaxation of the left ventricle was studied in six conscious dogs. The animals were previously instrumented with miniature solid state transducers for measuring left ventricular pressure and piezoelectric transducers for measurement of transverse internal diameter. Increasing heart rate from 97 ± 3.4 beats/min to 120, 150 and 180 beats/min by right atrial pacing increased -dP/dt by 7.4%, 13.6% and 14.6%, while significant increases in -dD/dt max (14.6%) were only observed at 180 beats/min. IV infusions of isoproterenol, at HR similar to pacing, did not effect -dP/dt max but resulted in a significant increase in -dD/dt max by 12.7%, 28.3% and 35.3%. Increments in end diastolic diameter (EDD) at a constant HR by rapid IV infusions of Ringer's solution, increased -dD/dt max by 11%, 25% and 32.8%, but did not significantly increase -dP/dt max. Increases in HR with EDD constant resulted in significant increases in both -dP/dt max (7.3 - 13%) and -dD/dt max (8 - 33%). With HR constant, increments in MAP (20 mmHg) with IV phenylephrine resulted in increases in -dP/dt max (16.6%) and -dD/dt max (8.4%. The results of this study suggest that -dP/dt max is related to the aortic diastolic pressure at end ejection, and -dD/dt max by the magnitude and duration of the rapid filling phase during diastole. (Supported in part by NIH #2 R01 HL12415-05 and AFOSR-71-2074.)

A Planar Tracking Model Composed of Discrete Neural Networks and Muscle Element Subsystems. George M. Barnwell, Robert E. Schuhmann, and Richard A. Albanese. (intr. by V. S. Bishop) Southwest Research Institute and USAF School of Aerospace Med., San Antonio, Texas.

The theoretical and conceptual foundations for a planar tracking system composed of discrete neural and muscular elements organized into several subsystems are developed. The neural system consists of a sensory, a memory and a comparator network, and four motoneuronal networks. The muscular system consists of four subsets of muscle fibers and their corresponding intrafusal fibers and Golgi tendon organs. Agonist-antogonist pairings control up-down and left-right movements. The comparator network compares the reference or desired control element position as stored in the memory network, with the actual control element position as seen in the sensory network, and generates a corrective signal to the appropriate subsets of motoneurons. A vector force is generated by activated muscle element subsets such that any deviation of the control element from its reference position is opposed by a restorative force. The vectorial restorative force allows full utilization of the distance and directional information generated by the neural networks. The model is useful for simulation of the human operator in a tracking task, reliability studies ofneuromuscular control systems, comparisons of the effects of degree of convergence and divergence between network layers on performance capability, and studies of the effects of any agent capable of affecting neuronal membrane potentials.

EFFECTS OF LONG TERM OZONE EXPOSURE ON LUNG ELASTICITY. D. Bartlett, Jr. C.S. Faulkner II* and K. Cook.* Departments of Physiology and Pathology; Dartmouth Medical School, Hanover, N.H.

We studied pulmonary growth and elasticity in young rats exposed to 0.2 ppm ozone for 30 days. Lung weight and alveolar number were not affected by this exposure, but lung volume, measured after fixation at 20 cm H_2O transpulmonary pressure, was increased by 16%. Static pressure-volume measurements in degassed, excised lungs showed that the lungs of the exposed animals were overdistended at high transpulmonary pressures, whether filled with air or with saline. We interpret these results to indicate that ozone exposure under these conditions causes a decrease in lung tissue elasticity, possibly mediated by an effect on collagen.

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"LUMINANCE" AND OTHER LUXO-TONIC UNITS IN SQUIRREL MONKEY STRIATE CORTEX. J.R. Bartlett* and R.W. Doty. Center for Brain Research, University of Rochester, Rochester, New York 14642.

In unanesthetized, painlessly immobilized monkeys about 70% of the units encountered in the foveal representation within the striate cortex show maintained, nonadapting changes in rate of discharge with increases or decreases in intensity of diffuse light. Upon changing illumination there is an abrupt increase or decrease in rate of discharge which, within 1-5 min, gradually assumes a new level. The mean frequency of discharge remains constant within roughly ± 10% indefinitely, several units having been followed for > 1 hr. For "luminance" units the maintained rate varies either directly or inversely as an exponential function of light intensity over a 10^4 range. In other cases such relation is less systematic, perhaps because all these luxo-tonic units are also strongly affected by normal or drug-induced changes in alertness. Nitrous oxide "anesthesia" (60:40 or 80:20) severely alters the properties of these units, i.e., such properties can probably not be observed in "lightly anesthetized" preparations. Receptive fields are usually hard to define, even though often limited to one eye, and seem to integrate luminous flux over a very wide area. Some luxo-tonic units, however, have fields as small as 0.2-0.8°. When they can be driven by electrical stimulation of optic tract, the latencies of either type unit (3.0 msec or less) suggest that they belong to the magnocellular system; a fact somewhat paradoxical considering their presence in foveal representation and probable relation to the tonic, slowly conducting units described by Gouras (J. Physiol. 204: 407, 1969) in the retina. (Supported by NS 03606 and NSF GB-7522X).

RELEASE OF GASTRIN BY ALCOHOL IN MAN AND DOGS. H.D. Becker*, D.D. Reeder and J.C. Thompson. Univ. Tex. Med. Branch, Galveston, Texas.

Ingestion of alcohol aggravates the peptic ulcer diathesis in man by stimulating gastric acid secretion. We studied the question of whether alcohol stimulates acid output by causing release of gastrin in 6 human volunteers and in dogs. Method: Man: Serum gastrin was measured by radioimmunoassay in each person before and at intervals after administration of 7% ethanol iv, or 80 ml of either 18% ethanol, 50% ethanol or water by mouth. Dogs: In 11 anesthetized dogs, the antrum was isolated and the antral vein cannulated. In 5 of these dogs the antral mucosa was perfused via a 2-way catheter first with saline (pH 5), then with 10% ethanol (pH 5), and finally with 10% ethanol (pH 1). Six dogs received a 2-hr iv infusion of 10% ethanol (20 ml/kg); during the second hour the antral mucosa was perfused with saline at pH 1. Gastrin levels were measured in the antral vein at intervals throughout all experiments. Results: Man: Ethanol iv produced a gradual rise in gastrin from 85 picograms (pg)/ml basal to 105 pg/ml at 50 min ($p < 0.05$). There was no increase in gastrin output after ingestion of water. Oral ingestion of 18% ethanol increased gastrin only slightly, but 50% ethanol caused a significant rise from 84 pg/ml basal to a peak of 109 pg/ml. Dogs: Topical saline (pH 5) did not change antral vein gastrin. Ethanol at pH 5 increased gastrin significantly from 92 to 338 pg/ml, and acidification of the ethanol decreased gastrin to 132 pg/ml ($p < 0.02$). Intravenous ethanol increased antral vein gastrin significantly from 105 to 310 pg/ml at 1 hr; subsequent antral acidification decreased gastrin to 147 pg/ml. Conclusion: These studies indicate that either topical or iv ethanol stimulates the release of gastrin as measured directly by radioimmunoassay. This increase in gastrin may be in part responsible for the increase in gastric secretion after alcohol.

THE ORGANIZATION AND VASCULAR PERFUSION OF CANINE RENAL TUBULES. R. Beeuwkes III and J. V. Bonventre*, Harvard Medical School, Boston. Mass.

Tubular function may be altered by changes in the distribution or physical properties of perfusing blood. To evaluate the influence of such factors it is necessary to determine the exact relations between blood vessels and tubules in each part of the kidney. Microinjected tubules and efferent blood vessels arising from single glomeruli were simultaneously photographed in cleared slices of fixed dog kidneys. Of 104 complete proximal injections, 16 continued through the loop of Henle and 5 distal tubules filled. In the sub-capsular zone 53 of 55 proximal convoluted tubules (PCTs) were associated with the efferents arising from the same glomerulus, while in mid cortex 31 of 35 PCTs were perfused over more than half their length by efferents arising from different glomeruli. In the inner cortex 10 of 14 PCTs were completely dissociated and the remaining 4 were associated only with minor branches. Regardless of the position of the parent glomerulus, each of the 80 straight parts, 16 thin descending limbs and 10 ascending limbs was perfused by efferents from many other glomeruli. Distal tubules were in contact with the proximal tubules from the same glomerulus and shared their perfusion. These results show that dependence of each nephron on perfusion by efferent blood from many glomeruli is a principle of canine renal organization. Because the nephron is not an independent unit, the roles of blood flow redistribution and of physical factors must be defined in terms of regional, rather than single nephron effects.

COMPARISONS OF ADRENAL, PITUITARY, AND GONADAL FUNCTION OF MALE NORWAY RATS WITH DIFFERING BREEDING HISTORIES. R. W. Belknap*, E. J. Keenan*, and R. V. Andrews. Creighton Univ., Omaha, Nebr.

Gravimetric and physiological tests of endocrine function reveal that breeding history influences sexual and social function in the Norway rat. Organ weight/body weight ratios of testes, seminal vesicles, prostates and epididymides demonstrate increased pituitary-gonadal activity for experienced breeders over inexperienced breeders and non-breeders. Sex accessory fructose values support these data, although pituitary gonadotrophin levels are higher only in naive breeders. Adrenal weight and corticosterone data are reciprocal in order to the sexual function indicators, i.e., show lower activity in breeders than in non-breeders. Similar findings are seen in relationship to the initiation of Spring breeding activity in wild rat populations. Sexual regression occurs on isolation of males or in response to short days and colder weather in the wild. Breeding activity appears to enhance the reproductive endocrine responses which promote sexual development and activity in mature rats. (Supported by USPHS Bureau of Community and Environmental Health Management (EC 00340)).

ALDOSTERONE-INDUCED PROTEIN (AIP) IN TOAD URINARY BLADDERS. William B. Benjamin* and Irwin Singer. University of Penna. School of Medicine, and Philadelphia Veterans Administration Hospital, Philadelphia, Penna.

Aldosterone is thought to stimulate sodium transport across the toad urinary bladder by inducing a specific RNA to code for the synthesis of a specific AIP responsible for sodium transport. However, neither a specific RNA or AIP has previously been demonstrated. Simultaneous electrophysiological and biochemical experiments were performed with paired hemibladders isolated from each toad (Bufo marinus). One hemibladder was used to monitor aldosterone-induced sodium transport in paired quarter-bladders by the short-circuit current (SCC) method in modified Ussing chambers. The corresponding hemibladder was used to study in vitro {^{35}S}-methionine incorporation into proteins isolated from scraped epithelial cells by gradient slab gel electrophoresis and autoradiography. Microdensitometric tracings of autoradiograms and tracings of gel slice radioactivity demonstrated that aldosterone (10^{-6}M) specifically increased {^{35}S}-methionine incorporation into a low molecular weight protein. Comparisons with histone proteins suggest the molecular weight of AIP is approximately 12,000 daltons. In each case (N=8) the presence or absence of an electrophysiological response correlated with the presence or absence of increased {^{35}S}-methionine incorporation into AIP. Dexamethasone (10^{-6}M) failed to induce either an electrophysiological or a biochemical response, suggesting mineralocorticoid specificity. Incubation with actinomycin D (2μg/ml) for 3 hrs prevented both the electrophysiological and the biochemical response to aldosterone. These data demonstrate that aldosterone specifically induces the synthesis of a low molecular weight protein (AIP), and that the production of AIP is correlated with the stimulation of sodium transport.

SKELETAL BUFFERING OF ACUTE METABOLIC ACIDOSIS. John Bettice* and James L. Gamble, Jr., Department of Physiology, The Johns Hopkins School of Medicine, Baltimore, Maryland 21205.

Decreases in the sodium content of bone were measured to evaluate the role of this tissue in the buffering of acute metabolic acidosis (by Na-H exchange). Radiosodium was injected into dogs (^{24}Na) and rats (^{22}Na) 18 hours before the infusion of HCl (0.25 N, 6-10 mEq/kg b.w.), and changes in the radioactivity were used to indicate loss of bone sodium. These losses were less than 1.0 mEq/kg bone during the first 1.5 hours of acidosis; whereas after 5.0 hours, canine rib and skull lost 9.0 mEq/kg and toe 5.3 mEq/kg. Not more than 2.5 mEq/kg bone sodium were lost during the infusions of isotonic sucrose used to determine the effects of the hyponatremia caused by the acid infusion. In 5.0 hour experiments with rats, losses of bone sodium were 14.6 mEq/kg with HCl and 7.5 with hyponatremia. In the aforementioned studies, the 18 hours of isotope equilibration resulted in labelling of 50% of the total bone sodium. To obtain more complete labelling, growing rats were placed on a 4-week diet containing ^{22}Na at a constant specific activity. This longer period allowed labelling of 89% of the total bone sodium. In these experiments, the mean loss after 5.0 hours of acidosis was 18.2 mEq/kg bone of which 10.5 was due to hyponatremia. After an infusion of HCl, the decrease in sodium is greatest in the smaller bones of the rat; and, in the dog, the losses from flat bones exceeded those from the long bones. These changes took place chiefly in the more rapidly exchangeable sodium. Soft tissue buffering must be more important initially; but, at the end of 5.0 hours, the quantity of sodium released from the skeleton is sufficient to account for most of the tissue buffering. (NSF Grant Number GB-35524)

LOWER ESOPHAGEAL SPHINCTER MECHANICS. P. Biancani*, J. Bejar*, H. M. Spiro*, R. M. Weiss and M. P. Zabinski*, Yale University, New Haven, Ct. and Fairfield University, Fairfield, Ct.

The mechanical factors involved in the genesis of lower esophageal sphincter (LES) pressure were studied in monkey and human sphincters. Various degrees of circumferential stretch were applied by introducing probes of different diameters into the in vivo LES. The closure pressure around each probe was measured and pressure-diameter curves were constructed. The pressure-diameter curve shows at first a decline followed by an increase in pressure with increasing probe diameters. Atropine lowered the entire pressure-diameter curve without change in shape. The intraluminal pressure in the LES is generated by tension developed in the muscle of the sphincter wall. Factors such as diameter of lumen and wall thickness play a role in determining the relationship between the wall tension and the intraluminal pressure. In the resting and electrically stimulated sphincter, wall tension is low near closure and increases as the diameter increases. It is concluded that the diameter of the pressure measuring probe affects the measured pressure; and that near closure, high intraluminal pressures may be produced by moderate tension in the wall muscles. Optimal tension is developed at large diameters and atropine affects the magnitude but not the shape of the pressure-diameter curves. (Supported by NIH Grant AM16021-01).

Permeability of water and non-electrolytes in the sheep placenta. J.M. Bissonnette, M. Haas, and R.C. Farrell (intr. by J.J. Faber) Univ. of Calif. at Irvine, and Univ. Oregon Med. School. Portland, Oregon.

Single injection multiple indicator dilution curves were used in an in vivo perfused placenta preparation previously described (Bissonnette J.M. and G.H. Gurtner, J. Appl. Physiol. 32:64, 1972). An injection of T-1824, tritiated water and a C^{14} labled non-electrolyte was made into the umbilical artery and the entire outflow collected from the umbilical vein into an automatic tube holder. The outflow pattern of the non-electrolytes and tritiated water were retarded relative to that of T-1824 (Goresky C.A., Am. J. Physiol. 204:626, 1963). Mean circulation time ($\bar{t}$) for T-1824 was 15.2 secs. and for tritiated water 29.4 secs. The ratio of the summation of the recovery of tritiated water to T-1824 was 0.6. Methanol, propanol, butanol and antipyrine showed $\bar{t}$ and recovery relative to T-1824 similar to water. Urea, thio-urea, ethylene glycol, glycerol and 1,7-heptanediol had $\bar{t}$ (22.6 secs) intermediate between T-1824 and water and recovery relative to T-1824 of 1.0. This pattern was analyzed with respect to the molecular weights, ether:water partition coefficients and number of weak hydrogen bonds which each non-electrolyte forms with plasma water. We would conclude that non-electrolytes which form 2 hydrogen bonds have permeability characteristics similar to tritiated water while those which must break 4 or more hydrogen bonds in order to enter the membranes separating fetus from mother diffuse into a smaller space and are not transferred during a single transit. Supported by Grant HD 06636-01 USPHS

A MODEL OF THE HUMAN RESPIRATORY SYSTEM. William B. Blesser‡ Ludwig Braun*, S. Finkelstein*, and Harold A. Lyons. Polytechnic Institute, Brooklyn, N.Y., SUNY at Stony Brook, Stony Brook, L.I., Polytechnic Institute, Brooklyn, N.Y., Downstate Medical Center, Brooklyn, N.Y. respectively. Supported by USPHS Grant #HE 13557.

A composite respiratory model will be described which includes some of the primary mechanisms related to transfer of gas from the mouth to the blood. The model features a section which deals with some of the mechanical properties of the lung such as resistance, compliance and dead space; a model configuration follows to simulate the mixing properties at the alveolar level; a diffusion section then follows to describe transport of gas to and from the pulmonary capillary bed and finally a section of the model is devoted to a description of blood flow through the capillary bed. The composite nature of the model permits an examination of gas flow into the pulmonary bed as a function of pulmonary blood flow, mechanical properties of the lung and a variety of other parameters.

A method for total brain ischemia (TBI) without circulatory arrest in the Rhesus monkey. A. Bleyaert‡ H. Morita‡ R. Carroll‡ P. Safar, B. Kirimli*and E. Nemoto. Dept. of Anes./CCM and Nuc. Med., Univ. of Pgh. Sch. of Med. and the Oakland VA Hospital, Pittsburgh, Pa.

Present models for TBI are inadequate because of extensive surgery, non-standardized post-ischemic (PI) life support, and undocumented completeness of ischemia. The result is greater data variability and non-CNS related morbidity and mortality. We have established a simple model for TBI by a high pressure (20 psi) neck tourniquet (2"x12") resulting in survival, neurologic deficit and low morbidity and mortality. Body temp., EKG, end-tidal CO_2, systemic art. (SAP), supra-cortical (SCP) and sagittal sinus (SSP) pressures were cont. monitored in halothane (1%) anesthetized monkeys (5-7kg) mechanically ventilated. A flat EEG in 20 secs., pupils fixed and dilated in 1 min., normal or subnormal SSP and SCP, absence of clinical signs of venous congestion were criteria for TBI. In several monkeys, these criteria were compared with brain scan data (8 mCi Tc^{99m}). We found that TBI can be effectively produced with this method on the basis of the criteria cited above. Brain scan calculations reveal approx. .06 ml/min brain blood flow (primarily post. fossa) during TBI. Success of the method required control of the hypertensive response during TBI (SAP maintained 80-125 mmHg) by halothane (1-3%)or alpha-blockers phenoxybenzamine, phentolamine. This also prevents the development of PI neurogenic pulmonary edema which is a frequent complication of severe brain damage. The mechanism of PI pulmonary edema has not been elucidated but is thought to be due to pulmonary venospasm. Xylocaine (1%) was used for arrhythmia control and agropine for bradycardia and restoration of SAP PI instead of vasopressors. This method for TBI is simple and reproducible with low morbidity and mortality enabling better correlation between duration of ischemia and neurologic deficit.

POSSIBLE RELEASE OF ATP AND ADENOSINE FROM EXERCISING SKELETAL MUSCLE. Emma L. Bockman* and Robert M. Berne. Univ. of Va., Dept. of Physiology, School of Medicine, Charlottesville, Va. 22901.

Based on the finding of ATP in the venous blood from exercising skeletal muscle, ATP has been suggested as a mediator of exercise hyperemia. However, it is not known whether the source of this ATP is the skeletal muscles, the nerves, or the formed elements of blood. To prevent ATP degradation, blood was collected in tubes containing EDTA. Tetanic contraction of dog hindlimb for 2 min caused an increase of venous plasma ATP from 0.36±0.16 nmoles/ml (range: 0.17-1.15 nmoles/ml; n=5) to 0.80± 0.23 nmoles/ml (range: 0.20-1.12 nmoles/ml) and a change in the arteriovenous difference of plasma ATP from -0.02±0.18 nmoles/ml to -0.56±0.27 nmoles/ml (n=4). However, there was a large variation among samples and control and experimental results did not differ significantly. Furthermore, the venous plasma ATP remained elevated (0.62±0.13 nmoles/ml) 45 min after the first period of tetany and did not increase significantly following a second period of tetany (0.70±0.11 nmoles/ml; n=5). In addition, the arteriovenous difference of plasma ATP was unchanged following a second tetanic period (-0.28±0.34 nmoles/ml vs -0.13±0.17 nmoles/ml; n=4). It is of interest that EDTA released ATP from the formed elements of blood resulting in a plasma ATP level of 0.39±0.11 nmoles/ml. This observation, in conjunction with the failure to obtain significant release of ATP following tetanic contraction (even in the presence of EDTA), casts considerable doubt on the role of ATP as a vasodilator in exercise hyperemia. Furthermore, in isolated, perfused rat hindquarters, no ATP was detectable in the venous effluents from either resting or contracting muscles (ATP<0.075 nmoles/ml). However, the levels of adenosine and its degradative products, inosine and hypoxanthine, in the venous effluents were greater in contracting than in resting hindlimbs. SUPPORTED BY GRANT # HL10384.

IMPROVEMENT OF CORONARY BLOOD FLOW IN ENDOTOXIC SHOCK WITHOUT IMPROVEMENT OF MYOCARDIAL CONTRACTILITY. C. T. Bohs*, M. E. Turbow* and S.N. Kolmen. Shriners' Burns Inst. and Univ. of Texas Med. Br., Galveston, Texas.

The effect of endotoxic shock on myocardial contractility is thought to be mediated via myocardial depressants released in later stages of shock. Since coronary constriction may be associated with this myocardial depression, it was thought enhancement of coronary flow might be of value. Healthy adult mongrel dogs were anesthetized with pentobarbital, placed on positive pressure ventilation and a left thoracotomy performed. A shunt containing an electromagnetic flowmeter was instituted from left carotid artery to left common coronary artery for measurement of coronary flow. Left ventricular and mean arterial pressures, cardiac output and heart rate were also continuously monitored. The peak value of dp/dt/P was used as an index of contractility. Dogs were divided into test (E. coli endotoxin, 0.75 mg/kg IV) and sham groups. After four hours each group was subdivided into treated (dipyridamole, 0.2 mg/kg IV) and untreated subgroups. Changes in heart rate, left ventricular and arterial pressures, cardiac output and coronary blood flow were as expected in dogs subjected to endotoxic shock; peak values of dp/dt/P were lower than pre-shock values throughout the experiment. Both sham and test subgroups receiving dipyridamole exhibited decreased heart rates and increased coronary blood flows with no change in myocardial contractility; the sham subgroup showed the greater increase in coronary flow. Apparently, the coronary vasculature in endotoxic shock is less responsive to dipyridamole. It also appears that the myocardial depression that does occur is not responsive to increased coronary flow.

THE EFFECT OF PHYSICAL CONDITIONING ON CARDIAC FUNCTION IN SQUIRREL MONKEYS FED AN ATHEROGENIC DIET. R.F. Bond, E.S. Manning*, T.B. Clarkson* and R.E. Parker*. Depts. of Phys. and Comparative Med., Bowman Gray School of Med. of Wake Forest Univ., Winston-Salem, N.C.

The purpose of these studies was to compare the functional myocardial reserve in sedentary and exercised atherosclerotic squirrel monkeys. The animals were divided into the following groups: 1) five free ranging controls (FRC), 2) five sedentary control animals fed an atherogenic diet for three years, and 3) five animals fed the same diet as group 2, but exercised 2 hrs./day for three years. Aortic arch pressure, mean and phasic cardiac output, cardiac power and lead I of the ECG were monitored while the myocardial oxygen demand was increased by electrical pacing. Aside from gaining control cardiovascular data on these animals, three critical pacing rates were obtained: a) lowest pacing rate at which repolarization changes occurred in lead I, b) pacing rate at which cardiac power demonstrated a significant decrease below control, and c) fastest pacing rate that the heart could follow. The data below is expressed as mean HR $\pm$ 1 SEM.

	FRC	DIET CONTROL	DIET TEST
T-WAVE	266 $\pm$ 15	273 $\pm$ 4	315 $\pm$ 19
POWER DROP	272 $\pm$ 10	350 $\pm$ 24	356 $\pm$ 30
MAX. RATE	314 $\pm$ 10	359 $\pm$ 24	386 $\pm$ 25

These data provide evidence that exercise improves the cardiac performance of monkeys consuming an atherogenic diet. Pathological studies indicated that the improvement was more likely related to lesser intramyocardial artery atherosclerosis (25$\pm$4 vs. 47$\pm$3% obstruction of arteries affected) than to increased collateral circulation (74$\pm$5 vs. 71$\pm$3 arteries seen on cross section).
(Supported by USPH, NHLI Grants HL 14164, HL 487 and HL 5392.)

THE CONFIGURATION AND VASCULAR PERFUSION OF HUMAN PROXIMAL TUBULES. J. V. Bonventre* and R. Beeuwkes, III, Harvard Medical School, Boston, Mass.

Proximal tubular reabsorption appears to be enhanced by increased oncotic pressure of the fluid perfusing the tubule. This may constitute a mechanism for filtration-reabsorption balance which could operate on a single nephron basis if close association existed between the proximal tubule and efferent capillaries arising from the same glomerulus. In the dog kidney, however, our studies have shown that these structures are generally dissociated. Normal human kidneys, donated for transplantation but found unusable, were rapidly fixed by arterial perfusion with glutaraldehyde solution so as to keep the proximal tubules open. Red "Microfil" silicone was injected via the artery to fill the vasculature. Kidneys were then dehydrated and cleared in methyl salicylate. Proximal tubules were injected with white silicone by means of micropipettes inserted into Bowman's spaces of chosen glomeruli. The efferent vessels of the glomeruli and the progress of the injections were filmed simultaneously. Each human proximal tubule was generally found to be perfused by the efferent vessels of other glomeruli. No one-to-one relationship or independent nephron was found to exist. This result indicates that if there is a balance between GFR and proximal reabsorption in the human nephron then this cannot be regulated by physical factors on a single nephron basis. A film demonstrating typical vascular-tubular relationships in the human kidney will be shown.

RENAL HANDLING OF CORTISOL IN DOGS. U. Boonayathap* and S.F. Marotta. Department of Physiology, University of Illinois at the Medical Center, College of Medicine, Chicago, Ill. 60680.

Although it is well known that adrenocortical steroids and their metabolites are excreted in the urine, little is known about the parameters which affect their excretion. To determine how the kidney regulates steroid excretion, free flow and stop flow studies were performed on anesthetized male dogs infused with cortisol. The concentrations of free (FC) and glucuronide (CG) cortisol were determined in plasma and urine. The results indicate that tubular reabsorption of FC reaches a maximum when the filtered load (FL) is approximately 14 µg/min. The tubular maximum (Tm) of FC is approximately 9 µg/min with the plasma threshold at 10 µg/100 ml. The FC clearance (C_{FC}) shows that at low FL (<14µg/min), C_{FC} remains essentially constant, then increases proportionally as the FL increases. CG does not show a Tm or plasma threshold; at low FL (<1.0µg/min) CG seems to be secreted by the renal tubules and then its reabsorption increases linearly as the FL increases. The CG clearance abruptly decreases at low FL up to 2 µg/min, then gradually declines as the FL increases. The stop flow studies show that FC is reabsorbed primarily in the distal tubules, but that CG is secreted along the entire length of the renal tubules. The administration of ACTH (2 U/min/dog) during the stop flow studies did not cause any appreciable changes in the reabsorption of FC in the distal tubules. In the proximal tubules, ACTH increased the reabsorption of FC. These findings suggest that the role of the kidney and the action of ACTH on this organ should be taken under consideration when describing the negative feedback mechanism which regulates plasma cortisol levels. (Supported in part by the Office of Naval Research Contract NR 101-580.)

EFFECTS OF CYCLIC AMP (cAMP) ON Ca TRANSPORT IN MITOCHONDRIA Andre B. Borle, Dept Physiology, Univ. Pittsburgh Sch. Med. Pitts., PA

The effect of cAMP on subcellular Ca turnover was studied in isolated kidney and liver mitochondria. The Ca concentration of the incubating medium was determined by fluorometric methods after its separation by millipore filtration. Control mitochondria take up Ca in exchange for H^+ and lower the medium Ca to 10^{-5}M in less than 2 min. cAMP produces an instantaneous release of Ca from mitochondria and a rise in the steady state Ca concentration of the medium. A new medium Ca level of 0.7 to $3 \cdot 10^{-4}$M is achieved in less than 5 sec. and is proportional to cAMP concentration between 10^{-7} and $3 \cdot 10^{-6}$M. cAMP is inactive above $5 \cdot 10^{-6}$M and below 10^{-7}M. cIMP, cGMP, 5'AMP, dibutyryl cAMP are inactive at any concentration. The same steady state Ca level is reached from higher or lower Ca concentrations i.e. whether cAMP is added before or after the addition of Ca to the mitochondrial suspension. At low Ca or P_i concentrations, the Ca released by cAMP is immediately reaccumulated by the mitochondria in less than 2 min. with a further release of H^+. This "pulse" can be repeated by sequential additions of cAMP. The transient or sustained response to cAMP depends on the medium Ca x P_i product and presumably on the presence or absence of Ca phosphate precipitate inside the mitochondria. These results support the hypothesis that cAMP regulates cytoplasmic Ca by controlling the mitochondrial Ca efflux rate. This mechanism may be involved in the regulation of Ca transport, in other hormonal effects mediated by cAMP, in stimulus secretion coupling and in the inotropic effect of catecholamines.

THE EFFECT OF FIRING RATE ON THE LOCAL THERMOSENSITIVITY OF PREOPTIC NEURONS. J.A. Boulant (intr. by J.D. Hardy). John B. Pierce Fndn. Lab. and Yale School of Medicine, New Haven, Conn. 06519

It has previously been shown that peripheral thermal stimulation may induce changes in the firing rate and local thermosensitivity of preoptic single units. During these changes, an increase in spontaneous firing rate (at 38°C) usually produced a decreased local thermosensitivity in "warm-sensitive" units and an increased thermosensitivity in "cold-sensitive" units. The present study sought to determine under neutral conditions, whether populations of preoptic neurons having different spontaneous firing rates, display analogous differences in their local thermosensitivities. In urethanized rabbits, the firing rates of preoptic single units were observed while local temperature was manipulated by implanted thermodes. Units were categorized in groups according to their firing rate at 38°C, and in each group the firing rates were averaged at regular intervals over the range 33° to 43°C. In the warm-sensitive units it was found that, in the hyperthermic range, there was a progressive decrease in thermosensitivity as spontaneous firing rate increased. In the cold-sensitive units, however, over the entire range of local temperatures, thermosensitivity increased as spontaneous firing rate increased. These results suggest that warm-sensitive neurons which are thermosensitive only in the hyperthermic range (possibly controlling heat-loss) have low firing rates, while neurons warm-sensitive only in the hypothermic range (possibly controlling heat-production) have high firing rates. It is proposed that input from peripheral thermal receptors contributes to these neuronal firing rates, and thus provides a basis for the separation of ranges of local thermosensitivity. (supported in part by NIH NB 04655 and ES00123).

RED CELL WASHOUT FROM CONTRACTING SKELETAL MUSCLE. T. Bowden*, S.H. Song and A.C. Groom. Biophysics Dept., Univ. Western Ontario, London, Ontario.

Gastrocnemius muscles of cats were isolated, placed in a bath of mineral oil at 37°C, and perfused with oxygenated cell-free Ringer solution at a constant flow rate of 5 ml/min. Throughout the perfusion the muscles contracted in response to electrical stimulation of the distal part of the cut sciatic nerve (0.5-1.5 V, 1 msec, 3-5 p.p.s). The infusion pressure at the arterial cannula, monitored with a Statham transducer, had a mean value of 51 $\pm$ 5 (S.E.) mm Hg, significantly less than that in perfused resting muscles. The concentrations of red blood cells in serial samples of the venous outflow were measured and plotted on a semilogarithmic scale as a function of time. The mean washout curve can be analyzed by a curve-peeling method and the results suggest that the overall curve is the sum of the washouts from four separate red cell compartments. In comparison with the results obtained from resting muscles there is little difference except that in the case of the compartment with the second slowest washout the $T_{\frac{1}{2}}$ is increased from 4 to 8 min. As yet we have not confirmed morphologically the identity of this particular compartment, but the change we found could signify the mobilization of vessels which in resting muscle would have been partially closed.

(Supported by the Ontario Heart Foundation)

TIME COURSE AND MECHANISMS OF THE VASCULAR RESISTANCE RESPONSE TO HYPERKALEMIA AND HYPOKALEMIA. R. A. Brace, J. B. Scott, and D. K. Anderson.* Depts. of Physiol. and Chem. Eng., Mich. State Univ., E. Lansing, Mich.

It is well established that a local decrease in arterial plasma $[K^+]$ increases vascular resistance to blood flow and an increase in plasma $[K^+]$ up to approximately 10 mEq/l initially decreases resistance. The purpose of the present study was to examine the time course of resistance changes produced by acute hypokalemic and hyperkalemic perfusion of the isolated canine forelimb. The study shows the initial decrease in resistance during hyperkalemia (7.1 mEq/l) is followed by a gradual increase in resistance which rises above the control value in approximately 5 minutes even though the hyperkalemic perfusion continues. With hypokalemic perfusion (2.4 mEq/l), only a slight waning follows the initial increase in resistance. After 10 minutes, the plasma $[K^+]$ was returned to normal. Resistance increased further before returning toward the initial value following hyperkalemia, whereas resistance simply decreased toward control following hypokalemia. The time course of the changes in resistance parallel almost exactly the time course of the changes in resting membrane potential calculated with a computer model of a vascular smooth muscle cell. The initial changes in resting potential are due to the effects of the changes in extracellular $[K^+]$ on the electrogenic Na-K pump while the secondary changes in resting potential are caused by the effects of changes in intracellular $[Na^+]$ on the electrogenic pump. These studies suggest that the changes in resistance produced by altered plasma $[K^+]$ are mediated in large part through changes in resting membrane potential.

EFFECTS OF ADH (ARGININE VASOTOCIN) ON SINGLE NEPHRON GLOMERULAR FILTRATION RATES (SNGFR) AND BLOOD PRESSURE IN BIRDS. Eldon J. Braun* and William H. Dantzler. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724.

Avian kidneys consist of large numbers of reptilian-type (RT) and smaller numbers of mammalian-type (MT) nephrons. SNGFRs of both types have been estimated in desert quail (Lophortyx gambelii), using modified Hanssen's technique. Previous work indicated that during control diuresis SNGFR was 6.4 nl/min for RT nephrons (71% of RT nephrons filtering) and 14.6 nl/min for MT nephrons. During intravenous salt loading, SNGFR of MT nephrons fell to 12.7 nl/min and RT nephrons stopped filtering. To assess factors contributing to regulation of SNGFRs, arginine vasotocin (AVT) was administered intravenously to desert quail in doses of 10, 50, and 200 ng/kg. The low, probably physiological doses (10 and 50 ng/kg) had no effect on mean arterial pressure but caused reduction in total-kidney GFR. SNGFR after 10 ng/kg was 11.3 nl/min for MT nephrons and 4.7 nl/min for RT nephrons (52% filtering). SNGFR after 50 ng/kg was 16.5 nl/min for MT nephrons and 6.9 nl/min for RT nephrons (26% filtering). High, probably pharmacological doses (200 ng/kg) produced increases, decreases, or biphasic changes in mean arterial blood pressure. Total-kidney GFR fell with all 200 ng/kg doses but SNGFRs were variable. With increases in mean pressure, MT SNGFR increased (24.7 nl/min) and RT nephrons ceased filtering. With decreases or biphasic changes in mean pressure MT SNGFR decreased (7.3 nl/min), RT SNGFR did not change (6.8 nl/min) but fraction of filtering RT nephrons fell to 43%. Shunting of blood away from RT nephrons into peritubular capillaries or away from groups of RT nephrons to MT nephrons may explain effects of AVT. It is concluded that AVT plays role in regulating total-kidney GFR in birds by regulating number of filtering RT nephrons and SNGFRs of both RT and MT nephrons. (NSF GB 28692X; NIH AM 16294; NIH HE 05884).

A KINETIC-DIFFUSION MODEL APPLIED TO RBC FLUX DATA, M.O. Breitmeyer and P.H. Newell, Jr.*, Bioengineering Program, Texas A&M University, College Station, Texas 77843.

Crank's (1) diffusion-reaction model for spherical particles is applied to Hoffman's (2) outflux data for isotopic sodium flux in human red blood cell ghosts. The model assumes simple diffusion coupled with first order reversible reaction. Diffusion is governed by equation (1) with simultaneous reversible reaction of the type described by (2).

$$(1) \quad \frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} - \frac{\partial S}{\partial t} \qquad (2) \quad \frac{\partial S}{\partial t} = \lambda C - \mu S$$

Where D = diffusion coefficient, λ = forward rate constant, μ = reverse rate constant, C = concentration of free solute, S = concentration of immobilized solute, x = distance, t = time.

When non-dimensionalized data of Hoffman's are plotted as dictated by the solution of Crank, the curve predicted by the model and the experimental data points nearly coincide. This agreement holds for "active" transport as well as in the strophanthidin inhibited case. Since the only parameters required are rate constants this model may be useful in the application of transport data to larger metabolic models.

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ROLE OF SKIN AND BLOOD TEMPERATURES AND OF dTs/dt IN CONTROL OF HUMAN SKIN BLOOD FLOW AND SWEAT RATE. George L. Brengelmann*, Craig Wyss*, John M. Johnson*, and Loring B. Rowell. University of Washington School of Medicine, Seattle, Washington.

To examine further the interaction of skin temperature (T_s) and blood temperature (T_b) in the control of skin blood flow (SkBF) and to compare this control with the control of sweat rate (SR), we drove T_s in a square wave followed by a ramp (.15°C/min). T_b (right atrial catheter), T_s (average of 10 sites), esophageal temperature, SR (dew point detection), SkBF (forearm plethysmography) and heart rate (HR) were monitored. Subjects were four healthy young men. With rising T_s the initial increase in SkBF (2 fold) was unaccompanied by any detectable change in SR; it occurred before any rise in T_b or HR (T_b fell slightly at the time). This flow increase was well correlated with T_s. When T_b rose above control, the pattern of responses changed; SR, SkBF, and HR then became strongly correlated ($R \geq 0.9$) with T_b. The relative sensitivities of SV, SkBF and HR with respect to T_b and T_s in this range exceeded the ratio of 15:1. During periods of high negative dTs/dt, SkBF, HR and SR for a given T_b, T_s pair were lower. Our findings fit with a scheme of control in which T_s governs release of skin vasoconstrictor tone and T_b dominates control of SR and active skin vasodilation. Negative dTs/dt is an inhibitory drive for both SkBF and SR. (Supported by NIH Grant HL 09773 and NASA Grant NGR-48-002-082.)

TUBULAR REABSORPTIVE RESPONSE TO HYPERNATREMIA. E.H. Bresler and K.T. Nielsen*, VA Hospital, New Orleans, La.; M. Clinton Miller, III* and M.R. Stroud*, Medical Univ. South Carolina, Charleston, S.C.

In dogs given ethacrynic acid a sustained steady diuresis was maintained by n-saline infusion at 10 ml/min. After a number of clearance periods 5% NaCl was administered to elevate plasma sodium concentration (P_{Na}) to values as high as 183 meq/L. GFR was determined by inulin clearance. The rate of tubular reabsorption (T_{Na}) was calculated. T_{Na}, adjusted for variation in GFR, was found to be closely correlated with P_{Na}. Since this constitutes a proportionality between changes in filtered loads of sodium produced by increments in P_{Na}, it is called glomerulotubular balance Type II in contrast to the more well known balance between filtered load and tubular reabsorption observed when GFR is varied (GT balance type I). The implications of these findings with respect to the nature of proximal tubular transport systems is discussed. The conclusion is drawn that these studies favor a reabsorptive system which generates bulk flow of solution rather than primary transport of sodium ion.

PERIODICITY DURING THE SHORT-TERM RESPONSE TO A STEP CHANGE IN INSPIRATORY GAS CO_2 CONCENTRATION. Alfred W. Brody, Steven S. Jewett*+, Suzanne Moshler*, Thomas H. Dee *+, Donald J. Schroeder*+: Chest-Asthma Research Institute, Creighton Medical School, Omaha, Nebraska 68131

By keeping the bag of CO_2 from which the subject rebreathes during determination of the equilibrated venous pCO_2, in the spirometer from which he breathes prior to and after the test, we have determined the response to pCO_2 during the two minutes of rebreathing, first in a small group of trained subjects, then in 75 untrained normal subjects, and in a large group of patients. The response to CO_2 increased during the entire two minutes of rebreathing and does not reach any maximum during this period; however, the response does not occur with the first breath and is not continuously augmented with each succeeding breath. The first response occurs in most people at 22-25 seconds after turn-in, following which the new rate and depth of breathing are constant for another 22-25 seconds after which there is another step-wise increase in ventilation. If the subject is calm and unworried with slow regular breathing immediately prior to turning into the bag, and if the resistance to breathing in the system is kept minimal, such step-wise responses to respiration continue during the whole two minute period of response. Nevertheless, the degree of response depends on the concentration in the first few breaths; in Normals, equilibration in our 1-2L bags of gas is complete within 3 breaths or 12-15 seconds, yet the response to an initial bag % of 10% is higher at every step than the response to an initial bag % of 8%, and to 8% is higher than to 6%. The response to step return to inspiratory air is cyclic with a slightly shorter period of 15-18 seconds initially and damps out in 1.5 to 4 cycles. (Supported in part by Nebraska TB Association, + Student Trainee supported in part by USPHS Grant 701HE5506.)

THE EFFECTS OF CARDIAC AGLYCONES ON THE Na EFFLUX IN SINGLE BARNACLE MUSCLE FIBERS. D. J. Brown,* E. E. Bittar (intr. by W. E. Stone). Univ. Wis. School of Med., Dept. Physiol., Madison, Wis. 53706

Recent studies of single muscle fibers from the barnacle Balanus nubilus loaded by microinjection showed that external but not internal application of ouabain caused a fall in the Na efflux. Also found was that the ouabain-insensitive Na efflux was markedly stimulated by raising the external K concentration, by acidification of the external medium and by microinjecting $CaCl_2$. By contrast, the aglycone, digitoxigenin, whether applied externally or internally, caused a fall in the Na efflux. Both effects caused by digitoxigenin were dose-dependent, with the minimal effective external concentration being 10^{-7} M, and the injected concentration 10^{-5} M. Internal application, followed by external application of digitoxigenin, failed to produce any further fall in the Na efflux. Sensitivity of the remaining Na efflux to a high external K concentration, external acidification or microinjection of $CaCl_2$, following external or internal application of digitoxigenin could also be demonstrated. The finding that an aglycone has the ability to slow down the Na efflux has been confirmed by internal application of ouabagenin, acetylstrophanthidin or strophanthidin. The simplest explanation of these results is that aglycones unlike glycosides are small enough to reach their point of action following micro-injection. That this may be so is suggested by the observation that other glycosides including digitoxin failed to influence the Na efflux following internal application. (Supported in part by grants from Wisconsin Heart Association, NSF and ONR).

NATURAL BREATHING PATTERNS AND THE EFFECT OF SUBJECT AWARENESS. P. Brusil, R. Kronauer (intr. by J. Mead). Harvard Univ., Cambridge, Mass.

Analysis of the naturally occurring ventilatory output allows inferences to be made about the natural respiratory control mechanisms. Using an indirect technique, the natural tidal volume time history was recorded from 25 normal, naive, supine subjects. In the average subject instantaneous, breath-to-breath ventilation varies about its mean by about 20%. The mechanisms controlling breath rate and depth, then, do not produce simultaneous compensatory changes on a breath-to-breath basis. Rather, because variations in breath duration are small, fluctuations in ventilation are produced by large fluctuations in tidal volume. In half the subjects, the fluctuations in depth are strongly correlated to fluctuations in the duration of inspiration (cf. 1,3). Regarding the effect of awareness of respiration upon the breathing pattern (cf. 2), the most prominent change following the transition from naive to "aware" breathing was that the average breath duration at first became significantly larger. Then it settled back to an average value that was still greater than that during naive breathing. The phenomenon is exaggerated for those subjects who are slow breathers in the naive state and is associated principally with changes in the duration of expiration. The time course of the transient phase is about 50 breaths.

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BIOASSAY OF THE INTRAVASCULAR CLEARANCE OF ENDOTOXIN AFTER ADRENALECTOMY AND TOLERANCE INDUCTION. Bernard J. Buchanan* and James P. Filkins. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Lead acetate iv sensitized rats to lethal shock as evidenced by a 2000-fold decrease in the LD_{50}. The present study evaluated the use of lead-sensitized rats as recipients for the evaluation by bioassay of the intravascular clearance of endotoxin. S. enteritidis lipopolysaccharide in 0.9% saline was administered iv at doses of 1.0, 0.5, and 0.25 mg to 300 g male rats of the Holtzman strain. Blood samples were obtained at 15, 30, 60, 120, 180 or 240 min, diluted 10-40 fold, and injected into assay rats which also received 5 mg of lead acetate iv. Blood endotoxin concentrations were calculated from a log-probit transformation of standard doses and from these data points the intravascular clearance half-times were computed. Similar analyses were performed after acute bilateral adrenalectomy which sensitized to endotoxin shock and after tolerance induction which increased resistance. In control rats the log endotoxin concentrations vs time plots for 1.0 and 0.5 mg doses were linear with half-times of 0.95 and 0.96 hrs, respectively. At a 0.25 mg endotoxin test dose multiphasic clearance occurred. Bilateral adrenalectomy did not alter the endotoxin clearance half-time. In contrast, clearance was markedly enhanced by prior treatment with endotoxin, such that little to no endotoxin was bioassayed 15 min after a 0.5 mg clearance test dose. These data suggest that (1) the lead-treated rat provides a sensitive and reproducible bioassay for endotoxin, (2) biologically active endotoxin is removed slowly from the circulation of rats, (3) the removal rate is not appreciably altered by adrenalectomy and (4) the clearance is markedly enhanced during endotoxin tolerance. (Supported by USPHS Grants HL 08682 and HL 14540 and NSF Trainee Grant 2/Z30-2253.)

INTERRELATIONS OF PLACENTAL BLOOD FLOW, O_2 TRANSFER AND INTRAUTERINE PRESSURE: A MATHEMATICAL MODEL. L. Allan Butler*, Lawrence D. Longo and Gordon G. Power. Departments of Physiology, Anesthesiology and Ob. & Gyn., Loma Linda Univ., Loma Linda, CA 92354.

In an attempt to understand the role of intrauterine pressure (P_{AM}) on maternal and fetal placental blood flows and O_2 exchange, we solved equations expressing their interrelations under various conditions. Some independent variables were: Mean maternal arterial pressure, maternal intervillous space compliance, uterine contraction duration and uterine contraction interval. Some dependent variables were: maternal placental inflow and outflow, intervillous space volume, fetal placental flow and the O_2 exchange rate. Results using Gaussian shaped contraction profiles indicate: 1) Increasing P_{AM} results in initially decreased maternal placental inflow and increased outflow leading to decreased intervillous space volume. 2)Maternal outflow varies as a function of intervillous lake pressure minus P_{AM}, i.e. "maternal sluice flow." 3) Fetal placental flow increases slightly, changing from sluice to non-sluice conditions. 4) O_2 exchange rate is decreased as a consequence of these changes. 5) Using assumed normal values, the maximum percentage changes were: maternal inflow -60%, outflow -30%, intervillous space volume -25% and fetal flow +20%. The O_2 transfer rate decreased 40%. 6) The effect of different labor patterns on the fetus were compared by integrating the milliliters of O_2 loss during a contraction. Fetal O_2 deprivation is greater with decreased mean maternal arterial pressure, increased P_{AM} and duration of contraction. Little effect was noted with change in interval between contractions, intervillous space volume and compliance. (Supported in part by USPHS Grants HD 03807 and HD 04394).

OXYGEN DELIVERY AND UTILIZATION IN DOGS WITH A SUBLETHAL DOSE OF COBALT CHLORIDE. S. M. Cain. U. of Ala. Med. Ctr., Birmingham, Al. 35294

Cobaltous chloride ($CoCl_2 \cdot 6H_2O$) causes depression of blood pressure, cardiac output, and oxygen uptake but the contribution of the stagnant hypoxia component to the histotoxic effect on oxygen uptake ($\dot{V}O_2$) has not been made clear nor has there been clear evidence that the reduced $\dot{V}O_2$ is associated with an energy deficit as indicated by a rise in arterial excess lactate (XL). Four groups of 8 anesthetized and paralyzed dogs were kept at constant ventilation and given 15 mg/kg $CoCl_2$ I.V. after a 30-min. control period. Gp I was given nothing else; Gp II received 1 mg/kg per hr propranolol (β-block); Gp III was given $NaHCO_3$ to correct pH changes after $CoCl_2$; Gp IV had both β-block and $NaHCO_3$. $\dot{V}O_2$ was measured every 10 min. for 4 hrs. and blood was taken frequently for lactate, pyruvate, and blood gas measurements. Depression of $\dot{V}O_2$ with β-block (Gps II and IV) was more marked (to 65% of control vs 79%, $P < 0.01$) but decreases in cardiac output and mean arterial blood pressure were not significantly different. Recovery of $\dot{V}O_2$ was complete, usually within 60 min., with little evidence of deficit repayment. In fact, Gp II had an average $\dot{V}O_2$ below control value throughout the experiment. Total O_2 delivery ($\dot{Q} \times Ca_{O2}$) became limiting to $\dot{V}O_2$ at 12 ml/kg·min which defined the stagnant hypoxia component. Histotoxic effects appeared limited at this dose of $CoCl_2$ to reduction of $\dot{V}O_2$ to 80% of control. XL in arterial blood was linearly correlated with the measured O_2 deficit during the acute reaction to $CoCl_2$ in all groups but Gp III. For β-block experiments, the regression line of XL and O_2 deficit was similar to previously obtained data from hypoxic hypoxia. Whether energy production was curtailed by low PO_2 or by poisoning of a Krebs cycle enzyme, XL was useful as a yardstick of the energy deficit incurred. (Supported by NHLI Grant HE-14693)

VOLUME REGULATION OF FLOUNDER, Pseudopleuronectes americanus, RED BLOOD CELLS. Peter M. Cala (intr. by B. Schmidt-Nielsen), Case Western Reserve Univ. and Mt. Desert Is. Biol. Laboratory, Salsbury Cove, Maine

When the nucleated red blood cells of the winter flounder, Pseudopleuronectes americanus, were placed in hypotonic media (200 mOsm vs 326 for isotonic), they swelled to 145% of control volume, then lost KCl and water until reaching a volume 111% of control. During the regulatory phase, the absolute amount of intracellular K^+ decreased to 79% of control values, while the absolute amount of intracellular Na^+ remained virtually unchanged.

The calculated osmolality of the transported fluid was 121 mOsm. A discrepancy of 70 mOsm existed between transported and extracellular fluid, of which some 25 mOsm could probably be accounted for by amino acids (Fugelli, K., 1967). Cells exposed to 10^{-4}M ouabain were able to regulate their volume as well as controls, although the ratio of intracellular K^+ to Na^+ was considerably decreased.

Cells placed in hypertonic media showed an initial rapid volume decrease to 75% of controls. At the conclusion of the regulatory phase, these cells had adjusted their volume to 95% of control values. The gain in cell water was apparently due to increases in the absolute amount of intracellular Na^+ and KCl, the gain in K^+ being approximately 1/3 that of Na^+. The transported fluid was essentially isosmotic since 90% of the water moved could be accounted for in terms of Na^+ and KCl.

It appears that volume regulation is passive, at least with respect to the Na-K dependent ouabain sensitive pump, and proceeds for the most part by making use of the steady state cation gradients. The possibility of an active component of flux during volume regulation, especially in the hypertonic media is being investigated. Supported by NIH Grant #AM 15972 and GB 22178 and by NIH Training Grant # GM 01699.

AIR BREATHING IN THE COCONUT CRAB, Birgus latro. J. N. Cameron and T. A. Mecklenburg (intr. by P. R. Morrison). Institute of Arctic Biology, Univ. of Alaska, Fairbanks, Alaska.

Aerial gas exchange was investigated in the coconut crab, Birgus latro, in Eniwetok, Marshall Islands. This animal has a well-developed lung, supplied with air by the pumping action of the scaphognathites. Air flow rates averaged 57 $mg \cdot kg \cdot min^{-1}$ at rest, and reached over $1L \cdot min^{-1}$ when the animals were stressed. Extraction was low (average 5.2%), but rose as high as 16% during moderate hypoxia ($P_{I_{O_2}}$ = 60 torr). Responses to hypercapnia were markedly different from those seen in aquatic crabs. Ventilation volume increased rapidly to a steady state value after an increase of ambient CO_2. The increased ventilation was accompanied by a decrease in CO_2 gradient across the lung, and by a drop in blood pH. After 14 hours of high CO_2 treatment, there was no compensatory change in pH, as would be seen in aquatic animals. We propose that this crab has evolved independently the same pH-regulating response to increased P_{CO_2} as have mammals. Various other aspects of gas transport were also noted, including the very high blood pressure (40-50 mm Hg) compared with other crabs. The high blood pressure is important in maintaining geometry (by inflation) of the lung, and may also be critical for support and locomotion of the animal's considerable mass (up to several kg). Some comparative data on Gecarcoidea lalandii will also be discussed.

EFFECT OF POSITIVE PRESSURE BREATHING ON FRC AND MVV DURING IMMERSION IN WATER. Enrico M. Camporesi,* Edward T. Flynn* and Sarah A. Nunneley,* (Intr. by H. Rahn). Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N.Y.

Lung volumes and maximal voluntary ventilation (MVV) were measured in 5 seated male volunteers immersed in water to the neck and breathing room air while applying positive counterpressures of 0, 10, 20, 30 cm H_2O. Lung volumes were measured with open circuit spirometry; RV was determined by lung N_2 dilution. MVV was calculated from the volume of the gas exhaled over 15 sec. The principal changes during immersion were in FRC and MVV, as indicated below.

		TLC (L)	FRC (L)	RV (L)	MVV (L/min)
Dry control		6.77	3.28	1.16	176
Immersion	0 cm H_2O	6.56	2.08	1.07	150
"	10 "	6.62	2.28	1.09	158
"	20 "	6.72	2.84	1.13	172
"	30 "	6.80	3.66	1.20	179

A positive counterpressure of 25 cm H_2O restored lung volumes and MVV to dry control values. The FRC was progressively displaced from the predicted position on the relaxation pressure-volume curve as the counterpressure increased, suggesting an increasingly active expiratory tonus at end expiration. (Supported in part by ONR Contracts N00014-68-A-0216 and N00014-71-C-0342, and by AF Contract F44620-72-C-0009.)

DISTRIBUTION OF ^{133}Xe BETWEEN ERYTHROCYTES AND PLASMA. Ronald Carlin* and Shu Chien, Department of Physiology, College of Physicians and Surgeons, Columbia University, New York, New York 10032.

^{133}Xe is commonly used for the study of microcirculatory dynamics by the indicator dilution technique. Since Xe has a high affinity for lipoid materials, quantitative treatment of Xe dilution curves necessitates precise information on its partitioning between erythrocytes and plasma as well as that between tissue and plasma. ^{133}Xe dissolved in saline was added to heparinized whole blood freshly drawn from healthy dogs and men. Under anaerobic condition the samples were allowed to equilibrate with mixing for 5-10 min. After centrifugal separation, plasma and packed cells were drawn anaerobically for the determination of ^{133}Xe activity. Studies on dog blood (average hematocrit 44%) at a temperature of 37°C yielded a RBC/plasma partition coefficient (λ) of 3.31 (S.D. = 0.06). Variations in the initial hematocrit of the blood sample from 20 to 70% did not significantly alter λ. Reductions in temperature from 37 to 22 and 5°C raised λ progressively. Preliminary studies on human blood at 37°C gave a mean λ value of 2.24. Therefore, ^{133}Xe has a high affinity for the erythrocytes in comparison to plasma, and the λ values vary with the temperature and the animal species used. (Supported by US Public Health Service Research Grant HL-06139 from the National Heart and Lung Institute, the US Army Medical Research and Development Command Contract DADA-17-72-C-2115, and the Scaife Family Charitable Trusts, Pittsburgh, Pa.)

INTERACTION BETWEEN NEUROGENIC AND PERIPHERAL DETERMINANTS OF RENAL VASCULAR RESISTANCE. Drew E. Carlson* and Lawrence P. Schramm. Johns Hopkins University School of Medicine. Experiments were performed on chloralose anesthetized cats. Renal blood flow to the left kidney was measured with an electromagnetic flowmeter. An estimate of renal vascular resistance (RVR) was computed on line as the ratio of aortic pressure to renal arterial blood flow. Renal vasoconstrictions (VC) were elicited by electrical stimulation of the left lateral hypothalamus (HP), central gray substance of the mesencephalon (CG) or left renal nerves. Renal vascular resistance was decreased by ureteral occlusion during an osmotic diuresis, and increased by graded ia infusions of norepinephrine (NE) or phenylephrine (PE). NE or PE infusions (which increased RVR 25 to 100% but did not elevate aortic pressure significantly) reduced the peak resistance attained and, therefore, the change in resistance achieved upon HP or CG stimulation. Decreased RVR, elicited by increasing ureteral pressure to 80-100mmHg, resulted in marked attenuation of both the rate of increase in RVR and peak values of RVR attained in response to HP, CG or renal nerve stiumlation. Identical increases in ureteral pressure in the contralateral kidney did not inhibit neurogenic VC's in the ipsilateral kidney. The mechanisms by which neurogenic renal vasoconstrictions were reduced by catecholamine infusion and by increased ureteral pressure are, as yet, unclear. However these experiments suggest that intrarenal rather than spinal or central reflex mechanisms may be involved.

EFFECTS OF AMILORIDE ON THE NUTRIENT MEMBRANE OF THE IN VITRO FROG GASTRIC MUCOSA. G. Carrasquer, M. Dinno*, Doris G. Fravert*, A. K. Olson*, and M. Schwartz, Depts. of Medicine and Physics, University of Louisville, Ky.

Amiloride decreases secretion of K^+ in the distal renal tubule. It occurred to us that this effect might be partially due to a decrease of the peritubular membrane permeability to potassium. This thought led to the speculation that amiloride might affect the K^+ permeability of the frog gastric mucosa.

Potential difference (PD), resistance ($R=\Delta PD/i$), and H^+ secretory rate of chambered frog gastric mucosae were determined in control and in the presence of 0.5 and 2.0mM amiloride in the nutrient solution. The nutrient solution contained either 4mM or 79mM K^+ Ringer's solution. In 4mM K^+ 0.5 and 2.0mM amiloride, respectively, R increased 36 and 150%; PD decreased 24 and 24%; and H^+ rate decreased 19 and 27%. In 79mM K^+ the respective changes by amiloride were: R increased 11 and 82%; PD increased negligibly and 20%; and H^+ rate decreased 21 and 25%. Our interpretation of these results is that amiloride decreased both K^+ and Cl^- permeabilities of the nutrient membrane. In low K^+ experiments the effect predominates on the Cl^- pathway whereas, in high K^+, the effect predominates on the K^+ pathway.

TRANSDUCTION FUNCTION OF PULMONARY STRETCH RECEPTORS. Richard Casaburi. Dept. of Biomedical Engineering, U.S.C., Los Angeles, California.

This study was undertaken to provide a general quantitative description of the dependence of pulmonary stretch receptor firing frequency on lung volume. Single fiber stretch receptor activity was recorded from the cervical vagus of pentobarbitalized, thoracotomized cats in response to both constant lung volume and constant inspiratory flow rate. The results were compared with a mathematical model which was derived on the assumptions 1) that the receptors are embedded in the smooth muscle of the walls of medium-sized bronchi, 2) that spatial adjustments in the smooth muscle medium allow the receptors to adapt to maintained inflations, and 3) that the receptors respond to the rate as well as to the amount of deformation. Data on each receptor's observed responses were used to evaluate the parameters of the general model for that particular receptor. The set of such transduction functions then provides a representative sample of the total population from which the total impulse traffic reaching the respiratory center from vagal pulmonary afferents may be modeled for any given respiratory frequency or tidal volume and any given airflow waveform. Contrary to previous studies, our experimental observations indicate that the firing frequency response of individual receptors to static inflations is not well described as a linear function of lung volume, and this is in agreement with our model predictions.
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THE EFFECTS OF PROCAINE AND La^{3+} ON ^{45}Ca EFFLUX FROM SINGLE MUSCLE FIBERS. Stephen S. Chen and B. Van Cleave.* Dept. of Physiology, Univ. of Wisconsin, Madison, Wis.

Single muscle fibers were isolated from the barnacle Balanus nubilus and then loaded with ^{45}Ca by microinjection. ^{45}Ca efflux was found to consist of three exponential phases, having half-times of 4.8 ± .6, 12.6 ± .7 and 111.1 ± 14.8 min (n = 6), respectively. Removal of external Ca^{2+} or Na^{+} 100 min or more after loading reduced the Ca efflux by 63 ± 2.0% (n = 30) and 61.9 ± 3.6% (n = 7), respectively. The effect of external Ca could be almost halved by external application of 10 mM procaine or abolished by 5 mM La^{3+}. 10 mM procaine at pH 7.8 exerted a dose-dependent effect which in turn depended on the external Ca^{2+} concentration; lowering the external Ca^{2+} concentration led to reduced inhibition of ^{45}Ca efflux by procaine. 10 mM procaine at pH 9.3, however, caused a biphasic response: inhibition was followed by stimulation and these fibers shortened when the ^{45}Ca efflux rose. Microinjection of .5 M procaine reduced the Ca efflux, no matter whether the external pH was 7.8 or 9.3. By contrast, microinjection of 1.5 M procaine often caused a prompt rise in ^{45}Ca loss followed by a fall. The stimulatory response could not be enhanced by raising the external pH from 7.8 to 9.3. Experiments with La revealed a similar pattern of behavior. External application of 5 mM La^{3+} reduced the ^{45}Ca efflux by half, whereas internal application of .5 M La^{3+} had the opposite effect. The above results lead to the conclusion that Ca-Ca exchange is suppressed by procaine and La^{3+} and that when present in high concentration in the sarcoplasm both stimulate Ca efflux probably by releasing some 'bound' Ca.

TRANSITORY CHANGES OF PLASMA PROGESTINS, ESTRADIOL AND LH PRIOR TO OVULATION IN THE BOVINE. J. R. Chenault*, W. W. Thatcher*, P. S. Kalra*, R. M. Abrams, and C. J. Wilcox*, Dairy Science Department, University of Florida, Gainesville, Florida, 32601.

Progestins (P), estradiol (E_2) and LH were measured in bovine plasma samples collected from indwelling jugular catheters: daily on days -7 to -4; every 6 h on days -3 and -2; every 2 h from day -1 to ovulation. Plasma P, E_2 and LH were measured by radioimmunoassays. An extensive series of least squares analyses were used to characterize hormonal interrelationships, animal effects (n=6) and time changes. Time of peak LH was designated as T_0. Plasma P decreased from 5.7 ng/ml at day -6 to 0.068 ng at T_0. Estradiol increased from 2 pg/ml at day -4 to 6 pg at -12 h and then increased abruptly to 7.4 pg at T_0. This latter increase in E_2 was synchronous with the acute preovulatory surge of LH. Average E_2 (days -7 to T_0) differed among cows ($p<.01$). A positive association was detected between E_2 and LH ($p<.01$), whereas a negative association was found between P and E_2 ($p<.01$). A 50% decrease in E_2 occurred by +5 h with a return to basal levels (2 pg) at +14 h. A linear increase of 0.1 ng LH/ml plasma/day was detected from day -7 to -0.3 day (-8 h). The least squares mean of LH for this period was 0.82 ng/ml. LH increased to a peak of 13.8 ± 6.1 ($\bar{X}$ ± S.D.) ng/ml over an interval of 4.67 ± 1.03 h and returned from the peak to basal levels during an interval of 5.03 ± 1.03 h. These results are consistent with the hypothesis that a proestrus increase in E_2, not P, triggers the preovulatory surge of LH in the bovine. (Supported in part by a Biomedical Science Grant, National Institute of Health).

VISCOELASTIC PROPERTIES OF ALVEOLAR WALL IN RELATION TO AGE.
S. Chihara* and C. J. Martin. Virginia Mason Res. Ctr. and Univ. of Wash., Seattle, Wash.

The viscoelastic properties do not change while the maximum extensibility of alveolar wall diminishes with aging in man (JAP 33: 93, 1972). This has been studied further in Sprague-Dawley rats (1-25 mo) and rabbits (1-48 mo). Following sacrifice by exsanguination, alveolar walls (~30 x 30 x 250 μ) with different orientation were dissected free and suspended between length and force transducers in a bicine buffer (pH 8.8) at 37°. Studies were made of the length-tension (L-T) and stress relaxation (SR) properties. Thereafter, swine pancreatic elastase (75 u) was introduced into the tissue bath and SR repeated after 30 sec incubation. Maximum extensibility (λ_{max} = maximum length/resting length), SR (% decay in peak force at 20 sec) and hysteresis ratio (HR = ratio of area within L-T loop to area beneath loading curve) were measured. The alveolar wall of rat shows a decrease in SR ($r = -0.75$) and HR ($r = -0.38$) with age. λ_{max} was not age related. In rabbit, a like decrease in SR ($r = -0.79$) and HR ($r = -0.40$) with age occurred. Again there was no relationship of λ_{max} to age. Following the short exposure to elastase, SR increased significantly ($p < .01$) but still showed a fall with age. Age related changes in the properties of alveolar wall from rodents are unlike those in adult man. Such differences in tissue properties of animals may prove crucial to modelling disease states in man, particularly those states in which the mechanical properties of lung are altered (obstructive pulmonary syndromes).

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Relative Sensitivity of Peak Aortic Flow Acceleration, Velocity and Stroke Volume During Cardiovascular Interventions in Unanesthetized Dogs. J.E. Chimoskey, E. Gams*, and L. Huntsman*. Center for Bioengineering, School of Medicine, University of Washington, Seattle, Washington 98195.

There is evidence that peak acceleration is the most sensitive aortic flow variable (Noble et al., Circ. Res. 19:139, 1966). During investigation of the degree of correlation of common carotid flow acceleration with ascending aortic flow acceleration in chronically instrumented dogs we observed that stroke volume may be more sensitive on occasion. Therefore we have compared peak flow acceleration, peak flow velocity and stroke volume in five trained dogs, (29-32 kg) chronically instrumented with electromagnetic flow probes on the ascending aorta. Experiments began seven to ten days after the operation. The aortic flow signal was processed electronically to give the first derivative (acceleration) and the intergal (stroke volume). We investigated the response to exercise, to sixty second occlusions of the circumflex, the anterior descending and both branches of the left coronary artery, to induction of short-acting barbiturate anesthesia, and intravenous infusion of three concentrations each of isoproterenol (0.8, 2.0, and 4.0 μgm/min.), levartenol (0.8, 2.0, and 4.0 μgm/min.), and acetyl choline (0.8, 2.0, and 4.0 mg/min.). Peak flow velocity, peak flow acceleration and stroke volume increased or decreased together. During exercise and the administration of all of the drugs peak acceleration is the most sensitive (undergoes the most change). During occlusion of either or both branches of the left coronary artery stroke volume is more sensitive than the other two variables. (Supported by USPHS Grants GM 16436-05 and HL 07293-12.)

RESPIRATION, OXIDATIVE PHOSPHORYLATION AND FATTY ACID CONTENT OF MITOCHONDRIA FROM REGENERATING LIVER. Sook Chong Choi* and James C. Hall. Dept. of Zoology and Physiology, Rutgers Univ., Newark, N. J.

Mitochondria from regenerating liver of Albino Sprague-Dawley rats were assayed polarographically for respiratory rate and oxidative phosphorylation and the concentrations of corresponding mitochondrial free fatty acids were assayed with gas-liquid chromatography. Approximately 65% to 70% of the liver was removed by simple surgical procedure and animals were sacrificed at different time intervals from 16 hrs to 4 wks after surgery. Mitochondria were isolated in an STE medium and incubated with succinate as a respiratory substrate, and free fatty acids were determined in corresponding aliquots. Significant changes in the rate of respiration and the concentration of free fatty acids were observed in mitochondria from regenerating liver. Respiratory control ratios and State 3 respiratory rates were increased during the regeneration period with the greatest increase in the groups studied at 24 hrs, 72 hrs, and 2 wks after partial hepatectomy. ADP/O ratios were also elevated, indicating a higher efficiency of ATP formation in mitochondria from regenerating liver. The concentration of total free fatty acid in mitochondria from regenerating liver was sharply decreased. The magnitude of this decrease was correlated with the increase of respiratory activity. The data indicate a tightly coupled oxidative phosphorylation and increased efficiency in mitochondria from regenerating liver and a possible shift in energy metabolism from predominant utilization of carbohydrate to an increased utilization of fatty acids during the period of liver regeneration. Supported by USPHS Grant No. RR7059.

STIMULATION OF GASTRIC MUCOSA ADENYLATE CYCLASE (AC) BY HISTAMINE (H) AND ITS METHYL DERIVATIVES AND ITS BLOCKADE BY H_2 RECEPTOR ANTAGONIST. C. F. Code and T. P. Dousa, Depts. of Physiology & Medicine, Mayo Clinic & Mayo Foundation, Rochester, Mn.

The action of H, its methyl derivatives and metiamide (H_2 receptor inhibitor) on the cyclic AMP metabolism was studied in a cell free system prepared from guinea pig gastric mucosa. H and N^{α}-methylhistamine (N^{α}MeH) in concentrations 10^{-6} - 10^{-3}M produced a dose-dependent stimulation of AC contained in 2000 x g sediment of homogenate from gastric mucosa epithelium. On the other hand, 1:4 N-methylhistamine had minimal stimulatory effect only in the highest concentration used (10^{-3}M). Metiamide, a new H_2 receptor inhibitor, selectively blocked the stimulation of AC by H and N^{α}MeH but had no substantial effect on the basal AC activity or AC stimulated by 10 mM NaF. Metiamide inhibited the H stimulation of AC at concentrations 100 x less than that of H. Neither H nor its methyl derivatives nor metiamide influenced the activity of cyclic AMP phosphodiesterase contained in 10,000 x g supernatant. Therefore, this study showed that H stimulates gastric mucosa AC via interaction with the H_2 receptor without influencing cyclic AMP breakdown, and that the methylation of H on the side chain preserves or even increases its stimulating ability. On the other hand, methylation of the ring nearly abolishes interaction with the H_2 receptor. The results support the hypothesis that stimulation of gastric secretion by H and N^{α}MeH is mediated in the mucosa by cyclic AMP and that the differential methylation of H in gastric mucosa provides a means of regulating its ability to interact with H_2 receptor. (Supported by NIH Grants AM-16105 & 5-501-RR-05530-10 and by the John A. Hartford Foundation, Inc. & Mayo Foundation.)

TRYPSIN INHIBITORY ACTIVITY OF SURFACTANT PROTEIN. W.K. Coester and S.C. Westerberg (intr. by U.C. Luft). Lovelace Foundation, Albuquerque, N.M. 87108

We have found that canine pulmonary surfactant protein inhibits the activity of trypsin and contains two components that appear to be serum proteins. Pulmonary surfactant was obtained by endobronchial lavage of Beagle dogs under halothane anesthesia and from isolated lungs following perfusion of the pulmonary vasculature with saline. Cells were removed from the crude lavage fluid by centrifugation for 10 minutes at 1500 rpm and surfactant material was obtained from the supernate by centrifugation at 20,000 rpm (4°C) for 30 minutes. Lipids were extracted from the surfactant pellet with 4:1 V/V hexane-ethanol. The surfactant protein was dissolved in saline and studied by immunoelectrophoresis. Trypsin inhibitory capacity was evaluated in terms of the ability of the surfactant protein to inhibit trypsin digestion of a fibrinogen agar substrate. Immunoelectrophoresis indicated the presence of two proteins antigenically identical to canine serum proteins. The surfactant protein exhibited trypsin inhibitory capacity intermediate between absence of inhibition observed in the saline controls and strong inhibition exhibited by whole serum. Immunoelectrophoretic patterns were identical in samples from perfused and non-perfused lungs indicating that the serum-like proteins are true components of the surfactant lipoprotein and are not a result of blood contamination.

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THE EFFECT OF MORPHINE ADMINISTRATION ON TYROSINE HYDROXYLASE ACTIVITY IN RAT BRAIN. S. L. Cohan*, J. R. Abbott* and G. N. Catravas*. (intr. by D. O. Carpenter) Armed Forces Radiobiology Research Institute, Neurobiology Dept., Bethesda, Md. and Georgetown University, Dept. of Neurology, Washington, D. C.

Male Sprague-Dawley rats (250-275 gm) were made tolerant to morphine by twice daily I.P. injections of morphine sulfate (30 mg/Kg/body wt) for one week and "naive" rats given a single injection of morphine (60 mg/Kg). Morphine-treated and saline injected controls were sacrificed 15 min to 24 hrs after their last injection and tyrosine hydroxylase (TH) activity determined in cerebrum, hippocampus, thalamus, hypothalamus, corpus striatum and mid-brain. In "naive" rats there was a 35% increase in TH activity in the hypothalamus with a return to control values within 30 min. In tolerant rats a 40% decrease in thalamic TH activity was seen 30 min after the last injection and a 30% decrease in corpus striatum activity in the basal ganglia 60 min after injection.

The rapidity of onset of changes in TH activity suggests that morphine influences the conformational state of TH rather than the rate of de novo synthesis. Furthermore, these alterations in TH activity produced by morphine support the concept that behavioral changes associated with morphine administration may be mediated by the catecholamine neurotransmitters.

LACTATE METABOLISM BY THE ISOLATED PERFUSED RAT KIDNEY. OXIDATION AND INTERCONVERSION RATES IN RELATION TO Na^+ REABSORPTION. Julius J. Cohen, J.R. Little*, Altamese Black*, and Margaret C. Bignall*. Dept. of Physiol. University of Rochester, N.Y.

We have quantified the utilization and the metabolic fates of lactate in the perfused rat kidney in relation to net Na^+ reabsorption (T-Na^+). The perfusate was 6% bovine albumin in Krebs-Ringer HCO_3^-, pH 7.4 (95% O_2, 5% CO_2) containing L-(+)-[U-^{14}C] lactate which was recirculated at 38°C. Three consecutive 20 min metabolic observations were made starting 15-20 min after perfusion was begun. We determined: a) net lactate utilization rate, b) lactate oxidation rate, c) glucose production rate and, by difference, d) the rate at which other products of lactate metabolism appeared. Total lactate utilization had not reached a maximum at 10mM (the highest [lactate] studied); lactate oxidation ($^{14}CO_2$ production) however, was maximal at a perfusate [lactate] of 5mM. The production rate of both glucose and the other products continued to increase as [lactate] was raised so that at 10mM lactate, lactate oxidation accounted for ∿30% of total lactate utilized. As net lactate utilization increased there was an increase in % T-Na^+ from 76% to 90%. These observations indicate that the metabolism of exogenous lactate can support a significant fraction (∿15%) of T-Na^+ while 76% of T-Na^+ which occurred without added lactate, was probably supported by substrates bound to the added albumin or by catabolism of renal tissue. Further, after the substrate requirements for oxidation are met, lactate utilization increases due to its conversion to other products.

MYOCARDIAL PERFORMANCE IN IRREVERSIBLE HEMORRHAGIC SHOCK. B. Coleman, J.E. Kallal*, L.P. Feigen* and V.V. Glaviano, Dept. of Physiol. & Biophys., The Chicago Medical School, Chicago, Illinois 60612

Myocardial performance was evaluated in 6 pancreatectomized dogs and 8 dogs without pancreatectomy by measuring left ventricular pressure (LVP) and its first derivative (Max dp/dt), left ventricular end-diastolic pressure (LVEDP), cardiac output (CO), pulmonary arterial pressure (PAP) and heart rate (HR) during standardized hemorrhagic shock. Left ventricular function curves were obtained in control dogs and in the late post-infusion period of hemorrhagic shock, by varying pre-load (LVEDP) over a range of 5-15 mmHg. Both groups of dogs (with or without the pancreas) showed similar responses to the shock procedure. In the immediate post-infusion period, LVP, Max dp/dt, LVEDP, mean arterial pressure and cardiac output returned to near control values while pulmonary arterial pressure was significantly elevated. The inability to maintain a normal arterial pressure became evident within 2-3 hours after reinfusion. The decline in arterial pressure was accompanied by a similar fall in LVEDP. Myocardial performance in hemorrhagic shock, as shown by the response of the heart to an increased pre-load, did not differ significantly from control dogs. Left ventricular stroke work and Max dp/dt were comparable at each level of end-diastolic pressure in the control period, as well as during the period of irreversible hemorrhagic shock. These data indicate that terminal hemorrhagic shock need not be accompanied by myocardial depression. It is suggested that the post-infusion decline in arterial blood pressure represents primarily an inadequate venous return to the heart. (Supported by ONR contract N00014-67-A-0397-0002).

PRESENTATION OF MATHEMATICAL MODELS OF PHYSIOLOGICAL SYSTEMS TO LARGE AUDIENCES. T. G. Coleman, A. H. Goodman*, J. H. Loflin*, & R. L. Darby*. Dept. Physiology & Biophysics, Univ. Miss. Sch. of Med., Jackson, Miss.

Mathematical models can be used to demonstrate the complex interrelationships that often occur in physiological systems and, particularly, the dynamic behavior resulting from these interrelationships. Most computing systems restrict participation in the modeling process to only one person at a time. Recognizing that the participation of larger groups is frequently desirable, we have developed an inexpensive system that presents mathematical analyses to classroom size audiences and allows the audience to participate, on-line, in the modeling process. The solution of the model is controlled from a portable classroom console that uses a Teletype for changing parameters and/or the basic configuration of the model. The results of the solution are displayed, in real-time, on four classroom TV monitors receiving a computer generated video signal containing both graphics and text. The lecturer adds annotation to this picture using a light pen at the classroom console in conjunction with a console TV monitor. The video signal(annotation) produced by the light pen is mixed with the computer generated video signal before being distributed to the classroom monitors. Video signals originating both at the computer and the classroom console are generated from analog voltages using Tektronix 4501 Scan Converter Units.

We feel that the capability of adding annotation in the classroom is essential to the success of this scheme, specifically because annotation allows the lecturer to emphasize various details of a given solution as the graphical display of the solution progresses. Preliminary applications have produced an enthusiastic response from both lecturer and students. Supported by NIH Grants HL 11678 and HL 70425.

EFFECTS OF ELECTROCHEMICAL DEPOSITION OF IRON ON LOCAL MULTIPLE UNIT ACTIVITY OF VARIOUS BRAIN REGIONS IN THE FEMALE RAT. J. A. Colombo*, D. I. Whitmoyer*, and C. H. Sawyer. Dept. of Anatomy and Brain Research Institute, UCLA School of Medicine, Los Angeles, Calif.

Since the original report by Everett and Radford (Proc. Soc. Exp. Biol. Med. 108, 604, 1961) a phenomenon called "electrochemical stimulation" has been widely used in the field of neuroendocrinology. It is developed by applying anodic direct current through stainless steel electrodes resulting in the deposition of iron in the tissue. Its effects on neuronal activity in the rat have generally been assumed to be stimulatory in nature, regardless of the brain site. In female rats under urethane anesthesia, with different electrode settings, we studied local multiple unit activity (MUA) changes within or close to the area of iron deposition as shown by the Prussian blue reaction. Electric charges ranging from 30 microcoulombs to 6 millicoulombs were applied through bipolar concentric or monopolar electrodes. MUA recording electrodes were placed from 20-600 u distant from the 'active' electrode. After the current was applied a transient (1-2 min) decrease was followed by a progressive increase above control levels in the integrated and spike rate of MUA in the medial-preoptic and hypothalamic areas, reaching its maximum 10-15 min afterwards. Recovery usually occurred between 30-60 min, but in some cases it took approximately two hours. Charges differing by a factor of two, applied to the same loci increased the amplitude rather than the duration of the increase. No significant differences could be detected between diestrous and proestrous animals. Similar changes were observed under pentobarbital anesthesia. (Supported by NIH grant NS-01162, the Ford Foundation and Foundation's Fund for Research in Psychiatry).

EVIDENCE FOR A SYNAPTIC AND NON-SYNAPTIC RESPONSE TO L-GLUTAMATE IN LOBSTER. C. Colton* and A.R. Freeman, Inst. of Psychiatric Research, Indiana University Medical Center, Indianapolis, Ind. 46202.

The amino acid, L-glutamate, when applied to the bathing medium perfusing the lobster neuromuscular junction at 18°C induced a depolarization and an increase in effective membrane resistance (R_{eff}). This action was inconsistent with the proposed role of glutamate as a synaptic transmitter. By lowering the temperature to 3°C a second glutamate response, that is, a depolarization and decrease in R_{eff}, was seen. Also noted was an apparent enhanced sensitivity of the membrane to glutamate at 3°C. Ion substitution studies on the glutamate induced responses at 18°C and 3°C, indicated that different mechanisms were involved. At 18°C, glutamate induced a decrease in K^+ selectivity and an increase in Na^+ selectivity, suggesting a depolarizing K^+ inactivation process typical of non-synaptic membrane. At 3°C glutamate caused a slight increase in K^+ selectivity over control at 3°C. Involvement of synaptic activation in the glutamate response was implicated by Na^+ replacement studies. In a Tris-substituted medium the glutamate response at 3°C was blocked while the effect at 18°C was not blocked. The membrane response to the inhibitory transmitter, GABA, at 3°C, was not affected by Na^+ replacement. Specificity for L-glutamate at 3°C was indicated by the lack of an effect of D-glutamate or L-aspartate up to a concentration of 1×10^{-4}M. At 18°C, 5×10^{-4} aspartate caused a depolarization and increase in R_{eff}. A potentiated excitatory effect was seen at 18°C when L-aspartate and L-glutamate were applied simultaneously.

ENDOTOXIN SENSITIVITY IN CADMIUM ACETATE AND LEAD ACETATE TREATED RATS. J. A. Cook* and N. R. Di Luzio. Dept. Physiology, Tulane University School of Medicine, New Orleans, Louisiana 70112

Lead acetate in well tolerated doses has been shown to markedly enhance the lethal effect of bacterial endotoxin. Recent observations in our laboratory have shown that cadmium acetate can also induce endotoxin hypersensitivity. To evaluate the role of the liver in the etiology of cadmium or lead induced endotoxin shock, hepatic function was comparatively evaluated in lead-endotoxin treated rats and in rats receiving equivalent doses of cadmium plus endotoxin. Rats receiving either cadmium- or lead-acetate demonstrated enhanced sensitivity to S. enteritidis endotoxin as denoted by increased mortality, impaired bromsulphalein (BSP) removal, hypoglycemia, and elevated levels of plasma glutamic oxalacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT). Mortality as well as the hypoglycemia and plasma enzyme activities were greater following combined treatment with cadmium and endotoxin than with lead and endotoxin. Increased intravascular clearance and hepatic localization of the RE test lipid emulsion were observed in rats treated with cadmium acetate, denoting enhanced macrophage function. In contrast, clearance rates and hepatic localization of the lipid emulsion were depressed following treatment with lead acetate. These data suggest that dysfunction of hepatic parenchymal cells contributes to the pathophysiology of cadmium or lead interaction with endotoxin. (Supported by the American and Louisiana Heart Associations).

DECOMPRESSION SICKNESS IN SIMULATED APOLLO-SOYUZ SPACE MISSIONS. Julian P. Cooke and William G. Robertson. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

The first joint manned space flight between the United States and the Soviet Union is tentatively scheduled for launch in 1975, and will unite a U. S. Apollo and a Russian Soyuz spacecraft. The American and Russian spacecraft have different atmospheres and different pressures, and interchange will take place by way of a docking module where space suit pressure may be necessary. Thus the present study evaluates the incidence of decompression sickness in men simulating passage from the Russian spacecraft atmosphere to the American space suit pressure. Following 8 hours of "shirtsleeve" exposure to 31:69::O_2:N_2 gas breathing mixture, at 10 psia, subjects were "denitrogenated" for either 30 or 60 minutes with 100% O_2 prior to decompression directly to 3.7 psia suit pressure equivalent while performing exercise at fixed intervals. Five of 21 subjects experienced symptoms of Grade I decompression bends after 1 hour of denitrogenation and 3 of these 5 noted the disappearance of all symptoms of bends while at 3.7 psia. In contrast, 6 among 20 subjects reported bends after 30 minutes of denitrogenation, and 2 of these progressed to Grade II bends. A 1 hour denitrogenation time is considered necessary for decompression from 10 psia to a space suit pressure of 3.7 psia. (Supported by NASA-MSC Contract T-82170, and performed in accordance with AFR 80-33. Further reproduction is authorized to satisfy the U. S. Government requirements).

REGIONAL METABOLIC MEASUREMENTS FROM ISCHEMIC AND NONISCHEMIC MYOCARDIUM. E. Corday, T.W. Lang, S. Meerbaum and J. Osher (intr. by J.V. Tyberg). Cedars-Sinai Medical Center, Los Angeles, California.

Following intracoronary balloon occlusion of the LAD coronary artery in 31 closed chest dogs, myocardial oxygen consumption (MVO_2), lactate extraction (LE) and potassium balance (K^+B) were measured simultaneously and separately from the occluded (O) and nonoccluded (NO) regions of the heart. Temporary balloon occlusion of the great cardiac vein provided separation of venous compartments for regional blood sampling and thermodilution coronary flow determinations. Following occlusion, myocardial metabolism in O differed significantly (* $p<0.05$) from that measured in NO (mean; C = preocclusion control).

	MVO_2 (ml/min)		LE (A-V)/A (%)		K^+B (A-V) (mEq/L)	
	C	3 Hrs O	C	3 Hrs O	C	3 Hrs O
NO Region	11.8	9.8	34.6	21.1	-0.05	-0.13
O Region	5.2	2.9*	34.8	10.5*	-0.06	-0.21*

The extent of the NO region was more than twice that of O, which explains the MVO_2 values in C. Five to 30 minutes after occlusion, both hemodynamics (H) and metabolism (M) indicated derangement of cardiac function, with maximal K^+ loss and lactate production in O. Subsequently, O exhibited little further change in the rate of K^+ loss and lactate production persisted. The NO zone M was depressed to a lesser extent. This may be related to compensatory hypercontractility and increased myocardial afterload due to elevation of systemic vascular resistance.

Regional measurements from both O and NO permit study of progressive post-O developments as well as evaluation of selective interventions which cannot be adequately assessed from global H and M.

GLUCONEOGENESIS IN ISOLATED RAT HEPATOCYTES AS A FUNCTION OF FASTING DURATION. Robert P. Cornell* and James P. Filkins. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Hepatocytes were prepared enzymatically by 0.05% collagenase and 0.10% hyaluronidase perfusion of isolated livers from either fed rats or rats fasted for 24, 48, 96, and 168 hrs. The integrity of the dispersed hepatocytes was verified by a high percentage (90%) of trypan blue exclusion and a low percentage (10%) of soluble enzyme (lactate dehydrogenase and glucose-6-phosphatase) loss through 120 min of incubation at 37C in glucose-free Krebs-Ringer bicarbonate medium. The addition of either 10 mM lactate or pyruvate--but not alanine--increased the rate of glucose production by 30% in cells from fed rats over the endogenous rate (3.04 μmoles of glucose/g of protein/min) which was high due to ongoing glycogenolysis. Gluconeogenic rates with the addition of 10 mM lactate, pyruvate, and alanine (1.71, 2.19, and 1.25 μmoles of glucose/g of protein/min, respectively) were 5 to 10-fold greater than the endogenous rate in cells from 24-hr fasted rats. Prolongation of the fast from 24 hr up to 168 hr resulted in no significant changes in the gluconeogenic rates when expressed per g of cell protein. Hepatocyte protein content decreased continually during this interval from 1.72 mg of protein per 10^6 cells for fed rats of 1.13 for 24 hr-fasted and 0.79 for 168 hr-fasted rats. Similar percentage decreases of total liver weight with fasting were determined. These findings support the concepts that during prolonged fasting in rats (1) the gluconeogenic pathway in liver remains intact despite marked hepatocyte proteolysis and (2) the presentation of substrate primarily from extrahepatic sources, viz. skeletal muscle, provides important physiological control of hepatic gluconeogenesis. (Supported by NIH Grants HL 08682 and HL 14540.)

EFFECTS OF DEHYDRATION ON MUSCLE METABOLISM DURING EXERCISE David Costill and Bengt Saltin*. Ball State University, Muncie, Indiana and Gymnastik-och idrottshögskolan, Stockholm, Sweden.

A greater reduction in physical work capacity has been observed after dehydration due to heavy exercise than when the sweating was induced by a thermal heat load. Measurements of intracellular and extracellular fluid compartments suggest that cellular disturbances are responsible for the greater "fatigue" experienced with exercise dehydration. The aim of this study was to compare the effects of exercise and thermal dehydration on selected metabolic responses during exercise. Six men performed a 5 min, standard cycling task (80% Vo_2 max) before and after dehydration and after rehydration. Blood, muscle tissue (vastus lateralis), heart rates and respired air were sampled in conjunction with each exercise bout. No differences were observed between the two forms of dehydration with regard to blood and muscle lactate concentrations following the exercise task. The water content of the muscle samples was not significantly altered by the 4% reduction in body weight. While exercise dehydration produced a significant decline in muscle glycogen concentration, prolonged exposure (3-3.5 hr) to a hot environment (80-95° C) resulted in a consistent rise in muscle glycogen. When compared to the thermal dehydration treatment, exercising heart rates and total oxygen consumption were greater when sweating was induced via prolonged exercise. These data suggest that the greater reduction in physical work capacity observed following exercise dehydration is a result of glycogen depletion rather than a decrease in intramuscular water.

ENHANCED PRESSOR RESPONSE PECULIAR TO VASOPRESSIN IN BARORECEPTOR DENERVATED AND AREFLEXIC DOGS. Allen W. Cowley, Jr. and Arthur C. Guyton. Dept. Physiol., Univ. Miss. Sch. Med., Jackson, Miss. 39216

Greatly enhanced pressor sensitivity to vasopressin (Pitressin) was obtained in conscious baroreceptor denervated dogs and studies were performed to quantitate the significance of the observations. One hour intravenous infusions of vasopressin were compared to infusions of norepinephrine in 3 types of dog preparations: unanesthetized normal dogs (N=7); unanesthetized sino-aortic baroreceptor dogs (N=6); and decapitated areflexic dogs (N=6). Doses of vasopressin infused ranged from 0.05 to 100 mU/kg/min; norepinephrine ranged from 0.03 to 2.0 ug/kg/min. The results showed that areflexic dogs were the most pressor sensitive to vasopressin infusions, followed by baroreceptor denervated dogs. Threshold pressor responses were obtained with doses approximating physiological secretion rates under various conditions. The regression equation for normal dogs was $y = 16.8 \log x - 1.7 (r = 0.74)$; denervated dogs $y = 23.0 \log x + 29.9 (r = 0.64)$; decapitated dogs $y = 51.7 \log x + 64.5 (r = 0.94)$. To obtain a 25 mmHg elevation in mean arterial pressure(MAP), 38.0 mU/kg/min must be infused in a normal dog, 0.61 mU/kg/min in a baroreceptor denervated dog, and only 0.18 mU/kg/min in decapitated dogs. In contrast the pressor sensitivity to norepinephrine between normal and denervated dogs was considerably less, yielding a regression equation of $y = 34.6 \log x + 43 (r = 0.80)$ in normal dogs compared to $y = 55.8 \log x + 79 (r = 0.8)$ in baroreceptor denervated dogs. An infusion rate of 0.3 ug/kg/min was required to obtain a 25 mmHg MAP rise in normal dogs compared to 0.1 ug/kg/min in denervated dogs. The results suggest that vasopressin could be actively involved in determining the overall gain of the sino-aortic baroreceptor reflex system and that under certain conditions could have a significant effect on arterial blood pressure. Supp. by NIH grants HL 14306 and HL 11678.

STUDENT LABORATORY EXERCISE IN TEMPERATURE REGULATION. Albert B. Craig, Jr., and William M. Abraham* Department of Physiology, University of Rochester School of Medicine and Dentistry, Rochester, New York 14642.

A very simple and inexpensive laboratory exercise using only clinical rectal thermometers, an accurate scale for body weight, and a basketball court has been organized for several years to demonstrate the principles of temperature regulation. After control observations the students form two equal teams and play basketball for one hour interrupting play briefly for experimental measurements. During the 30 minute recovery period, they are told to drink enough water "to satisfy their needs."

Average	Control	Exer.15	30	60 min.	Recovery
Rectal Temp.	37.4	38.7	39.3	39.5	38.4 C
Heart Rate	75	128	137	136	94/min
Weight	76.11	-	-	75.14	75.52 kg

Water intake during recovery was 460 ml or 47% of weight loss. Conferences which are held on a different day, emphasize the control of body temperature, mechanisms of heat loss, role of thirst in the control of body fluids, and interrelationships of temperature and cardiovascular responses. The laboratory exercise is well received by the students. Although our experience is limited to medical students, the experiments may be useful to many other types of students at both the graduate and undergraduate level.

EFFECTS OF EXERCISE ON HEAT BALANCE DURING HEAD OUT IMMERSION IN WATER. Albert B. Craig, Jr., and Maria Dvorak* University of Rochester School of Medicine and Dentistry, Rochester, N. Y. 14642

Heat balances were measured in eight normal subjects during exercise in water at 28 C. Heat exchanges between the subject and the water were measured by direct calorimetry. Heat balances were calculated as the differences between heat production and the sum of heat losses from the respiratory tract, head, and those to the water. The temperature of the insulated external auditory canal (T_e) showed an increase in the first 15 minutes and was the same as control at the end of 30 minutes of immersion at rest. The subject then began exercise which doubled the oxygen consumption. The T_e decreased precipitously, .49 C, during this second half hour. In another series of experiments in which the subjects exercised during the first half hour, the T_e decreased .17 C, and during the next half hour when they were at rest, the T_e decreased another .20 C. By contrast the heat balance, expressed as change in mean body temperature, was -1.25 C and -.57 C during the first and second half hours respectively in the rest-exercise and -1.46 C and -.83 C during the exercise-rest experiments. These data indicate that light exercise in water of 28 C does not significantly increase loss of heat from body stores but causes an internal shift of heat from central to the peripheral parts. Supported in part by USPHS, NIH Grant 5RO1 HL09676-08.

EFFICIENCY OF EVAPORATIVE COOLING FROM WET CLOTHING. F. N. Craig and J. T. Moffitt.* Biomedical Laboratory, Edgewood Arsenal, Aberdeen Proving Ground, MD.

Two men wearing fatigue clothing walked on the treadmill and stored heat at rates of from -14 to +121 W/m^2. Twenty-one tests were made to relate the efficiency of evaporative cooling, E/E', to the water content of the clothing, D. The heat lost from the body by evaporation, E, was obtained from the equation E = M+R+C-S, where metabolism, radiation and convection were estimated, and storage was determined from changes in skin and rectal temperatures. The total heat of evaporation, E', was determined from the change in clothed body weight. D was the ratio of the average wet weight of the clothing to the standard dry weight; the wet weight varied during the walk with the rates of evaporation and sweating and with the amount of water added initially. As D increased there was little change in M, R and C, but E' increased more than E and the increase in E was counterbalanced by a decrease in S. The approach of E/E' to unity at minimum values of D supported the validity of the estimates of M, R and C. In six sets of tests under different conditions the average data were D 1.05, E/E' 0.96, for no water added; D 1.20, E/E' 0.72, for 400 g added; and D 1.47, E/E' 0.59, for 1000 g added. A decrease in E/E' with an increase in D was to be expected, but the extent of the decrease could not have been predicted.

REGIONAL LIPID AND GLYCOGEN UTILIZATION ACROSS THE ISCHEMIC DOG LEFT VENTRICULAR WALL. M. F. Crass, III and J. W. Holsinger, Jr.*
University of Nebraska Medical Center and Veterans Administration Hospital, Omaha, Nebraska.

Biochemical and histological evidence has suggested a greater susceptibility of the subendocardium (SENDO) to ischemic damage and necrosis as compared with the midmyocardial (MID) and subepicardial (SEPI) layers. Regional metabolism of exogenous fatty acids was studied by infusion of 5 μc ^{14}C-palmitic acid bound to albumin into the left circumflex artery of mongrel dogs. The artery was either occluded by ligation (L) or left patent (C). After 2 hours transmural tissue samples were obtained and frozen in liquid nitrogen. Sections (2-3mm thick) were cut from SEPI, MID and SENDO layers. Extraction and analysis of total and ^{14}C-lipids and glycogen determinations were performed. In C: SENDO contained only 20% of total ^{14}C-lipids found in MID and SEPI; in all layers, glycerides (GLY) comprised 30-38% and phospholipids 60-70% of total ^{14}C-lipids; a gradient in glycogen content from SEPI to SENDO (SEPI<MID<SENDO) was observed. In L: a similar gradient in total ^{14}C-lipids was demonstrated, however GLY-^{14}C was increased 10-fold in MID and SEPI and 15-fold in SENDO as compared with respective C values; ischemic (hypoxia)-induced net glycogenolysis was observed transmurally, however glycogen breakdown was significantly greater in SENDO. These data suggest that regional variations exist in the metabolism of exogenous fatty acids and glycogen in normal and ischemic dog left ventricle.

ACQUISITION OF A CONDITIONED EYEBLINK RESPONSE DURING DENERVATION OF ORBICULARIS OCULI MUSCLES IN THE CAT. T.J. Crow* and C.D. Woody. Laboratory of Neurophysiology, Mental Retardation Center, UCLA, Los Angeles, Calif. 90024.

Studies examining the importance of the integrity of peripheral motor pathways in conditioning as opposed to movement or proprioceptive feedback have produced contradictory results. Our experiment investigated the effect of crushing the VIIth nerves on the acquisition of a conditioned eyeblink response. Following crush lesions of the facial nerves, cats (N=5) received 13 training sessions consisting of 150 pairings of a click CS followed by glabella tap (interstimulus interval of 400 msec). EMG activity recorded from the denervated muscle provided a precise measure of motor responses, thus ensuring that subliminal myokinetic responses did not occur during the training period. The subsequent behavioral tests following recovery of nerve function demonstrated that acquisition of a blink CR does not require the integrity of the peripheral motor pathway. The nerve crush group reached a level of 66% CRs as compared with 61% CRs for a group of normal control cats (N=5) receiving 13 training sessions. Although anatomical evidence suggests that crush lesions of the facial nerve result in a displacement of synaptic terminals from the surface of the soma membranes of facial motoneurons, electrophysiological evidence has shown that EPSPs can be evoked in facial motoneurons following injury to facial nerves. Our results and the electrophysiological evidence are of significance in view of recent findings that antidromic activation of facial motoneurons by electrical stimulation of the VIIth nerve may be a sufficient condition for acquisition of a conditioned eyeblink. (Supported by USPHS HD-05958, HD-04612 and Calif. Dept. of Mental Hygiene.)

RIGHT ATRIAL RECEPTORS MEDIATE THE ADRENOCORTICAL RESPONSE TO SMALL HEMORRHAGE. GEORGE L. CRYER* AND DONALD S. GANN. The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.

Previous experiments have shown that cardiac receptors (low-pressure system) are involved in changes in secretion of cortisol in response to hemodynamic changes. Arterial receptors (high-pressure system) are also involved in this response. When the high- and low-pressure receptor areas are pitted against each other by a controlled pressure difference of 15-20 mmHg (aortic or pulmonary artery constriction) the low-pressure receptor area predominates, causing a decrease in secretion of cortisol. Further, vagotomy abolishes the response to 5 ml/kg hemorrhage. The present experiments were performed to determine the role of right atrial receptors in the adrenocortical response to small (5 ml/kg) hemorrhage. 21 dogs were studied one day after adrenal vein cannulation and placement of a small inflatable balloon inside the right atrium. Timed adrenal venous blood samples were collected before and after hemorrhage with and without simultaneous balloon inflation and were analyzed for cortisol (RIA). 5 ml/kg hemorrhage without balloon inflation leads to increased secretion of cortisol (31% maximal, ± 7%); whereas 5 ml/kg hemorrhage with simultaneous balloon inflation leads to a diminished response (13% maximal, ± 3%). The difference in the two responses was significant ($P<0.025$). These results, with previous data, suggest that right atrial receptors play a primary role in the adrenocortical response to small hemorrhage.

THE FLOW LIMITING SEGMENT IN THE AIRWAY. B. Culver*, J. Friend*, V. Loverde*, and J. Butler. Department of Medicine, University of Washington, Seattle, Washington.

Forced expiratory flow rates from the lung reach a maximal value for a given lung volume which cannot be exceeded by additional effort. This can be explained by collapse of a portion of the airway to limit flow in the manner of a Starling resistor. We have studied maximal expiratory flow in normal excised and in situ dog lungs using an isovolume preparation in which air flow is introduced into the lung via multiple retrograde catheters. Lung volume and the driving pressure (between alveolar and tracheal outlet pressure) can be varied independently and maintained in a steady state. The equal pressure point (EPP), where airway transmural pressure is zero, occurred predominantly in the lobar bronchi just upstream from a segment along which a marked pressure change occurred. We consider this to be the flow limiting segment (FLS). At low lung volume the EPP moved upstream, but the FLS remained fixed in its location through a wide range of lung volumes. The FLS was very short (<1cm) and consistently occurred between the lobar and main bronchus. The position of the FLS was the same in this preparation as in pressure-flow deflation studies performed on the same lobe. The retrograde catheters bypass the most peripheral airways, but in studies using buttons glued on the pleura the air flow was introduced directly into the lung parenchyma and the characteristics of the FLS were the same. Preparations using two or more lobes and both lungs were studied using both dynamic deflations and the isovolume technique. The FLS was again in the same location as in the single lobe experiments, showing it to be independent of downstream events. Results in lobes studied in living open-chested dogs have not differed from those of excised lungs. (Supported by NHLI Grant HL-14152-03 and USPHS Grant HL-12630).

ROLE OF THE CAROTID BODIES IN THE SENSATION OF BREATHLESSNESS.
J. Terrance Davidson*, Karlman Wasserman, Brian J. Whipp, Sankar Koyal*, and Robert Lugliani*. Harbor General Hospital, Torrance, UCLA School of Medicine, Los Angeles, Ca. and Hadassah University Hospital, Jerusalem, Israel.

To determine the role of the carotid bodies in the sensation of breathlessness during hypoxia and hypercapnia, breath-holding studies were performed in normal subjects and subjects with asymptomatic asthma who had had bilateral carotid body resection (C.B.R.). The breath-holding times and the alveolar O_2 (P_AO_2) and CO_2 (P_ACO_2) tensions were determined in each subject following inspiratory vital capacity breaths of 100%, 50%, 20% and 12% and after breathing 12% O_2 for one minute. Breath-holding time averaged 2.2 minutes after a single breath of 100% O_2 in both groups. In normal subjects, breath-holding time and P_ACO_2 at the breaking point progressively decreased as P_AO_2 decreased. In the normal subjects, P_ACO_2 was approximately 10 mmHg. lower than that for the C.B.R. group at a P_AO_2 = 50 mmHg. In contrast, there was no change in P_ACO_2 or breath-holding time at the breaking point until P_AO_2 decreased below 50 mmHg., in the C.B.R. group. In the latter group, breath-holding time decreased at P_AO_2 values between 25 and 50 mmHg. but was still twice that of the control subjects when their P_AO_2 = 50 mmHg., the lowest value reached by the normal subjects. These studies indicate that 1) the carotid bodies play a role in the breaking point of breath-holding, when P_AO_2 is below 300 mmHg. 2) the well recognized interaction of CO_2 and O_2 tension on respiratory control appears to occur exclusively at the level of the carotid bodies, and 3) the sense of "breathlessness" in hypoxic states is reduced in the C.B.R. subjects as evidenced by prolonged breath-holding times and increased P_ACO_2 and decreased P_AO_2 values at the breaking point. (Supported by NIH Grant HL 11907.)

GAS-BLOOD Pco_2 GRADIENTS DURING AVIAN GAS EXCHANGE. D. G. Davies*and R. E. Dutton. Department of Physiology, Albany Medical College, Albany, New York 12208.

It has been suggested that the avian respiratory system is a cross-current gas exchange system (Scheid and Piiper, Resp. Physiol. 16: 304-312, 1972). One of the aspects of this type of gas exchange system is that end expired gas Pco_2 can be higher than arterial Pco_2, the limiting value being mixed venous Pco_2. Steady-state measurements of arterial, mixed venous and end expired Pco_2 were made in 5 anesthetized, spontaneously breathing chickens during administration of room air and 2, 4, 6 and 8 % CO_2. End expired Pco_2 was found to be higher than both arterial and mixed venous Pco_2, the magnitude of the differences being directly related to the $[H^+]$ and $[HCO_3^-]$ of the mixed venous blood: (ΔPco_2 (end expired-mixed venous) = $^-0.2873\ [H^+]\bar{v} - 7.05$, $p < .001$ and $\Delta Pco_2 / [HCO_3^-] = 0.0128\ [H^+]\bar{v} - 0.308$, $p < .001$). These observations are explainable by the charged membrane hypothesis proposed by Gurtner, Song and Farhi (Resp. Physiol. 7: 173-187, 1969) to account for similar alveolar to mixed venous Pco_2 differences under conditions of no gas exchange. The fact that end expired Pco_2 was higher than arterial Pco_2 in the chicken can be explained on the basis of cross-current gas exchange. However, positive differences between end expired and mixed venous Pco_2 must be accounted for by some other mechanism. If the charged membrane effect were present in the avian respiratory system, this could explain these observations. This study suggests that the avian respiratory system can be used as a model for testing the validity of the charged membrane hypothesis.
(Supported by NIH grant HL 12654 and Heart Association of Eastern N. Y.)

Effect of Physical Training on Canine Ventricular Fibrillation Threshold
Albert K. Dawson*, Henry L. Taylor, & Marvin Bacaner.

Stainless steel electrodes were implanted in the left ventricular myocardium of adult, 13-26 kg., mongrel dogs and a snare placed around the left anterior descending coronary artery (LAD) approx. 2 cm. distal to its origin. After recovery (about one month), the dogs were randomly assigned to either an exercise (E) or a control (C) group. Average exercise was 6.5 mph at 30% grade for 30 min. once daily for 5-6 weeks. Ventricular fibrillation thresholds (VFT) were determined under sodium pentobarbital anesthesia in all dogs in the normal (N) (i.e., snare not pulled or heart not made ischemic) and in the ischemic (I) (snare temporarily closed) heart just prior to (B) and at the end of (A) this 5-6 week experimental period. Out of a total of 114 measurements made in 9 E and 10 C dogs NVFT [means ± S.E. (ma.)] were

	Exercise Dogs	Control Dogs
B	26.22 ± 2.66	24.20 ± 1.94
A	41.06 ± 5.55	27.34 ± 2.70
Mean differences (A-B)	14.83 ± 3.97*	3.14 ± 2.62*

*significantly different ($0.02 < p < 0.05$)

From 20 measurements made in 6 E and 4 C dogs, the mean differences in I VFT (A-B) for E and C dogs were 23.67 ± 12.73 and 6.00 ± 4.50 ma. resp. (not significantly different). 4 C and 4 E dogs underwent limited additional NVFT at the end of the experimental period while conscious (CN) and while under sodium pentobarbital anesthesia (PA). Mean differences in NVFT (CN-PA) for E and C dogs were 14.58 ± 3.77 and 2.58 ± 1.88 ma. resp. These mean differences were significantly different ($0.02 < p < 0.05$). These findings indicate that exercise may modify VFT. Further study of this problem is warrented.

ISOLATION AND CHARACTERIZATION OF SIALIC ACID-LIKE SUBSTANCES FROM BEETLE HEMOLYMPH

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Two substances have been isolated from 4th larval instar hemolymph of the Colorado potato beetle, Leptinotarsa decemlineata, by molecular filtration and ion exchange chromatography. Each compound develops a different chromogen in Warren's thiobarbituric acid (TBA) assay. Compound I forms a TBA chromogen with an absorption maximum at 532nm, identical to the TBA chromogen formed from 2-deoxyribose, while compound II forms a chromogen with an absorption maximum at 549nm, identical to the TBA chromogen formed from 2-keto, 3-deoxyaldonic acids, such as sialic acids. Neither compound develops color in the direct Ehrlich test nor do they form pyrroles upon treatment with weak base, tests specific for sialic acids. Molecular weights, determined on Sephadex G-10, are 325 and 160 for compounds I and II, respectively. Behavior of both compounds on Dowex resin is strongly anionic. Both substances are found free in the hemolymph but there is evidence that compound I may be bound to a high molecular weight molecule by an acid labile bond, readily cleaved with 0.1N H_2SO_4 at 80° for 1 hr. The evolutionary significance of sialic acid-like materials found in a protostomic organism is discussed.

LYMPH FLOW ALTERATIONS SECONDARY TO CHANGES IN SERUM CALCIUM. Maximo Deysine, Milan Mader*, Eliseo Rosario* and Charlotte Mandell*. L.I. Jewish-Hillside Med. Ctr., New Hyde Park, N.Y. and Health Science Ctr., SUNY, Stony Brook, N.Y.

To clarify our observation that increases in serum calcium (Ca) augment thoracic duct lymph flow (TDLF), we injected this ion in increments of .5mg.Kg./BW in five intact and five parathyroidectomized dogs observing a linear dose related response. To rule out artifacts altering TDLF, all animals in this and the following series were rendered apneic with I.V. nembutal and ventilated with a respirator through a cuffed endotracheal tube. Dogs were divided in groups of five and subjected to the following procedures: Striated muscle paralysis obtained by L tubocurarine (.53mg.Kg./BW) or succinylchlorine chloride (.2mg.Kg./BW-minute) failed to prevent the TDLF raise after Ca injection. Atropinization (.40mg.Kg./BW) also could not prevent the response producing instead a 500% increase over control values (.3 ml. to 1.5 ml. of lymph per minute). Because increases in arterial blood pressure (ABP) are followed by TDLF raises and calcium augmented ABP, the effect of complete sympathetic blockage was studied in two groups of five control and five parathyroidectomized dogs. All animals were adrenalectomized and treated with reserpine (.5mg.Kg./BW in three doses 24 hours apart), phenoxibenzamine hydrochloride (4mg.Kg./BW infused in 45 minutes) and propranolol (1mg.Kg./BW infused in 30 minutes). Ca injected after all drugs were administered (5mg. of Ca ion per Kg./BW) produced a significant augmentation in the ABP ($P<.01$) and a very significant raise in TDLF ($P<.001$). This TDLF raise was significantly less than that obtained by atropinization. These experiments suggest that the sympathetic system exerts some control on lymph propulsion by direct action or by raising ABP.

TUMOR DEVELOPMENT AS INFLUENCED BY HUMORAL RECOGNITION FACTORS. N. R. Di Luzio, R. McNamee*, I. Olcay*, A. Kitahama*, R. H. Miller*, and E. O. Hoffmann*. Departments of Physiology and Surgery, Tulane University School of Medicine, New Orleans, Louisiana 70112

The reticuloendothelial (RES) system constitutes a fundamental surveillance mechanism by which foreignness in the internal environment can be detected. Recognition factors, which are present in the α-globulin fraction of plasma have been demonstrated in our laboratory to constitute one component of macrophage surveillance since phagocytic expression is deficient in the absence of recognition factors. Since our laboratory has also demonstrated that depletion of recognition factors occurs in experimental and clinical neoplasia, studies were undertaken to clarify the contribution of macrophages and recognition factors to neoplasia. Recognition factors, isolated from human plasma, were employed to possibly enhance tumor cell detection and destruction. Employing Shay chloroleukemic cells as the transplant, recognition factor administration at the tumor cell site at the time of transplantation induced an 86% decrease in tumor weight and increased the degree of tumor rejection. Specificity of the recognition factor inhibitory response on tumor growth was demonstrated by the observation that administration of human serum albumin resulted in no modification in tumor growth. The isolated recognition factor fraction enhanced phagocytosis *in vitro* and *in vivo* and also exerted a pronounced chemotactic effect. These studies denote that macrophages and recognition factors by their phagocytic promoting and chemotactic influences may be of significant importance in tumor cell detection and rejection mechanisms.

ADRENERGIC EFFECTS ON POSTPACING ASYSTOLE IN AV BLOCK.
J. DiSalvo, G. Newman,* and G. Grupp. Depts. of Med. & Physiol., Coll. of Med. Univ. of Cinn., OH 45229.

Cessation of ventricular pacing in dogs or man with AV block causes ventricular asystole of variable duration. The possibility exists that the variable duration of post-pacing asystole (PPA) or the resumption of ventricular beating depends on adrenergic mechanisms. To test this hypothesis we studied effects of beta-adrenergic drugs on time required for ventricular escape, or duration of PPA in unanesthetized dogs with chemically induced chronic AV block. The duration of PPA increased from 1 to 6 sec as pacing rate was increased from 90 to 150 bpm. Similarly, when the duration of pacing at 120 bpm was lengthened from 5 to 120 sec, PPA increased by about 1 to 8 sec. Further increases in pacing rate or duration of pacing either decreased or produced no further change in PPA. After administration of either dl-propranolol, practolol, or sotalol PPA increased by 2 to 40 sec. above control values. In contrast d-propranolol which has only about 1/50 the beta-blocking effect of dl-propranolol, but comparable "quinidine"-like action, had only minimal effects on PPA. The findings suggest that the canine ventricular pacemaker is dependent on adrenergic activity and that duration and rate of ventricular pacing influences the development of the ventricular pacemaker potential. (Supported by Am. H. Assoc. S.W. Ohio Chap., and USPHS-HL6307.)

Factors Influencing Dynamic Lung Compliance in Man.
J. Dosman*, R. Antic*, F. Bode*, J. Urbanetti*, R. Martin* and P.T. Macklem. Meakins-Christie Laboratories, McGill University Clinic, Royal Victoria Hospital, Montreal Canada.

We measured dynamic compliance (Cdyn) at different frequencies (bpm) in 34 non-smoking normal males and females age 30-59 yrs. In those aged 30-49 the Cdyn at 90 bpm was significantly higher than at 15 bpm while those aged 50-59 showed no significant difference. Assuming an inertance of 0.01 $cmH_2O/l/sec^2$ and a sinusoidal breathing frequency Cdyn at 60 and 90 bpm was corrected for inertia. This resulted in no significant difference between Cdyn at 15, 60 and 90 bpm in the 30-49 age group whereas in the 50-59 age group Cdyn at 15 bpm was significantly higher than at 90 bpm ($p < 0.05$). In this group 4 out of 8 subjects were significantly frequency dependent when corrected for inertia. These findings indicate that inertia significantly influences Cdyn at breathing frequencies of 60 per min. and above. Unless this is taken into account frequency dependence of compliance may be missed. The results also indicate that frequency dependence of compliance is normal in some older individuals but is not normal in the younger age group.

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CLONAL ISOLATION OF DIFFERENTIATED RAT LUNG CELLS.
William H.J. Douglas,* M. Edward Kaighn,* Ralph A. Redding,* and Myron Stein. W. Alton Jones Cell Center, Lake Placid, New York, and Brown University, Providence, Rhode Island.

Retention of tissue-specific characteristics and biochemical functions of in vitro cells obtained from liver and other organs is now well established. These successes directed our efforts to isolate cell strains possessing characteristics typical of type II pneumonocytes from normal lungs. Suspensions of cells were obtained from adult rat lung utilizing enzymatic digestion. Thirty clones derived from single cells were isolated, individually grown into populations of 10^7 cells, frozen, and stored in liquid N_2. The clonal approach avoids the problem of selective overgrowth of one cell type by another. All clones thus far examined possess a diploid female rat karyotype. Although some clones were fibroblastic, among the epithelial cell types, were four clones which contained osmiophilic lamellar bodies in their cytoplasm when examined by electron microscopy. The lamellar bodies were morphologically identical to those found within in situ type II cells from whole lung. In addition, lamellar body fractions were isolated both from cultured cells and whole lung tissue utilizing differential osmotic gradient centrifugation, and were found to be morphologically similar. These observations suggest that the four clones were derived from type II alveolar cells because they retained some tissue-specific characteristics and biological function. (Supported in part by NIHL-15266).

THE EFFECTS OF ANTIDIURETIC HORMONE (ADH), PARATHYROID HORMONE (PTH) AND THYROCALCITONIN (TCT) ON THE CYCLIC AMP FORMATION IN KIDNEYS OF SUBMAMMALIAN VERTEBRATES. Thomas P. Dousa, Depts. of Medicine and Physiology, Mayo Clinic & Foundation, Rochester, Minnesota 55901

The effect of ADH, PTH and TCT on the cyclic AMP formation in membrane preparations (washed 600 x g sediments) from kidneys and some other tissues of submammalian vertebrates have been studied in vitro. Adenylate cyclase was found in all preparations from all studied species and was several fold stimulated by 10mM sodium fluoride. Vasotocin, the submammalian ADH, stimulated cyclic AMP formation in kidneys of bullfrog and toad but did not influence adenylate cyclase prepared from pigeon, chicken, alligator goldfish and catfish kidneys or from goldfish gills. Adenylate cyclase prepared from amphibian urinary bladders was markedly stimulated by vasotocin while the enzyme from rat urinary bladder gave no hormonal response. Marked, dose-dependent stimulation by bovine PTH was observed in preparations from kidneys of birds and alligator but not from amphibian kidneys or urinary bladders or from teleost fish kidneys and gills. No stimulation of cyclic AMP formation by porcine TCT was detected in preparations from all tested vertebrate tissues with the exception of preparations from rat kidneys.

Results suggest that the renal response to ADH in amphibians and the renal response to PTH in birds and reptiles are mediated by cyclic AMP in the similar way as it is in mammals. Lack of hormonal stimulation of cyclic AMP formation in vitro in some studied tissues might reflect either the total absence of hormonal receptors associated with cyclic AMP-generating system in these respective organs, or its presence in only very small quantity.

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INHIBITION OF CORONARY FLOW BY A SLUICE MECHANISM AND AN ESTIMATE OF THE INTRAMYOCARDIAL PRESSURE. James M. Downey and Edward S. Kirk (Intr. by Carleton H. Baker). Univ. of South Florida, Col. of Med., Tampa, Fla. and Peter Bent Brigham Hosp., Boston, Mass.

The present study examines the mechanism whereby systole inhibits coronary blood flow. The pressure flow relationship was examined in the canine left coronary artery which was maximally dilated with continuous infusion of adenosine. By periodically arresting the heart with vagal stimulation the pressure flow relationship during asystole (PF_A) could be compared to that in the beating state (PF_B). The PF_A was found to be linear from 20 to at least 250 mm Hg. The PF_B was shifted to higher pressures and in the range above peak ventricular pressure was also linear and parallel to the PF_A. Below peak ventricular pressure, however, the PF_B was markedly convex to the pressure axis. These results were compared to data from a model of the coronary bed consisting of numerous parallel channels, each responding to local intramyocardial pressure (LIP) by formation of vascular sluices; local flow = K· (perfusion pressure - LIP). When LIP was assigned values from 0 at the epicardium and increasing to ventricular pressure at the endocardium the model duplicated the experimental data. Increasing LIP in the model to values greater than ventricular pressure produced curves clearly different from those obtained experimentally. Thus, it was concluded that systole inhibits coronary perfusion by a vascular sluice mechanism and that the compression experienced by the coronary vessels does not exceed ventricular pressure. Supported by Hillsborough County Heart Association and USPHS Grant # 5T01-HL-05890.

EFFECTS OF AN ANTAGONISTIC ANALOGUE OF OXYTOCIN ON THE ELECTRICAL AND MECHANICAL ACTIVITY OF UTERINE SMOOTH MUSCLE Rosemarie S. Drake[1] (intr. by E. L. Gasteiger) Department of Physical Biology, N. Y. S. Vet. Col. Cornell University, Ithaca, N. Y. 14850

The effects of oxytocin and 1-deaminopenicillamine-oxytocin (Schulz, H. and V. du Vigneaud. J. Med. Chem. 9: 647-650, 1956) on the electrical and mechanical activity of the non-pregnant rat uterus have been studied in vitro by use of intracellular microelectrode recordings and isometric tension measurements. It was determined that the transmembrane potential of the estrous uterine muscle is relatively low (-41.52 mv, S.E. ± 0.97, n=200), spontaneous contractions were associated with membrane activity and the pattern of spontaneous discharges was irregular. The amplitude of the action potentials was small (13.36 mv, S.E. ± 0.68, n=38); no overshoot potentials were observed. Oxytocin (1.16×10^{-10} moles) increased the force, frequency and duration of the uterine contractions. No depolarizing effect was associated with oxytocin, i.e. the resting potential was not significantly affected (E_m = -39.05 mv, S.E. ± 1.02, n=200). Increased spike amplitude was observed. 1-Deaminopenicillamine-oxytocin (2.25×10^{-9} moles) was devoid of oxytocic activity. It had no effect on the mechanical activity, the resting potential (E_m = -42.02, S.E. ± 1.15, n=200), the action potential amplitude or the pattern of discharge. The analogue consistently inhibited the effect of oxytocin. The results are consistent with those previously reported by Chan et al. (Endocrinology 81: 1267-1277, 1967) for isotonic contractions. 1-Deaminopenicillamine-oxytocin has high specificity for the oxytocic receptor, since it does not inhibit the spontaneous activity of this tissue.

1. Fellow of AID, U.S. Dept. of State)

THE EFFECT OF CHRONIC HUNGER ON GUSTATORY RESPONSES IN THE FROG.
S. Dua-Sharma*, K. N. Sharma* and H. L. Jacobs. Dept. of Physiology, St. John's Med. Col., Bangalore, India, and Pioneering Res. Lab., U. S. Army Natick Labs., Natick, Massachusetts 01760.

Unit responses were recorded from glossopharyngeal afferents in well-fed (Type I) or on frogs deprived of food for over six months (Type II). Responses to NaCl, glucose, amino acids, and quinine sulphate were measured. Number of papillae responding to glucose and amino acids and magnitude of response to these two substances increased in Type II animals. Repeated trials with threshold stimuli produced responses with each application in Type II animals, whereas Type I gave less stable responses. Gastric distention inhibited the glossopharyngeal response to gustatory stimuli in Type I and facilitated this response in Type II animals. Gastric vagotomy (or electrical stimulation) and cervical sympathectomy (or stimulation) showed a dual control system mediating these effects, biased by the nutritional state of the animal. Gastric-evoked gustatory inhibition was mediated via vagal fibers in Type I animals while the facilitatory effect was mediated via sympathetic fibers in the Type II preparations.

Bioelectric Regulation of Attachment of Omentum
A. E. Dumont, R. O. Becker*, S. McIlveen*, A. Martelli*
Dept. of Surgery, New York University School of Medicine, N.Y., N.Y. and Dept. of Orthopedic Surgery, V.A. Hospital, Syracuse, N.Y.

A localized bipolar electrical field was induced in the peritoneal cavity of rabbits to determine effects on attachment of the omentum. Bimetallic, insulated devices, 2-3cm long, an exposed silver wire at one end and a platinum wire at the other, were designed to produce voltages ranging from 0-350 mv. Control devices of exposed or coated silver wire were expected to produce little or no current or voltage. One device was inserted into the peritoneal cavity of each of 29 rabbits via laparotomy and sutured to parietal peritoneum away from the incision Forty eight hours later animals were sacrificed and the area inspected. Omentum was firmly attached to the peritoneum around the device in the case of all 4 expected to produce a current of about 4 nA at 10 megohms and 50 mv and with all 3 yielding the highest current at 0. megohms and 0. mv. Attachment was absent with all 3 devices of 1 megohm and 10 mv and with 3 of 10 megohm and 70 mv. Attachment was also absent with 4 of 6 of the highest voltage (350 mv) and lowest current and with 6 of 10 expected to yield almost no currents or voltages. Exceedingly slight alterations in bioelectric activity, particularly increased flow of current, in a small area of parietal peritoneum appear to attract and attach the omentum. Lack of uniform results with silver wire controls may be due to release of cell damaging silver ions from long, exposed wire ends.

POTASSIUM EFFLUXES IN GOAT RED BLOOD CELLS. P.B. Dunham and J.S. Bleier.* Dept. of Biology, Syracuse Univ., Syracuse, N. Y.

In human red cells, a portion of K efflux is inhibited by ouabain and promoted by intracellular orthophosphate (P_i) (Glynn et al., J. Physiol. 207:371). Depending on the external medium, this K efflux is associated with reversal either of the entire Na-K pump or of the K entry step alone. We have investigated these kinds of K effluxes in red cells from HK goats. Unidirectional K effluxes were measured using ^{42}K in cells depleted overnight at 37°C. The cells then either received no further treatment (control cells), or were exposed for 1 hour to medium with 100 mM P_i or with 10 mM inosine, to raise or lower, respectively, cellular P_i. K effluxes were either in K-free medium or 10 mM K medium. All media contained Na as the major cation. The K efflux from control cells in K-free medium was 1.26 mM/l cells x hr. With 10^{-4} M ouabain the K efflux was reduced by 0.12 mM/l x hr. Raising external K, $(K)_o$, to 10 mM had no effect on this K efflux. After cellular P_i was reduced by inosine, the ouabain-sensitive K efflux was completely abolished. After incubation in high P_i medium, ouabain-sensitive K efflux was increased to 0.32 mM/l x hr, but remained independent of $(K)_o$. However there was an increased K efflux of 0.22 mM/l x hr induced by 10 mM K in the high-P_i cells which was ouabain-insensitive. The ouabain-sensitive K efflux in K-free medium represents reversal of the entire Na-K pump process; it has the same characteristics as the K efflux accompanying pump reversal in human red cells. The $(K)_o$-stimulated K efflux in high-P_i goat cells is a K-K exchange representing reversal of the K entry step of the pump alone. In goat cells the K-K exchange requires a higher cellular P_i level than that which allows reversal of the entire pump. K efflux in goat red cells also differs from that in human cells in that the P_i-dependent K-K exchange is ouabain-insensitive.
Supported by NIH grant AM 16196.

A PROPOSED APPROACH TO DERIVE AN INTEGRATED CONCEPT OF THE CONTROL MECHANISMS FOR CIRCULATORY SYSTEM DYNAMICS UTILIZING MODELING BASED ON THE ANALOGOUS DESIGN REQUIREMENTS OF AN E M F POWER DISTRIBUTION SYSTEM R. B. Dunham* and Saul Boyarsky. HEW, FDA, BU Drugs, Rockville, Md. and Urodynamics Laboratory, Washington Univ. School of Med., St. Louis, Mo.

The Physicist's and Electrodynamics Engineer's approach to problem definition, hypothesis formulation, and experimental proof of a principle offers a high order of product/cost efficiency in a time of constricted financial support for research. The principal research effort cost is his thinking time, wherein he examines the phenomenon, abstracts and analyzes the quantum order of its limiting conditions, perceives and segregates essences from attributes, and erects and demolishes with known or derivable data numerous hypotheses in order to identify several of promise, each of which is subjected to test of a single elegant demonstrative experiment, frequently entailing little more laboratory cost than a few coils of wire, electronic components, and an E M F source. It is proposed that the control mechanisms of the circulation, to accomplish their function, must meet design requirements analogous to E M F power distribution systems. Observations and data of limiting conditions derived from "experiments of nature" and proprietary data acquired for other purposes are offered supporting the proposition that an interdisciplinary approach utilizing such integrative concept should prove fruitful. Animal laboratory costs of definitive demonstrations should be low relative to yield of new principles and new openings for therapeutic interposition.

EARLY CAPILLARY EXTRACTION OF SODIUM IN RESTING AND EXERCISING CANINE SKELETAL MUSCLE. Walter N. Durán (intr. by Eugene M. Renkin). Dept. of Physiol. & Pharmacol., Duke Univ. Med. Ctr., Durham, N. C. 27710.

Experiments were performed in the isolated gracilis muscle perfused with blood at constant flow. Muscular contraction was produced by electrical stimulation of the nerve. A mixture of sodium-22 and Cr^{51}-hemoglobin was injected in the arterial cannula, and thirty samples were collected from the venous outflow in 20-80 seconds depending on the flow rate. A system of coupled injection-withdrawal syringes was used to avoid changes in perfusion pressure produced by the injection of the tracers. Capillary extraction, E, of sodium was estimated from the average ascending limb sodium/hemoglobin venous concentration ratios; these ratios did not show any clear trend either to increase or decrease. The product capillary permeability-surface area (PS) was calculated as: $PS = -F \ln(1-E)$, where F is plasma flow (ml/min.100 g). PS increased with flow at rest and during exercise, and no constant value for PS-Na was reached. Assuming that the highest PS obtained during exercise (14.2 ml/min.100 g) represents the transport capacity of most of the exchange surface area (70 cm^2/g muscle), a capillary permeability coefficient of at least 3.4×10^{-5} cm/sec can be calculated for sodium. At any given flow, muscle exercise increased PS up to 100% of the resting level (range of increase: 30-103%). The present results indicate that about one-half of the capillaries are open in resting skeletal muscles in agreement with observations made using Rb^{86}.

(Supported by USPHS Grant HL-12749.)

NADH OXIDIZING FACTOR FROM IN VITRO HEART PREPARATIONS. Beatrice C. Durham and Harvey I Miller. Hahnemann Medical College and Hospital, Philadelphia, Pa.

In studies designed to measure the rates of incorporation of ^{14}C-palmitate into triglyceride fatty acid by rat heart slices, it appeared that glycerol (determined by the enzymatic method of Pinter, Hayashi and Watson) was being rapidly released by the tissue in vitro. A pre-incubation period did not prevent apparent glycerol output. Previous work on adipose tissue had failed to show glycerol in the incubation medium although there was measureable lipolysis as shown by FFA release. We obtained evidence that the enzymatic determination of glycerol proceeded at a more rapid rate when used with the medium from the incubation flasks. When glycerol was determined according to the chemical method of Lambert and Neish, however, no glycerol release was seen. Therefore, characterization of the substance responsible for the false glycerol reaction in the enzymatic test was deemed necessary. When the enzymatic determination was performed in the absence of added glycerol kinase, the reaction proceeded at approximately half the normal rate. However, assaying for glycerol kinase was negative in the presence of medium previously incubated with myocardial tissue. The initial reading in the glycerol determination records the absorbance of NADH after it has been partially oxidized in a coupled reaction with any ADP or pyruvate in the sample. Since we noted a marked decrease in NADH absorbance, in the absence of glycerol kinase, it is suggested that either pyruvate or ADP or both are released by the tissue during the course of incubation and constitute the interfering agent(s) responsible for the false glycerol measurements obtained in this study. Further characterization is necessary, but careful interpretation of glycerol values obtained by the enzymatic method of Pinter et al is indicated. (Dr. Miller is an Est. Investigator of Am. Heart Assn.)

COMPARATIVE ACTIONS OF GLUCAGON AND SECRETIN ON RENAL FUNCTION. Leslie E. Edwards and Anne C. Brehme*. Department of Physiology, Medical College of Virginia, Richmond, Virginia 23219.

Previous investigators have shown that glucagon alters renal reabsorption of Na^+, Cl^-, K^+, Ca^{++}, Mg^{++} and H_2O. This study compares the actions of a structurally related compound, secretin, to that of glucagon on renal function in the dog. The evidence obtained indicates that glucagon and secretin have some antagonistic actions on renal function. Glucagon decreased the acidity and decreased the reabsorption of Na^+, K^+, Cl^-, and HCO_3^- while secretin increased the acidity of the urine and increased the reabsorption of Na^+, Cl^- and HCO_3^-. These results not only confirm earlier studies showing glucagon inhibition of sodium transport in the kidney but also indicate that changes in sodium transport may be associated with changes in acid secretion by the kidney. The results suggest also that secretin increases sodium transport by the kidney. This investigation implies that both glucagon and secretin can play a role in acid-base balance in the body.

OSMOTIC STIMULATION OF VASOTOCIN SECRETION IN ORGAN CULTURES OF THE TOAD'S PREOPTICO-NEUROHYPOPHYSEAL SYSTEM. Patrick Eggena (intr. by Irving L. Schwartz). Mount Sinai Medical and Graduate Schools of the City University of New York, N.Y..

The hypothalamo-neurohypophyseal complex of the toad containing vasotocin secretory neurons has been maintained in organ culture for 1-4 days. The explant was found to release 0.54 ng/hr vasotocin into 240 mOsm/l culture medium and 1.98 ng/hr into culture medium to which NaCl had been added to raise the tonicity to 450 mOsm/l. Hypertonic mannitol solutions were also effective in triggering vasotocin release from the explant, whereas hypertonic urea solutions were not effective. When the preoptico-neurohypophyseal tract was sectioned at the infundibulum and the hypothalamic and neurohypophyseal parts of the tract cultured separately, only the hypothalamic tissue slices were found capable of releasing vasotocin in response to osmotic stimulation. While the isolated neurohypophysis was unresponsive to osmotic stimuli, vasotocin release from this tissue increased 17-fold in the presence of 55 mM KCl-medium. These findings suggest that the osmoreceptors responsible for triggering vasotocin secretion in the toad are located in the anterior hypothalamus rather than in the neurohypophysis.

This work was done during the tenure of an Established Investigatorship of the American Heart Association and supported by U.S. Public Health Service Grant AM 15622 of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

END PRODUCT INHIBITION--A POSSIBLE FEEDBACK CONTROL MECHANISM FOR ANGIOTENSIN GENERATION.

Peter Eggena*, Jack D. Barrett*, and Mohinder P. Sambhi, Department of Medicine, University of California at Los Angeles, and Veterans Administration Hospital, Sepulveda, California.

We have previously reported a progressive inhibition of renin-substrate reaction in plasma that paralleled angiotensin generation but was not attributable to angiotensin per se. We have now studied this phenomenon during incubation of partially purified human renin (Haas) and homologus substrate (approx. 80% purity by salt fractionation, gel and ion exchange chromotography). Incubated mixtures were subjected to gel filtration to separate renin from generated end products. Renin inhibitory action was located in a fraction with M.W. similar to that of renin substrate, but without angiotensin generating ability with added renin. These experiments indicate that angiotensinogen molecule following cleavage of angiotensin I acts as an end product inhibitor of the renin reaction. Assuming similar metabolic clearance rates for angiotensinogen and the cleaved renin substrate, a possible in vivo role is suggested for this feedback mechanism to modulate angiotensin generation.

THE EFFECT OF MEAN CRITICAL CLOSING PRESSURE AND TOTAL ARTERIAL RESISTANCE ON BLOOD PRESSURE IN UNANESTHETIZED DOGS. W. Ehrlich, F. Schrijen*, T. Solomon*, E. Rodriguez* & J. Brady*. Johns Hopkins Univ., Sch. of Medicine and Sch. of Hygiene, Baltimore, Md. 21205.

Raising the heart rate of unanesthetized standing dogs by electrical pacing enhances cardiac output and raises the arterial blood pressure immediately. After 6 seconds baroreceptor reflexes diminish the original blood pressure rise. The original blood pressure rise is believed to be caused by the enhancement of flow through still unchanged arteries. The slope of a straight line connecting the prepacing flow-pressure values with the values 4 or 6 seconds after the onset of pacing indicates the total arterial resistance if we assume that the mean arteriolar critical closing pressure is the effective downstream pressure. The zero-flow-intercept of this straight line on the pressure axis indicates the mean critical closing pressure. The mean critical closing pressure in average values from repeated experiments with 3 dogs was about 50 mmHg and the total arterial resistance, 0.01 mmHg ml^{-1} min. We conclude that the blood pressure of unanesthetized dogs is dependent on the cardiac output, the mean critical closing pressure, and to a lesser degree on the total arterial resistance. The state of the circulation downstream of the point of critical pressure does not contribute to arterial blood pressure being below the arteriolar "vascular waterfall." (Permutt, S. & Riley, R. J. Appl. Physiol., 18(5), 924-932, 1963.)

MICROVASCULAR REACTIVITY TO PROSTAGLANDINS IN NORMOTENSIVE AND SPONTANEOUSLY HYPERTENSIVE RATS. E.F. Ellis* and P.M. Hutchins. Dept. of Physiology, Bowman Gray School of Medicine, Winston-Salem, N.C.

Prostaglandins A and E (PGA,PGE), which produce vasodilation and increased cardiac output, have been suggested to be reduced in essential hypertension. A decrease in PGA and PGE would cause an increased peripheral resistance and a decreased cardiac output. However, the pre-hypertensive stage is often characterized by a decreased total peripheral resistance and an elevated cardiac output. In the advanced hypertensive stage cardiac output becomes fairly normal and is associated with an increased peripheral resistance. We wish to consider the possibility that during the pre-hypertensive stage, increased prostaglandin actions cause vasodilation and increased cardiac output and later, in the advanced hypertensive stage, physiologic or anatomic vascular changes occur to reduce the resultant overperfusion and maintain the hypertensive state. Previous anatomic studies in our laboratory have found a decreased number of skeletal muscle arterioles in the pre-hypertensive stage in the spontaneously hypertensive rat. This may represent an anatomical compensation to reduce overperfusion. To examine differences in reactivity, changes in skeletal muscle microvessel diameters where compared during i.a. infusion of PG in spontaneously hypertensive rats during the pre-hypertensive stage and normotensive rats. This study helps clarify the role of prostaglandins in the development of essential hypertension. (Supported by HL 5392 and HL 13936)

EXISTENCE OF A NEGATIVE FEEDBACK LOOP BETWEEN TWO HYPOTHALAMIC SYSTEMS WHICH SEPARATELY CONTROL FEEDING AND SATIETY. R. Emmers. Department of Physiology, College of P & S, Columbia University, New York, N. Y.

Previous work (Fed. Proc. 30: 663, 1971) has indicated that some neurons of the entopenduncular nucleus (Ep) and the lateral hypothalamic area (LHA) respond to intracarotid infusion of a glucose solution by decreasing their activity, while others of the ventromedial hypothalamus (VmH) respond to such an infusion by increasing their activity. When the thalamic taste nucleus (thtn) was stimulated with single electrical pulses at 1/sec, the firing of the Ep-LHA neurons showed inhibitory-excitatory (I-E) oscillations. These appeared to emerge from the activity in a reverberatory feedback loop. To explore this loop, experiments were performed in which stimulation of the thtn in cats anaesthetized with Nembutal was coupled with the recording of activity from single Ep-LHA neurons before and after destruction of the VmH. Before destruction, the activity of these neurons exhibited the I-E oscillations; after destruction, the oscillations vanished. Moreover, stimulation of the VmH inhibited the activity of the Ep-LHA neurons, whereas stimulation of the Ep-LHA excited the VmH neurons. Therefore, the path from the Ep-LHA to the VmH is excitatory, the feedback from the VmH to the Ep-LHA is inhibitory. (Aided by grant NS-03266 from NINDS.)

Airway Closure in Man. L.A. Engel*, A. Grassino*, and N.R. Anthonisen, Meakins-Christie Laboratories, McGill University Clinic, Royal Victoria Hospital, Montreal, Canada.

We studied airway closure during the "closing volume" maneouver in seated man. In each of 3 subjects Xe^{133} boli were introduced into the lung in three different ways. The regional distribution of a bolus injected intravenously (Xe_{iv}) was compared with that inhaled (Xe_{in}), and that carried in during a breathhold (Xe_{car}). The last was obtained by partially equilibrating the lungs with 80% N_2O and then breathholding with open glottis (BH). The gas flow into the lung induced by gas absorption during isovolumic BH carried in a Xe^{133} bolus injected at the mouth. The subject held his breath until regional distribution of the bolus was complete. Lung volume was monitored by two pairs of magnetometers and was constant during BH. With open airways distribution of Xe_{car} should reflect regional perfusion and be similar to that of Xe_{iv}. This was the case in each subject at FRC. At a lung volume 4% VC above RV ($\sim$RV) much less Xe^{133} entered dependent regions during BH than after intravenous injection. In fact, at $\sim$ RV distribution of Xe_{car} matched closely that of Xe_{in}. The results indicate that airways in dependent lung regions close in the course of a deflation from TLC to RV in man. Furthermore, the uneven distribution of a bolus inhaled from near RV is entirely accounted for by airway closure.

Supported by the DRB and MRC of Canada.

STIMULATION OF GASTROINTESTINAL TRACT DNA SYNTHESIS BY PENTAGASTRIN. M Rebecca Enochs,* Paul D. Guthrie,* and Leonard R. Johnson. Univ. of Texas Medical School at Houston, Houston, Texas.

Several lines of investigation have indicated that gastrin is a trophic hormone for certain tissues of the gastrointestinal tract. Such an effect would necessarily involve the stimulation of DNA synthesis in these tissues. Rats were fasted for 24 hr and then injected intraperitoneally with either pentagastrin (250 ug/kg) or an equal volume of saline. At various times following injection the animals were killed and small pieces of tissue from the oxyntic gland area of the stomach, duodenum, ileum and liver were incubated for 30 min in tissue culture medium containing ^3H-thymidine. The reaction was stopped with 0.4N perchloric acid containing carrier thymidine, the DNA extracted, and the incorporation of thymidine determined. Results were expressed as DPM per mg tissue and per ug DNA. DNA synthesis in the liver was not affected by pentagastrin at any time period. Four hours following injection duodenal DNA synthesis was significantly increased to 194% of the control. By 8 hours synthesis was significantly increased in the gastric and ileal tissue of the pentagastrin injected animals as well. These studies demonstrate that pentagastrin stimulates DNA synthesis at varying rates in different tissues in the gastrointestinal tract and has no effects on tissues outside the tract. (Supported by NIH Grant AM 16505).

EFFECTS OF INERT GASES UPON THE O_2 AND CO_2 GRADIENT ACROSS THE EGGSHELL OF THE INCUBATING HEN'S EGG. Beth DeW. Erasmus* and H. Rahn. Dept. Physiol., State Univ. N.Y. at Buffalo, Buffalo, N.Y.

The gas exchange of the incubating egg depends upon passive diffusion of gases across the pores of the egg shell. For a given metabolic rate the O_2 and CO_2 gradients across the shell are determined by pore geometry and the binary diffusion coefficient between O_2 or CO_2 and the inert gas. By changing the inert gas from N_2 to SF_6 or He one would predict a large change in the diffusion coefficient and an equivalent change in O_2 and CO_2 gradient. This was tested by determining the percent O_2 and percent CO_2 in the air cell when eggs (15-17 d. incubation) were exposed to normal O_2 in N_2, SF_6 and He. In air the percent CO_2 in air cell is about 5%, rises to 9% in SF_6 and falls to 2% in He. The percent O_2 in the air cell is normally about 16%, falls to 11% in SF_6 and rises to 18% in He. (Supported in part by NIH 1 P01 HE 14414-01.)

SERUM LH AND PROLACTIN FOLLOWING RESTRAINT STRESS IN THE RAT. J. Euker*, J. Meites and G. Riegle. Dept. of Physiology, Michigan State University, East Lansing, Michigan 48823.

The effect of acute 2 hr restraint stress on serum LH and prolactin was studied in Long-Evans male and female rats. Hormone levels were measured by RIA in serial orbital sinus blood samples taken before and after the rats were restrained. Male and female diestrus rats with low initial prolactin (35 - 50 ng/ml) levels had a 3 - 4 fold increase in prolactin following stress. Serum prolactin concentrations were reduced in proestrus and estrus female groups which had high initial prolactin levels (400 - 600 ng/ml). Low serum LH concentrations (15 - 25 ng/ml) in males and diestrus and estrus females were not affected by restraint. The high initial level of LH in proestrus females (650 ng/ml) was sharply reduced by the stress. Changes in serum hormone concentration during the restraint period were studied in a separate group of male rats. Prolactin levels were greater in the stressed than in the control rats 15 min after initiation of the stress and remained high throughout the restraint. The duration of hormone alterations in rats subjected to restraint was measured in serial blood samples taken at the end of the restraint and after 2 and 4 hrs of recovery in male and proestrus female groups. Serum prolactin had returned to control levels after 2 hrs of recovery in both groups. Two hours of restraint stress administered between 3:30 and 5:30 PM blocked the proestrus LH surge for the duration of the sampling period. (Supported in part by NSF grant GB 8687 and NIH grant AM-07484.)

FETAL ARTERIAL BLOOD PRESSURE AND BLOOD VOLUME. Faber, J.J., Gault,* C.F., Green,* T.J., Thornburg,* K.L. Department of Physiology, University of Oregon Medical School, Portland, Oregon.

Intravascular catheters and intrauterine catheters were placed in 14 sheep fetuses in the last one-third of gestation. Five of these underwent bilateral nephrectomy, and 9 were equipped with electromagnetic flow sensors on the distal aorta. Three to nine days after surgery, fetal blood volumes were changed by injection or withdrawal of blood, or by injection of Ringer's or dextran solutions. Control values of femoral artery pH and pCO_2 were 7.35 (± 0.04 SD) and 53 (± 4.6 mm Hg SD) respectively. These changed little during experimentation; mean difference from control -0.04 (± 0.07 SD) and + 1.9 (± 3.4 mm Hg SD) respectively. Distal aortic blood flow was 81% (± 4.8% SD) placental flow, independent of fetal blood volume ($P \approx 0.3$). Fetal arterial pressure was proportional to blood volume ($P < 0.001$) and depended somewhat on hematocrit ($P < 0.01$). Fetal central venous pressure depended strongly on blood volume ($P < 0.001$). There were no significant differences between normal and 5 nephrectomized fetuses or 7 fetuses treated with 7-14 mg/kg hexamethonium i.v. Only after hexamethonium did fetal heart rate depend on blood volume. Within the observed narrow ranges of pH and pCO_2, there was no effect of these variables on arterial pressure. Placental flow was proportional to arterial pressure, with some dependence on hematocrit. We calculate for the baroceptor mechanism an open loop gain of ~ 0.2 (N.S.) and renal regulation of arterial blood pressure through direct vasoconstrictive effect of angiotensin is also absent or weak. Regulation of fetal blood volume could be a common link in the regulation of fetal arterial blood pressure and fetal placental blood flow.

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REGENERATIVE RELEASE OF CALCIUM WITHIN "SKINNED" CARDIAC CELLS OF DIFFERENT SPECIES. Alexandre Fabiato and Françoise Fabiato*, Peter Bent Brigham Hospital and Harvard Medical School, Boston, Mass. 02115

In fragments of rat ventricular cardiac cells in which the sarcolemma was disrupted and mechanically removed (Fed Proc 32:685, 1973), the threshold for direct activation of myofibrils was pCa 6.25 when the SR was destroyed with Brij 58 or functionally eliminated by a high level (1mM) of EGTA buffering. When SR function was eliminated by caffeine 10mM or deoxycholate 1mM, the pCa threshold was 6.5-6.7 in the presence of either 1mM or 0.03mM of EGTA. This result may be explained by a slight modification of the sensitivity of myofibrils to Ca^{2+} induced by these drugs. With 0.03mM EGTA and no other drug, a contraction followed by a relaxation was elicited by a perfusion at pCa 7.3, while the cell was quiescent at pCa 7.6. This phasic contraction was cyclically repetitive if the pCa was maintained at 7.3, while it remained single with brief exposure to pCa 7.3, followed by return to pCa 7.6. It is proposed that the diastolic myoplasmic free $[Ca^{2+}]$ in the intact tissue would be $\leq 10^{-7.6}$. A small flux of calcium across the surface membrane would increase free $[Ca^{2+}]$ up to $\geq 10^{-7.3}$, which would trigger a release of Ca^{2+} from SR, increasing myoplasmic $[Ca^{2+}]$ above $10^{-6.25}$, then activating the myofibrils. A reduction of myoplasmic $[Ca^{2+}]$ below $10^{-7.6}$ would be required for relaxation and absence of repetitive beating. These results obtained on rat ventricle were also observed in atria of mammalian species. In rabbit ventricle and in frog ventricle or atria, phasic contractions were not observed for a free Ca^{2+} lower than the threshold for direct activation of myofibrils. It is proposed that in these latter species most of the coupling calcium would come from superficial sites rather than SR.

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SEASONAL SYMPATHO-ADRENAL AND METABOLIC RESPONSES OF SNOWSHOE HARES TO COLD. Dale D. Feist and Mario Rosenmann*. Institute of Arctic Biology, Univ. of Alaska, Fairbanks, Alaska 99701.

In order to assess sympatho-adrenal responses to cold in different seasonal groups of snowshoe hares (Lepus americanus macfarlani), urinary catecholamines were analyzed in November hares at -5°C, February hares at -20°C, and June and August hares at +13°C. In spite of the differences in ambient temperature, these different seasonal groups excreted the same levels of norepinephrine (NE) (2 to 4 μgNE/Kg/24hrs) and epinephrine (E) (1 to 2 μgE/Kg/24hrs). Exposure of the summer group (June) to -20°C elicited an immediate, significant, 4-fold increase in urinary NE (12.0 μgNE/Kg/24hrs) and a significant 6-fold increase in E (6.6 μgE/Kg/24hrs) by the second day. Exposure of this same group to -45°C failed to cause a further increase in the NE response and two hares died. In contrast to the summer hares, the winter group (February) when exposed to -45°C, showed a 3-fold increase in urinary NE after the second day and this output dropped to about 2-fold by the third day of exposure. The E level in winter group at -45°C increased only slightly by the second day of exposure. Seasonal values of thermal conductance ($cc O_2/g \cdot hr \cdot °C$) were lower in winter than in summer hares. Upon increasing heat loss by wetting, shaving, and cold exposure in air and helium (80%):oxygen (20%), metabolic rate increased to levels expected in air at temperatures lower than -100°C.

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A DEMONSTRATION OF RECEPTOR NERVE ACTIVITY (VIDEOTAPE). Carlos M. Ferrario, James W. McCubbin, Jerome B. Senturia and John J. Wright,* Department of Biology and Health Sciences, Cleveland State University and Research Division Cleveland Clinic Foundation, Cleveland, Ohio.

Physiologists have long been interested in the mechanisms which regulate heart rate, blood pressure and respiration. Unfortunately, some of these mechanisms are difficult to demonstrate to large groups of students, particularly nerve activity from peripheral sensory receptors. Some of the difficulties encountered are the time, skill and equipment necessary to prepare the demonstration, and the relatively small field of view available. The problems can be overcome by the use of videotape recorded demonstrations. Examples of nerve activity from receptors in atria, aorta and lung are illustrated. This tape was made by recording from single fibers in the vagal-sympathetic trunk as it travels within the neck of the dog. Arterial pressure and electrocardiogram were also recorded to correlate receptor activity with changes in physiologic function.

HYPOGLYCEMIA AND DEPRESSED HEPATIC GLUCONEOGENESIS DURING ENDOTOXIN SHOCK. James P. Filkins and Robert P. Cornell*. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Previous studies in rats rendered sensitive to endotoxin by co-treatment with lead salts have implicated depressed hepatic gluconeogenesis, hypoglycemia, and the resultant sympathetic hyperactivity in the development of endotoxin shock. (Proc. Soc. Exp. Biol. & Med. 142: 915, 1973). In order to evaluate this metabolic pattern in a non-sensitized animal model, blood glucose levels, hepatic glycogen contents, and hepatic gluconeogenesis were evaluated in rats with unimpaired endotoxin resistance. Salmonella enteritidis lipopolysaccharide administered iv to well-nourished, 300 ± 20 gram male rats of the Holtzman strain produced rapid depletion of liver glycogen, an accompanying initial hyperglycemia, but subsequently a profound and terminal hypoglycemia which occurred simultaneously with the characteristic mucosal congestion and bowel syndrome of shock. While the LD_{50} for fed rats was 1.12 mg endotoxin iv, overnight fasting increased the LD_{50} to 2.57 mg. Concomitant with the fasting-induced resistance to endotoxin, gluconeogenesis was maximally enhanced as assessed by either an in vitro procedure using isolated hepatocytes or in vivo methods employing both the chemical and radiotracer conversion of alanine to glucose. Endotoxin at LD_{50}-75 doses administered either prior to or after fasting induction of gluconeogenesis depressed the maximal hepatic gluconeogenic rates when evaluated by either in vitro or in vivo assays. Endotoxin did not however affect gluconeogenesis when added to isolated hepatocytes in vitro. These data suggest that the depression of hepatic gluconeogenesis accompanying endotoxemia may underlie the progression of hypoglycemia and thus contribute to the development of endotoxin shock. (Supported by USPHS Grants HL 08682 and HL 14540.)

COMBINED EFFECTS OF OZONE AND PHYSICAL ACTIVITY ON EXERCISE VENTILATION L.J. Folinsbee, R.J. Shephard, F. Silverman*, Gage Research Institute and School of Hygiene, University of Toronto, Canada

Pulmonary effects of experimental ozone exposures have been measured previously only under resting conditions. Accordingly, we have now tested the response of 11 subjects to a 3-stage bicycle ergometer test (approx. 25, 50, 75% of aerobic power) before and in the first 10 minutes after exposure to ozone. Exposures were to 37, 50, 75 pphm of O_3 for 2 hrs with or without intermittent exercise (15 min rest alternated with 15 min exercise at a load adjusted to increase $\dot{V}_E$ by a factor of 2.5). Resting exposure to 37 and 50 pphm produced no marked changes in ventilatory response to exercise. Resting exposure to 75 pphm or with intermittent exercise at 50 pphm led to a decrease of vital capacity and $FEV_{1.0}$. Subjects complained of throat irritation, cough, and discomfort on taking a deep breath. The ventilatory response to exercise showed an increase of $\dot{V}_E$ and respiratory frequency at a given load with a smaller tidal volume than before exposure. However, the heart rate was similar to that found initially. The post-exposure $\dot{V}_{O_2}$ during effort tended to be lower and the O_2 debt (total 6 min after exercise) tended to be increased relative to the pre-exposure values. It is suggested that respiratory control is modified by the combined effects of exercise and an irritant gas. (Supported in part by MRC Grant MA4984 and Fellowship to LJF and OTRDA of Canada.)

EVIDENCE FOR A HUMORAL MECHANISM OF EXERCISE HYPERPNEA. W.E. Fordyce*, S.M. Yamashiro*, and F.S. Grodins. Biomedical Engineering, University of Southern California, Los Angeles, California.

The humoral mechanism of exercise hyperpnea was investigated by employing a cross circulation technique in which the exercising hindlimbs of one dog (neural) were perfused exclusively by a second dog (humoral). The animals were anesthetized with either pentobarbital or pentothal. Exercise was induced in the cross-perfused hindlimbs of the neural dog by percutaneous electrical stimulation. Steady state values of blood gases, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, ventilation, and cardiac output were measured at rest and during exercise in the humoral dog. Previous investigators using similar preparations studied animals breathing 100% O_2; in the present experiments both dogs inhaled room air. Thirteen exercise experiments were performed on six preparations and thirteen experiments on four similar preparations in which the humoral dog inhaled 5% carbon dioxide in air, the neural dog inhaled air, but exercise was not induced. The ventilatory response of the humoral dog to exercise in the neural dog was greater than could be accounted for by changes in $P_{a_{CO_2}}$, $(H^+)_a$, or $P_{a_{O_2}}$; hypoxia was never present. These results are compatible with the hypothesis of a humorally mediated exercise stimulus and incompatible with earlier results rejecting this hypothesis during 100% O_2 inhalation.
(Supported in part by USPHS, NIH Grant GM 16437.)

EFFECT OF HYPOXIA AND HISTAMINE ON THE VOLUME/PRESSURE RELATIONSHIPS IN PULMONARY ARTERIES AND VEINS. T.E. Forrester*, C.A. Dawson and L.H. Hamilton. Med. Col. of Wis. and Wood VA Ctr., Milwaukee, Wis. 53193.

The volume/pressure relationships of the arteries and veins of isolated cat lungs were examined during forward and retrograde perfusion respectively. Changes in reservoir height reflected changes in lung fluid content (LFC). The ether bolus technique was used to estimate arterial (V_a) and venous (V_v) blood volumes. During forward perfusion the control arterial pressure (P_a) was 12.2 mmHg and V_a was 3.3 ml. Hypoxia (hyp) decreased LFC, increased P_a and decreased V_a. Histamine infusion (hist) increased both LFC and P_a but did not change V_a. During retrograde perfusion the control venous pressure (P_v) was 13.0 mmHg and V_v was 5.5 ml. Hyp increased both LFC and P_v but did not alter V_v. Hist increased both LFC and P_v but decreased V_v. Compliance of vascular segments was calculated from changes in segmental volume and inflow pressure which accompanied induced changes in outflow pressure with constant flow. During forward perfusion control arterial compliance (C_a) was 0.104 $ml \cdot mmHg^{-1}$. During retrograde perfusion control venous compliance (C_v) was 0.057 $ml \cdot mmHg^{-1}$. During hyp and hist C_a and C_v did not change significantly. Hyp decreased V_a and hist decreased V_v. Since vascular pressures were higher during hyp and hist, these changes caused a downward displacement of the C_a curve during hyp and of the C_v curve during hist. The effects of hyp and hist on the measurements indicate that hyp increased arterial resistance more than venous resistance while hist had a greater effect on the veins. (Supported in part by the Wis. Heart Assoc.)

OXYGEN COST AND HEART RATE DURING TREADMILL WALKING IN SIMULATED SUBGRAVITY ENVIRONMENTS. E. L. Fox, J. Hoche*, R. L. Bartels*, E. C. Chaloupka*, J. E. Klinzing*, Exercise Physiol. Res. Lab., Ohio State U., Columbus, and Naval Aeromed, Res. Labs., Pensacola, Fla.

The purpose of this study was to determine O2 cost(VO_2) and heart rate(HR) during treadmill walking in simulated subgravity environments. The long axis of the body of the subjects(n=2) was suspended parallel to the floor in a slow rotation room(SRR) with their feet aligned on the running surface of a treadmill mounted 90° on the wall. Without rotation, the subjects were virtually weightless against the treadmill; with centrifugation environments of ¼, ½ and 1G were simulated. VO_2 (open circuit) and HR (electrocardiogram) were measured during the 5th min of walking at 3.2, 4.7 and 6.1 km/hr as follows:

	¼G		½G		1G	
Speed km/hr	VO_2 ml/kg	HR b/min	VO_2 ml/kg	HR b/min	VO_2 ml/kg	HR b/min
3.2	6.0	85	6.9	87	11.8	108
4.7	7.4	90	9.8	91	16.9	120
6.1	9.0	99	14.0	107	19.0	146

In addition, VO_2 and HR measurements determined during treadmill walking at ½G using the inclined plane technique(long axis of body suspended 30° to the floor) were no different than those obtained at ½G in the SRR. It was concluded that since exercise VO_2 and HR were significantly lower in subgravity as compared to 1G environments, and since inclined plane subgravity simulation appears valid, then this latter method of exercise at reduced O2 cost and cardiac work may benefit patients undergoing exercise rehabilitation. Supported by the office of Naval Research and NASA.

RYANODINE EFFECTS ON GUINEA PIG ATRIAL MEMBRANE VESICLES. M. Frank* and W. W. Sleator, Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois 61801.

A search for the subcellular basis of the negative inotropic effect of ryanodine (RD) on guinea pig atrium has led to the isolation and study of subcellular membrane vesicles. Sucrose density ultracentrifugation (1.07ρ and 1.15ρ) of the tissue results in a relatively pure membrane fraction consisting mainly of vesicles with an average diameter of 800 A (range: 500 A to 1500 A). Cytochrome oxidase determinations indicate that there is minimal mitochondrial contamination. Analysis of the fraction for AMPase activity, a plasma membrane marker, has demonstrated a specific activity of 1.10±0.12 (SEM) μmoles PO_4/mg protein/min, which is unaffected by the addition of $5x10^{-5}$M RD. Examination of the Ca^{++}-binding activity (in the absence of oxalate) of the fraction shows no significant RD effect. However, we have demonstrated that RD does significantly reduce the ATP-dependent Ca^{++} uptake activity (in the presence of oxalate) during 1,5,10, and 30 min incubation periods. For the 30 min incubation period, RD reduced Ca^{++} uptake from 0.90±0.03 to 0.74±0.04 μmoles Ca^{++}/mg protein. The decrease in Ca^{++} uptake was associated with a significant increase in the Ca^{++} activated ATPase activity from 0.18±0.02 to 0.34±0.02 μmoles PO_4/mg protein/min. This effect of RD on Ca^{++} uptake and Ca^{++} activated ATPase was associated with a decrease in the ratio of μmoles Ca^{++} sequestered/μmoles ATP hydrolyzed from 1.00 to 0.50. These results indicate that the negative inotropic effect of RD in guinea pig atrium is associated with the uncoupling of Ca^{++} transport from ATP hydrolysis.

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KINETICS OF ICG CLEARANCE IN HYPERTHERMIC RATS. H.M. Frankel and T. Einhorn*. Dept. of Physiol. and Bur. Biol. Res., Rutgers University, New Brunswick, New Jersey 08903.

The concept of carrier mediated transport kinetics was used to evaluate the effect of hyperthermia on liver function in rats at T_r's of 37 and 41°C. Using micro sampling techniques, half-time disappearance ($t_{1/2}$) and initial plasma concentration ($/\overline{ICG}/$) were measured in rats given doses of indocyanine green (ICG) varying between 0.2 and 2.0 mg/100 gms body weight. Initial velocity of dye removal (J_D) was calculated from the equation: $J_D = 0.693\ /\overline{ICG}/t_{1/2}$. J_{max} and K_m were estimated from the x and y intercepts on plots of $1/J_D$ vs $1/\overline{/ICG/}$. The plots of data from rats given a single dose of dye were linear at T_r of 37°C ($r = 0.97$) and 41°C ($r = 0.92$). Estimates of J_{max} for initial dye injections were 109 and 104 mg/100 ml/min and K_m was 33 and 30 mg/100 ml at 37 and 41°C, respectively. Additional experiments suggested the presence of ICG in hepatocytes altered the kinetics of transport. Under the conditions of our experiments liver function did not change significantly with hyperthermia.

(The authors wish to acknowledge the generous contribution of ICG as Cardio-Green by Hynson, Westcott and Dunning, Balto., Md.)

RENIN RELEASE DURING URETERAL OCCLUSION, PAPAVERINE INFUSION, AND ETHACRYNIC ACID ADMINISTRATION. R.H. Freeman*, J.O. Davis, R.W. Gotshall*, B. Braverman*, and J.A. Johnson. University of Missouri School of Medicine, Columbia, Missouri 65201.

In 2 groups (n=6/group) of dogs maintained on a normal Na diet of 65 mEq/day, ureteral occlusion (UO) increased renin secretion (RS) from a mean control value of 460±150 to 2173±519 ng/min ($P<.025$) in group #1 and from 309±71 to 1455±318 ng/min ($P<.025$) in group #2 within 10 to 20 min after occlusion. In group #1, papaverine, an inhibitor of vascular smooth muscle contractility, was infused (3 to 7 mg/min) into the renal artery during the next 20 min of UO; RS was 2173±519 ng/min before and 2473±457 ng/min during papaverine infusion ($P>.15$). At this time, UO was removed and RS determined 5,12, and 27 min later. Analysis of serially collected aliquots of urine revealed that urinary Na concentration reached a plateau in less than 5 min after UO was removed. During the 35 min post-UO, excreted Na increased from pre-occlusion control values of 60-65 to 225 μEq/min ($P<.05$). RS decreased from 2473±457 ng/min before removal of UO to -203±210, 236±74, and 491±227 ng/min 5, 12, and 27 min after UO removal ($P<.01$ for all 3 values). In group #2, ethacrynic acid (EA) was administered (50 mg, i.v.) 20 min after UO, and RS was determined during the next 20 min of UO; RS was 1455±318 ng/min before and 1677±351 ng/min after EA administration ($P>.20$). Again, UO was removed, and urinary Na concentration plateaued in less than 5 min; during the 35 min post-UO, excreted Na increased 7-fold above pre-occlusion control values ($P<.005$). RS was 1677±351 ng/min before and 1468±292 ng/min ($P>.25$) 5 min after removal of UO; RS decreased significantly to 545±218 and 657±99 ng/min at 12 and 27 min after removal of UO ($P<.05$ for both values). The data suggest that UO increases RS via a non-baroreceptor mechanism, but fail to support the idea that increased Na concentration at the macula densa increases RS.

ORAL CONTRACEPTIVE-INDUCED SALT APPETITE IN RATS. M.J. Fregly and D.G. Newsome*. Dept. Physiol., Univ. Fla., Coll. Med., Gainesville, Fla.

Earlier studies have shown that dietary administration of the oral contraceptive, Enovid, to male and female rats given a choice between distilled water and either 0.15 or 0.25 M. NaCl solution to drink was accompanied by a spontaneous NaCl appetite. The present objectives were to determine both the lowest dose and shortest duration of administration of Enovid inducing a spontaneous NaCl appetite as well as to study the specificity of the NaCl appetite. Twenty-eight female rats were divided equally into a control and 3 treated groups. The latter received 1.25, 2.50 and 5.00 mg Enovid/kg food respectively. Rats were caged individually and daily intakes of distilled water and 0.15 M. NaCl solution measured for 3 weeks. During the remainder of the experiment, daily intakes of water and the following NaCl solutions were measured for 1 week: 0.15 M. (week 6); 0.25 M. (week 8); 0.35 M. (week 15). An appetite for 0.15 M. NaCl solution was detectable within 1 week of drug administration in all treated groups. Further, all 3 treated groups ingested more 0.25 and 0.35 M. NaCl solution than controls. A second group of 12 female rats, of which 6 received Enovid at 7.5 mg/kg food for 12 months, was used to test the specificity of the NaCl appetite. Rats were offered a choice between distilled water and salt solution (either NaCl, $NaHCO_3$, $NaNO_3$, KCl, $KHCO_3$ or KNO_3). Each salt solution was offered for 2 days at the following concentrations: 0.075, 0.15 and 0.25 M. Enovid induced an appetite for all these salt solutions. Thus, as little as 1.25 mg Enovid/kg food can induce an appetite for 0.15 M. NaCl solution within 1 week. When administered at 7.5 mg/kg food for 12 months, an appetite was also observed for other salt solutions. Hence, the appetite does not appear to be specific for NaCl solutions, but may reflect a general salt appetite. (Supported by grant HL-14526-02 from NIH).

ASCORBATE STIMULATION OF CHLORIDE TRANSPORT IN THE AMPHIBIAN CORNEA Deborra F. Friedenthal* and Walter N. Scott, Dept. of Ophthalmology, Mount Sinai School of Medicine of CUNY, New York, New York.

Ascorbic acid (AA) is actively secreted by the ciliary processes with the result that the concentration of AA in the aqueous humor may be 20-fold greater than the plasma levels of AA. The physiologic role of AA in the aqueous is not known. Corneas of the toad, Bufo marinus, were mounted in Ussing-style chambers and both surfaces bathed in a modified Conway-Ringers solution. AA (2mM) added to the baths caused a marked increase in short-circuit current (207%) and potential difference (136%). Similar results were obtained in corneas of the frog, Rana catesbiana. The concentration of AA in the aqueous humor of amphibians is 0.1-0.2 mM; the addition of 0.1 mM AA stimulated SCC by 139%. Concentrations of AA as low as 10 uM caused a significant increase in both SCC and PD. Dehydroascorbic acid had no significant effect upon SCC or PD. Inhibitors of mitochondrial oxidative phosphorylation caused no significant reduction in the response to AA, suggesting that AA might be an electron donor to an electron transport system coupled to ion transport. The amphibian cornea transports chloride from the epithelial surface to the endothelial surface, and to a lesser extent, sodium in the opposite direction. We measured the unidirectional fluxes of ^{24}Na and ^{36}Cl and found that AA stimulates the net flux of chloride but has no effect upon sodium flux. These data suggest that ascorbic acid, secreted by the ciliary processes, may play a significant role in maintaining normal corneal function.

Supported by Fight for Sight Inc., New York. WNS is an Established Investigator of the American Heart Association.

INFLUENCE OF 24 HR AT 4,267 m ON THE HYPOXIC VENTILATORY DRIVE OF MAN R.A. Gabel and R.B. Weiskopf (intr. by S.M. Robinson). U.S. Army Res. Inst. Environ. Med., Natick, Mass. 01760; and Dept. Anes., Peter Bent Brigham Hosp. and Harvard Med. Sch., Boston, Mass. 02115

Persons with lifelong hypoxia owing to residence at high altitude (HA) have a lesser ventilatory response to acute hypoxia than natives of sea level (SL). Effects of shorter durations of hypoxia have been less certain. We studied the ventilatory responses of 5 healthy young men to a progressive isocapnic fall in Pa_{O_2} over 4 min from greater than 100 torr to 40-45 torr: first, at SL; then, after 24 hr of acclimatization to 4,267 m in an hypobaric chamber. SL tests were performed at resting Pa_{CO_2}. After 24 hr of hypoxia, tests were carried out at resting HA Pa_{CO_2} and at resting SL Pa_{CO_2}. Ventilatory response to acute hypoxia was expressed as $\Delta\dot{V}_E$ (L/min BTPS), the difference between $\dot{V}_E$ during normoxia and $\dot{V}_E$ at the Pa_{O_2}, Pa_{CO_2}, and pH_a shown:

CONDITION	Pa_{O_2}	Pa_{CO_2}	pH_a	$\Delta\dot{V}_E$
(1) SL @ SL Pa_{CO_2}	43.3	35.1	7.424	16.3
(2) HA @ HA Pa_{CO_2}	39.2	26.1	7.453	7.0
(3) HA @ SL Pa_{CO_2}	43.5	33.2	7.381	43.7

Interpretation: 1. $[H^+]$ at central chemoreceptors (CC) should have been comparable under conditions 1 and 2 (C1,C2); so the greater $\Delta\dot{V}_E$ in C1 than in C2 was from interaction of hypoxia with CO_2 or $[H^+]$ at peripheral chemoreceptors (PC). 2. CO_2 at PC was comparable under C1 and C3; so the greater $\Delta\dot{V}_E$ in C3 than in C1 was apparently from interaction of hypoxia at PC with increased $[H^+]$ at CC. 3. $[H^+]$ and CO_2 at both PC and CC were higher under C3 than under C2; so the greater $\Delta\dot{V}_E$ in C3 than in C2 may have been from interaction of hypoxia with $[H^+]$ or CO_2 at PC or CC. There was no change in PC sensitivity to acute hypoxia which could not be explained by changes in $[H^+]$ or CO_2 at PC or CC.

HISTIDINE DECARBOXYLASE ACTIVITY IN TRAUMATIC SHOCK. Michael J. Galvin, Jr.*, Rebecca Bunce* and Sherwood M. Reichard, Div. Radiobiology, Medical College of Georgia, Augusta, GA 30902, and Dept. Pharmacology, University of Georgia, Athens, GA 30601.

Histamine is known to play an important role in the alterations that occur in the microcirculation after exposure to local or systemic stimuli. The formation of this vasoactive amine has been shown to be related to the activity of the inducible enzyme histidine decarboxylase (HD). In the present study, HD activity was determined in lungs and spleens of rats at various times following the production of traumatic shock. Shock was produced in rats by exposure to an LD_{50} dose of trauma in a Nobel-Collip drum. Histidine decarboxylase activity was determined by incubating 10μCi ^{14}C L-histidine with tissue extracts and assaying ^{14}C-histamine by isotope dilution as dibenzenesulfonyl-histamine (BSH), according to the method of Schayer. At 15 minutes following exposure, the enzyme activity in the lung was elevated from 350 to 810 cts/min/ 100 mg BSH/100 mg tissue. This reached a maximum of 1240 cts by four hours, and returned to normal by 10 hours. The enzyme activity in the spleen did not increase at 15 minutes, but was elevated at four hours from 500 to 1700 cts/min and returned to normal by 10 hours. These results indicate that histidine decarboxylase activity is altered following drum trauma, and may be important in explaining the changes in the microcirculation in traumatic shock.
(Supported in part by NIH Grant HE-08982)

INITIAL CHARACTERIZATION OF NEURAL TYPE CELL FROM MAHE HUMAN EMBRYONIC SKIN CULTURES. V. F. Garry, Jr., R. D. Moore, and L. W. Harris, (intr. by F. W. Stemler) Biophysics Division, Biomedical Laboratory, Edgewood Arsenal, Aberdeen Proving Ground, MD 21010

Cultures of human embryonic skin cells obtained from Microbiologic Associates, Bethesda, MD, were found to contain neuroepithelial-like cells. These cells formed discrete cell aggregates within the fibroblastic monolayers. The neural-like cell aggregates were separated and have been grown in culture for seven months. By electron microscopy the cytoplasm of the isolated cells was found to contain numerous ribosomal aggregates and rosettes, well formed myelin and intracellular myelin figures, large and small dense core granules, multivesicular bodies,, and microtubules. By light microscopy axon-like processes were seen. Silver impregnation studies showed fibrillar material. Nissl-like material was identified. The cell nuclei are large and have a prominent centrally placed nucleolus. Some cells within the cultures are multinucleate. Cholinesterase activity has been demonstrated biochemically. No viral material has been demonstrated either within the cells or by transfer of the cell free supernate to other cultures for the demonstration of cytopathologic effects. The cells possess a karyotype compatible with human origin.

STEADY STATE GLUCOSE OXIDATION RATE BY DOG KIDNEY IN VIVO. R. Garza-Quintero*, Julius J. Cohen, Paul H. Brand and Y. J. Kook*. Dept. of Physiology. University of Rochester, Rochester, N.Y.

The contribution of glucose oxidation in vivo to renal energy production during the steady state has not been quantified. Using the indicator dilution technique, Chinard et al reported that very small amounts (if any) of glucose were oxidized to CO_2. In 9 experiments we have now quantified the rate of glucose oxidation by the dog kidney in vivo in relation to: a) decreases in Na^+ reabsorption ($\dot{T}$-Na^+) due to raised ureteral pressure (mean decrease in T-Na^+=37%), or b) respiratory alkalosis. In 9 experiments, tracer amounts of either [1-^{14}C]-or[U-^{14}C]-D-glucose was infused at a constant rate into one renal artery. Oxidation of glucose by that kidney was calculated from the renal $^{14}CO_2$ production rate (corrected for recirculation). Under all conditions, glucose oxidation rate was low. Control (N=8) =4.4±0.9 µmoles/100g.min (mean ± SE). A mean decrease in $\dot{T}$-Na^+ of 37% (N=5) or a rise in ECF-pH (Resp Alkalosis N=2) had no significant effect on glucose oxidation rate (9.11 ± 42 and 4.7 ± 1.7 µmoles/100 g.min respectively). Thus under all conditions, there was a small but significant oxidation of glucose. This low oxidation of glucose requires ∿6% of the renal O_2 utilization and hence makes a relatively small but constant contribution to the total aerobic renal energy requirements. It is suggested that glucose oxidation may provide energy for basal renal energy requirements or to some portion of renal transport not affected by our experimental techniques. Supported by NIH-AM-03602.

Effect of exercise on glucose and palmitate metabolism by rat lung in vitro. L.N. Gassenheimer*, R.A. Rhoades, and E.R. Buskirk. The Pennsylvania State University, University Park, Pa. 16802

Increased ventilation in response to muscular exercise is well documented, but whether increased ventilation (greatly enhanced surfactant film compression–expansion) leads to quantitative differences in substrate metabolism by the lung is not known. Glucose $-U-^{14}C$, glucose $-6-^{14}C$, glucose $-1-^{14}C$ and palmitate $-1-^{14}C$ utilization was examined in vitro on lungs from male Long Evans Hooded Rats following a regimen of exercise. The exercise regimen consisted of treadmill running at 1 mph 4% grade. Thus, 1 mile/day was run 3 days/week for 8–9 weeks. Three weeks of conditioning preceded the exercise period. All measurements were made 24 hrs. after the last bout of exercise. Body weights decreased 17% ($P < 0.05$) in the exercise group. Corrected lung, heart, and adrenal weights were significantly higher than those in the sedentary controls. The ability to oxidize labeled glucose was increased 41% in lung slices from exercised rats. C_1/C_6 ratio was significantly lower in the exercised group, suggesting a decrease in hexose monophosphate shunt pathway activity. Palmitate oxidation was unaltered following exercise. Glucose $-U-^{14}C$ and palmitate $-1-^{14}C$ incorporation into total lipid, phospholipid, neutral lipid and phospholipid–hydrolytic products were relatively refractory to exercise. Lung glycogen content (mg/100mg lung) was also unaltered, indicating glycogen stores remain stable following exercise. The data show that glucose oxidation by lung was accelerated by the exercise regimen, whereas lipid synthesis was unaltered.
(Supported in part by NSF Grant GU 3695.)

FACTORS INFLUENCING RADIATION INDUCED INCAPACITATION IN THE RAT
E. L. Gasteiger and Mark Windt* Dept. of Physical Biology, N. Y. S. Vet. Col. and Section of Neurobiology and Behavior, Div. of Biol., Cornell University, Ithaca, N. Y. 14850

Rats exposed in a nuclear reactor to high levels of pulsed gamma-neutron radiations experience a 10-20 min. period during which they can not perform learned behavior; they display early transient incapacitation (ETI). This phenomenon has been studied by modifying the operant conditioning jump-box paradigm of Casarett and Comar (Rad. Res. 53: 455-461, 1973) to permit minute to minute assay of the behavioral state of animals after pulsed irradiation. Observation of irradiated unconditioned animals revealed reduction in motor activity but no ETI except for complicated activities such as rearing on hind limbs and grooming. Animals occasionally swayed their heads, rolled or toppled backwards. Recovery curves for conditioned animals pulsed at various doses revealed threshold for ETI at about 2,570 rads with no recovery within 30 min. for 13,600 rads. At intermediate doses the animals showed swift growth of incapacitation to maximum at 3 min. Recovery then began and proceeded to completion in 20 min. Recovery will occur without shock or provoked motor activity as determined by delayed shock experiments. Parallel with ETI is a marked increase in breathing rate following pulse, with a stepwise return to normal rates during the 5th through 9th minutes. Recovery was promoted by the presence of 100% oxygen or increased shock intensity. Capacity for motor performance and detection of shock stimuli appeared to be normal. ETI can be characterized by disequilibration or disorientation, probably caused by hypoxia.

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SELECTIVE INCREASE IN SERUM FSH FOLLOWING TREATMENT OF FEMALE RATS WITH DIHYDROTESTOSTERONE. Vernon L. Gay. University of Pittsburgh School of Medicine, Pittsburgh, Pa. 15261.

At the time of castration, adult female rats received subcutaneous implants of silastic capsules containing crystalline dihydrotestosterone (DHT). Following 10 days of treatment with the appropriate implant (10 mm/100 g BW) serum LH levels were significantly decreased (5ng/ml, RP-1 standard) as compared with intact controls (10.4 ± 1.0,S.E.) while serum FSH had increased (543 ± 71 ng/ml) as compared with controls (170 ± 11). However, untreated castrates had significaltly higher levels of FSH (2202 ± 224) and LH (317 ± 37). Since these hormonal responses could be interpreted as a differential inhibiton of LH secretion, intact females were also treated with DHT. In such intact rats DHT implants caused an increase in serum FSH (487 ± 39 vs. 218 ± 21) while LH did not increase, and resulted in FSH levels comparable to those observed in untreated females on the day of estrus and in intact males. Since we (Jarvis and Gay, unpublished) and others have observed a "peak" of serum testosterone on the day of proestrous in the rat, these responses to androgen suggest that the post-ovulatory increase in serum FSH may not be dependent on events which stimulate LH release but may result from an increase in circulating androgens which causes an increase in the rate of FSH release or an alteration in the rate of FSH metabolism.

HEAT LOSS OF MAN IN TOTAL WATER IMMERSION. G. K. Gee* and R. F. Goldman. US Army Research Institute of Environmental Medicine, Natick, Mass.

Heat loss and surface transfer coefficients were studied in 15 men immersed in water. Heat flow, measured by 5 heat flow transducers, averaged 35, 87, 163, 235 and 290 watt/m^2 at 35, 32, 28, 24 and 20°C, respectively. Calculated transfer coefficients were linear with water temperature and constant at a given temperature, but increased with decreasing temperature partly from increased natural convection, but especially increased shivering movement. Heat transfer coefficients, calculated from heat sensor, skin (T_s) and water (T_w) temperature were 38, 96, 208, 358 and 537 watt/m^2°C in water of 35, 32, 28, 24 and 20°C. The measured gradients ($T_s - T_w$) were:

T_w	5'	15'	30'	60'
35°C	-.02±.18°C	.12±.11	.13±.08	.14±.08
32	.41±.26	.39±.23	.37±.25	.34±.14
28	1.20±.13	1.04±.24	.92±.21	.75±.24
24	1.78±.47	1.22±.24	1.07±.14	.97±.21
20	2.80±.53	1.76±.32	1.77±.40	1.49±.31

Previously reported gradients in 20°C unstirred water were 3.3°C after 5 min, 2.4°C after 15, 1.6°C after 30 and 0.7°C after 60 min. The predicted coefficients for a 3°C ($T_s - T_w$) in 20°C water were 140 w/m^2 for forced, and 250 for free convection, a total of 390 w/m^2°C; as the gradient falls to 2-3°C and shivering begins, the predicted forced convection is 780 w/m^2°C and the free is 225 - a total of 1005 w/m^2°C. The 537 w/m^2°C, in 20°C water (from the heat flow sensors) agrees with these predictions and with the observed severe sporadic shivering.

PARASYMPATHETIC INFLUENCE ON CARDIAC RATE AND RHYTHM IN THE NEWBORN. W. Peter Geis and Robert J. Herfkens.* Department of Physiology and Surgery, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Supramaximal electrical stimulation of vagus nerves in adult dogs typically elicits profound sinus bradycardia or cardiac arrest. These responses are interrupted by ganglionic blocking agents. Further, partial denervation studies have elucidated bilateral parasympathetic influence on both sinus and AV nodes in adults. Since the autonomic system continues to develop during perinatal life, the aforementioned responses may differ considerably in neonates. Accordingly, distal ends of right and left vagus nerves were electrically stimulated during recording of ECG and systemic pressure in 18 newborn puppies. Stimulations were repeated after intravenous injections of hexamethonium HCl and following atropine sulfate. Newborns exhibited bradycardia during right vagal stimulation with alteration in rhythm from sinus to AV junctional. Following hexamethonium, the negative chronotropic response declined to 37% of the initial response and sinus node remained dominant. Left vagal stimulation effected moderate decline in sinus rate and complete AV block. Hexamethonium interrupted AV block and reduced negative chronotropic effect on the sinus node while atropine interrupted all chronotropic effects. These data delineate that parasympathetic fibers of right-sided origin are pre-ganglionic to the sinus node, while those of left-sided origin are pre-ganglionic to AV node in newborns. Moreover, continued sinus slowing following hexamethonium strongly suggests presence of post-ganglionic parasympathetic fibers in neonates. These findings strongly suggest incomplete bilateral parasympathetic nodal innervation and continued ganglion cell migration in perinatal life. (Supported by Grants NHLI HL 08682 and Chicago Heart Association A7151.)

ELECTRICAL PROPERTIES AND DIFFUSION POTENTIALS OF GALLBLADDERS FROM VARIOUS SPECIES. R.T. Gelarden* and R.C. Rose. The Pennsylvania State Univ., College of Medicine, Hershey, Pa. 17033.

Gallbladders were mounted in a lucite Ussing-type chamber and bathed on each surface with buffered electrolyte at 38°C. Rabbit gallbladder developed a small spontaneous serosa-negative transmural PD; dog gallbladder developed essentially zero PD; gallbladders of goose, monkey and human developed serosa-positive PD's which were reduced by ouabain, low temperatures, or the absence of O_2 or Na. Diffusion potentials, established to determine whether the cation-anion selectivity of the tight junction correlated with the magnitude and orientation of the spontaneous PD's, were generated across the membrane by diluting the mucosal solution 50% with isotonic mannitol. All gallbladders were found to be cation selective. The Cl:Na permeability ratios do not correlate with the orientation and magnitude of the spontaneous PD's. The possibility that diffusion gradients, established in the intercellular space subsequent to cellular NaCl absorption, produce the serosa-positive PD's seen in goose, monkey and human gallbladders does not seem likely in view of the cation selectivity of the tight junction.

	Rabbit	Dog	Monkey	Human	Goose
Spontaneous PD (mv)	-0.4	0	+4.1	+5.5	+5.7
R (Ω-cm^2)	26	46	37	44	28
Diffusion PD (mv)	-8.6	-3.0	-8.4	-2.3	-8.8
P_{Cl}/P_{Na}	.32	.70	.33	.75	.32

(Supported by N.I.H. grant AM 15926)

A MATHEMATICAL MODEL OF THE RESPIRATORY CENTERS. S.Geman and M.Miller (intr. by S.M.Tenney). Dept. of Physiol., Dartmouth Med. Sch., Hanover, N.H.

A mathematical model of the brainstem respiratory system composed of two mutually inhibiting populations (inspiratory and expiratory) of computer simulated neurons, has been devised. Each population consists of randomly interconnected subpopulations of excitatory (E) and inhibitory (I) neurons. A sufficient condition for neuronal coupling, as defined by the Poincare-Bendixson Theorem, is used to insure that either the inspiratory or expiratory population alone is capable of cyclic activity. The phase difference in oscillation of well coupled E and I subpopulations is extremely small relative to the cycle time of the coupled system. Thus a single, well connected network of E and I neurons cannot account for the reciprocating activity of the two distinct populations of inspiratory and expiratory neurons. Weak inhibitory connections between inspiratory and expiratory populations provides satisfactory reciprocating activity independent of the natural frequency of either population alone. Initiation and persistence of rhythmic activity is dependent upon a diffuse non-cyclic excitatory input.

CO_2 stimulation, simulated by uniform facilitation of synaptic connection, increased discharge rate of inspiratory and expiratory populations, with minor effect on frequency. Vagal discharge, simulated by phasic inhibition of inspiratory neurons, results in increased respiratory frequency with decreased inspiratory activity. Interaction of CO_2 and vagal input reproduces physiological experiments. The system demonstrates inspiratory-expiratory and expiratory-inspiratory phase-spanning activity, as well as predicting paradoxical effects of CO_2 and vagal inputs on inspiratory and expiratory neurons, as observed in experimental animals.

Supported by PHS Grant HL 02888-17.

EFFECTS OF SODIUM ON PAH TRANSPORT IN RABBIT KIDNEY SLICES. G.A. Gerencser*, Y.S. Park*, and S.K. Hong, Dept. of Physiology, Univ. of Hawaii School of Medicine, Honolulu, HI 96822.

Na is needed to induce maximal PAH accumulations in vertebrate kidney slices. We conducted the following study in order to further define the specific function of Na in relation to active organic solute secretion using PAH as a model organic compound. When measuring PAH accumulation as a function of time in the presence and absence of metabolic inhibitors (N_2 and Iodoacetate) at constant Na concentration (10 or 100 mM/L) and a fixed PAH concentration (70μM/L), the maximal rate of active PAH uptake occurs between 0 and 60 minutes for either Na concentration. The mean slice to medium ratio (S/M) are 1.60 $\pm$ 0.10 (n = 20) and 9.43 $\pm$ 0.47 (n = 20) for 10 and 100 mM Na, respectively. Efflux of PAH from preloaded slices is independent of the Na concentration in the bathing medium. The oxygen consumption of slices in the 10 and 100 mM Na media was 0.73 $\pm$ 0.06 (n = 10) and 0.70 $\pm$ 0.01 (n = 10) μl/hr per milligram initial wet weight respectively. PAH accumulation as a function of PAH concentration in either Na media increases curvilinearly and tends to saturate at a high PAH concentration. Kinetic data of PAH uptake yields the following results: the mean maximal velocity (V_{max}) in 100 mM Na is 4.10 $\pm$ 0.75 (10) while in 10 mM Na it is 1.31 $\pm$ 0.18 (10), and the mean Michaelis constant (Km) in 100 mM is 0.31 $\pm$ 0.03 (10). While in 10 mM Na it is 0.33 $\pm$ 0.04 (10). These results suggest that Na plays a role in PAH accumulation perhaps by mobilizing the carrier through its binding at a site other than the active or allosteric sites. (Supported by a Grant-in-Aid from the American Heart Association and supported in part by the Hawaii Heart Association).

INTRACELLULARLY-RECORDED RESPONSES OF OLFACTORY RECEPTORS IN NECTURUS. R. C. Gesteland and A. I. Farbman*. Northwestern Univ., Evanston, Ill.

Olfactory receptor neurons in the mudpuppy, Necturus, are larger than those in most other vertebrates. Using 150 megohm, 2.5 M KCl micropipette electrodes we can record intracellularly for periods of many minutes in live, pithed animals. An advancing electrode encounters cells with negative resting potentials of 20 mv in which no spikes occur (most likely supporting cells) and cells with resting potentials of 30 mv in which two sorts of spike activity occur. Regular interval spikes with amplitudes of 30 mv are seen immediately after penetration. The firing rate slows and the amplitude declines in less than a minute. This firing pattern may continue until the spikes are lost in the noise. Alternatively, spikes in some cells reach a stable amplitude of a few mv and continue as long as the electrode remains in the cell. When this happens the firing rate becomes slow and very irregular, successive intervals differing by factors up to 30:1. We infer that the large, declining amplitude, regular interval spikes arise locally where the penetrating electrode damages the soma membrane. The smaller, constant amplitude, irregular interval spikes are normal action potentials originating at the hillock or axon which electrotonically invade the soma region near the electrode. The spikes are monophasic and positive-going. Olfactory stimulation with various vapors and solutions may increase the firing rate, decrease the firing rate, or have no effect on any particular cell. Effective stimuli cause changes in the membrane potential of less than a mv. A typical response consists of a sequence of negative and positive potential fluctuations. (Supported by NSF Grant No. GB-30520.)

EFFECTS OF METIAMIDE, AN H-2 ANTIHISTAMINE, ON GASTRIC H^+ AND PEPSIN SECRETION IN THE DOG IN RESPONSE TO VARIOUS STIMULI. R. G. Gibson*, G. Hutchison*, and B. I. Hirschowitz. Division of Gastroenterology, Dept. of Med., Univ. of Ala. Medical Center, Birmingham, Ala.

In 3 fistula dogs, 45 minute consecutive step-dose response control studies were undertaken using histamine (2-100 μg base/kg.hr), pentagastrin (PG) (0.1 to 5 μg/kg.hr), urecholine (UR) (20-160 μg/kg.hr) and a single response to 100 mg/kg 2-Deoxy-glucose (2-DG), a vagal stimulant. In repeat studies Metiamide* was given as background in 2 doses, 0.5 and 2.5 mg/kg.hr respectively. H^+ output in response to all stimuli was reduced significantly by Metiamide. At the lower dose of Metiamide the H^+ response to all stimuli was competitively inhibited (Vmax unchanged, Km increased), but at the highest dose inhibition was so great (> 80%) that no kinetic calculations could be performed. By contrast, pepsin secretion with histamine was not changed by Metiamide, but with PG, UR and 2-DG stimulation, pepsin secretion was increased by Metiamide 2 to 7 x and pepsin:H^+ ratios were increased 20 - 50 x, reflecting the simultaneous H^+ reduction. Thus, the receptors for stimulation of the peptic cell are clearly different from those affected by the H-2 antagonist on the parietal cell. The action of Metiamide against all stimuli raises the question of specificity of this compound for the parietal cell histamine receptors. NIH Support.

*Metiamide kindly supplied by Dr. J. W. Black, SKF, England

HYPOXIC RESISTANCE OF SHIVERING THERMOGENESIS IN MINI-PIGS. Thomas M. Gilbert* and Clark M. Blatteis. Dept. of Physiol. and Biophys., Univ. of Tenn. Med. Units, Memphis, TN.

Because visible shivering continues unabated in the cold during moderate hypoxic hypoxia, it has been suggested that the hypoxic reduction of the metabolic response to cold of certain sensitive species might be due to the selective depression of their nonshivering thermogenesis (NST). To test this possibility, four adult, cold-acclimatized, miniature pigs were exposed to 7 C for two hours while breathing air or 10% O_2 (in N_2). These animals, even when cold-acclimatized, are alleged not to possess NST; therefore, their metabolic response to cold should be unaffected by moderate hypoxia. The absence of NST was inferred in these mini-pigs by the lack of a large calorigenic response to the iv infusion of norepinephrine (2 µg/kg for twenty minutes). In 7 C, neither the increase in O_2 consumption nor the visible shivering activity which accompanied it were different in the two gaseous environments. Colonic temperature did not change during cold exposure under both conditions. These results would support, therefore, the earlier suggestion that shivering thermogenesis is not depressed by moderate hypoxia, whereas NST might be.

EFFECTS OF SHORT-TERM HEAT-ACCLIMATION ON THE ABILITY OF MEN TO PERFORM PROLONGED WORK IN THE HEAT. Carl V. Gisolfi*(intr. by C. M. Tipton). Stress Physiology Laboratory, Univ. of Iowa, Iowa City, Iowa 52242.

In March, 6 healthy untrained ($\dot{V}O_2$ max = 52 ml/kg·min) young men acclimated to work in the heat (50/27°C db/wb) by walking 100 min/day at 5.6 km/hr on a level treadmill for 7 consecutive days. On day 8 each man walked for 3 to 4 hrs under the same conditions. In 4 of the men short-term heat-acclimation followed by prolonged work in the heat was studied in both the trained ($\dot{V}O_2$ max = 62 ml/kg·min) and untrained ($\dot{V}O_2$ max = 51 ml/kg·min) state. The latter experiments were performed 1 year apart. Training consisted of short (10 sec to 10 min) bouts of intense treadmill running alternated with brief (10 sec to 5 min) periods of rest or moderate work 30 min/day, 5 days/week for 11 weeks in a cool (21°C) temperature controlled environment. On day 7 of heat-acclimation in the untrained state terminal rectal temperature, mean weighted skin temperature, heart rate, and sweat rate for the 6 men averaged 38.0°C, 37.0°C, 123 beats/min, and 605 g/m^2·hr respectively. On day 8 after 3 hrs of walking in the same environment corresponding mean terminal values were 38.2, 36.8, 134, and 613 respectively. The rate at which heat-acclimation occurred, the final degree achieved, and the ability to perform prolonged work in the heat were similar in the trained and untrained states (4 men) when heat-acclimation in the untrained state was preceeded by 5 days of walking 100 min/day at 5.6 km/hr in a cool (25°C) room. These data suggest that (a) intense interval training eliminates the need for a 5 day adjustment period in a cool room prior to heat-acclimation, (b) short-term heat-acclimation enables men to perform prolonged (3-4 hrs) work in the heat, and (c) the ability to acclimate and to perform prolonged work in the heat is not related to $\dot{V}O_2$ max.
(Supported by ONR Contract N00014-68-A-0196-0008)

RESPIRATORY EFFECTS OF VARIED TIME INTERVALS BETWEEN PNEUMOTAXIC AREA LESIONS AND VAGOTOMY. R. L. Glasser, R. A. King*, W. M. St. John, and G. M. McClain*. Univ. of North Carolina at Chapel Hill, N. C.

Bilateral lesions were placed in the pontine pneumotaxic area in anesthetized cats. After varied time intervals ranging from one hour to three months, both vagal nerves were sectioned in these cats under short-acting anesthetics. Regardless of the time interval, vagotomy induced conspicuous apneustic breathing. After vagotomy, the animals with chronic pneumotaxic lesions of one - three months exhibited remarkably rapid and extensive recovery from the anesthetic state and from apneustic breathing. Within two - four hours these animals were awake and their respiratory patterns characteristically were eupneic. Cats with lesion to vagotomy intervals of one - two weeks also exhibited good recovery. However, these animals recovered at a slower rate and to a lesser extent than did the one - three months animals. Cats with lesion to vagotomy intervals of one - two days required significantly longer times after vagotomy before they exhibited signs of wakefulness and a return to more normal patterns of breathing; after six - eight hours, normal respiratory activity was frequently interrupted by prolonged apneustic inspirations. Acute lesion animals with lesion to vagotomy intervals of one - three hours stood in sharp contrast to the other animals. The acute lesion animals failed to regain the awake condition and failed to exhibit a restoration of normal respiration. Some of these animals were monitored for sixty or more hours; they tended to display apneustic breathing interspersed with other abnormal forms of respiration and apnea. These data indicate that the duration of the interval between placement of pneumotaxic area lesions and vagotomy is a significant determinant of the rate and the extent of recovery from apneustic breathing.

RELATIVE STABILITY OF AIR/WATER FILMS OF PALMITOYL, MYRISTOYL- AND DIPALMITOYL-PHOSPHATIDYLCHOLINES AT 37°C. Jon Goerke* and John A. Clements. CVRI, UCSF, San Francisco, Calif. 94122.

1-palmitoyl, 2-myristoyl-3-sn-glycerophosphorylcholine (16,14-PC) is reported to be the principal lung surfactant in human fetuses prior to 36 weeks gestation, while the closely related 1,2-dipalmitoyl-3-sn-glycerophosphorylcholine (di 16-PC) is said to be the major contributor to lung stability in infants nearer term and in adults.[1] We synthesized 16,14-PC by degrading pure synthetic di 16-PC with Crotalus phospholipase A_2 to form the palmitoyl lyso derivative and reacting this with myristoyl chloride. The product was chromatographically pure and contained equimolar amounts of palmitic and myristic acids. By hydrolysis of the product with phospholipase A_2, we found the myristic acid >95% in the 2 position. With phospholipase C, only 16,14-diglyceride was formed. Using both 16,14-PC and di 16-PC on a Langmuir-Wilhelmy surface balance thermostated at 37°C we followed the time course of surface tension (γ) during film collapse from initial γ values of 20, 12 and 5 dynes/cm. In companion experiments we maintained γ constant at these same values by compressing the film, and recorded the film area (A) as a function of time. Two indices of collapse rate $(d\gamma/dt)_A$ and $(d\ln A/dt)_\gamma$, showed surface films of 16,14-PC to collapse ~40 times as fast as those of di 16-PC. This finding makes it unlikely that 16,14-PC can act as a lung surfactant at 37°C.

1. Gluck, L., et al. Pediat. Res. 6: 81, 1972

THE DISSOCIATION OF MYOCARDIAL INOTROPISM FROM METABOLISM BY CARBACHOL IN DOGS SUBJECTED TO CARDIOPULMONARY BYPASS. J.M. Goldberg, M. Pindok* and V.V. Glaviano. The Chicago Medical School, Chicago, Illinois 60612

The effects of the cholinergic agent, carbamylcholine chloride (carbachol) on cardiac metabolism were studied in dogs subjected to total cardiopulmonary bypass. In the paced, contracting, nonworking heart, the cardiac extraction and uptake of oxygen and plasma free fatty acids (FFA), glucose (G) and triglycerides (TG) were determined before and after an intracoronary infusion of carbachol (1 μgm/Kg/min) for 6 min. Aortic and coronary perfusion pressures together with total coronary inflow and myocardial contractile force from the right ventricle were continuously monitored. The infusion of carbachol caused a slight decrease in mean aortic and coronary perfusion pressures and a marked decrease in myocardial force of contraction (40%), while coronary flow increased on an average of 45%. In this period, the extraction of O_2 decreased markedly (av. 40%) while uptake underwent little or no change. In contrast, the myocardial extraction and uptake of FFA, G, and TG were significantly elevated during the infusion of carbachol. The uptake of FFA increased from 1.7 to 7.5 μEq/min/100 gm while the TG shifted from -0.1 to 6.8 mg/min/100 gm. Glucose uptake increased from 5.1 to 43.0 μM/min/100 gm. Thus, with the work of the heart held at a minimum by total cardiopulmonary bypass, a decrease in contractility due to the infusion of a cholinergic agent was associated with an increase in the myocardial uptake of carbohydrate and lipid substrates in the presence of no change in O_2 consumption. These experiments indicate that in the absence of external cardiac work, parasympathomimetic agents can cause dissociation between negative inotropism and metabolism. (Supported by NIH grant HL 14673 and ONR NOOO14-67-0397-01).

Metabolic rate and induced obesity in man. R.F. Goldman, M.F. Haisman* and E.A.H. Sims*. US Army Research Institute of Environmental Medicine, Natick, MA 01760 and University of Vermont, Burlington, VT.

A discrepancy between sustained excess caloric intake, energy expenditure and the weight gained has been frequently reported. In two separate investigations (1 and 2), energy metabolism was measured at rest and during standardized and self-paced exercise in two groups of four men (seven individuals) before and after overfeeding. The primary objective was to determine if the increase in metabolism after overfeeding, reported by others, could be demonstrated with two different regimes of overfeeding. In experiment 1 the basal diet was supplemented with fat for 3 months; in 2, carbohydrate supplement was given for 18 days. These dietary regimes resulted in mean body weight gains of 11.2 kg (15.2%) and 4.5 kg (5.1%). In experiment 1, resting metabolic rate in a controlled environment chamber (26.7°C, 50% R.H.) was essentially unchanged and, correspondingly, reduced when expressed per unit of body size. Metabolic rate during exercise (treadmill, bicycle ergometer, stair climbing and self-paced walking) was generally elevated at the end of the overfeeding period; these increases could be accounted for largely by increased body weight. In experiment 2, resting metabolic rate was somewhat higher after the overfeeding period, particularly after standardized meals. Skin temperature also tended to be higher in the overfed state. The exercise responses however, did not show any consistent trend to increase after overfeeding; changes observed were within normal physiological variability. Our studies do not allow separation of metabolic effects of either the duration or nature of the overfeeding. From this limited available data, "luxus consumption" is manifested more as an increase in resting post prandial heat production after overfeeding carbohydrate, than as an exercise associated effect.

LANTHANUM AS A CARDIOPLEGIC AGENT. Frank Gollan, Michael H. Cleman* and Albert F. De Loskey*, Veterans Administration Hospital and University of Miami School of Medicine, Miami, Florida.

The trivalent cation lanthanum has a greater electrostatic attraction for any extracellular, negative binding site than calcium. Previous investigations by other authors have shown that lanthanum can substitute for calcium in the lobster axon membrane, the barnacle muscle, smooth muscle of the intestine and uterus, and the striated muscle of the frog sartorius. The present communication deals with its effects on the isolated, perfused heart. Rabbit hearts were perfused first with blood, then with a plasma expander and then various concentrations of lanthanum chloride were added to the asanguineous perfusate. The optimum concentration was one millimole of lanthanum which reduced the contractility to about one-tenth and the rate to about one-third of the normal response to blood. During lanthanum inactivation the minute work of the perfused heart was reduced to 6% and the oxygen consumption to 12% of the control value. The time for complete recovery of function was directly related to the lanthanum concentration. For every millimole of lanthanum the heart required five times more time in minutes to regain its original contractility, rate and oxygen consumption. The fact that ionized lanthanum displaces extracellular calcium receptor sites, whereas potassium penetrates the cells, may account for the rapid and complete recovery of myocardial contractility when isolated hearts are reperfused with blood. Thus a Langendorf heart preparation may also serve to give functional information on the neutralization of calcium transport in the sarcotubular system. (This work was partially supported by a grant from the Norman Olsen Memorial Fund and the Florida Heart Association).

GLYCOGEN DEPLETION IN HUMAN SKELETAL MUSCLE FIBERS DURING ISOMETRIC EXERCISE. P.D. Gollnick, J. Karlsson+, and B. Saltin+, Department of Physiology, Gymnastik- och idrottshögskolan, Stockholm, Sweden.

Muscle glycogen is used as a substrate during exercise. The pattern for glycogen depletion in the individual muscle fibers may vary as a function of the type of exercise performed. In the present study the glycogen depletion pattern in the fibers of human skeletal muscle was examined after different programs of isometric work. Exercise consisted of exerting tension with the knee extensors with the knee joint at a 90^{o} angle. Muscle biopsy samples were taken from the vastus lateralis before, during, and after the work. Isometric tensions ranging from 10 to 40% of maximal voluntary contractile strength (MVC) were held to exhaustion either continuously or intermittently. Muscle glycogen and lactate were determined chemically. Muscle fibers were identified histochemically and their glycogen content estimated with the PAS reaction. Muscle glycogen declined from a resting concentration of 48 mmoles of glucose units x kg^{-1} wet weight at all work loads but it was never completely depleted. Resting muscle lactate averaged 2.3 mmoles x kg^{-1} wet weight. No increases in lactate occurred in the muscle at the lowest tensions studied (10-15% MVC) or at the high tensions when short work bouts were separated with short rest pauses. Peak lactates occurred at a tension of 25% MVC held to exhaustion. At tensions below 20% MVC, regardless of the experimental protocol, glycogen was preferentially lost from the slow twitch (high-oxidative) fibers. At tensions of 20% MVC and higher the fast twitch (low-oxidative) fibers were the only fibers to become PAS negative. These fibers were the most darkly stained for glycogen in the pre-exercise samples. These data indicate that a changing pattern of glycogen usage exists in human skeletal muscle as a function of the tension developed.

HEART RATE RESPONSE TO PARTIAL FACE IMMERSION IN TRAINED DOGS. B. A. Gooden*, C. L. Jones* and H. L. Stone. Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas.

Dogs were trained to partially immerse the face under water for durations up to 30 seconds. Commands initiated and terminated immersion. The ECG was recorded from sternal electrodes. Average resting heart rate in the dogs was 85 $\pm$ 10 (S.D.) bpm. At the moment of partial face immersion the dogs exhaled and held their breath. The heart rate fell 36 $\pm$ 6 bpm below the resting level after 10 to 15 seconds of immersion. A post-immersion tachycardia, 41 $\pm$ 20 bpm above the resting level, occurred within 1 to 5 seconds after removal of the muzzle from water. The magnitude of post-immersion tachycardia was inversely related to the magnitude of immersion bradycardia. Intravenous propranolol (2 mg/kg) had no effect on the magnitude of immersion bradycardia or post-immersion tachycardia. Intravenous atropine (0.2 mg/kg) greatly reduced or abolished immersion bradycardia. These findings support the view that diving bradycardia in the dog results from increased vagal tone. The post-immersion tachycardia does not appear to result from increased sympathetic tone but may result from inhibition of vagal tone. Therefore, the role of the vagus nerve appears to be the dominant cardiac effect of the diving response in these trained dogs.

EARLY POSTNATAL PATTERN OF MATURATION OF BODY TEMPERATURE IN MICE. Cecilie A. Goodrich. Cleveland State Univ., Cleveland, Ohio.

A simple method has been devised for obtaining repeated measurements of body temperature with minimal stress. A precision thermocouple is attached to the skin of the thorax in the region of the heart with warm beeswax. The mouse is then placed in an insulated sling during recording of temperature. During the measuring period animals may sleep or groom themselves; more active animals can be induced to sleep by placing a piece of gauze over their head. Ambient air temperature near the mouse is recorded simultaneously (22-25° C). Body temperature measured by this method in CFW mice averages 2-3° C. above ambient for the first 3 days after birth. On the 4th day, body temperature is about 4.5°, and then continues to increase steadily with respect to ambient. Adult levels of temperature are reached by the third to fourth week. Individual mice may mature at different rates with respect to both body temperature and body weight. "Runts" (as defined by low body weight at 7 days) have significantly lower body temperature over the first two weeks, but are indistinguishable from littermates in weight and temperature at 8 weeks (adult). This method of temperature measurement should provide a useful tool for screening drug effects on maturation. (Supported by NIMH grant MH 22213.)

VASCULAR RESPONSIVENESS OF THE PERFUSED DOG PANCREAS TO VASOCONSTRICTORS AND GLUCOCORTICOIDS. Richard J. Gorczynski,* James A. Spath, Jr.,* and Allan M. Lefer. University of Virginia School of Medicine, Department of Physiology, Charlottesville, Virginia 22901.

Pancreatic ischemia is an early pathophysiologic event in a variety of types of circulatory shock, which subsequently leads to the plasma accumulation of hydrolytic enzymes and toxic factors. The purposes of this study are to determine: (a) the role of humorally released vasoactive agents in the maintenance of the pancreatic hypoperfusion of shock, and (b) the effectiveness of glucocorticoids in vasodilating the pancreatic vasculature as a possible mechanism of their protective action in shock. The hemodynamically-isolated dog pancreas was perfused *in situ* under constant flow conditions at a perfusion pressure of 130 mm Hg. Concentrations of vasoconstrictors comparable to those observed in plasma during shock were administered: norepinephrine (10 ng/ml),angiotensin II (9 ng/ml) and vasopressin (3 mU/ml). Norepinephrine produced a mean increase in pancreatic perfusion pressure of 49±3%, angiotensin 25±3, and vasopressin 27±3. These data indicate that catecholamines induce a greater vasoconstrictor response than the peptide vasoconstrictor agents at the plasma concentrations present in shock. Thus the release of vasoconstrictor agents in shock may contribute to the observed pancreatic hypoperfusion in hypotensive states. In contrast, neither methylprednisolone nor dexamethasone in doses which have been shown to protect in shock, 30 mg/kg and 6 mg/kg respectively, exerted any significant vasodilator effect when compared to appropriate vehicle controls. The preparation however was responsive to vasodilators; an acetylcholine concentration of 1 µg/kg produced a 36±3% decrease in perfusion pressure. These data fail to substantiate the hypothesis that glucocorticoids protect in shock by virtue of their ability to dilate the splanchnic vasculature. (Supported by an NIH Grant.)

INCREASED RENIN RELEASE DURING RENAL AUTOREGULATION IN ADRENALECTOMIZED DOGS WITH A DENERVATED, NONFILTERING KIDNEY.
R.W. Gotshall*, J.O. Davis, E.H. Blaine*, R. Freeman*, and J.A. Johnson. University of Missouri School of Medicine, Columbia, Missouri 65201.

A nonfiltering kidney model was used to study renin release in response to graded constrictions of the suprarenal aorta. In six dogs with a single denervated nonfiltering kidney, decreases in renal perfusion pressure of 30, 50, and 80 mm Hg resulted in significant increases in renin release at each level. Renal vascular resistance (RVR) decreased with each constriction as renal blood flow (RBF) either decreased or did not change. Release of the constriction at each level of pressure resulted in a decrease in renin secretion, an increase in RVR and an increase or no change in RBF. In five adrenalectomized dogs with a single denervated nonfiltering kidney, decreases in renal perfusion pressure within and below the autoregulatory range resulted in increased renin release with each constriction as RBF did not change or decreased. RVR decreased or did not change with each suprarenal aortic constriction. Release of the constriction was associated with a decrease in renin release as RBF remained the same or increased to the control level while RVR increased or failed to change. Thus, in dogs with or without intact adrenals and with a denervated nonfiltering kidney, renin secretion was associated with renal arteriolar dilatation. It is concluded that changes in renin secretion are mediated by a renal vascular receptor in the presence of decreased renal vascular resistance as well as during increased renal resistance, a finding observed previously. (Supported by USPHS Grants--HL 05810 and HL 10612)

A 3-SPECIES, 3-COMPONENT MODEL FOR OSMOTIC TRANSIENTS IN MYOCARDIUM. E.F. Grabowski* and J.B. Bassingthwaighte, Mayo Clin., Rochester, Mn.

In order to reconcile differences in estimates of capillary permeability(P) and reflection coefficient(σ) obtained with osmotic transient and tracer techniques (Yipintsoi and Knopp, Biophys.J.12,137a,1972) water and solute exchange across barriers between capillary, interstitium(ISF) and cell were modeled. Estimates of P, σ and the capillary filtration coefficient(L_p) are interdependent and cannot be obtained simply from initial rates and time constants of weight changes, but rather must account for factors whose neglect gives errors in parameter estimates:

Neglected Factor	Est./True Value Lp	σ	P
1.Time-dependent vol. of distribution(V_d) of test solute.	1	>1	>1
2.Transient ISF and cell V_d's and concentrations of electrolyte and protein.	<1	<1	<1
3.Cell permeability to water, but not solutes.	1	>1	<1

The effect of 1. dominates for small hydrophilic solutes. The model was used to analyze weight responses in Langendorff, modified-Ringer-perfused rabbit hearts subjected to step changes in perfusate osmolarity at 23-25°C (flows >1.3 ml/min-g with albumin, >5.6 with sucrose, permitting neglect of flow-limitation to exchange). Assuming surface area = 500cm^2/g, from albumin transients, for weight losses, L_p (cm/sec.cm.H_2O)x10^8= -8 7.6±3.4 (mean ± SD, N=5), and for gains,10.2±4.7 (N=4). Using L_p=8.8x10^{-8} with step increases in osmolarity, estimates of σ were: sucrose 0.055 - 0.062 (avg=0.058,N=3); raffinose 0.054-0.079 (avg=0.066,N=3); inulin 0.32 & 0.56. Permeabilities, Px10^5cm/sec, were: sucrose 1.8-2.6 (avg=2.3, N=3), raffinose 1.5 & 2.5, inulin 0.55 & 0.55. These values for σ and P, lower than ones obtainable by less complex analysis, are compatible with values from tracer studies. (Supported by NIH-HL9719)

MICROVASCULAR REACTIVITY TO NOREPINEPHRINE AND ISOPROTERENOL IN RAT SKELETAL MUSCLE. A. Wayne Greene*, Phillip M. Hutchins and Thomas D. Rains*. Departments of Physiology and Bio-Medical Engineering, Bowman Gray School of Medicine, Winston-Salem, N.C. 27103.

Studies were performed in an attempt to localize the alpha and beta adrenergic reactivities within skeletal muscle arterioles. Graded concentrations (10^{-8} - 10^{-4} gm/ml) of norepinephrine and isoproterenol, alpha and beta agonists, respectively, were injected retrograde via the ipsilateral femoral artery into the cremaster muscle of the rat. Changes in arteriolar diameters, as observed microscopically, were used as an indication of alpha and beta adrenergic reactivities. Dose-response curves (concentration agonist verses diameter-per cent of control) were constructed for four classifications of arterioles whose diameters ranged from 5 to 100 micra. Comparison of the curves indicates that both alpha and beta adrenergic reactivities seem to be increased in the vessel classes of smallest control diameters. This would indicate that both reactivities have the same distribution within the arteriolar microcirculation. These results would lend support to the hypothesis that alpha and beta receptors may operate through similar mechanisms. (This work supported in part by grants NC Heart 1972-73-A-13, Title IV of NDEA and HL 13936.)

ADRENAL CORTICAL ACTIVITY IN RESPONSE TO MYOCARDIAL INFARCTION AND CO INHALATION. Charlotte H. Greene and Domenic A. DeBias. Department of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pa. 19107

Adrenal cortical activity was monitored in the Cynomolgus monkey in response to myocardial infarction and exposure to carbon monoxide. Non-fatal myocardial infarction was experimentally induced by selectively depositing polystyrene spheres directly into the coronary artery through a catheter guided into the ostium under image intensifying flouroscopy. Infarction was confirmed by characteristic electrocardiographic changes, elevated leucocyte counts and pathological examination of the hearts at sacrifice. Immediately post infarction one group of infarcted monkeys and one group of non-infarcted monkeys were exposed to CO (100ppm) for 6 hours. Comparable control groups continued breathing ambient air during this period. Plasma corticosteroid levels were determined by competitive protein binding radiosterioassay before and after insertion of catheter, post infarction, and post CO exposure. Although there was a significant increase in measured corticosteroids in response to cut-down, this response was significantly lower than that which was obtained 30-40 min. post infarction. Maximal response was detected directly proceeding exposure in infarcted animals but the response did not appear to be influenced by CO inhalation. (Supported in part by Coordinating Research Council contract APRAC-CAPM-4-68 , and in part by PHS General Research Grant No. RR-5414)

ELECTROPHYSIOLOGIC EFFECTS OF APRINDINE: ANTIARRHYTHMIC MECHANISMS. Kalman Greenspan, Mitchell Steinberg*, Donald Holland*, and Alan R. Freeman, Depts. of Medicine and Psychiatry, Ind. Univ. Sch. of Medicine and Eli Lilly Co., Indianapolis, Indiana.

Studies on isolated Purkinje fibers from the canine heart superfused with 10^{-5} M Aprindine [N-phenyl-N(3-diethylamino propyl)-2-indanylamine HCl] was initiated utilizing intracellular electrodes in order to determine the effects of this agent upon action potential amplitude, duration, rate of rise of phase 0, membrane potential and impulse conduction. In normal non-automatic fibers, Aprindine depressed the rate of rise of phase 0 with a concomitant reduction in action potential amplitude, duration and frequently in membrane potential. With prolonged superfusion, conduction became altered with varying degrees of block, and exhibited the clinical counterpart of the Wenkebach structure. In fibers rendered automatic by stretch, hypoxia, digitalis or catecholamines, the slope of phase 4 depolarization was reduced and eventually abolished with Aprindine. The onset of automaticity, by the above interventions, was prevented by prior administration of Aprindine. The conduction depression (and block) occurring with this agent at times led to reexcitation. The latter, resulting from impulses arriving at cells which were non-homogenous in refractoriness and reduced in resting potential could also abolish a tachycardia. Thus, alterations in conduction and refractoriness, associated with abolition of automaticity are the antiarrhythmic mechanisms of Aprindine.

ANALYSIS OF NUTRITIONAL STRESS ON DEVELOPMENT OF RAT CEREBELLUM. W.S.T. Griffin*, D. J. Woodward, and R. Chanda*. University of Rochester, Rochester, N. Y.

We compared here the effect of nutritional stress (raising in large litters (LL) of 20 pups/dam versus small litters (SL) of 6 pups/dam) on production of cell number and constituents measured in terms of total cerebellar DNA, RNA, protein and fresh weight. SL animals had 2.43 ± 0.09 mg DNA/cerebellum (mean ± S.D.) at 21 days whereas LL animals had 1.89 ± 0.10 mg DNA/cerebellum. By comparing values on days 3, 4, 8, 11, 14, 17 and 21, we conclude: a) statistically significant differences appear by day 4, indicating little nutritional reserve at the time of birth and b) the difference in DNA accumulates throughout the 21-day period. Other tissue constituents roughly parallel alterations in DNA, indicating that most quantitative measures reflect differences in cell numbers. Histological measurements of mid-sagittal H&E stained sections of cerebellum from SL and LL litters show deficits in total and regional areas well correlated with biochemical measures. A test of whether a transient nutritional stress is followed by quantitative recovery was done by raising pups in LL days 0-8 and SL days 9-21. A persistent deficit to 2.01 ± 0.05 mg DNA/cerebellum indicated a lack of total recovery. A stress even as short as 4 days, from days 4 to 8, resulted in a permanent deficit to 2.19 ± 0.10 mg DNA/cerebellum. Other schedules of nutritional stress also support our conclusion that deficit in cell numbers and constituents can result from deprivation at any time in the post-natal phase of cell proliferation. (Supported in part by NIH Grant #NS09820.)

HYPOTHALAMIC AREAS ASSOCIATED WITH NEURAL CONTROL OF ACTH. William E. Grizzle*, Mary F. Dallman*, Lawrence P. Schramm*, and Donald S. Gann. The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205 and University of California San Francisco, San Francisco, California 90033.

We have identified the medial aspect of the dorsal hypothalamus as a region where single units are found which are sensitive to stretch of the right atrial-venal caval junction, to carotid constriction and to hemorrhage (Fed. Proc. 32:295 abs, 1973). Electrical stimulation (20 sec at 200 and 400 μA) of the caudal part of this region was reported to cause significant ($P<0.05$) inhibition of peripheral plasma ACTH (radioimmunoassay) 1.5 minutes after stimulation. Further experiments confirmed that 20 second stimulations of the medial dorsal posterior hypothalamus at 200 μA caused significant ($P<0.01$) inhibition in peripheral ACTH plasma levels 1.5 minutes following stimulation. In contrast, identical stimulation of the more rostral part of the receptive area resulted in significant ($P<0.01$) increases in peripheral ACTH plasma levels. When the two groups of responses were compared, they were significantly different ($P<0.001$). These results suggest that this medio-dorsal hypothalamic area, which is sensitive to hemodynamic changes, may include anatomically distinct components which mediate respectively facilitation and inhibition of the release of ACTH. (Supported in part by NIH grants AM14952 and NS09528)

PERMEABILITY OF THE HUMAN ERYTHROCYTE TO AMMONIUM CITRATE. Maureen E. Groër*and Akira Omachi. University of Illinois at the Medical Center, Chicago, Illinois 60680.

Entry of citrate ions into human red blood cells was studied by suspending cells in isotonic solutions of ammonium citrate. NH_3 penetrates the membrane and NH_4^+ reforms intracellularly. If citrate ions can follow NH_4^+ entrance in this manner, water will also enter the cell and cause swelling which can be followed photometrically. There is clearly entry of NH_4^+ citrate at pH 6.0 and 37°C. A slower rate of penetration was discernible at pH 6.8 and 7.2. There was no apparent permeation at a temperature of 23°C. These changes were osmotic in nature as ascertained by osmotic reversal of the swelling by hypertonic sodium citrate. Citrate entry was elevated in a hypotonic (200 mOsm) solution of NH_4^+ citrate. As blood is generally stored in citrate-containing media, the effect of storage on citrate permeability was investigated. There was no systematic change in the rate of swelling of human erythrocytes suspended in isotonic NH_4^+ citrate after different periods of storage.
(Supported by USPHS Grant 13567.)

Further evidence for a specific O_2 carrier in the placenta. G. Gurtner and B. Burns*. The Johns Hopkins University. Baltimore, Maryland

In previously reported experiments we observed that compounds which bind to cytochrome P-450 decrease O_2 flux across the sheep placenta while not affecting argon flux. (Nature 240:473-475, 1972). This is strong evidence that cytochrome P-450 acts as an O_2 carrier. There is also physiologic evidence that the O_2 diffusing capacity of the placenta is greater than inert gas diffusing capacity. In additional experiments, we perfused the fetal side of the placenta with fluids exhibiting different solubility properties for O_2 and argon. The perfusion media were dextran, blood and an emulsion containing 33% of the fluorocarbon FC-80, in which O_2 and argon are almost equally soluble. PO_2 and Pargon as well as O_2 content were measured in arterial and venous vessels on both maternal and fetal sides of the placenta. The flux of both gases increased as the solubility for the gases increased in the perfusion media. In all experiments there were large partial pressure differences for argon between maternal and fetal veins (Δ P argon). Δ P argon increased as the solubility for argon increased in the perfusion medium. The flux of argon divided by ΔP argon is an index of the diffusing capacity of the placenta and did not vary with differences in solubility. These results indicate that argon does not reach equilibrium between maternal and fetal capillaries. Similar measurements of O_2 transfer indicate that O_2 diffusing capacity of the placenta is from 15-70 times that of argon, a gas with similar physical properties. This is consistent with a specific O_2 carrier in the placenta.

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CARDIAC BRADYDYSRHYTHMIAS IN RESPONSE TO SMALL VAGAL NERVE STIMULATIONS. Gilbert R. Hageman*, Walter C. Randall, and J. Andrew Armour. Dept. of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Alterations in cardiac pacemaker location and conduction were induced in adult anesthetized mongrel dogs by electrical stimulation of the thoracic vagi and their small branches. Electrical activity from contiguous bipolar silver electrodes was amplified and recorded on photographic paper using an optical oscillograph. The electrodes were over the SA node, anterior (AIN), middle (MIN), and posterior (PIN) internodal pathways, the left atrium, and ventricular epicardium. A Hoffman type plaque electrode was sutured over the distal AV node to record a His electrogram. A lead II ECG was also recorded. Electrical stimulation of an individual branch of the left recurrent cardiac nerve sometimes induced selective bradycardia with no effect on A-H interval. The bradycardia was attenuated by cervical vagotomy indicating reflex as well as direct innervation. Stimulation of small left vagal branches caudal to the recurrent nerve often induced reflex bradycardia and increased A-H interval. Stimulation of the right recurrent cardiac nerve induced atrial bradycardia with heart block above the His bundle without ventricular escape. Stimulation of intermediate level right side parasympathetic branches often induced increased heart rate with increased AH interval, indicating sympathetic components in these branches. Stimulation of individual right vagal branches near the heart induced bradycardia, shifts in atrial pacemaker location or a His pacemaker. The establishment of the His rhythm indicated selective inhibition of supraventricular pacemakers but not of the His bundle. These reflex effects were abolished by vagotomy. When right thoracic vagal stimulation induced atrial fibrillation, the SA node often continued to depolarize at a rapid rate. (Supported by NIH Grants HL 08682 and GM 999.)

RESTORATION OF RESPONSIVENESS TO ELECTRICAL STIMULATION IN PAPILLARY MUSCLES FROM HUMAN QUIESCENT HEART. Anwar A. Hakim. University of Illinois Medical Center, Chicago. Ill. 60680.

Responsiveness to electrical stimulation in papillary muscles from quiescent heart was restored with metanephrine. Right ventricular papillary muscles from these hearts were excised and placed in oxygenated Krebs-Ringer bicarbonate solution. The muscles were devided longitudinally to strips of 0.85-1.0mm in diameter and suspended between two electrodes into a 50 ml chamber. They were stimulated at a rate of 12/min. by square wave pulses with stimuli discharged through the solution. The stimulus was of 5-30msec duration and 15-30% above threshold voltage. Electrical stimulation alone did not generate contractions. Aliquots of 0.05-0.20ml of 10^{-6}M metaphrine solution was added, and electricalstimulation continued until contractions were generated at a steady state. The muscles were flushed with the Krebs solution. The length-active tension curve was then determined for each muscle. Force-velocity curves were constructed from the maximum velocity of shortening in each contraction and the total force (preload and afterload). The Vmax increased significantly with increasing muscle length and was 1/40 that of papillary muscle from beating rat heart at comparable frequencies. Resting and developed tension at the top of the length-tension curves was similar, but time to peak tension was 10 times shorter in the rat while peak rate of tension develpment was correspondingly higher. These differences suggested basic differences in the control of calcium movements and in the contractile process.

SELECTIVE INHIBITION USING AN ATP ANALOG OF VARIOUS HUMAN RED CELL GHOST CATION-STIMULATED ATPases. B. Haley*, R. Yount* and J.F. Hoffman. Dept. of Physiol. Yale Univ. Sch. Med., New Haven, Conn. and Dept. of Chem., Wash. State Univ., Pullman, Wash.

The interactions of several ATP analogs with ATPases and ATP regulated enzymes have given valuable information as to the role of ATP in the control and regulation of physiological phenomenon. Consequently, an ATP analog, 6-thioinosyl-imidodiphosphate, has been used to inhibit human erythrocyte membrane ATPase activities stimulated by Mg and/or Ca and by the combination Mg +Na +K. The inhibitor is covalently bound to the membrane through a disulfide bond. Inhibition can be reversed slowly with dithiotreitol. The conditions under which the inhibitor reacts with the membrane controls the selectivity of inhibition. The effects of temperature, pH, nucleotides, and various metal ions on the inhibition of the ATPases have been evaluated. It is possible to inhibit completely the Ca and Mg stimulated ATPase activities with very little or no effect on the ouabain-sensitive ATPase activity. The selectivity is found to be temperature and pH dependent with selective inhibition being lost at higher temperatures and increased pH values above 7.5. It has not been possible to inhibit the Mg stimulated activity without also inhibiting the Ca stimulated activity. High concentrations (>1mM) of ATP protect against inhibition when added before the inhibitor. However, at low ATP concentrations (<1mM) the effects are much more complicated and increased rates of inhibition are found under certain conditions.

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NEURALLY AND HUMORALLY MEDIATED VASCULAR RESPONSES TO HEMORRHAGE. J. Hall*, B. Lalone*, J. Schwinghamer* and T. Adams, Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

The contributions of sympathetic nerves and circulating hormones to large and small vessel constriction in skin (S) and muscle (M) during hemorrhage were examined in naturally perfused, innervated (N=15) or denervated (N=17) forelegs of 32 anesthetized dogs. Mean systemic arterial blood pressure (Pa) was reduced by bleeding from a carotid artery into a pressurized reservoir. Total and segmental vascular resistances (R) in S and M were calculated from pressure-flow determinations made during the prehemorrhage control period and at Pa's of 100, 75, 50 and 35 mmHg. In all experiments bleeding to Pa's of 100 mmHg and below elicited progressive increases in total S and M vascular R. In the experiments with innervated forelimbs, R ($mmHg/ml \cdot min^{-1}$; $\bar{x} \pm SE$) in the large artery segment supplying S was 0.40±0.02 during the prehemorrhage control period. When the animals were bled to Pa's of 100, 75, 50 and 35 mmHg, R in the innervated S arteries increased to 0.70±0.07, 1.07±0.13, 2.43±0.35 and 2.98±0.44 respectively. In experiments with denervated forelimbs, average R in S arteries was 0.39±0.02 during the prehemorrhage control period. Bleeding to the Pa's described above caused R in the denervated S arteries to increase to 0.47±0.03, 0.56±0.06, 1.04±0.08 and 1.83±0.19 $mmHg/ml \cdot min^{-1}$. Denervation did not significantly reduce the magnitude of the hemorrhage induced constriction in any M vascular segment or in S small vessels and veins. These observations suggest that circulating vasoconstrictor agents are the primary mediators of hemorrhage induced constriction in all forelimb vascular segments except the large arteries supplying S, which appear to be controlled by both neural and humoral inputs.

CARDIAC HYPERTROPHY: ISOTONIC QUICK RELEASE FORCE-VELOCITY AND STRESS-STRAIN RELATIONSHIPS OF PAPILLARY MUSCLES. Burt B. Hamrell* and Norman R.Alpert, University of Vermont College of Medicine, Burlington, Vermont

Isotonic quick-release shortening was used to obtain force-velocity and stress-strain data at selected early instants in the isometric twitch of right ventricular papillary muscles from non-failed hypertrophied (H) and normal (N) hearts. H was produced by pulmonary artery banding in rabbits. H and N preparations were studied at 24°C at external lengths 96% to 100% L_o. Isometric data at L_o:

	Tension gm/mm^2		TPT* msec	T1/2R+ msec
	Active	Passive		
N	4.72	0.92	376	855
H	4.56	0.98	557	1053

*Time to peak tension. +Time to 1/2 relaxation.

At L_o and at that time in the twitch where peak dp/dt occurred the velocity of muscle shortening with 0.4 gm/mm^2 total load was depressed in H (0.55 L_o/sec) as compared to N (1.20 L_o/sec). Series elastic moduli at a number of levels of stress were identical in N and H. Parallel elastic moduli (obtained with quick-stretches between twitches) versus stress manifested a steeper slope: slope N/slope H= 1/3. The effect of length on the force-velocity relationship early in the twitch was the same in N and H; V_{max} was constant. In hypertrophy active tension development is maintained at normal levels by prolongation of depressed contractile element activity during a twitch. The relationship of V_{max} to length is unchanged. Passive chord compliance is decreased.

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THE MORPHOLOGY OF TERMINAL AIRWAYS IN THE HUMAN LUNG. James E. Hansen, Edgar P. Ampaya*, Gordon H. Bryant*, and James J. Navin*. Tripler Army Med. Center, Honolulu, Hi.

Accurate knowledge of the three-dimensional morphology of the terminal airways is essential in understanding gas and particulate movement in the lung. We prepared eighty 20-micron thick serial sections of inflated, formalin fixed lung. These we serially projected at a magnification of 320 onto 6.4 mm sheets of polyurethane foam. After cutting and removal of areas equivalent to the lumen of airways and alveoli, the resultant sheets were glued and reassembled into 24 blocks, each equivalent to approximately 1 mm^3 of lung. The largest airway in the model, generation 1 (G1), is a terminal bronchiole which has two rudimentary alveoli (AL) and bifurcates into respiratory bronchioles (RB). Generations 2, 3, and 4 (G2-4) include RB formed by consecutive bifurcations, alveolar sacs (AS) and AL, but not alveolar ducts (AD). The amount of bronchial epithelium decreases to less than one percent by G5, which includes 9 first order AD. The RB are cylindrical with length twice their diameter but AD are more spherical. The AD of successive generations gradually decrease in size and number of exits. Mean number of exits for G5 AD are 2.4 AD, 4.0 AS and 8.2 AL; for G8 AD are 1.5 AD, 2.5 AS and 3.8 AL; and for G11 AD are 0.4 AD, 3.4 AS and 2.3 AL. AS of all generations terminate in 2-8 AL. Although many terminal branches are not included in the model, AL are found from G2-14. It is calculated that G9-13 include over 85% of all the AL. Contrasted to conventional methods, examination of the lung using this positive model discloses a greater complexity of airway branching, a larger number but shorter length of individual airways, and fewer AL per AS. This suggests an even more efficient gas transport system than previously recognized.

SEIZURES IN THE OFFSPRING OF RATS EXPOSED TO SEVERE STRESS DURING THE LATE STAGES OF A PRIOR PREGNANCY. Carolyn M. Hardin. Meharry Medical College, Nashville, Tennessee.

Female Sprague Dawley rats, 15-20 days pregnant, were accidently exposed to high temperature for about 2 hours during the course of shipment from the supplier. 18 of 30 pregnant rats died. 7 of the remaining 12 rats delivered viable litters. All 12 rats produced apparently healthy litters when subsequently remated. Male offspring from either the second or third litters were injected with 1 mg/kg d-amphetamine-SO_4 (6 injections over a 2 week period) or saline at age 1-3 months. 67% (10 of 15) of the amphetamine-treated rats and 50% (7 of 14) of the saline-injected rats had 1 or more seizures during the subsequent 5 months. Animals were removed from their cages and observed for seizures at approximately weekly intervals. The stress of the novel environment appeared to precipitate the seizures although minor seizures involving myoclonic jerks of the face muscles were occasionally observed when the animals were in their cages. Seizures began in amphetamine-injected rats at age 149 $\pm$ 6 days and in saline controls at 186 $\pm$ 17 days ($p<0.05$). 18 tonic spasms (1.3 $\pm$ 0.3 per rat) were observed in amphetamine-treated rats as compared with 5 (0.4 $\pm$ 0.2 per rat) in saline controls ($p<0.01$). Generalized tonic-clonic convulsions began at age 198 $\pm$ 16 days in amphetamine-treated rats and at age 211 $\pm$ 14 days in saline-injected controls. 15 seizures of the grand mal type were observed in amphetamine-injected rats (1.1 $\pm$ 0.3 per rat) as compared with 10 for the saline controls (0.8 $\pm$ 0.4 per rat). The 2 groups did not differ in terms of frequency of occurence or age of onset of generalized tonic-clonic convulsions. Supported by GM17806-03.

COMPOSITION OF GLOMERULAR FILTRATE IN THE MUNICH-WISTAR RAT. Carol A. Harris*, P.G. Baer*, E. Chirito* and J.H. Dirks. Renal and Electrolyte Division, Department of Medicine, McGill University, Montreal, Canada.

The composition of mammalian glomerular filtrate is not precisely known due to the inaccessibility of glomeruli to micropuncture in most species. Surface glomeruli are readily apparent in female Munich-Wistar (MW) rats. Samples of glomerular filtrate (GF) from a total of 38 glomeruli were collected by micropuncture and analyzed for inulin, sodium, chloride, calcium and phosphorus in 19 female MW rats. Sodium and calcium were analyzed by helium glow photometry, chloride by electrometric titration, phosphate by a microadaptation of the Chen method, and inulin by fluorometry. GF values were related to corresponding plasma water (P) values. Tubule fluid (TF) was collected from 40 random or late proximal tubules for comparison with GF. GF/P inulin was 1.01 $\pm$ 0.02 (mean $\pm$ S.E.) and was unchanged over a wide range of plasma inulin concentrations. Mean GF/P Na was 0.96 $\pm$ 0.02 and TF/GF Na was 0.99 $\pm$ 0.01. Mean GF/P chloride averaged 1.00 $\pm$ 0.01. Mean GF/P Ca was 0.62 $\pm$ 0.07, and TF/GF Ca was 1.03 $\pm$ 0.05. Mean GF/P phosphorus was 0.96 $\pm$ 0.05 and TF/GF phosphorus was 0.92 $\pm$ 0.05. End proximal fractional phosphate delivery averaged 51 $\pm$ 6% compared to a fractional excretion of 26 $\pm$ 3%. The late proximal TF/P inulin averaged 2.04 $\pm$ 0.10. These data indicate 1) inulin, Na and Cl are fully ultrafilterable at the glomerular membrane. 2) approximately 62% of total plasma Ca is ultrafilterable. 3) phosphorus is fully ultrafilterable in female MW rats, is reabsorbed proportionately to fluid reabsorption in the proximal tubule and continues to be reabsorbed more distally.

PRESENCE OF AN ANGIOTENSINOGEN STIMULATING FACTOR AFTER NEPHRECTOMY. H. Hasegawa* and G.M.C. Masson. Research Division, Cleveland Clinic Foundation, Cleveland, Ohio 44106.

These experiments were based on the assumption that the increase in angiotensinogen formation after nephrectomy is due to the presence of a stimulating factor in plasma and that contact of normal liver slices with such a plasma may be sufficient to elicit a detectable and persistent increase in rates of angiotensinogen formation (RAF). The procedure consisted of 2 steps: first, preincubation of liver slices with the test material and secondly, after washing, incubation of the same slices in an angiotensinogen-free medium (Robinson solution) to measure formation of angiotensinogen. Plasma and liver slices from normal, 5 hr-and 15 hr-nephrectomized rats were used. Without preincubation, RAF in normal liver slices incubated with Robinson solution averaged 9.3 ± 0.9 ng/g/hr. This value increased to 20.1 ± 1.7 and 39.5 ± 5.8 ng/g/hr respectively with slices from 5 hr-and 15 hr-nephrectomized rats. These rates were not altered by preincubation with Robinson solution or with normal plasma. They were increased however by preincubation with nephrectomized plasma. Preincubation of normal liver slices with plasma from 5 hr-and 15 hr-nephrectomized rats gave the respective RAF values of 21 ± 2.7 and 41.9 ± 4.6 ng/g/hr; with slices from 5 hr-nephrectomized rats the corresponding values were 35.5 ± 2.8 and 49.1 ± 3.9. Maximum stimulation to about 80 ng/g/hr was obtained when slices from 15 hr-nephrectomized rats were preincubated with plasma from 5 hr-or 15 hr-nephrectomized rats. It is suggested that after nephrectomy, there is accumulation of an angiotensinogen stimulating factor of extra-renal origin which is normally inactivated or destroyed by the kidney. (Supported in part by NIH Grant HL-6835).

EFFECT OF COMPLETE HYPOTHALAMIC DEAFFERENTATION ON THE SECRETION OF TSH IN RATS. E. Hefco* and L. Krulich. Department of Physiology, Univ. of Texas Southwestern Medical School, Dallas, Texas 75235.

Using the technique of Halasz, completely isolated hypothalamic islands were made in normal adult male rats. The islands were cylindrical, 3 mm in diameter and 2 mm high, with their anterior border approximately 1 mm behind optic chiasma and contained all the major structures of the middle hypothalamus and a large part of the posterior hypothalamus. Sham operated animals were used as controls. The following results were obtained: (1) Resting levels of plasma TSH, measured by radioimmunoassay, were decreased as early as 4 days after deafferentation and remained at the same low level as long as three months. (2) Thyroid blockade induced by 2-mercapto-methylimidazol (MMI) (5 mg priming dose i.p. followed by 0.05% in drinking water for 7 days) caused an increase of plasma TSH levels, but the rise was considerably smaller in operated animals than in controls. A single large dose of T_3 (10 µg/100g b.w.) given after 7 days of MMI treatment caused a rapid and equal decrease of TSH levels in operated and control animals. (3) The rise of plasma TSH levels during cold exposure was abolished by deafferentation if the exposure to cold took place 4 days after operation, but was partly restored one month after deafferentation. On the basis of these results, it may be concluded that (1) the isolated hypothalamic island is able to produce TRF in resting condition and possibly enhance the TRF secretion during hypothyroid state, but in both situations, at considerably reduced rates in comparison to controls. The inhibition of TSH secretion by large doses of T_3 is not affected by deafferentation. (2) The reappearance of the response to cold one month after deafferentation is difficult to explain, but it suggests that some kind of restorative process takes place if enough time is allowed after operation. (Supported by NIH grants.)

EFFECTS OF VASODILATOR DRUGS ON CAROTID CHEMORECEPTORS.
Donald D. Heistad, Francois M. Abboud, Allyn L. Mark, and Phillip G. Schmid. Cardiovascular Division, Department of Internal Medicine, University of Iowa College of Medicine and V.A. Hospital, Iowa City, Iowa 52242.

This study was done to test the hypothesis that the vasodilator drugs, nitroglycerin and bradykinin, might depress ventilation, perhaps by increasing blood flow to chemoreceptor sensors. Drugs were injected in anesthetized dogs into the carotid artery, close to the carotid chemoreceptor. Intracarotid injections of nitroglycerin produced a small decrease in ventilation in 6 of 25 dogs breathing room air and in 2 of 9 dogs during hypoxia. This depression of ventilation was abolished by denervation of the carotid body. Intracarotid injection of bradykinin, 1 to 10 μg, caused apnea, bradycardia, and hypotension. These effects were blocked by simultaneous infusion of carboxypeptidase. The response to intracarotid bradykinin was not altered detectably by denervation of the carotid chemoreceptor or by sectioning the nodose ganglion. Systemic injections of the same doses of bradykinin had no effect. Apnea, bradycardia, and hypotension were observed, however, after injection of bradykinin into the vertebral or internal carotid arteries. We conclude that 1) intracarotid injections of nitroglycerin may cause a small decrease in ventilation which is mediated through carotid chemoreceptors and 2) intracarotid or intravertebral injections of bradykinin cause apnea, bradycardia, and hypotension, which may be initiated in the central nervous system.

REGULATION OF BODY TEMPERATURE IN EUTHERMIC AND HIBERNATING GROUND SQUIRRELS. H.C. Heller (intr. by H.T. Hammel). Dept. of Biological Sciences, Stanford University, Stanford, California 94305.

The characteristics of the CNS regulator of body temperature were determined for two species of hibernators (Citellus Lateralis and C. beldingi) during hibernation and euthermia. Water perfused thermodes were used to heat and cool the pre-optic tissue while metabolic rate was simultaneously measured as oxygen consumption. The euthermic proportionality constants (α) for metabolic heat production in response to POH temperatures below threshold were approximately -.09 cal/g min°C for lateralis and -.05 cal/g min°C for beldingi. These extremely high α values mean that the T_b regulators of these two species of small mammals have the same open loop gain as the regulator of the dog, i.e. between 12 and 14. Changes in ambient temperature shift the threshold temperatures of the regulator and do not change its temperature sensitivity. Animals in deep hibernation respond in two ways to POH cooling. They may show an arousal response during which the threshold temperatures of the regulator rapidly rise or they may show proportional heat production with thresholds remaining constant. α values for torpid animals (T_b between 2° and 8°C) averaged about 15 times lower than α values for euthermic animals. High α values in the euthermic animals may be related to their small body size and reflect greater dependence on core rather than peripheral temperature reception for regulation. High α values may also be a consequence of the need to regulate T_b while in hibernation.

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NET SODIUM FLUX IS LESS THAN THE SHORT-CIRCUIT CURRENT IN FROG SKIN: EFFECTS OF MEDIA AND ALDOSTERONE. S.I. Helman and B.M. Koeppen.* University of Illinois, Urbana, Ill.

Net sodium flux (I_{Na}) was determined isotopically in non-edge damaged frog skins (Rana pipiens) continually short-circuited. Skins from non-treated and aldosterone-treated frogs (.05 mg injected subcutaneously 24 hours before study) were bathed in either Cl or SO_4 Ringer. In all four groups, I_{Na} was less than I_{sc}. These data are consistent with the existence of the active transport of a non-Cl ion other than Na.

	I_{sc} ($\mu A/cm^2$)		$I_?$ (% of I_{sc})		E_1 (mv)		E_2 (mv)	
	Cl	SO_4	Cl	SO_4	Cl	SO_4	Cl	SO_4
Control	22.0 ±3.3	39.1 ±4.6	11.8 ±3.7	20.0 ±3.0	91.8 ±4.6	171.4 ±14.9	9.9 ±2.2	64.6 ±10.5
+Aldo.	33.0 ±3.1	57.4 ±4.6	8.4 ±3.2	7.1 ±0.9	106.8 ±4.3	162.5 ±6.1	18.1 ±4.7	87.0 ±10.5

(Mean ± S.E., N ≥ 6.)

The current-voltage relationship (Science 173:146, 1971) revealed that voltages E_1 and E_2 were elevated in SO_4 Ringer as was the I_{sc}. Moreover, the increase in I_{sc} with aldosterone occurred with little or no change in voltages E_1 and E_2. If E_1 and E_2 represent the emf's of the ion pumps, the increase in I_{sc} with aldosterone occurred by virtue of a decrease in resistance to sodium flux, whereas the increase in I_{sc} with SO_4 Ringer occurred by virtue of an increase in pump emf's.
(Supported by USPHS Grant AM 16663)

THE FORCE-VELOCITY CHARACTERISTICS AND SERIES ELASTIC COMPONENT (SEC) OF VASCULAR SMOOTH MUSCLE. J. T. Herlihy* and R. A. Murphy. Dept. of Physiology, Univ. of Va. Sch. of Med., Charlottesville, Virginia.

Vascular strips were teased from the media of hog carotid arteries and the length at which maximal tension was developed (l_o) was determined using transverse electric field stimulation (60 Hz, 20 V/cm). The force-velocity characteristics were determined by the method of quick-release to a known afterload. Strips contracted isometrically for 10 sec before quick-release and isotonic shortening. Shortening after release showed two phases: a fast undamped component due to the SEC and a slower component due to shortening of the contractile component (CC). Shortening velocities of the CC decreased during the response. This was presumably due to the transformation of the preload (10% of P_o at l_o) to an afterload during shortening. The relationship between the initial shortening velocity of the CC and the afterload was hyperbolic and could be fitted by the Hill equation. A linearized plot of the data for 6 strips yielded the following force-velocity constants (± SEM): V_{max} = 0.126 ± 0.007 l_o/sec; b/l_o = 0.021 ± 0.002 sec^{-1}; P_o = 1.88 ± 0.34 kg-wt/cm^2; and a/P_o = 0.17 ± 0.02. In addition, the stress-strain curve for the SEC was determined from quick-release measurements obtained during stimulation by potassium depolarization. The curve depicting the SEC (as % l_o) as a function of developed force increased monotonically and was most compliant at loads under 0.3 P_o. At P_o (= 2.2 kg-wt/cm^2) the SEC was 6 - 8% l_o, a value lower than reported in other studies of smooth muscle strips *in vitro*.
(Supported by NIH grant HL 14547)

The Response of Thoracic Sympathetic Afferent Nerves to Changes in Ventricular Dynamics. G.L. Hess, J.P. Kampine, R.L. Coon, and E.J. Zuperku. (Intr. by H. Klitgaard) Medical College of Wis. Milwaukee, Wis.

The sympathetic nervous system has been shown to carry afferents from receptors in the left ventricle back to the spinal cord. The purpose of this research was to study the effect of changes in preload, afterload, and the inotropic state on sympathetic afferent discharge in an isolated ejecting left ventricle. Dogs were placed on total heart-lung bypass to maintain arterial circulation and prevent the activation of peripheral reflexes. A left heart preparation was used in which the preload of the ventricle could be controlled by adjusting the height of a reservoir which fed the left atrium. A large bore cannula equipped with an artificial valve was inserted into the ventricular apex, and a variable resistor distal to the valve was used to alter afterload. The coronary circulation was maintained by a separate perfusion pump and the peak pressure adjusted to prevent ventricular ejection through the aortic valve. Afferent nerve activity was measured at the third thoracic white ramus and stored on tape along with the hemodynamic data. A window discriminator and spike frequency analyzer were used to analyze nerve discharge according to maximum, total, and average activity. Preloading, afterloading, and independent changes in the inotropic state of the ventricle produced by epinephrine infusion all resulted in increased sympathetic afferent discharge. The relative contributions of peak pressure, myocardial contractility as measured by dP/dt, and stroke work were correlated with afferent activity at different levels of preload and afterload. Maximum discharge coincided with the upstroke of the left ventricular pressure curve. Stroke volume was not a contributing factor in afferent stimulation since maneuvers which elevated left ventricular pressure, accompanied by either an increased or decrease in stroke volume, resulted in an enhancement of afferent activity.

CHOLINERGIC RESPONSE OF THE LOWER ESOPHAGEAL SPHINCTER FOLLOWING ANTRECTOMY AND/OR VAGOTOMY. R. H. Higgs* and D. O. Castell* (intr. by F. P. Brooks). U.S. Naval Hospital, Philadelphia, Pa.

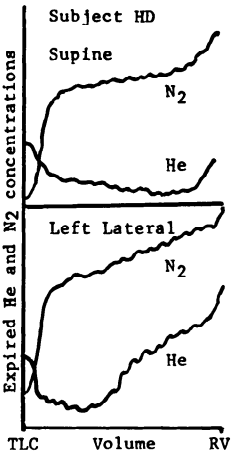
Cholinergic innervation and endogenous gastrin have been shown to be important in maintenance of lower esophageal sphincter (LES) pressure. Therefore, the effect of a cholinergic agent on the LES in patients with antrectomy and/or vagotomy should be of interest. Using an infused open-tip system we have monitored resting LES pressure and the response to four doses of bethanechol (0.01, 0.02, 0.04, and 0.08 mg/kg, subcutaneously) in controls (C), patients with vagotomy and pyloroplasty (V & P), patients with vagotomy and antrectomy (V & A), and patients with antrectomy alone (A). There was no significant difference in mean resting LES pressure for all groups (C: 15.9 $\pm$ 1.5 mm Hg, SEM; V & P: 11.8 $\pm$ 2.2 mm Hg; V & A: 15.8 $\pm$ 1.7 mm Hg; A: 15.4 $\pm$ 4.1 mm Hg). All patients showed a significant ($p < 0.01$) change in LES pressure after bethanechol injection. Controls and V & A patients showed similar dose response curves (maximal pressure increase = 28.8 $\pm$ 1.0 mm Hg for controls and 34.5 $\pm$ 3.4 mm Hg for V & A). Mean pressure increases for V & P patients were significantly ($p < 0.01$) greater than controls at the three higher doses, with a maximal increase of 40.8 $\pm$ 2.4 mm Hg. For A patients mean pressure changes were significantly ($p < .01$) less than those for V & A patients at all four doses. The maximal increase for A patients was only 9.0 $\pm$ 1.0 mm Hg. Conclusions: 1) Patients with antrectomy and/or vagotomy show definite response of LES to cholinergic stimulation. 2) Vagotomy alone produces supersensitivity of the LES. 3) Antrectomy alone results in an attenuated response to cholinergic stimulation.

CIRCADIAN RHYTHM IN PLASMA CORTICOSTERONE LEVELS AND HEPATIC REDUCTASE ACTIVITY IN RATS. L. G. Hiles*, D. M. Lanuza*, U. Boonayathap*, and S. F. Marotta. Departments of General Nursing and Physiology, University of Illinois at the Medical Center, Chicago, Illinois 60680.

The circadian rhythm in plasma corticosterone (Cpd. B) is commonly attributed to a similar rhythm existing in the hypothalamo-hypophyseal-adrenocortical system; however, since the plasma level of this steroid is considered to be a balance among secretion, metabolism and excretion, it is possible that the circadian rhythm in plasma Cpd. B may be influenced by factors other than the secretory activity of the adrenal cortex. Thus, to ascertain whether the liver, the major site of Cpd. B catabolism, also exhibits a circadian rhythm, hepatic Δ^4-reductase activity and plasma Cpd. B levels were determined in male albino rats (approximately 225 gms.). The animals (8/group) were maintained on a 12L:12D cycle for 10 days and then sacrificed by decapitation at 4 hr intervals commencing at 0400 hr over a 24 hr period. The plasma Cpd. B levels were analyzed fluorometrically while portions of the liver were homogenized and incubated with Cpd. B and the necessary cofactors in order to determine Δ^4-reductase activity (Glenn et al., 1957). Protein content was also ascertained on these hepatic homogenates (Lowry et al., 1951). The results showed that liver protein (mg P/100 mg wet liver) was higher during the evening while the hepatic Δ^4-reductase activity (µg Cpd. B metabolized/100 mg P/hr) was significantly lower in the evening than in the morning. In general, this hepatic reductase activity showed an inverse relationship with plasma Cpd. B levels. These data suggest that the circadian rhythm in hepatic reductase activity may influence the circadian rhythm observed in plasma Cpd. B levels. (Supported in part by the Office of Naval Research Contract NR 101-580.)

"CLOSING VOLUME" IN THE LATERAL POSITION. Hillary Don, Malcolm Green, (intr. by Jere Mead). Dept. of Anaesthesia, Peter Bent Brigham Hospital, and Harvard School of Public Health, Boston, Mass.

In 4 normal volunteers aged between 31 and 41 years, "closing volume" was measured using simultaneously the helium bolus and nitrogen techniques first in the sitting and supine positions. "Closing volumes" were similar in the two postures and consistent with published data for this age group. However, when the subjects were studied in either the right or left lateral positions, the shape of the alveolar plateau was strikingly different (figure). An abrupt rise in expired helium concentration occurred at 60.6 (S.D. 6.0)% VC in the left, and 60.8 (S.D. 5.5)% VC in the right, lateral positions. This rise might represent the heart and mediastinum reaching a mechanical limit, and slowing the emptying of the dependant lung. At very low lung volumes a second rise in concentration was seen in some subjects, reflecting perhaps delayed closure. The nitrogen concentration during the alveolar plateau also tended to show an inflection at about 60% VC, but was not present in all subjects.



EVALUATION OF THE ROLE OF A CIRCULATING MYOCARDIAL DEPRESSANT FACTOR IN SHOCK. L. B. Hinshaw, L. T. Archer*, M. R. Black*, P. P. Brown*, and L. J. Greenfield. V.A. Hospital and University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma.

The purpose of the present study was to investigate the role of a myocardial depressant factor (MDF) in shock. Experiments were carried out on 29 dogs subjected to either splanchnic arterial occlusion (SAO) shock or endotoxin shock. An isolated working heart was subjected to blood released during SAO shock or endotoxin shock in pancreatectomized animals. Changes in LVEDP, dP/dt, coronary hemodynamics and myocardial oxidative metabolism were monitored in all heart preparations. The first series of experiments tested the hypothesis that MDF is released in SAO shock. Results demonstrated normal myocardial performance at afterloads of 100-150 mm Hg during early and late phases of SAO shock. The second series of experiments examined the hypothesis that MDF is released primarily from the pancreas in shock and depresses the myocardium. Hearts failed after 4-5 hrs in animals acutely pancreatectomized and administered endotoxin, while pancreatectomized controls exhibited normal performance. Pancreatectomy did not lessen the degree of heart failure in endotoxin shock. The third series of experiments evaluated the hypothesis that MDF exerts a depressant action on the heart only subsequent to a sustained period of deficient myocardial perfusion. Two to 3 hrs of pre-existing myocardial hypoperfusion (afterload 30-50 mm Hg) in the SAO shock model provided no evidence for the presence of MDF, even when myocardial dysfunction was elicited by diminished pressure prior to the precipitation of SAO shock. In conclusion, the above findings fail to reveal any instance of myocardial dysfunction due to an MDF action and suggest that the MDF hypothesis is inadequate to explain the pathogenesis of SAO or endotoxin shock.

ISOLATION OF COUNTERPULSATION SUCTION PHASE FOR STUDY OF ITS OPTIMIZATION. S. Hirose, S. Meerbaum, T. W. Lang and E. Corday (intr. by J. V. Tyberg). Cedars-Sinai Medical Center, Los Angeles, California.

An experimental system was developed for isolation of the suction phase (sink) in order to (1) separate its effects from those of the diastolic augmentation phase and (2) to evaluate the influence of timing and characterization of sink on counterpulsation effectiveness. A counterpulsation cannula and a modified pulse pressure generator, with two one-way valves, were used in conjunction with a SIMAS control programmer to provide isolated suction from the ascending aorta. The withdrawn blood was returned to the femoral artery. The descending aorta was transsected and a one-way valve was inserted to minimize retrograde diastolic aortic pressure augmentation. Satisfactory stable sink isolation was achieved in 17 normotensive open-chest dogs. Diastolic augmentation was minimal. The sink was controlled to start either 50 msec before end-diastole (E) or within the isovolumetric period (L). Aortic end-diastolic pressure was reduced 40% in E and 7% in L (control 58 mm Hg). Peak systolic pressure (PSP) dropped 20% in E and 13% in L (control 100 mm Hg). Cardiac output (CO) was lowered 2% in E but increased 7.5% in L (control 1210 ml/min). Myocardial oxygen consumption (MVO_2) was reduced by 21% in E and by 8.5% in L (control 7.2 ml/min).

It is concluded that the L timing of sink is advantageous because it results in increased CO, but E timing exhibits significantly larger reductions in MVO_2. PSP is reduced with both E and L. The isolated sink preparation lends itself well to separate study of the effects of different modes of suction phase counterpulsation.

The Effects of Dry Air and Subsequent Humidification on Tracheal Mucous Velocity in Dogs. J.A. Hirsch and J.L. Tokayer (intr. by M.A. Sackner) Division of Pulmonary Diseases, Mount Sinai Medical Center, Miami Beach, Florida 33140.

Tracheal mucous velocity (TMV) was determined in twenty-six healthy mongrel dogs which were anesthetized with sodium pentobarbital. Teflon discs (0.68x0.13mm, weighing 0.13mg), filmed at constant speed through a bronchofiberscope, were used as markers of mucous motion (Sackner,Rosen, Wanner. J. Appl. Physiol. 34:495, 1973). Sixteen dogs were exposed to air from a compressor dried with calcium sulfate (10% relative humidity, 25°C) for three hours and ten of these dogs were subsequently placed on a Puritan nebulizer (100% relative humidity, 37°C). Ten dogs, similarly breathing nebulized air (100% relative humidity, 37°C), served as controls. Both groups breathed air through uncuffed endotracheal tubes and their muzzels were sealed with tape. Dry air depressed average TMV from 5.0mm/min SD 2.5 to 3.0mm/min SD 1.8 ($p<0.01$) after one hour. Almost no particle motion was observed after three hours (0.1mm/min,SD 0.2). After rehumidification,TMV increased and did not differ significantly from initial values two hours later (3.8mm/min SD 1.2). In the control group, at no time did TMV differ significantly from the initial values. Values of TMV in the control group did not differ significantly from the values obtained in anesthetized dogs breathing room air (60-70% relative humidity, 25°C) through their noses in work previously reported. In conclusion, acute exposure to dry air significantly depresses TMV in anesthetized dogs (a decrease of 40% after one hour),while reversal of this response by subsequent humidification to values not significantly different from initial values does not take place until after two hours of rehumidification. (Supported in part by NLHI:NIH 71-2205).

RESPONSE OF HEPATIC ARTERIAL FLOW TO REDUCTION OF PORTAL VENOUS FLOW OR RESISTANCE. Leroy J. Hirsch and Gerald Glick. Cardiovascular Institute, Michael Reese Hospital & Medical Center, Chicago, Illinois.

In a new experimental canine model which, for the first time, allows measurement of total hepatic blood flow, we have observed a mechanism that may serve to preserve hepatic integrity in the face of hypotension or other disturbances that would tend to reduce total hepatic blood flow. Electromagnetic flow probes were implanted around the portal vein, and the hepatic and superior mesenteric arteries. A group of 8 animals was subjected to: 1) superior mesenteric artery occlusion, 2) portal vein occlusion, and 3) infusion of isoproterenol, 0.1 μg/kg/min, into the portal vein. In a second group of 4 dogs, myocardial infarction and cardiogenic shock were induced by mercury embolization of the circumflex artery. Hepatic arterial flow increased 30±3.5% after superior mesenteric artery occlusion, 46±5.2% after portal vein occlusion, 75±17.2% during isoproterenol infusion, and 105±1.0% during shock. (All $p<0.01$.) Occlusion of the portal vein or its major feeder artery, the superior mesenteric artery, produced an increase in hepatic arterial flow within several beats, indicating that the increase in flow was not due to the accumulation of metabolites. Thus, when portal flow or resistance is reduced, compensatory increases in hepatic arterial flow ensue. The still larger increases in hepatic arterial flow during shock probably stem from decreased superior mesenteric artery flow (-60.0±7.9%) and accumulation of vasoactive metabolites. Therefore, hepatic arterial flow is regulated by a complex system of internal and external control mechanisms.

TRANSIENT STATE DIFFUSION OF DIETHYL ETHER IN SUBCUTANEOUS TISSUE. M.P. Hlastala* and J. Butler. Department of Medicine, University of Washington, Seattle, Washington, 98195.

The initial transient state of growth or decay of a decompression sickness bubble is very important since it involves a major change in bubble volume. Gas flux is heavily dependent on the diffusion characteristics of surrounding tissue. Transient state diffusion of an inert gas was measured in the subcutaneous tissue of rats. An existing subcutaneous gas pocket was surgically opened exposing the inner surface with the perfusion intact and a rigid, transparent chamber was mounted on the exposed surface. The chamber could be completely flushed with gaseous diethyl ether in four seconds. The uptake of gas by tissue was measured as a change in chamber pressure using an attached pressure transducer. The uptake rate could be accurately predicted using a mathematical model in which the tissue is perfused by an infinite number of infinitesimally small capillaries.

This technique allowed measurement of the rate of gas flux across the gas tissue interface during both the initial transient state - the build-up of a diffusion gradient in the tissue - and the later steady state. The transient state was relatively independent of tissue perfusion and allowed measurement of the diffusivity of diethyl ether which was .000752 $\pm$ .000058 cm^2/min (mean $\pm$ SEM) at a mean temperature of 38.4°C. This phase was over in 5 to 10 minutes depending on the perfusion. The steady state was strongly dependent on tissue perfusion and allowed measurement of perfusion which varied between experiments. (Supported in part by NIH Grant HL 12174).

MULTIPLE END PRODUCTS OF ANAEROBIOSIS IN DIVING VERTEBRATES. P.W. Hochachka, Dept. of Zoology, University of British Columbia, Vancouver 8, B.C., Canada.

When oxygen availability to working muscle in diving animals is limited by peripheral vasoconstriction, the muscle ferments carbohydrate and amino acids simultaneously, in effect coupling two additional energy-yielding reactions to those of glycolysis. Multiple anaerobic end products accumulate as a result. Succinate is the chief end product of anaerobic amino acid catabolism, alanine is a minor end product, while pyruvate and lactate are produced by glycolysis. During recovery following diving, increased blood concentrations of all four metabolites can be readily measured in the green sea turtle, the harbor seal, the sea lion, and the porpoise.

RELATIONSHIP BETWEEN ELASTIC RECOIL AND CLOSING VOLUME IN SMOKERS AND NON-SMOKERS. Vernon H. Hoeppner*, David M. Cooper*, Noe Zamel and Henry Levison. Dept. of Peds., Univ. of Toronto, Res. Inst., Hospital for Sick Children, and Dept. of Med., Toronto General Hospital, Toronto.

Closing volume (CV) by the single breath nitrogen technique and static elastic recoil were measured in 87 apparently normal subjects of whom 46 were smokers and 41 non-smokers. CV as a percent of total lung capacity (TLC) was higher in smokers, 40 $\pm$ 7.7%, than in non-smokers, 33.6 $\pm$ 7.5% ($p<0.01$). However, "closing pressures", obtained by an exponential extrapolation of the static pressure volume curves, were the same (smokers 3.3 $\pm$ 1 cm H_2O and non-smokers 3.1 $\pm$ 0.9 cm H_2O). The higher CV corresponded to a loss of elastic recoil demonstrated by the smokers. At 60% TLC, the recoil pressures for smokers were 5.7 $\pm$ 1.7 cm H_2O and for non-smokers 6.8 $\pm$ 2.1 cm H_2O ($p<0.02$). This suggests that changes in CV in smokers are primarily due to a loss of elastic recoil and do not necessarily reflect intrinsic small airways disease.

EFFECTS OF Ca, Ba, AND Sr ON RATE OF EFFLUX OF 45-Ca FROM VASCULAR SMOOTH MUSCLE MICROSOMES. Charles J. Hofbauer* and David F. Bohr. Department of Physiology, University of Michigan, Ann Arbor, Michigan.

Microsomes from hog carotids were labeled with 45-Ca and its efflux rate was studied in the presence of different concentrations of Ba, Sr, and Ca. Minced arteries were subjected to a polytron homogenization and the microsomes isolated using a variable centrifugation technique. The microsomes were resuspended in a tris buffer solution and labeled with 45-Ca in an uptake medium containing 10 mM oxalate for a period of 15 min. At this time the protein was associated with 20.20 nmoles Ca per mg microsomal protein. The labeled protein was then diluted twenty times in a medium identical to the uptake medium with the exception that no calcium was present. The calcium efflux then occurred with a rate constant of 0.025. After a 20.5 min efflux period Ca, Ba, or Sr was introduced. Each cation initiated a unique two-phase efflux response, an initial efflux complete in two minutes and a slow efflux. Quantitative comparisons of the initial and secondary 45-Ca efflux rates following the introduction of these cations permitted the establishment of a hierarchy which describes the relative affinities of Ba and Sr for the calcium binding sites in the microsomal protein. It was found that barium has a greater affinity for the calcium binding sites than does Sr.

Arterial Blood Pressure Regulation in Iguanas following Graded Hemorrhage and Passive Tilt. Lyle A. Hohnke (intr. by Jay W. Constantine). Univ. of Calif. School of Med., Los Angeles, Calif.

In reptiles, cardiovascular reflexes are poorly characterized although important evolutionary changes in vascular anatomy appear in these animals. Arterial blood pressure (ABP) changes in response to graded hemorrhage and passive head-up tilt were studied in restrained, anesthetized and unesthetized iguanas. Heart rate, arterial pressure, femoral arterial blood flow and central venous pressure were recorded via indwelling catheters and electromagnetic flow equipment. ABP fell slowly in response to hemorrhage up to a critical blood volume deficit of 35±18% of the estimated blood volume. The rate of ABP fall then increased nearly 40 fold ($p.<.001$) to continued hemorrhage. Heart rate increased and femoral arterial blood flow decreased progressively throughout hemorrhage; central venous pressure was stable initially then declined. Propanolol (2-3 mg/kg) and atropine (.01-.1 mg/kg) did not appreciably alter arterial pressure-hemorrhage curves. Heart rate fell nearly 50% following propanolol administration but increased steadily in response to hemorrhage. Atropine had little effect on either the blood pressure or heart rate changes induced by hemorrhage. During passive tilts of 0-90° carotid arterial pressure fell 33% before returning to control levels (2 min.). Heart rate increased, femoral arterial blood flow and central venous pressure fell in response to head-up tilts. Atropine plus propanolol lowered tilt induced heart rate increases by 77% but did not appreciably change the ABP responses; atropine alone had little effect. It is concluded that hemorrhage and passive head-up tilt induce reflex changes in heart rate and peripheral resistance that assist ABP regulation in iguanas.

EFFECT OF PENTAGASTRIN AND SECRETIN ON GASTRIC ADENYL CLCLASE.
O. Holian*, L. M. Nyhus, C. T. Bombeck*
Department of Surgery, The Abraham Lincoln School of Medicine, University of Illinois at the Medical Center, Chicago, Ill.

Cyclic AMP has been implicated as a "second messenger" in hormonally regulated reactions. Recent experimental findings suggest that cAMP may also participate in the production of gastric acid. In an attempt to evaluate the role of cAMP in gastric secretion, we have studied the cAMP forming enzyme, adenyl cyclase. We have studied the effects of pentagastrin and secretin on the adenyl cyclase activity both in "in vitro" and "in vivo". Pentagastrin (1 μg/100 μl), when added to the reaction mixture "in vitro", did not change the rate of adenyl cyclase activity over control value (250 pmoles cAMP formed/mg protein/20 min.). "In vivo" administration of pentagastrin by subcutaneous injection (20 μg/100 g. body weight) resulted in stimulation of adenyl cyclase activity at both 15 (150-200% of control level) and 30 minutes (300% of control level). Secretin had an inhibitory effect on the rate of adenyl cyclase activity when added "in vitro", and the degree of inhibition depended on the concentration of secretin: 0.05 units gave activity that was 50% of the control level, while 0.50 units reduced adenyl cyclase activity to 10% of control levels. Secretin, when administered "in vivo", also inhibits adenyl cyclase activity, but the "in vivo" inhibition appears to be less pronounced than the "in vitro" inhibition. Our data suggests that cAMP does play a role in the hormonal regulation of gastric secretion.

STATISTICAL EVALUATION OF THE BINDING CONSTANTS OF TROPONIN; VALIDITY OF THE 2-CLASS MODEL. Carl R. Honig and Gerald Gulden.* Univ. of Rochester, Roch. N.Y., and Univ. of Hawaii.

The equation currently used to analyze Ca binding to muscle proteins assumes 2 classes of independent, non-interacting sites. This was tested by applying the model to Scatchard plots of Ca binding to 7 preparations of troponin and 40 preparations of native tropomyosin. A computer searched for all possible combinations of affinities and binding capacities which fit each data set. An accepted criterion for selecting the best fit is the method of least squares. Accordingly, the combination of parameters with the lowest least squares sum (LSS) was chosen. If such a combination is a unique solution, (which it must be if the model is valid) one can change each of the 4 parameters in turn and observe an increase in LSS. A ± 5% change was used for this purpose. Many combinations of parameters gave a good visual fit to the data; in some cases affinities could be varied 5 orders of magnitude! 12 preparations could not be fitted with all parameters at least squares minimum, and in 1/2 the cases where a minimum was found, one or more of the parameters was biologically uninterpretable. Since interacting sites and multiple classes of independent sites can yield identical Scatchard plots, both models may fit some of the data. The correct model, however, should fit all the data. We therefore conclude the 2 class model is incorrect as applied to Ca binding to muscle proteins. This is significant in that interaction models yield totally different explanations for the effects of associated proteins, pH, etc. Supported by USPHS grant HL-03290.

FORCED EXPIRATORY FLOW IN RELATION TO ELASTIC RECOIL OF EXCISED RABBIT LUNG. T.Horie*, R.Ardila*, and J.Hildebrandt. Virginia Mason Research Center, Seattle, WA 98101.

In order to study the interaction between recoil (Pel) and forced flow($\dot{V}m$), recoil pressure at a given volume was varied in two ways in 9 rabbit lungs. Six lungs were ventilated for 1 hr with a V_T of 50% TLC, after which PV curves were significantly shifted toward higher Pel. For the same tracheal driving pressures (Ptr), $\dot{V}m$ always increased after ventilation. However, when $\dot{V}m$ was plotted against Pel, no consistent change in slope could be detected. Using Ptr down to -50 cm H_2O, IVPF curves usually reached a plateau only at volumes below 50% TLC. When Ptr was large, oscillations in $\dot{V}$ were present, and $\dot{V}$ dropped fairly abruptly to low values at volumes below 50% TLC while deflation continued. The cause of this transition is uncertain, but could represent the sudden buckling of a partially rigid airway system. Peak $\dot{V}$ in the rabbit was 5-8 TLC/sec, compared to about 1.4 TLC/sec in man.

Deflation of a partially inflated lung also produces increased Pel, when compared to a normal deflation path from 100% TLC. Therefore, partial $\dot{V}$-V curves beginning at 50% TLC (7 cases) and 75% TLC (5 cases) on an inflation limb were compared with partial $\dot{V}$-V curves beginning at the same volume on a deflation limb. Forced flow beginning from inflation limbs was always larger. However, when $\dot{V}m$ was again plotted versus Pel, no difference was seen. Data between rabbits could be compared and averaged by normalizing flow ($\dot{V}m$/TLC) and volume (% TLC). When $\dot{V}m$/TLC was plotted against Pel, data from all rabbits were quite similar regardless of ventilation or volume histories. In this type of plot, there was usually a small negative intercept on the P axis (up to 0.5 cm H_2O), indicating some flow at zero Pel.

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EFFECTS OF CAROTID SINUS DISTENTION ON NICTITATING MEMBRANE TENSION AND SWEAT GLAND POTENTIALS. I.S. Horwitz and A.I. Kaufman (intr. by - K. Koizumi). Downstate Medical Center, Brooklyn, New York.

Peripheral sympathetic neurons have often been identified as innervating vascular smooth muscle if their activity was changed by changing carotid sinus pressure. The question of whether baroreceptor reflexes can extend to effector organs beyond the cardiovascular system has not, however, been thoroughly studied. We have begun studying this by recording nictitating membrane tension (NMT) and sweat gland potentials (SGP) in 11 chloralose anesthetized cats. Both carotid sinuses were isolated to enable raising sinus pressure suddenly from 0 mmHg to 150-200 mmHg. Sinus pressure and systemic arterial pressure were simultaneously recorded. The cats were immobilized with Flaxedil and artificially ventilated. Marked reductions of spontaneous fluctuations in NMT or SGP were seen to follow sinus distention in 7 cats, though not consistently, and to precede the reduction in systemic arterial pressure. The latency to onset of reduction in NMT and SGP ranged from 1-5 sec. Reductions lasted 4-20 sec. and did not outlast the distention. When spontaneous fluctuations were absent, distention did not change NMT or SGP. In all 8 cats where NMT or SGP could be reflexly increased by sciatic n. stimulation or asphyxia, distention could reduce the reflex activity, including 3 of the 4 cats where spontaneous fluctuations were not affected. In one cat where femoral arterial flow was kept constant while recording SGP from the corresponding foot, sinus distention markedly reduced rises in SGP following asphyxia. We conclude that baroreceptor reflexes can affect activity in sympathetic neurons innervating non-cardiovascular structures. (Supported by USPHS Grants GM-00968 and NS-846)

THERMAL REGULATION IN LONG-EVANS RATS EXPOSED TO 2450 MHZ MICROWAVE RADIATION.[1] W.M. Houk,* S.M. Michaelson, and A. Longacre, Jr.* Univ. of Rochester, School of Med. and Dentistry, Dept. Radiation Biology and Biophysics, Rochester, N.Y.

Colonic temperature was measured in 500 unrestrained male Long-Evans rats that had been exposed to various power flux densities (3, 10, 20, 30 mW/cm^2) of 2450 MHz far-field microwave radiation maintained under constant environmental conditions. Noteworthy was the requirement for long equilibration times of three or more hours to avoid masking the temperature effects induced by the thermal input of this unique volume heating agent. Temperature responses were related to power-density and duration of exposure. Microwave irradiation appears to cause a resetting of hypothalamic regulatory centers in a manner analogous to a fever without altering environmental conditions external to the animal and without creating the problems of analysis when pyrogens are used to induce fever.

[1]This report is based on work performed pursuant to Contract No. FDA 73-30 with the Public Health Service, Food and Drug Administration, U.S. Department of Health, Education, and Welfare and under contract with the U.S. Atomic Energy Commission at the University of Rochester Atomic Energy Project and has been assigned Report No. UR-3490-330.

THE EFFECT OF VARIOUS GASTRIC LOADS ON FOOD INTAKE IN SUCKLING RATS, Katherine Albro Houpt* and T. Richard Houpt. N.Y.S. Vet. Col., Cornell Univ., Ithaca, N.Y. 14850

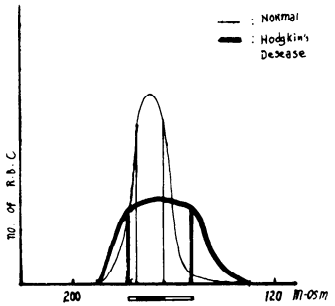
Following a 4-hr deprivation period with a non-lactating foster mother, suckling rats, 3 to 7 days old, were given gastric loads equal to 4% of their body weight by gavage. Controls were intubated only. When NaCl solutions were given, 3% NaCl (n=12) depressed intake to 48% ($p<0.001$) of the control (n=24) intake of 1.1±0.3g/4-hr, while 0.9%NaCl (n=12) depressed intake to only 78% ($p<0.025$) of control, indicating that osmotic factors may be involved in controlling food intake in suckling rats. When the various components of rat's milk were given as gastric loads, factors other than osmo-concentration appeared to be involved. All gastric loads significantly depressed intake in comparison to controls ($p<0.01$ or lower). In order of increasing effectiveness in depressing intake: milk (n=23) depressed intake to 68% of that of the controls (n=127) which gained 1.2±0.4g/4-hr; water (n=14) depressed intake 67%; heavy cream (n=17) 63%, 5% lactose (n=18) 60%; protein hydrolysate (n=18) 59%; 5% glucose (n=14) 44%; and corn oil (n=12) 10%. Corn oil, an unsaturated fat, is not a natural component of rat's milk and appeared to have a toxic effect in suckling rats: intake was depressed for 20 hours which was not the case with any other gastric load. Glucose was most effective in temporarily depressing food intake. (Supported by the Pennsylvania Plan to Develop Scientists in Medical Research, Univ. of Pa.)

RESPIRATORY PROPERTIES AND 2,3-DIPHOSPHOGLYCERATE (DPG) CONCENTRATION IN BLOOD OF THE ADULT OPOSSUM. A. S. Hoversland, D. S. Dhindsa, W. S. Murphy*, J. T. Parer* and J. Metcalfe. Heart Research Laboratory, Department of Medicine, University of Oregon Medical School, and Oregon Zoology Research Center, Portland, Oregon.

Oxygen dissociation curves (O_2 DKs) were constructed at 35° C on whole blood (WB), on incubated whole blood (IWB), and on incubated, hemolyzed, dialyzed blood (IHDB) from adult American opossums (Didelphis marsupialis virginiana). The influence of DPG was studied by adding 30 μm/g hemoglobin (Hb) to the IHDB. The pH gradient across the red cell membrane of WB averaged 0.300, so all P_{50} values were corrected to an intraerythrocytic pH of 7.10. Incubation was at 37° C for 24 hrs, hemolysis was achieved by alternate freezing and thawing and dialysis was carried out in Visking bags (15-20 ml capacity) against 10 L of bicarbonate buffer for 24 hrs. The mean P_{50} values ± SD were: 42.3 ± 3.9 mm Hg (n = 22) for WB; 25.7 ± 0.9 mm Hg (n = 6) for IWB; 36.0 ± 1.3 mm Hg (n = 3) for IHDB; and 44.4 ± 1.3 mm Hg (n = 2) when DPG was added to IHDB. Mean concentration of DPG was 16.41 ± 4.44 μm/g Hb (n = 15) in WB. Other mean values for WB were hematocrit 35.5 ± 7.0%, Hb concentration 12.2 ± 2.2 g%, and Bohr factor ($\Delta \log P_{O_2} / \Delta$ pH) -0.526. Starch gel electrophoresis (8 volts/cm, pH 8.6, 4 hrs, 5° C) showed only one major component migrating slightly faster than human A Hb. (Supported in part by USPHS, NIH grants HL 05499, HL 06042, HL 14121, HL 14979, and the Oregon Heart Association.)

THE DEFINITION OF AN ERYTHROCYTE OSMOTIC FRAGILITY INDEX WITH A NEW FRAGILIGRAPH. J. Hsu*, D. Ostrowski*, M. Polanyi* and G. G. Nahas. Col. Phys. & Surgs., Columbia Univ., New York, N. Y., and American Optical Corp., Framingham Centre, Mass.

The A. O. fragiligraph, prototype II, consists of light-emitting diodes which transilluminate a sample of blood diluted (1/600) in isotonic saline. A constant delivery pump adds distilled H_2O so as to progressively decrease osmolarity and produce hemolysis. Two curves are recorded: one which relates light scattering of the erythrocytes to osmolarity; the second which is a derivative of the first, and a function of the rate of light scattering to the change in osmolarity. This derivative is a display of the distribution curve of erythrocytes undergoing hemolysis. Using this curve, a new osmotic fragility index of erythrocyte was defined. This index is equal to the change in osmolarity (ΔOsm) which will produce hemolysis of 25% to 75% of the cell population. In normal man this index was 11.8 ± 1.1 mOsm. In patients with blood dyscrasias this index was 25.5 ± 6.9 mOsm. Such a ΔOsm is a significantly more precise index of erythrocyte osmotic fragility than the older measurements correlating the start or the end of hemolysis to % dilution of an isotonic saline solution. Such measurements presented a considerable standard deviation and were not always significantly different in normal and abnormal blood cell populations.



DEPRESSED-VENTILATORY RESPONSE TO HYPOXIA IN CHRONIC OBSTRUCTIVE LUNG DISEASE. Chin T. Huang and Harold A. Lyons. Downstate Medical Center, Pulmonary Disease Division, Brooklyn, N.Y. Supported by USPHS Grant #HL 05862, #PN 12832, #HE 11932.

The ventilatory response to breathing graded degrees of hypoxia was compared for seven normal subjects and ten patients with hypercapnic chronic obstructive lung disease. The oxygen concentrations used were 0.1, 0.12, 0.15 and 0.21. Alveolar carbon dioxide concentration was kept constant during each study. The ventilatory response to the hypoxic stimulus of the patients was shifted to the right and flattened. This response was markedly different from normal subjects being approximately 50% less for each grade of hypoxia. Ventilatory response curves to increased concentrations of carbon dioxide for the patients showed responses which indicated that the poor responses to hypoxia were not limited by mechanical factors of respiration. The depressed response to hypoxia observed in the patient is similar to that found in residents at high altitude or in congenital cyanotic cardiacs. The exact mechanism remains unknown. The results suggest that the peripheral chemoreceptors are inhibited in response to hypoxia in patients with chronic obstructive lung disease.

STUDIES OF BICUCULLINE BLOCK OF GABA CEREBRAL SYNAPTIC INHIBITION BY MONITORING NEURONAL MEMBRANE CHANGES. Chuong C. Huang* and Amedeo S. Marrazzi, Univ. of Missouri Inst. of Psychiatry, St. Louis, Mo. 63139.

By the evoked potential technique and close arterial injection Marrazzi, et al. have demonstrated cerebral synaptic inhibition by biogenic amines, and their differential block by chlorpromazine (CPZ). Thus they have shown differential block of 5HT by CPZ and of GABA by bicuculline. Using the microelectrode technique, we also reported that CPZ is a specific competitive inhibitor of 5HT and LSD, each of the three producing similar synaptic changes, i.e. reduced or stopped spike firing, hyperpolarization, reduced EPSPs (evoked by V.L. thalamic stimulation) and appearance of IPSPs, and decreased conductance. On the other hand, GABA and glycine have shown increased conductance during spike inhibition and membrane hyperpolarization. In the present studies, the intracellular and extracellular recordings were from the Betz cells in the pericruciate area of the cat and the drugs were injected close arterially through the ipsilateral common carotid artery. Bicuculline blocks GABA inhibition of spontaneous unitary activities but is unable to block 5HT. It is found that bicuculline produces membrane changes similar to those of GABA, viz., increased conductance, hyperpolarization and reduced or stopped spike firing. It is thereby shown that bicuculline accomplishes its specific inhibition of GABA by competing for the identical membrane site, i.e. receptor, ionic channel or transport mechanism. Equilibrium potential studies are expected to help identify the specific ion channels that may be involved. Aided by Psychiat. Research Fndn. of Mo.

THE MECHANISM OF BICARBONATE SECRETION IN RABBIT ILEUM EXPOSED TO CHOLERAGEN. K. A. Hubel, Department of Medicine, University of Iowa, Iowa City, IA.

Bicarbonate may be secreted into the intestinal lumen in cholera because: 1) HCO_3^- ions are transported, or 2) OH^- ions accumulate and react with dissolved CO_2 to form HCO_3^-. If HCO_3^- ions are transported into the lumen from the interstitial fluid, lumenal PCO_2 should increase ($HCO_3^- \rightleftharpoons OH^- + CO_2$); if OH^- accumulates, PCO_2 should diminish. Net movement of H_2O, and HCO_3^-, and changes in pH and PCO_2 in lumenal fluid were studied in adjacent segments of rabbit ileum in vivo, one of which was exposed to choleragen (Wyeth 001). Four hours after exposure, segments were drained and infused with gassed Krebs-Henseleit solution whose PCO_2 exceeded arterial PCO_2. After 45 minutes, fluid was collected anaerobically from control and cholera segments. Among 13 cholera segments, lumenal PCO_2 diminished by a mean of 8.4 Torr and was less than femoral arterial blood PCO_2 in 6 instances. In the paired control segments, mean PCO_2 increased by 4.4 Torr, and was always greater than arterial PCO_2. Dilution could not account for the low PCO_2 in cholera segments because in hypertonic solutions which caused water to move into the lumen, the PCO_2 did not differ from control values obtained with isotonic solutions. The results suggest that OH^- accumulation (by addition of OH^- or removal of H^+) causes HCO_3^- secretion in cholera. This does not result from secretion of some other base (e.g., $HPO_4^=$), because HCO_3^- accounts for most of the base in the lumenal fluid. The PCO_2 changes suggest that OH^- reacts with CO_2 at the cell-lumen interface, but reaction at the cell-interstitial fluid interface cannot be excluded.

CORONARY AND SYSTEMIC HEMODYNAMIC EFFECTS OF HYPERTONIC MANNITOL IN THE CONSCIOUS, INTACT DOG. I. Hutton*, G.H. Templeton*, D.E. Fixler* and J.T. Willerson* (intr. by J.H. Mitchell). U. Tex. Southwestern Med. Sch. at Dallas, Dallas, Texas.

In this study the effects of mannitol on regional myocardial blood flow (RMBF) and on systemic hemodynamics have been determined in 10 conscious dogs. RMBF was measured using radioactive microspheres (8 μ in diameter). Heart rate was maintained constant by atrial pacing. Mannitol (25%) was administered intravenously and either isotonic dextrose or saline was given as control at the same rate of infusion. Serum osmolality increased following mannitol by 22 ± 2 mOsm. Maximum left ventricular rate of pressure rise (dp/dt) increased by 23% from 2061 ± 346 to 2529 ± 377 mm Hg/sec ($p < 0.005$) and mean systemic arterial pressure increased from 101 ± 5 to 116 ± 8 mm Hg ($p < 0.001$). There were small but nonsignificant increases in left ventricular end-diastolic pressure following mannitol from 3 ± 1 to 6 ± 2 cm H_2O and in cardiac output from 2.5 to 3.1 L/min. There were modest but not significant increases in RMBF after volume expansion with either dextrose or saline. However, mannitol significantly increased flow to the right ventricle by 77 ± 14%, to the left ventricle by 81 ± 13%, and to the ventricular septum by 82 ± 16%. These data suggest that hypertonic mannitol significantly increases regional myocardial blood flow to the right and left ventricles and ventricular septum and has a positive inotropic effect in the conscious, intact dog.

A HISTOCHEMICAL AND ELECTRON MICROSCOPIC STUDY OF COMPENSATORY MUSCULAR HYPERTROPHY. C. D. Ianuzzo*, R. B. Armstrong*, W. Costello*, and P. D. Gollnick. Dept. of Health Sciences and Biology, Boston Univ. Dept. of Physical Education for Men, Washington State Univ.

Histochemical and electron microscopic changes that occur with skeletal muscle hypertrophy have been investigated. Compensatory hypertrophy of the plantaris and soleus muscles was induced in Sprague-Dawley albino rats following the surgical removal of the ipsilateral gastrocnemius muscle. The corresponding muscles from the sham operated contralateral leg and muscles from non-operated animals served as controls. Animals were sacrificed approximately 60 days following gastroxectomy. Myofibillar ATPase and DPNH-diaphorase activities were estimated histochemically. The cross-sectional areas of the three animal muscle fiber types were determined by direct planimetry. Muscle samples prepared for electron microscopy were fixed in glutaraldehyde and embedded in epon-araldite. The soleus and plantaris muscles were found to have hypertrophied 40% and 100% by weight, respectively. A 2-fold increase was observed in the cross-sectional areas of the fast-twitch-oxidative-glycolytic(FOG), fast-twitch-glycolytic(FG), and slow-twitch-oxidative(SO) fibers in the hypertrophied plantaris muscle. The findings indicate the plantaris to have an increase in the percent of SO and FOG fibers. The hypertrophied soleus muscles were found to consist of only SO fibers. Electron microscopic findings indicate a change in the size and number of myofibrils per muscle fiber. One group of animals received a subcutaneous injection of Dianabol (5 mg/kg) 3 times/week. These findings were similar to sham injected animals.

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MODEL FOR THE CIRCADIAN NEURONAL ACTIVITY OF THE EYE OF APLYSIA. Jon W. Jacklet, Dept. Biology, SUNYA, Albany, N.Y.

The isolated eye of Aplysia exhibits a precise endogenous circadian rhythm in the frequency of autoactive compound action potentials (CAP) recorded from the optic nerve while the eye is cultured in darkness in vitro for a week. Studies with low calcium and high magnesium indicate that chemical synapses are not necessary for rhythm expression. Intracellular recordings show three basic types of response. Two of these responses are prolonged depolarization or hyperpolarization to light and are shown to be from cells of the pigmented retina by dye injection of these cells. The third response type is correlated with the CAP and shown to be from the non-pigmented secondary cells by dye injection. Antidromic activation of these cells suggests that they have axons in the optic nerve. Ablation of part of the eye demonstrates that the secondary cells, mainly at the base of the eye, generate the circadian rhythm. The available evidence suggests a model in which all three cell types have processes in the nerve and interact by electrotonic coupling to produce the synchronous optic nerve CAP. The secondary cells are the source of the autoactivity in darkness and the receptor types, during illumination, modulate the optic nerve activity. The circadian rhythm does not appear to be the property of one cell but is dependent on a population of cells for its extraordinary range and regularity. Supported by NIH grant NS 08443.

CARDIOVASCULAR EFFECTS OF ACUTE HYPOXIA IN CONSCIOUS RESTING DOGS. D. B. Jennings and J. Sparling *, Department of Physiology, Queen's University, Kingston, Ontario.

The relations between cardiovascular function and minute ventilation and oxygen consumption were studied in conscious resting dogs breathing different combinations of low oxygen and high carbon dioxide gas mixtures. The dogs breathed through an endotracheal tube in a chronic tracheostomy and catheters were placed in the right heart and in an exteriorized carotid artery by indirect techniques. These studies of hypoxia and asphyxia (hypoxemia plus hypercapnia) were compared with the cardiorespiratory relationships in dogs breathing air. Breathing 12% O_2 ($P_{a_{O_2}}$ = 46 mm Hg; $P_{a_{CO_2}}$ = 28 mm Hg) there were no consistent changes in cardiovascular function with respect to minute ventilation. Breathing 10% O_2 ($P_{a_{O_2}}$ = 37 mm Hg; $P_{a_{CO_2}}$ = 22 mm Hg) there were no changes in the relationships between cardiac output, mean arterial blood pressure or total peripheral resistance and minute ventilation; however, at every level of minute ventilation heart rate was increased and stroke volume was decreased. When breathing gas mixtures low in oxygen and high in carbon dioxide (6% to 10% O_2; 5% to 10% CO_2), cardiac output was decreased at every level of minute ventilation associated with a decrease in stroke volume, whereas heart rate was normal or reduced. Cardiac output was also reduced with respect to oxygen consumption in asphyxia but not in hypoxia. Mean arterial blood pressure was maintained within normal limits during asphyxia and therefore total peripheral resistance was increased.

Supported by grants from the Ontario Heart Foundation and the Defence Research Board of Canada.

AN ELECTRONYSTAGMOGRAPHIC STUDY OF POST-ROTATORY NYSTAGMUS DURATION, NUMBER OF BEATS, AND FREQUENCY IN 10 ATMOSPHERES ABSOLUTE HELIUM AND OXYGEN AND DURING DECOMPRESSION. C. B. Jensen*, S. J. Brumleve, and B. De Boer. Department of Physiology and Pharmacology, University of North Dakota, Grand Forks, N.D. 58201

Adult, male guinea pigs weighing 700 gm (± 100 gm) were chronically implanted with periorbital, silver, disc electrodes for the purpose of recording electronystagmus. Each was individually restrained in a plexiglas restraining cage, secured to a turntable, and placed in a hyperbaric chamber for subsequent experimentation. Vestibular nystagmus was induced by rapidly stopping the turntable following ten rotations at 40 rpm. Post-rotatory electronystagmograms were recorded by a polygraph, and all eye movements were monitored on an oscilloscope. Nystagmus duration, number of eye beats, and frequency were manually determined from the polygraph recordings. Post-rotatory nystagmus samples were recorded in room air, 1 atmosphere absolute (ata) helium and oxygen ($He-O_2$), 10 ata $He-O_2$, and at four stages (7.7 ata, 5.0 ata, 3.5 ata, and 1.0 ata) during six different decompression rates (0.04, 0.06, 0.08, 0.10, 0.12, and 0.15 ata/min). Slight changes in post-rotatory nystagmus duration, number of beats, and frequency were observed in each of the test environments. The greatest post-rotatory nystagmus variations occurred during decompression, and the fastest decompression rates provided the most significant alterations. Spontaneous nystagmus was present during rapid decompression, and the possibility of its serving as a warning of impending decompression trauma was evaluated. (Sponsored by ONR Contract N00014-68-A-0499)

THERMOREGULATION IN MACACA MULATTA: A THERMAL BALANCE STUDY. George S. Johnson* and Reynaldo S. Elizondo. Department of Anatomy and Physiology, Indiana University, and Indiana University Medical School, Bloomington, Indiana 47401.

An indirect calorimetric study was performed on three male rhesus monkeys (Macaca mulatta), weighing 3.09-3.66 kg., over an ambient temperature (Ta) range of 15-40°C. Oxygen consumption, CO_2 production, mean-weighted skin temperature($\bar{T}s$), rectal temperature(Tre), respiratory evaporative water loss (Eres), and total evaporative water loss (Etot) were measured continuously after equilibration at each Ta. $\bar{T}s$ changed linearly with Ta, whereas Tre was maintained within the range of 37.8 - 39.9°C at Ta's of 15-40°C. The lower critical Ta for the increase in metabolic heat production was 26.8±0.2°C, and corresponds to a critical $\bar{T}s$ of 29.4± .2°C; heat production (M) was elevated so that at 15°C (M= 91.0±3.0 W/m^2) it was almost twice that at 26.8°C (M=52.2±3.0 W/m^2). Above the upper critical Ta of 31.9±.7°C, heat losses were facilitated by eccrine sweating so that at 40°C Etot (54.8±4.7 W/m^2) was over eight times that in the thermal neutral zone, TNZ, (6.33±.9 W/m^2), whereas Eres (4.7±.4 W/m^2) increased only 2.1 times neutral zone levels (2.2±.3 W/m^2). Panting was not observed. The critical $\bar{T}s$ for the onset of sweating was 34.4±.7°C. Tissue conductance (k) in the cold(15-26.8°C) had a minimum value of 18.6±1.4 W/(m^2°C), and increased to 131.9±5.9 W/(m^2°C) at 40°C. These data illustrate that in Macaca mulatta thermoregulation is achieved in the TNZ (26.8±.2-31.9±.7°C) by vasomotor control. Above the upper critical limit, eccrine sweating is the major avenue of heat loss and the role of Eres in dissipating metabolic heat production is insignificant. Below the lower critical limit, thermal balance is maintained by an apparent increase in M which is attributable to shivering thermogenesis. (Supported by AF-72-2383)

EFFECT OF 1-SARCOSINE-8-ALANINE-ANGIOTENSIN II ON ARTERIAL PRESSURE IN MALIGNANT AND CHRONIC RENAL HYPERTENSIVE DOGS. J.A.Johnson, J.O.Davis, W.S.Spielman*, and R.H.Freeman*. Department of Physiology, University of Missouri School of Medicine, Columbia, Missouri 65201.

Earlier studies from this laboratory have shown that the angiotensin II analog, 1-sar-8-ala-angiotensin II, acts to antagonize both the pressor and the steroidogenic effects of angiotensin II in the dog. The present experiments were undertaken to determine the effect of this analog on arterial pressure (AP) in renal hypertensive dogs. Eight dogs were subjected to right nephrectomy and reduction of left renal blood flow by a Goldblatt clamp; 5 of these dogs developed malignant hypertension while 3 dogs developed chronic hypertension. Intravenous infusion of the A-II analog at 6 ug/kg min. into conscious malignant hypertensive dogs resulted in a decrease in AP from an average control level of 170 mm Hg to 144, 137, and 137 mm Hg after 15, 30, and 45 min. of analog infusion. After increasing the analog infusion rate to 12 ug/kg min. for 15 min. the AP was still 140 mm Hg. However, these pressures were higher than the average pre-hypertensive value of 110 mm Hg. During infusion of the A-II analog, plasma renin activity (PRA) increased from an average control value of 41 ng A-II/ml to 61, 77, and 77; infusion of the analog at the higher dose resulted in a PRA of 88 ng/ml. In conscious chronic hypertensive dogs with an average control AP of 172 mm Hg, infusion of the A-II analog (6 ug/kg min) resulted in an AP of 170, 172, and 170 mm Hg at 15, 30, and 45 min. Control PRA was 7 ng A-II/ml and during infusion of the analog averaged 9, 10, and 12 ng/ml. These studies indicate that A-II contributes significantly to the elevated AP in malignant hypertension, but suggest that some additional factor may also be involved. A role for A-II in maintaining the elevated AP in chronic hypertension could not be demonstrated.

BIOCHEMICAL MANIPULATION OF MYOCARDIAL FUNCTION BY PHOSPHODIESTERASE INHIBITION OR BY INTRODUCTION OF CYCLIC PHOSPHATES. Weldon B. Jolley, Danny M. Anderson*, David B. Hinshaw* and Louis L. Smith*. Loma Linda University School of Medicine, Surgical Research Laboratory, Loma Linda, CA.

Sutherland postulated that cyclic 3',5'-adenosine monophosphate (C-AMP) is the intracellular messenger activating cell response to a variety of stimuli. The enzyme phosphodiesterase (PDE) converts C-AMP to the inactive form 3',5'-adenosine monophosphate. We have studied cardiovascular responses to two methods for controlling the intracellular level of C-AMP. The first was by inhibiting PDE activity; the second was by administering structural analogs of C-AMP which are presumed to enter the cell because of the response effected. It was hoped that alterations in intracellular C-AMP levels would improve myocardial function and hence be beneficial in low perfusion states. Twenty-two adult dogs were lightly anesthetized following which baseline hemodynamic measurements were obtained. Experimental observations included arterial pressure (AP), central venous pressure (CVP), heart rate (R), cardiac output (CO), and a standard limb lead EKG. Infusion of the drug in normal saline was begun and continued for 120 minutes. Measurements were made at 30 min. intervals during the test and for 120 min. following completion. Identical volumes were employed in all groups. Control dogs received received the same volume of normal saline only. Four different phosphodiesterase inhibitors were studied and each effected an immediate response which was cumulative but which ceased with the termination of the infusion. CO increased by up to 80%. AP, CVP and R showed no statistically significant changes. Peripheral resistance decreased during the period of the infusion. By contrast, cyclic phosphate compounds effected a slower response which was cumulative and prolonged in effect. The CO showed a progressive and prolonged rise to 75% over baseline. This effect continued for up to 120 min. following completion of the infusion. No cardiac arrythmias were noted in either group. Studies are now in progress to dermine the effectiveness of these compounds in improving myocardial function following endotoxic shock.

EFFECTS OF TEMPERATURE ACCLIMATION ON CATECHOLAMINE TISSUE LEVELS AND SYMPATHETIC CAPACITY IN THE HAMSTER. Stephen B. Jones* and X. J. Musacchia, Dept. of Physiol., Dalton Res. Ctr., Univ. of Missouri, Columbia, Mo. 65201

Changes in tissue catecholamines at different temperature acclimation states were investigated by: 1) measurements of tissue levels and 2) assessment of biosynthetic capacity using a pharmacologic inhibitor. Groups of 8-10 Mesocricetus auratus were placed in either cold (7°C), control (22°C) or warm (34°C) environments for 4 to 7 weeks. Heart, liver, kidney and adrenal from each animal were quickly frozen for analysis of norepinephrine (NE) and epinephrine (E). NE in hearts of heat exposed animals, 1.98±.11 ug/g, were significantly higher ($P<.001$) than control values, NE=1.31±.05 ug/g, while heart NE in cold exposed animals, 1.00±.06 ug/g, were significantly depressed from controls ($P<.05$). Alterations in kidney NE levels were similar to heart, but liver catecholamines appeared unchanged. Adrenal changes were in the opposite direction from heart and kidney. Sympathetic capacity was measured in animals exposed to 34°C for 4 to 5 months and compared with 22°C ambient controls. After a single dose of α-methyl-p-tyrosine (160mg/kg, 50mg/ml) or saline animals were sacrificed at 1, 4 or 8 hrs; heart was assayed for NE and E. Heart NE in controls decayed linerally, 1.43±.05 ug/g to 1.10±.16 ug/g in 8 hrs; with heat acclimation there was no linear decay. Heat exposure may reflect increased biosynthetic capacity (sympathetic capacity). Supported by NASA NGL 26-004-021, S7-9.

VENTILATORY RESPONSES TO NON-OCCLUSIVE DISTENSION OF THE MAIN PULMONARY ARTERY IN THE CONSCIOUS DOG. C.E. Juratsch*, B.J. Whipp, M. Laks, D. Garner*, J. Beazell* and J. Jengo*. Divs. of Cardiology and Respiratory Medicine, Harbor General Hospital, Depts. of Medicine and Physiology, UCLA, and Physiology, University of So. California, Los Angeles, Calif.

Acute, non-occlusive inflation of a chronically implanted balloon in the main pulmonary artery (MPA) of the conscious dog results in constriction of pulmonary arterioles (Fed. Proc. 32:442, 1973). We subsequently observed that minute ventilation ($\dot{V}_E$) also increases during this procedure. To elucidate the mechanism of this hyperpnea we performed 24 balloon inflation experiments in four conscious dogs. V_E, tidal volume (V_T), breathing frequency (f), and end-tidal CO_2 ($P_{ET}CO_2$), were determined. In addition, arterial blood gas and acid-base status, physiological dead space (V_D)/V_T and cardiac output ($\dot{Q}$) were measured. $\dot{V}_E$ increased with balloon inflation, from a mean control of 5.5 L/min and reached a steady-state value of 7.7 L/min within one minute. This increase was predominantly due to an increased V_T. $P_{ET}CO_2$ decreased an average of 4 mmHg. V_D/V_T increased (31%) with no decrease in P_aCO_2. P_aO_2 decreased 15 mmHg and $\dot{Q}$ was elevated (32%). These data demonstrate a redistribution of pulmonary blood flow with P_aCO_2 being regulated by increases in $\dot{V}_E$ that are proportional to both the regional increases in perfusion and the overall increase in $\dot{Q}$. Possibly the regional variations in pulmonary blood flow result from unequal constriction of pulmonary arterioles and/or physical redistribution of blood flow by the balloon. We conclude that in the conscious dog a highly sensitive ventilatory control mechanism exists which is responsive to small transient elevations of P_aCO_2, resulting from the increased $\dot{Q}$ (Fed. Proc. 32:385, 1973) and the uneven distribution of $\dot{V}_A/\dot{Q}$.

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MORPHOLOGIC EVIDENCE OF DIRECT INNERVATION OF PARIETAL CELLS IN RATS
N. G. Kalahanis*, L. M. Nyhus, and T. K. Das Gupta*. Department of Surgery, University of Illinois Hospital and Abraham Lincoln School of Medicine, Chicago, Illinois.

The object of this investigation was to study the morphology of nerve fibers in the rodent gastric mucosa. An attempt has been made to correlate the findings of light and electron microscopy with possible demonstration of a synapse with the parietal cell. Gastric mucosa from fasting male rats was divided into control and vagotomized groups. Vagotomy was performed to study degenerated nerve fibers. Tissue from vagotomized rats was taken on the fourth, seventh, and eleventh post-operative days and processed for Araldite embedding. Semi-thin sections were treated with modified Nauta's and Holmes' methods, and for electron microscopy, before embedding in Araldite, the blocks were treated with the above silver techniques. By these methods, we have traced the nerve fibers to their termination, both in normal and in vagotomized rats. In light microscope, we found structures ending in the cell membrane of the parietal cell. These structures are similar to the "Button Terminale" and were also confirmed by electron microscopy. Therefore, we can conclude that in rats the peripheral nerves directly innervate the parietal cells.

ROLE OF THE ROSTRAL CINGULATE GYRUS IN THE REFLEX MUSCULAR INHIBITION FROM TYPE-J PULMONARY RECEPTORS.
Madhu Kalia (intr. by S. Lahiri), Cardiovascular-Pulmonary Division, Dept. of Med., University of Pa., Philadelphia, Pa.

Earlier work on the cerebral pathways involved in the J-reflex, i.e., the reflex muscular inhibition from the type-J pulmonary receptors, has shown that the main centers concerned are not associated with the cerebral cortex but with deeper structures (Kalia, 1969). More precise localization has been done by making small subcortical lesions in acute and chronic experiments on 25 cats. The J-reflex was studied by eliciting the effect of injections of phenyl diguanide (pdg) into the pulmonary circulation (a procedure which is known to stimulate type-J pulmonary receptors) on the knee jerk that was used as an index of monosynaptic reflex. Electromyograms of the leg muscles, respiration and aortic blood pressure were also monitored. Injections of pdg were administered through a right atrial catheter in a dose of 150 µg in 1.5 ml saline at 37° C. In all control runs a dramatic reduction in the knee jerk occurred 2 seconds after the pdg injection. Acute bilateral lesions were then made in the region of the cingulate gyrus by subpial suction and the experiment repeated. Chronic bilateral cingulate lesions were also produced in 5 cats for testing of the J-reflex 5 weeks later. All lesions were reconstructed from serial celloidin sections stained with cresyl violet. The smallest lesion sufficient to abolish the J-reflex was found to involve the rostral part of the cingulate gyrus. It was concluded that the rostral cingulate region is an essential part of the pathway for the J-reflex. (Supported in part by the Alexander von Humboldt Stiftung).

PULMONARY VASCULAR COMPLIANCE CHANGES IN RESPONSE TO STELLATE STIMULATION. J.E. Kallal* and B. Coleman, Dept. of Physiol. & Biophys. The Chicago Medical School, Chicago, Illinois 60612

A series of experiments were performed in which simultaneous recordings or pulmonary arterial and aortic blood flow were obtained in nine opened chest, artificially respirated dogs anesthetized with chloralose (125 mg/kg). The difference between these two mean flows was integrated by use of an analog computer to indicate changes in volume of the pulmonary vascular bed. Along with these electromagnetically derived flow recordings, the pulmonary arterial pressure, left atrial pressure, and aortic pressure were measured. An evaluation of resistance and compliance changes could be made from pressure-flow measurements and pressure volume measurements within the pulmonary vascular bed in response to stellate ganglion stimulation and to sympathomimetic agents.

The results of these experiments indicate that right and left stellate stimulation decrease the compliance of the pulmonary vascular bed. Stellate stimulation with a frequency of 15/sec. and magnitude of 2-4 volts when applied for 6-12 seconds resulted in a greater aortic flow than pulmonary arterial flow within a range of 20-65 ml. during the first 40 seconds after the initial stimulus. During this interval, the mean pulmonary arterial pressure increased 1-6 mmHg. These effects were mimicked by epinephrine (0.5 μg - 0.8 μg/Kg), blocked by propranolol (0.5 mg - 1.0 mg/Kg), but not blocked by phenoxybenzamine (1.5 mg - 2.5 mg/Kg). These data indicate that the volume of blood contained within the pulmonary bed is dependent upon sympathetic nervous activity. (Supported by Grant HE-12285 from The National Heart & Lung Institute).

EFFECT OF α-METHYLTYROSINE ON CYCLIC CHANGES IN MONOAMINOXIDASE ACTIVITY AND 17β-ESTRADIOL RISE IN PROESTRUS RATS. I.A. Kamberi and E.S. Bacleon*. Dept. of OBG, UCLA School of Medicine, Harbor General Hospital Campus, Div. Reproductive Biology, Torrance, California.

Four day cyclic female rats, untreated or injected with α-methyltyrosine (α-MT) (200 mg/kg) were autopsied at the fixed time of estrus cycle. Estradiol-17β (E_2) was measured by radioimmunoassay. Method of Otsuka and Kobayashi (Biochem. Pharmacol. 13, 995, 1964) was used to measure monoamineoxidase (MAO) activity in brain tissue. The MAO activity in the hypothalamus (Ht) of untreated rats changed cyclically during the estrus cycle. Highest levels occurred at 10 A.M. on the day of proestrus (P) and at 10 A.M. and 2-3 P.M. on the day of estrus (E). Lowest levels in MAO activity occurred at 6-7 P.M. on the day of P during metestrus and diestrus (D). The amygdala (Am) showed cyclic activity which followed the pattern of the Ht, but was less marked. Frontal and lateral brain cortex possessed much lower levels of MAO activity and showed no cyclic changes. Plasma levels of E_2 rise in the morning of the day of P reaching the peak at noon of the same day. Elevations in E_2 always preceeded well known gonadotopin surge in the afternoon of the day of P. Administration of α-MT, an inhibitor of catecholamine (CA) synthesis, in the morning or afternoon in the day of D, prior to the day of P, effectively inhibited the P rise in plasma E_2, abolished cyclic changes in MAO activity in Ht and Am during the day of P, and prevented P surge of gonadotropins. These results suggest that CA are involved in regulation of secretion of gonadotropins and gonadotropin releasing hormones. In addition, these studies indicate that effect of α-MT is exerted via mechanism(s) which is linked to the ovarian estrogen secretion. (Supported by GRS grant RR05551 from N.I.H.).

EFFECT OF PRE-INSPIRATORY LUNG VOLUME ON CLOSING VOLUME BY THE NITROGEN METHOD. K. Kaneko*, J. Mohler* and O. Balchum. LAC/USC Medical Center, Los Angeles, Calif.

Recently, by adding a deadspace prior to inspiration of O_2, that is, by increasing the pre-inspiratory lung volume, Mansell, et al. (J. Appl. Physiol. 33:6, 1972) were able to detect the measurable closing volume (CV) in children, which were previously undetectable by the "original N_2 method" (Resp. Physiol. 8:58, 1969/70). Yet its theoretical explanation has not been clarified. In the present investigation, the effect of the pre-inspiratory lung volume on CV was studied in simulated CV determination with a lung model and also in two normal subjects. Both studies supported our hypothesis that inspiration of O_2 initiated at the "closing capacity" (CV+RV) would improve the resolution of the inflection point between Phases III and IV (Resp. Physiol. 2:234, 1967). In practice, the modification can simply be made by adding a deadspace with its capacity equal to CV (600-700 ml in adults) between the O_2 bag and mouthpiece (modified N_2 method). The lung model analysis further indicated that if the inflection point were located by extrapolating the terminal portion of Phase IV, then the original N_2 method could underestimate CV systematically as much as five percent VC, because of the relatively small rise in N_2 concentration at the beginning of Phase IV. Conversely, the value obtained by the modified N_2 method should be reasonably close to the value obtained by the "tracer gas method" (J. Appl. Physiol. 28:448, 1970; J. Clin. Invest. 47:81, 1968).

DIRECT EFFECT OF TESTOSTERONE (T) AND ITS METABOLITES ON PITUITARY (AP) LH AND FSH RELEASE IN VITRO: CHANGE IN PITUITARY RESPONSIVENESS TO STALK MEDIAN EMINENCE EXTRACT (SME). Lidia W. Liu Kao and Judith Weisz (intr. by C. W. Lloyd). Div. Reprod. Biol., Dept. of Ob-Gyn, M. S. Hershey Med. Center, Hershey, Pa.

The effects of T, dihydrotestosterone (DHT), 5α-androstane-3α, 17β-diol (3α-Adiol), & its 3β isomer (3β-Adiol) on SME induced LH & FSH release by AP in vitro were studied using a continuous flow incubation (perifusion) system. Four hemi-pituitaries were incubated at 37°C. Buffered medium 199 was infused continuously at a rate of 12 ml/hr. LH & FSH were measured by radioimmunoassay in 10 min collections of effluent. In this system repeated 10 min pulses of SME during a period up to 12 hrs produce rapid and reproductible release of LH & FSH & the output of LH & FSH is proportional to the log dose of SME from 1/4 to 8 SME/pulse. After 1-1/2 hr preincubation, two successive identical test pulses of SME were administered. Then T or its metabolites (0.1 µg/0.1 µg ml or 1 µg/ml) was added to the medium & the responsiveness of AP to the test pulses of SME was re-examined at hourly intervals. DHT caused first an augmentation of FSH & LH output in response to test pulses of SME (150-210% of control) then a suppression (40-90% of control) T and 3α or 3β-Adiol also caused an initial augmentation of LH output but predominantly a suppression of FSH output. Within 2 hrs after withdrawal of the steroids LH release in response to the test pulses of SME returned to control values while FSH tended to remain low. The results indicate both positive & negative feedback action of androgens on the AP with the different metabolites having different effects. These effects were not seen when epitestosterone was used. The findings contrast with those previously reported for estradiol which caused first a suppression & then augmentation of SME induced GTH release.

RETICULOENDOTHELIAL RESPONSE TO INJURY IN ADRENALECTOMIZED RATS. John E. Kaplan,* Thomas M. Saba, and William A. Scovill.* Dept. of Physiology, Albany Medical College, Albany, N. Y. 12208.

Failure of the reticuloendothelial system (RES) mediated by hypoopsonemia following surgical trauma has been previously demonstrated (Surgery 71:675, 1972). In the present study, the potential role of an adrenal response following trauma in the etiology of this RE depression was investigated. RE function was determined by the vascular clearance of an ^{131}I test colloid (50 mg/100 g) and opsonin levels were evaluated by isotopic bioassay. The standardized trauma consisted of a sterile 5 cm laparotomy with jejunal enterotomy under light ether anesthesia. In contrast to a control pre-surgery clearance half-time of 10.13 $\pm$ 1.7 min, the clearance was maximally depressed ($p < .01$) by 60 min post-surgery. Early RE depression was followed by RE hyperactivity at 24 hr post-surgery. Opsonin levels abruptly decreased ($p < .01$) 70-75% by 30-60 min post-trauma. While the trauma induced RE clearance depression was primarily reflected in a hepatic phagocytic failure, livers from traumatized animals manifested normal colloid phagocytosis in the presence of normal pre-surgery plasma. Sham-adrenalectomized and adrenalectomized rats manifested comparable states of opsonic and phagocytic depression following subsequent standardized trauma. With the use of ^{125}I purified opsonic protein (80 µg/rat), which is an alpha-2-globulin, it was demonstrated that plasma opsonic protein sequestration at the site of tissue injury was initiating the rapid post-injury hypoopsonemia. While the data demonstrate that an adrenal response to trauma is not critical in the post-injury RE depression, the findings suggest that opsonic protein administration during surgery may circumvent the post-surgical RE failure (USPHS AM-14382).

REFLEX BRADYCARDIA DUE TO AORTIC NERVE STIMULATION IN ONE R-R INTERVAL. Merrill B. Kardon*, D. Fred Peterson and Vernon S. Bishop. The University of Texas Medical School at San Antonio, San Antonio, Texas.

The central end of the cut left aortic nerve was stimulated electrically in 17 rabbits to determine the response to a single burst of impulses within one cardiac cycle. Stimulus pulse number, stimulus burst frequency and stimulus burst duration were each held constant while the other two parameters were varied. A PDP-8 digital computer was used "on-line" to determine average responses to 10 successive trials. All stimulations were performed using supramaximal intensity for the rabbit aortic nerve; 10 volts, 0.3 msec. A single burst of 10 pulses at 80/sec caused an 8.4 $\pm$ 0.3 b/min (SEM) decrease in heart rate. No significant differences were found to depend upon location of the stimulus burst within the R-R interval. Beat interval began to lengthen within 2 beats after the stimulus burst. Peak response was reached between the 7th and 10th beat after the stimulus burst, then gradually returned toward the control value. Holding burst frequency constant at 80/sec an increase in pulse number from 5 to 10 caused a 70% increase in the reflex response. While burst duration was constant at 125 msec, increasing burst frequency from 80/sec to 160/sec caused a 93% increase in the peak response. With pulse number constant at 10, increasing pulse frequency from 80/sec to 160/sec caused a 29% decrease in the peak bradycardia. These results indicate that reflex bradycardia can be produced by changes in aortic nerve activity in one R-R interval and that total pulse number is the primary determinant of the degree of response. This work supported in part by NIH #2 R01 HL12415-05, AFOSR-71-2074 and the San Antonio Heart Association.

SEGMENTAL SUPERSENSITIVITY OF THE REINNERVATING HEART. M.P. Kaye, W.P. Geis, G.R. Hageman*, W.C. Randall, and D.V. Priola. Dept. of Physiology Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Little is known concerning the alterations in norepinephrine (NE) sensitivity of the myocardium during the dynamic processes of adrenergic cardiac reinnervation. Twenty five dogs were subjected to cardiac denervation and acutely studied at intervals from 5 days to 26 months. During acute studies, strain gauge arches recorded myocardial contractile force on right (RA) and left atria, (LA) left ventricular base and apex, and right ventricular sinus and conus. The stellate ganglia were electrically stimulated and graded doses of NE and tyramine were administered. Tissue samples from beneath the strain gauge placements were analyzed for catecholamine content. Generally at four months post-denervation, LA inotropic supersensitivity was absent and was accompanied by functional and pharmacological evidence of adrenergic reinnervation. Ventricular supersensitivity to NE was present with no evidence of reinnervation of this tissue. At six to eight months, left stellate stimulation resulted in a normal inotropic response of not only the left atrium but also the left ventricular base. Tyramine infusion demonstrated release of neurotransmitter from both areas. NE (0.1µg total dose) caused marked inotropic response of the LV apex with no response in LA or LV base. Functional evidence for reinnervation of LA seemed to correlate with rising LA catechol content. In contrast, functional reinnervation of ventricular myocardium occurred in the absence of rising levels of tissue catecholamines. These data elucidate segmental myocardial supersensitivity to NE which is sequentially reversed during progressive adrenergic reinnervation. Further, they strongly suggest that the labile Tyramine releasable pool, although small, is restored and accounts for functional reinnervation. (Supported by NIH Grants HL 08682 and GM 999.)

OXYGEN CONSUMPTION ($\dot{V}_{O_2}$) IN THE UNIFORMLY COOLED DOG. Barbara B. Kent* and E. Converse Peirce II. Depts Surgery, Mount Sinai School of Medicine and Bronx Veterans Administration Hospital, New York.

Accurate Q_{10} for $\dot{V}_{O_2}$ during hypothermia has not been available for large animals because usual methods of cooling (immersion or perfusion alone) produce large temperature gradients and no measureable temperature is available for reference. $\dot{V}_{O_2}$ was measured in dogs uniformly cooled by combined immersion and perfusion. Eleven mongrel dogs (14 $\pm$ 2 kg), anesthetized (α-chlorolose, 80mg/kg), heparinized (200u/kg) and cannulated for total cardiopulmonary bypass following ventricular fibrillation were perfused by an extracorporeal circuit which included a 1M^2 G.E. - Peirce membrane lung. The dogs were cooled by total body perfusion with cold blood and by simultaneous surface cooling with a cold water spray to 30, 25, 20, 15, and 10°C (1 hr at each level). Arterial and venous O_2 content was determined by a Lex-O_2-con oxygen analyzer. $\dot{V}_{O_2}$ was calculated as the product of extracorporeal circuit flow times arteriovenous (A-V) O_2 difference. With combined immersion-perfusion cooling, temperature gradients within the body at each level of hypothermia are less than 1°C. Esophageal temperature (T_E) remains within $\pm$1 S.D. of the mean of temperatures measured at 13 anatomical sites. A least squares fit of the relationship between $\dot{V}_{O_2}$ and T_E to the Arrhenius semi-log model is as follows: $Y=0.3835+0.0446X+0.1158$ (SSE), when $Y=\log(((\dot{V}_{O_2}$ at $T_E)/(\dot{V}_{O_2}$ at 37°C))x100) and $X=T_E$°C. The Q_{10} is 2.8. The fraction of $\dot{V}_{O_2}$ in the form of dissolved O_2 increases from less than 2% at 37°C to 9% at 10°C. The A-V difference in hemoglobin saturation falls from 22.1% at 37°C to 0.1% (N.S.) at 10°C as the p50 of the O_2 dissociation curve falls from 1?.7 to 5.8 Torr. By using combined immersion and perfusion, dogs can be brought to successive series of uniform temperatures. When uniform temperature is maintained throughout the body, $\dot{V}_{O_2}$ is meaningful, predictable and accurately described by the Van't Hoff-Arrhenius relationship.

PROSTAGLANDIN DEPENDENT CORONARY VASODILATOR RESPONSES. Kenneth M. Kent, R. Wayne Alexander*, John J. Pisano*, Harry R. Keiser* and Theodore Cooper. National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland.

Prostaglandins have been demonstrated to be important substances in the regulation of blood flow in several organs including the kidney and adipose tissue. The purpose of the present experiments was to evaluate the role of endogenous prostaglandin synthesis in the regulation of coronary blood flow (CBF). The left main coronary artery was cannulated and total left CBF was measured in 5 intact dogs and 6 canine heart-lung preparations. Coronary vasodilatation was elicited by left main coronary occlusion of 10, 15 and 20 seconds (reactive hyperemia) and by decreasing the inspiratory O_2 tension (hypoxia) before and after blockade of prostaglandin synthetase by indomethacin (IND) or meclofenamate (MEC). Both drugs caused a marked reduction in the vasodilator responses to reactive hyperemia and to hypoxia. In addition, in the heart-lung preparations there was a progressive increase in CBF during the testing procedures. This increase in blood flow was accompanied by an increase in prostaglandin E in the coronary sinus blood but no change in myocardial O_2 consumption. After IND or MEC the CBF decreased to control levels and the concentration of prostaglandin E decreased in the coronary sinus. Therefore endogenous prostaglandin synthesis appears to be important in the regulation of CBF and there is a prostaglandin dependent stress induced vasodilator system in canine hearts.

CHANGES OF ABNORMAL SEGMENTAL MOTION OF ACUTELY INFARCTED MYOCARDIUM IN RESPONSE TO POSITIVE INOTROPIC AGENTS. Richard E. Kerber* and Francois M. Abboud. Cardiovascular Division, University of Iowa and Veterans Administration Hospitals, Iowa City, Iowa.

Previous studies have suggested that positive inotropic agents may worsen aneurysmal bulging of acutely infarcted myocardium. We tested this hypothesis by producing true posterior wall infarction by coronary ligation in open-chest anesthetized dogs. Ultrasound recordings obtained by direct reflection off the infarcted posterior wall revealed characteristic dyskinesis: aneurysmal bulging during isometric contraction and markedly reduced posterior wall velocity (PWV) and excursion (PWE) during ventricular ejection. Isoproterenol (I), Norepinephrine (N), Ouabain (O) and Glucagon (G) were then administered intravenously in graded doses. Increased aneurysmal bulging during the isometric contraction phase was produced (I=O>G>N), but during ventricular ejection significant improvements in PWV and PWE occurred: (I>G>O>N). I and G returned PWV to control levels. Simultaneous hemodynamic measurements showed the drugs also caused improvement in cardiac output (I=G>O=N) and left ventricular dp/dt (I>G>N). Increasing the heart rate by atrial pacing did not produce similar improvement in ultrasound or hemodynamic parameters, indicating that the drug-induced changes were not due to tachycardia alone.

Inotropic agents thus do increase the aneurysmal bulging of infarcted myocardium. However, this effect is limited to the isometric contraction phase and is accompanied by improved wall velocity during the phase of ventricular ejection, which contributes to the observed improvement in simultaneously measured cardiac output and dp/dt. Acutely ischemic myocardium retains the capacity to respond to pharmacologic stimuli.

EFFECT OF HEAT ACCLIMATION (32°C) ON RAT LIVER AND BRAIN SUBSTRATE LEVELS. J.S. Kerr*, R.L. Squibb* and H.M. Frankel. Dept. of Physiol. and Bur. Biol. Res., Rutgers Univ., New Brunswick, New Jersey 08903.

Liver and brain tissue substrate levels were determined in female rats maintained at T_e of either 26 or 32°C for 30 to 45 days. Brain aspartic, citric, glutamic, α-ketoglutaric and malic acids, NAD^+, NADH and glutamic, lactic and malic dehydrogenase were determined in tissue samples removed within 15 seconds, frozen and maintained in liquid N_2. The same procedures and determinations were used for liver tissue. In addition, liver $NADP^+$, NADPH, mono-, di- and triglycerides, cholesterol and free fatty acids were determined on samples held at -5°C until assayed. It was observed during exposure at 32°C that the activity level of the animal and its food intake were decreased. On autopsy, total liver weight was less in the heat acclimated group. Heat acclimation did not change tissue substrate levels significantly ($p < 0.01$) except for a decrease in liver glutamate (253 vs 216 μg/gm tissue) and brain malate concentrations (74 vs 56 μg/gm tissue). Dietary habit rather than temperature, per se, may have accounted for the observed changes in mild heat acclimation stress.

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MEASUREMENT OF THE SPONTANEOUS ACTIVITY OF URINARY BLADDER MUSCLE IN RESPONSE TO URECHOLINE USING A DIGITAL COMPUTER George F. Keyser* and Peregrina Labay. Washington University, St. Louis, Missouri

When 5mm x 0.5mm strips of detrusor muscle from the urinary bladder of rabbit are suspended and stretched in an organ bath from an isometric force transducer, rhythmic contractions ensue. Urecholine, a drug long used to combat bladder atony profoundly affects the frequency, magnitude, and uniformity of contractions. Ten to fifteen-minute lengths of the rhythmic activity in response to known concentrations of Urecholine were recorded on magnetic tape. This data was subsequently converted and analyzed by a LINC computer to yield three characterizing parameters: (1) mean tension, $\bar{X}$; (2) average force of contractions about the mean tension, $\bar{D}$; (3) frequency of contractions, f. At Urecholine concentrations from $3x10^{-7}$M to $3x10^{-5}$M, f and $\bar{X}$ rose monotonically from 6±1 cycles/min. and 0.08±0.04 grams to 19±6 cycles/min. and 0.65±0.35 grams respectively. In contrast, $\bar{D}$ rose to a peak in the vicinity of $3x10^{-6}$M or $6x10^{-6}$M and thereafter decreased with increasing concentrations. Over the recording period, the parameters were uniform when the concentration was $6x10^{-6}$M or less whereas at higher concentrations they became erratic and nonstationary in time. The results at the lower concentrations show the existence of a functional steady state between tissue and bath environment.

ESTROGEN BINDING PROTEIN IN BOVINE ENDOMETRIUM AND CORPUS LUTEUM DURING THE ESTROUS CYCLE. Frances A. Kimball* and William Hansel, Dept. of An. Sci., Cornell University, Ithaca, N.Y. 14850

Estrogen binding by endometrial and luteal cytosol protein was determined by a dextran-charcoal adsorption method and correlated with plasma hormone levels in the same animals. The cytosol preparations of both tissues were saturable and demonstrated high affinity (10^{-9}M) for estradiol. Both were specific for estradiol-17B when centrifuged in a 5-20% linear sucrose gradient. Inhibition of endometrial protein binding of ^{3}H-estradiol-17B was obtained with estradiol-17B> , estrone > , estradiol-17< > , diethylstilbestrol at 0°C. The luteal protein binding could be inhibited with estradiol-17B> estrone. The concentration (pmole/mg protein) of endometrial estrogen binding protein increased ($p < .025$) between the 15th and 21st days of the estrous cycle when compared to the 2nd, 5th and 10th days. The concentration of day 15 binding protein was highly correlated with the estradiol-17B and estrone plasma levels found at that time ($p < .01$). The surge of plasma estrone at day 10 may increase cellular activity in the endometrium, stimulating induction of new estrogen binding protein. The concentration of luteal estrogen binding protein increased from day 5 to day 10 ($p < .01$) and remained at this level through day 15. There was a significant decline in binding protein concentration at day 17-18, at the initiation of luteal regression. The concentration of binding protein at day 21 was higher than at any other time during the cycle. Luteal estrogen binding protein concentration reached a maximum in the presence of high plasma progesterone and estrone levels. Plasma progesterone and estrone levels declined at day 17-18 while plasma estradiol levels increased. This specific luteal estrogen binding protein may be important in the initiation of luteolysis in the cow.

EXERCISE PERFORMANCE OF RATS IN LONG DURATION SWIMMING. Nancy W. King*, Edward L. Hunt*, and Richard D. Phillips. Battelle, Pacific Northwest Laboratories, Richland, WA.

A fully automated swim alley was devised for continuously testing rats' exercise performance in long duration swimming sessions. Swimming speed was measured on repetitive traverses in a 6-m alley. After the rats had been appropriately trained, they performed reliably and their speed scores were highly predictable.

Experiments were conducted to determine the conditions necessary for optimum performance. Swimming speed was measured during a 3-hr test session at water temperatures of 19°, 22°, and 24°. Water at the colder temperatures motivated the rats to swim faster initially. The long term effect of colder water was to decrease swimming speed, and at the coldest temperature, the animals were unable to complete the session.

The rest interval between traverses was also varied. Swimming speed was measured for 3 hrs using a rest interval of 10, 17, 34, or 51 sec. Trained rats would not reliably perform the task with a 10-sec rest interval, indicating a lack of motivation to complete the traverse. With the other three rest intervals, increasing rest time led to faster swimming. However, with longer rest intervals, the animals spent less time swimming and fewer traverses were completed during the test.

With the selection of appropriate water temperatures and rest times, rats will swim reliably for 13- and even 24-hr sessions. The use of this technique can provide a measure of both immediate and prolonged effects of experimental variables on performance and capacity.

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THE RADIOIMMUNOASSAY OF PULMONARY SURFACE ACTIVE MATERIAL IN SHEEP LUNG.
Richard J. King*, Elias Gikas*, John Ruch* and John A. Clements+.
Cardiovascular Research Institute, Univ. of Calif., San Francisco, CA.

We have developed a radioimmunoassay for pulmonary surfactant capable of detecting 1 to 10 picomoles of surfactant apoprotein. The procedure is based upon the "sandwich" technique developed by Salmon et al. (J. Immunol. 103: 129, 1969) and is carried out as follows. Polystyrene tubes are coated with antiserum directed against pulmonary surfactant purified from sheep endobronchial lavage fluid. Samples of lung homogenate, unfractionated endobronchial lavage fluid, or purified surface active material are incubated in these tubes for 12 to 18 hours at 37°C. 3,000 to 5,000 CPM of surfactant apoprotein, labelled with $Na^{125}I$, are added to each tube, and the tubes are incubated for an additional 3 hours. The tubes are removed from the 37°C water bath, washed three times with distilled water, and the bound radioactivity is counted in a scintillation spectrophotometer. The amount of antigen in the sample can be calculated from the amount of ^{125}I-antigen bound to the polystyrene tubes, and is dependent upon the competition for antibody binding sites between the antigen in the sample and the added antigen labelled with $Na^{125}I$. The assay is specific for the apoprotein isolated with pulmonary surfactant, and is not affected by added lipid or serum. Because of its sensitivity, the assay should be useful for estimating the amount of surfactant in preparations of isolated cells; in lung fluids where surfactant concentration is low, such as tracheal or amniotic fluids; or in very small amounts of lung tissue, such as might be harvested by biopsy techniques.

+ Career Investigator, American Heart Association.
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EFFECTS OF AHR-2666 ON FROG SKELETAL MUSCLE.
E.B. Kirsten and K.C. Lustig*. Columbia Univ., College of Physicians and Surgeons, New York, N.Y. 10032.

AHR-2666 is a substituted phenoxypyrrolidine with both central and peripheral muscle relaxant effects (Johnson et al., Fed. Proc. 31:535, 1972). When studied on sartorius muscle, AHR-2666 produces a dose-related, reversible decline in isometric twitch tension. Following a 30 min pretreatment with AHR-2666 (1.0 mM) both the potassium contracture and the rigor induced by 10 mM caffeine are blocked. The Ca-45 efflux produced by 10mM caffeine is also blocked by 1.0 mM AHR-2666; higher concentrations of caffeine are less completely blocked. By itself, the drug has no effect on either the uptake or release of Ca-45 from resting muscle. Electrical studies indicate that the transmembrane potential is uneffected by AHR-2666 although the action potential is depressed. The data indicates that the peripheral muscle relaxant effects of AHR-2666 are due to a local anesthetic mechanism.
(Supported in part by NIH Grant HL-12738).

EFFECTS OF THE CALCIUM IONOPHORE, X-537A, ON QUANTAL ACH RELEASE AT THE FROG NEUROMUSCULAR JUNCTION. H. Kita* and W. Van der Kloot. SUNY at Stony Brook.

The antibiotic X-537A selectively binds divalent cations and is lipid soluble, so it can carry the ions across biological membranes (B.C. Pressman, Ann. NY.Acad Sci. 147;753, 1971). Increases in the rate of quantal release at the neuromuscular junction are thought to be triggered by the entry of Ca^{++} into the terminals. Therefore we have studied the effects of X-537A by recording min.e.p.p.s with an intracellular electrode. In some preparations 10 μM X-537A increases the min.e.p.p. frequency. In almost all preparations 20 μM X-537A raises the min.e.p.p. frequency and the increases are often substantial: for example from 0.46/sec to 116/sec. The rise in frequency begins as the drug-containing Ringer is flowing into the chamber. The increase is always transient. Usually after five minutes the min.e.p.p. frequency is below the pre-treatment level. A second treatment with X-537A at the same concentration does not cause an increase in frequency. Following treatment with the antibiotic, the amplitude of the min.e.p.p.s. may be somewhat reduced, we are not yet certain whether this effect is pre- or post- synaptic. Therefore the preliminary results suggest that X-537A carries Ca^{++} into the nerve terminals and that the entering Ca elicits a greatly enhanced quantal release. There is not enough data to decide whether the transitory effect is owing to depletion of available quanta or to some other action of the drug. After the period of rapid release, stimulation of the nerve still causes a contraction of the muscle. The threshold concentration of X-537A required to accelerate min.e.p.p. release seems to be lower in Sr^{++} Ringer than in Ca^{++} Ringer.

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DISSOCIATION OF PLASMA VOLUME FROM REGULATION OF PROXIMAL REABSORPTION. Franklyn G. Knox, Edward G. Schneider, L.R. Willis*, Jack W. Strandhoy*, Cobern E. Ott*, Dept. of Physiology, Mayo Clinic, Rochester, MN

Preferential expansion of the plasma volume by infusion of salt-poor hyperoncotic albumin solution decreases sodium reabsorption by the proximal tubule. The present micropuncture studies test the thesis that albumin infusion depresses proximal reabsorption by an effect unrelated to expansion of the plasma volume, perhaps due to an effect of parathyroid hormone (PTH) on proximal sodium reabsorption. Salt-poor hyperoncotic albumin was found to bind sufficient calcium to provide a stimulus for PTH release. In the absence of the control of PTH release, albumin infusion resulted in significant decreases in sodium reabsorption by the proximal tubule ($-9.2 \pm 1.7\%$ $p < .001$) in 12 dogs. In contrast, in 12 parathyroidectomized dogs given a constant infusion of PTH, albumin infusion had no significant effect on proximal reabsorption ($-0.2 \pm 1.5\%$). Similarly, infusion of albumin, in which the ionized calcium was restored to normal plasma levels, had no significant effect on proximal reabsorption in 7 intact dogs ($-1.3 \pm 3.2\%$). Single nephron and kidney filtration rates were not significantly changed following albumin infusion in any group and therefore absolute reabsorption changed in parallel with fractional reabsorption. Plasma volume was expanded $54 \pm 5\%$, $P < .001$ in dogs without control of PTH and $49 \pm 4\%$, $P < .001$, in dogs with control of PTH. Efferent arteriolar protein concentration was not significantly changed in any group indicating that differences in proximal reabsorption were not due to altered peritubule Starling forces. These findings suggest that PTH may play a significant role in the decrease in proximal reabsorption following salt-poor hyperoncotic albumin infusion and clearly dissociate changes in plasma volume from changes in sodium reabsorption by the proximal tubule.

THE EFFECT OF CARDIAC ANTISERA ON THE PERFORMANCE OF PAPILLARY MUSCLE.
M.M. Knudson,* T. Rogers,* P.K. Bajpai. Univ of Dayton, Dayton,Ohio.

Cardiac antibodies play a role in rejection of heart transplants as well as in some coronary diseases. Experiments were designed to observe the effect of antisera developed against rabbit heart muscle on the in vitro performance of rabbit papillary muscle. The antisera was prepared by immunizing guinea pigs with heart muscle extract in Freund's complete adjuvant as well as polyuridine and polyadenine nucleotide adjuvants. After the papillary muscle developed its maximum force of contraction (120 mins) in oxygenated Krebs-Ringer's solution the muscle was exposed to fresh Krebs-Ringer's solution or 10% normal sera or 10% to 20% antisera. Addition of fresh Krebs-Ringer's solution increased both force and duration of contraction. Normal sera (10%) caused an increase in force of contraction. Antisera (10% and 20%) produced with Freund's adjuvant decreased the duration of contraction whereas antisera produced with the aid of polynucleotide adjuvants decreased both force and duration of contraction. In our opinion the above effect of the cardiac antibodies is due to their interference with the calcium binding and release mechanism of the contractile system. (Supported by the Miami Valley Chapter of The American Heart Association).

DIMENSIONS OF CARDIAC MUSCLE CELLS DURING THE LIFE SPAN OF RAT.
B.Korecky, K.Rakusan, Dept. of Physiology, Univ. of Ottawa, Canada.

Rat hearts were perfused on a Langendorf preparation with Ca^{++} free Krebs-Ringer bicarbonate solution (KRB) containing 0.1% hyaluronidase and 0.05% collagenase at 36°C for 40 min. at pH 7.4. The free wall of the left ventricle (LV) was then separated, cut into small pieces and incubated in KRB for 5-10 min, with constant stirring. The length and width of "undamaged" individual cardiac muscle cells (20-50% of the final yield) were measured in a chamber under a phase contrast microscope. Only cells with identifiable sarcolema and with distinct cross-striation were considered. Four age groups of normal male Sprague-Dawley rats were investigated: young (mean body weight 82g), young adults (160g) adults (366g) and old (648g). The corresponding average cell lengths were 80,85,103 and 128μ , the average widths 15.2, 16.7, 20.5 and 25.1μ . The length to width ratio remained constant in all groups. The average estimated cell volume using cylindrical model was 15.2, 19.7, 35.6 and $67.2\mu^3 x10^3$, all the successive groups being significantly different. The ratio between the % increase in the cell volume to the corresponding % increase in LV mass changes with age; from young to young adults is .46, from young adults to adults is .94, from adults to old rats is 1.66. This may indicate some hyperplasia in the early stage and some numerical atrophy in the latest stage assuming constancy of extracellular space and of proportion of cardiac to non cardiac muscle cells.
(Supported by the Ontario Heart Foundation and MRC of Canada)

ACTION OF IMIDAZOLE AND 2-METHYL IMIDAZOLE ON FROG MUSCLE EXCITABILITY AND CONTRACTION. Zofia Korsak*[1] and Richard S. Tuttle. Masonic Medical Research Laboratory, Utica, N.Y.

Imidazole (I) and 2-methyl imidazole (2 MI) in concentrations of 10^{-2} molar can increase the force of contraction of frog skeletal muscle by up to 50%. The effect of 2 MI is of somewhat lesser magnitude and slower in appearance. In an attempt to relate changes in contraction to changes in excitability, the muscle action, end plate and single fiber potentials were recorded during exposure to I and 2 MI. Using preparations similar to those of del Castillo and Engbaek (J. Physiol. 124:370-384, 1954) and standard intracellular techniques, we were able to show that I and 2 MI increased the muscle action potential from 100 to 200%, developing in the same time course as the contractility changes. The effects on muscle action potential were most pronounced at subthreshold and threshold stimulus voltages. The single fiber action potential was not significantly modified by either drug. We suggest that imidazole may possibly increase the receptor sensitivity to acetylcholine.

1. Olsen Memorial Fellow

SPINAL TRACT TRANSECTIONS AND THE LORDOSIS REFLEX IN FEMALE RATS. L.-M. Kow* and D. W. Pfaff. The Rockefeller Univ., New York, N. Y.

Somatosensory stimulation on certain parts of the rear body surface can trigger the lordosis mating reflex in the estrous female rat. To localize ascending somatosensory pathways mediating lordosis, we have conducted a systematic study of spinal tract transections. Transections were done under direct visual control at the lower thoracic level of the spinal cord of ovariectomized female rats brought into estrus by estrogen treatment. Rats were tested for lordosis in response to mounting by male rats or to manual stimulation before and after transections of the dorsal columns, dorsolateral columns, combined dorsal and dorsolateral columns, or anterolateral columns. Transections were confirmed by histological examination. Before surgery, all rats performed lordosis in response to both the male rat and to manual stimulation. After a postoperative recovery period, rats with dorsal column, dorsolateral column or combined dorsal and dorsolateral column transections still performed lordoses in response to the male rat or to manual stimulation. However, in 4 rats with anterolateral column transections, the lordosis reflex was abolished or reduced in intensity. In these 4 rats, signs of general motor deficits were also observed. The results suggest that sensory information carried by the dorsal and dorsolateral columns is not necessary for lordosis, and conversely that information carried by sensory fibers located in the anterolateral columns of the spinal cord is sufficient for triggering the lordosis reflex in the female rat. (Supported by NIH grant HD-05751.)

SINOAORTIC REFLEXES AND THE CUSHING RESPONSE. J.A. Krasney, M.G. Levitzky*, and R.C. Koehler* Dept. Physiol., Albany Medical College.

Elevation of intracranial pressure (ICP) elicits a bradycardia and a pressor response (Cushing response). The bradycardia may be reflexly mediated by the arterial baroreceptors secondary to the rise in arterial pressure, or it could be caused by ischemia or pressure/stretch of CNS centers controlling heart rate. Accordingly, graded 60-sec elevations of ICP were produced by injecting saline into the epidural space in 8 dogs anesthetized with morphine and chloralose. Cerebral perfusion pressure (CPP) was estimated by subtracting the ICP from the dog's control arterial pressure. Reduction of CPP to levels of 30 mm Hg, 20 mm Hg, and 10 mm Hg caused heart rate to decline significantly by 34, 30, and 33 beats/min, respectively, from heart rates averaging 82 beats/min (±5.6 SE). With sustained elevation of ICP, a significant bradycardia of lesser degree persisted. Arterial pressure was not altered until CPP's in the negative range were produced. Subsequently, the buffer nerves were sectioned by a technic which leaves vagal efferents intact. When CPP was again reduced to 30, 20, and 10 mm Hg, an initial bradycardia was still observed of 40, 24, and 47 beats/min, respectively, from control levels of 193 beats/min (±8.4). Significant increases in arterial pressure now occurred each time CPP was reduced, and with this increase in pressure heart rates returned to control levels. These results indicate that sinoaortic reflexes act to minimize the tendency for arterial pressure to rise during periods of reduced CPP. Since bradycardia occurred in the absence of arterial pressure changes in the intact situation and occurred only transiently after denervation, disappearing as arterial pressure rose, it appears that the mechanism responsible for the bradycardia component of the Cushing response is largely independent of sinoaortic influences. (Supported by NIH grant HL-11982).

FREQUENCY CONTENT OF INTRAVASCULAR AND INTRACARDIAC PRESSURES AND THEIR TIME DERIVATIVES. L. Jerome Krovetz and Stephen D. Goldbloom.* The Johns Hopkins University School of Medicine, Baltimore, Md.

Accurate recording of intravascular and intracardiac pressure requires knowledge of the frequency content of these pulses before one can specify recording systems needs. Catheter-tip manometers provide high-fidelity responses well beyond physiologic requirements but they are expensive, fragile and difficult to calibrate. Frequency response of commonly employed fluid-filled catheter systems is often too low to record details of the pressure waves. For this study, pressures obtained by catheter-tip manometers were recorded on magnetic tape. Fourier analysis of 72 representative tracings was performed using a Varian 620/L minicomputer. Pressure waveforms were then resynthesized using varying numbers of harmonics and compared to original waveforms. As the number of harmonics utilized decreases, the curve becomes progressively smoother but it is difficult to decide when increasing smoothness represents elimination of noise rather than loss of signal. Therefore, significant changes were defined as exceeding 1) 2% for systolic pressure, 2) 5% for pulse pressure, and 3) 10% for peak dp/dt. The atria require the highest, an average of 15 harmonics, while the iliac artery required only 3. For each site, dp/dt requires about 6x the harmonics. There was wide variation at each site; e.g., brachial artery recordings needed from 5-19 Hz for pulse pressure and from 16-51 Hz for dp/dt. Analysis of 164 conventional catheter setups showed that only 8% were capable of measuring dp/dt accurately. Slight changes in frequency response or heart rate may produce significant changes in measured peak dp/dt. Frequency response of catheter-manometer systems should be measured at least once during every experiment or catheterization, since frequent measurement often leads to improvement of the system through more careful attention to details of assembly and connection.

MODULATION OF CAROTID SINUS BARORECEPTOR REFLEX BY STIMULATION OF HYPOTHALAMIC DEFENSE AREA. M.Kumada, L.P.Schramm, R.A.Altmansberger*, K. Sagawa. Dept.Biomed.Engineering, Johns Hopkins Univ., School of Med., Baltimore, Maryland

In anesthetized and vagotomized dogs relationships between intrasinus pressure (ISP) and various cardiovascular responses were compared, with an aid of curve-fitting, before and during stimulation of the defense area within the lateral hypothalamus (HT stimulation). HT stimulation increased the slope (or gain) of the ISP-arterial pressure (AP) curve at ISPs between 150 and 240 mmHg. Stimulation raised the equilibrium point (the value of ISP at which ISP equaled AP) from 146 to 163 mmHg. It also raised both the maximum gain (by 15%) and the ISP at which maximum gain was achieved from 152 to 162 mmHg. Thus, HT stimulation modulated the reflex such that disturbances of AP could be buffered more effectively about an elevated AP level. Modulation of the reflex response of AP was ascribed largely to that of total peripheral resistance. There was no positive evidence for participation of cardiac output in the modulation of the gain. For the purpose of comparing modulatory effects on different vascular beds we obtained an index which reflected alterations in reflex response of arterial resistance (AR) by HT stimulation. The index was less subject to experimental variations in strength of HT stimulation or briskness of carotid sinus baroreceptor reflex. Comparison of the index of four vascular beds revealed that the hypothalamic modulation was exerted nonuniformly among these beds in the following order of intensity: renal > superior mesenteric > femoral (contralateral to HT stimulation) > femoral (ipsilateral to HT stimulation). Modulation of the reflex response of AP was thus the result of nonuniform modulation of AR in various vascular beds. (Supported by NIH Grant #1 ROl HL 15434-01).

HEMODYNAMIC EFFECTS OF METHYLPREDNISOLONE ON PULMONARY MICROCIRCULATION IN HYPOVOLEMIA. Katsuyuki Kusajima*, Watts R. Webb, Stennis D. Wax, Frederick B. Parker, Jr.*, I. Ayhan Ozdemir*
Department of Surgery, SUNY, Upstate Medical Center, Syracuse, N.Y. 13210

Hemorrhagic hypotension to 40 mmHg for two hours followed by reinfusion of the shed blood produces the full pathologic picture of congestive atelectasis. Studies in 12 control dogs of pressures in pulmonary artery (PA), pulmonary artery wedge (PAW), pulmonary vein wedge (PVW) small pulmonary vein (SPV), and left atrium (LA) showed the initial response to be SPV constriction and later alveolar capillary obstruction. Gradients developed between PAW and SPV and between PA & PV of about 5 mm Hg. Methyl prednisolone (MP) (30 mgm/Kg) given in mid shock in 18 dogs almost completely eliminated the gross & microscopic changes in the lungs. On reinfusion, arterial pressure rose to 90% of base line versus 70% in control ($p < .01$). The early rise in SPV was not seen and late gradients between PAW and SPV and between PA and PVW were reduced ($p < .01$). Other studies in 8 dogs each with diuretics (furosamide) and atropine showed no effect. These data demonstrate that MP protects the lung by reducing the SPV constriction and also the alveolar capillary blockage. (Supported by Heart Association Grants).

THE RELATION BETWEEN INITIAL CHEMICAL BREAKDOWN AND RECOVERY METABOLISM IN MUSCLE. M.J. Kushmerick and R.J. Paul*, Harvard Medical School, Boston, MA 02115.

We have reported at the spring meeting of this Society [Fed. Proc. 32, 346 Abs (1973)] that the relation between the high energy phosphate breakdown (Δ~P) and the recovery oxygen consumption (ΔO_2) was constant for isometric tetani of durations from 5 to 20 s in frog sartorius muscles at Lo at 0°C. ΔO_2 and Δ~P vs. the tension time integral ($\int$Pdt), scaled to a P/O of 2, were superimposable. Both relations were linear with statistically significant intercepts. The meaning of these intercepts is unclear and indicates either the presence of a reaction during contraction not proportional to $\int$Pdt, or a non-steady state actomyosin ATPase activity. For these reasons the relation between Δ~P and ΔO_2 for tetani of durations of less than 5 s were studied as a function of $\int$Pdt. Δ~P vs. $\int$Pdt was found to be curvilinear in the range of 1-5 s with the apparent ATPase rate during the maintained tetanus decreasing monotonically to a stable rate at 5 s. Experiments at the limit of resolution for single tetani indicate that the relation between ΔO_2 and $\int$Pdt in short tetani is similar to that of Δ~P. To help elucidate the nature of this region multiple tetani were studied. ΔO_2 was a function of the interval between tetani. This result suggests (1) an ATP requiring process other than actomyosin ATPase occurs during a brief (<5 s) tetanus and (2) a period without stimulation is required before that process can recur. (Supported by Massachusetts Heart Association #1104 and #1145-F and by Medical Foundation, Inc.)

THE IN VIVO EFFECT OF OZONE ON THE FORMATION AND RELEASE OF SURFACE ACTIVE LIPIDS FROM RABBIT LUNG. K. Kyei-Aboagye*, M. Hazucha*, I. Wyszogrodski*, D. Rubinstein* and M.E. Avery. Montreal Children's Hospital Res. Inst. and Depts. of Physiol. and Biochem., McGill Univ., Montreal, Canada.

In normal animals ten hours after i.v. injection of ^{14}C-palmitate and ^{3}H-oleate, the specific activities of ^{3}H and ^{14}C in the lecithins (PC) isolated from the lung tissue and the alveolar wash are in equilibrium and remain so for 30 hours. We investigated the effect of ambient ozone on the incorporation of ^{14}C-palmitate and ^{3}H-oleate into tissue PC and the appearance of labeled PC in the alveolar wash. Sixteen hours after the injection of the isotopes, rabbits exposed to 1 ppm ozone for four hours showed a significant decrease in incorporation of ^{3}H-oleate into lung tissue PC, while there was only a slight decrease in ^{14}C-palmitate incorporation, when compared to controls. However, the ratio of S.A. of wash PC to tissue PC increased significantly for both labels. The ^{3}H/^{14}C ratio decreased significantly in the tissue PC but remained the same in the alveolar wash PC. The above changes were accompanied by increased lung weight/body weight ratios. Furthermore, the absorption of lung tissue lipids at 235 mμ increased. This study demonstrates that, in vivo exposure to ozone for a short time causes, in addition to peroxidation of lipids and edema, decreased formation of tissue PC from fatty acids particularly oleate, and increased release of surface active lipids, without affecting the species of PC released.

A POSSIBLE MOLECULAR MECHANISM OF CAROTID CHEMORECEPTOR EXCITATION IN THE CAT. S. Lahiri and R.G. DeLaney*, Cardiovascular-Pulmonary Div., Dept. of Med. and Dept. of Physiol., University of Pennsylvania, Philadelphia, Pa.

As an oxygen receptor the first order of business for the carotid body is to recognize oxygen as a source of stimulus. The nature of this recognition function can be reflected in the activity of its single fibers. In order to explore the mechanism of this chemoreception, the steady-state effects on single fiber activity of various levels of PaO_2 (at constant levels of $PaCO_2$) were investigated in anesthetized cats. In all 24 units examined in 18 cats the activity was increased by low PaO_2. This response was enhanced by higher levels of $PaCO_2$. The relation between unit activity and PaO_2 resembled partly the oxygen equilibrium curve of hemoglobin with a distinct "Bohr effect", suggesting a conformational change at the receptor site as a basis of the regulation of response. Such a molecular change at the chemoreceptor site may very well be the first step which determines the stimulus response relationship between oxygen and carotid chemoreceptors, although the ultimate development of regenerator potential may involve several intermediate steps. (Supported in part by NIH grant HL-08805).

THE ELASTIC CONSTANTS OF INFLATED DOG LOBES, Stephen J. Lai-Fook*, Robert E. Hyatt†, Joseph R. Rodarte† and Theodore A. Wilson*. University of Minnesota, Minneapolis, Minnesota and †Mayo Clinic, Rochester, Minnesota.

Tests were made to determine the elastic constants of inflated dog lobes. The lobes were subjected to deformations which approximated the conditions of uniaxial loading. The data on deformation under uniaxial loading together with the bulk modulus obtained from the local slope of the pressure-volume curve are used to determine the two elastic constants needed in an analysis of non uniform deformations about an initial state of uniform inflation. The Young's modulus for the lung is found to vary from approximately 3 to 12 cm. H_2O with increasing pressure in the range of inflation pressures from 4 to 16 cm H_2O. The Young's modulus is therefore small compared to the bulk modulus. The Poisson ratio is found to be about 0.45. Estimates of the three second order elastic constants are also obtained.

EFFECTS OF ELECTRICAL VAGAL STIMULATION ON GASTRIN AND ACID OUTPUT IN THE ANESTHETIZED DOG. G. Lanciault*, L.S. Adair* and F.P. Brooks. Dept. of Physiol., Univ. of Pa. School of Med., Philadelphia, Pa. 19174.

Electrical vagal stimulation in the ex vivo dog stomach produces a significant increase in gastrin output and acid secretion (Fed. Proc. 32, 410 (1973). Using chloralose anesthetized intact dogs, we have studied the effects of electrical stimulation on these parameters. The dogs were prepared according to the method of Lanciault et al (Fed. Proc. 30, 478 (1971). A non-cannulating electromagnetic flow probe was placed on the portal vein proximal to the liver. Flow was continuously monitored and recorded. Gastric juice was collected and total acid was determined electrometrically. Portal blood was sampled frequently and serum gastrins were determined by the method of McGuigan (Gastroenterology 54, 1005 (1968). An electrical stimulus of 7 V, 5 msec duration with varying frequency was applied bilaterally to the cervical vagus. Frequencies from 1 through 10 Hz were changed every 15 min. Portal blood flow was found to vary inversely with the stimulus frequency. Resting portal blood flows of 40 $\pm$ 3 decreased to 5 $\pm$ 4 ml/kg/min(10 Hz). Blood flow returned promptly to control levels when the stimulus was removed. Gastrin concentrations increased significantly with increasing stimulus frequency (from 56 $\pm$ 8 to 142 $\pm$ 35 pg/ml at 10 Hz). In contrast gastrin output decreased from 2.31 $\pm$ 0.40 to 0.42 $\pm$ 0.9 ng/ml/kg/min(10 Hz). Gastric acid output was increased to a maximum of 145 $\pm$ 46 µEq/kg/15 min, peaking at 8 Hz. Although mucosal blood flow was not measured, it appeared that the gastric mucosa was receiving adequate blood flow to maintain acid production. We conclude that in the chloralose anesthetized dog, gastrin output varies inversely with gastric acid output in response to electrical vagal stimulation.
(Supported by USPHS, NIH Grant 5R01-AM14563-03)

CIRCADIAN INTERRELATIONSHIPS OF PLASMA CORTISOL AND CATIONS IN WOMEN. D. M. Lanuza* and S. F. Marotta. Departments of General Nursing and Physiology, University of Illinois at the Medical Center, Chicago, Illinois 60680.

Recent studies from our laboratory have shown that the infusion of Ca^{++} or PTH into dogs activates the hypothalamo-hypophyseal-adrenocortical system. The present study was undertaken to ascertain the basal and circadian interrelationships among plasma cortisol, Ca^{++}, Mg^{++}, Zn^{++} and Cu^{++} concentrations in female subjects. This study consisted of two parts. Part I involved withdrawing venous blood from 41 healthy subjects prior to breakfast. Part II, the circadian study, involved withdrawing blood every 3 hr during a 24 hr period from 4 healthy nurses when their activity period occurred during the day, as well as after they had reversed their activity from day to night. These studies reveal that: 1) under basal conditions, plasma cortisol levels were independent of plasma Ca^{++} and/or Mg^{++}; 2) no differences between subjects in the follicular and luteal phases were observed in plasma cortisol and cations; 3) plasma Ca^{++} and Mg^{++} were highly correlated; 4) a circadian rhythm was demonstrated for plasma cortisol and Mg^{++} in subjects on a regular sleep-wake cycle, while reversing the sleep-wake cycle for 6-7 days was sufficient time for the form of the rhythmicity of plasma cortisol and Mg^{++} to adjust but not to re-establish a significant circadian rhythm, and 5) variations in plasma Ca^{++}, Zn^{++}, and Cu^{++} were noted though no significant rhythms were observed. These data suggest that the mechanisms regulating plasma cortisol are not unduly influenced by physiological levels of Ca^{++} and/or Mg^{++}. (Supported by 5A11-NU00102-10 Professional Nurse Traineeship and NR 101-580.)

AN ANALYSIS OF THE FIDELITY OF LONG-TERM BEDREST AS A METABOLIC ANALOGUE OF WEIGHTLESS FLIGHT. C. S. Leach, P. C. Rambaut* and P. C. Johnson*. Johnson Space Center and Baylor College of Medicine, Houston, Texas.

A series of two week bedrest studies have been undertaken in order to simulate the hypokinetic and hypogravic conditions of weightless flight. Controlled dietary intakes and complete metabolic collections have been maintained. Measurements have been performed of total body water, intra- and extracellular water, plasma volume and total exchangeable potassium. Anthropometric parameters have included body volume, body mass, limb girth and bone density. A similar series of measurements have been made on the Apollo and Soyuz space missions. Losses in total body calcium inflight have been found to occur at approximately twice the rate observed at bedrest. Phosphorus losses have been greater inflight than calcium losses which is unlike bedrest. Weight changes inflight have exceeded those occurring in bedrest by a factor of approximately five and include tissue losses. Water excretion is elevated in bedrest and reduced in spaceflight. Increases in intracellular water have been observed inflight but not in bedrest. Among the significant hormonal changes noted has been an increase in aldosterone excretion inflight but not in bedrest. There have been larger losses of potassium inflight than in bedrest. Bedrest is still a good way to simulate weightlessness but the differences between it and spaceflight must be considered in metabolic studies.

RENAL MICROCIRCULATION AND PHYSIOLOGICAL STATE. C. Lechene and M.F. Poirey (intr. by A.C. Barger). Harvard Medical School, Boston, Mass.

A silicone rubber,"microfil", was injected into rat kidneys, in vivo, through an aortic catheter at the level of the renal artery and at aortic pressure. The rate of injection was roughly equivalent to renal blood flow. After polymerization of the "microfil" the kidneys were cleared in methyl salicylate. The results show very reproducible filling of the microvasculature and characterize clearly the four zones of the vascular distribution:cortex, juxtamedullary cortex, outer medulla and inner medulla. Under all conditions the filling was homogeneous for a given zone, but the distribution in and between zones changed in a very reproducible fashion with alteration of physiologic state. Compared to the filling observed in normal animals one can see:after the angiotensin (1 or 50ng/min),non-homogeneous distribution;after bleeding, the superficial glomeruli are not injected but the juxta medullary glomeruli and the vasa recta are well filled. After saline loading(NaCl 2%-0.3ml/mn)the capillary plexus between the bundles of VR of the outer medulla are richly injected. However after furosemide(.15mg/min/100g)the same capillary plexus is very poorly injected. One can assume that the distribution of the "microfil" reflects the intrarenal distribution of the blood flow and that the reproducible change observed reflect different distribution of intrarenal blood flow in different physiological conditions. It emphasizes 1. that the redistribution of the blood to the deeper region of the kidney is perhaps as important as the so called redistribution of SGFR measured in the cortex. 2. that one cannot rely solely on the study of the tubular function to interpret the integrated physiology of the kidney.

PURIFICATION OF AN ANOREXIGENIC SUBSTANCE ISOLATED FROM URINE OF RATS. Young-woo Lee* and Ira J. Lichton. Department of Food and Nutritional Sciences, University of Hawaii, Honolulu, Hawaii 96822

Spontaneous intake of food by 200g male rats is depressed 30-40% in the first 24 hours following a single i.p. injection of 12 mg of an alkaline extract of material precipitated from rat urine at pH 5.3 in cold ethanol saturated with benzoic acid. The chemical characteristics of this substance, called fat-mobilizing substance 1A (FMS 1A) by previous workers, have not been fully identified. Accordingly, FMS 1A was partially purified by means of Amicon ultrafiltration, anion exchange chromatography on DEAE-cellulose and by gel filtration on Sephadex G-75. The fraction of apparent molecular weight 30,000-50,000 was the most potent of all fractions separated by ultrafiltration; 12 mg caused a 98% reduction in food intake. Chromatography of FMS 1A on DEAE-cellulose yielded one major peak (peak I_D); 12 mg of material from this peak caused a 66% reduction in food intake. Gel filtration also yielded one major peak (peak I_S) with an apparent molecular weight larger than 80,000; 1.5 mg of material from this peak caused a 40% reduction in food intake. Thus material from peak I_S was at least 8 times more potent than the starting material, FMS 1A. The response to peak I_S material was not linear with dose, as injections of 0.9, 1.8, 2.7 and 3.6 mg/rat caused reductions in food intake of 65.0, 46.9, 45.6 and 58.0% respectively. Material from peak I_S is the purest available anorexigenic preparation derived from FMS 1A.

CLOSING VOLUME CHANGES IN DOGS WITH ELEVATION OF LEFT ATRIAL PRESSURE. R. Lemen, G. Cowan, J. G. Jones, P. Graf (Intr. by W. Gold). Cardiovascular Research Institute, Univ. of California, San Francisco, Calif.

We measured closing volume in 10 intact anesthetized dogs. A subatmospheric pressure of 5 cm H_2O was applied to the airways followed by a slow inflation with an oxygen-filled syringe to an airway pressure of 30 cm H_2O. During slow expiration with a controlled flow rate produced by a vacuum source, we simultaneously recorded airway pressure and alveolar nitrogen concentration plotted against expired volume. Lung water was determined by the double isotope dilution method using tritiated water and I^{125} Serum Albumen in 6 dogs. Closing volume (CV), total respiratory resistance (R_L) and lung water (Qwl) were measured before, during and after elevation of left atrial pressure (LAP) to 10-15 mm Hg with a balloon-tipped catheter. In 8 dogs closing volume increased 10-15% with elevated LAP and returned to near control values after LAP was lowered to normal. The R_L did not change significantly ($\bar{X}$=0.4 cm H_2O/l/sec) with elevated LAP in 6 dogs but increased 60% in two dogs. Lung water did not increase significantly in the six dogs studied by the double isotope dilution method. Vagotomies performed in two dogs studied during the control period did not change CV. Vagotomies in two other dogs with increased LAP, CV and R_L reduced the CV and R_L to near control levels. Post mortem compartmental analysis showed a small or no increase in Qwl. Histology of the lungs frozen in liquid nitrogen revealed small or no cuffs of edema around small airways. Increased LAP in the intact anesthetized dog produced an increase in CV which in two dogs studied was partially reversible by vagotomy when changes in Qwl are minimal or absent.

DEPTH SEPARATION OF MULLER CELL ON-AND-OFF RESPONSE. J. Levett (intr. by A. Rovick), Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois.

Müller cells generate the b-wave in the mudpuppy retina. These cells also show a depolarizing off-response similar to the off-response of the ERG (1,2). The b-wave of the isolated frog retina is attenuated at levels of extracellular K^+ that do not effect retinal neurons and Müller cell membrane permeability appears to be K^+ dominated. Both the b-wave and the d-wave of the ERG result from the K^+ electrode properties of the Müller cell with the d-wave being more sensitive to K^+ (3). Microelectrode depth penetrations of the frog retina were undertaken to establish the retinal depth location of the b- and d-waves of the ERG. They are distinctly separable with the d-wave located proximal to the b-wave leading to the suggestion that two radially oriented dipoles are generated one for light-on and the other for light-off. This implies the existence of either two Müller cell populations or a single population characterized by two distinctly different locations at which K^+ permeability changes can originate. Furthermore, if light causes a build-up of extracellular K^+ then different ionic equilibrium conditions most probably exist for a steady light level versus a sinusoidally modulated light of the same average intensity. Using the latter stimulus a dc response results which is a function of both the amplitude and frequency of stimulus modulation. A dipole model of the b- and d-waves will be presented. (1) Miller, R.F. and Dowling, J.E., (1970) J. Neurophysiol., 33: 323. (2) Miller, R.F. and Dowling, J.E. (1970) ISCERG Symp. 8, 85. (3) Miller, R.F. (1973) J. Neurophysiol., 36: 28. Supported by a grant from Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois.

ANTI-COAGULANT ACTIVITIES OF CYCLIC-AMP AND ITS DIBUTYRYL DERIVATIVE-ELECTROKINETIC AND CURRENT INDUCED THROMBOSIS INVESTIGATIONS. Levine, R.L.*, Margulies, J.L.*, Solash, J.*, Srinivasan, S.*, and Sawyer, P.N. Electrochemical and Biophysical Laboratories, Department of Surgery, State University of New York, Downstate Medical Center, Brooklyn, NY 11203

Cyclic AMP and its dibutyryl derivative inhibit the ADP induced aggreation of platelets. Our previous studies have shown that anti-coagulants increase or maintain the negative charge densities of the vascular components (blood vessel wall and blood cells) while procoagulants have the opposite effect. In the present work, the effects of cyclic AMP and its dibutyryl derivative on (i) the electrophoretic mobilities of human platelets and (ii) the current induced occlusion times in rat mesenteric vessels were determined. Cyclic AMP has a biphasic effect on electrophoretic mobilities - below 10^{-5}M, the mobilities are higher than controls while above 10^{-5}M, the opposite behavior is observed. Dibutyryl cyclic AMP increases the electrophoretic mobility of platelets at all tested concentrations (10^{-12} to 10^{-4} M). Except at one concentration (2.5×10^{-12}M), cyclic AMP shortens the current induced occlusion times in rat mesenteric vessels while the dibutyryl derivative was markedly anti-thrombogenic at all concentrations. The enhanced activity of DB-c-AMP over its parent nucleotide in increasing the surface charge density of platelets, in the extension of current induced occlusion times in rat mesenteric vessels and inhibition of platelet aggregation may be associated with the increased uptake of DB-c-AMP by platelets.

COMPARISON OF THE AWAKE BABOON'S SENSITIVITY TO INHALED AND SYSTEMICALLY ADMINISTERED CO_2. Steven M. Lewis* and Allan C. Young. Department of Physiology and Biophysics, University of Washington Seattle, Washington 98195

Several theories of the exercise response postulate a greater sensitivity to CO_2 produced in the body than to inhaled CO_2. Receptors in the great veins, the right ventricle, the pulmonary artery or response of the arterial chemoreceptors to oscillations in PCO_2 have been proposed. We have tested this postulate by administering CO_2 to an awake undrugged baboon via membrane oxygenator inserted into a chronic femoral shunt. Steady state $PaCO_2$ and mean end tidal CO_2 were compared for CO_2 administered via the shunt and CO_2 administered via the inhaled air at a level which produced comparable minute volumes. A major problem was the maintenance of a chronic (over several months) preparation which gave reproducible respiratory data. Throughout the experiment the animal performed a task and his performance was a criteria of his state. Data from such an animal shows that the CO_2 sensitivity (as measured by end tidal CO_2) to systemically administered CO_2 was not more than 20% greater than that when CO_2 is given via the inhaled air. (Supported by NIH grants GM00260 and RR00166)

EFFECTS OF DEXTRO-PROPRANOLOL ON LEFT VENTRICULAR FUNCTION IN CONSCIOUS DOGS BEFORE AND AFTER ACUTE MYOCARDIAL INFARCTION. Chang-seng Liang* and William B. Hood, Jr. University Hospital and Boston University School of Medicine, Boston, Mass.

Propranolol (racemic) has been shown to have myocardial depressant effects in animals, especially in the presence of myocardial infarction and heart failure. To study whether these effects are a result of its local anesthetic action, we infused dextro-propranolol, an isomer with full local anesthetic potency but devoid of beta-adrenoceptor blocking action, into conscious dogs before and after acute myocardial infarction. A stable preparation of heart failure was produced by inflating a balloon implanted previously around the left anterior descending or circumflex coronary artery. Doses of 0.03, 0.1, 0.3 and 1.0 mg/kg body wt were administered at 15 min intervals. Cardiac output (CO) by dye dilution method, heart rate, arterial blood pressure, left ventricular end-diastolic pressure (EDP), and rate of left ventricular developed tension (dp/dt) were measured. None of these parameters were affected significantly by d-propranolol either before or after acute myocardial infarction. Similar administration of dl-propranolol produced an increase in EDP and a dose-dependent decrease in CO and dp/dt with a 50% reduction at the highest dose. Therefore, it is concluded that d-propranolol did not depress left ventricular function and the cardio-depressant effects of dl-propranolol could not be accounted for by the local anesthetic action of the drug alone.

SPIKE RESPONSES OF CAUDATE NEURONS TO CORTICAL, NIGRAL AND ENTOPEDUNCULAR NUCLEAR STIMULI IN CATS. Samuel L. Liles. Louisiana State University Medical Center, New Orleans 70112.

Single-unit discharges of caudate neurons were recorded extracellularly in response to frontal cortex, substantia nigra (SN) and entopeduncular nucleus (EN) stimuli in unanesthetized cats. Significant differences were noted in latencies and frequency-sensitivity characteristics of excitatory responses elicited from motor and orbitofrontal cortical areas. Antidromic spike responses to EN and SN stimuli were characterized by invariant latency to single stimuli, faithful following of repetitive stimuli and occasional complete fractionation of the "A-B" spike with uncovering of the "A" spike component. Only 6% of the neurons which were antidromically activated by EN or SN stimuli showed orthodromic excitatory responses to cortical stimuli, and collision extinction of the antidromic responses was demonstrable in these units. Anatomical analyses revealed that neurons responding to motor cortex stimuli were located mainly in the dorsolateral part of the caudate head, while units responding to gyrus proreus stimuli were found in the medial and ventral areas of the rostral caudate. Neurons in the medial two-thirds of the dorsal part of the caudate tended to receive excitatory or inhibitory inputs from more than one cortical area. Units antidromically activated by SN stimuli were found mainly in the medial and ventral caudate area, while EN-activated units were more widely distributed. These findings are in agreement with anatomical data of others which indicate that inputs to the striatum terminate mainly on interneurons, and that regional differences may exist in the integrational functions of these neurons in relation to frontal cortical input. (Supported by USPHS, NIH Grant NS-08907)

DEPRESSION EFFECT OF RESPIRING HELIUM-OXYGEN (80-20%) ON THE HEART RATE IN THE UNANESTHETIZED MALE NORMOTENSIVE AND SPONTANEOUSLY HYPERTENSIVE RATS. Y.C. Lin. Univ. of Hawaii Sch. of Med. Honolulu, HI.

Until recently, He gas has been considered devoid of cardiovascular actions. However, over the past 3 years, there have been reports that breathing He-O_2 mixture induces a protection against the arrhythmic effect of coronary ligation in dogs. It is of interest to see whether He affects the heart rate in the intact animal. The comparison of the heart rates under the two breathing gas mixtures was based on the iso-aerobic requirements. The oxygen consumption ($\dot{V}_{O_2}$) was varied by altering the ambient temperatures (T_a), and was measured with a ventilated chamber and an oxygen analyzer. The T_a was varied from 10-35°C and 25-35°C for breathing air and He, respectively. The heart rate was obtained by direct wiring through an air-tight entry port to the animal chamber which was submerged in water for temperature control. The results are summarized in the following table, where X is $\dot{V}_{O_2}$ in ml/min/kg ml/min/kg, and Y is heart rate in beat/min:

	Normotensive (Sprague-Dawley)	Hypertensive (Okamoto)
air	Y = 5.4X + 191 (n=40, r=.6304)	Y = 3.8X + 210 (n=26, r=.7558)
He-O_2	Y = 5.0X + 161 (n=16, r=.7537)	Y = 3.4X + 115 (n=22, r=.6331)

The heart rate was lower in the rats breathing He than rats breathing air at all $\dot{V}_{O_2}$ as indicated by similar regression coefficients with distinct intercepts. The effect of He breathing was similar in both normotensive and hypertensive rats. However, the sensitivity of the heart rate changes in response to the changes in $\dot{V}_{O_2}$ was lower in the spontaneously hypertensive rats than that of the normotensive rats as indicated by lesser slopes of the regression lines. (Supported by ONR Contract N00014-67-A-0387-0014 and Univ. of Hawaii Intramural Grant).

SYMPATHOMIMETIC ALTERATIONS OF ELECTRO-MECHANICAL COUPLING IN CANINE VENTRICLES. D.B. Lippincott and M.P. Kaye. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

The effects of several positive inotropic interventions on the electro-mechanical (EM) coupling of various segments of left and right ventricular muscle were studied. Walton-Brodie strain gauge arches, with an attached unipolar electrode were sutured to the anterior, lateral and posterior left ventricle and the right ventricular sinus of the canine heart. Left (LSS) and right (RSS) stellate stimulation, right atrial pacing, Ca^{++} and norepinephrine, before and after propranolol, were used in this study. During control the LV segments contracted almost simultaneously and 10-15 msec before the RV segment. The EM coupling interval for the RV-sinus was longer than the LV segments. During LSS the EM coupling of all areas shortened significantly (8-15 msec) with the LV lateral base (15 msec) and RV sinus (14 msec) showing the greatest shortening. Mechanical sequence also changes with both LV posterior and lateral base contracting 6-8 msec before LV anterior and RV sinus. RSS showed a significant decrease in EM coupling in all areas with LV lateral base (16 msec) and RV sinus (15 msec) showing the greatest decrease. During RSS all gauges contracted within an 8 msec period compared to 12 msec during LSS. Right atrial pacing up to rates equal to or higher than rates reached during LSS or RSS showed a shortening of EM coupling time but not to the extent seen with LSS and RSS. LSS and RSS during the pace further shortened the EM coupling time. NE (1γ/Kg I.V.) shortened EM coupling times significantly in all areas. After propranolol, the NE failed to elicit any change. Ca^{++} before and after propranolol, gave similar reductions in EM coupling. All positive inotropic interventions also caused reductions in EM coupling. (Supported by NIH Grants HL 08682 and GM 999.)

AN ANALYSIS OF THE FACTORS WHICH MAY INFLUENCE THE EFFECT OF ACETYLCHOLINE ON K TRANSPORT IN THE SINUS NODE. S. Lipsius* and M. Vassalle. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Sino-atrial nodes from guinea-pig hearts were perfused in a tissue bath in close proximity to a beta probe. The tissue was loaded to equilibrium with ^{42}K and then washed in inactive Tyrode. Tissue radioactivity was recorded at intervals, as well as membrane potentials. The K uptake was estimated by the increase in tissue counts after reexposure of the preparation to radioactive Tyrode. Acetylcholine (Ach) increased K uptake as a function of its concentration (10^{-7}M to 10^{-4}M). In lower concentration (10^{-9}M) acetylcholine caused a decrease in K uptake, but not consistently. The stimulatory action of acetylcholine on K uptake was abolished by atropine. No consistent differences were found whether the fiber was electrically driven or spontaneously active during acetylcholine exposure. In the presence of propranolol, the acetylcholine-induced uptake was slightly larger. Acetylcholine still provoked an increase in K uptake in pretreated reserpinized tissue. The Ach-induced uptake was about the same before and after acute reserpinization and also before and after a norepinephrine load. The increase in K uptake during simultaneous exposure to acetylcholine and norepinephrine was the same as during acetylcholine alone. It is concluded that acetylcholine may have an inhibitory and excitatory action of K uptake, depending on the concentration. Also, changes in rate of discharge play little role in changes in K uptake induced by acetylcholine. Acetylcholine provokes most of its effect without the intermediary action of norepinephrine. With acetylcholine and norepinephrine simultaneously present, the unaltered uptake is probably due to an inhibition of norepinephrine action by acetylcholine.

Supported by a NIH grant.

FEVER PRODUCED IN THE SQUIRREL MONKEY BY INTRAVENOUS AND INTRACRANIAL INJECTIONS OF S. TYPHOSA ENDOTOXIN. J.M. Lipton and D.E. Fossler (intr. by R.M. Dowben). Psychiatry and Physiology Departments, Southwestern Medical School, Dallas, Texas 75235

Unlike man, the Rhesus macaque (Sheagren, Wolff and Shulman, AJP, 212, 884) and the chimpanzee (Tully, Gaines and Tigertt, J. Infect. Dis., 115, 445) do not develop large and reliable fevers in response to intravenous administration of bacterial endotoxins. In a search for a more responsive primate model for fever studies, squirrel monkeys, which were accustomed to sitting in a restraint chair, were given injections of endotoxin via the saphenous vein. Rectal temperature and three skin temperatures were automatically recorded every five minutes throughout a one hour baseline period and a five hour post-injection period. All of the experiments were conducted in an environment controlled at 23°C. Beginning 20 to 75 minutes after the injections were made, dose-related fevers developed which reached peaks 1-2 hours post-injection. In animals implanted with chronic intracranial cannulae, 500 ng of endotoxin in one microliter of saline produced maximal fevers (40.5-40.9°) when injected into some sites, and lesser fevers when injected into other sites, in the diencephalon. Submaximal fevers were produced by injecting prostaglandin E_1 (500 ng), a possible mediator of fever, or of sodium pentabarbital (2-5% concentration) into the brain sites that were most sensitive to endotoxin. It is concluded that the squirrel monkey is an appropriate primate model for fever research since it is sensitive to both systemic and central administration of an endotoxin that is pyrogenic in man and many other species. (Supported by PHS Research Grant #1-RO1-NS-10046 from the NINDS.)

MUSCLE DEGENERATION AND THE ESCAPE OF MUSCLE PROTEINS INTO BLOOD. Richard A. Lockshin (intr. by E. F. Adolph). U. of Rochester School of Medicine and Dentistry, Rochester, New York.

The very rapid involution of the intersegmental muscles of moths is a truncated version of slower processes in vertebrate muscle pathology, such as denervation atrophy and muscular dystrophy. In the insect, it is possible to state definitively that a given fiber is going to degenerate within a specific time, and thus to assign a temporal and causal sequence to the events which ensue. The question which we asked is, do cathepsins or other intracellular proteases control the catabolism of the contractile filaments? The answer, which is that cathepsins apparently do not digest the contractile filaments, has been documented by several techniques. Electron microscopy, done in collaboration with Jacques Beaulaton, reveals in degenerating muscle the presence of large numbers of lysosomes but the absence from these organelles of myofilaments. Intracellular recordings do not suggest major ionic or pH changes during the first phase of rapid histolysis. Furthermore, experiments have documented by the following techniques the appearance in the blood of intact muscle protein: release of isotope from pre-labeled muscle; 2- to 15-fold rises in circulating enzymes considered to be clinical indicators of muscle damage; and the appearance in the blood of a muscle antigen which reacts with anti-muscle antibody and cross-reacts with a preparation of insect actomyosin. These several arguments suggest that an early phase of degeneration consists in the solubilization without complete digestion of contractile and other proteins. The mechanism of this solubilization is under study.

A ONE-DIMENSIONAL VISCO-ELASTIC MODEL OF HEART MUSCLE. Louis Loeffler* and Kiichi Sagawa. Johns Hopkins Univ., Baltimore, Maryland.

A model of heart muscle was developed under a fixed inotropic state, temperature (20°C), and stimulation rate (10/min). The passive properties of muscle were determined by using step changes in length of no more than 1.2% L_{MAX} for a range of initial lengths from 85 to 100% L_{MAX}. We fit the resulting passive force by a sum of two decaying exponentials and a constant, suggesting the model of Fig. 1. All five parameters were small at muscle lengths below 95% L_{MAX} but increased markedly at longer lenghts. The active (total minus passive) properties of muscle were studied by perturbing isometrically contracting muscle with a sinusoidal length change of amplitude less than .15% L_{MAX} over the frequency range from .1 to 35 Hz. Plotting the log of active stiffness ($\equiv \Delta F/\Delta L$) versus the log of frequency gave a curve that was flat at high and low frequencies and increased in a first-order manner at intermediate frequencies. Such a frequency response suggests the model of Fig. 2. We determined the dependency of K, K_S and C on length and time by recording the dynamic response at various combinations of length and time. K_S was found to vary linearly with active force, F_a, i.e. $K_S = BF_a$ where B is independent of both length and time. K and C exhibited time courses roughly paralleling F_a up to t_{MAX}, maintained their values until 1.8 t_{MAX}, and then fell towards zero. K was essentially independent of length up to 95% L_{MAX} and then began to decline, while C varied in proportion to muscle length. A parallel combination of the two models constitute whole muscle properties and could be used to simulate muscular contraction. (Partly supported by NIH Grant HL 14903).

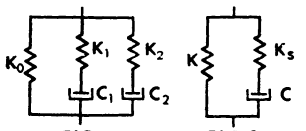

FIG.1

FIG.2

Lysosomal Enzyme Changes in Liver, Spleen, Pancreas, Intestinal Mucosa and Plsama During Hemorrhagic Shock in Dogs. Daniel J. Loegering*, Robert C. Arfman*, John C. Garancis*, and James J. Smith. Dept. of Physiol., Med. Col. of Wis., Milw., Wis. 53233.

This study was carried out to determine the source of the elevated lysosomal enzyme levels in the plasma during shock. Male dogs were hemorrhaged into a pressurized reservior to a mean arterial pressure of 35 mmHg. Experimental groups were based on the percent of spontaneous uptake of maximal shed volume: 5% uptake (5), 30% uptake (30), and 1 hour after 30% uptake (30+1). At the end of the experiment, samples of liver (L), spleen (S), pancreas (P), and proximal jejunal mucosa (I) were assayed for cathepsin and acid phosphatase. Arterial and venous P_{O2}, P_{CO2}, pH and arterial lactate were monitored. Plasma levels of acid phosphatase and cathepsin, determined hourly, progressively increased with time in each shock group, except for acid phosphatase in the 5 group. In the tissues, L cathepsin increased at 5 and 30 but L acid phosphatase did not change. Cathepsin increased in the I at 30; acid phosphatase was not assayed in I. The S showed an increase in cathepsin at 5, 30 and 30+1, while the acid phosphatase increased at 5 and 30. P showed no changes in lysosomal enzyme activities. The general trend of changes in enzyme levels for all tissues except P was an increase at 5 and 30 with a decrease to or toward preshock levels at 30+1. This decrease was taken as an indication of enzyme loss to the plasma. Histological examination of the tissues showed severe changes in I and L, minor changes in S and no changes in P. It was concluded that I, L and to a lesser extent S but not P contributed to the increased plasma lysosomal enzyme levels in shock. (Supported by a grant from the Wisconsin Heart Association and research grant NHLI06588).

CARDIOVASCULAR RESPONSES TO ORTHOSTATIC STRESS WITH β-ADRENERGIC BLOCKADE. J.A. Loeppky (intr. by U.C. Luft). Lovelace Foundation, Albuquerque, N.M. 87108

The single-breath (SB) method of Kim et al. was employed for serial measurements of cardiac output ($\dot{Q}$) before, during and after orthostasis in 6 subjects. Previously the SB method had been validated against direct (Fick) determinations at rest and exercise (NASA Rep., Feb. 1973, Contract NAS 9-12572). In the control tests heart rate (fr) increased and pulse pressure (pp) dropped immediately on tilting to 60°, while $\dot{Q}$ and stroke volume (V_s) declined gradually over 21 minutes upright. After β-adrenergic blockade (40 mg Inderal) fr was 10 bpm lower supine and 20 bpm less at 60° than in the controls with slightly reduced $\dot{Q}$ but higher V_s. With the drug $\dot{Q}$ and V_s also dropped during the first 10 minutes of tilting but recovered approaching pre-tilt levels during the latter part of the tilt without any change in fr or pp. As a result of increased V_s, $\dot{Q}$ was higher on the average at the end of the tilt with β-receptor blockade than in the controls. On return to supine there was a transient increase in V_s and $\dot{Q}$ with a drop in fr in both experimental and control tests. At the same time, arterio-venous O_2 difference and apparent $\dot{V}_{O_2}$ rose sharply, reflecting return of more unsaturated blood to the lungs after extrathoracic pooling. (Supported in part by Contract NAS 9-12572 with NASA-MSC).

Intestinal Mesenteric Blood Vessel Catecholamine Concentrations During Prolonged Hemorrhagic Stress. J. Lombard*, F. Loo*, S. Contney*, and W.J. Stekiel, Dept. of Physiol. Med. Col. of Wis., Milw. Wis. 53233.

Male dogs (18-28 kg), anesthetized with Na-pentobarbital, were hemorrhaged to 35 mmHg MABP and were divided into four experimental groups based on the magnitude of maximum bled volume taken back: 5%, 30%, 30%+1 hr. and 30% glucocorticoid pretreated. Four non-hemorrhage control groups included: immediate, 2 hr., 4 hr., and 4 hr. with controlled ventilation. Superior mesenteric artery (SMA), and small mesenteric artery (SA) and vein (SV) tissue concentrations of epinephrine (E) and norepinephrine (NE) were determined fluorometrically (μg/gm wet wt.). In controls, the SA mean NE level (3.1 $\pm$ .19) was significantly greater than that of SV (1.8 $\pm$ .16) which in turn, was greater than SMA (1.0 $\pm$ .14). A similar distribution occurred for E controls with SA, SV and SMA levels respectively, at 1.2 $\pm$ 0.11, 0.7 $\pm$ .10 and 0.4 $\pm$ .06. Duration of anesthesia appears to elevate E but not NE tissue levels. Hemorrhagic stress led to a significant fall in mean catecholamine levels of the SA beginning with the 5% group for NE and the 30% group for E. In SV and SMA, the fall in mean catecholamine levels during stress was not significant. Glucocorticoid pre-treatment prevented the fall in both E and NE observed in the SA of the non-treated 30% group. It is suggested that depletion of neurotransmitter in compensatory vascular beds is an initial step in the peripheral vascular collapse resulting from the ischemia associated with prolonged hemorrhagic stress. The beneficial action of glucocorticoids may result from an ability to help maintain normal levels of neurotransmitter in compensatory beds. (Supported by a grant from the Wisconsin Heart Association.)

PLASMA ALDOSTERONE AND GLUCOCORTICOID LEVELS DURING NEONATAL DIARRHEA IN CALVES. G. A. Lopez* and R. W. Phillips. Dept. of Physiology and Biophysics, Colo. State Univ., Ft. Collins, Colo.

This research was designed to determine whether the calf's adrenal gland is capable of responding to the profound hypovolemia of diarrhea. Diarrhea was induced in healthy, newborn bull dairy calves by oral administration of a viral inoculum. Clinical diarrhea occurred 22-40 hrs following inoculation. Serial blood samples were taken throughout the experiment to either recovery or death. Electrolyte therapy was initiated in a group of diarrheic animals and a second group was left untreated. Corticoids were determined by radioimmunoassay and competitive protein-binding assay following previous purification by paper chromatography. Diseased calves had significantly higher plasma aldosterone levels than controls from just prior to the onset of diarrhea until death. Additionally, plasma aldosterone values were higher in the untreated than in the treated diarrheic animals. Plasma cortisol tended to decrease with age in normal calves. With diarrhea, levels of cortisol were higher than those seen in the control animals as were corticosterone and progesterone. The hematocrit (% change) increased significantly with time for the diseased animals as opposed to controls. The results show the classical stimulation of water-electrolyte retaining mechanisms through an increased aldosterone production and also suggest that adrenal corticoid synthesis during diarrhea is adequate, even during the critical stage prior to death when substrate availability may be limiting as judged by the absence of food intake. Also, during the severe stage the biosynthetic pathway leading to aldosterone formation appears to be preferentially stimulated even at the expense of cortisol biosynthesis. We conclude on this basis that the very young neonatal calf has a competent adrenal response mechanism. (Supported in part by Experiment Station Project W220 and U.S.P.H.S. Grant 5S01-RR-5458-10.)

STIMULATION INDUCED POTASSIUM ACCUMULATION IN CONFINED SPACES OF THE NERVE BUNDLE OF THE LOBSTER CNS. Eugene Lovelace* and Alan R. Freeman. Inst. of Psychiatric Research, Ind. Univ. Sch. of Med., Indianapolis, Ind. 46202.

The potential across the ensheathment cell of the nerve bundle connecting the brain and the first thoracic ganglion of the lobster CNS was measured. Microelectrode studies revealed that a positive voltage on the order of 5 mv in artificial sea water exists and that stimulation of the nerve bundle alters this potential in a repeatable manner which appears to be stimulation dependent. Variation of the potassium level of the bathing medium alters the unstimulated potential, but does not appear to significantly change the time course of the stimulation dependent potential changes. The post-stimulation potential does not return to steady state for some time, often of the order of minutes. Desheathed preparations were placed in a chamber containing 0.5 ml of 0 mM potassium artificial sea water. The bundle was bathed in this medium for varying times after which the fluid was replaced with a new sample. Potassium levels in the collection samples were measured directly using a flame photometer. By altering the bathing time, the kinetics of the system were found to be those of a simple diffusion regime. Moreover, upon stimulation, the departures from the steady state were consistent with increases in the average potassium concentration in the diffusion pathway. Finally, the post-stimulation concentrations returned to the original diffusion kinetics with a slight time delay. The results show evidence for perineuronal potassium accumulation at stimulation rates as low as five per second. In addition, the ensheathment cell appears to be an effective diffusion barrier to potassium.

ANGIOTENSIN INDUCED RELEASE OF NOREPINEPHRINE FROM CANINE HEART. R. F. Lowe (intr. by J. C. Pisano). Dept. Physiology, Tulane University School of Medicine, New Orleans, Louisiana 70112

It has been suggested that the cardioaccelerator action of angiotensin (AT) can be attributed to the release of catecholamines from myocardial adrenergic neurons (Am. J. Physiol. 213:134, 1967). These studies test the ability of AT to release ^{3}H-norepinephrine (NE) from the canine heart. Hearts were isolated and perfused with blood in situ basically as described by Chidsey et al. (Circulation Res. 12:220, 1968). Myocardial adrenergic neurons were exposed to ^{3}H-NE (58.8 μC) which was infused into the right coronary artery (RCA) and venous blood was drained from the right atrium and right ventricle. Radioactivity in the venous blood was assayed by scintillation counting. Twenty-five AT (1 μg/kg) injections were made into the RCA in 18 dogs. Injections were made at 10, 20 and 30 minutes (min) following isolation of the heart. All AT injections resulted in a rapid transient increase in the efflux of radioactivity from the heart. Percent increase in efflux produced by AT decreased with time from isolation: 10 min (503 ± 129 S.E.)> 20 min (168 ± 74)> 30 min (58 ± 23). Coincident with the increase in efflux of radioactivity, an increase in heart rate was observed in 19 of 25 trials. Percent increase in heart rate also decreased with time from isolation: 10 min (20.2 ± 3.8)> 20 min (8.3 ± 2.4)> 30 min (4.8 ± 1.3). RCA injections of tyramine led to qualitatively similar results. Results of these studies indicate that AT can release NE from myocardial adrenergic neurons and that this NE participates in part in the cardioacceleration observed following injection of AT. (Supported by the Louisiana Heart Association).

EFFECTS OF PROLACTIN ON THE RENAL RESPONSE TO VOLUME EXPANSION IN THE RAT. Marjory Lucci*, Howard Bengele and Sidney Solomon. Department of Physiology, University of New Mexico School of Medicine, Albuquerque, New Mexico 87131.

Mammalian prolactin has been shown to have profound influence on water and electrolyte balance in teleost fish and amphibia. For this reason the effects of prolactin on renal sodium and water handling during volume expansion in the rat were studied by renal clearance techniques. Both control and experimental adult male Wistar rats were prehydrated with an oral water load equal to 2.5% body weight. At least three hours later, a continuous infusion of ovine prolactin (NIH-P-S8), 1.2 ng/min/gBW, was started in the experimental group. After a one hour steady state period, both groups of rats were given an intravenous infusion, 2.5% body weight, of either hypotonic (0.45%) or isotonic (0.9%) saline, or fresh donor blood. In control saline expanded animals, approximately 50% of the volume load was excreted within one hour with no difference between hypotonic and isotonic infusions. In comparison, rats receiving prolactin demonstrated significantly reduced volume excretion following both hypotonic and isotonic loads. With respect to the sodium response to expansion, control rats receiving a hypotonic infusion tended to excrete a smaller percentage of the sodium load than those receiving an isotonic infusion. Prolactin significantly reduced sodium excretion after an isotonic load, and there was a reduction in sodium excretion after a hypotonic load, although this was not significant. In contrast to the effects of prolactin on the renal response to saline infusions, it did not alter the sodium or volume response to blood expansion. These results may be interpreted as prolactin, in some way, counteracting the effects of physical factors regulating sodium reabsorption in the proximal tubule. (Supported by NSF Grant GB-35637X).

PARIETAL ASSOCIATION CORTEX NEURONS ACTIVE DURING HAND AND EYE TRACKING OF OBJECTS IN IMMEDIATE EXTRAPERSONAL SPACE.
J. C. Lynch*, H. Sakata*, A. Georgopoulos*, and V. B. Mountcastle, The Johns Hopkins University School of Medicine, Baltimore, Maryland.

In the course of an investigation of the posterior parietal areas of the monkey we have applied the method of single unit analysis in 15 waking monkeys trained to perform a number of appropriate tasks. Among several populations of neurons identified, two are of special interest as regards operations within immediate extrapersonal space. The first lies in that portion of area 5 lining the anterior bank of the intraparietal sulcus. These neurons discharge when the monkey actively projects an arm towards, or tracks, a desired object or a meaningful target. They show no correlated activity during other arm movements, and are not activated by passive manipulation or stimulation of the arm. Cells of the second class are located in area 7, and are active when the animal fixes his gaze upon or visually tracks the movement of an object of high motivational potency - a lighted target whose tracking and accurately timed contact leads to reward, moving food objects, etc. These neurons are always directionally sensitive, most commonly to movements in the contralateral half of visual space; they are inactive during spontaneous eye movements. Often they do not discharge during visual tracking of otherwise effective moving targets if they are beyond arm's reach. These sets of neurons are thus neither sensory nor motor in the usual sense, and are active before and during the animal's active projection of hand or eye into his immediate extrapersonal space. Motivational drive is a necessary condition for that discharge. (NINDS Grant 5 PO1 NS0 6828).

LARGE OSMOTIC GRADIENTS ACROSS A LIVING CELLULAR EPITHELIUM.
John Machin, Dept. of Zoology, University of Toronto, Toronto, Ontario, M5G 1G6, Canada.

The presence of a highly waterproof barrier somewhere in a single layer of epidermal cells has been advanced as a hypothesis to explain extremely low rates of water loss (0.02 mg/cm^2/h per mmHg vapor pressure difference) from dormant land snails. A previous experimental study indicates the barrier to be located beneath a small hygroscopic compartment in equilibrium with the external air. Other observations show this mechanism of water conservation commences when normally active mucus glands cease to secrete. As a means of further locating the barrier, frozen sections of living epithelial tissue were examined. They demonstrate considerable osmotic gradients, a difference of greater than 5,000 milliOsmols across a cell 15μ deep. Additional observations suggest that the barrier is principally associated with a zone of apical microvilli, in cells having very low membrane permeability to water. (Supported by National Res. Council, Canada grants.)

SODIUM ACTIVATION OF INTESTINAL BRUSH-BORDER SUCRASE: DESENSITIZATION BY FRACTIONATION OF MEMBRANES SOLUBILIZED WITH SODIUM DODECYL SULFATE AND Mg^{++}-DEPENDENT RE-SENSITIZATION. Akhtar Mahmood* and Francisco Alvarado. University of Puerto Rico, Med. Sch., San Juan, P.R. 00936.

The effect of Na^+ on the sucrase activity of various preparations derived from brush-borders of guinea pig intestine has been studied. Maximal activation (6-8 fold) is obtained above 50 mM Na^+, the result being similar in crude brush-border preparations (BB) or in BB lysed with 0.1% sodium dodecyl sulfate (BBL). With extensive dialysis against either 5 mM Li^+ or Li^+ plus 10 mM Mg^{++}, the Na^+ activation pattern of both BB and BBL does not change appreciably. Fractionation of BBL on Sepharose 2B (Pharmacia) gives two broad protein peaks. In the second peak (P-2), 80-100% of the sucrase activity is recovered, but activation by Na^+ is absent (the enzyme can be said to be "desensitized"). However, after dialysis of P-2 against 5 mM Li^+ plus 10 mM Mg^{++} for 3-5 days (but not against Li^+ alone), membrane-like structures are regenerated containing sucrase that is again fully susceptible to Na^+ activation (the enzyme can be said to be "re-sensitized"). The results suggest that desensitization of sucrase towards Na^+ is due to separation of some component(s) from the sucrase particle; and that restoration of sucrase sensitivity to Na^+ (re-sensitization) depends on the reassociation of the dissociated components of the particle in presence of Mg^{++}. (Supported in part by NIH Grants and Research Career Development Award K04-AM 2383 to F. A.).

INTRACELLULAR pH IN TURTLE (*PSEUDEMYS SCRIPTA*) TISSUES AS A FUNCTION OF BODY TEMPERATURE. Andre Malan* and Robert Blake Reeves, Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N.Y.

Reeves (*Respir. Physiol.* 14: 219, 1972) proposed that alphastat regulation of acid-base balance in air breathing poikilotherms has as a central function preservation of intracellular protein charge state when body temperature changes. This hypothesis requires that intracellular dpH/dT change in parallel with blood dpH/dT. We have measured intracellular pH in four tissues using the DMO technique. DMO-^{14}C and Inulin-^{3}H were injected intracardially 12 hours before sampling in 13 animals which had been kept at a constant ambient temperature (range 6 - 35°C) for a minimum of one week. The following are the least squares fitted slopes (dpH_i/dT) and significance of difference between tissue dpH_i/dT and blood dpH/dT:

Blood	-0.021 u/°C	-
Striated Muscle	-0.019	NS
Ventricular Muscle	-0.012	$p<.01$
Liver	-0.023	NS
Smooth Muscle:Esophagus	-0.014	NS

These results for striated muscle are similar to those reported on DMO studies of bullfrogs (*Fed. Proc.* 28: 782, 1969) which have independent support from CO_2 content pH_i estimates (*Physiologist* 15: 246, 1972). Cardiac muscle in both species presents a significantly lower slope than striated muscle. These findings are in general agreement with the alphastat hypothesis. (Supported in part by ONR Contract N00014-68-A-0216, NIH Grant 1 P01 HE 14414-01, and NSF Award.)

EFFECTS OF HYPOXIA AND CSF CORTISOL IN MODULATING THE ADRENOCORTICAL RESPONSES TO VARIOUS CSF [H+]. L. J. Malasanos* and S. F. Marotta. Department of Physiology, University of Illinois, College of Medicine, Chicago, Illinois 60680.

Previous work from this laboratory has demonstrated the similarity of arousal for the hypothalamo-hypophyseal-adrenocortical (HHA) and respiratory systems via hypoxic activation of the aortic and carotid bodies at the peripheral level as well as through the action of CSF [H+] at the central nervous system level. Acute hypoxia induced by respiring 10% O_2 added to the stimulus schedule of dogs undergoing pH alterations of CSF perfusate exhibited modification of cortisol secretory rates: the increase seen at CSF pH 7.20 (4.9±4.5μg/min/gm) was $\cong$ doubled (10.0±1.1μg/min/gm), whereas the decrease observed at CSF pH 7.60 (6.4±2.2μg/min/gm) was $\cong$ halved (2.8±0.7μg/min/gm). Hypoxia coupled with ventriculocisternal perfusion at CSF pH 7.40 failed to change the cortisol secretory rate. When only perfusion of the cerebral ventricular system is performed no alterations of peripheral PaO_2, $PaCO_2$, arterial pH or mean pressure, as well as respiratory rate, pulse rate, adrenal blood flow or rectal temperature were observed; however, simultaneous presentation of 10% O_2 with CSF pH alterations produced changes in these parameters consistent with the change in ventilation. The addition of cortisol hemisuccinate (0.1μg/ml or 0.2μg/min) to these perfusates two hours before and during the experimental period obviated the changes in cortisol secretory rates either to acidic or basic CSF perfusate. These data indicate that the HHA responses to alterations in CSF pH are synergistic with the hypoxic stimulus and can be inhibited by cortisol.
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COMPARISON OF VENTRICULAR HYPERTROPHY INDUCED BY PRESSURE AND VOLUME OVERLOADING. A.B. Malik, H.O. O'Kane*, T. Abe* and A.S. Geha. Washington University School of Medicine and The Jewish Hospital of St. Louis, Missouri. 63110.

Stable left ventricular hypertrophy (LVH) was induced in dogs either by volume overloading (A-V fistulas) or by pressure overloading (aortic banding). Aortic and LV pressures, LV dp/dt, cardiac output, and arterial, mixed venous and coronary venous O_2 contents were measured at rest and over similar exercise loads until exhaustion. Cardiac oxygen extraction was maximal at rest in LVH induced by pressure (P) and by volume (V) overloading and did not increase with exercise as in normal dogs, suggesting that the hypertrophied myocardium meets the increased O_2 demands of exercise only by increasing coronary flow. Indices of LV function such as cardiac output, stroke volume, minute work, stroke work, peak LV dp/dt and ratio of peak LV dp/dt to isovolumic pressure were in the normal or above normal range at rest in both forms of LVH. These indices of LV function increased similarly with exercise in P and normal dogs, but the increases in V were attenuated. Thus, ventricular function in LVH induced by V and P is not depressed at rest in conscious dogs. At comparable levels of exercise, indices of LV function increased more significantly in the pressure overloaded hypertrophied hearts than in the volume overloaded ones. The reduced functional reserve of the volume overloaded hearts may be due to a combination of factors such as increased myocardial tension, operation of these hearts at higher levels on the Frank-Starling curve and decreased coronary flow. (Supported by United States Public Health Services Grant 5 RO 1 - HE13088-02.)

DEMONSTRATION OF TONIC CIRCULATORY RESTRAINT FROM THE HEART AND FROM THE LUNGS IN DOGS. Giuseppe Mancia*, David E. Donald and John T. Shepherd. Mayo Foundation, Rochester, Minnesota.

Vagal afferents from receptors in the heart and the lungs exhibit tonic activity throughout the cardiac and the respiratory cycle. The present experiments were designed to determine if this tonic activity is implicated in control of the circulation. Dogs were anesthetized with chloralose, paralyzed with gallamine, thoracotomized and ventilated at 12 cycles per minute with a peak pressure of 12 cm H_2O. The carotid sinuses were denervated, the aortic nerves cut and the vagi divided at the diaphragm. Thermodes were applied around the cervical vagi to permit reversible block by cooling. Two series of experiments were performed: A) blood was pumped by the right ventricle to an oxygenator and returned at constant flow to the left atrium. The lungs were removed and the pumping heart left in situ to support the systemic circulation. Intracardiac and aortic pressures were similar before and after removal of the lungs. B) blood was drained by gravity to the oxygenator from both venae cavae and returned at constant flow into the aorta. This allowed removal of the heart, leaving the lungs in situ. Ventilatory and aortic pressures were not altered by these maneuvers. In A, vagal cold block caused mean aortic pressure to increase 44±7 mm Hg (mean ± SE) before and 34±6 after lung removal (5 dogs). In B, the increases in mean aortic pressure obtained with the block were 68±13 before and 21±4 after heart removal (5 dogs). The increases in aortic pressure were statistically significant. These experiments demonstrate that vagal afferents from the heart and from the lungs 1) affect tonically the circulation 2) act in both instances to inhibit the sympathetic vasomotor drive. The role of this inhibition under normal circumstances remains to be determined. (Supported by NIH grant HLO 6143).

HEMODYNAMIC TRANSIENTS DURING THE ONSET OF SALT LOADING HYPERTENSION. R. Davis Manning, Jr.*, Thomas G. Coleman, Roger A. Norman, Jr.*, Robert E. McCaa*, and Allen W. Cowley, Jr., Dept. of Physiology & Biophysics, Univ. Miss. Sch. Med., Jackson, Miss.

Experimental hypertension was produced in subtotally nephrectomized dogs by increasing their salt and water intake. Hemodynamic data was collected on 12 mongrel dogs during the initial phases of this hypertension. The animals previously had renal mass surgically reduced to 30% normal and were equipped with chronic catheters in the aorta and right atrium. Isotonic saline was continuously infused at 190 cc/kg-day for 13 days following a one week period of baseline measurements. Arterial pressure was elevated during the entire infusion period and reached a final value of 132% baseline. Initial salt and water retention was evidenced by an increase in blood volume from 82 cc/kg to 101 cc/kg on the 3rd day and an increase in sodium space from 332 cc/kg to 422 cc/kg on the third day. Both the blood volume and sodium space returned close to baseline after 13 days. The mean circulatory pressure increased from a baseline value of 7.3 mm Hg to 12.0 mm Hg on the 3rd day and then decreased to 9.4 mm Hg on the 13th day. Cardiac output reached a maximum value of 138% baseline on the 3rd day and progressively decreased to a final value of 110%, while total peripheral resistance increased to a final value of 120% baseline. Salt loading resulted in a reduction of plasma renin activity from 1.1 ng A_I/cc/hr to an undetectable concentration after the 6th day, while plasma aldosterone concentration decreased from 9.6 ng% to 7.0 ng% on the 13th day. These data show that the elevated arterial pressure is initially caused by an increased cardiac output and is maintained by an increased total peripheral resistance. The increase in cardiac output is a result of fluid retention and elevated mean circulatory pressure. Suppported by NIH Grants No. HL 11678 and 5-TL-HE 5184.

FUNCTIONAL AND STRUCTURAL IDENTIFICATION OF NEURONS IN THE CATFISH RETINA. PART I. P. Z. Marmarelis* and K. -I. Naka, Information Science Department, California Institute of Technology, Pasadena, California 91109.

Two-inputs white noise analysis was performed on the neuron chains which subserve the catfish concentric retinal receptive fields. The light-to-horizontal cell system is nearly linear, within a restricted range, having a small dynamic nonlinearity persistent even for "small signals". The surround (annular) response is faster (latency and frequency responses) than the center (spot) response, when each one alone is present. The center response becomes faster and its gain increases in presence of an annular signal, while the surround response is unaffected by the presence of a center stimulus. The dynamic interaction between the two components is linear and synergetic and affects only the center response but not the surround. The light-to-ganglion cell system is strongly nonlinear (half-wave rectification). The center response is slower in the absence of surrounding stimulation but becomes faster in the presence of it. No corresponding change is observed for the surround response. The dynamic interaction between these two receptive-field components is linear, antagonistic and reciprocal.

Evidence indicates that a feedback mechanism exists from the horizontal cells to the receptors which acts to improve the frequency response performance of these initial stages.

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NIGROSTRIATAL BUNDLE (NSB) DAMAGE AND FEEDING. John F. Marshall* and Philip Teitelbaum, University of Pa., Phila., Pa. 19104

Bilateral intrastitial injections of 6-hydroxydopamine along the NSB, at the level of substantia nigra or globus pallidus, produce a syndrome of feeding and drinking impairments similar to that seen after electrocoagulation of lateral hypothalamus (LH). Rats with NSB destruction become aphagic and adipsic, and reject food that is offered. Such rats progress through the same sequence of stages in the recovery of feeding as do rats with LH lesions. After aphagia/adipsia, they eat moist, palatable foods, but not enough to maintain body weight; then, they regulate their body weight and caloric intake on palatable foods but refuse to drink water; and finally they maintain a stable weight on dry pellets and water. Rats with NSB damage have long-term impairments in responding to regulatory challenges which are similar to those seen after LH lesions. They overeat in the cold, but not in response to glucoprivation. They fail to drink when food is absent or in response to cellular dehydration or hypovolemia. However, rats with NSB damage are less finicky to bad-tasting diets than are rats with LH lesions. Sensorimotor impairments (difficulty localizing stimuli, hypokinesia, limb dys - function and rigidity) observed after NSB damage seem to contribute to the ingestional losses, but cannot fully account for the regulatory and motivational deficits seen after destruction of this dopamine-containing pathway.

EVIDENCE FOR CONGENITAL GROWTH HORMONE (GH) DEFICIENCY IN THE MUNICH-WISTAR RAT. J.B. Martin*, Carol A. Harris* and J.H. Dirks. Department of Medicine, McGill University, Montreal, Canada.

The Munich-Wistar (MW) rat is typified by a renal abnormality in which some glomeruli are present on the kidney surface. Studies using these rats for micropuncture led to the chance observation that body growth was significantly retarded when compared to normal Wistar (W) rats. The body weight in male MW rats, age 5-6 months was 201 ± 4 g (mean ± S.E.) compared to 335 ± 10 g in controls of the same age. In females the body weights were 137 ± 5 g (MW) and 216 ± 4 g (W) respectively. Mean glomerular filtration rate in 15 female MW rats was 0.67 ± 0.06 ml/min or 0.33 ± 0.03 ml/min/100 g body weight and single nephron filtration rate averaged 16.5 ± 2.4 nl/min in 6 rats; values lower than in comparable Wistar rats. Plasma GH levels (as determined by radioimmunoassay) in nonstressed decapitated rats were unmeasurable (<1 ng/ml) in male MW rats (n=10), compared to 33.5 ± 11.7 ng/ml in 10 control animals. In 10 female MW rats plasma GH levels were less than 4 ng/ml; in 7 out of 10 animals values were less than 1 ng/ml. In contrast, normal female Wistar rats had plasma GH levels of 22.1 ± 9.6 ng/ml. Pituitary GH concentration was significantly higher in both female (13.9 ± 1.2 (MW) vs 10.4 ± 1.0 (W) µg/mg; $p<.05$) and male (22.1 ± 1.9 (MW) vs 15.7 ± 0.6 (W) µg/mg; $p<.01$) MW rats. Plasma prolactin, corticosterone and T.S.H. levels were normal. It is postulated that MW rats have a hereditary defect in pituitary GH release, deficient GH possibly accounting for the low glomerular filtration rate. The basic cause of this defect in GH secretion and the resulting growth retardation remains to be established.

ABSENCE OF RELATIONSHIP BETWEEN NASAL BLOODFLOW AND NASAL AIRWAY RESISTANCE IN HEALTHY SUBJECTS. John S. Martin* and M.H.F. Friedman. Dept. of Physiology, Jefferson Med. College, Thomas Jefferson Univ., Philadelphia, Pa. 19107.

Over 1400 continuous simultaneous recordings of nasal airflow, nasal intraluminal pressure, thoracic respiration, nasal septal bloodflow, digital bloodflow, heart rate and spectographic analyses of nasal respiratory sounds were made in 24 adult subjects in good health. Nasal airway resistance was calculated from nasal pressure and airflow data. The effects on these variables of compression of the carotid artery or jugular vein, application of cold or warmth to the face, immersion of the hand in cold or warm water, and nasal insufflation of sympathomimetic agents were studied. The influence of instituting maximum (forced) respiratory effort, exercise, and total breathing by mouth were also studied. No statistically significant difference was found between Caucasion and Afro-American subjects for either nasal airflow or nasal bloodflow. The sinus arrhythmia patterns in nasal bloodflow which are exhibited when the subject breaths through the nostril are markedly reduced when he breaths through the mouth. No correlation between nasal airway resistance and nasal blood flow was found. Airway resistance may be increased or decreased independently of nasal vasodilation or vasoconstriction. The results do not support the view that in the subject without nasal pathology the caliber of the nasal airways is determined by the state of the nasal mucosal vasculature. This study suggests that some other portion of the upper airway (larynx?) is responsible for much of the airway resistance which is measured at the level of the nostrils.

EFFECT OF AGING AND ALTITUDE ACCLIMATION ON THYROID FUNCTION. Loren G. Martin*, John M. Connors*, Thomas J. Doubt*, James J. McGrath and Grace E. Wertenberger. Department of Physiology, Temple University School of Medicine, Philadelphia, Pa. 19140 and Department of Basic Sciences, Peoria School of Medicine, Peoria, Il. 61606.

While previous studies in our laboratory have demonstrated that acclimation to simulated high altitude is capable of depressing thyroid function, the effect of this environmental parameter has not been adequately assessed on the basis of age. Rats whose ages were 1, 3, 15 and 39 months of age were maintained on a thyroxine-free synthetic diet and tap water ad libitum. Altitude-exposed animals (23,000 feet for 5 weeks) and Philadelphia controls (150 feet above sea level) were compared on the basis of thyroid wet weight per 100 gm body weight, thyroidal histology, and serum PBI values. Thyroid weights were maximal in the 1 month-old controls, decreased at 3 months of age, and increased progressively with age in the 15 and 36 month-old groups. All animals showed an increased thyroid weight with altitude exposure, but this change was not significant in the older animals. As a result of altitude exposure, PBI values were increased in the 1 month-old group, not significantly changed in the 3 month-olds, and were decreased in the older animals. These results were substantiated by histoligical examination. (Supported by NIH General Research Support Grant awarded to Temple University School of Medicine, 5S01RR05617-10.)

PULMONARY FUNCTION MEASUREMENTS IN LABORATORY PONIES. J. L. Mauderly, W. C. Nenno, and G. A. Morrison (Introduced by B. A. Muggenburg). Lovelace Foundation for Medical Education and Research, 5200 Gibson Blvd. S. E., Albuquerque, New Mexico 87108.

The pulmonary function of 2 male and 2 female adult grade ponies was measured without anesthesia or sedation. Parameters included respiratory frequency, tidal and minute volumes, functional residual capacity, nitrogen clearance equivalent, CO diffusing capacity, fractional uptake of CO, alveolar and arterial P_{O_2} and P_{CO_2}, alveolar-arterial gradients for O_2 and CO_2, O_2 saturation of hemoglobin, arterial pH, O_2 uptake, CO_2 output, respiratory exchange ratio, specific ventilation, and alveolar ventilation. The values for alveolar and arterial O_2 and CO_2 tensions, arterial pH, and O_2 saturation of hemoglobin were similar to those obtained from Beagle dogs and human subjects at the same elevation. Other parameters demonstrated typical differences related to body size. The practicality of handling ponies as experimental subjects in the laboratory and the similarities between equine and human lung ultrastructure suggest the usefulness of the pony in respiratory studies. (Research performed under U. S. A. E. C. Contract AT(29-2)-1013 in facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.)

CONTROL OF PRE-CAPILLARY SPHINCTER DYNAMICS. H.N. Mayrovitz*, A. Noordergraaf, and L.H. Peterson, Dept. of Bioengineering and Bockus Res. Inst., Univ. of Penna., Phila., Pa.

In vivo pre-capillary sphincter (PCS) contraction duration (T_C) and dilation duration (T_D) are quite variable. To evaluate the role of fluid pressure in the tissue (P_T), PCS dynamics were predicted by means of a microvascular model in which the lumen diameter in the vicinity of the PCS was intrinsically controlled by P_T which depended on the capillary-tissue osmotic pressure difference (P_D) and the overall microvascular hemodynamics. The bat wing was used as the experimental model for developing a topological and functional hybrid computer simulation of the microcirculation. The results were tested for compatibility with available experimental data. Changes in the fundamental period (T) of PCS dynamics and of the ratio (T_C/T) were then obtained as a function of perfusion pressure (P_{AV}) and P_D. The results show: 1. for a given P_D, T is a double valued function of P_{AV}. With increasing P_{AV}, T first decreases, then increases. The pressure at which the minimum T occurs depends on P_D. T ranged between 10 and 30 seconds which is quantitatively compatible with measurements of duration of RBC flux through capillaries. 2. Increases in P_D reduce T at a given P_{AV}. 3. The ratio (T_C/T) monotonically increases with increasing P_{AV}. This predicted increase is in quantitative agreement with direct in vivo measurements. 4. Elevations of P_D increase this ratio by an amount that depends on P_{AV}. The possibility that tissue fluid pressure plays an important role in the control of PCS dynamics is compatible with the present results. Though the double-valued relationship between T and P_{AV} predicted by the model needs to be experimentally verified, it may well be possible to exploit the dependence of this control on osmotic values as a means of distinguishing between the mechanism investigated here and other postulated mechanisms such as myogenic control.

AMINO ACIDS IN INDIVIDUAL AXONS FROM THE LOBSTER. W.J. McBride,* A.R. Freeman, L.T. Graham, Jr.*, R.P. Shank*, and M.H. Aprison. Sections of Neurobiol. and Neurophysiol., Inst. of Psychiatric Res., Ind. Univ. Med. Ctr., Indianapolis, Ind. 46202.

The levels of alanine, proline, glycine, GABA, glutamate and aspartate were measured in 6 giant axons and several medium size axons in the nerve bundle connecting the supraesophageal ganglion and first thoracic ganglion in the CNS, the external cellular sheath covering this connective, and identifiable inhibitory and excitatory axons and bundles of sensory axons from the walking limbs. In the external cellular sheath (non-neuronal material), the content of glycine was 2.4, 3.7, 4.9 and 650 times higher than the levels of alanine, proline, glutamate and aspartate, respectively. In contrast, aspartate was present in the highest amounts in the 6 giant and medium size axons. In general, the pattern observed for the axon with the largest diameter was also found to be the case for the other 5 giant axons. Comparison of the concentrations found for the amino acids in this axon with respect to the inhibitory (I), excitatory (E) and sensory (S) axons revealed the following: the mean level (in mM) of alanine in the giant axon was 8.60 vs. 20.2 (I), 21.3 (E) and 5.99 (S); that for proline was 2.0 vs. 3.5 (I), 18.6 (E) and 5.78 (S); that for glycine was 18.6 vs. 39.8 (I), 64.0 (E) and 28.8 (S); that for glutamate was 7.19 vs. 24.2 (I), 31.8 (E) and 4.98 (S); and that for aspartate was 70.6 vs. 109.1 (I), 101.8 (E) and 37.8 (S). GABA was detectable only in the inhibitory axons (36.9 mM). On the basis of the data obtained, it would appear that neither GABA nor glutamate are likely candidates for neurotransmitters in the 6 giant axons of the CNS. The relatively high content of aspartate in these latter 6 axons as well as in the inhibitory and excitatory axons may point to some specialized neuronal function for aspartate. This research was supported by NSF and NIMH grants.

SEPARATION OF FREE AND BOUND STEROID IN THE RADIOIMMUNOASSAY FOR ALDOSTERONE: ACCURACY AND REPRODUCIBILITY. Connie S. McCaa and Robert E. McCaa*. Department of Biochemistry and Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

Various agents may be used to separate antibody-bound from free antigen in radioimmunoassay procedures and the accuracy, sensitivity, and reproducibility of the procedure are dependent upon the choice of agent. We have compared three of the agents used in radioimmunoassay of aldosterone (Florisil, dextran-coated charcoal, and saturated ammonium sulfate solution) with consideration of technical simplicity. Antiserum to aldosterone carboxymethoxime coupled to bovine serum albumin was obtained from rabbits and used at a dilution of 1:50,000 in the assay of aldosterone over the range of 0 to 200 picograms. Maximum sensitivity was obtained with ammonium sulfate with a 61% decrease in binding from 0 to 200 picograms as compared to 46% for dextran-coated charcoal and only 25% for Florisil. A comparison of the accuracy by t-test at each concentration showed no significant difference between the three methods. However, the reproducibility of each technique, as determined by analyzing the coefficient of variation of replicate samples, was significantly better for the ammonium sulfate method. This higher degree of reproducibility coupled with its relative simplicity indicates that the ammonium sulfate precipitation method of separating antibody-bound from free aldosterone is the technique of choice. Supported by USPHS Grant HL 09921.

EFFECT OF ACUTE SODIUM DEPLETION WITHOUT A CHANGE IN PLASMA POTASSIUM CONCENTRATION OR FLUID VOLUME ON ALDOSTERONE SECRETION IN ANEPHRIC MAN. R.E. McCaa*, J.D. Bower* and C.S. McCaa. Department of Physiology and Biophysics, University Medical Center, Jackson, Mississippi.

Plasma aldosterone concentration (PAC) can increase in anephric man during hemodialysis. Since metabolic clearance rate of aldosterone does not change during hemodialysis, aldosterone secretion must increase in response to sodium and/or volume depletion. This study was designed to determine the relative influence of sodium and volume depletion and plasma sodium concentration per se on PAC in anephric man. Fluid volume was reduced (605 ml) in 13 anephric subjects by ultrafiltration. Plasma sodium and potassium concentration did not change, but total body sodium and potassium decreased during ultrafiltration. PAC did not change significantly after ultrafiltration. An additional 1100 ml fluid was removed from 5 anephric subjects by ultrafiltration and hemodialysis without changing plasma sodium concentration. PAC did not change significantly in response to volume reduction in anephric man. An additional 1000 ml fluid was removed from 8 anephric subjects by ultrafiltration and hemodialysis and plasma sodium concentration was lowered from 138.0 to 130.5 mEq/L. PAC increased from 9.3 to 19.4 ng% ($p < 0.05$). Three anephric subjects were hemodialyzed for 8 hours against a dialysate containing 125 mEq/L sodium while plasma potassium concentration and body fluid volume were held constant. Plasma sodium concentration decreased from 138.5 to 125.0 mEq/L and PAC increased from 7.4 to 24.3 ng% ($p < 0.01$). These data indicate that decreasing plasma sodium concentration without changing plasma potassium concentration or total body fluid volume can stimulate aldosterone secretion in man by some mechanism that excludes the renal renin-angiotensin system.

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PRE-OPTIC ANTERIOR HYPOTHALAMIC SENSITIVITY TO LOCALIZED COOLING IN THE UNRESTRAINED ADULT NEW ZEALAND WHITE RABBIT. G.N. McEwen Jr.* and J.E. Heath. Department of Physiology & Biophysics, University of Illinois, Urbana, Illinois 61801.

These experiments were designed to investigate whether rabbits respond to pre-optic cooling at different ambient temperatures by changing the set point for shivering as in the dog, or by changing the pre-optic sensitivity as in the cat. Two male and two female adult white rabbits were implanted with thermodes and re-entrant tubes stereotaxically in the pre-optic anterior hypothalamic area. Three experimental protocols; alternate heating and cooling; cooling, recovery, cooling; and cooling by steps with no recovery period between each step; were used at ambient temperatures of 20,10,0, and -8°C. Pre-optic, rectal, ear temperature, and O_2 consumption were continuously monitored. A total of sixty experiments were conducted. In 28% of these, the animals responded by changing the set point while maintaining a relatively constant preoptic sensitivity of -.81 W/Kg-°C. In 72% of the experiments, the animals had preoptic sensitivities of -.10 W/Kg-°C at 20°C, -.16 W/Kg-°C at 10°C, -.29 W/Kg-°C at 0°C, and -.50 W/Kg-°C at -8°C. The type of response could not be predicted from rectal temperature, ear vasomotor state, pre-optic temperature change, beginning O_2 consumption values, or experimental protocol. We have previously determined that postural changes play a significant role in rabbit thermoregulation, and it seems likely that the mode of response of these animals is determined by some combination of behavioral changes and possibly awareness state of the animals. (Supported in part by NSF grant GB-13797.)

TIME BEHAVIOR OF SERIES ELASTICITY IN CARDIAC MUSCLE
Robert J. McLaughlin,* Freddy Epstein,* and Edmund H. Sonnenblick
Peter Bent Brigham Hospital and Harvard Medical School, Boston, Mass.

Series elasticity (SE) of cardiac muscle was studied at various times in an isometric contraction to find evidence of compliance changes due to changing numbers of myofilament cross-bridges. Controlled-length quick releases at constant velocities were applied to cat papillary muscles at 25°C. Force and length were measured continuously during each release, thus providing a complete SE curve without recourse to multiple releases or extrapolation methods. The force-extension curve of the SE was exponential, and the compliance varied with force independently of time. Initial muscle length did not affect SE compliance relative to time, and SE force-extension curves at different initial lengths were virtually identical. Conventional comparisons of SE compliance in terms of SE shortening between peak tension and preload, however, showed wide variation with initial muscle length because of the different portions of the force-extension curve traversed. This problem was avoided by expressing SE compliance in terms of the length change x_e necessary to reduce force by $1/e = 0.368$ anywhere on the force-extension curve. x_e averaged $1.87 \pm .26\%$ of initial muscle length, which is about 25% smaller than reported previously. Because of the exponential shape of the SE force-extension curve it is theoretically impossible to identify the origin of the series elasticity by tests of this kind. However the large compliance of cardiac muscle relative to skeletal muscle makes it seem unlikely that cross-bridge compliance contributes substantially to total myocardial compliance.

EFFECT OF HISTAMINE ON ISOGRAVIMETRIC CAPILLARY PRESSURE IN THE GRACILIS MUSCLE. J. McNamee* and F.S. Grodins. Department of Biomedical Engineering, University of Southern California, Los Angeles, California.

Recent observations indicate that histamine can produce accumulation of edema fluid even in tissues perfused at arterial pressures below average normal capillary pressure. This phenomenon, which cannot be explained by an altered pre- to post-capillary resistance ratio, suggests that there is a lowering of equilibrium capillary pressure due to the action of histamine. To test this hypothesis, isogravimetric capillary pressure (P_{C_i}) was measured in the isolated perfused canine gracilis muscle, with and without the presence of histamine in the perfusion circuit. Mean P_{C_i} without histamine was 15.5 $\pm$ 4.0 mmHg while P_{C_i} with histamine was 2.4 $\pm$ 2.9 mmHg and sometimes net fluid filtration could not be stopped. In another group of experiments, albumin or dextran was added to increase control P_{C_i}. Mean P_{C_i} without histamine was 23.7 $\pm$ 2.6 mmHg and 5.7 $\pm$ 2.4 mmHg with histamine present. The fall in P_{C_i} in both groups was found to be significant ($P < .01$), and was greater than that observed in heterogeneous preparations (e.g., hindlimb). It is concluded that histamine acts to diminish the osmotic gradient between plasma and tissue, thereby reducing P_{C_i}. (This work was supported in part by USPHS Grants GM 01724 and GM 16437.)

LEFT VENTRICULAR, CORONARY AND REGIONAL VASCULAR EFFECTS OF DOBUTAMINE IN CONSCIOUS DOGS. Robert J. McRitchie*, Stephen F. Vatner, Ronald Tuttle* and Eugene Braunwald. Depts. Med., Harvard Med. Sch. and Peter Bent Brigham Hospital, Boston, MA, and Lilly Res. Lab., Indianapolis, IN.

Dobutamine, a synthetic sympathomimetic amine, was developed in order to provide an inotropic agent with minimal effects on arterial pressure and heart rate. Dobutamine was administered i.v. in graded doses (4-40 ug/kg bolus and 8-40 ug/kg/min by infusion) in 7 conscious dogs 2-4 weeks after instrumentation with Doppler flow probes on the left circumflex coronary, mesenteric, renal and iliac arteries, arterial catheters, left ventricular (LV) P gauges for LVP, dP/dt and dP/dt/P and endocardial diameter (D) gauges for LVD, dD/dt, i.e., velocity (V_{iso}). Dobutamine infusion, 40 ug/kg/min, resulted in little change in mean arterial pressure, heart rate, and end diastolic D, while increasing dP/dt/P (+85%) and V_{iso} (+76%) and decreasing end systolic D(-5mm) and resistance in the coronary (-44%), mesenteric (-20%), renal (-19%) and iliac (-41%) beds. Practolol 4 mg/kg blocked the inotropic response, and with the addition of phentolamine 1 mg/kg dobutamine decreased resistance in the coronary (-32%), mesenteric (-24%), renal (-28%) and iliac (-50%) beds. After propranolol 1-2 mg/kg, the inotropic response was again blocked but dobutamine now increased resistance in the coronary (+10%), mesenteric (+22%), renal (+12%) and iliac (+30%) beds, while the addition of phentolamine resulted in abolition of these vasoconstrictor responses, indicating that dobutamine possesses relatively minor adrenergic alpha constricting and beta$_2$ dilating vascular effects. Thus, dobutamine exerts a potent inotropic action associated with little chronotropic effect and does not produce marked alpha adrenergic vasoconstrictor effects, resulting in maintenance of arterial pressure near control levels while cardiac output rises. Therefore, dobutamine possesses unique actions, which make it a potentially valuable therapeutic agent.

WASH-IN KINETICS OF ALBUMIN IN PULMONARY INTERSTITIAL FLUID AND RIGHT DUCT LYMPH.
E. C. Meyer and R. Ottaviano (intr. by M.H.F. Friedman). Mercy Catholic Medical Center, Darby, Pennsylvania 19023.

We measured the transport kinetics of radioiodinated albumin (RISA) from plasma to right duct (RD) lymph, and compared this with plasma to pulmonary interstitial fluid RISA transport. Five days after giving intravenous 125-RISA to 8 dogs, when equilibration with total body albumin was established, we cannulated the RD, injected 131-RISA intravenously, and maintained plasma concentration constant. We collected lymph to T 1/3 131-RISA equilibration. Only a single wash-in exponential (K_R) could be identified. From lung homogenates at the end of the experiments, we measured total extravascular water (Q_{wl}), 14C-Sucrose extravascular space (Q_{iw}), Evans Blue Dye plasma volume, total albumin in Q_{iw} (A_I), and the transported 131-RISA in Q_{iw}. Mean $K_R = 2.08 \pm 0.82 \times 10^{-3}$ (min^{-1}), Q_{wl} = 4.6 ± 1.1 ml/kgm, Q_{iw} = 2.41 ± 0.2 ml/kgm, and A_I = 0.53 ±0.15 gm. The calculated 131-RISA/125-RISA ratio in Q_{iw} was 0.34 ± 0.12. The measured 131-RISA/125-RISA ratio in RD lymph at death was 0.33 ± 0.10 for an experimental time of 240 ± 54 min. These data indicate that the normal turnover time of albumin in pulmonary interstitial fluid is approximately 500 min., and this is reflected by the fastest exponential observed in RD wash-in kinetics.

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SERUM LEVELS OF GONADOTROPIN-RELEASING HORMONE (GN-RH) THROUGHOUT THE ESTROUS CYCLE OF RATS.
M. H. Meyer, J. F. Masken, T. M. Nett and G. D. Niswender (Intro. by M. L. Hopwood). Dept. of Physiology and Biophysics, Colo. State Univ., Ft. Collins, Colo.

Adult female Sprague-Dawley rats were maintained in a 14 hr light 10 hr dark regime and estrous cycles were monitored with daily vaginal smears. After exhibition of at least two cycles 4 days in length, the rats were divided into 4 groups: diestrus day 1 (I), diestrus day 2 (II), proestrus (III), and estrus (IV). Approximately 4 rats were sacrificed by decapitation at 0800, 1000, 1200, 1400, and 1600 in each group and blood samples were collected. Serum was obtained and Gn-RH and luteinizing hormone (LH) concentrations were determined by radioimmunoassay. In groups I and II Gn-RH levels were low ($<$20 PG/ML) at 0800, rose by 1000 and remained high (80-120 PG/ML) at 1200 and 1400 but had declined ($<$10 PG/ML) by 1600. In group III and IV Gn-RH levels were high at 0800 and remained elevated through 1000, 1200, and 1400 (50-120 PG/ML). In group III Gn-RH had declined to 12.5 ± 2.7 PG/ML at 1600 while in group IV the levels at 1600 were very high 148 ± 48 PG/ML. Elevated levels of LH were noted in all rats in Group III killed at 1600. These results suggest a daily pattern of release for Gn-RH rather than a single release on proestrus. It is possible that the steroid hormonal environment in the rat is optimal for LH release only on proestrus or that some factor other than Gn-RH is responsible for the proestrus LH surge in the rat. (Supported in part by a Grant from Abbott Laboratories, G. N.).

BRONCHIAL MAST CELLS AND HISTAMINE IN EXPERIMENTAL CANINE ASTHMA. J. L. Meyers*, D. Dain*, W. M. Gold, R. L. Miller*, and H. R. Bourne* Cardiovascular Research Institute and Department of Medicine, University of California San Francisco, California 94122.

We have previously shown that antigen inhalation by allergic dogs results in histamine release from lung correlating with the severity of the respiratory reaction. This study was done to determine the effect of inhaled antigen on mast cells and histamine concentration in the airways of allergic dogs. Histologic specimens were fixed in Carnoy's solution and stained with toluidine blue. Histamine was measured by the enzymatic double-isotope dilution method. In 6 open-chested dogs, mast cell counts and bronchial histamine concentrations were determined in the right lower lobe resected before and in the left lower lobe resected after antigen inhalation. Arterial plasma histamine and respiratory resistance (Rrs) were measured before, and after antigen inhalation. In controls, mast cell counts were 126 ± 12 (mean ± SE) per 25 hpf in proximal airways and 228 ± 15 in distal airways, and correlated closely with histamine concentrations of 4.6 ± 0.7 ng/gm in proximal and 10.9 ± 2.5 ng/gm in distal airways. Following antigen inhalation, proximal airway mast cells decreased 31 ± 7% ($P < .01$); distal airway counts and bronchial histamine concentrations remained unchanged. Arterial plasma histamine increased to 143 ± 43 ng/ml and correlated with increased Rrs (989 ± 166% above control). Conclusion: antigen induced bronchoconstriction is associated with histamine release from proximal airway mast cells. The lack of change in bronchial histamine may indicate that most of the histamine released remains in airway tissue or that small changes in concentration cannot be detected in the presence of large tissue stores. Supported in part by USPHS grants HL-14201 and HL-09964.

THE IMPORTANCE OF SPECIFIC SENSORY FIBERS OF THE SUPERIOR LARYNGEAL NERVE TO SWALLOWING AND RESPIRATION. Arthur J. Miller and Robert F. Loizzi. Univ. Illinois Med. Center, Chicago, Illinois.

The importance of sensory input from the larynx to a number of brain stem reflexes involving glottic closure, respiratory inhibition, coughing, swallowing, and mucosal secretion raises the question of the contribution of the fibers carried by the superior laryngeal nerve (SLN). Histological preparation of the sensory internal branch (ILN) of the SLN with both light and electron microscope analysis indicates that unlike most extremity nerves, this cranial nerve contains predominantly myelinated fibers with a unimodal distribution (range, 1.3-16.7 μ; median, 3.8 μ). Reconstruction of the compound action potential from the myelinated fiber distribution using the Landau et al. method indicates three major peaks. Electrically stimulating the ILN at low current intensities while recording centrally on the SLN indicates a two peak compound action potential. At maximum intensities, the first major negative potential differentiates into two separate peaks, giving a three component action potential. Correlation of the recorded three peak compound action potential with the reconstructed action potential indicates that the first major potential evoked at low intensities incorporates fibers ranging in size from 6.7-16.7 μ. Stimulation of the ILN of the anesthetized cat at 3/sec indicates that this first major negative potential reaches its maximum amplitude (2.6 T) before either the inhibition of respiration (3.2 T) or the evoking of swallowing (8.4 T), or the threshold of the second potential (9.8 T). Stimulation at 30/sec demonstrates a lower threshold for apnea (2.0 T) and swallowing (2.7 T) and definitely incorporates fibers contributing only to the first major potential indicating that the largest fibers of the ILN, comprising less than 20% of the total number, effect both respiration and swallowing. (Supported by NIDR, NS 10154-01)

CANINE FORELIMB LYMPH FLOW AND PROTEIN CONCENTRATION FOLLOWING THE RELIEF OF PROLONGED ISCHEMIA. G.L. Miller*, R.L. Kline*, J.B. Scott, F.J. Haddy, and G.J. Grega. Department of Physiology, Michigan State University, East Lansing, Michigan 48823.

Ischemia has been reported to increase microvascular permeability to plasma proteins and increase extravascular fluid volume. However, we found no evidence for a rise in extravascular fluid volume following the relief of prolonged ischemia (2 hr.) in canine forelimbs perfused either naturally or at constant inflow, suggesting that ischemia fails to increase microvascular permeability in canine forelimb (The Physiologist, Vol. 15, 1972). To further test the effect of ischemia on protein permeability, lymph flow and protein concentration were measured in the forelimb of male dogs anesthetized with sodium pentobarbital. Ischemia was induced by clamping the brachial artery for 2 hours in collateral-free, innervated naturally perfused canine forelimbs or by stopping arterial inflow for 2 hours in intact forelimbs utilizing a pressure cuff. Lymph flow and protein concentration were measured during a control period and at regular selected intervals during a 60 min. period following the relief of the ischemia. Lymph flow and protein concentration failed to change relative to control throughout the 60 min. post-ischemic period. These data fail to provide evidence for an ischemia induced increase in microvascular permeability to plasma proteins or increase in protein efflux in the canine forelimb. Hence, the concept that ischemia increases microvascular permeability to plasma proteins needs to be carefully re-examined.

HEMODYNAMIC PROPERTIES OF PARALLEL REGIONS DRAINED BY THE INFERIOR VENA CAVA. W. Mitzner*, H. Goldberg*, and S. Permutt. Johns Hopkins Univ. School of Hygiene & Public Health, Baltimore, Maryland 21205.

We have used a model consisting of an arterial resistance, R_a, venous compliance, C_v, and venous resistance, R_v, in a series arrangement to investigate the effect of both transmural pressure and epinephrine on those parameters in parallel regions drained by the inferior vena cava (IVC). The IVC flow was divided into splanchnic (S) (drainage through the liver), and non-splanchnic (NS) portions. A preparation was utilized that allowed control of outflow pressure (P_{IVC}) for each region and adjustment of cardiac output. Outflow from each region and aortic pressure were measured. For each region the pressure within the compliance portion was considered equal to the plateau in P_{IVC} which occurred following 4-10 sec. of simultaneous occlusion of inflow and outflow. R_v and R_a could then be calculated. With constant arterial inflow, volume could be added to each region by increasing outflow pressure. The volume increment divided by the increase in P_{IVC} was considered equal to the compliance. Experiments in 5 dogs before and during administration of epinephrine (60 µg/min i.v.), with aortic pressure kept at or near control by adjusting cardiac output, have shown the following: 1. $R_a(S)$ and $R_a(NS)$ were both elevated during epinephrine but the per cent increase in $R_a(NS)$ was greater; 2. For P_v in the range of 0-18 mmHg, $C_v(S)$ and $C_v(NS)$ were both found to decrease with increasing P_v. Epinephrine caused a small reduction in $C_v(S)$ but had little effect on $C_v(NS)$; 3. In the experimental range of P_v both $R_v(S)$ and $R_v(NS)$ were independent of P_v, and both were elevated with epinephrine. However, $R_v(S)$ during epinephrine decreased with increasing P_v approaching control levels at high P_v. (Supported in part by PHS grants HL-14153 and HL-05453.)

A SIMPLE METHOD TO DETERMINE THE MEAN SPECIFIC VENTILATION AND VARIANCE. J. Mohler*, J. Butler* and J. Hackney. LAC/USC Medical Center and Rancho Los Amigos Hospital, Los Angeles, Calif.

A lung model with continuous distribution of both ventilation and perfusion (Math. Biosc. 9:195-203, 1970) describes a volume weighted linear distribution of alveolar ventilation (β). Mean specific ventilation ($v=Vt/Vo$, $Vo=FRC-V_D$) and its variance (σ) for the lung, and in some cases the distribution function β can be determined from the first 15 breaths of a standard N_2 washout procedure. By definition, the differential number of units with v between v and v+dv is proportioned to the distribution function (ρ): $d\xi/Vo=\rho(v)\int dv(Vo=\int d\xi, d\xi$ is an infinitely small volume weighted lung slice). We can then define $1=\int dv\rho(v)$, $\bar{v}=\int (dv)v\rho(v)$, $\bar{v}^2=\int dv\ v^2\rho(v)$ and $\sigma^2=\overline{v^2}-\bar{v}^2$ and expand $f(v)$ about $\bar{v}$ in a Taylor series: $f(v)=f(\bar{v})+(v-\bar{v})f'(\bar{v})+\frac{1}{2}(v-\bar{v})^2f''(\bar{v})+\ldots$ Neglecting higher order terms, doing the integral $\int dv\rho(v)f(\bar{v})=f(\bar{v})+\frac{1}{2}\sigma^2f''(v)$. We can by substitution and use of the law of Parsimony (Occam's Razor) yield $\ln \bar{C}n/Co=-n\ln 1+\bar{v}/1+(V_D/Vo)+\ln[1+\frac{1}{2}\sigma^2(n((n-1)\bar{v}-2)/v(1+\bar{v})^2)]$. A curve fit of the plotted data by a polynominal yields $\ln \bar{C}n/Co=\mu n+\gamma n^2$ where $\mu=\ln 1+\bar{v}/1+V_D/Vo)+\frac{1}{2}\sigma^2[\bar{v}+2/\bar{v}(1+\bar{v})^2]$ and $\gamma=\frac{1}{2}\sigma^2[1/(1-\bar{v})^2]$. We can now solve for $\bar{v}$, σ and $\beta=\sqrt{3}/\bar{v}\ \sigma$.

We have used this model on data collected from normal and diseased subjects and find the discrimination good. Normal: n=25, $\bar{v}=.266\pm.07$, $\sigma=0.74\pm.02$, $\beta=.49\pm.12$; Obstructive lung disease: $\bar{v}=.120$, $\sigma=.75$, $\beta=1.09$ (not rational); Acquired heart disease: $\bar{v}=.205$, $\sigma=.061$, $\beta=.205$; D.I.F.: $\bar{v}=.379$, $\sigma=.07$, $\beta=.3$.

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SPINAL REFLEX VARIABILITY: A CORRELATION WITH SPONTANEOUS SPINAL CORD ACTIVITY. J. T. Molt* and E. L. Gasteiger. Dept. of Physical Biology, N. Y. S. Veterinary College and Section of Neurobiology and Behavior, Div. of Biol. Cornell Univ., Ithaca, N. Y. 14850.

The spinal electrogram (SEG) as recorded from the dorsal spinal gray matter of the cat consists of low voltage background activity, (25 μV) upon which occur random, monophasic, large amplitude (50-200 μV) potentials. These large potentials, termed negative sharp waves (NSW) are typically 40 msec in duration at their base and are recorded as negative in the dorsal gray matter, the suspected site of the interneuronal pools generating them. To test for possible functional significance, flexor (withdrawal) reflexes were elicited by stimulation of the superficial peroneal nerve during the occurrence of NSWs and at random. The reflexes recorded from the deep peroneal nerve were significantly greater in amplitude if they were evoked during NSWs as compared to those evoked at random. To test if this effect was due to altered levels of polarization in the primary afferent terminals, antidromic compound action potentials were recorded from the superficial peroneal nerve following stimulation in the spinal cord dorsal gray matter. The antidromic action potentials elicited during the occurrence of NSWs were significantly smaller in amplitude than those elicited at random. This is interpreted as being an indication of hyperpolarization of the primary afferent terminals (PAH) during the occurrence of NSWs and is considered the cause of the enhancement of the reflex potential. A model in which tonic depolarization present in the primary afferent terminals is transiently reduced during NSWs will be presented.

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EFFECT OF VASOPRESSIN AND NOREPINEPHRINE ON LARGE DEFORMATION MECHANICS OF CANINE ARTERIES IN VITRO. Emil Monos*, Robert H. Cox and Lysle H. Peterson. Bockus Research Institute, Univ. of Penna., Philadelphia, Pa.

Our recent studies have indicated a significant role of endogenous levels of vasopressin in the control of arterial mechanical properties in vivo. These studies were designed to clarify the regional specificity in responsiveness over a wide pressure range. The reactivity of cylindrical segments of common carotid (CC) and iliac (IA) arteries held at constant length to 150/μU/ml arginine-vasopressin (VP), and to 0.05 μg/ml norepinephrine (NE) was studied in vitro. The segments, incubated in physiological salt solution, were continuously inflated and deflated by air in 5-250 mmHg pressure (P) range at a rate of 100 mmHg/min, and their internal P, outer diameter (D) and axial tension were recorded continuously. By comparing the control and hormone activated P/D characteristics, the change in CC and IA strain (active strain) was computed. 3-5 min after NE administration, the peak CC active strain (-6.6±1.5%) developed at 60 mmHg, while in the case of IA (-23.5±4.2%) at 40 mmHg. The shape of CC and IA active strain curves differed substantially. VP alone was not effective within 5 min after its administration, but significantly potentiated the NE effect on both CC (peak: -9.5±1.5%) and IA (-25.3±4.2%). VP changed the shape of active strain characteristics of NE activated CC, but not of IA. Three-dimensional stress-strain characteristics of the vessel segment were determined before and after activation. VP augmented the active isometric stress responses produced by NE for both the CC and IA. The data suggest that endogenous levels of VP may enhance the effects of norepinephrine on vascular smooth muscle. The individual and combined effects of NE and VP can be the largest in hypotensive states. Significant regional variations in the effects of NE and the interaction of NE and VP have been demonstrated.

QUANTIFICATION OF INTERDEPENDENCE. M.S. Morgan*, S.V. Dawson*, F.G. Hoppin, JR. and G.C. Lee*. Harvard Sch. Pub. Health, Boston and SUNY Buffalo.

Distortion of the lung parenchyma is important to the size of airways, blood vessels, regions of inhomogeneity within the lung, and the distribution of pleural pressure. We have attempted to model the effect of lung distortion as follows. First, we have measured the mechanical properties of the lung in distortion. Second, we have developed a model of lung parenchyma as a collection of randomly arrayed non-linear elastic fibers and have compared the results to the experimental observations. Finally, we have applied the model to a physiological situation.

We set sixteen small hooks in each face of a 1 cm^3 cube of dog lung and applied normal loads. With equal loading of the faces, the cubes showed pressure-volume behavior both in saline and air which was typical of whole lungs. Unequal loading gave the stress-strain data for distortion. We then developed a model based on an array of fibers. Conceptually, the length-tension properties of the fibers themselves are related directly to the P-V curve. By considering the random array of fibers with these length-tension properties as it is distorted and by viewing it as a continuous material with the same properties, we derived the elastic coefficients. Then we predicted the mechanical response of the model to the experimental distortions and found good correspondence. Therefore the predictions of the model are probably valid for distortions of lung parenchyma (as long as the distortions are relatively small and extend over a distance which is large relative to alveoli).

We have used the model to predict the relationship between the radius of a cylindrical hole in the parenchyma and the stress applied to the inside of the hole (peribronchial pressure). The results show that at any given lung volume, the hole is on the order of four times stiffer than the original lower bound prediction of Mead et al JAP(28)5:596,1970. (supported by USPHS-HL-14580).

HYPOXIC VENTILATORY DEPRESSION. C.G.Morrill*, J.R.Meyer*, J.V.Weil*, and R.F.Grover. Univ. Colo. Med. Ctr., Denver, Colorado 80220

The question has been raised whether or not the full ventilatory response of an animal to hypoxia (HPX) is partially masked by HPX ventilatory depression. When an intact animal is made progressively HPX, $\dot{V}_E$ increases in a hyperbolic or exponential fashion until at very severe levels of HPX, a critical P_AO_2 is reached (14 to 25 mm Hg) at which abrupt ventilatory depression occurs. It has been suggested that HPX has two opposing effects on respiration: 1) stimulation of the peripheral chemoreceptors (PCR) to increase $\dot{V}_E$, and 2) CNS HPX which results in ventilatory depression. If this is correct, then PCR denervation should shift the P_AO_2 at which ventilatory depression occurs to a much higher value. Ten dogs, anesthetized with chlorolose, were studied intact, after carotid glomectomy or vagotomy to denervate the aortic bodies, and after both (complete PCR denervation). The mean P_AO_2 values given below for ventilatory depression were obtained from isocapnic, progressive HPX studies.

		Carotid glomectomy	complete PCR
critical	Intact	or vagotomy	denervation
P_AO_2 (mm Hg)	18.6±0.6 (SEM)	20.8 ± 0.9	21.8 ± 0.8

Only small changes were noted in the P_AO_2 at which ventilatory depression occurred after denervation. However, the difference between the intact and complete PCR denervation means did achieve statistical significance ($P < 0.05$). Following carotid glomectomy and complete PCR denervation, $\dot{V}_E$ was unchanged by HPX until ventilatory depression resulted at the critical P_AO_2. Thus, the probability of ventilatory depression occuring during hypoxic testing as the technique is normally used is minimal ($P_AO_2 \geq 40$ mm Hg).

CHOLINERGIC AND α-ADRENERGIC PARTICIPATION IN CENTRALLY-INDUCED NATRIURESIS. M. Morris and R. Orias (intr. by V. Sallee). Department of Physiology, Univ. of Texas Southwestern Medical School, Dallas, Texas 75235

The role of the central nervous system in the control of Na excretion was investigated by studying the changes in urine composition following the intraventricular (IVTR) injection of norepinephrine (NE), carbachol (C) and hypertonic saline (HS) in the rat. The mechanism of the natriuresis was then studied through the use of adrenergic and cholinergic blockers. Conscious male Holtzman rats (250-270g) with chronic cannulae in the third ventricle, bladder and jugular vein were infused with a 5% dextrose solution (.19 cc/min) and urine samples were collected at 15 min intervals. Control IVTR injections of 2 µl saline (.9%) or drug diluent caused no change in Na+ excretion. IVTR injection of 2 µl HS (2M), NE (5 µg) and C (.6 µg) caused a significant increase in Na^+ and K^+ excretion with an antidiuresis. When the B adrenergic blocker, Propranolol (PR) (30 µg), was given IVTR prior to NE or HS, the Na^+ excretion was greater than that produced by NE or HS alone. This increase was due to PR itself since when injected alone it significantly increased Na^+ excretion and the Na^+/K^+ ratio. IVTR injection of 30 µg of phentolamine, an α-adrenergic blocker, prior to NE and HS abolished their natriuretic properties. Treatment with IVTR atropine (150 µg) also blocked the response to both NE and HS. Thus, natriuresis can be induced by the IVTR injection of hypertonic NaCl as well as cholinergic and catecholaminergic drugs. Cholinergic and α-adrenergic synapses seen to be involved in the neuroendocrine pathway(s) regulating Na excretion. (Supported by NIH grant.)

INTERACTIONS OF THE VASCULAR, INTERSTITIAL AND LYMPHATIC SYSTEMS IN THE CAT INTESTINE. Nicholas A. Mortillaro*and Aubrey E. Taylor. Dept. of Physiology, Univ. Miss. Sch. Med., Jackson, Miss. 39216

An in-situ, isovolumetric intestinal loop was made using 10-30g of cat ileum in which the lymphatic vessel draining the loop was also cannulated. Venous outflow pressure (P_v) was altered from 0 to 30 mmHg, in steps of 5 mmHg, and the following parameters were measured and/or calculated. 1) Isovolumetric capillary pressure (P_c) was measured by the zero flow technique. 2) Colloid osmotic pressure of the plasma (π_p) and lymph (π_L) were determined. 3) Lymph flow (J_L) was measured. 4) Capillary filtration coefficient (K_f) was measured using the filtration portion of the volume change curve. 5) Tissue pressure (P_T) was calculated using the following equation: $P_T = P_c + \pi_L - \pi_p - J_L/K_f$. 6) Pre ($r_a$) and post ($r_v$) capillary resistances were calculated. Preliminary results indicate the following: a) approx. 65% of ΔP_v is transmitted to the capillaries; b) a decrease in K_f; c)increase in r_a and a decrease in r_v; d) an increase in J_L with a simultaneous decrease inπ_L; e) a slight increase inπ_p; f) the calculated P_T showed an increase from -1.2 to +4.5 mmHg. The results indicate that at a P_c of 13-14 mmHg and a P_v of 7-8 mmHg, that P_T is approximately zero. In addition, filtration into the intestinal lumen was seen at P_v's greater than 26-27 mmHg, which corresponds to P_T's greater than or equal to 4 mmHg. (Supported by NIH grant HL 15680).

CARDIOPULMONARY FUNCTION OF AWAKE, SEDATED, AND ANESTHETIZED BEAGLE DOGS. B. A. Muggenburg and J. L. Mauderly,* Lovelace Foundation for Medical Education and Research, 5200 Gibson Blvd., S. E., Albuquerque, New Mexico 87108.

Ventilation, lung mechanics, gas exchange, venous admixture and hemodynamics in the right heart were measured in four Beagle dogs awake, sedated and anesthetized. Some parameters varied with each pharmacologic agent. Trifluprom azine hydrochloride administered intravenously resulted in only small changes in ventilatory pattern gas exchange and ventilation-perfusion patterns, and a reduction in stroke volume and cardiac output. Fentanyl-droperidol given intramuscularly along with atropine produced small changes in ventilation, a reduced diffusing capacity of carbon monoxide and fractional uptake of carbon monoxide and an increase in specific ventilation. Heart rate was increased, stroke volume and cardiac output reduced and total pulmonary resistance was increased. Sodium pentobarbital, given intravenously, induced significant changes in ventilation, lung mechanics, gas exchange, matching of ventilation and perfusion and hemodynamics. The data obtained on this study suggest that the use of chemical restraint in untrained dogs in lifespan studies would introduce variables in the values obtained from periodic examination of the circulatory and pulmonary systems. (Research performed under U. S. A. E. C. Contract AT(29-2)-1013 in facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.)

ADAPTATION OF THE RABBIT DIGASTRIC MUSCLE TO AN ABRUPT CHANGE IN LENGTH-A RADIOGRAPHIC AND HISTOLOGIC STUDY. Z.F. Muhl* and A.F. Grimm. University of Illinois at the Medical Center, Chicago, Illinois.

The rabbit digastric muscle has a simple fiber arrangement and long tendon. Several small pieces of barbed steel were surgically implanted along the length of the belly. Orthogonal radiographs were taken periodically. The actual distance between the metal markers was calculated from measurements made on the paired radiographs. Baseline distances were established during an initial one month period. In a second surgical procedure the tendon was shortened by forming it into a loop. Radiographic observation of the metal markers in eleven animals revealed that the shortening operation produced an immediate increase of 11% in muscle length. Soon thereafter, the tendon began to lengthen and the muscle belly shortened. After two weeks, the muscle belly length stabilized at 84% of baseline length. Muscle shortening to less than the baseline length could be explained in terms of the properties of the passive tension system. Muscles were fixed in situ with the jaws closed by arterial perfusion of formalin. Sarcomere lengths were measured on histologic preparations with the optical microscope. Mean sarcomere length of control muscles was 2.62 μm. (This value is significantly greater than that at optimum length). The immediate effect of tendon shortening was an increase in sarcomere length. After a considerable period of time, sarcomere lengths in muscles subjected to shortening were found to be no different from control values.

UREA SYNTHESIS IN THE CANINE KIDNEY. M.M. Mullins and R.O. Banks. (Introduced by D.L. Kline) Dep't. of Physiology, Univ. of Cincinnati Coll. of Med., Cincinnati, Ohio 45219.

Renal urea synthesis was investigated in 13 anesthetized mongrel dogs during antidiuresis. Eight of these dogs were maintained for 8 days on protein-restricted diets. Following a priming dose, unlabeled inulin and 14-C-urea were infused at a slow rate. In each experiment one hour was allowed for the dogs to attain steady state, followed by 10 clearance periods of combined left and right ureteral urine (average clearance period was 30 minutes). In the 8 protein-restricted animals and in one animal on control diet the urea specific activity ratio (S.A. plasma/S.A. urine) was greater than 1.0, demonstrating intrarenal synthesis of urea. The specific activity ratio was negatively correlated with plasma urea concentration ($r = -0.82$, $p < 0.05$). In these 9 animals, 9-65% of the total excreted urea had been synthesized in the kidney. These results indicate that the comprised concentrating ability of the canine kidney during protein deprivation is in part minimized by renal urea synthesis. This work was supported by USPHS grant HL-14348-01.

EYE MOVEMENTS AND VISUAL PROCESSING. John B. Munson. Department of Neuroscience, College of Medicine, University of Florida, Gainesville.

1. Eye movements in awake and sleeping cats are accompanied by gross potentials in lateral geniculate nucleus (LGN) and visual cortex (VC). These potentials (LGN and VC spikes) occur synchronously with the termination of saccadic eye movements; i.e., the moment of visual fixation. Electrical stimulation of midbrain reticular formation (MRF) evokes LGN and VC spikes similar to those seen with eye movements. LGN spikes or MRF stimulation can be used as conditioning stimuli for the geniculo-cortical evoked response; the resulting response augmentation is identical in each case. These and other experiments suggest an MRF-mediated augmentation of visual activity at the termination of saccadic eye movements; i.e., "fixation augmentation" of visual function.

2. Antidromic LGN-ON responses are augmented during LGN spikes of both awake and sleeping cats. Orthodromic postsynaptic "r" waves in LGN are augmented with LGN spikes of sleeping, but not alert cats (Malcolm, et al., EBR, 1970). Bilateral transection of the optic nerves (ON) reduces the amplitude of LGN spikes in sleeping cats to about 50% of pre-operative amplitudes; in alert cats the spikes disappear. These experiments suggest that LGN spikes in the normal sleeping cat are composed of postsynaptic potentials (psps) both in ON terminals (which are lost following ON section) and in relay and interneurons in LGN (which persist following ON section). Since (i) LGN spikes in the alert cat disappear following ON section; (ii) the "r" wave is not augmented with LGN spikes in alert cats; and (iii) LGN spikes in alert cats are normally half the amplitude of those in sleeping cats, it appears that the LGN spikes in alert cats are composed solely of psps in ON terminals, the pathway to the postsynaptic LGN relay and interneurons then being inactive. (NSF Grant GB-7622).

MYOSIN CONTENT AND THE INTRINSIC STRENGTH OF THE CONTRACTILE SYSTEM OF ARTERIAL SMOOTH MUSCLE. R. A. Murphy and J. T. Herlihy.* Dept. of Physiology, Univ. of Va. Sch. of Med., Charlottesville, Virginia.

Potassium depolarized strips prepared from the media of hog carotid arteries develop a maximal active tension of $2.22 \pm 0.17 \times 10^6$ dynes/cm^2 at their optimum length. Smooth muscle cells occupy 60% of the strip cross-section as determined by electron microscopy of glutaraldehyde fixed tissue. Strips from weanling hogs with a cell area of 36% strip cross-section show a correspondingly lower active force development ($1.04 \pm 0.10 \times 10^6$ dynes/cm^2). Since tension is proportional to cell cross-sectional area, the smooth muscle cells should develop a tension of 3.73×10^6 dynes/cm^2, a value somewhat greater than the average mammalian striated muscle. A better comparison of the contractile force might be based on contractile protein content. About 1 mg myosin can be isolated and purified per g arterial media, *i.e.* 7-12% of that obtained from skeletal muscle. However, losses may be correspondingly larger in the smooth muscle preparation. An independent estimate of myosin content is given by: [μMoles ATP split by myosin/g homogenized media]/[μMoles ATP split/mg pure myosin] = mg myosin/g media. Measurements of Ca^{++} or EDTA activated ATPase activity of myosin and medial homogenates after inhibition of other ATPases by azide, ouabain, deoxycholate, and pretreatment with Dowex 50 to remove Mg^{++} led to an estimated myosin content of 1.5 - 4.5 mg/g media. These values are 10% or less than estimated for skeletal muscle. Although many potential errors exist in this approach, most would lead to an overestimation. Thus, on the basis of myosin content assessed by extraction or from enzymatic measurements, force development by the smooth muscle contractile system would greatly exceed that of striated muscle. (Supported by NIH grant HL 14547)

EFFECT OF ENDOGENOUSLY-RELEASED ACETYLCHOLINE ON K UPTAKE OF THE SINUS NODE. Ezio Musso* and Mario Vassalle. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Guinea-pig sinus nodes were perfused in a tissue bath located in close proximity to a beta probe. The tissue was loaded to equilibrium with ^{42}K and then washed for 30 min in inactive Tyrode solution (efflux period). After counting tissue radioactivity, the sinus node was exposed once more to the radioactive Tyrode solution (uptake period) and this was followed by another efflux period. The increase in tissue radioactivity at the end of the uptake period was taken as a measure of K influx. The whole procedure was repeated in the presence of the variables under study. Small concentrations of atropine (10^{-7}-10^{-11}M) had little effect on K uptake but large concentrations (10^{-5}, 10^{-6}M) had an inhibitory effect which was not abolished by 10^{-7}M propranolol. Eserine at 10^{-9}M in spontaneously discharging preparations provoked a small decrease and at 10^{-5}M a small increase in K uptake. In electrically driven preparations this increase was greater and was reduced by tetrodotoxin (3 x 10^{-6}M). The increase was present even when the stimulus was made subthreshold for the sinus node fibers but presumably not for the nerves. Inhibitory doses of acetylcholine (10^{-9}M) became stimulatory when administered in the presence of 10^{-7}M eserine. Eserine at that concentration had no or little effect of its own. Choline stimulated K uptake and this action was increased by eserine 10^{-7}M. The present results show that acetylcholine released from the sinus node perfused in vitro increases or decreases K uptake depending on the amount liberated. The increase of K uptake with electrical stimulation which does not excite sinus cells suggests that most of the mediator is released from nervous structures. Acetylcholine is synthetized in the perfused preparation since choline enhanced K uptake.

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SKIN (S) AND MUSCLE (M) VASCULAR RESPONSES TO HYPOTHERMIA. J. Musson, B. Lalone, J. Hall and J. Schwinghamer (intr. by T. Adams), Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

The internal body temperature (T_{re}) of 8 pentobarbital anesthetized dogs was lowered from 37 to 28°C (cooling period) and maintained at 28± 0.5°C for 2 hours (hypothermia period) by pumping arterial blood through a heat exchanger into the inferior vena cava. Responses of the forelimb S and M circulations to cooling and hypothermia were examined with a combined gravimetric and segmental vascular resistance (R) technique. Total vascular R (mmHg/ml·min; $\bar{x}$ ± SE) increased (↑) from 1.86±0.24 (S) and 3.17±0.45 (M) at T_{re} = 37°C to 11.28±2.12 (S) and 14.14±2.05 (M) at the end of the cooling period, and to maximum values of 21.65±5.6 (S) and 20.60±5.13 (M) at the end of the hypothermia period. All three vascular segments (arteries, small vessels and veins) in S and M contributed to these R ↑'s. Limb wt. decreased (↓) throughout the cooling and hypothermia periods with a maximum loss of 0.2±0.1 g/min occurring at T_{re}=30°C. Arterial hematocrit ↑ progressively from 44±1% at T_{re}=37°C to 49±2% and to a maximum value of 52±2% at the end of the cooling and hypothermia periods respectively. These data indicate that R in all S and M vascular segments ↑'s when T_{re} ↓'s due to an ↑ blood viscosity and also to vascular smooth muscle cell contraction. Contrary to previous reports (J. Appl. Physiol. 10:146-150, 1957 and Am. J. Physiol. 219: 1772-1778, 1970.) we did not observe active vasodilation in the M vasculature at any time during cooling or hypothermia. Since the limbs lost wt. throughout the cooling and hypothermia periods we conclude that the ↓ circulating blood volume which reportedly accompanies hypothermia does not result from net storage of fluid in the intra- and extravascular compartments of S and M.

EFFECT OF THYROCALCITONIN ON CALCIUM AND MAGNESIUM METABOLISM IN THE SPINAL RAT. N.E. Naftchi, A.T. Viau*, G.H. Sell*, and E.W. Lowman* Inst. of Rehab. Med., N.Y.U. Med. Cntr., New York, N.Y.

Urinary and fecal excretion of calcium and magnesium was measured by atomic absorption spectroscopy in male Wistar rats after transection of the spinal cord at the level of T_5. Thyrocalcitonin (TC), administered subcutaneously (4 MRC units/day/rat), increased the survival rate from 25% to 85% and markedly reduced the incidence of hydronephrosis which often occured after spinal cord transection. Excretion of urinary calcium (µg/day) changed from a control value of 204 to 556 in 5 to 10 days, and returned to control levels two weeks after transection. After treatment with TC the excretion of urinary calcium increased to 3166 µg/day within 10 days after transection. Fecal excretion of calcium changed from 15.5 mg/day in control animals to 27 mg/day in rats 5 to 10 days after transection and was lowered to 8.6 mg/day after treatment with TC. Calcium balance was depressed from +27.9 to +7.2 mg/day in 5 to 10 days after transection and was restored to normal levels after TC therapy. The urinary excretion of magnesium, although showing the same trend as that for calcium, was less pronounced. Fecal excretion of magnesium was lowered to control levels after treatment with TC. Although magnesium balance improved with TC, it did not reach control levels. The results indicate thet treatment of spinal cord injured rats with TC increases the survival rate possibly by normalizing kidney function and improves calcium balance probably by enhancing the absorption of calcium through the intestinal tract.

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EFFECT OF ACETAZOLAMIDE ON WATER AND ELECTROLYTE SECRETION BY THE COMMON BILE DUCT. D.L. Nahrwold and R.C. Rose. The Pennsylvania State University, College of Medicine, Hershey, Pa. 17033.

Previous studies suggested that the distal portion of the biliary duct system secretes a bicarbonate-rich fluid in response to secretin. The present experiments were designed to determine the effect of acetazolamide, a carbonic anhydrase inhibitor, on the secretory processes of the distal bile duct. Four dogs were prepared with an isolated segment of common bile duct around which bile was shunted by cholecystojejunostomy. The common duct, intubated at both ends, was perfused at 1.5 ml/hr with 0.15M NaCl. In control studies net flux from blood to lumen was found for water (135 µL/hr) and for all electrolytes (Na^+ 24.6, K^+ 1.6, HCO_3^- 5.8, Cl^- 24.1 µEq/hr). After intravenous acetazolamide (loading dose 12.5 mg/kg, then 12.5 mg/kg/hr) there was a decrease in net flux from blood to lumen for water (66 µL/hr) and for all electrolytes (Na^+ 15.6, K^+ 1.2, HCO_3^- 2.9, Cl^- 16.9 µEq/hr). Acetazolamide decreased net fluid secretion into the duct lumen by 51% and net HCO_3^- secretion into the duct lumen by 50%. HCO_3^- concentration in the recovered perfusion fluid decreased from a mean control value of 3.4 meq/L to 1.7 meq/L after acetazolamide, whereas Cl^- concentration increased from a mean control value of 155 meq/L to 159 meq/L after acetazolamide. The study confirms previous reports that there is a net secretion of fluid from blood to lumen in the distal biliary duct system, and that this net secretion is decreased by acetazolamide. The results suggest that $NaHCO_3$ transport may be a driving force for movement of water and electrolyte into the duct system, and that this process may be dependent on carbonic anhydrase. (Supported by N.I.H. grant AM 15244)

FUNCTIONAL AND STRUCTURAL IDENTIFICATION OF NEURONS IN THE CATFISH RETINA. PART II. K.-I. Naka, P. Z. Marmarelis* and R. Y.-F. Chan.* Information Science Department, California Institute of Technology, Pasadena, California 91109.

Two-input white noise analysis was performed on the dye-identified bipolar and (true) amacrine cells in the catfish retina.

In all bipolar cells so far identified the center and surround of the receptive field gave rise to responses which were opposite in polarity. Presence of the other input increased the dynamic gain of the opposite member of the receptive field. In the presence of annular input the spot component became faster, both latency- and frequency-wise, while presence of the spot input did not produce a similar change in the annular component.

In those neurons which were identified as amacrine cells, both center and surround stimuli gave rise to responses of the similar polarity. In presence of the surround input the gain of the spot component was markedly depressed while presence of the spot input did not affect the annular component. Within the range of stimulus modulation used, both the bipolar and amacrine cells behaved linearly.

Our procion-dye identification has consistently missed one class of bipolar cells (bipolar cells with a large dendritic field) which have been seen often in the golgi preparations. In the "amacrine cell layer" we have found a class of neurons which produced spike discharges (with a marked nonlinearity) but we do not know whether these neurons have axons or not.

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PROSTAGLANDIN DEHYDROGENASE ACTIVITY IN THE LUNG AND KIDNEY OF ENDOTOXEMIC RATS. J. Nakano and A. V. Prancan Univ. of Oklahoma Coll. of Med., Oklahoma City, Okla.

Plasma prostaglandin (PG) levels have been found to increase in animals in septic shock. However, its underlying mechanism remains uncertain. The present study was undertaken to examine the prostaglandin dehydrogenase (PGDH) activity in lung and kidney homogenates of rats in endotoxin shock. Male Holtzman rats were treated with an i.p. injection of 0.5 ml of 0.9 % NaCl solution (Control Group) or of 10 mg/kg of E. coli endotoxin (Shock Group). Eight hrs. later, the rats were anesthetized with an i.p. injection of pentobarbital (30 mg/kg), and systemic arterial pressure (SAP) was measured from a femoral artery with a Statham pressure transducer. Thereafter, the rats were sacrificed and the heart and kidneys removed. After rapid freezing in dry ice, the tissues were homogenized with 9 vol. of Bucher medium. After differential centrifugation, soluble fractions were harvested. PGDH activity was measured by a modification of the method described previously (Nakano et al.: Biochem. Pharmacol. 20: 2512, 1971). It was found that 8 hrs. after the injection of 0.9 % NaCl or endotoxin, SAP of control rats and endotoxemic rats were 121 $\pm$ 4 and 52 $\pm$ 6 mm Hg, respectively. Within 5 min. the control lung and kidney homogenates metabolized approximately 90 and 75 % prostaglandin E_1 (PGE_1) respectively. In contrast, the shock lung and kidney homogenates inactivated PGE_1 at considerably slower rates. Usually, the decreased PGDH activity was considerably greater in the lung than in the kidney. It is suggested that the increased PG levels found in animals with endotoxin shock may be partly due to the impairment of PG metabolism than decreased PGDH activity in the lungs and kidneys.

DISAPPEARANCE OF BRADYKININ IN THE RENAL CIRCULATION OF DOGS. A. Nasjletti and J. C. McGiff. Med. Col. of Wisc., Milwaukee, Wi., 53233.

The kidney is a rich source of kallikrein and kininases. The intrarenal activity of the kallikrein-kinin system is presumed to be a function of both, the capacity of the kidney to generate and to inactivate bradykinin. In chloralose anesthetized dogs, we investigated the ability of the kidney to remove bradykinin on passage across the renal vascular bed. The peptide was infused into the renal artery at doses ranging from 5 to 200 ng/kg/min; renal blood flow (electromagnetic flowmeter) and kinin content of renal venous blood were determined and the percent survival of bradykinin on passage across the kidney was calculated. Bradykinin caused a dose related increase in renal blood flow, urine flow, sodium excretion and kinin content of renal venous blood. In all instances, however, more than 85% of the infused peptide was removed or destroyed in the kidney (less than 15% survival). Intravenous administration of SQ-20881 (300 µg/kg), a synthetic peptide which potentiates the hemodynamic effects of bradykinin, by itself produced significant increases in renal blood flow, urine flow, sodium excretion and kinin content of renal venous blood. In addition, SQ-20881 treatment resulted in marked potentiation of the renal vasodilator, diuretic and natriuretic properties of bradykinin infused intrarenally. This was associated with a striking increase in the survival of bradykinin on passage across the kidney (35 to 50% survival). It is concluded that the bradykinin potentiating effects of SQ-20881 are mediated in large part by diminished destruction or removal of the peptide. In addition, these results indicate that variations in the capacity of the kidney to inactivate bradykinin may be a major determinant of the intrarenal activity of the kallikrein-kinin system. (Supported by NIH Grant # HL 15791-01 and American Heart Association Grant # 73-720).

LIGHT DIFFRACTION IN CARDIAC MUSCLE. Rashid Nassar*, Andres Manring*+, and E.A.Johnson. Dept. of Physiology, Duke University Medical Center, Durham, N.C.

The technique of light diffraction was used to measure sarcomere spacing in resting and contracting cardiac muscle. Trabeculae (50-100µ in diameter) of frog atrium were chosen which were relatively free of bifurcations and rich in contractile material. The preparation was immersed in frog Ringer at 20-22°C. A small beam (50µ diameter) of monochromatic light (He-Ne laser) illuminated the trabeculae. A diffraction pattern was obtained in the back focal plane of a lens. The diffraction pattern obtained from cardiac muscle, like that of skeletal muscle, consisted of several straight, bright lines or diffraction maxima. When the muscle was stimulated the first and higher orders in the diffraction pattern momentarily moved away from the zero order, returning to their original position. The distance between the two first order maxima was smapled at rates up to 60 sec^{-1} and a record of local sarcomere motion was constructed. Overall developed and resting tension were also measured. Changes in sarcomere motion produced by inotropic interventions that increase the contractile tension of the overall muscle were examined : Increasing the Ca++ concentration increased the velocity, duration and total amount of sarcomere shortening. An increase in the rate of stimulation (from 0.2 sec^{-1} to 0.5 sec^{-1}) increased the velocity and total amount of sarcomere shortening with no significant change in the duration of the contraction cycle. A reduction in temperature increased the duration of the cycle of sarcomere motion, largely as a result of delay in relaxation, the velocity of shortening being relatively unaffected. (This work was supported by USPHS Grants HL11307 and HL12157 and N.C.Heart Grants 1971-72-A-15 and 1972-73-A-29.)+Recipient,Special Health Research Fellowship HL50791.

INTERACTION OF CHRONIC METABOLISM ALKALOSIS WITH POTASSIUM AND CHLORIDE IMBALANCE IN THE CONTROL OF BREATHING. E.E.Nattie* and S.M.Tenney. Dept. of Physiol., Dartmouth Med. Sch., Hanover, N.H.

The degree of hypoventilation in chronic metabolic alkalosis may depend, in part, on co-existing alterations in potassium and chloride balance. As a first step in elucidating responsible mechanisms, experiments were performed on rats fed a low K diet for 14-17 days. Muscle electrolyte concentrations indicated moderate K depletion while serum and blood samples from unanesthetized rats indicated hypokalemic, hypochloremic alkalosis and increased P_aCO_2. Ventilatory studies in unanesthetized rats showed that the low K group hypoventilated at rest with a low f and normal to elevated V_T. The low K animals had a diminished ventilation breathing CO_2 (6.7%) or hypoxic air (8.3% O_2) entirely due in each case to a diminished f. However, the slopes of the response curves in low K and control groups were similar. CSF samples 2-5 min after ether anesthesia showed lactate concentrations which were not significantly different in the two groups and were within the reported normal range. CSF K and Cl concentrations were significantly lower in the diet group while CSF bicarbonate was significantly higher. Comparing diet to control rats, $\Delta CSF[HCO_3^-]$ (5.9 mEq/kgm water)/Δarterial $[HCO_3^-]$ (9.0 mEq/kgm water) was greater than reported for similar uncomplicated metabolic acid-base disturbances in the rat. Regional tissue electrolyte analyses of brainstem, hypothalamus and cerebrum indicated a significant decrease only in hypothalamic K and Cl concentrations. These results suggest: 1) alkalotic hypoventilation may be related, in part, to direct effects of K or Cl depletion in the hypothalamus. 2) Diminished serum and CSF K and Cl concentrations may affect ventilation indirectly by altering CSF bicarbonate or H ion homeostasis.

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SIMULTANEOUS ASSESSMENT OF SEVEN INDICES OF MYOCARDIAL CONTRACTILITY. N.S. Nejad*, E.F. Uretz*, H.G. Tobin*, and M.P. Kaye. Test and Evaluation Facility, IITRI, Chicago, Illinois 60616.

Various indices for determining myocardial contractility have been suggested utilizing either developed or absolute left ventricular pressure (LVP) and its first derivative. There has been much controversy concerning the validity and sensitivity of these indices for assessing myocardial contractility. A study to critically compare these indices was carried out on twenty canine heart-lung preparations. The Xerox Sigma-3 computer was programmed to simultaneously measure the following indices during various hemodynamic interventions: 1) the peak value of the ratio of the first derivative of LVP to instantaneous LVP (dp/dt/p) max; 2) Vmax using absolute LVP; 3) Vmax using developed LVP; 4) peak dp/dt; 5) (dp/dt)max over corresponding instantaneous LVP; 6) dp/dt/p at 40 mm Hg of absolute LVP; 7) dp/dt/p at 40 mm Hg developed LVP. Varying either preload or afterload changes the last five indices as much as 15-50%. Of all the indices under study, (dp/dt)max was the most sensitive to load. Only the first two indices proved to be independent of either preload or afterload. As much as a two fold increase in load had little or no effect on these two indices. Isoproterenol administration (0.1μg/min) at constant heart rate with atrial pacing augmented all indices from 10-40%. The (dp/dt/p)max was the most sensitive index to Isuprel. EDTA infusion (14mg/min) lowered all seven indices from 10-25%. Again (dp/dt/p)max responded most significantly in the failing heart. These results suggest that only (dp/dt/p)max and V max using absolute LVP are reliable indices of myocardial contractility and (dp/dt/p)max is more sensitive and accurate than V max. (Supported by Contract No. NIH-NHLI-69-2125.)

BODY COMPOSITION, UREA METABOLISM, AND LIVER ARGINASE ACTIVITY IN BEARS BEFORE AND DURING WINTER SLEEP. Ralph A. Nelson, James D. Jones,* Heinz W. Wahner* and Douglas B. McGill.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The study was done to determine (1) if bears can withstand food and water deprivation in summer as they do in winter, (2) if urea is produced during winter sleep, and (3) if the activity of liver arginase changes during winter sleep. Two bears were studied in summer without food and water but under "winter sleep" conditions (ambient temperatures 5 or 10°C). They became dehydrated and total body urea increased. When starved but given water, total body urea and lean body mass decreased. The same bears were studied in winter and no changes were noted in total body water or lean body mass; total body urea decreased. Urea production was measured while the animals were eating and drinking and found to be 722 and 715 mg/hr. By contrast, in winter sleep, urea production was 100 and 112 mg/hr respectively. Values for half-life of ^{14}C urea for the two bears were 9 and 12 hours in summer and 90 and 25 hours in winter. The ratio of activity in expired air to plasma was always less in winter than in summer. In both animals liver arginase activity increased threefold in winter. It is concluded that bears respond like other mammals to starvation in summer; in winter, however, during food and water deprivation, they do not become dehydrated, lean body mass remains constant, and total body urea decreases. Urea production in winter, though lower, continues, suggesting that urea nitrogen must be recycled through some unknown pathway because lean body mass remains constant. Carbon is also conserved as suggested by its decreased loss via expired air in winter.

EFFECTS OF ISOPROTERENOL ON INTERNAL AND EXTERNAL MECHANICAL WORK OF THE LEFT VENTRICLE. Wilmer W. Nichols, William E. Walker*, and William R. Milnor. The Johns Hopkins School of Medicine, Baltimore, Maryland.

Isoproterenol (.5μg/kg) was injected directly into the left ventricular chamber of anesthetized open-chest dogs and the resulting changes in mechanical work were observed. Ascending aortic flow was measured with an electromagnetic flowmeter, aortic and left ventricular pressures with catheter-tip micromanometers and ejection fraction by thermodilution. Internal (contractile element) work was obtained by integrating the product of tangential wall force (F) and contractile element velocity (V_{CE}) ($V_{CE} = 2\pi r\, dF/30Fdt$, r = internal radius) over the period of isovolumic contraction. External work, the integrated product of pressure and flow, was obtained from harmonic analysis of the aortic pressure and flow waveforms, computing separately: (1) the energy associated with pulsations (oscillatory work); and (2) that associated with steady flow. Data were collected and analyzed before and at various time intervals (5, 7, and 9 seconds) after the injections of isoproterenol. Internal work increased steadily from an average control value of 54 (range 27-68) to 83 (51-101) millijoules (mj) at the last sampling point (9 seconds) and external work increased from 131 (91-169) to 155 (112-219) mj. Oscillatory work increased from 13 (9-17) to 30 (21-44) mj and accounted for 10% to 19% of the external work, respectively. Isoproterenol produced a 54% increase in the internal work while producing only an 18% increase in the external work, most of the latter due to oscillatory work. The slight increase in external work after isoproterenol, combined with an increase in heart rate, produced a 56% increase in external power (work per unit time).

THE GABA-MEDIATED DEPOLARIZATION OF PRIMARY AFFERENT NEURONS. S. Nishi, S. Minota* and A.G. Karczmar*. Neurophysiology Lab., Dept. of Pharmacology, Loyola Univ. Med. Ctr., Maywood, Illinois.

The responses to gamma-aminobutyric acid (GABA) of the primary afferent terminals and cell bodies were studied in bullfrogs by the sucrose-gap and intracellular recording techniques, respectively. GABA (10^{-5}-10^{-4}M) depolarized the terminals as well as the cell bodies. The specificity of GABA action could be demonstrated in two ways. First, none of eight additional amino acids induced a depolarization comparable to that caused by GABA. Second, the GABA antagonists such as picrotoxin (10^{-5}M) and bicuculline (10^{-5}M) were very effective in antagonizing the GABA depolarization. The GABA depolarization of cell bodies was associated with a marked reduction of membrane resistance, and the response was increased by hyperpolarization and decreased and reversed by depolarization. The mean reversal level of GABA depolarization (E_{GABA}) was -9.3 mV and -33.7 mV when measured with KCl-microelectrodes and with K-citrate-microelectrodes, respectively. Reduction of $[Na]_o$ to 1/10 by replacing tris buffer for sodium displaced E_{GABA} slightly (<5 mV) in the hyperpolarizing direction. The decrease in $[K]_o$ to 1/10 or its increase to 5 times the normal concentration did not alter E_{GABA}. On the other hand, the replacement of chloride by methylsulfate caused a concentration dependent diminution of E_{GABA}; a clear semilogarithmic relationship was observed between E_{GABA} and $[Cl]_o$. These data demonstrate conclusively that the GABA-mediated depolarization of primary afferent neurons is due predominantly to an increased chloride conductance. Supported by PHS Grant NS06672.

BETA-ADRENERGIC STIMULATION OF RENIN RELEASE IN VITRO. H.L. Nolly*, I.A. Reid* and W.F. Ganong. Department of Physiology, University of California, San Francisco, California 94122.

Results obtained from in vivo studies indicate that the increases in renin secretion produced by sympathetic stimuli or administration of catecholamines are mediated via β-adrenergic receptors and probably involve the formation of cyclic AMP. The present study was designed to study the effects of norepinephrine, theophylline and adrenergic blocking drugs on renin release in vitro. Paired rat kidney slices weighing approximately 100 mg were incubated for 1 hr in a modified Krebs-Ringers solution and the rate of renin release was measured using a radioimmunoassay for angiotensin I. Addition of norepinephrine in concentrations of 10^{-5} M or 2 x 10^{-5} M increased the rate of renin release from 4.76 ± 0.80 (S.E.) to 7.43 ± 1.05 ($P<0.02$) and from 5.89 ± 0.74 to 10.92 ± 1.61 ng AI/mg tissue/hr ($P<0.005$) respectively. These increases were accompanied by significant increases in the renin content of the slices. Theophylline (10^{-3} M) had no effect by itself but potentiated the renin response to norepinephrine. The α-blocking agents phenoxybenzamine (10^{-4} M) and phentolamine (10^{-4} M) increased, rather than decreased, the effect of norepinephrine on renin release. The response to norepinephrine was unaffected by D-propranolol but was prevented by D,L- or L-propranolol. These results indicate that norepinephrine stimulates renin release in vitro by a β-adrenergic mechanism which probably involves the formation of cyclic AMP. (Supported by USPHS Grant AM06704, Skaggs Foundation, and Bay Area Heart Research Committee).

SITE OF ACTION OF Ba^{++} ON IN VITRO FROG GASTRIC MUCOSA WITH MICROELECTRODE TECHNIQUE. J. O'Callaghan,* S. S. Sanders, R. L. Shoemaker and W. S. Rehm. Medical Center, Univ. of Ala. in Birmingham, Ala. 35294

Four macroelectrodes are used, two for transmucosal PD [V(NS), N = nutrient, S = secretory] and two for transmucosal current sending. A microelectrode (M) is placed in a surface cell. Addition of Ba^{++} (1 mM) to the N medium produces a rapid and marked increase in the transmucosal resistance [R(T) = $\Delta V(NS)/i$] and the increase is rapidly reversed (<1 min) by changing N fluid to 86 mM K^+ + 1 mM Ba^{++}. The rapidity of the responses (plus other evidence) indicates that the site of these actions is the N membranes of the surface and/or tubular cells and that the resistances of the S membranes are unchanged. Three ΔV's due to current sending were measured, the relationship being: $\Delta V(NS) = \Delta V(NM) + \Delta V(MS)$. With resistance of the S membrane of the surface cells constant, changes in PD across this membrane [$\Delta V(MS)$] determine how Ba^{++} and high K^+ affect the distribution of applied current between the surface and tubular cells. Ba^{++} increases $\Delta V(MS)$ about 3-fold (indicating current via surface cells increased 3-fold) and in presence of Ba^{++}, high K^+ decreased $\Delta V(MS)$ by about the same amount. Hence Ba^{++} produces a greater % increase in resistance of the tubular cells than of the surface cells and high K^+ produces a greater % decrease in resistance of tubular cells than of the surface cells. Data on ratios of ΔV's indicate that sum of the resistances of N and S membranes of surface cells is not changed significantly by Ba^{++}. Therefore the primary site of the increase in resistance due to Ba^{++} and of the decrease in resistance in the presence of Ba^{++} due to high K^+ is the nutrient membrane of the tubular cells. Surprisingly, analysis of the data permits us to conclude that under control conditions (4 mM K^+ and 0 Ba^{++}) the average resistance across the tubular cells is <1.5 R(T) and that across the surface cells is >3 R(T). (NSF and NIH support.)

INTENSITY AND FREQUENCY OF CONDITIONING AS DETERMINANTS OF CARDIOVASCULAR RESPONSE DURING WORK. P.Oja,* W.C.Nicholas,* J.Hodgson,* and J.Kollias. Laboratory for Human Performance Research, University Park, Pa. 16802.

Forty-one clinically healthy, 28-55-year-old, sedentary men were randomly assigned to four conditioning programs with the following exercise intensities and frequencies: low intensity(65% $\dot{V}O_2$ max)/twice a week(Group 1), low intensity/four times a week(Group 2), high intensity(80% $\dot{V}O_2$ max)/twice a week(Group 3)and high intensity/four times a week (Group 4). Heart rate(HR),oxygen consumption($\dot{V}O_2$) and cardiac output($\dot{Q}$)were measured during submaximal and maximal treadmill work before and after 10 weeks of conditioning,which consisted of jogging-running for 20 minutes at individually prescribed constant speed.The mean exercise intensities,as determined from the running HR,for groups 1, 2,3, and 4 were 69,67,82 and 84 percent of $\dot{V}O_2$ max respectively.The following pre-post-test changes were observed:

		Group 1	2	3	4
HR REST	bpm	-1.6	1.5	-6.6	-5.2
HR 3mph/5% grade	bpm	- .5	-2.1	-3.5	-7.0
$\dot{Q}$ 3mph/5% grade	L/min	- .8	- .6	- .8	-1.2
HR max	bpm	3.4	-2.3	-3.4	-6.6
$\dot{V}O_2$ max	ml/kg·min	2.5	5.3	4.2	5.6
$\dot{Q}$ max	L/min	1.6	1.0	1.6	1.0

Interpretation from an analysis of variance indicates that with the given conditioning programs exercise frequency may be more important than intensity in determining the increase in maximum aerobic power.

RETICULOENDOTHELIAL (RE) DYSFUNCTION AND ENDOTOXEMIA FOLLOWING PORTAL VEIN OCCLUSION (PVO). I. Olcay*, A. Kitahama*, R. H. Miller*, R. A. Trejo*, and N. R. Di Luzio. Departments of Physiology and Surgery, Tulane University School of Medicine, New Orleans, Louisiana 70112

The mechanism by which acute, temporary ligation of the portal vein (PV) produces death in various animal species is unknown. Our previous studies have indicated a relationship of RE dysfunction and endotoxemia with death following occlusion of the portal vein and hepatic artery of Papio papio baboons. To further define this relationship, studies were undertaken to evaluate endotoxemia and RE function in both conventional and germ free rats following 30 minutes of PVO. Endotoxin was measured by the Limulus lysate test. RE function was evaluated by measuring the I.V. clearance and tissue distribution of the ^{131}I-labeled lipid emulsion. Although endotoxin was not detected in portal or systemic blood samples prior to surgery, endotoxin was present in the portal circulation 5 minutes after PVO. The portal endotoxin concentration continued to increase throughout the occlusive interval. Systemic endotoxemia was detected late during the occlusion episode. Following the restoration of portal flow, endotoxin levels initially increased and subsequently returned to near normal levels within six hours. Systemic endotoxemia was invariably associated with portal endotoxemia. Endotoxin was not detected in portal vein or systemic samples of germ free animals prior to or during PVO. RE function, measured six hours post PVO, was significantly depressed in both the conventional and germ free animals. Thus, RE depression following ischemic insult to the liver is not due to endotoxemia. The demonstration of the development of systemic as well as portal endotoxemia following gut vascular stasis in association with RE dysfunction may well contribute to the pathophysiology of portal vein occlusive injury.

EFFECTS OF OXYGEN ADMINISTRATION FOLLOWING CORONARY OCCLUSION. J. Osher, T.W. Lang, S. Meerbaum and E. Corday (intr. by W.W. Parmley). Cedars-Sinai Medical Center, Los Angeles, California.

Oxygen was administered for one hour after 90 minutes of LAD coronary artery occlusion in seven closed chest dogs to assess hemodynamic and regional [occluded (O) and nonoccluded (NO)] effects on myocardial metabolism. Measurements were carried out prior to occlusion (P), 90 minutes following occlusion (OC) and at 60 minutes of oxygen administration (O_2). Data are given as mean, and significance is indicated (* $p<0.05$; O_2 relative to OC):

		P	OC	O_2
LV end-diastolic pressure (mm Hg)		7.0	10.4	10.6
Max LV dP/dt (mm Hg)		3190	2304	1990*
Stroke work (g. m)		44.8	27.6	21.0
Coronary flow (ml/min)	NO	112	61	75
	O	51	28	16
Lactate extraction (A-V)/A (%)	NO	34.6	24.5	25.0
	O	34.4	5.2	9.9
Potassium balance (A-V) (mEq/L)	NO	0.06	0.03	0.02
	O	0.03	-0.08	-0.15
Myocardial oxygen consumption (ml/min)	NO	12.3	8.7	10.4
	O	4.1	3.5	2.1

Oxygen administration during coronary occlusion caused significant reduction in max LV dP/dt. The coronary flow in the O region decreased slightly. Other hemodynamic and metabolic changes were nonsignificant. There was no indication of improvement in metabolic or hemodynamic function as a result of oxygen administration following coronary occlusion.

DYNAMIC EFFECT OF PLASMA GLUCOSE ON GLUCAGON SECRETION IN THE ISOLATED, BLOOD-PERFUSED, CANINE PANCREAS. L. Ostroy*, M. Sperling*, B. Haller*, R.N. Bergman*and D.J. Marsh. Univ. of California, Los Angeles, and University of Southern California, Los Angeles, California.

The dependence of pancreatic glucagon secretion on pancreatic arterial glucose concentration was explored in the isolated blood perfused canine pancreas. Glucagon was measured by a specific radioimmunoassay which is 100 fold more sensitive to pancreatic than to gut glucagon. Glucagon secretion rate averaged 6.3 $ng \cdot min^{-1} \cdot kgBW^{-1}$ when pancreatic arterial glucose concentration was 100mg%, and fell when arterial glucose concentration was raised by steps of 25mg% or 100mg%. Still higher glucose steps produced no further fall in glucagon secretion; secretion persisted at 2.5 $ng \cdot min^{-1} \cdot kgBW^{-1}$ in the presence of the highest glucose concentrations used. When the arterial glucose concentration was set initially at 200mg% and then decreased by steps of 25mg% or 100mg%, glucagon secretion did not increase until the glucose concentration was brought down to 125mg% or less. When arterial glucose concentration was either increased or decreased, the new steady glucagon secretion rate was reached in less than 1 min, and no overshoots or undershoots were consistently found. The relationship between arterial glucose concentration and glucagon secretion rate can be approximately represented by the equation:

$$\dot{G} = \dot{G}_0 - aS, \qquad S \leq 140mg\%$$

$$\dot{G} = b, \qquad S > 140mg\%$$

where $\dot{G}$=glucagon secretion rate, S=arterial glucose concentration, and $\dot{G}_0$, a and b are constants in these experiments. From the data in these experiments, the values of these constants are: $\dot{G}_0$=15.75 $ng \cdot min^{-1} \cdot kgBW^{-1}$, a=0945, b=2.52 $ng \cdot min^{-1} \cdot kgBW^{-1}$. Supported by NIH Grants AM15145 & HD07087.

FAILURE OF INDOMETHACIN TO ALTER REACTIVE HYPEREMIA IN THE DOG HEART. T.L. Owen, I.C. Ehrhart*, W.T. Chen* and J.B. Scott. Mich. State Univ., E. Lansing, Michigan 48823.

Indomethacin (I), a drug which blocks prostaglandin synthesis, has recently been reported to block reactive hyperemia (RH) in the kidney (Herbacynska-Cedro and Vane, V Int. Cong. Pharm. 100, 1972). Other data suggest that prostaglandins are released during RH in the heart (Kramer and Folts, Fed. Proc. 32:454 Abs, 1973). In order to investigate the possible role of prostaglandins in RH in the heart, we infused I directly into the coronary circulation. Eight mongrel dogs were anesthetized with urethane-chloralose. Blood flow in left circumflex or anterior descending arteries was measured with the Pieper flowmeter in closed-chest dogs. In each animal, 90 mg of pure I dissolved in 100 ml saline was infused into the coronary branch under study over a period of 30 to 60 minutes. Blood pressure, heart rate, and coronary blood flow were not affected by I. Hyperemic flow was measured following relief of a 15 second occlusion before and at 15 minute intervals for at least one hour after I. The table reports flow during the first 10 seconds after release of occlusion.

	Control Flow (ml/min)±SE Before Occlusion	Reactive Hyperemia (% Control)±SE	
		0-5 Sec Post-Occlus.	5-10 Sec Post-Occlus.
Pre-indometh.	25.25±2.5	679±80	517±77
30 min post-indo.	22.71±2.4	705±81	596±66
60 min post-indo.	25.28±2.5	603±70	426±55

Under the conditions of these experiments, I, in a dosage exceeding that which has been reported to block renal RH, is ineffective in blocking coronary RH. These studies provide no evidence for a role of prostaglandins in RH in the dog heart.

IMMUNOLOGICAL HOMOGENEITY OF RAT URINARY KALLIKREIN WITH KIDNEY TISSUE KALLIKREIN. N.B. Oza*, L.A. Fernandez*, and O.A. Carretero. Dept. of Med., Henry Ford Hospital, Detroit, Mich.

Kinin generating enzymes are widely distributed in the mammalian system and are described as two major types: glandular and plasma kallikrein. The glandular kallikreins are found in urine, kidney, pancreas, salivary and sweat glands. The possibility that urinary kallikrein is formed in, and secreted by the kidney, has not yet been proven; although some indirect evidence has shown that both enzymes are similar. The aim of this work was to compare the urinary kallikrein with the kidney kallikrein. For this, rat urinary kallikrein was purified by precipitation, followed by chromatography through CMC, DEAE, and sephadex. The final product was homogeneous on sephadex chromatography and migrated as a single protein band on acrylamide disc gel electrophoresis. Antibodies against this preparation were generated by repeated injections of this enzyme with Freund's adjuvant in rabbits. Heterogenous antiserum was also generated by injecting a protein concentrate of rat urine. Immunodiffusion tests further confirmed the purity of the kallikrein preparation and indicated that the anti-kallikrein antibody was monospecific. This antibody to rat urinary kallikrein cross-reacted with kidney kallikrein. This is a direct evidence that urinary kallikrein and kidney kallikrein are immunologically similar. This could indicate therefore, that urinary kallikrein is similar to kidney kallikrein; and further, that urinary kallikrein is formed and secreted by the kidney. (Supported in part by grants from the Michigan Heart Association and the N.I.H. Grant No. HL 15839-01).

ROLE OF SEROTONIN AND SEROTONIN ANTAGONIST ON PULMONARY HEMODYNAMICS AND MICROCIRCULATION IN HEMORRHAGIC SHOCK

I. Ayhan Ozdemir*, Katsuyuki Kusajima*, Frederick B. Parker, Jr.*, Watts R. Webb, and Stennis D. Wax
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Previous studies showed similar pulmonary pathologic changes after hemorrhagic shock or continuous (2 hours) serotonin infusion with congestive atelectasis, interstitial and intra-alveolar edema and hemorrhage, and red cell aggregation. Studies in 25 dogs compared pulmonary hemodynamics during 2 hours of hemorrhagic hypotension (40 mm Hg) with and without methysergide (serotonin antagonist) and the effect of serotonin (75 ug/Kg/min) alone. During serotonin infusion in normovolemia, cardiac output rose 25% and peripheral resistance fell 45%, while pulmonary artery resistance rose 60%. Pulmonary artery (PA) pressure rose 50% as did the Pulmonary Vein Wedge (PVW). Pulmonary Artery Wedge (PAW) and Small Pulmonary Vein (SPV) both rose 10% while left atrial pressure fell 50%. These changes are due to pulmonary arteriolar and small pulmonary venous constriction and are statistically and physiologically significant. Pretreatment with methysergide prior to hypovolemia prevented the SPV pressure rise and reduced the PA and PVW rise ($p < 0.02$) seen in the control shock dogs. Lung changes, grossly, microscopically and by cinemicroscopy were greatly reduced by the methysergide. These results suggest that serotonin - possibly released by the hypoxic intestine, hypoxic brain or instable platelets - plays a significant role in the pulmonary changes secondary to hypovolemic hypotension. (Supported by Heart Association Grants).

RELATIVE WATER VAPOR PERMEABILITIES OF THE SHELL AND SHELL MEMBRANES OF THE HEN'S EGG. Charles V. Paganelli, Amos Ar,* and Hermann Rahn. Dept. Physiol.,State Univ. of N.Y. at Buffalo,Buffalo,N.Y.

The exchange of water vapor, O_2, and CO_2 across the avian egg shell occurs by diffusion through gas-filled pores in the shell and shell membranes. We here address ourselves to the following question: How much resistance to water vapor diffusion is offered by the shell itself, and how much is contributed by the shell membranes? To answer this question, we measured the diffusive permeabilities to water vapor (K_{H_2O}) of the following preparations: 1) a hen's egg shell, with its membranes intact, into which Ringer's solution was placed; 2) an egg shell from which both inner and outer shell membranes were removed, and which also contained Ringer's solution. K_{H_2O} was determined by following weight loss with time under a known ΔP_{H_2O}. K_{H_2O}'s (cm^3 STP $cm^{-2}sec^{-1}torr^{-1}$) were: preparation 1: 6.8 ± 0.12 (SEM); preparation 2: 6.9 ± 1.1 (SEM). It is clear that within the limits of experimental error the barrier to diffusive exchange of water vapor lies in the shell itself; the shell membranes play a quite minor role. (Supported by ONR Contract N00014-68-A-0216, (NR 101-722).)

EFFECT OF MEDIUM POTASSIUM CONCENTRATION ON UREA PRODUCTION BY LIVER SLICES. B. Pal* and D.E. Kamm. Roch. Gen. Hosp. and Univ. of Roch. Sch. of Med., Rochester, New York.

We have previously demonstrated increased urea production following K administration (Abst. V. Int. Cong. Nephrol., 1972). To determine whether this effect is mediated in part through direct stimulation of hepatic metabolism by increased extracellular fluid (ECF) [K], urea production has been examined in liver slices incubated in Krebs-Henseleit medium containing lactate, ornithine, ammonia or amino acids (10 mM) and varying [K]. As shown in the Table, increasing [K] signifi-

Medium [K] mEq/l	Alanine	Glutamine	Threonine	Serine
	(Urea Production in μM/100 mg d.wt./hr.)			
2.95	2.15±0.22(12)	2.85±0.39(12)	1.62±0.12(8)	3.31±0.19(12)
5.90	2.88±0.30(12)*	3.67±0.54(12)†	2.16±0.23(8)**	4.06±0.31(12)**
11.80	2.89±0.30(12)*	3.72±0.50(12)*	2.38±0.31(8)**	3.74±0.22(12)†

Significantly different by paired T-test when compared with results found with [K] 2.95 mEq/l, *P < 0.01, **P < 0.02, †P < 0.05.

cantly enhanced urea production from alanine, glutamine, threonine or serine. In similar studies, increasing [K] did not influence urea production from ammonia, glutamate, aspartate, glycine or lysine. We conclude: 1. that increasing ECF [K] per se does not directly stimulate hepatic urea cycle activity, since it did not enhance urea production from ammonia, glutamate and aspartate, 2. ECF [K] does influence the transport and/or metabolism in liver of several gluconeogenic amino acids, and 3. that the latter effect accounts, at least in part, for the enhanced urea production found after K administration in vivo. (Supported by NIH AM-11023)

VASOACTIVITY OF RENAL VENOUS BLOOD AFTER RENAL ARTERY CONSTRICTION. M.B. Pamnani*, G. Simon* and H.W. Overbeck. Mich. St. Univ., E. Lansing, Mich.

To better understand the systemic vasoconstriction that occurs after renal artery constriction we bioassayed venous blood, using the isolated denervated pump perfused gracilis muscle. We perfused the muscle of each of 10 pentobarbital anesthetized dogs at constant flow with blood from his vena cava (VC) and then from each of his renal veins (RRV and LRV) sequentially before and during the 45 minutes after constriction of his left renal artery ("experimental group"). A control group of 10 dogs underwent sham constriction. Venous blood hematocrit did not change during the procedure. We detected no rise in systemic blood pressure in either group. Mean ± SEM of % change in gracilis perfusion pressures:

		Time Following Constriction (min): 25	35	45
Exper. Group	LRV Blood	+24.5±2.6	+27.0±2.8	+29.9±3.4
	VC Blood	+21.2±2.2	+23.9±3.0	+26.4±4.0
	RRV Blood	+8.4±3.3	+11.1±3.4	+13.7±3.8
Control Group	LRV Blood	+4.2±0.9	+5.9±1.2	+7.2±1.6
	VC Blood	+3.2±1.8	+4.4±2.2	+5.0±2.6
	RRV Blood	+2.8±1.1	+4.8±1.4	+6.6±1.9

In the experimental group, as compared to the control group, perfusion with LRV blood after tightening the clamp evoked vasoconstriction ($P < .001$). Similar levels of gracilis vasoconstriction were evoked by VC blood in these dogs, but, interestingly, no vasoconstriction was evoked by RRV blood ($P > 0.2$). Our results suggest that, upon acute clamping of one renal artery, a vasoconstrictor substance, probably angiotensin, is added to blood. Our interesting finding, however, is that the untouched kidney either inactivates this vasoconstrictor substance and/or secretes a vasodilator substance. This action of the untouched kidney may help to explain its "protective" function in renal hypertension. (Supported by USPHS Grant HL15146 and a Mich. Heart Assoc. grant).

PHYSIOLOGICAL STRAIN DURING LIGHT EXERCISE IN HOT-HUMID CONDITIONS. K.B. Pandolf,* R.R. Gonzalez, and A.P. Gagge. John B. Pierce Foundation and Yale School of Medicine, New Haven, Conn. 06519

Previous work by Kamon and Belding (Human Factors 13:153, 1971) demonstrated heart rate (HR) increases ~ 1 beat/min (bpm) for each °C of ambient temperature (T_a) above 20°C, when relative humidity (RH) < 30%. During the present experiments physiological strain was compared at 25, 32 and 40°C for both low and high humidity, while male unacclimatized subjects pedalled on a bicycle ergometer for 30-40 min at 25% $\dot{V}O_2$max. Ambient vapor pressure (P_a) was held constant at 8 Torr for the low humidity series and increased towards saturation for the high humidity series. Mean skin ($\bar{T}_{sk}$) and esophageal temperature (T_{es}), HR, evaporative heat loss (E_{sk}) due to sweating, local forearm sweat rate ($\dot{S}$), and local chest skin conductance by a heat flow disc were recorded continuously. At 25, 32 and 40°C (when P_a ~ 8 Torr), HR equilibrated at 106, 112 and 119 bpm, respectively (or ~ 1 bpm/°C in T_a), while ΔT_{es} rose 0.3-0.5°C above resting. At the end of exercise during high humidity (T_a = 32 and 40°C), HR was elevated 4-5 bpm for each °C above 25°C and there was no equilibrium. T_{es} and $\bar{T}_{sk}$ increased progressively with humidity and E_{sk} was hampered by excessive dripping of sweat, especially when dew point was above $\bar{T}_{sk}$. At this extreme, chest skin conductance was 48-60% above resting values and was associated with increased HR and T_{es}. The relation of the sweating drive ($\dot{S}$) to the maximum evaporative capacity of the environment (E_{max}), as well as changes in HR and T_{es}, better define the physiological strain of hot-humid environments. Supported by NIH Grant ES-00354.

Regulation of CSF $[HCO_3^-]$ during chronic hypercapnia with superimposed metabolic alkalosis. S.S.Park and A. D'Orazio*
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Our previous investigation has indicated that an effective ionic regulatory mechanism prevents an excessive increase of CSF $[HCO_3^-]$ during chronic administration of CO_2 and $[HCO_3^-]$ in cats (Fed.Proc.:30:269,1971). In order further to elucidate the mechanism responsible for such an ionic regulation, the CSF/blood electric potential difference has been measured. Confirming the previously reported species difference, the CSF/blood electric potential difference in cats was found to decrease with increasing arterial P_{CO_2}. In addition, it was established that this P_{CO_2} dependent change of potential is little influenced by the change of arterial pH and is sustained during chronic hypercapnia. The $PaCO_2$-CSF/blood electric potential relationship thus established allowed us to evaluate the contribution of active and passive transport to the actual ionic distribution of bicarbonate across the blood-brain barrier obtained during chronic CO_2 exposure with and without superimposition of metabolic alkalosis. The results indicate that the concerted action of two processes, an arterial pH dependent active process and P_{CO_2} dependent passive process, is responsible for the prevention of an excessive increase of CSF $[HCO_3^-]$ in our experimental condition. Such regulation of CSF $[HCO_3^-]$ may play an important role in maintaining the effectiveness of respiratory regulation through the central chemoreceptor. Administration of THAM as an alkalizing agent, however, appeared to overcome this regulatory mechanism, resulting in further respiratory suppression.

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VASCULAR REACTIVITY AND METABOLIC ALTERATIONS DURING ENDOTOXIN SHOCK. J.L. Parker* and T.E. Emerson, Jr., Dept. of Physiol., Mi. State Univ., E. Lansing, Mi. 48823.

The effects of endotoxin shock upon cerebral blood flow (CBF), cerebral vascular resistance (CVR), cerebral perfusion pressure (CPP=aortic pressure-CV pressure) and arterial and cerebral venous (CV) pO_2, pCO_2, and pH were studied in 12 spontaneously respiring dogs. CBF was measured from the cannulated confluence of the sagittal, straight, and transverse (lateral) sinuses with the transverse sinuses occluded (Rapela, et al., Fed. Proc. 20:100, 1961). Purified E. coli endotoxin (2 mg/Kg) was infused intravenously over a 5 min. period and the animals followed for 4 hrs. The average data for these experiments is illustrated below. The percent change was calculated at 240'. (*=$p<0.05$)

TIME		CONTROL	30'	120'	240'	%Δ
CBF	(ml/min)	34.1	20.9 *	18.3 *	16.9 *	-50
CPP	(mmHg)	127.4	87.0 *	79.0 *	96.2 *	-24
CVR	(PRU)	4.21	4.43	4.59	6.00*	+43
CV pO_2	(mmHg)	42.0	40.0 *	34.0 *	35.0 *	-17
CV pCO_2	(mmHg)	49.4	46.3	47.0	47.1	0
CV pH	(units)	7.29	7.23*	7.21*	7.25*	

Arterial pO_2 increased from 84 to 93 mmHg; arterial pCO_2 decreased from 42 to 28 mmHg by 30 min after endotoxin and remained depressed; arterial pH decreased from 7.33 to 7.30. Cardiovascular parameters in 8 control dogs were stable over the four hours. Cerebral autoregulation was unaffected by 4 hours of shock, however the vascular response to 10% CO_2 inhalation was significantly depressed. The venous-arteriolar response was maintained. This study demonstrates that CBF is severely depressed during endotoxin shock due to a rise in cerebral vascular resistance. (Supported by grants from NIH, NE14774, and the Michigan Heart Association.)

MEMBRANE STABILIZING EFFECTS OF NEWER NONSTEROIDAL ANTIINFLAMMATORY AGENTS. S. S. Parmar*, V. Kishore*, and S. J. Brumleve. Dept. Physiol. & Pharmacol., Univ. N. Dak., Med. Sch., Grand Forks, N. Dak., and Dept. Pharmacol. & Therap., K. G. Medical Coll., Lucknow, India.

Membrane stabilizers not only depress excitability in nerves and muscles but also protect erythrocytes against hypotonic hemolysis. In the present study ability of 5-(α-naphthyl methyl)-1-substituted-S-triazole-2-thiols (NST), their precursor 1-α-naphthyl-acetyl-4-substituted thiosemicarbazides (NSTS) and 5-(α-naphthyl methyl)-1-substituted-S-triazole-2 yl-mercapto acetic acids (NSTM) to stabilize red cell membrane and to afford protection against carrageenin-induced oedema in rat was investigated. All compounds were found to decrease hypo-osmotic hemolysis of canine erythrocytes where cyclization of NSTS into corresponding NST in no way altered their concentration dependent antihemolytic activity. Masking of the free mercapto group of NST to form NSTM was found to cause marked decrease in their activity. Bovine serum albumin was found to decrease antihemolytic activity of these compounds indicating their possible interaction with cell membrane proteins where presence of mercapto group facilitates the binding. All compounds were found to exhibit antiinflammatory activity where no structural activity relationship was observed. Failure to observe correlationship between antiinflammatory and antihemolytic activity provides evidence for different cellular basis of antiinflammatory activity of these compounds. (Supported by Sch. of Med. Gen. Res. Support USPHS NIH Grant 5 S01 RR0 5407 and the Council of Scientific and Industrial Research, New Delhi.)

SEROSAL Na BUT NOT K IS NEEDED TO MAINTAIN FROG SKIN EPIDERMIS SHORT-CIRCUIT CURRENT. R. H. Parsons* and T. Hoshiko. Biology Dept., Rensselaer Polytech. Inst., Troy N.Y. 12181 and Physiology Dept., Case Western Reserve U. Sch. of Med. Cleveland OH. 44106.

The presence of a Na-K active transport mechanism at the inside or corium side of isolated frog skin is commonly accepted, following Ussing's model of frog skin. However relatively little work has been reported on the precise role of potassium. Occasionally we had observed that skins in K-free corium-bathing solutions maintained short-circuit current for substantial periods of time. No further experiments were pursued since the presence of the corium made it impossible to know if the potassium concentrations at the epithelial cell border were actually reduced to zero. The split-skin preparation has made it possible to restudy this question. Our results indicate that the presence or absence of 5 mM K in sulfate Ringer's at inner border does not alter the the skin current. Removal of all sodium however results in a prompt fall in current to zero. Presence of even 5 mM sodium on the corium side results in a current of significant magnitude. Cell sodium content tends to be somewhat lower in the absence of potassium, but the scatter in the potassium data obscures any effect on potassium content if present. Large vacuoles appear in epithelial cells incubated in sodium free solutions, but removal of potassium with sodium present does not produce such gross changes. These results suggest a complex role for sodium in maintenance of cellular integrity and active transport at the corium border. (Supported by USPHS grant AM 05865.)

COMPUTER BASED SYSTEM FOR BREATH-BY-BREATH MEASUREMENT AND ANALYSIS OF RESPIRATORY RESPONSES TO CONTROLLED BICYCLE ERGOMETER LOADS. David H. Pearce*, H. T. Milhorn, Jr. and W. J. Reynolds*. Univ. of MS Med. Ctr., Jackson, MS 39216.

In order to examine the respiratory responses to exercise on a breath-by-breath basis, a computer based system was devised which allows the examination of the responses to various work loads. This system (1) generates the command signals for a subject on a bicycle ergometer, (2) controls the ergometer load, (3) records selected signals, and (4) computes and plots the responses. The subject breathes into a two-way mouthpiece, the expiratory side of which is connected to a pneumotachograph. Gas sample lines run from the mouthpiece to oxygen and carbon dioxide analyzers and EKG electrodes are connected to the subject's chest. Expired flow rate, a trigger pulse indicating the completion of a breath, fractions of expired O_2 and CO_2, EKG, and the exercise command signal are recorded on FM analog tape. Before each experiment, calibration signals are recorded on the FM tape system and are later replayed, along with the experimental signals, through a low-pass filter into the computer (DEC PDP-9) via an analog-to-digital converter. The computed variables are tidal volume, respiratory frequency, end-tidal P_{CO_2} and P_{O_2}, oxygen consumption and carbon dioxide production rates, and heart rate, all determined on a breath-by-breath basis. The computed breath-by-breath values are stored on magnetic tape and printed out on a lineprinter. An editing program permits the removal of artifacts after which the data can be automatically plotted either as 10 second averages or on a breath-by-breath basis. (Supported in part by NIH Grant HE 11678.)

REFLEX CONTROL OF RENAL SYMPATHETIC ACTIVITY. L. Conrad Pelletier (intr. by John T. Shepherd). Mayo Foundation, Rochester, Minnesota.

In 10 anesthetized dogs, with vagosympathetic trunks cut, neurograms were obtained from multifiber preparations of sympathetic nerves to the left kidney. In 4 of the dogs, the two carotid sinuses were isolated and carotid sinus pressure controlled. Taking the mean renal nerve activity measured at a sinus pressure of 40 mm Hg as 100%, it was decreased to 17 $\pm$ 9% (mean $\pm$ SE) by increasing carotid sinus pressure to 250 mm Hg; stimulation of muscle receptors of the hindlimb by injecting capsaicin 0.3 mg in one iliac artery while sinus pressure was maintained at 40 mm Hg caused the mean renal nerve activity to increase to 211 $\pm$ 16%. In 6 dogs with intact carotid sinuses, bilateral carotid occlusions were performed during room-air ventilation (mean arterial P_{O_2}=100 mm Hg) and during ventilation with 10% O_2 (mean arterial P_{O_2}=40 mm Hg). Before the occlusions, there was little or no activity in the renal nerve during normoxia, and only a slight increase in mean renal nerve activity (12%) occurred after 2 minutes of hypoxia. Bilateral carotid occlusions caused mean aortic pressure to increase by 56 mm Hg during normoxia and by 90 mm Hg during hypoxia. The increase in mean renal nerve activity with carotid occlusion averaged 56 $\pm$ 10% greater during hypoxia than during normoxia. Prior experiments suggest that this potentiation by hypoxia is the result of carotid chemoreceptor stimulation. Ganglionic blockade abolished the changes in aortic pressure and the sympathetic activity in the renal nerves. Thus, the reflex increase in sympathetic outflow to the kidney caused by withdrawal of baroreceptor activity can be markedly potentiated by the simultaneous stimulation of muscle receptors or peripheral chemoreceptors. (Supported by NIH Grant #HL5883 and the Medical Research Council of Canada).

CONTINUOUS CARBON MONOXIDE EXPOSURE: EFFECTS ON HEART SIZE IN RAT. D. Penney, M. Benjamin and E. Dunham. (intr. by - W. Weathers) Dept. of Biol. Sci., Univ. of Ill. at Chicago Circle, Chicago, Ill. 60680

Male rats 60 days of age were exposed continuously over 21-46 days to 100, 200 and 500 p.p.m. carbon monoxide in air. Carboxymethemoglobin levels of 9.26%, 15.82% and 41.12% of the total hemoglobin and 0.94, 2.08 and 10.05 gm/100 ml increases in hemoglobin were observed at sacrifice, respectively. Significant increases in heart weight over equal age and body weight controls were detectable following exposure to 200 p.p.m. (12.03%) and 500 p.p.m. (46.06%) CO, but not at 100 p.p.m. CO. At 500 p.p.m. CO increases in heart weight resulted from significant increases in left ventricular (LV) (34.3%), right ventricular (RV) (47.6%) and atrial weights (81.8%). The ratios of RV/LV weights were similar to controls, 0.352 vs 0.320, respectively. Same aged rats acclimated to a simulated altitude of 5,500 m for 11 weeks also showed increases in hemoglobin (5.93 g/100 ml) and heart weight (30.34%) over equal body weight controls. However, here the RV was the major site of significant weight increase (79.64%). The RV/LV ratio rose to 0.500. Apparently, CO levels of 100 p.p.m. and above result in significant increases in hemoglobin, while 200 p.p.m. CO is the threshold for measurable affects on cardiac size. These data also suggest that unlike altitude cardiac enlargement which primarily involves the RV, CO exposure produces an overall increase in heart mass.

ARTERIAL BLOOD GASES IN UNANESTHETIZED RATS EXPOSED TO HYPOXIA, HYPERCAPNIA OR BOTH. William E. Pepelko and Gene A. Dixon*. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

Catheters were implanted into the caudal arteries of 120 adult male rats under anesthesia. Upon awakening, an animal was placed in a restrainer and exposed individually to the experimental environments in a small, thermally controlled, cylindrical chamber. Catheters were ducted through the end of the chamber to permit arterial blood collection. Blood samples were collected and analyzed for pH, P_{O_2}, and P_{CO_2} prior to and during exposure to 20 different experimental gas mixtures. The $P_{I_{O_2}}$ levels were controlled at 146, 122, 98, 79 or 63 mm Hg. These were combined with $P_{I_{CO_2}}$'s of 0, 30, 60 or 90 mm Hg. Six animals were exposed to each gas mixture. During air breathing pH averaged 7.466 $\pm$ 0.020 S.D., $P_{a_{O_2}}$ 91.8 $\pm$ 3.46 mm Hg and $P_{a_{CO_2}}$ 41.2 $\pm$ 1.87 mm Hg. During exposure to the experimental gases the mean arterial pH ranged from 7.150 $\pm$ 0.020 to 7.604 $\pm$ 0.039, $P_{a_{O_2}}$ ranged from 30.8 $\pm$ 2.03 mm Hg to 140.8 $\pm$ 5.10 mm Hg and $P_{a_{CO_2}}$ ranged from 25.8 $\pm$ 2.77 mm Hg to 102.0 $\pm$ 1.81 mm Hg. It was concluded that the rat differs from man in that bicarbonate buffering is greater in the rat, resulting in a higher pH during air breathing and smaller decrease in pH with increasing P_{aCO_2}. Differences between arterial and inspired CO_2 were very small at 60 and 90 mm Hg and were not influenced by $P_{I_{O_2}}$ at these CO_2 levels. This suggests that respiration may not be increased further by increasing the $P_{I_{CO_2}}$ above 60 mm Hg or by decreasing the $P_{I_{O_2}}$ at 60 or 90 mm Hg $P_{I_{CO_2}}$.

Glutathione S-aryltransferase activity in hepatic "Y" protein.
I. W. Percy-Robb*, Neil Kaplowitz*, Norman B. Javitt.
University of Edinburgh, Scotland and Cornell University Medical College.

Transfer of bromsulphthalein (BSP) from plasma to bile may be mediated in part by a hepatic soluble protein called 'Y' protein or ligandin[1] which binds organic anions. During Sephadex gel filtration of hepatic 100, 000 g supernatant, containing BSP as a marker, significant conjugation of BSP with glutathione was found to occur. Glutathione was shown to bind to 'Y' protein in a pattern identical with BSP, and the enzyme conjugating activity (glutathione S-aryltransferase) for these ligands was demonstrated to reside exclusively in the fractions containing 'Y' protein. Using a kinetic assay for glutathione S-aryltransferase with 3, 4-dichloronitrobenzene, the pattern of enzyme activity was identical with that of glutathione binding. The elution pattern from Sephadex G75 of partially purified glutathione S-aryltransferase[2] revealed a peak for protein, BSP, glutathione and enzymic activity corresponding precisely to the elution volume of 'Y' protein in whole supernatant on the same column. These data can be interpreted as evidence for an enzymic function for 'Y' protein and require a reappraisal of its role in hepatic anion transport.

1. Nature 234:466, (1971)
2. Biochem. J. 79:516, (1961)

HEMODYNAMIC EFFECTS OF ALTERNATELY BEATING VENTRICLES AND TOTAL CIRCULATORY SUPPORT. J. L. Peters, J. L. Foote*, J. Kawai*, and W. J. Kolff. Department of Surgery, University of Utah, Salt Lake City, Utah.

Increased survival of calves with artificial hearts have stimulated a new approach to the study of the effects of cardiac function. Independent control of the right and left ventricle allows evaluation of acute single or biventricular failure and the effects of multiple driving modes: In three chronically instrumented calves with total Kwan-Gett artificial hearts the ventricles were driven synchronously initially to establish a control and then driven alternately with systole of one ventricle occurring during diastole of the other ventricle for periods of four to 20 hours. Outflow pressures AoP=150/90 mmHg and PAP =64/12 mmHg; mean inflow pressures RAP = 6 mmHg; LAP = 4 mmHg; ventricular pressures LVP = 225/0 mmHg; and RVP=105/0 mmHg; and cardiac output of 8 to 10 l/min. with alternately driven ventricles didn't vary significantly from those driven synchronously. These preliminary studies suggest that pumping synchrony between left and right ventricles isn't a requirement for total circulatory support and that single ventricular bypass of the natural heart need not be synchronized with the unsupported ventricle.

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SPECIFICITY OF REFLEX INFLUENCES ON THE HEART DURING ACUTE MYOCARDIAL ISCHEMIA IN CONSCIOUS DOGS. D. Fred Peterson, Robert L. Kaspar* and Vernon S. Bishop. Dept. of Pharmacology, The University of Texas Medical School at San Antonio, San Antonio, Texas.

The functional significance of the autonomic nervous system in regulating the inotropic performance of the heart during one minute occlusion of the left circumflex coronary artery (CO) was studied in 13 conscious dogs previously instrumented for the measurement of left ventricular pressure (LVP) and internal diameter (D). During control CO the end diastolic diameter (EDD) increased 0.6 ± 0.2 mm and the end systolic diameter (ESD) increased 3.8 ± 0.4 mm. Thus, reducing the extent of shortening by 3.2 ± 0.4 mm. Left ventricular end diastolic pressure and heart rate (HR) increased progressively (6.8 ± 0.6 mmHg and 38 ± 5 b/min). dP/dt and dD/dt were significantly reduced. Following parasympathetic blockade with atropine (0.1 mg/kg), the left ventricular (LV) responses to CO were similar to control with the exception of the increase in EDD (1.5 ± 0.4 mm) and a much reduced increase in HR (12 ± 5 b/min). After beta adrenergic blockade with propranolol (0.5 - 1.0 mg/kg) or surgical cardiac sympathectomy, LV responses to CO were also qualitatively similar to the control responses. The principle difference was in the reduction in the change in ESD (3.2 ± 0.4 mm) and HR (9 ± 3 b/min). Thus, CO in the conscious dog does not produce measurable reflex changes in the inotropic state of the heart, and, therefore, these results in conscious dogs cannot explain the previously reported reflex changes in efferent vagal and cardiac nerve activity during coronary occlusion in anesthetized animals. All values are mean ± SEM. This work is supported in part by grants NIH #5 RO1 HL12415-05 and AFOSR-71-2074.

ISOMETRIC ENDURANCE IN MEN WHO ARE OVERWEIGHT. J. Petrofsky* and A.R. Lind. St. Louis Univ. Sch. Med., St. Louis.

Being overweight can limit mans capacity for dynamic exercise. On the treadmill, where man must carry his own weight, dynamic exercise is recognized to present a greater physiological strain for overweight men. On the other hand, the capacity to work on the bicycle ergometer is considered to be independent of the body weight because the bulk of any excess weight is carried by the saddle. From these established views, it can be argued that in isometric exercise not involving support of the body, being overweight should not limit muscular performance. That is not our finding. On the contrary, in sustained isometric hand grip contractions carried to fatigue, we have found a significantly negative correlation between the endurance time of a 40% MVC contraction and the excess body weight of our subjects.

PHYSIOLOGIC RESPONSE OF RATS TO HYPERTHERMIA INDUCED BY EXPOSURE TO 2450 MHz MICROWAVE RADIATION. Richard D. Phillips, Edward L. Hunt*, and Nancy W. King*. Battelle, Pacific Northwest Laboratories, Richland, WA.

This study was undertaken to determine the thermoregulatory, metabolic and cardiovascular response of rats to relatively low levels of microwave radiation. Young-adult male rate (430 g) were exposed to microwaves for 30 minutes in a microwave cavity at absorbed dose rates of 0, 4.5, 6.5 or 11.1 mw/g. Immediately after exposure, measurements were made for five hours of colonic and skin temperatures, O_2 consumption and CO_2 production rates, and heart rate. ECG tracings also were made. Rats exposed at 4.5 mw/g (27.7 cal/min) differed from controls only by a slight initial elevation in colonic and skin temperatures. The group exposed at 6.5 mw/g (40.1 cal/min) had greater elevations in colonic and skin temperatures immediately after exposure, then overcompensated and had a lower colonic temperature than controls from 40 to 180 minutes postexposure. The metabolic rate was depressed in this group for three hours after exposure. Bradycardia developed within 20 minutes after exposure and persisted for 3 hours. The group exposed at 11.1 mw/g (68.2 cal/min) had a response similar to that of the 6.5 mw/g dose group, but the changes were more pronounced and lasted longer: the initial elevations in colonic and skin temperatures were higher and lasted longer; the thermoregulatory overcompensation was more severe and persisted for 5 hours; the depressed metabolic rate was more pronounced and lasted 5 hours; the bradycardia was more abrupt and greater. In addition, a number of abnormalities were noted in the ECG tracings of this group, including incomplete heart block. The physiologic responses of rats to microwave exposure at these doses can be attributed to the hyperthermia induced by irradiation. (Work supported by Bureau of Medicine and Surgery and ONR, contract N00014-70-C-0332)

A DIRECT METHOD FOR THE SPECTROPHOTOMETRIC DETERMINATION OF HEMOGLOBIN OXYGEN SATURATION IN MICROVESSELS. Roland N. Pittman* and Brian R. Duling. University of Virginia, Charlottesville, Va. 22901.

Whole blood does not obey Beer's law. Therefore, independent calibrations for path length and hematocrit are usually required for each measurement of blood hemoglobin oxygen saturation. Our method differs from former oximetric techniques in that a wavelength independent correction factor, based upon theoretical predictions, is computed. This correction factor is determined from the measured optical density (OD) of the red blood cell suspensions (RBC) at two isosbestic wavelengths and can be applied to other wavelengths to obtain corrections for light scattering. As a test of this method the light absorbing properties of RBC were compared to those of hemoglobin solutions (Hb) over the wavelength range of 500 to 600 nm. The ratio of the corrected OD of the RBC to the OD of Hb was found to be a constant and independent of wavelength (eq. 1). It is known that a linear proportionality exists between oxygen saturation of a hemoglobin solution and the ratio of the solution's OD's at two appropriate wavelengths (eq. 2).

$$OD^{Hb} = K \cdot OD^{RBC}, \quad \text{eq. 1} \qquad Sat = m \cdot \frac{OD_1^{Hb}}{OD_2^{Hb}} + b, \quad \text{eq. 2}$$

Substituting equation 1 into equation 2 makes it apparent that blood Hb saturation should also be linearly proportional to the ratio of the corrected OD's of the RBC at the two wavelengths. The method has been tested in systems with optical path lengths from 25 μ to 2 mm and with hematocrits between 3 and 50%. Applicability to microvascular measurements has been assessed through the use of TV microdensitometry on micropipettes with flowing RBC.

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Pathophysiology of Cestode Infections: Movements of Water and Electrolytes in the Rat Jejunum Infected with the Tapeworm, Hymenolepis diminuta. R.B. Podesta and D.F. Mettrick, intr. by J. Machin, Department of Zoology, University of Toronto.

Net movements of NaCl, water and bicarbonate in rat jejunum were studied in vivo in control rats and in animals infected with tapeworms. Absorption by the worms was also investigated. Acidification of fluids, as determined by the method of dis-equilibrium pH[1], in the control jejunum occurred via H ion secretion. The increased acidification in the parasitized jejunum was due to H ion secretion by the worms. Rates of NaCl and water absorption by normal intestine were increased by increasing the pH from 6 to pH 7, and, to a lesser extent, by the presence of glucose; stimulation by bicarbonate was small and insignificant. In the parasitized jejunum, with the worms removed, water and ion absorption were less, and secretion into glucose-free solutions at initial pH 6 greater, than in normal animals. Changing the pH had less effect on absorption but stimulation of ion and water absorption by glucose was greater than in normal jejunum. In the worms the presence of bicarbonate stimulated sodium and water, but not chloride absorption; low pH stimulated sodium, water and chloride absorption. Evaluation of the comparative data lends insight into the possible mechanisms by which bicarbonate, glucose and pH affect water and electrolyte absorption.

[1]Turnberg, L.A. et al. 1970. J. clin. Invest. 49, 548-556.

IONIC DISTRIBUTION IN RAT VENTRICLE. P.I. Polimeni (intr. by E. Page). Pritzker School of Med., University of Chicago, Chicago, Ill.

The determination of intracellular content and concentration of substances which are predominantly extracellular is crucially dependent upon the accuracy with which the extracellular space (ECS) is measured. For the purpose of determining the cellular water and electrolyte contents and concentrations in ventricular muscle, two independent methods were used to measure ECS: the in vivo tracer ($^{35}SO_4$) distribution in the nephrectomized animal, and the morphometric (point counting) analysis of histological preparations fixed by immersion in a saline-glutaraldehyde solution isosmotic with rat blood plasma (osmolality of vena caval samples (N=6): 312 $\pm$ 1 (SEM) m-osmoles). The ECS determined by these two methods was 0.187 $\pm$ 0.002 gm/gm and 0.193 $\pm$ 0.003 cm^3/cm^3, respectively (N=24). Ventricular water content was 3.32 $\pm$ 0.02 gm water/gm dry wt., of which 0.82 $\pm$ 0.01 gm (25%) consisted of extracellular water. Electrolyte contents (m-mole/kg dry wt.) of ventricular samples (N=16) were: Na, 164 $\pm$ 3; K, 367 $\pm$ 3; Cl, 125 $\pm$ 2; Ca, 3.59 $\pm$ 0.08; and Mg, 44.5 $\pm$ 0.4. Plasma concentrations (mM) were: Na, 143 $\pm$ 1; K, 4.0 $\pm$ 0.1; Cl, 107 $\pm$ 1; Ca, 2.38 $\pm$ 0.06; and Mg, 1.05 $\pm$ 0.02. Propagated errors of the analytical procedures were evaluated. The calculated (nominal) cellular concentrations (m-mole/kg cell water $\pm$ propagated analytical error at 99% confidence limits) were: Na, 16 $\pm$ 4; K, 144 $\pm$ 12; Cl, 13 $\pm$ 5; Ca, 0.6 $\pm$ 0.2; and Mg, 17 $\pm$ 1. The cellular concentration of Cl appears to be greater than that predicted on the assumption that Cl is passively distributed across the plasma membrane. (Supported by USPHS Heart Research grant 5-R01 HL-10, 503-07, Myocardial Infarction Research Unit contract # PM 43-NHLI-1334, and a grant from the Chicago and Illinois Heart Associations).

REACTIVE HYPEREMIA IN THE CAT MESENTERY CAPILLARIES. George P. Pollock* and Paul C. Johnson, Physiology Department, College of Medicine, University of Arizona, Tucson, Arizona 85724.

The hyperemia following release of an arterial occlusion has been most commonly attributed to metabolic factors such as oxygen depletion and accumulated metabolites. Some investigators, however, have suggested that the pressure reduction during the occlusion induces a myogenic relaxation of the resistance vessels. Since the mesentery has a low metabolic rate we felt that myogenic mechanisms during reactive hyperemia might be observed more clearly in this tissue. The dual slit method for red cell velocity measurement was used to measure flow in mesenteric capillaries of an isolated, autoperfused cat intestine preparation. Arterial occlusions of 15-60 sec duration were performed by clamping the arterial inflow circuit. Analysis of these responses were performed measuring several variables as functions of duration of occlusion. The peak responses for 15 and 60 sec occlusions were $1.36 \pm .77$ and $1.45 \pm .93$ mm/sec respectively. For the same occlusion durations, the times to peak flow were 10.4 ± 7 and 16.4 ± 10 sec, while the durations of hyperemia were 18.8 ± 13 and 22.4 ± 11. Excess flow values were 7.2 ± 6 and 7.3 ± 6 and peak velocity to control velocity ratios were $2.5 \pm .8$ and 2.7 ± 1.6 respectively. These data did not indicate an important role for metabolic regulation during reactive hyperemia in mesentery. When arterial pressure was pulsed (20-80 mmHg) for 5 to 20 seconds, a brief initial hyperemia was followed by a marked decrease in flow. This decrease was a function of the magnitude of the pressure pulse. However, a slow ramp increase in pressure of the same magnitude did not produce an initial hyperemia or a secondary fall in flow. We conclude therefore that myogenic activity plays an important role in reactive hyperemia in the cat mesenteric microvasculature. (Supported by NIH grants HL 15390-07, 05884-03, and grant-in-aid from American Heart Association)

HEMODYNAMIC EFFECTS OF ACETALDEHYDE IN DOGS. A. V. Prancan, R. B. McCloy and J. Nakano, Univ. of Oklahoma Coll. of Med., Oklahoma City, Okla.

Ethanol (ETOH) has been found to cause dose-related myocardial depression in vitro, but mild to moderate ETOH intoxication is accompanied by tachycardia and slight hypertension in healthy individuals. Since ETOH is metabolized to acetaldehyde (ALD) in the body, cardiovascular changes observed during ETOH intoxication may be due to the hemodynamic effects of both ETOH and ALD. The current study was undertaken to investigate the effects of ALD on the systemic, pulmonary and regional circulations in open chest dogs anesthetized with pentobarbital. Systemic arterial pressure (SAP), pulmonary arterial pressure (PAP) and left atrial pressure (LAP) were measured with Statham pressure transducers. Cardiac output (CO), systemic venous return (SVR) and regional blood flow were measured with electromagnetic flow meters. The intravenous injection of graded doses (2-16 mg/kg) of ALD caused dose-related increases in heart rate, SAP, PAP, CO, SVR and dp/dt, while LAP decreased. The intraarterial injection of ALD constricted the peripheral vascular beds in the brachial, femoral, renal, carotid, and superior mesenteric arteries, and dilated those in the coronary and hepatic arteries. Alpha- and beta-adrenergic blocking agents not only blocked the cardiovascular effects of ALD but reversed its pressor effect. It is concluded that most of the hemodynamic effects of ALD resulted from the release of catecholamines from nerve endings and adrenal medulla. Furthermore, this study suggests that the cardiovascular changes during early or moderate ETOH intoxication are mostly due to ALD.

AUTOREGULATION OF BLOOD FLOW IN SKELETAL MUSCLE CAPILLARIES. Russell L. Prewitt* and Paul C. Johnson. Department of Physiology, University of Arizona College of Medicine, Tucson, Arizona 85724.

It has been demonstrated by a number of investigators that a decrease in blood pressure supplying skeletal muscle results in a decrease in blood flow which may be sustained or followed by an autoregulatory response. The autoregulatory response has been shown to be accompanied by an increase in the capillary filtration coefficient which is interpreted as an increase in the number of flowing capillaries. However, there is little information at present on the patterns of flow in autoregulating and non-autoregulating capillaries. These studies were designed to determine whether the autoregulatory response involves principally an increase in the velocity of flowing capillaries or an opening of more capillaries. Red cell velocity was measured in individual capillaries of an isolated cat sartorius muscle during a five minute control period in which the blood pressure averaged 100-120 mmHg, a five minute period in which the pressure was reduced by 50%, and a five minute recovery period. Venous pressure and gross flow were also measured. We found that individual capillaries in the same muscle respond in a variety of ways ranging from virtual stoppage to increases in the steady state velocity. In some of the autoregulating capillaries the percentage of time the vessel was flowing increased as did the velocity. Thus the autoregulatory response is due, at least in part, to an increase in velocity in flowing capillaries. We could not rule out a possible increase in the number of flowing capillaries as well. (Supported by NIH grant number HL 15390-07 and a grant-in-aid from the American Heart Association).

EFFECTS OF TRANSPLANTATION ON MECHANICAL PERFORMANCE OF RAT CARDIAC MUSCLE. D.V. Priola*, H.A. Spurgeon, C.P. Montoya*, R.D. Lueker* and D. Robillard*. University of New Mexico School of Medicine, Albuquerque, New Mexico 87131.

There is little information available on the effects of cardiac transplantation on isotonic and isometric contractility and sensitivity of rat cardiac muscle to Ca^{++} and adrenergic agents. To investigate these changes, a series of hearts from Wistar-Furth (WF) rats were grafted to the abdominal aortae and venae cavae of WF recipients. This procedure produces donor hearts which are not rejected and remain mechanically active for at least the 21 day period studied. Length-tension (LT) and force-velocity (FV) characteristics were determined for papillary muscles removed from the left ventricle of donor hearts. In addition, the isometric and isotonic responsiveness to a series of norepinephrine (NE) and Ca^{++} doses was determined. In the first day after surgery, both performance curves are shifted downward and responsiveness to NE and Ca^{++} is diminished. By day 3, LT and FV curves had returned to control levels. However, the response to 5 mM Ca^{++} was never re-established and isometric and isotonic responses to 0.25 g/L of NE were diminished or absent after day 3. From day 3 through day 21, the FV and LT curves were steadily depressed with values for maximum isometric tension and Vmax dropping to 70% and 50% of control values, respectively. The data suggest that transplantation of the rat heart leads to a diminished NE responsiveness. This diminished adrenergic response is probably not the result of decreased receptor sensitivity but may be secondary to a diminished reactivity of the contractile elements to external Ca^{++}. (Supported by NHLI Grants 10869 and 15912 and Grants from the American and New Mexico Heart Associations.)

CORONARY REPERFUSION. CORRELATION BETWEEN RECOVERY OF CONTRACTILITY AND HIGH ENERGY PHOSPHATES. Pritpal S. Puri, Wayne State Univ., Sch. of Med., Det. Gen. Hosp., Detroit, Michigan.

Effects of coronary occlusion followed by reperfusion on regional changes in contractility were studied in dogs and correlated with tissue content of energy rich phosphates. Contractility was recorded by means of a strain gauge tipped two-prong probe which measures myocardial fiber shortening. Contractility was lost at 15 seconds after coronary occlusion. Release of coronary occlusion at any time up to 45 minutes was followed by prompt return of contractility. Recovery of adenosine triphosphate and creatine phosphate was 95% (normal adenosine triphosphate - 5.75 μmoles/g, normal creatine phosphate - 8.54 μmoles/g). When period of coronary occlusion was extended beyond 45 minutes reperfusion at 1 to 3 hours was followed by a delayed return of contractility at two weeks thereafter. Recovery of adenosine triphosphate was 91%, 81% and 73% upon release of coronary occlusion of one hour, two hours and three hours respectively. Corresponding values for creatine phosphate were 95%, 90% and 85% at 1 hour, two hours and three hours respectively. In conclusion, return of contractility upon reperfusion after extended periods of coronary occlusion was accompanied by significant recovery of energy rich phosphates.

TWENTY-FOUR-HOUR RHYTHMICITY OF PINEAL CANALICULI AND EVIDENCE FOR THEIR INTRINSIC HUMORAL REGULATION. W.B. Quay. Neuroendocrinology Section, Waisman Center on Mental Retardation and Human Development, and Dept. of Zoology, University of Wisconsin, Madison, Wisconsin 53706.

Intercellular canaliculi (0.2-0.4μ diameter) were discovered in rat pineal glands perfused *in situ*. They enmesh the pinealocytes and join the pericapillary spaces or networks within the pineal gland. The present investigation is an initial step in the determination of their physiological significance and control mechanisms.

All experiments employed perfusions of adult rat pineal glands in isolated heads mounted in a stereotaxic apparatus. After parenchymal perfusions with india ink solutions by standardized procedures, the pineal glands were fixed and processed for stained, serial (7μ) tissue sections.

Partial dehydration or exposure to hypertonic solutions inhibited perfusion of pineal canaliculi, and either $CaCl_2$ or trypsin in the ink blocked perfusion. Hyaluronidase was without apparent effect. Maximum canalicular perfusion distance followed a 24-hour rhythm, with a peak (mean max. distance = 95μ)near the end of the daily light phase, and a trough (13μ) during the dark phase. The rhythm resembled that in rat pineal content of 5-hydroxytryptamine (5-HT). Dark phase perfusion distances equivalent to those of the light phase were obtained when 5-HT (5×10^{-3}M) was added to the perfusate. Melatonin, heparin and norepinephrine had no effect in similar experiments.

It is concluded that: (1) circadian and local patency of the pineal canaliculi may be regulated, at least in part, by release of 5-HT by pinealocytes; and (2) the canaliculi may constitute a transport route between pinealocytes and blood vessels, especially during the daily light phase.

THE IMPORTANCE OF THYROTROPIN RELEASING HORMONE (TRH) ON THYROID GLAND HOMEOSTASIS IN NORMAL AND X-IRRADIATED BEAGLES AS DETERMINED BY A RADIOIMMUNOASSAY FOR CANINE THYROID STIMULATING HORMONE (TSH).[1] W.J. Quinlan* and S.M. Michaelson. Univ. of Rochester, School of Med. and Dentistry, Dept. Radiation Biology and Biophysics, Rochester, N.Y.

Following the successful development of a radioimmunoassay for canine TSH, a series of experiments were carried out on the response of normal and X-irradiated beagles to varying doses of TRH. Intravenous administration of TRH in normal dogs resulted in a delayed release of TSH by the pituitary gland. Baseline TSH levels were 5.0 ± 4.1 ng/ml, reaching a maximum of 20 ± 5.0 within 20 minutes following injection. Dogs with X-irradiation induced primary hypothyroidism had elevated basal, TSH levels of 38 ± 7.0 which rose dramatically following TRH administration. Both thyroxine (T4) and triiodothyronine (T3) serum measurements were also carried out by a slight modification of radioimmunoassays for T3 and T4 in man. Changes were observed in T3 and T4 levels in both normal and X-irradiated beagles within 260 mins following TRH administration. The importance of altered TSH, depressed T4 and elevated T3 in dogs with radiation-induced thyroid dysfunction, and the usefulness of the dog as a model for studying thyroid feedback mechanisms will be discussed. (The cooperation of Dr. A.E. Wilhelmi for assistance in extracting TSH from dog pituitaries and Dr. M.S. Anderson of Abbott Laboratories for TRH are acknowledged.)

[1]This paper is based on work performed under contract with the U.S. Atomic Energy Commission at the University of Rochester Atomic Energy Project and has been assigned Report No. UR-3490-329.

EFFECTS OF BLOOD VOLUME INCREASES AND PAPAVERINE ON O_2 IN THE RESTING AND EXERCISING ISCHEMIC CANINE FORELIMB. D. Radawski*, W. Hoppe*, R.S. Underwood*, T. Burns* and R. Daugherty. Mi. State Univ. School of Med., E. Lansing, Mi.

We have reported that local papaverine infusion or systemic blood volume expansion alone or together substantially increase blood flow in resting ischemic canine forelimb skeletal muscle (Fed. Proc. 29:259, 1970). We now report the effects of these procedures on the O_2 delivery to O_2 utilization ratio (RO_2) in the exercising as well as resting muscle. In 20 dogs the brachial artery was completely ligated to produce ischemia. Arterial and brachial venous O_2 content, brachial venous (muscle, F_m, ml/min) outflow and brachial artery (P_{BA}) and vein (P_{BV}) pressures were measured during control periods, local papaverine infusion (0.6 mg/min), after volume expansion (30 min Dextran infusion=2% body weight) and during papaverine infusion superimposed on this volume expansion. Skeletal muscle vessel resistance (R_m, mmHg/ml/min) was calculated from P_{BA}-P_{BV}/F_m. Papaverine decreased R_m from 3.0 to 1.1 and increased RO_2 from 82 to 672. Volume expansion decreased R_m from 3.5 to 2.4 and increased RO_2 from 90 to 145. The combination of papaverine and volume decreased R_m from 3.5 to 0.8 and increased RO_2 from 90 to 1196. In 10 of these animals the forelimb was locally exercised (E) for 3-5 min periods by faradic stimulation of the skeletal muscle (5v, 6/sec, 1.6 msec) alone and during each of the above maneuvers. With E alone R_m fell from 2.4 to 1.3 and RO_2 fell from 74 to 42. During papaverine and E, R_m fell from 2.8 to 0.6 but RO_2 increased from 76 to 210. After volume expansion corresponding values were 3.2 to 1.2 and 83 to 132 with E. The combination and E reduced R_m from 3.2 to 0.5 and increased RO_2 from 83 to 318. Thus, local papaverine infusion and/or volume expansion increase ischemic limb RO_2 at rest and prevent it from falling during E. It is not known if the decrease in R_m is in nutriative vessels.

ENVIRONMENTAL-BEHAVIORAL INFLUENCES ON CARDIAC DYNAMICS IN THE NORMAL AND CARDIAC DENERVATED MONKEY. D.C. Randall*, M.P. Kaye, W.C. Randall and J.V. Brady*. Div. Behavioral Biology, Johns Hopkins Univ. Sch. Med., Baltimore and Dept. Physiology, Loyola Univ., Chicago

Chair-restrained Rhesus monkeys in an isolation chamber were classically conditioned to both a 1-minute, 900 Hz tone (CSf) followed by food, and a 1-minute, 3.4 KHz tone (CSs) followed by shock. Catheters were then implanted in the aorta and the right and/or left ventricles. Each CS produced sudden, large magnitude and sustained increases in the systemic and ventricular pressures, ventricular dP/dt and heart rate. Following analysis of these responses, the hearts of the animals were surgically denervated by transection of nerves along the origin of the great vessels and transection and reanastomosis of the atria and great veins. The completeness of the denervation was confirmed by absence of heart rate and dP/dt changes during supramaximal stimulation of the vagus nerve and stellate ganglion. The animals were tested beginning the first week following surgery and then daily until clear evidence of parasympathetic and sympathetic reinnervation was obtained. The immediate, large conditioned increases in heart rate and dP/dt demonstrated preoperatively were completely abolished by cardiac denervation. Frequently a definite tachycardia and increase in dP/dt occurred starting about 20 sec after onset of CSs which demonstrates an endogenous secretion of catecholamines conditioned to an aversive stimulus. Six to 8 weeks postoperatively, incipient parasympathetic reinnervation was noted; about 16 weeks postoperatively, initial sympathetic reinnervation was manifest by abrupt increases in dP/dt to conditioned stimuli. These studies demonstrate that the primary cardiovascular adaptation during environmental stress is via the cardiac autonomic nerves. Furthermore, the denervated monkey heart demonstrates functional reinnervation at about four months. (Supported by NIH grants HL 06945 and HL 08682.)

SHORT-TERM EFFECTS OF RENAL ARTERIAL OCCLUSION ON METABOLISM AND FUNCTION OF DOG KIDNEY IN VIVO. Howard M. Randall, Jr. Department of Physiology, Louisiana State University Medical Center, New Orleans, Louisiana, 70112.

Studies were designed to determine whether the decreases in renal function that occur after a discrete period of ischemia are due to tubular dysfunction or to hemodynamic changes. Experiments were carried out on dogs in which the left renal artery was occluded completely for 1 hour and then released while the right kidney served as a control. Clearance determinations including: PAH, inulin, osmolar, Na^+ and K^+ were carried out on both kidneys while $\dot{Q}O_2$, TRBF, and Qglucose were made on the left kidney only. 10 minutes after release TRBF was 23% below preocclusion rates and fell to about 35% by 190 min. In contrast, the C_{IN} of the ischemic kidney was reduced by 60%, 10 minutes after release, and recovered to within 35% of control by 190 min. Changes in urine flow, Cosm, and the excretion rates of Na^+ and K^+ were similar to those of C_{IN}. The % of filtered Na^+ reabsorbed did not change significantly from controls. Coincident with the decrease in C_{IN} was a decrease in $\dot{Q}O_2$ of 50%; by 190 min. the $\dot{Q}O_2$ had recovered to within 30% of controls. The fall in $\dot{Q}O_2$ was not as great as the fall in $\dot{T}Na^+$ suggesting a decrease in efficiency of $\dot{T}Na^+$. Net gluconeogenesis changed to net utilization during the initial postischemic period but by 190 min., net gluconeogenesis was again evident. It would appear that 1 hour of RA occlusion does reduce subsequent renal function due largely to a decrease in GFR and not to tubular dysfunction. These in vivo results are consistent with previous in vitro findings. (Supported by USPHS Grant No. HE 11987).

PRESSOR AND DEPRESSOR REFLEXES MEDIATED BY THE VAGUS NERVES. W.C. Randall and J.A. Armour. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Depressor reflexes incorporating bradycardia, slowed A-V conduction, and systemic hypotension are well known responses to afferent excitation of the cervical vagus and aortic depressor nerves. Profound pressor responses to afferent excitation of selected, small thoracic cardiac nerves have been described in recent papers from this laboratory. Systematic stimulation at different anatomical levels of the thoracic vagosympathetic complex in the anesthetized dog, beginning at the pulmonary veins and progressing rostrally to the caudal cervical ganglion and the cervical trunk, elicited successive changes from predominantly depressor to sustained pressor responses. Stimulation of the thoracic vagus at a point caudal to the pulmonary veins invariably failed to elicit any alteration in cardiovascular responses, whereas, excitation at the central end of the transected cervical vagus resulted in marked elevation in blood pressure. At the level of the caudal cervical ganglion, combined stimulation of sympathetic and parasympathetic fibers gave rise to competetive autonomic responses in the heart with consequent suppression in atrial contractile force and severe bradycardia, but marked augmentation in ventricular contractile force and elevation in arterial blood pressure. These pressor responses are presumably related to activation of large numbers of afferent nerves arising from the thoracic viscera although the specific origins and nature of the receptors remain unknown. Efferent components of the pressor reflex are contained within the vagi as well as in the sympathetic supply to the heart, adrenal medulla, and the peripheral vascular system. (Supported by NIH Grants HL 08682.)

THE EFFECT OF SURGICAL STRESS ON THE MACROSCOPIC DISTRIBUTION OF THE UTERINE AND UMBILICAL BLOOD FLOWS IN THE NEAR TERM SHEEP PLACENTA. John H.G. Rankin and J. M. Schneider.*Physiol. & Gynec.-Obstet. Univ. of Wis. School of Med. Madison, Wis.

The distribution of the uterine and umbilical blood flows to 1 gram slices of near-term sheep placenta are reported to be uneven in the acute preparation (Power et.al. J. Clin. Invest. 46:2053, 1967). Subsequent experiments showed that in the chronic preparation, the uterine and umbilical blood flows were very evenly distributed (Rankin et.al. Am. J. Physiol. 219:9, 1079). In subsequent years, it has been generally accepted that these two results reflect the differences between the acute and chronic preparation. In an attempt to test the validity of this difference, 9 experiments were performed upon pregnant sheep under conditions that closely approximated those reported by Power et. al. Primary differences were as follows: 1. We used 25 micron radioactive microspheres labelled with one of the following isotopes: CE^{141}, CR^{51}, SR^{85}. 2. The whole placenta was assayed for radioactivity. The uterine blood flow, umbilical blood flow and the ratio of the uterine to umbilical blood flow were observed to be evenly distributed over the surface of the placenta. It was determined that the uneven distributions observed in this study could have caused the transplacental clearance of a very diffusible molecule to decrease by no more than 2%. This result should be compared with the value of 25% obtained from the results of Power's group. The difference between this work and the early experiments may therefore be ascribed to the inadequacy of macroaggregates of iodinated albumin in measuring the distribution of blood flow in an organ. We conclude that in both the acute and chronic condition, the uterine and umbilical blood flows of the near-term sheep, as measured in 1 gram slices, are evenly distributed over the surface of the placenta. Supported by grant no. HD 06736.

THE EFFECT OF ATROPINE ON CIRCULATING LEVELS OF GASTRIN IN MAN. D.D. Reeder, H.D. Becker* and J.C. Thompson. Univ. Tex. Med. Branch, Galveston, Texas.

Atropine is an effective inhibitor of basal or gastrin-stimulated gastric secretion. The effect of atropine on gastrin release from the antrum is not totally understood. Methods: Eight healthy adult volunteers participated in these studies. The effect of the intermittent injection of atropine, 0.5 mg, on basal and food-stimulated serum gastrin was determined by radioimmunoassay. Results: Mean basal serum gastrin was 121 picograms (pg)/ml. Atropine caused a significant decrease in basal serum gastrin to 80 pg/ml at 20 mins ($p<0.02$). One hour after the last injection of atropine serum gastrin had returned to basal levels. In the studies on the effect of atropine on food-stimulated serum gastrin levels, the mean basal gastrin was 117 pg/ml in the control study and 105 pg/ml in the test study. All gastrin levels after the initial injection of atropine were higher than control levels. At 30 mins after food the serum gastrin was 149 ± 28 pg/ml in the control study and 191 ± 24 pg/ml when atropine was administered ($p<0.05$). Conclusions: Atropine significantly depressed basal levels of serum gastrin in normal man, indicating that basal gastrin release is, at least in part, mediated by cholinergic mechanisms. Atropine significantly increased the serum gastrin response to food; this increase may be due to diminished acid inhibition of gastrin release from the antrum or to decreased motility resulting in antral stasis.

ANOMALOUS RESPONSE OF INTERCELLULAR POTENTIALS OF IN VITRO FROG GASTRIC MUCOSA TO CHANGE IN $[K^+]$ IN PRESENCE OF Ba^{++}. W. S. Rehm, J. O'Callaghan,* S. S. Sanders and R. L. Shoemaker, Univ. of Ala. in Birmingham, Medical Center, Birmingham, Ala. 35294

Mucosae of Rana pipiens were mounted between chambers and bathed with nutrient (N) and secretory (S) fluids. With a microelectrode (M) in a surface cell, potential differences were measured between M and a N electrode [V(MN)], between a S electrode and M [V(SM)] and between S and N [V(SN)]. V(SN) = V(SM) + V(MN); when e.g. V(SM) is positive it means S is positive to M. With Ba^{++} present (1 mM) in nutrient fluid the total resistance R(T) is high and V(SN) is negative. A step elevation of nutrient K^+ (Ba^{++} still 1 mM) from 4 to 86 mM (K^+ replaces Na^+) results in rapid (<1 min) decrease and inversion of V(SN); S becomes positive to N. Changes in V's due to elevation of K^+ are given by DV(SN) = DV(SM) + DV(MN); when e.g. DV(MN) is positive M becomes more positive to N. In representative experiment DV(SN) was about +35 mv, DV(SM) about +20 mv and DV(MN) about +15 mv. Possible explanations are based on assumption that changes in V's are so rapid that concentrations of ions in cells are not changed. If there were no transcellular electrical coupling 1) between surface and tubular cells and 2) between surface and transintercellular (leak) pathways then we would expect DV(SM) to be zero (but DV(SM) $\neq$ 0). If coupling exists only between the surface cells and the leak pathways then we expect DV(SM) to be negative (it is not). We conclude that with Ba^{++} and high K^+ there must be electrical coupling between surface and tubular cells and that changes in emf's and resistances of nutrient membranes are such as to result in an increase in current flow from S into surface cell (or a decrease in current flow from surface cell to S) which would result in positivity of DV(SM)--furthermore Δemf of N membrane of tubular cells is > Δemf of N membrane of surface cells. (NIH and NSF support.)

EFFECT OF INTERCOSTAL AFFERENT STIMULATION ON THE RESPIRATORY RHYTHM OF ANESTHETIZED CATS. J.E. Remmers, I. Marttila* and C. Von Euler*. Nobel Institute of Neurophysiology, Karolinska Institute, Stockholm, Sweden and Dept. of Physiology, Dartmouth Med. Sch., Hanover, N.H.

Experiments were carried out on cats anesthetized with pentobarbitol and paralyzed with gallamine. The central, cut ends of the external intercostal nerves of segments T6-T8 were stimulated electrically (0.2 msec pulse at 100-200 Hz). Phrenic discharge was recorded off the C5 root. Intercostal nerve stimulation during the inspiratory phase shortened inspiration, and stimuli delivered during the expiratory phase prolonged expiration. Dorsal root neurograms revealed that these effects were associated with recruitment of group II muscle afferents. Sustained alterations of the respiratory rhythm were demonstrable in cats ventilated with a low tidal volume and a high respiratory frequency, so that the neural respiratory period exceeded the cycle duration of the respiratory pump. Intercostal nerve stimulation during the phase of inspiratory activity shortened inspiration, and caused the neural respiratory cycle to become synchronous with the pump cycle. In cats made apneustic by bilateral vagotomy and pontine lesions, intercostal nerve stimulation shortened inspiration and converted apneustic breathing into a more nearly normal respiratory pattern. The results indicate that intercostal muscle afferents of the mid-thoracic region synapse with bulbopontine respiratory neurons which set the rhythm of the breathing.

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ACTIONS OF X537A ON CA-RELEASE AFTER CA-BINDING AND CA-UPTAKE BY RABBIT SKELETAL SARCOPLASMIC RETICULUM. D.I. Repke* and A.M. Katz, Dept. of Medicine, Mount Sinai Sch. Med., New York, N.Y. 10029

Accumulation and release of Ca^{2+} by sarcoplasmic reticulum (SR), play key roles in contraction-relaxation cycle of skeletal muscle. Isolated SR can remove Ca^{2+} from solution by two kinetically dissimilar mechanisms: Ca-binding and Ca-uptake (BBA,298:270, 1973). Both are inhibited by the Ca-ionophore X537A. To elucidate the mechanism of this inhibition, SR was loaded with Ca^{2+} in 0.12 M KCl, 40 mM histidine (pH 6.8) and 5 mM MgATP, in the absence (Ca-binding) and presence (Ca-uptake) of 2.5 mM Tris-oxalate. X537A (12 μM) caused rapid release of Ca^{2+} (∿ 0.08 μmoles/mg) when added after Ca-binding had reached steady state. Loss of Ca^{2+} from Ca-binding was the same whether X537A was added before the addition of Ca^{2+} or after Ca-binding had reached steady state. Almost complete inhibition of both rate and extent of Ca-uptake was seen when 12 μM X537A was added to the reaction mixture before Ca^{2+}, whereas 12 μM X537A added during the initial phase of Ca-uptake after addition of Ca^{2+} caused only slight slowing of uptake without decreasing the plateau level (∿ 4 μmoles/mg). Addition of 12 μM X537A after Ca-uptake reached this plateau caused a rapid release of a small amount of Ca^{2+} (∿ 0.08 μmoles/mg, the amount of Ca^{2+} released from Ca-binding measured under similar conditions). This released Ca^{2+} was again taken up within one minute and no further release occurred. When Ca-uptake was limited to ∿ 0.4 μmoles/mg by adding less Ca, 12 μM X537A again caused release of Ca^{2+} (∿ 0.08 μmoles/mg), but Ca-uptake initiated by further addition of Ca was not inhibited. These findings support the view that Ca-binding and Ca-uptake represent two different mechanisms. Supported by NYHA & NIH-NHLI Contract No. 72-2973-M.

Influence of adrenalectomy on glucose utilization by rat lung.
R.A. Rhoades, L.N. Gassenheimer*, and W. R. Blackburn*. The Pennsylvania State University, and the Hershey Medical Center, University Park, Pa. 16802

Glucose $-U-^{14}C$, glucose $-1-^{14}C$, and glucose $-6-^{14}C$ utilization was examined in vitro in lung slices from adrenalectomized (ADX) male rats. All animals received food and fluids ad libitum, but 1% NaCl was added to the drinking water of the ADX group. Plasma corticosterone levels from rats killed 3 weeks following adrenalectomy averaged 0.88 μg/100 ml plasma $\pm$ 0.32 and their lungs showed a significant ($P < 0.05$) increase in lung weight (g/100 g body weight) compared to normal lungs. No differences were observed in body weight. Incorporation of glucose $-U-^{14}C$ by the lung was significantly depressed by 30% in total lipids and by 32% in phospholipids (PL) in the ADX group. Hydrolysis of PL revealed that the depressed incorporation was proportionately greater in the PL–fatty acid than in the PL–glyceride–glycerol moiety, suggesting depressed fatty acid synthesis by lung. The ability to oxidize labeled glucose was also significantly reduced (26%) in the ADX animals. The C_1/C_6 ratio was significantly lower in the ADX group, suggesting relatively less carbon flow through the hexose monophosphate shunt. The data show that adrenal deficiency has a profound influence on glucose metabolism and lipogenesis in the adult rat lung.

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THE PRETEST AS A TOOL FOR EVALUATING LEARNING IN A CONVENTIONAL LECTURE FORMAT. Daniel R. Richardson, Dept. of Physiology & Biophysics, School of Medicine, University of Kentucky, Lexington, Kentucky 40506.

Evaluation of learning in an academic course is usually based on examination performance during and/or after a semester. This procedure fails to take into consideration any prior knowledge a student may have obtained. In order to achieve a better evaluation of knowledge gained by our students, we administered a 100 question multiple choice pretest (unannounced) during the first class meeting of a graduate level course in human physiology which was taught in a conventional lecture format. The pretest contained both factual and conceptual questions of the same degree of difficulty as those asked on course examinations. Comparison of pretest and course examination performances showed that the class as a whole had a 69% increase in knowledge for the entire course. With respect to various topics of the course, this gain varied from 47% in the endocrine section to 200% in the gastrointestinal section. This difference was manifested in the pretest, since course examination performances for these two sections were about the same. Without the added dimension of the pretest, such differences in knowledge gain would have been overlooked.

The amount of knowledge gain for individual students over the entire course varied from 2% to 240%, and there was no correlation between pretest and course examination performances among the students. Thus, while the pretest proved valuable as a tool for evaluating knowledge gain, it was found that such a test can not be used to predict individual student performance in an academic course.

The Effect of Norepinephrine on Myocardial Cell pH During Acidosis. K. M. Riegle* and R. L. Clancy, Dept. of Physiology, KUMC, Kansas City, Kansas.

It has been shown that buffer capacity of cardiac muscle is less in vitro than in vivo. The present study was undertaken to determine if norepinephrine, (NE), modifies the change in cardiac intracellular hydrogen ion concentration, ($[H^+]_i$). The $[H^+]_i$ was calculated using the DMO method of Waddell and Butler. An isolated rat heart preparation was perfused with a Krebs-Henseleit's solution. The following series of experiments were performed. MJ-1999 and NE refer to experiments in which a beta blocking agent or NE was added to the perfusate respectively.

Series	$[H^+]_e$nM	pCO_2	$[H^+]_i$nM
1. Normocapnia +MJ-1999	51	45	87
2. Normocapnia	49	44	87
3. Normocapnia +NE	60	56	92
4. Hypercapnia +MJ-1999	135	124	185
5. Hypercapnia	139	129	151
6. Hypercapnia +NE	144	134	126

It was observed that the $[H^+]_i$ of series 1 through 3 was not significantly different. However, when the pCO_2 was increased, $[H^+]_i$ of series 5 and 6 were less than that of series 4. Therefore, it would appear that NE can modify the increase in $[H^+]_i$ occurring in respiratory acidosis. Similar results have been found in metabolic acidosis. Additional experiments suggest that the action of NE on $[H^+]_i$ is related to the presence of calcium. (Supported by: Kansas Heart Association.)

VIDEOMETRIC DETERMINATION OF DYNAMIC REGIONAL SHAPE AND DIMENSIONS OF AN ISOLATED WORKING CANINE LEFT VENTRICLE. E. L. Ritman*, D. E. Donald, K. Tsuiki*, R. E. Sturm*, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

The left main coronary artery of a dog heart was cannulated and perfused at constant flow with donor arterial blood. The right atrium and ventricle were resected and the heart placed in an artificial perfusion circuit filled with Ringer's/dextran solution containing 10% renovist. Atrioventricular conduction block permitted independent control of atrial and ventricular pacing. The heart was positioned at the intersection of two orthogonal x-ray beams and video angiograms recorded in continuous 20-second sequences at a rate of 60 biplane images per second. Comparison of stroke volume measured by volumetric (X) and videometric (Y) techniques showed the relationship $Y = -0.9 + 1.06X$, $r = 0.96$ using endocardial silhouettes, and $Y = 2.0 + 1.02X$, $r = 0.98$ using epicardial silhouettes. Serial analysis of the endocardial silhouettes parallel diameters measured at 0.5-mm intervals on a base-apex axis showed: 1) the onset of volume change of the apex during systole lagged behind that of the basal third, 2) this delay was greater with increase in left ventricular end-diastolic pressure, and reduced with increased heart rate. Absolute change, and rate of volume change were greatest in the basal third. (Supported in part by NIH grants HL3532, HL4664, HL06143, and RR-7; NASA NGR 24-003-001; and AHA CI 10.)

CENTRAL AND PERIPHERAL MECHANISMS OF HEAT AND EXERCISE ACCLIMATION. M.F. Roberts*, K.B. Pandolf*, and E.R. Nadel. John B. Pierce Fndn. Lab. and Yale Univ. Sch. Med., New Haven, Ct. 06519.

A number of recent studies have shown increases in sweating rate accompanying combined exercise and heat acclimation. Some authors have suggested that physical training itself produces an acclimation to heat. We designed experiments to test this idea, and also to determine whether the potentiation in sweating in an acclimated individual is due to 1) an increase in sweat gland sensitivity (peripheral effect), or 2) a shift in the point of zero central drive (central effect). The program of exercise and heat acclimation was as follows: $\dot{V}O_2max$ was determined on 3 untrained, unacclimated males. Their local sweating rate/internal temperature relation was determined on 2 consecutive days in 10-min. exercise bouts (80% $\dot{V}O_2max$, Ta=22 C). Sweat rate was determined by resistance hygrometry, internal temperature was measured with an esophageal thermocouple, and skin temperature was measured at 3 sites. Subjects then trained 1 hr/day for 10 consecutive days at 70% $\dot{V}O_2max$ and T_a=22 C. Average $\dot{V}O_2max$ increased from 41 to 46 ml/kg. min during the training period. Following training, sweating response was again determined in experiments identical to pre-training tests. Next the subjects were heat acclimated by exercising 1 hr/day for 10 consecutive days at 50% $\dot{V}O_2max$ at T_a=45 C (T_{wb}=25 C). Following this, the sweating response was again obtained in experiments identical to pre-training and post-training tests. Results showed that exercise training alone increased the responsiveness of the sweat glands (peripheral effect) without changing the point of zero central drive. Heat acclimation lowered the point of zero central drive without altering the responsiveness of the glands. Besides clarifying some of the processes in acclimation to heat, these experiments point out the differences between heat and exercise acclimation.

INHIBITION OF ELEVATED CORE TEMPERATURE IN MICE BY CENTRAL NERVOUS SYSTEM GLUCOPENIA WITH 2-DEOXY-D-GLUCOSE. S. M. Robinson and M. Mager, U. S. Army Research Institute of Environmental Medicine, Natick, MA 01760

We demonstrated previously that 2-deoxy-D-glucose (2-DG), a competitive inhibitor of glucose utilization, resulted in hypothermia when administered into men or mice (N. Engl. J. Med. 287:841-845,1972). We postulated that intracellular glucopenia in the brain affected centers involved with the control of heat production, and was characterized by decreased utilization of fuel in the periphery. In the present study, 2-DG was injected into the cerebral ventricles (i.c.) of conscious mice to determine if it would affect the fevers induced by prostaglandin E_1 (PGE_1) and Brewers yeast. Results: PGE_1, 600 ng i.c., elevated core temperature (Tr) by 3.3° C within 15 min, with return to normal by 90 min. Tr rose only 0.9° C when 4 mg 2-DG was injected simultaneously with PGE_1; 6 mg 2-DG completely obtunded the response to PGE_1. Brewers yeast suspension (10%, 0.4 ml s.c.) elevated Tr by 1° C within 24 hrs; Tr returned to normal within 30 min. after 4 mg 2-DG i.c., remained normal for 3 hrs. and then returned to the fevered state. By comparison, sodium salicylate (300 mg/kg i.p.) reduced the fever from Brewers yeast, but not PGE_1. These data suggest that central nervous system glucopenia negates the hyperthermic actions of PGE_1 or yeast.

VOLUME AND ION INFLUX RATE CONSTANTS OF THE PLEURAL SPACE IN UNANESTHETIZED RATS. Lester L. Rolf* and David M. Travis, Dept. Pharmacol., Univ. Fla., Col. Med., Gainesville, 32601.

Rolf and Travis (Am. J. Physiol. 224(4):57-61, 1973) determined the major ionic components of normal pleural fluid in the rat and have demonstrated that a positive pleural fluid to venous plasma bicarbonate gradient of 5-8 mM exists in this space. The present study was designed to determine the normal volume of fluid/hemithorax and the rate of ion influx into this compartment. Three ml volumes of 5% dextrose were rapidly injected into the pleural space of 6 rats weighing 300-350 grams. The fluid was allowed to remain for 30 seconds and then withdrawn for analysis of Na^+, Cl^- and HCO_3^-. Based on the dilution of known Na^+, Cl^- and HCO_3^- concentrations and the volume of fluid injected, volumes/hemithorax (ml) of 0.49, 0.50 and 0.47 were calculated. The accumulation of Na^+, Cl^- and HCO_3^- into a 10 ml volume of 5% dextrose injected into the space was studied over a period of 38 minutes in 12 rats weighing 300-400 grams. Samples withdrawn at 3 and 8 minutes after instillation were used to calculate influx rate constants for the three major ions. These were found to be 0.042, 0.039 and 0.041 min^{-1} for Na^+, Cl^- and HCO_3^-, respectively. These studies were repeated on rats pretreated with the potent carbonic anhydrase inhibitor benzolamide (50 mg/kg i.m.). Rate constants calculated from these data were 0.047, 0.039 and 0.046 min^{-1}, respectively for Na^+, Cl^- and HCO_3^-, values indistinguishable from the controls. Based on the known volume, ionic composition and rate constants, and assuming that water moves isotonically with Na^+, the total pleural fluid volume could theoretically be exchanged every 29 hours. We conclude that the previously demonstrated bicarbonate gradient in this space can not be attributed to a differential influx of the bicarbonate ion and the influx of all ions is independent of enzymic activity of carbonic anhydrase. (Supported by NIH grant GM-AI-16934-02)

THE EFFECT OF PINEALECTOMY ON PLASMA GONADOTROPINS AND PROLACTIN IN THE RAT. O. Rønnekleiv* and S.M. McCann. Univ. of Texas Southwestern Medical School, Dallas, Texas 75235

Pinealectomy was performed in rats and its effect on plasma gonadotropin and prolactin levels was determined by radioimmunoassay. Plasma levels were determined at various times by drawing jugular blood samples while the rats were lightly etherized. The weights of ovaries, thyroids and adrenals were significantly enlarged two months after pinealectomy in female rats. In males, only anterior pituitary and prostate weights were increased following the operation. In females the estrous cycle remained normal following pinealectomy and plasma levels of LH at different stages of the cycle were unchanged except for a significant reduction in the preovulatory peak observed on the afternoon of proestrus. Following ovariectomy there were higher levels of plasma FSH but not LH in the pinealectomized females. There was no effect of pinealectomy on gonadotropin levels in intact or castrated males. The most dramatic effect of pinealectomy was an alteration in plasma prolactin observed in males. In normal males an early morning rise in plasma prolactin was detected with peak levels around 5 A.M. This was abolished by pinealectomy, and at 125 days after the operation pinealectomized animals also had significantly lower day time levels of plasma prolactin than controls. Superior cervical ganglionectomy was performed to denervate the pineal. Three weeks after bilateral ganglionectomy there was a decrease in plasma prolactin. Nocturnal activity of the pineal mediated via the superior cervical ganglion appears to be responsible for the early morning rise of plasma prolactin in the male rat. (Supported by grants from NIH, the Ford Foundation and the Texas Population Crisis Foundation.)

Blood Nitrogen Equality, Fact or Fiction? Edith Rosenberg and Donald H. Wood*
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A recent study by Cissik et al (J. Appl. Physiol. 32:155, 1972) in which they observed that the amount of expired nitrogen greatly exceeded the inspired nitrogen 1.5 hours after ingestion of high protein meals casts doubt on the axiom that gaseous nitrogen is neither used nor produced in the human body. They postulate that gaseous N_2 is produced metabolically and transported to the lungs in the venous blood by an as yet unknown mechanism. If they are correct, mixed venous nitrogen content ($C_{\bar{v}N_2}$) should be substantially higher than arterial nitrogen content (C_{aN_2}) after ingestion of a high protein meal. To test this postulate, catheters pretreated with carbon and heparin were implanted into the pulmonary artery and aorta of 2 dogs. The catheters were irrigated daily with heparin to prevent clotting. Blood was withdrawn simultaneously from both catheters and the samples analyzed for O_2, CO_2, and N_2. The nitrogen content was measured by Van-Slyke extraction coupled with gas chromatography. One of the animals was studied over a period of 18 days and 14 bloods were compared after the animal ingested food containing 82.5 to 142 gm. of protein. $C_{\bar{v}N_2}$ was 9.41 + 0.93 μL/ml and C_{aN_2} was 9.20 + 0.98 μL/ml blood, a difference which was neither significant nor related to the amount of protein eaten. $C_{\bar{v}N_2}$ of all 25 samples studied was 9.09 + to 0.97 μL/ml. C_{aN_2} was 9.22 + .93 μL/ml. These data do not support the postulate of Cissik et al.

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MESENTERIC VASOCONSTRICTOR ESCAPE IN ISOLATED ARTERIAL SEGMENTS.

Gordon Ross. UCLA School of Medicine, Los Angeles, California 90024.

Arterial segments 3-4 mm long and 1 mm diameter from the distal trunk of the cat superior mesenteric artery were superfused at 37°C with Krebs-bicarbonate solution equilibrated with 95% O_2-5% CO_2. The solution contained (mM)-NaCl 123, KCl 5, $CaCl_2$ 1.6, $MgSO_4$ 1.2, Na_2 EDTA 0.026, glucose-11.1. Addition of norepinephrine 1 µg/ml (NE) produced a contraction which slowly declined after its initial peak despite the continued presence of NE (NE escape). Phenylephrine, angiotensin and histamine behaved similarly. Substitution of NaCl by LiCl, $NaClO_4$, or Na I or reduction of the KCl concentration increased the initial NE contraction and reduced the rapidity of escape. Substitution of NaCl by Na_2SO_4 or Na isethionate reduced the initial contraction and the escape. Ouabain 10^{-6}M increased and verapamil 10^{-5}M and ryanodine 10^{-5}M reduced the initial NE contraction. All three agents reduced the rapidity of the escape. When the vessel was superfused with a depolarising solution (containing, mM-K_2SO_4 79, KCl 10, $KHCO_3$ 16, $CaCl_2$ 1.6, $MgSO_4$ 1.2) an initial contraction occurred which rapidly lessened to reach a stable level. Addition of NE produced a further contraction and escape did not occur. It is concluded that NE contraction of mesenteric arteries is strongly anion-dependent and that vasoconstrictor escape is an intrinsic property of mesenteric vascular smooth muscle which can be modified by changes in the ionic environment and by agents which influence excitation-contraction coupling.

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HUMAN SPLANCHNIC AND FOREARM VASOCONSTRICTION DURING RIGHT ATRIAL VS. AORTIC PRESSURE CHANGES. Loring B. Rowell, John M. Johnson*, Manfred Niederberger*, and Martin M. Eisman*. University of Washington School of Medicine, Seattle, Washington.

The objective was to cause separate reductions in right atrial pressure (RAP) and then in aortic mean (MAP) or pulse pressure (PP) and to determine degrees of splanchnic and forearm vasoconstriction in response to each change. In 30 experiments on 9 normal men, lower body negative pressure (LBNP) was applied in a slow (-1 mm Hg/min) ramp to simulate gradual hemorrhage. RAP fell gradually with LBNP. MAP remained constant until LBNP reached at least -30 mm Hg. PP stayed constant until LBNP reached about -20 mm Hg; thereafter PP fell and heart rate (HR) rose continuously as the ramp of LBNP continued. Changes in PP and HR were highly correlated (r=-.92). Forearm blood flow (FBF) (plethysmography) began to fall at the onset of LBNP and on the average was reduced by 35% before LBNP reached -20 mm Hg. Splanchnic blood flow (SBF) (via constant infusion of indocyanine green dye) was significantly ($P<.05$) reduced below control values when LBNP reached -15 mm Hg, and was reduced an average of 12% at LBNP of -20 mm Hg. Average SBF and FBF were 30% and 45% below controls, respectively, at -50 mm Hg of LBNP. We conclude that when RAP falls, the significant splanchnic and forearm vasoconstriction can occur without measurable change in MAP or PP. This suggests an influence from cardio-pulmonary stretch receptors with greater effect on FBF than SBF. (Supported by USPHS Grant HL 09773.)

PURINE NUCLEOSIDE PHOSPHORYLASE: LOCALIZATION AND ROLE IN THE TISSUE DISTRIBUTION OF PURINES. Rafael Rubio and Robert M. Berne, Dept. of Physiology, University of Virginia, Charlottesville, Virginia 22901.

Measurement of adenosine (Ado), inosine (Ino) and hypoxanthine (Hx) in isolated guinea pig hearts and their perfusates show Hx:Ado:Ino ratio of 0.6:1:1.2 for tissue and 6:1:7 for perfusates. The greater proportion of Ino and Hx with respect to Ado in the intracoronary than in the extravascular compartment suggested that Ado released from myocardial cells is degraded to Ino and Hx as it passes through the vessel wall. In support of this idea, nucleoside phosphorylase (NP), the enzyme catalyzing the conversion of Ino to Hx, was found to be localized principally in the vascular endothelium (Am. J. Physiol. 222: 550, 1972). To determine the degree of uniformity of the distribution of this enzyme and the correlation with the purine distribution, histochemical localization of NP was done in brain, kidney, liver, lung and skeletal muscle from rats and guinea pigs and Ado, Ino and Hx were measured in venous effluents and extravascular spaces of isolated saline perfused lungs, kidneys and livers. The purine content in urine and in tracheal and biliary effluents were taken as representative of extravascular purine content. In all organs NP was most active in the cytoplasm of vascular endothelium and pericytes. Little or no activity was detected in other cells. Purine analysis revealed ratios of Hx:Ado:Ino of 14:1:6, 1:1:0.5 and 3:1:3 for lung, kidney and liver extravascular compartments, respectively, and their respective intravascular ratios were 6:1:6, 7:1:4 and 235:1:110. With the exception of the lung, Ino and Hx are relatively greater in the intravascular than the extravascular compartment. These results are in accordance with the concept that the Ado produced by the cells in an organ is degraded to Ino and Hx as it passes through the vessel wall. SUPPORTED BY GRANT # HL10384.

EFFECT OF HEPARIN ON RELATIVE HEPATIC AND PULMONARY LOCALIZATION OF BLOOD-BORNE MICROPARTICLES FOLLOWING TRAUMA. Thomas M. Saba and T. G. Antikatzides.* Dept. of Physiology, Albany Medical College, Albany, N. Y. 12208.

The influence of heparin injection (IV) on the vascular clearance and relative hepatic and pulmonary localization of a labeled particulate fat emulsion (1 u) was evaluated in normal and post-surgically traumatized (celiotomy plus intestinal manipulation) rats. Surgical manipulation resulted in an impairment in the vascular clearance of the test emulsion (50 mg/100 g) by the reticuloendothelial system (RES) at 1 hr post-surgery and an associated increment in the lung localization of the microparticles. Heparin injection (100 USP/100 g) 3 min prior to colloid injection into normal rats resulted in a hepatic clearance depression and excessive 8-fold increment ($p < .001$) in lung particle localization. The combination of surgical trauma plus heparin injection maximized the RE phagocytic depression ($p < .001$) and intense pulmonary localization (11-fold) of the microparticles. The depressant effect of heparin on hepatic phagocytic activity within 3 min post-injection increased with dose (50-500 USP/100 g) and was not apparent below 25 USP/100 g. In contrast, the heparin induced increase in the pulmonary localization response was minimized with increments in the intervals between heparin administration and systemic particle injection. In this regard, it was maximal with a 3 min interval, significantly reduced by 30 min, and not apparent over a 60-240 min interval. The data demonstrate that heparin can alter RE function, and that pulmonary localization of blood-borne particulate matter appears to be inversely related to the hepatic clearance capacity. Impairment of the RES following trauma may lead to abnormal pulmonary localization of particulate matter (USPHS AM-14382).

CORRECTION FACTOR REPLACEMENT OF REGRESSION EQUATIONS USED IN ANGIOCARDIOGRAPHIC DETERMINATION OF LEFT VENTRICULAR VOLUMES. William P. Santamore* and Peter R. Lynch. Temple Univ. School of Med., Philadelphia, Pa. 19140

Twelve canine left ventricular casts were sliced at various intervals perpendicular to the base-to-apex axis. The outline of each slice was fed into a computer. The computer, then, calculated for a desired view a correction factor (CF), the CF being the relationship between the cross-sectional area of the slices and the estimate of the area based on the assumption that the shape of the slice is circular. The CF for different ventricular slices were averaged for each specific view. For the anteroposterior view, the average correction factor (ACF) was .786 for biplane data. Estimates of left ventricular volume were then obtained by multiplying the ACF by the uncorrected volumes obtained by the ellipsoid and Simpson's rule models. For the Simpson's rule biplane model, values of r=.96 and a standard error of estimate (SEE) of 6.5 ml were obtained using the ACF method. This compares to values of r=.97 and SEE= 9.2 ml obtained by use of regression equations. For the ellipsoid biplane model, values of r=.93 and SEE=8.9 ml were obtained using the ACF method as compared to r=.94 and SEE=10.8 ml obtained by using regression equations. This data demonstrates that the ACF can be used instead of the regression equations. Furthermore, since the ACF by use of the computer can be generated for any desired view, the necessity for calculating new regression equations for different views is eliminated. (Supported in part by NIH, NHLI Grant HL08886-09 and NIH, NHLI Training Grant 5-T-01-HL05362

OXYTOCIN RESPONSIVENESS OF MORPHOLOGIC CELL TYPES ISOLATED FROM TOAD URINARY BLADDER. Victor S. Sapirstein*, Monroe J. Yoder*, and Walter N. Scott, Dept. of Ophthalmology, Mount Sinai School of Medicine of CUNY, and Dept. of Biology, New York University, New York, New York.

The urinary bladder of the toad, Bufo marinus, responds to vasopressin and related hormones by increases in hydro-osmotic permeability and in sodium transport. There is considerable evidence to indicate that these responses are both mediated by cyclic AMP, although different hormone receptors may be involved. The mucosal epithelium consists of at least two major morphologic cell types: "mitochondria-rich" and "granular". The mitochondria-rich cells have been implicated as being responsible for the hormone-induced transport of sodium. We have removed the mucosal cells and separated the mitochondria-rich and granular cell types to determine their responsiveness to oxytocin. Mucosal cells were removed by incubation in EDTA-Ringers and then layered over a discontinuous Ficoll gradient. Four bands of material were apparent after centrifugation at 27,000 rpm for 45 min. The material was collected and studied by electron microscopy. Two bands contained intact cells identified as predominently mitochondria-rich (Band #2) and granular cells (Band #3). The cells were washed and resuspended in Ringers solution containing 1.5 mM Ca^{2+} and the cAMP content measured by radioimmunoassay. The basal cAMP levels in bands 2 and 3 were 11.33 $\pm$ 0.56 and 12.69 $\pm$ 0.54 pMoles/mgm protein, respectively. After six minutes exposure to oxytocin (10^{-8} M), the cAMP levels in bands 2 and 3 were 37.87 $\pm$ 2.11 and 13.58 $\pm$ 0.45 pM/mgm protein, respectively. These data indicate that the mitochondria-rich, but not the granular, population of toad bladder mucosal cells is responsive to neurohypophyseal hormones.

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THE INFLUENCE OF VARIATION IN INSPIRED OXYGEN CONCENTRATION ON THE VENTILATORY RESPONSE TO ADRENERGIC STIMULATION AND INHIBITION. Tapan K. Sarkar*, Harold Keltz* and Daniel J. Stone, Veterans Administration Hospital, Bronx, N.Y., and Mount Sinai School of Medicine, New York.

Minute ventilation ($\dot{V}_E$) was measured during control periods, and following the infusion of norepinephrine, norepinephrine and propranolol, propranolol alone, and propranolol and norepinephrine. These observations were made in ten healthy male subjects, using heart rate and expired carbon dioxide monitoring as indices of steady state; measurements were made after ten minutes of exposure of the subject to two inspired gas mixtures, oxygen 25%, and 10%, with the balance nitrogen. $\dot{V}_E$ while breathing F_{IO2} of 25% averaged 3.3 l/min/m^2 and rose to 4.3 l/min/m^2 on breathing the 10% mixture ($P < .001$). Norepinephrine had no effect on $\dot{V}_E$ during 25% oxygen breathing, whereas at F_{IO2} of 10%, it caused a rise in $\dot{V}_E$ of 0.6 l/min/m^2 ($P < .001$) above that due to low oxygen breathing per se. The rise in $\dot{V}_E$ due to norepinephrine, during low oxygen breathing, was completely inhibited by propranolol. However, the rise in $\dot{V}_E$ due to the stimulus of low oxygen breathing alone was not inhibited by propranolol. It is concluded that modest elevations of the inspired oxygen tension inhibit the stimulating effect of norepinephrine on ventilation. Beta adrenergic inhibition abolishes the effect on ventilation of norepinephrine, but not that of low oxygen breathing.

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EFFECTS OF VALINOMYCIN ON THE ELECTRICAL PROPERTIES OF EMBRYONIC CHICK HEART MUSCLE. T.Sawanobori*,M.Lieberman,J.Vereecke*,E.A.Johnson.Dept. of Physiology, Duke University Medical Center, Durham, N.C. 27710.

Since the antibiotic,valinomycin (Val) is known to specifically increase membrane permeability to potassium (K) in systems other than heart muscle, it was of interest to determine its effects on preparations of cultured embryonic chick heart muscle which are differentially sensitive to acetylcholine(10-100μg/ml)but respond to changes in external K(0-20mM) in a manner similar to that reported for adult mammalian Purkinje fibers. Synthetically grown strands of heart muscle in culture were exposed to Val (0.2-20μg/ml)in DMSO for as long as two hours. Intracellular microelectrodes were used to study passive and active membrane properties in the presence of bathing solutions containing Val and K at concentrations of 0-10mM.The effects of Val were shown to be more pronounced at $[K]_o$ = 5.4mM. Using the square-pulse technique, decreases up to 25% were observed in the measurements of length constant, input resistance and time constant.In addition, Val produced a slight decrease in the input slope resistance for hyperpolarizing currents,yet reduced by a factor of 2 the normally high input slope resistance during the plateau phase.In spontaneously beating preparations,the slope of the diastolic depolarization decreased without altering the maximal diastolic potential.The most noticeable changes in action potential configuration were increases in the resting(take-off)potential and maximum rate of depolarization($\dot{V}_{max}$); a decrease in duration(50% level) occurred without a concomitant change at the 90% duration level.No changes were observed in the S-shaped relationship between $\dot{V}_{max}$ and membrane potential.Action potentials obtained from intact embryonic chick ventricle responded in a similar manner to the presence of Val. It is concluded that valinomycin increases K permeability in embryonic chick heart muscle.

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CATION TRANSPORT BY RAT LIVER-SLICES IN HEMORRHAGIC SHOCK. M.M. Sayeed, M. Hass*, I.H. Chaudry, M.A. Wurth, and A.E. Baue. Washington University School of Medicine and The Jewish Hospital of St. Louis, Mo. 63110

We have demonstrated previously a loss of active Na, K transport capability of liver slices in hemorrhagic shock. In this study we have investigated if this cellular function can be restored. Fasted albino rats were bled and maintained at a mean arterial pressure of 40 mm Hg for varying periods of time and then sacrificed with or without reinfusion of blood plus lactated Ringer's solution (LR). Liver slices were initially chilled at 0.5 C in Krebs-Ringers bicarbonate (KRB) for 90 min. This allowed equilibration of tissue Na and K with medium. The slices were then incubated at 37 C in KRB for 1 hr and tissue Na and K measured. Rates of active transport were expressed in units of mEq/(hr x Kg dry wt). In liver slices from 6 unbled control animals, Na was extruded and K accumulated at 37 C at an average rate of 147.83 and 119.38 respectively. The rate of K accumulation in animals bled for ½, 1 or 2 hrs without reinfusion of blood plus LR was about 10% of control (14.29-16.94). Not only Na extrusion was absent in liver slices from these animals but Na contents increased by an average rate of 5.33 in 7 animals bled ½ hr, 108.40 in 10 animals bled 1 hr and 188.09 in 6 animals bled 2 hrs. In 10 animals bled for ½ hr and then treated with blood plus LR, Na extrusion and K accumulation returned to near control level (Na, 118.97; K, 92.28). Treatment with blood plus LR in 10 animals after 1 hr bleeding restored Na,K transport activity to about 35% of control level. These treatment effects were not studied in animals bled for 2 hrs because of high mortality in this group. These data suggest that the loss of Na, K transport with hemorrhagic shock is restored to normal in early but not in later stages of shock. (Supported by USPH grant 5 RO 1 HL 12278-05 and US Army contract DADA-17-69-9165.)

MODE AND SITE OF WATER PERMEATION IN ISOLATED RABBIT CORTICAL COLLECTING TUBULES. J. A. Schafer, S. L. Troutman*, and T. E. Andreoli. University of Alabama Medical Center, Birmingham, Alabama.

Previously, we reported that the vasopressin-dependent osmotic (P_f, μsec^{-1}) and diffusional (P_{D_W}, μsec^{-1}) water permeability coefficients in isolated collecting tubules were, respectively, 186 and 14, and the urea efflux coefficient was 0.03 μsec^{-1}. Further, we proposed that vasopressin increased water diffusion in luminal surfaces, and that the P_f/P_{D_W} ratio was due to cellular constraints to water diffusion but not bulk flow (J. Clin. Invest. 51:1264, 1972). The possibility that such restricted diffusion is the consequence of area limitations for water flow in the cell layer has been supported by a theoretical and experimental analysis of the osmotic transient phenomenon in these tubules (Fed. Proc. 32:397, 1973). In order to evaluate the contributions of tight junctions relative to luminal membranes for water flow, we measured vasopressin-independent osmotic flow rectification and, simultaneously, urea influx and efflux. The lumen contained hypotonic and hypertonic (with urea or sucrose added) Krebs-Ringer buffer for, respectively, osmotic volume inflow and outflow; the bath was isotonic Krebs-Ringer buffer. $P_{f_{in}}$ and $P_{f_{out}}$ were, respectively, 73 $\pm$ 7 (SEM) and 22 $\pm$ 4. For urea and sucrose dependent volume inflow, the urea efflux coefficients were, respectively, 0.19 $\pm$ 0.02 and 0.046 $\pm$ 0.01, but the urea influx coefficient was 0.033 $\pm$ 0.002 for volume inflow with either solute. The data suggest that luminal hypertonicity opens tight junctions to permit rectified osmotic volume flow, urea but not sucrose permeation of tight junctions, and, anomolous solvent drag for urea. We conclude that tight junctions are negligible paracellular shunts for osmotic volume outflow and that vasopressin increases water diffusion primarily in luminal membranes. (Supported by NIH, AHA, NSF and VA research grants, an NIH RCDA and an AHA Est. Investigator Award.)

Hypothermic Kidney Preservation With A Low Chloride Solution, Paul R. Schloerb, R. Bhasker* and N.C. Babcock*. University of Kansas Medical Center, Kansas City, Kansas 66103

Studies in vitro by Whittembury et al. suggest that hypothermic preservation of the dog kidney is associated with reduced cellular swelling using a chloride-free intracellular electrolyte perfusate. We are evaluating this suggestion by autotransplantation of the preserved dog kidney. The perfusate solution (G.W. Whittembury) contains, in one liter K_2SO_4-60 mM, $NaHCO_3$-15 mM, glucose -200 mM and 10% Dextran in 5% glucose -200 ml. Under Na pentobarbital anesthesia one dog kidney is removed, perfused at 100 cm H_2O pressure with about 500 ml of the solution and kept in the refrigerator. After at least 24 hours, the kidney was autotransplanted to the neck by standard vascular surgical methods and with skin ureterostomy. The opposite kidney was removed immediately or later, following autotransplantation. Prompt urine production was observed and life-sustaining function without uremia was demonstrated. Results from this continuing study suggest that the dog kidney may be preserved at 0°C for at least 24 hours, using a brief wash-out perfusion consisting of a simple low-chloride, intracellular-type, hypertonic perfusate

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VASCULAR EFFECTS OF VASOPRESSIN: CORRELATION WITH PLASMA LEVELS. Phillip G. Schmid, Eric S. Ramberg*, Francois M. Abboud, Allyn L. Mark, and Donald D. Heistad. Cardiovascular Division, Department of Internal Medicine, University of Iowa College of Medicine and V.A. Hospital, Iowa City, Iowa 52242.

Vasopressin (VP) has been implicated in regulation of the peripheral circulation, but plasma concentrations of VP required to produce direct vascular effects are not known so that a regulatory role in normal as well as pathophysiological states remains unsettled. In the present experiments, plasma VP (rat bioassay) was determined in six anesthetized, hexamethonium treated dogs given intravenous infusions of vasopressin (2, 4 and 8 mU/kg/min) and these levels were correlated with changes in systemic arterial pressure, heart rate, cardiac output, and blood flow to superior mesenteric, renal and iliac arteries (electromagnetic flow meters). During the low dose of VP, plasma concentration averaged 115±12.9 μU/ml (±SE) compared to the baseline average of 66±8.4 μU/ml. Systemic arterial pressure increased and iliac conductance decreased in five of six dogs. During the middle dose of VP, plasma concentration averaged 209±19.8 μU/ml and increases in total vascular resistance as well as further increases in systemic arterial pressure and decreases in iliac conductance were noted. Mesenteric and renal conductance were unchanged. During the high dose of VP, plasma concentration averaged 280±36.8 μU/ml; cardiac output and conductance in mesenteric artery decreased and other changes persisted. In eight different dogs, a smaller dose of VP (0.96 mU/kg/min) produced direct coronary vasoconstriction. These results indicate that coronary and hindlimb vascular beds are more sensitive to constrictor effects of VP than mesenteric and renal beds and support a direct role of VP in regulating the peripheral circulation in pathophysiological states when VP levels are > 100 μU/ml but not normally since VP levels rarely exceed 20-25 μU/ml.

ENDOGENOUS RELEASE OF PARATHYROID HORMONE AND SODIUM REABSORPTION BY THE PROXIMAL TUBULE OF THE DOG. Edward G. Schneider, Dept. of Physiol, Mayo Graduate Sch. of Med., Rochester, Minnesota

Exogenous parathyroid hormone (PTH) has been shown to inhibit fractional sodium reabsorption by the proximal tubule (FR). Thus, infusion of 0.05 units/kg/min of purified bovine PTH into the renal artery of 12 dogs increased significantly phosphate clearance from 15.2 ± 2.1 to 30.7 ± 2.8 ml/min/100 ml GFR while FR, measured by micropuncture, decreased significantly from 0.38 ± .02 to 0.33 ± .03 (59 tubules; $P < .025$). To determine if endogenous parathyroid hormone has a similar effect, the ionized calcium of blood perfusing the parathyroid gland of 8 unilaterally thyroid parathyroidectomized dogs (TPTX) was reduced from 4.1 ± .1 mg/100 ml to 3.2 ± .4 mg/100 ml by infusion of an isotonic sodium citrate plus sodium chloride solution into the blood supply of the parathyroid gland. The clearance of phosphate increased significantly from 14.6 ± 3.2 to 24.5 ± 3.2 ml/min/100 ml GFR and FR decreased from 0.41 ± .04 to 0.35 ± .03 (39 tubules; $P < .025$). Systemic plasma calcium increased .31 ± .10 mg/100 ml which was significantly greater than the change of plasma calcium obtained in sodium chloride infused control dogs. In the 8 normal control dogs which received isotonic sodium chloride infusion neither FR ($\Delta = .00 \pm .02$; 35 tubules) nor phosphate clearance ($\Delta = +3.2 \pm 2.1$ ml/min/100 ml GFR) were significantly altered. In 5 bilaterally TPTX dogs which received a sodium citrate plus sodium chloride infusion FR by the proximal tubule was not significantly altered ($\Delta = .00 \pm .02$; 23 tubules). There were no significant changes in glomerular filtration rate or renal plasma flow in any of the groups. The data suggest that increases in either exogenous or endogenous parathyroid hormone can cause a small but significant decrease in fractional sodium reabsorption by the proximal tubule.

RESPONSES OF VESTIBULAR NEURONS TO SINUSOIDAL ANGULAR ACCELERATIONS. L.W. Schneider and D.J. Anderson (intr. by N.B. Gross), Kresge Hearing Research Institute, Ann Arbor, Michigan.

Discharge patterns of first and second order vestibular neurons responding to angular acceleration were studied in gerbil. Sinusoidal oscillations ranging in frequency from .0125 to 5.0 hertz were delivered by a velocity controlled rate-table. Resting discharge activity was studied by measuring the coefficient of variation and coefficient of skewness of the interval distributions. Fourier analysis of the period histograms was used to determine the phase of cell response to sinusoidal rotations, while the D.C. level and amplitude were determined by a least squares fitting algorithm applied over the fraction of the stimulus period where the cell discharged. First order neurons were found to have high discharge rates and bidirectional responses to rotation and were composed of two groups called regular and irregular according to their resting discharge patterns. The second order neurons have low discharge rates, more unidirectional responses and are of a single population. The Bode plots of the regular first order cells are similar to that of a first order system with a time constant of 2 seconds as predicted by the torsion pendulum theory for cupula movement. The irregular first order cells show an increasing gain above .5 hertz and a large phase lead re velocity above 1.0 hertz. The second order cells show the phase and gain characteristics of the regular first order cells and thus transmit a unidirectional coding of head angular velocity for frequency components of head movements above 1.0 hertz.

Supported by: The John A. Hartford Foundation.

EFFECTS OF SIMULTANEOUS ACTIVATION OF MULTIPLE CNS VASOMOTOR SYSTEMS ON SKELETAL MUSCLE AND RENAL VASCULAR BEDS. Lawrence P. Schramm, Richard A. Altmansberger* and Mamoru Kumada. Johns Hopkins Univ. Sch. of Med. Numerous central neural vasomotor systems have been described. It is commonly assumed that complex cardiovascular behavior is the product of patterned activation of these systems. But little is known about their interactive properties. The present study investigated interactions between two systems, one in the hypothalamus (HT) and the other in the central gray (CG). The HT system mediated active sympathetic vasodilation in skeletal muscle (SVD) and neurogenic vasoconstric- (VC) in the kidney. The CG system mediated VC in both vascular beds. Experiments were performed in cats anesthetized with chloralose. Constant current stimulation of central vasomotor systems was delivered through stainless steel electrodes under stereotaxic control. Renal and skeletal muscle blood flows were measured electromagnetically. SVD evoked by supramaximal HP stimulation was only slightly blocked by CG stimulation which, by itself, elicited large vasoconstrictions. Submaximal excitation of SVD, however, was blocked by CG stimulation in a graded fashion. Quantitatively identical interactions between SVD and skeletal muscle VC's were observed when VC's were elicited by ia norepinephrine (NE) or phenylephrine (PE) infusions. These results suggest that the site of interaction between HP and CG effects on skeletal muscle vasculature may be peripheral. CG stimulation at intensities which elicited only small renal VC's greatly potentiated HP-evoked renal VC's. Similar facilitation of HP-evoked renal VC's was not observed when renal resistance was raised by NE or PE infusions indicating that the site of interaction between HP and CG-evoked effects on renal vasculature may be central.

A MODEL OF CORONARY FLOW ADAPTATION TO SOMATIC ACTIVITY. F. Schrijen*, W. Ehrlich, T. Solomon*, E. Rodriguez*, & J. Brady*, Johns Hopkins Univ. School of Medicine & School of Hygiene, Baltimore, Md. 21205.

Our experimental studies so far lead us to postulate this model of coronary adaptation to somatic activity: (1) With the onset of exercise a gradual shift in autonomic nervous function enhances rate and strength of myocardial contractions and this together with the subsequent rise in stroke volume enhances the extravascular pressure on, and the resistance to flow in, the coronary arteries. At the onset of exercise this rise in resistance is more effective in influencing coronary flow than any other factor and the coronary flow diminishes during the first 4 seconds of exercise. (2) The metabolic needs of the myocardium increase gradually with the rise in rate and force of heartbeat, and subsequently with the rise of stroke volume. At the onset of exercise the growing metabolic needs are faced with a decreasing blood supply. After the first 4 seconds of exercise, therefore, a large number of coronary arterioles start to recruit and the coronary flow increases during the next 20 seconds, in spite of the simultaneously rising extravascular pressure.

Electrical pacing however raises the rate but not the strength of the heartbeat. The extravascular pressure on the coronaries is less enhanced than with exercise. The heart rate increase is not gradual, it is switched on at once. The metabolic stimulus to recruit new vessels is therefore stronger at the onset of pacing than at the onset of exercise and the extravascular pressure is less enhanced. In contrast to the response at the onset of exercise, at the onset of paced heart-rate-increase the coronary flow rises immediately.

ISOLATION AND PARTIAL CHARACTERIZATION OF CARBONIC ANHYDRASE OF THE TOAD, *BUFO MARINUS*. Walter N. Scott, Department of Ophthalmology, Mount Sinai School of Medicine of CUNY, New York, New York.

It has recently been observed that the urinary bladder of the toad, *Bufo marinus*, is capable, under certain conditions, of acidifying the urine. The fact that acidification is inhibited by Diamox suggests that carbonic anhydrase (CA) is involved. Neither the characteristics of CA in toad RBC's nor the presence of CA in the toad bladder mucosal epithelium have been biochemically defined. We have purified toad RBC-CA by affinity chromatography. The toad RBC contains approximately 400 Enzyme Units (EU) of CA per gram cell. Although our preparation was homogeneous by gel chromatography and gel electrophoresis, four peaks of enzyme activity were obtained when the enzyme was analyzed by isoelectric focusing. These isolated peaks were homogeneous upon re-focusing. Activity of the enzyme was not stimulated by histamine, histidine, or vasopressin. The CA was inhibited by oxidizing agents and required the presence of reducing agents (e.g., mercaptoethanol) to maintain activity. The toad CA catalyzes the hydrolysis of p-nitrophenyl acetate and related esters as well as the hydration of CO_2. Mucosal cells were removed from bladders by incubation in EDTA-Ringers and disrupted by sonication. CA activity in the supernatant fraction of the cells amounted to 24 EU/gm cell (wet wt.), equivalent to the CA activity in toad kidney. Analysis of CA in the mucosal cell extracts by isoelectric focusing showed one major peak whose pI (6.0) corresponded to that of the major fraction of toad RBC-CA. The affinities of these two enzymes for ^{3}H-Diamox were similar. Our results indicate that there may be four isozymes of carbonic anhydrase in the toad RBC and that the CA in toad bladder mucosal cells may be identical to the major component of RBC-CA.

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Chemically "Skinned" Coronary Smooth Muscle. C.L.Seidel* & H.V.Sparks
Univ. of Michigan, Ann Arbor.
In 1971 Winegrad (J.Gen. Physiol. 58:71) described a technique for chemically "skinning" cardiac muscle. We have successfully applied this technique to coronary vascular smooth muscle. Canine left circumflex coronary arteries (OD=2mm) were cut into helical strips (1.5x10mm) and suspended with a resting tension of $1.3x10^4$ dynes/cm^2 in a muscle bath containing a physiological salt solution (PSS). The mechanical responsiveness of the strips to increased extracellular Ca concentration and to phenylephrine (P) was determined. The PSS was then replaced with the "skinning" solution of the following composition (mM): EDTA-Na_2,3; Na_2ATP, 5; Tris, 10; KCl, 140. The vessels remained in this solution for 20min and then were placed in a Ca free solution of the following composition (mM): EGTA, 3; Na_2ATP, 5; Tris, 10; KCl, 140; $MgCl_2$, 1.17. After determination of the mechanical response of the strips to increased extracellular Ca, the EGTA solution was replaced with PSS and at various times the mechanical response to P was determined. "Skinned" strips have a greatly increased sensitivity to extracellular Ca. Prior to "skinning" an increase in extracellular Ca from $1.6x10^{-3}$ to $4.3x10^{-3}$M (an increase of $2.7x10^{-3}$m) was associated with the development of only 56±15 dynes of force, whereas after "skinning" an increase in Ca from 0 to $8x10^{-4}$M was associated with the development of 401±99 dynes. "Skinning" appears to be a reversible process since within 60min after returning to PSS, the mechanical response to P ($3.2x10^{-6}$M) returned to 72±11% of the pre-"skinned" response. This "skinning" technique has several advantages over the technique of glycerol extraction: 1)"skinning" is more rapid; 2)the contractile response of "skinned" vessels is large; 3)"skinning" is a reversible process; 4)a given strip can be "skinned" and "healed" several times. Supported by USPHS Grant HL-13538.

PLASMA PROTEIN AND VOLUME CHANGES DURING HEAT ACCLIMATIZATION. L.C. Senay, Jr., D. Mitchell*, and C.H. Wyndham*. Human Sciences Lab., Johannesburg and St. Louis Univ. Sch. Med., St. Louis.

Four males who had undergone a prolonged training program (bicycle ergometer) were first exposed on three control days to 25°C D.B., 18.1° C W.B. while working at a rate of 400 watts for 4 hr. Following the final control day, the subjects were then acclimatized to heat by exposure to 45°C D.B., 32.2°C W.B. for 4 hr. on 10 consecutive days while working at the same rate. Numerous observations relating to heat transfer, the cardiovascular and respiratory systems were obtained but this presentation is only concerned with certain changes in and of the vascular volume. Free flowing venous blood samples were taken before and 1/2, 1 1/2, 2 1/2, and 3 1/2 hr. after starting work on control and heat exposure days. Results indicated that between days 1 and 2 of heat exposure there was an 11.6% increase in total circulating protein (TCP) and a 9% increase in plasma volume. Pre exposure values (Time 0) slowly increased until day 6 of heat exposure. TCP increased some 22% as did plasma volume. Protein fractions were not uniformly elevated i.e. B globulin had the largest proportionate increase. During each 4 hr. exposure the movement of protein fractions into and out of the vascular compartment appeared to be similar in control and acclimatizing subjects but the latter always maintained a greater amount of protein and fluid within the vascular volume. There was no evidence of salt and water retention. The increase in vascular volume was thought to be due to a transfer of interstitial protein and water to the vascular volume. Results for individual subjects indicated that a 10% expansion of plasma volume was necessary to effect a decrease in heart rate during heat exposure. These results indicate that a critical event in heat acclimatization is expansion of the vascular volumes. This work was accomplished during the tenure of an Anglo-American Fellowship by LCS.

AORTIC BLOOD FLOW MEASUREMENTS IN AN UNRESTRAINED, UNANESTHETIZED HIBERNATOR, THE WOODCHUCK, MARMOTA MONAX (VIDEOTAPE). Jerome B. Senturia, John R. Chessar* and Carlos M. Ferrario, Department of Biology and Health Sciences, The Cleveland State University and Research Division, Cleveland Clinic Foundation, Cleveland, Ohio

Blood flow measurement is critical for the evaluation of cardiac responses to the lowered body temperatures associated with mammalian hibernation. Until recently, available techniques have prohibited serial measurement over periods extending to days or months. Refinements in electromagnetic flowmeter technology, including transducer miniaturization, allow application of the method for continuous measurements of cardiac output from unrestrained, awake woodchucks. Blood flow transducers were implanted in anesthetized woodchucks under sterile conditions. Details of the procedures are described by the use of a videotape demonstration. Simultaneous measurement of aortic blood flow, stroke volume, heart rate, cardiac output, aortic blood flow acceleration, ECG, and body temperature could be obtained in the awake woodchuck as early as 1 hour post operative and continued daily for periods in excess of two months. In euthermic, conscious unrestrained woodchucks mean values ranged as follows: Aortic Blood Flow 16-23 ml/sec, Stroke Volume 1.7-1.9 ml, Heart Rate 173-183 b/min, Cardiac Output 274-359 ml/min, Flow Acceleration 5.6-5.7 g. The results indicate the feasability of serial measurement of blood flow in the woodchuck and opens a new avenue for more comprehensive study of cardiac responses during hibernation.

INFLUENCE OF TRIGEMINAL NUCLEUS CAUDALIS AND INTERACTION OF TACTILE AND NOXIOUS STIMULI ON CAT TRIGEMINAL NEURONES. B.J. Sessle and L.F. Greenwood (Intr. by A.T. Storey). Univ. of Toronto Fac. of Dentistry, Toronto, Canada, M5G 1G6.

In studies of brain stem mechanisms that may contribute to oral-facial sensory and motor functions, extracellular recordings were made from more than 150 single trigeminothalamic relay neurones and interneurones located in histologically verified microelectrode penetrations of the trigeminal main sensory and oralis nuclei in anaesthetized (chloralose) or decerebrate cats. The response in over 90% of neurones with an oral-facial mechanoreceptive field to a reproducible and accurate mechanical stimulus applied within the field could be depressed by reversible cold block of synaptic transmission through nucleus caudalis or by trigeminal tractotomy at the obex. Mechanoreceptive field size was also markedly reduced. Neurones activated by a noxious (bipolar tooth pulp) stimulus were also located, but were usually not influenced by cold block of caudalis. The antidromic response of trigeminothalamic neurones and trigeminal motoneurones and the activity of trigeminal primary afferents were also apparently unaffected by this procedure. Moreover, cold block did not abolish the conditioning effects of oral-facial single or vibratory mechanical stimuli or single or repetitive shocks to tooth pulp. These conditioning stimuli produced a prolonged (200-300 msec) inhibition or short (30 msec) facilitation in neurones activated by tactile and/or pulp stimuli. Facilitation following the inhibition was not observed. These findings do not entirely support proposals for a presynaptic modulatory role of nucleus caudalis, although the interaction of tactile and noxious stimuli and the regulatory effect of caudalis on the tactile input to trigeminal neurones may have a presynaptic basis.

EFFECT OF ANGIOTENSIN II ON THE ADH RESPONSE TO CONTINUOUS SLOW HEMORRHAGE IN ANESTHETIZED DOGS. R.E. Shade* and L. Share. Dept. of Physiology & Biophysics, U. of Tenn. Med. Units, Memphis, TN. 38103

These experiments were designed to determine if exogenous angiotensin II (AII) could potentiate the increase in plasma antidiuretic hormone (ADH) produced by a continuous, nonhypotensive hemorrhage. Changes in endogenous plasma levels and high initial values of AII were prevented by bilateral nephrectomy at least 2 hours before the experiment. In a control group of 9 dogs continuous hemorrhage was applied during an I.V. infusion of 0.9% NaCl at 0.28 ml/min. A second experimental group (8 dogs) received an infusion of AII at a dose of 10 ng/kg.min in 0.28 ml/min in a femoral vein. A third group received an identical infusion of AII in the left carotid artery. The rate of hemorrhage was 0.44 ml/kg.min, with blood samples for plasma ADH determination taken after 0,5,10 and 30 minutes of hemorrhage. Plasma ADH concentration increased significantly after 5($p<.05$), 10($p<.05$), 20($p<.01$) and 30($p<.01$) minutes of hemorrhage in dogs with femoral vein infusion of AII. Carotid artery infusion dogs had an increase in plasma ADH after 5 minutes; statistically significant increases were seen only after 10,20 and 30 minutes of hemorrhage ($p<.01$ for each). Control dogs had a significant increase in plasma ADH only after 20($p<.05$) and 30($p<.01$) min. An analysis of variance could not detect any significant differences in plasma ADH levels between any of the 3 groups at any time interval. Mean arterial blood pressure increased 20 mmHg ($p<.01$) with both infusions of AII. Mean arterial blood pressure, plasma osmolality and arterial pulse pressure did not change during hemorrhage in all 3 groups. In conclusion, we were unable to detect any effect of AII on the plasma ADH response to a continuous, nonhypotensive hemorrhage.

ROLE OF ASPARTATE IN NEUROMUSCULAR EXCITATION IN THE LOBSTER. R.P. Shank*, A.R. Freeman, C.A. Colton*, W.J. McBride* and M.H. Aprison, Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, Indiana 46202.

We have confirmed and pursued the observation made previously by Kravitz and his colleagues (in Excitatory Synaptic Mechanisms, Eds: P. Anderson and J.K.S. Jansen, Universitetsforlaget, Oslo, 1970) that aspartate, which by itself has very weak excitatory activity, can potentiate the action of glutamate on lobster muscle fibers. When included in an artificial sea water solution being perfused over the muscle fibers, aspartate at concentrations which by itself has no effect, greatly reduces the concentration of glutamate required for maximum excitatory activity. Thus the difference between the concentration of glutamate having a minimal effect and that having a maximal effect is greatly reduced by aspartate. The concentrations of aspartate and glutamate in excitatory axons were found to be approximately 100 mM and 30 mM, respectively. The potentiative effect was most pronounced when the ratio of aspartate to glutamate was similar to that present in the axons (i.e., 4:1). Our observations are consistent with the view that neuromuscular excitation in the lobster is mediated by glutamate and aspartate acting synergistically. One possible advantage of such a "team" action is that the on-off time for maximal receptor activation and subsequent inactivation may be shortened appreciably. (Supported in part by Postdoctoral Training Grant MH 10965 and Research Grant GB 28715X from the National Science Foundation).

Influence of Chronic Administration of Ethanol on Function and Morphology of Parietal Cells in Dogs. R.N. Sharma*,W.Y.Chey,R.Escoffery*, C.B. Lillibridge*. The Isaac Gordon Center for Digestive Diseases, The Genesee Hospital and University of Rochester School of Medicine and Dentistry, Rochester, New York.

Effect of daily administration of ethanol on the function and morphology of parietal cells was investigated in 11 dogs with esophagostomy and gastric cannula. To 6(Group I)of 11 dogs, 40% ethanol solution, in a daily dose of 4.4 gm/kg was given for one month in 5 equal portions through esophagostomy at half hourly intervals, starting one hour after meals. The remaining 5(Group II)received 15% ethanol solution parenterally at the rate of 1.5 ml/minute for 3 hours daily through an indwelling catheter in superior vena cava for one month also. Peak Blood Alcohol level ranged from 260 mgs. to 320 mgs% in both groups. Within one month of the ethanol administration, the mean maximal acid output in response to histamine increased significantly in all dogs with mean increase of 56.02% in Group I and 66.13% in Group II. The mean parietal cell mass(PCM)determined in 3 each of Group I and Group II was 204.4x 10^6/kg and 214x10^6/kg which were approximately 50% greater than that of 5 control dogs. The mean diameter of parietal cell in these dogs was 16.5u while that of 5 control dogs was 12.5u. The difference between the two was statistically significant ($P < .05$). Electron microscopy of these parietal cells revealed hyperplasia of vesicotubules and swollen mitochondria with bleb formation. The observations indicate that alcohol per se influences the acid secretory function of the stomach by increasing its secretory capacity significantly. They suggest further that the acid secretory changes were well correlated with the structural alterations of the parietal cells which included hyperplasia and hypertrophy.

ANOMALOUS RETINAL PROJECTIONS AFTER TECTAL REMOVAL IN ADULT GOLDFISH. S.C. Sharma. New York Medical College, New York, New York.

Experiments involving size disparity between the retina and the optic tectum in adult goldfish have suggested the rearrangement of the regenerating retinal axons in their terminations while retaining a certain order. In the present experiments, regenerating optic axons formed a "normal" retinotopic order of projections to the ipsilateral tectum when the contralateral optic tectum was completely removed. Thus, both eyes projected to one tectum yet retained their normal order of fiber distribution. Furthermore, when one eye and its ipsilateral tectum were removed, the remaining eye innervated its ipsilateral tectum, thus restoring partial vision. Behavioral visual recovery was noticed within a few weeks following surgery. The factors responsible for such anomalous retinal projections will be discussed.

EFFECT OF PROSTAGLANDIN E_2 ON THE ISOLATED PERFUSED STOMACH OF THE DOG. Jane E. Shaw and John Urquhart, ALZA Research, Palo Alto, CA 94304.

We have initiated studies to determine the mechanism whereby prostaglandins inhibit gastric acid secretion. Using the isolated canine stomach perfused with blood by the pilot organ method, we have defined certain parameters associated with control of gastric acid secretion in this preparation; we have documented the effect of graded infusions into the gastric artery of histamine ($0.5\text{-}1 \times 10^{-8}$ g/ml) or pentagastrin (ICI 50123; $2\text{-}4 \times 10^{-10}$ g/ml) and the effect of vagal stimulation on acid secretion, perfusion pressure, blood flow and motility. In addition, we have investigated the effect of vagal stimulation on antral output of immunoreactive gastrin and determined the effect of varying the frequency on acid secretion and gastrin release. Further studies have been directed towards elucidation of the mechanism whereby prostaglandins inhibit gastric acid, pepsin, and mucous secretion induced by either chemical or nervous stimulation; such effects have been recorded in both dog and man following intravenous injections or infusions. The finding that prostaglandins inhibited so many aspects of gastric function indicated that they may be effective via reduction in mucosal blood flow. We have confirmed that PGE_2 when added to the perfusing blood ($0.5\text{-}10 \times 10^{-8}$ g/ml) inhibits the action of all stimulants, an effect which is associated with an unexpected marked increase in total gastric blood flow.

CONCLUSION: The inhibitory effect of PGE_2 on acid secretion in the isolated canine stomach is not associated with a decrease in tissue blood flow. Thus, PGE_2 may be effective by a direct action on the secretory cells or may modify the interaction of stimulants with these cells.

BODY COMPOSITION IN THE ESKIMO. R. J. Shephard, J. Hatcher,* and A. Rode.* Depts. Envtal. Hlth. and Epidemiology and Biometrics, Sch. Hygiene, Univ. Toronto.

The body composition of 74 adult Eskimos (33 males, 41 females) has been determined by Deuterium oxide dilution. Lean mass is comparable with that for the "white" population when reported on an absolute basis, but is larger if expressed per unit of standing height. Percentages of body fat (average 13.4% in males, 22.6% in females) are relatively high despite very low skinfold readings; possibly, the regional distribution of body fat in the Eskimo differs from that in the "white" man. Blood volumes measured by a carbon monoxide method are in the high normal range (95.7 ml/kg in the males, 91.0 ml/kg in the females); however, lower values in hunters (83.6 ml/kg) than in settlement Eskimos (94.6 ml/kg) suggests that dehydration may be incurred during hunting trips. If so, the deuterium method may overestimate the body fat of the hunters.

Blood volumes are related to body water in the females, but not in the males. Perhaps because skinfold readings are so low, there is no relationship between skinfold thickness and body fat in the male Eskimos. In the females, also, the best equation accounts for only 25% of the variance in the data.

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PLASMA MEMBRANE POLARITY OF PROXIMAL TUBULE AND COLLECTING DUCT CELLS OF RAT AND BOVINE KIDNEY IN RELATION TO THE MECHANISM OF ACTION OF PTH AND ADH. L. J. Shlatz*, R. Kinne*, E. Kinne-Saffran* and I. L. Schwartz. Dept. Physiol., Mount Sinai Sch. of Med. of the City Univ. of New York, N.Y.C. and Max Planck Inst. für Biophysik, Frankfurt/M.

In the rat kidney the adenylate cyclase specifically activated by parathyroid hormone has been shown to be localized in the basal infoldings of the proximal tubule cell (Kinne et al., Abstracts, 9th Intl. Congr. Biochem., Stockholm, 1973). Since the effect of cAMP in various tissues involves the activation of protein kinases, we investigated the possibility that such an enzyme might be a component of the plasma membrane. The incorporation of P^{32} from γ-P^{32}-ATP into the plasma membrane was found to be catalyzed by an endogenous protein kinase localized in the brush border fraction. This phosphorylation was increased approximately 100% at a cAMP concentration of 10^{-7}M.

To determine whether the plasma membrane of the renal collecting duct possesses a similar enzymatic polarity, membranes from bovine papillae were prepared by a modification of the method of Heidrich et al. (J. Cell Biol. 54:232, 1972). Separation by free flow electrophoresis resulted in two distinct membrane fractions, one containing Ca^{++}-ATPase and ADH-stimulated adenylate cyclase activities and the other containing HCO_3^--ATPase and cAMP-dependent protein kinase activities. These results suggest that the adenylate cyclase and protein kinase of the collecting duct and of the proximal tubule are localized on the contraluminal and luminal cell surfaces, respectively.

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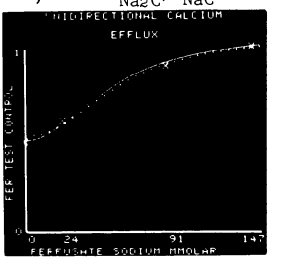
Na^+-Ca^{2+}EXCHANGE IN PERFUSED RAT HEARTS. P.M. Sidell*, R.E. Safford*, and J.B. Bassingthwaighte, Mayo Grad. Sch. of Med., Rochester, Mn. 55901

Control ^{45}Ca fractional escape rates, FER, where FER = dM/dt/M and M = heart tracer content, were obtained with Tyrode perfusate concentrations of Na_o = 147mM, Ca_o = 1.8mM. Test perfusates with raised Na_o or Ca_o (maintaining osmolality with sucrose) increased the FER's; tests with lowered Na_o or Ca_o decreased FER's. Low Na_o increased diastolic tension, zero Na_o gave contracture. Analysis was in terms of a sarcolemmal carrier binding 1 Ca or 1 or 2 Na ions, each bound form having a different permeability. Experimental, test/control FER's are X's on the figure. For a model solution assuming carrier internally facing free sarcoplasmic concentrations of Na=2mM & $Ca_i=10^{-7}$M (continuous line in fig.) binding constants for Na, outside & in, were $KNa_o=KNa_i=(65mM)^2$; for Ca, $KCa_o = 5.4\times10^{-3}$ M, $KCa_i=5\times10^{-8}$M. Permeabilities of free carrier, P_c, and of single-Na-complex, P_{NaC}, were very low compared to P_{CaC} & P_{Na_2C}. The dotted solution was obtained assuming the carrier to be at the site of cisternal SR-sarcolemmal apposition and Na_i=80mM, $Ca_i=5\times10^{-5}$M; values were: $KNa_o=(100mM)^2$, KCa_o=6.5mM, KCa_i=0.5mM, with P_{Na_2C}/P_{NaC} >100. This latter solution is compatible with observations of the reversal potential for Ca^{2+} currents being around +40mV. Both solutions provide net Ca efflux driving the concentrations toward the equilibrium given by:

$$\frac{Na_o^2/KNa_o}{Na_i^2/KNa_i} = \frac{Ca_o/KCa_o}{Ca_i/KCa_i}$$



(Supported by NIH-HL9719)

EFFECTS OF PROSTAGLANDIN $F_{2\alpha}$ ($PGF_{2\alpha}$) ON DEHYDROEPIANDROSTERONE-3β-HYDROXYSTEROID DEHYDROGENASE (DHA-3β-HSD) ACTIVITY IN THE OVARY OF THE IMMATURE LABORATORY RAT. Martin A. Sidor,* Barbara A. Kasprow,* Fred Buddingh,* Leslie A. Emmert* and Joseph Thomas Velardo. RILAMSAT, Veterans Administration Hospital, Hines, Illinois and Department of Anatomy, Loyola University, Stritch School of Medicine, Maywood, Illinois.

A series of experiments was undertaken to observe the effects of $PGF_{2\alpha}$ and aspirin on estrogen biosynthesis in the ovary as revealed histochemically by the localization of DHA-3β-HSD (Kalvert and Bloch, 1968). Two of three major groups of thirty 22 day old female albino rats (controls and two experimental groups) were given subcutaneous injections of 75 μg of $PGF_{2\alpha}$ or 5 mg of aspirin twice daily. All rats were housed in plastic cages (five animals per cage) on ground corn-cob bedding and fed Purina Rat Chow and water ad libitum. Sub-groups of ten rats in each major treatment category were necropsied, and the ovaries frozen, at 27, 33 and 37 days of age. Average semi-quantitative estimates of DHA-3β-HSD activity in ovarian sections revealed a statistically significant ($P < 0.05$) increase in enzyme activity at day 27 in the $PGF_{2\alpha}$ group and at day 33 in the aspirin group. Adrenal gland weights, on a milligram per 100 gram body weight basis, showed statistically significant increases at day 27 in both the $PGF_{2\alpha}$ and aspirin groups. It was postulated that $PGF_{2\alpha}$ and aspirin, a specific prostaglandin antagonist, exert their effects at different levels of hormone action, i.e. at the pituitary or ovarian levels, to produce or modulate estrogen biosynthesis. (Supported by Veterans Administration Hosp., Hines, and U.S.P.H.S.-G.R.S.G., Pr.Velardo)

MAGNESIUM MODULATION OF CALCIUM UPTAKE BY HEART MITOCHONDRIA. Burton B. Silver* and Louis A. Sordahl. Department of Physiology and Biophysics, University of Louisville School of Medicine, Louisville, Kentucky, and Division of Biochemistry, University of Texas Medical Branch, Galveston, Texas.

Correlative ultrastructural and biochemical evidence indicates that the presence of magnesium alters both the rate and characteristics of calcium uptake in neonatal cardiac mitochondria compared to adult heart mitochondria. The ultrastructure of electron-opaque calcium granules appeared to be either amorphous granules or crystal-like deposits within the cristae, depending on the amount of calcium loading and the type of mitochondria. In the absence of Mg^{++}, mitochondria accumulate calcium at higher rates than when Mg^{++} is present. Neonatal heart mitochondria, in the presence of Mg^{++}, accumulated calcium at higher rates compared to adult heart mitochondria. However, the calcium deposits associated with the neonatal cristae tended to be rounded dense amorphous structures. Calcium loading in adult heart tended to form a second type of crystal structure apparently destructive to mitochondrial integrity. In both neonatal and adult heart,stimulation by calcium was also lower in the presence of Mg^{++}. A marked stimulation of respiration in the presence of Mg^{++} occurred with addition of ADP after calcium uptake. Mg^{++} appears to protect and modulate the ATP synthesizing and calcium transport activity of both neonatal and adult cardiac mitochondria. (Supported by grants from American Heart Association, Texas Affiliate, Eli Lilly and DHEW 5S01-05427-11.)

THE IN VIVO LOCALIZATION OF ^{3}H-PHLORIZIN BINDING IN DOG KIDNEY. Melvin Silverman. University of Toronto, Toronto, Canada.

The intrarenal distribution of ^{3}H-phlorizin was studied in anesthetized mongrel dogs by the multiple indicator diluter method. Renal vein and urine outflow curves were obtained for tracer ^{3}H-phlorizin relative to simultaneously injected, TI824-albumin (vascular reference), and creatinine (extracellular reference). ^{3}H-phlorizin emerges ahead of creatinine in the renal vein and its recovery in venous blood is greater than creatinine. It is calculated that 10-15% of the injected drug binds immediately to some component in whole blood. In vitro experiments confirm that the binding is to red cells. The remaining free ^{3}H-phlorizin has an extracellular distribution from the postglomerular circulation (no interaction with the antiluminal membrane). In contrast, about 95% of the filtered ^{3}H-phlorizin binds to the luminal membrane. This labelled phlorizin can be washed off the brush border surface by a bolus of systematically administered cold phlorizin or by D-glucose. Phloretin loading has no effect. It is concluded that there is only one set of high affinity phlorizin receptor sites in dog kidney and that these are distributed along the brush border of the proximal tubule.

DECREASED VENOUS COMPLIANCE AND NORMAL BLOOD FLOW IN THE MESENTERY OF RENAL HYPERTENSIVE DOGS. G. Simon*, M.B. Pamnani*, D.N. Pugh* and H.W. Overbeck. Michigan State University, East Lansing, Michigan.

Mesenteric hemodynamics have not been investigated in experimental renal hypertension (RHT). Therefore, we studied mesenteric (ileal) blood flows, segmental vascular resistances and venous pressure-volume (compliance) relationships in 9 pentobarbital-anesthetized (35 mg/kg) dogs in the early (<4 weeks) stage of RHT and in 10 normotensive, control dogs. We used the isolated, innervated, naturally-perfused intestinal loop preparation. We measured venous compliance by injecting blood into temporarily isolated, standardized segments of mesenteric vein in vivo or Krebs-Henseleit solution into standardized segments of the superior mesenteric vein in vitro. Although arterial pressure in hypertensives (181.6±5.4 SEM mm Hg) was greater ($P<0.001$) than in normotensives (145.2±2.0), blood flow (ml/min/100 gm) and resistances: total, arterial, small vessel and venous (mm Hg/ml/min/100 gm) in hypertensives (57.2±5.4, 3.22±.27, .94±.16, 2.14±.16, .135±.022, respectively), were not significantly different ($P>0.05$) from values in normotensives (52.1±2.7, 2.70±.15, .74±.09, 1.86±.13, .091±.010). In comparison to veins from normotensives, the in vivo pressure-volume curves for hypertensive veins were shifted toward the pressure axis at pressures up to 35 mm Hg ($P<0.01$). In vitro, similar shifts occurred in hypertensive veins ($P<0.05$) but only up to 15 mm Hg. We detected no tendency for sigmoid configuration of curves in hypertensive veins. We suspect that the decreased venous compliance we found in hypertensives represents structural changes, which persist in vitro in the absence of neural or humoral stimuli. This decreased venous compliance may contribute to the increase in cardiac output reported to occur in this stage of RHT. However, the mesenteric vascular bed appears not to share in the increased total peripheral blood flow. (Supported by USPHS Grant HL15146 and by the Mich. Heart Assoc.)

REGULATION OF VERTEBRATE COLLAGENASE: A POSSIBLE ROLE FOR A MAST CELL FACTOR. John W. Simpson and A.C. Taylor*. University of Texas Dental Science Institute, Houston, Texas.

Mechanisms for the regulation of vertebrate collagenase activity are not clearly understood. When rat mesentery was incubated with rat gingival tissue culture media, the collagen fibers surrounding each of its mast cells became digested. This experiment suggested that collagenase activity was dependent upon an interaction between a mast cell factor and collagenase. Rat gingival cells cultured in serum-free media produced enzyme activity which reduced the viscosities of collagen solutions, and electrophoretic analysis of collagen-culture media reaction mixtures verified the viscosity reduction to be catalyzed by collagenase. In the presence of 2% bovine or rat serum the collagenase was inactivated. Addition of a mast cell extract to the serum-inhibited collagenase blocked the inhibitory action of serum. Serum inhibited collagenase was capable of degrading collagen fibers in the presence of the mast cell extract but not in its absence. Therefore, collagenase activity in tissues could be regulated, in part, by a mast cell factor which reverses the inhibition of collagenase. The nature of the mast cell factor has not been established; however, the active component is nondialyzable and heat stable but is destroyed by 20% TCA. Neither extracts from muscle, kidney, liver, intestinal mucosa and leucocytes nor heparin, histamine and 5-hydroxytryptamine could substitute for mast cell extracts in the activation of gingival collagenase.
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EFFECTS OF PROSTAGLANDIN E_2 (PGE_2) ON RENAL FLUID DYNAMICS. R. J. Sinclair*, R. D. Bell and M. J. Keyl. Univ. of Oklahoma Health Sciences Ctr. and VA Hospital, Oklahoma City, Okla.

PGE_2 has been demonstrated to be a potent vasoactive agent. The role of this naturally-occurring substance in the kidney is not clear. The present studies were designed to determine the effects of PGE_2 on renal fluid dynamics. PGE_2 was infused into the renal artery of the anesthetized dog. Renal blood flow (RBF), arterial pressure (AP), renal venous pressure (RVP), intrarenal venous pressure (IRVP), subcapsular pressure (SCP), lymph flow or pressure (L_cP), lymph protein concentration, urine flow and osmolality were measured. PGE_2 increased RBF, IRVP, SCP, lymph flow, L_cP and urine flow while AP, RVP, renal venous resistance and lymph protein concentration remained unchanged. Urine osmolality and prevenous resistance decreased. PGE_2 alters renal fluid dynamics by decreasing arteriolar resistance. The increased RBF acts against an unchanged venous outflow resistance, elevating IRVP. SCP and L_cP increase secondary to the change in IRVP. PGE_2 did not alter vascular permeability to protein as evidenced by unchanging lymph protein concentrations. Thus, with the exception of the greater potency of PGE_2 the effects are not unlike those previously demonstrated for acetylcholine on the kidney.

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VISIBLE LIGHT AND OXYGEN: Production of Retinal Changes. Thomas R.C. Sisson*, E.M. Glauser and S.C. Glauser, Temple University School of Medicine, Philadelphia, Penna., U.S.A. This study was designed to investigate the effect of broad-spectrum, and narrow-spectrum (420-470nm), visible light and various concentrations of oxygen in the inspired air upon the retinas of the newborn piglet. Forty-two piglets were studied half in darkness and half in light, in room air at 100% O_2, 40% O_2 and 10% O_2. Exposures to these various combinations of oxygen and light-dark were for 24 hours in environmental chambers at three days of age. Indirect ophthalmoscopy, electroretinography, and retinal photography were performed immediately preceding exposure and 21 days after exposure. At 24 days of age the piglets were sacrificed and eyes enucleated and processed for histologic examination. Vascular changes were seen in eyes following exposure to 40% and 100% oxygen in the dark on indirect ophthalmoscopy, and changes in fundal background homogeneity were noted after exposure to light and to light plus elevated oxygen concentrations. Histologic sections revealed narrowing of retinal vessels and proliferation, with degeneration of some arterioles after oxygen exposure, similar to the changes in the human newborn eye with retrolental fibroplasia. Degeneration of visual receptors and nuclei of the ganglion layers, and alterations in the pigment epithelial layer were noted in eyes exposed to blue light. ERG recordings established loss of visual reception after light exposure both with and without oxygen exposure. Generalized edema of retinal layers was observed. These results indicate that pathologic changes in the retina of the piglet was increased when exposure to visible light is added to increased oxygen in the atmosphere, even at concentrations (40%) considered "safe" for newborn infants. Reduced O_2 conc. (10%) did not produce the vascular changes of higher conc., with or without light.

RELATIONSHIP BETWEEN CARDIAC DIGOXIN CONCENTRATIONS AND DRUG TOXICITY. D. S. Skelley, P. D. Allmendinger, J. Dawson and J. Burdine (intr. by P. K. Besch). Dept. Ob. Gyn. Baylor College Med. and Depts. Surgery, Cardiology and Nucl. Med., Texas Heart Institute, Houston, Texas 77025.

The blood and cardiac tissue levels of digoxin in 30 patients undergoing cardiopulmonary bypass were correlated with symptoms of toxicity and with preoperative levels. The right atrial appendage was removed at surgery, weighed, placed in alcohol and homogenized with a Willems Polytron Homogenizer for 5 seconds. The homogenates were then centrifuged and the filtrated supernatants analyzed for digoxin by radioimmunoassay in quadruplicate. The levels of serum digitalis was dose-related and decreased as a function of increased withdrawal time preoperatively (1-4 days) from 0.83 ± 0.041 ng% (SEM) to 0.55 ± 0.05 ng%. Similarly, digoxin tissue levels decreased from 214.3 ± 41.5 ng/gm to 111.6 ± 28 ng/gm. In two patients exhibiting ventricular tachyarrhythmias intra- and postoperatively, the digoxin levels were in excess of 300 ng/gm. Blood digoxin levels were similarly studied in patients prior to death and were correlated with toxicity and pathological findings. The absolute tissue levels and relative proportions among the various tissue specimens and plasma samples varied widely. These preliminary studies illustrate the ease with which these relationships may be investigated and underscore the need for further evaluation of the blood and tissue levels of such widely used therapeutic agents.

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INTRACELLULAR KILLING OF PS. AERUGINOSA BY RAT ALVEOLAR MACROPHAGES STIMULATED BY NORMAL LUNG LAVAGE FLUID. William A. Skornik*, Donald P. Dressler*, and Paul Nathan, Harvard Med. School, Boston, Mass. and Shriners Burns Institute, Cincinnati Unit, and University of Cincinnati, Ohio.

Rapid in vivo killing of Ps. aeruginosa delivered by aerosol to the lungs of normal rats is thought to be due to alveolar macrophages. The present work describes stimulation of this function of the alveolar macrophage in vitro by factors present in lung lavage fluid. Macrophages washed from normal rat lungs were incubated with Ps. aeruginosa in Medium 199 and 10% pooled normal rat serum alone or with the wash fluid added. The total incubation volume was one and one-half ml. In the experimental group 1/2 ml of the media was lavage fluid. The pulmonary factors were obtained from the lung washout fluid by centrifugation following separation of the alveolar macrophages. After 30 min. incubation, antibiotics were added to the controls and to the test mixture to kill nonphagocytized bacteria. The duplicate tubes were reincubated for 30 min. Intracellular killing was determined by comparing the number of viable bacteria taken up by the cells after the initial 30 min. incubation to the bacteria remaining after reincubation. The mean number of alveolar macrophages ± S.D. washed from the lungs of normal rats was $2.05 \pm .74 \times 10^6$. These cells were 91% viable, while 32% appeared morphologically activated. At a bacteria-macrophage ratio of 10:1 in vitro, these cells phagocytize $7.8 \pm 2.4 \times 10^3$, and kill 27% of the bacteria. Following incubation with the lung wash fluid, phagocytosis remained normal while intracellular killing by cells exposed to wash fluid was 60% ($P < .01$). It is suggested that activating agents present in the lavage fluid from the lungs of normal rats markedly stimulates in vitro intracellular killing by alveolar macrophages.

GLUCONEOGENESIS IN RELATION TO THE ESTROUS CYCLE IN RATS. Celia D. Sladek (intr. by S. F. Marotta) Dept. of Physiology, University of Illinois, College of Medicine, Chicago, Illinois 60680.

Considerable evidence has accumulated suggesting a relationship between carbohydrate metabolism and the levels of circulating sex hormones. In this study, gluconeogenesis was assessed in the whole animal to determine if hormonal fluctuations related to the estrous cycle resulted in alterations in glucose production. The stages of the estrous cycle were determined in virgin female rats by vaginal smears performed daily for 2-3 weeks. Gluconeogenesis was evaluated, following a 24 hr. fast, by measuring incorporation of intravenously injected U1-C^{14}-alanine (0.75 mmole in 0.5 cc) into blood glucose and hepatic glycogen. Blood samples were obtained at 5,10,20, and 30 min. post-injection. Glycogen analyses were performed on liver samples obtained 30 min. post-injection. C^{14}-glucose was isolated from C^{14}-alanine in the blood samples using ion-exchange resins. Percentage alanine conversion to glucose was calculated as described by Herrera, et al. (J. Clin. Invest. 48:2260, 1969). Significantly more alanine was converted to glucose in diestrus animals than in animals in the other stages of the estrous cycle (i.e., proestrus, estrus, metestrus; $p<.025$). Incorporation of alanine into hepatic glucogen was also significantly greater at diestrus than estrus ($p<.005$). Serum insulin levels were significantly lower at diestrus than estrus ($p<.025$). Thus, the increased gluconeogenesis seen at diestrus may be a reflection of decreased insulin inhibition due to lower blood insulin levels. Hepatic glycogen content fluctuated with the phases of the estrous cycle; however, these fluctuations were not related solely to the changes in circulating insulin levels.

HISTOCHEMICAL AND BIOCHEMICAL CORRELATES OF SEROTONERGIC DEVELOPMENT IN MONKEY BRAIN, Sladek, J.R., Jr., Tabakoff, B. and Garver, D., (Intr. by H.A. Hakim), Department of Anatomy, University of Rochester, Department of Biochemistry, Chicago Medical School and Illinois State Psychiatric Institute.

Difficulty has been previously encountered in visualization of serotonin (5HT) containing neurons in non-pharmacologically pretreated animals with the use of the Falck-Hillarp fluorescence technique. In our search for material suitable for the demonstration of serotonergic fluorescence in brain stem neurons, without pharmacologic pretreatment, two-day old, twelve-week old and adult Macaca speciosa were examined for 5HT histofluorescence. Such fluorescence was most intense in the neonate, and decreased with age. Only faint 5HT fluorescence was seen in adults. To account for this developmental pattern, biochemical determinations were made of: 5HT levels in brain stem; its subcellular distribution; monoamine oxidase (MAO) activity; and the levels of the major degradation product of 5HT, 5-hydroxyindoleacetic acid (5HIAA). Significantly higher levels of 5HT were demonstrated in the neonate with concommitantly lower levels of MAO activity. Differences were also noted in the subcellular distribution of 5HT with markedly higher levels appearing in the crude mitochondrial fraction (containing nerve endings) of the neonate. Although a greater percentage of the total 5HT appeared in the soluble fraction of the adult, the absolute values (ng/g) were similar in neonate and adult. The adult brain stem contained significantly higher amounts of 5HIAA. Therefore, fluorescence intensity differences might be accounted for by both higher levels of 5HT and its lower turnover rate in the neonate.

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A COMPARISON OF CRITICAL AIR AND WATER TEMPERATURES IN HAWAIIAN RESIDENTS. Richard Merrill Smith and Joel M. Hanna (intr. by Suk Ki Hong). Dept. of Physiology, Univ. of Hawaii, School of Medicine, Honolulu, Hawaii 96822.

Previous studies from this laboratory have suggested that Hawaiian Scuba divers have a reduced critical water temperature. In an attempt to generalize our results and to determine critical water and air equivalents, we have determined the lower critical air temperature (LCAT) of recumbent semi-nude subjects by the method recently described by Wilkerson, Raven, and Horvath (J. Appl. Physiol. 33:451, 1972). Previous estimates of LCAT have ranged from 24-27°C with considerable individual variation. We hope that much of this variation can be eliminated through use of Hawaiian residents who have a more uniform thermal history. Metabolic rate ($\dot{V}O_2$) was measured at air temperatures (T_a) of 30, 25, 20, and 10°C presented in random order in a controlled temperature chamber. Rectal temperature (T_{re}), surface temperature (T_s) and heat flow were simultaneously recorded. Preliminary analysis of data suggests that LCAT in Hawaiian residents taken as a group may be somewhat lower than that reported in the literature. The lower value seems to result from a decreased $\dot{V}O_2$ at 10°C rather than a generally depressed $\dot{V}O_2$ at all temperatures. It is further noteworthy that T_{re} fell significantly as T_a was decreased from 25 to 10°C ($.02 < p < .05$) rather than increasing as has been previously reported. It is suggested that Hawaiian residents do not increase their $\dot{V}O_2$ to the same degree as do non-tropical peoples when exposed to 10° air. These air data tend to confirm the low critical temperature data determined in Scuba divers by water immersion. (Supported in part by NOAA Sea Grant 04-3-158-29 and in part by an intramural grant from the Univ. of Hawaii.)

Separation of Prolactin Cells from the Female Rat Adenohypophysis
J. Snyder°, W. Wilfinger° and W. C. Hymer. Department of Biology, The Pennsylvania State University, University Park, Pa.

Pituitary glands from female rats were trypsinized and the resulting cells (yield = 2.4 x 10^6 cells/gland) separated according to type by sedimentation at unit gravity (Hymer et al., Endocrinology, 92, 275 1973). Thirty-three percent of the cells in the initial suspension were prolactin cells as estimated by cytochemical staining. As determined by radioimmunoassay, the concentration of prolactin in these initial cell suspensions ranged between 4.5-8.5 ng/1000 cells. After unit gravity sedimentation, certain gradient fractions were enriched with prolactin cells (60-70%) and contained a level of hormone consistent with this degree of enrichment. Electron microscopic study of the separated cells showed their morphology to be virtually identical to those seen in situ.

Prior administration of estradiol benzoate (1-20 µg EB/day/5 days) resulted in elevated cellular prolactin which appeared to be proportional to dose of EB administered. Prolactin cells from the estrogen-primed animals sedimented further into the gradient, a result which suggests that the steroid causes hypertrophy of some of the prolactin cells. The degree and size of the cytoplasmic hormone granules, as well as the development of ER and golgi material, present a picture of heightened synthetic activity in these cells.

Conclusion. The unit gravity cell separation procedure is an effective way of obtaining enriched fractions of prolactin cells and offers a way of studying hormone secretion from this cell type.

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Sodium-Stimulated E·ATP with no Exogenous Magnesium.
R.J. Sohn*, W.A. Brodsky, C. Matons* and A.S. Chin*, Mt. Sinai School of Medicine/CUNY, New York, New York

The addition of Na to Mg-containing mixtures of eel electroplax microsomes and ATP causes a decrease in the Mg-dependent level of E·ATP (Brodsky, Sohn & Etra, 1973) together with increases in the level of Na·E·P and P_i release. Present experiments were designed to study the effects of Na and/or K on the functions of electroplax ATPase in the absence of exogenous Mg, - using α-^{32}P-ATP as a tool to estimate E·ATP; and γ-^{32}P-ATP, to estimate Na·E·P and P_i release. Microsomes, tris buffer and EDTA were incubated for 5 to 360 sec. with ATP (0.2 to 10 µM) at 0°C. Addition of Na or K alone or together produced distinct enzymatically-induced increments of α-^{32}P labelling (0.5 to 10 pmoles/mg of E·ATP). The α-^{32}P labelling in the absence of cations (other than tris) was greater than that in the presence of cations except when ATP was 10 µM or more, at which point the Na increment of E·ATP exceeded the tris increment which in turn exceeded the K increment of E·ATP. The levels of E·P and P_i release under Mg-free conditions were much less than those under Mg-rich conditions; but the level of E·ATP under Mg-free conditions was similar to or greater than that under Mg-rich incubation conditions. Tentatively, the primary enzyme-substrate production is stimulatable by Na or Mg, but not dependent on Mg. But the Na·phosphoenzyme production is much greater in the presence than in the absence of Mg. These data suggest a correspondence between the enzymatic steps and the active Na transport steps which will be presented.

RENAL FUNCTIONAL RESPONSE TO DOC ADMINISTRATION BY IMMATURE RATS. Sidney Solomon and Howard Bengele. Department of Physiology, University of New Mexico School of Medicine, Albuquerque, New Mexico 87131.

The renal functional response to either 4 or 5 days DOC administration or 7-10 days administration has been studied using clearance procedures. Wistar rats aged 20 to 46 days and weighing from 30 to 235 gms. were utilized. Because DOC administration causes renal hypertrophy, renal functional variables are normalized by being expressed as a function of body weight. In control rats there is a slight increase in $U_{Na}\dot{V}$ with development but $U_K\dot{V}$ remains constant. Administration of DOC for 3-5 days does not cause sodium retention until animals are 25 days old. After that, one finds the usually described anti-natriuresis. No "escape" from 7-10 day treatment is evident until animals weigh about 100 gms. Unlike the situation in mature animals, $U_K\dot{V}$ is usually suppressed by DOC administration with only a few sporadic animals showing normal K excretion. The failure to show "escape" from DOC until animals are quite large is consistent with the previous observations of lack of response to blood volume expansion until rats are 32 days old. (Supported by NSF Grant GB-35637X).

INTRATUBULAR PRESSURE IN ISCHEMIC RENAL FAILURE IN RATS. Samaisukh Sophasan (intr. by George A. Tanner). Dept. Physiology, Indiana Univ. Sch. Med., Indianapolis, Indiana 46202.

Ischemic renal failure in rats was induced by completely occluding a renal artery for 1 hr. Clearance and micropuncture measurements were made ½ and 24 hr after the occlusion was released. Polyfructosan clearance was decreased significantly ($P<.001$) from a control value of 470±110 SD (n=27 rats) µl/min-100 g body wt-kidney to 28±23 (n=19) and 25±32 (n=7) ½ and 24 hr, respectively, after ischemia. The corresponding urine flow rates were 2.51±1.00, 6.19±5.80, and 2.61±2.09 µl/min-100 g body wt-kidney. Proximal tubular pressure (PTP), measured with a Kulite pressure transducer, increased significantly ($P<.001$) from a control mean of 13±2 mm Hg (n=181 tubules) to 39±11 (n=328) and 25±8 (n=77) ½ and 24 hr after temporary artery occlusion. Stop-flow pressure (SFP), measured at the first loop of the proximal convoluted tubule or in Bowman's capsule, was 39±6 mm Hg (n=42) in control, and 46±10 (n=24, $P<.01$) and 37±7 (n=17) at ½ and 24 hr after ischemia. Glomerular capillary pressure, estimated from the SFP plus plasma colloid osmotic pressure, averaged 55±6 mm Hg (n=42) in control, and 64±10 (n=24, $P<.001$) and 51±7 (n=17) at ½ and 24 hr after the insult. Increased PTP, possibly due to tubular obstruction and reduced fluid reabsorption, contributes to the decreased glomerular filtration rate after ischemia. Defective renal function in this model of acute renal failure is not due to a decrease in glomerular capillary pressure. (Supported by Rockefeller Foundation and USPHS NIH Grant HL 13929).

Underclothing and Physiological Performance in a Hot-Dry Environment. R.G. Soule, F.R. Winsmann* and R.F. Goldman. US Army Research Institute of Environmental Medicine, Natick, MA 01760.

When underclothing of any type was worn, data collected from our copper manikin clearly indicated there was decreased evaporative transfer. In clothing, particularly with underwear in light clothing the trapped still air layer is important, but may be significantly altered with movement. In order to assess air movement in the dynamic state ("pumping") the present study involved 8 men (21.2 yr., 175.2 cm and 69.1 kg) to evaluate four underclothing systems with desert uniform outer clothing: a) No Underwear; b) Std boxer shorts and t-shirt; c) Fish net; and d) Ladder net. Each subject walked at 4.8 km/hr for each condition (40 min walk, 20 min rest and 40 min walk) at 49°C 20% R.H. (≈29°C WB). Three point MWST, T_{re}, H.R., sweat production (P) and sweat evaporation (E) were measured. Results: 1) No Underwear resulted in significantly cooler MWST at minutes 60, 80, and 100; 2) T_{re} was slightly lower at a given time interval with No Underwear; 3) there was a rise in heart rate across time during the work periods, but no differences among underwear systems; 4) sweat production showed no differences; 5) the ratio of Produced/Evaporated Sweat (P/E) showed No Underwear allowed better evaporative cooling ($P < .01$) than any of the other three systems. This P/E ratio is a measure of stress of a clothing system and clearly favors the No Underwear condition. These data indicate that there was either (1) no additional cooling by moving the trapped still air layer of the fishnet or ladder system or (2) there wasn't sufficient air "pumping" to enhance cooling. If evaporative cooling is the objective, it seems apparent that any underclothing added within a clothing system inhibits evaporative transfer, and neither fish nor ladder net underwear appears to offer any advantage over regular underwear; subjective comfort ratings agree with these conclusions.

RELATION OF PANCREATIC ISCHEMIA AND PROTEOLYSIS TO THE PATHOGENESIS OF SHOCK. James A. Spath, Jr.,* Richard J. Gorczynski* and Allan M. Lefer Department of Physiology, University of Virginia School of Medicine, Charlottesville, Virginia 22901.

Prominent among the metabolic alterations of circulatory shock is a marked increase in proteolysis. Furthermore, proteolysis correlates closely with the severity of the shock state. Proteolysis was evaluated in dogs subjected to hemorrhagic shock (mean arterial blood pressure 45 mm Hg for three hours), and in cats subjected to splanchnic arterial occlusion (SAO) shock for two hours. Three indices of proteolysis were measured in plasma: activity of the lysosomal protease cathepsin D, amino-N, and the activity of a toxic peptide myocardial depressant factor (MDF). In hemorrhagic shock, the plasma cathepsin D, amino-N and MDF activities increased 25-fold, 2.5-fold and 3.5-fold, respectively, Similarly, following release of the occlusive clamps in SAO cats, plasma cathepsin D, amino-N and MDF activities rose 2.5-fold, 4-fold and 4-fold, respectively. The observed increases in proteolysis occurred after two hours of essentially zero pancreatic perfusion in SAO shocked cats and after an 83% reduction in pancreatic blood flow in hemorrhaged dogs. Moreover, pump-perfusion of the pancreas at normal flows in hemorrhaged dogs resulted in less than half the usual increases in plasma activities of cathepsin D and amino-N, and almost completely prevented the increase of MDF activity. Pancreatic pump-perfusion in normovolemic dogs did not alter any of the proteolytic indices. Furthermore, incubation of pancreatic homogenates resulted in 3-fold increases in amino-N and MDF activities. These data suggest that about half of the proteolysis and most of the MDF production during shock is related to pancreatic ischemia. Moreover, toxic factor production appears to be closely related to pancreatic proteolysis. (Supported by a grant from NHLI).

RELEASE OF PREVIOUSLY RETAINED FLUORIDE IN MAN. Herta Spencer, Dace Osis*, and Emilie Wiatrowski*. Metabolic Section, VA Hosp., Hines, IL.

Following the administration of 10 mg fluoride as sodium fluoride given daily for 30 days, the urinary and fecal fluoride excretions were determined for several weeks. These excretions were related to the amounts of fluoride excreted in the control study and to the retention of fluoride during fluoride supplementation. This retention was calculated from the fluoride balances. The average total retention of fluoride for the stated period of time was calculated to be 162 mg. After discontinuation of the intake of sodium fluoride, the excretions of fluoride in both urine and stool decreased markedly and were only slightly higher than in the control study for 10-12 days. The excess fluoride excretion totalled 6.5 mg in the first 6 days and 3.3 mg in the next 6 days after the intake of sodium fluoride was discontinued. Most of this excess excretion was eliminated in urine and only a small amount in stool, the total excess excretion in urine and stool corresponding to 5.9% of the previously retained fluoride. After these initial 12 days the urinary and fecal fluoride excretions were similar to control values. On a high fluoride intake of 48 mg/day, given for 76 days to patients with osteoporosis, the fluoride balance averaged +11 mg/day. After discontinuing this large dose of fluoride the urinary and fecal fluoride excretions also returned promptly to relatively low levels. The excess fluoride excretion in both urine and stool totalled 16.7 mg in 8 days, corresponding to about 2% of the calculated amount of fluoride retained (836 mg). Thereafter, the urinary and fecal fluoride excretion also returned to control levels. The data indicate that only a small amount of the previously retained fluoride is released. (Supported by USPHS research grant DE-02486.)

EFFECTS OF AORTIC OR CAVAL CONSTRICTION ON ALDOSTERONE SECRETION IN THE INTACT AND NEPHRECTOMIZED RAT. W.S. Spielman*, J.O. Davis, and B. Braverman*. Department of Physiology, University of Missouri School of Medicine, Columbia, Missouri 65201.

The importance of the renin-angiotensin system in the regulation of aldosterone secretion has been questioned in the rat. Recent experiments in the sodium-depleted rat have demonstrated that a competitive angiotensin II antagonist was ineffective in altering the secretion of aldosterone (W.S. Spielman and J.O. Davis, Endocrine Society abstracts, 1973). In view of this apparent uniqueness of the sodium-depleted rat, two other stimuli were studied in order to evaluate further the role of the renin-angiotensin system. In two groups of animals, a control sample of adrenal venous blood was followed by either suprarenal aortic constriction or suprahepatic caval constriction for 30 min., followed by another adrenal vein blood sample. Aldosterone secretion in the aortic constriction group (n=7) increased from a control value of 0.73± .09 ng/min to 1.69±.36 ng/min ($p<.05$). Likewise, aldosterone secretion increased in the rats with caval constriction (n=7) from a mean of 0.53± .20 ng/min to 1.13±.21 ng/min ($p<.05$). In two additional groups of rats the same experiments were performed and differed only in that the rats were nephrectomized 2 hr prior to experimentation. In the nephrectomized rats (n=7), aortic constriction resulted in no significant change in aldosterone secretion (1.20±.26 ng/min to 1.5±.40 ng/min, $p>.05$). Similarly, caval constriction in nephrectomized rats (n=5) failed to stimulate aldosterone secretion (1.50±.29 ng/min to 2.0±.61 ng/min, $p>.05$). These results suggest a renal mechanism in the control of aldosterone secretion in the aortic or caval constricted rat but additional observations are needed to confirm this. (This work was supported by USPHS Grants, HL 05810 and HL 10612.)

THE EFFECT OF MANGANESE ON CANINE PURKINJE AND VENTRICULAR MYOCARDIAL CELLS. Kenneth W. Spitzer* and Perry M. Hogan. Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, N.Y.

Action potentials were recorded from Purkinje fibers and regular myocardial cells isolated from canine ventricles and *superfused* with tyrode solutions containing 1.25, 2.5, 5.0 and 10.0 mM $MnCl_2$. At the three lower concentrations, manganese caused hyperpolarization of membrane potential (V_m), a decrease in maximum upstroke velocity ($\dot{V}_{max}$) and no change in overshoot potential (V_{OS}). The duration of the action potential was lengthened largely through a decrease in the slope of phase 3. The plateau phase increased in duration at 1.25 and 2.5 $[Mn^{++}]_o$ with no change in slope. In contrast, 5.0 mM $[Mn^{++}]_o$ caused the plateau to increase in slope and shorten in duration. Preceeding the plateau a "notch" developed which increased in amplitude with $[Mn^{++}]_o$ concentration. The initial effects of 10 mM $[Mn^{++}]_o$ were similar to those at lower concentrations. However, after longer exposure there occurred a marked decrease in action potential duration, a depressed plateau phase, decreases in V_m and V_{OS}, and a further reduction in $\dot{V}_{max}$. Low $[Mn^{++}]_o$ had similar effects on regular myocardial cells except V_{OS} was depressed at all $[Mn^{++}]_o$. At 10.0 mM $[Mn^{++}]_o$ V_m was either unchanged or depolarized. Analysis of strength duration curves in Purkinje fibers indicated a decrease in excitability directly related to $[Mn^{++}]_o$. In 10 mM $[Mn^{++}]_o$ the membrane was frequently depolarized to the point of inexcitability (-60 to -50). The relationship between $\dot{V}_{max}$ and V_m was shifted downward & to the left of normal by 5 and 10 mM $[Mn^{++}]_o$. Simultaneous analysis of Purkinje and regular myocardial cells suggest that the former are more sensitive to higher $[Mn^{++}]_o$. This study suggests that manganese may have effects on Purkinje and regular myocardial cells other than blocking a slow inward current. (Supported by USPH, NIH Grant HL 12780, and ONR Contract N00014-68-A-0216, (NR 101-722)).

COLD ACCLIMATION INCREASES SENSITIVITY OF FROG CUTANEOUS COLD RECEPTORS. D.C. Spray, Dept. Physiology, U. Florida Coll. Med., Gainesville, Fla.

Acclimation of *Rana pipiens* to 9°C increases maximum dynamic sensitivity (impulses/°C-sec) and increases the range of static sensitivity (impulses/sec at a static temperature) but decreases the peak temperature of maximum static sensitivity. Cold receptors of cold-acclimated animals were markedly less sensitive to the application of epinephrine to the inner skin surface than were warm-acclimated animals (23°C), and showed much less enhancement of maximum dynamic sensitivity by sympathetic stimulation. Since circulating catecholamines are known to be elevated in the cold-acclimated amphibian, these results may be interpreted as evidencing hormonal modulation of sensory input.

OBSERVATIONS SUGGESTING MEAN LENGTH DURING A CONTRACTION DETERMINES OXYGEN UPTAKE FOR THE CONTRACTION. W. N. Stainsby, J. K. Barclay,* and P. D. Allen.* Dept. of Physiology, Coll. of Med., Univ. of Florida, Gainesville, Florida.

Oxygen uptake (Vo_2) by in situ dog semitendinosis muscle was calculated from measurements of blood flow and a-v O_2 differences during brief tetanic contractions which began at a wide range of initial lengths (L_i). When L_i was at or below mechanical optimal length (L_o), Vo_2 increased with load during afterloaded contractions, and maximal Vo_2 occurred when the load was sufficient to make the contractions isometric. When L_i was slightly greater than L_o, Vo_2 was greatest at intermediate loads, and Vo_2 under isometric conditions was nearly the same as for minimal load. When L_i was considerably greater than L_o, maximal Vo_2 occurred at a low load and isometric Vo_2 was less than Vo_2 at minimal load. When L_i was adjusted to keep mean length during the contractions constant, Vo_2 was constant for the entire load range. Vo_2 was directly related to external work and shortening, as described in similar previous myothermic or chemical energetic studies, only when L_i was considerably greater than L_o. For these conditions the preload required was in the range of 10 to 50 grams per gram wet weight of muscle. This range of preloads was generally used in the previous myothermic and chemical energetic studies. The present data suggest Vo_2 is mainly determined by mean length during each contraction with Vo_2 increasing with mean length up to L_o and then decreasing with further increases of mean length. The data further suggest that the presence of direct relationships between Vo_2 and work and shortening occur under such special conditions that they are probably irrelevant. (Supported in part by NIH Grant GM 06264 and in part by a Pharmaceutical Manufacturers Association Starter Grant.)

SUBCELLULAR FRACTIONATION STUDIES OF RED AND WHITE AVIAN SKELETAL MUSCLE. William T. Stauber* and B. A. Schottelius, Dept. of Physiology and Biophysics, University of Iowa, Iowa City, Iowa 52242.

Avian anterior (ALD) and posterior (PLD) latissimus dorsi muscles (100-200 mgm) were homogenized in 0.25 M sucrose and fractionated by differential centrifugation into five subcellular fractions: nuclear fraction, N, 510 g x 10 min; heavy mitochondrial fraction, M, 10,000 g x 5 min; light mitochondrial fraction, L, 40,000 g x 10 min; microsomal fraction, P, 100,000 g x 45 min; and soluble fraction, S. These fractions were identified as to biochemical homogeneity by measurement for cytochrome oxidase, Cathepsin D, catalase, Ca-ATPase, EGTA-ATPase, 5'-nucleotidase activities and protein concentration. Calcium uptake ability was measured in all fractions using p-nitrophenyl phosphate as the substrate. Distribution of the enzymes was similar for both muscles but the ALD demonstrated more cytochrome oxidase, Cathepsin D, and catalase activities and less Ca-ATPase and calcium accumulating ability than the PLD. Electron microscopy revealed similar morphology in the respective fractions from both muscles. (Supported in part by USPHS, NIH Grant NS 08550.)

ENERGY REQUIREMENT FOR UPTAKE OF 5-HYDROXYTRYPTAMINE BY ISOLATED GUINEA PIG LUNG. Harry Steinberg*, David Bassett*, and Aron Fisher. Dept. of Physiology, U. of Pa. School of Med., Phila., Pa.

5-hydroxytryptamine (5-HT) is taken up by pulmonary endothelium and metabolized to 5-hydroxyindoleacetic acid (5-HIAA). To study the energy requirement for uptake, isolated guinea pig lungs were perfused at constant flow rate for 75 minutes with Krebs-Ringer bicarbonate solution containing 4% bovine serum albumin, 5 mM glucose and 0.2 μM ^{14}C-5-HT. The lungs were ventilated with 95% O_2:5% CO_2 or, for anoxic experiments, 95% N_2:5% CO_2. Tracheal and perfusion pressures and lung weight were monitored continuously. The perfusate was recirculated and aliquots were removed at various time intervals. ^{14}C-5-HT and ^{14}C-5-HIAA were measured by scintillation counting after separation on Sephadex columns. In control experiments, 42% of 5-HT entering the lung was removed, and decrease of ^{14}C-5-HT in the perfusate was logarithmic at a rate of 6.0±0.5%/min. During anoxia, perfusate ^{14}C-5-HT decreased 3.2±0.3%/min. Inhibitors were preincubated for 30 minutes and ^{14}C-5-HT disappearance was determined. Decrease per min in perfusate ^{14}C-5-HT was: KCN (10^{-3}M) 3.4±0.8%; ouabain (10^{-5}M) 2.8±0.3%; Thorazine (10^{-5}M) 1.3%, and Imipramine (10^{-4}M) 0.2±0.07%. Lung edema did not account for the decreased ^{14}C-5-HT removal in the presence of inhibitors. 75% of infused ^{14}C was subsequently recovered as ^{14}C-5-HIAA. Iproniazid (10^{-4}M) markedly inhibited the conversion of ^{14}C-5-HT to ^{14}C-5-HIAA but did not affect ^{14}C-5-HT uptake by lung. The removal of ^{14}C-5-HT by pulmonary endothelium appears to be an energy requiring process. Once uptake occurs, ^{14}C-5-HT is rapidly metabolized to ^{14}C-5-HIAA. Supported by HL 15061.

CYTOPHOTOMETRIC ANALYSIS OF AZURE B-RNA IN MYOCARDIAL TISSUE FROM HYPOXIA EXPOSED RATS. Athleen J. Stere* and Adam Anthony. Dept. of Biology, Pennsylvania State University, University Park, Pa.

Cardiac responses to hypoxia exposure include hyperplasia of coronary vessels, muscular hypertrophy, increased myoglobin concentration. Increased protein synthesis is required to effect these responses and one might expect concomitant changes in RNA metabolism. The purpose of this study was to determine whether hypoxia-induced cardiac hypertrophy involves increased cytoplasmic RNA content as indicated by enhanced affinity for azure B stain. Azure B stains both DNA and RNA but is specific for RNA if DNA is removed prior to staining. Myocardial tissue from rats exposed to reduced barometric pressure (380 mm Hg) for 0,1,4,7,14,21,28,42,56 days was stained with azure B after DNAse hydrolysis. Cytoplasmic RNA was measured using the two wavelength method of cytophotometry. Hearts from all hypoxia exposed rats weighed more (mg heart/100 g body weight) than hearts from corresponding control animals. Cytophotometric data, however, showed an initial drop in RNA content during the first day of hypoxia followed by a gradual return to control level or slightly above by day 7. At all subsequent exposure periods, RNA levels in experimental hearts were greater than corresponding controls. Since the first two days of exposure at 380 mm Hg constitute an emergency situation, nonessential synthesis will be postponed until after this critical period. The fact that RNA content decreased at the start of exposure rather than remaining at control level may indicate a temporary lack of maintenance of RNA with degradation continuing at the usual rate. We propose that initiation of hypertrophy is delayed for at least 48 hours after the onset of exposure and then is accompanied by an increase in cytoplasmic RNA.

CHARACTERISTICS OF CAT LGN RECEPTIVE FIELDS. John K. Stevens* and George L. Gerstein. Depts. of Physiology and of Biophysics, Univ. of Penna., Phila., Penna. 19174.

Spatial and temporal properties of LGN receptive fields were studied by flashing a small bar of light across the field in 28 discrete steps. The flashes at each of the spatial positions were used to produce 28 PST histograms. These histograms were in turn displayed as a plane, with space on the X axis, time on the Y axis and probability of firing on the Z axis. These response planes clearly show the classic spatial center and antagonistic spatial surround of LGN fields. The response planes have also revealed a powerful temporal inhibitory surround which is itself a function of spatial position. Using response planes it is possible to divide LGN neurons into five field categories: 1) Heterogeneous ON: ON fields with OFF response latencies that vary as a function of space; 2) Homogeneous ON: ON fields with constant response latencies; 3) Heterogeneous OFF: OFF fields with spatially varying OFF response latencies; 4) Homogeneous OFF: OFF fields with constant response latencies; 5) ON,OFF: fields with ON, OFF response in both center and surround. Neurons whose responses could be classified as sustained (X type) always had heterogeneous fields while neurons with transient responses (Y type) had homogeneous fields. Supported by NIH Grant #NS 05606.

EVALUATION OF AN ON-LINE COMPUTER CALCULATION OF N_2 "CLOSING VOLUME". Helen Strobach*, Pierre Vaillancourt* and Margaret R. Becklake. McGill Univ., Montreal, Canada.

With a view to using N_2 "Closing Volume" (CV) and/or "Closing Capacity" (CV + RV) as a field test in epidemiologic studies, we have developed an on-line data collection, processing and reporting system. Criteria for trial acceptance (e.g. expiratory flow rates less than .5l/sec) and for trial selection (e.g. Vital Capacity (VC) differed by $<5\%$ between trials) were applied before computer analysis of three trials each on 10 volunteers. Both N_2 and volume signals, sampled at the rate of 12 points/sec for a maximum of 1 min., were digitized using an A-D converter, and the means of successive paired samples stored in core, using less than 2K. The onset of Phase IV (marking the "CV") was recognized as the lung volume at which FEN_2 departs permanently from the expected value, as derived from the regression line of Phase III, calculated as FEN_2 rise between 70% and 40% of expired VC. Integration of the area under the curve allowed for determination of Residual Volume (RV) with calculation of Total Lung Capacity (TLC) as suggested by Buist and Ross (Amer. Rev. Resp. Dis., 107, 744, 1973). Using this logic the computer misinterpreted two curves because of more than one slope in Phase III; in 25 of the remaining 28, "Closing Capacity"/TLC% was with 2SE of results obtained by one observer. Computer calculation of all values for VC and TLC agreed with the observer's analysis within $\pm$ 2.5% indicating that the sampling rate for the volume signal was adequate. (Supported by the MRC of Canada).

EVIDENCE FOR PARTIALLY CARRIER MEDIATED CO TRANSFER IN THE HUMAN LUNG. W. Summer* and G.H. Gurtner. The Johns Hopkins University, Baltimore, Maryland 21205.

In previously reported experiments we have observed that compounds which bind to cytochrome P-450 decrease O_2 transfer in the placenta and isolated lung without affecting inert gases and CO_2 transfer (Nature 240:473-475, 1972, Fed. Proc. 15:156, 1972, Drug Metabolism and Disp. 1:368-373, 1973). These results are consistent with a specific transport mechamism for O_2 involving cytochrome P-450 (c.f. Nature). O_2 and CO have similar affinities for cytochrome P-450 so that CO transfer should also be decreased after administration of drugs which bind to the cytochrome. We have observed in sheep and dogs that the diffusing capacity of the lungs (DL_{CO}) is decreased significantly after administration of the same drugs which decrease placental O_2 transfer. (Drug Metabolism and Disp. 1:374-379, 1973). In the course of additional experiments on the placenta, the antihistamine diphenhydramine was also found to decrease O_2 transfer. Diphenhydramine also decreased DL_{CO} in dogs. In 15 normal volunteers we measured DL_{CO} by the single breath method before and 1 to 2 hours after an oral dose of diphenhydramine (50 or 100 mg). All subjects were studied in the supine position at TLC after breathing 100% O_2 for 15 minutes. The subjects were studied in the supine position at constant lung volume because DL_{CO} at any constant lung volume in the supine position was not affected by changes in pulmonary blood flow even during exercise (J. Appl. Physiol., 30:619-626, 1971). In 14 of 15 studies DL_{CO} decreased 8 to 27% after the drug. The mean decrease was 14.2% of the control value. This decrease was statistically significant $P<.001$. These results are consistent with partial carrier mediation of CO transport in the lung.

INTERDEPENDENCE IN INTACT PIG LUNGS. J.T. Sylvester*, H.A. Menkes and F. Stitik*. Depts. of Medicine, Environmental Medicine and Radiology, The Johns Hopkins University, Baltimore, Maryland 21205.

If a region of lung is obstructed and its volume (Vr) held constant, an increase in the volume of the surrounding lung (V_L) generates an outward-acting pressure on the region because of mechanical linkage, or interdependence, between the lung and the region. This outward-acting pressure causes a fall in the pressure within the obstructed region (Pr) relative to pleural pressure (Ppl). If the change in (Pr -Ppl) is measured relative to the change in the transpulmonary pressure of the surrounding lung (P_L), the resulting ratio, $-\Delta(Pr-Ppl)/\Delta P_L$, constitutes an expression of the effectiveness of interdependence, K, which equals 0 when there is no interdependence and increases when the effectiveness of interdependence increases. The purpose of this study was to determine how K changed as a function of Vr when V_L was at functional residual capacity (FRC). We measured K in obstructed lower lobe regions of lungs in pigs with closed chests and found that K increased when Vr was high. This result was contrary to our expectation that the effectiveness of the outward-acting pressure exerted by the surrounding lung would decrease at higher Vr. The observed increase in K is difficult to explain unless the elastic recoil of the obstructed region is considered to be a function not only of Vr but also of V_L. For example, if Vr is constant at its FRC value and V_L increased a small amount above FRC, the shape of the region departs from its resting geometry. This distortion leads to an increase in the elastic recoil of the region which decreases K. On the other hand, when the region is inflated relative to the surrounding lung, distortion has already occurred. In this case, a small increase in V_L from FRC with Vr constant acts to reduce distortion. This leads to a decrease in the elastic recoil of the region which increases K.

STIMULATION BY ALDOSTERONE OF SODIUM EFFLUX IN SINGLE BARNACLE MUSCLE FIBERS. R. B. Tallitsch* and E. E. Bittar. Dept. of Physiology, Univ. of Wisconsin, Madison, Wis. 53706.

Because of some basic disagreement about the mode of action of aldosterone on Na transport in asymmetric cells, and because of a paucity of information about its mode of action in symmetric cells, we thought it worthwhile to check whether its mechanism of action can be investigated with giant muscle fibers from the barnacle Balanus nubilus. This approach seemed reasonable in view of the finding by Bittar (BBRC 23:868, 1966) that crab muscle fibers can be rendered sensitive to aldosterone by pre-exposing the crab in vivo to a dose of the steroid. The ^{22}Na efflux in barnacle fibers loaded by microinjection was insensitive to externally applied aldosterone. However, the Na efflux in fibers isolated from specimens injected with aldosterone in vivo some 16 hours earlier, was stimulated by externally applied aldosterone in concentrations as low as 10^{-10} M. This response was biphasic: first there was a change in slope followed by a slow step-up in the rate of Na efflux; then there was a sharp but transient rise in the Na efflux, the magnitude of which averaged 37.3% (n = 24) and 46.6% (n = 12) (employing 10^{-6} and 10^{-5} M aldosterone). The initial kinetic changes, viz. slow reduction in the rate of decline of the Na efflux, and fractional Na loss becoming constant, are interpreted as indicating that aldosterone acts at first by mobilizing the sequestered (or 'bound') fraction of Na. That the effect of aldosterone is not on the outer side of the plasma membrane is further shown by the fact that the Na efflux was similarly affected by internal application of 10^{-6} M aldosterone (n = 12). (Supported by NSF).

AN EVALUATION OF NEURAL INFLUENCES ON THE SPHINCTER OF ODDI IN THE DOG. M.F. Tansy, D.L. Innes* and F.M. Kendall*, Department of Physiol. & Biophys., Temple University School of Dentistry, Philadelphia, Pa.

The purpose of these studies was to conduct a systematic evaluation of nervous influences upon the opening pressure of the canine sphincter of Oddi using a pressure ramp technique. Acute experiments were performed on 25 fasted mongrel dogs of both sexes which were anesthetized with a chloralose-urethan mixture. Opening pressures were estimated from the hydraulic pressure which was present in a polyethylene cannula which was inserted via the fundus of the gall bladder and advanced to the vicinity of the choledochoduodenal junction. The hydraulic stimulus consisted of a linear pressure ramp with a constant rate of pressure rise which was maintained during both the control and the experimental states. Utilization of a pressure ramp of 7.5 cm of saline per second produced control opening pressures which ranged from 18 to 33 cm of saline. The following observations were made using this technique: Bilateral vagotomy did not significantly change mean opening pressure. No combination of electrical stimulus parameters was effective in producing changes in opening pressure when the stimuli were applied to the central ends of the vagi or to the peripheral splanchnic nerves. No electrical stimuli were effective in altering opening pressures when applied to the peripheral vagi at a supradiaphragmatic level. Inhalation of amyl nitrite vapor significantly reduced mean opening pressures and intravenous infusion of 20ml/kg of saline solution produced a significant elevation of opening pressures. It is concluded that opening pressures can be significantly changed by hydraulic factors but are apparently unresponsive to direct neural influences.

RENAL FUNCTION IN HELIUM-COLD HYPOTHERMIC HAMSTERS (M. AURATUS). George E. Tempel* and X. J. Musacchia, Dept. of Physiol., and Dalton Res. Ctr., Univ. of Missouri, Columbia, Mo. 65201

Renal function in a depressed metabolic state was studied. Plasma and urine concentration of Na^+, K^+, and urea; and renal cortico-medullary concentration gradients of Na^+ and urea were examined. Hamsters were studied as follows: (C) control (T_{re} 37°C); (H) hypothermia, 48 hrs (T_{re} 7°C); (R1) rewarming from hypothermia (T_{re} 18°C); and (R2) rewarmed from hypothermia (T_{re} 37°C for 2 hrs). Plasma Na^+ and K^+ appear unaffected by 48 hrs of hypothermia. In normothermia mean concentrations were 117.4±7.0 and 6.5±0.8 mEq/l for Na^+ and K^+ respectively. Mean values for (H) animals were 110.3±12.6 mEq Na^+/l and 5.5±0.7 mEq K^+/l. By contrast, plasma urea levels increased from 0.5± 0.05 mM/l for (C) animals to 0.8 mM/l for the (H) group. Urinary Na^+ showed little difference between (C) and (H) hamsters. Mean concentrations were 99.4±45.2 for the former and 80.4±37.7 for the latter. However, concentrations of K^+ and urea were both reduced in samples obtained after 48 hrs T_{re} 7°C. (C) hamsters demonstrated a K^+ concentration of 299.2±90.8 mEq/l which declined to a value of 78.3±45.9 in (H) animals. Likewise, urea concentration declined from a control value of 98.1±16.5 mM/l to levels of 1.8±1.2 mM/l for the (H) group. Tissue slice analysis showed no solute gradient for either Na^+ or urea in hamsters hypothermic for 48 hrs. (R1) animals sacrificed at T_{re} 18°C also lacked a gradient. However, the normal gradient returns in (T_{re} R2) animals. Supported by NASA NGL 26-004-021, S7-9.

ELECTRON MICROSCOPIC EXAMINATION OF THE STEADY STATE CONCENTRATIONS OF EXOGENOUS FERRITIN IN THE 27-29 DAY RABBIT PLACENTA. Thornburg*, K.L., Gault*, C.F., Green*, T.J., and Faber, J.J. Department of Physiology, University of Oregon Medical School, Portland, Oregon 97201

Fetuses anesthetized with sodium pentobarbital were injected in utero with cadmium free ferritin (~ 1 mg/g) I.V. One to 24 hours later the animals were re-anesthetized and placentas of living fetuses were processed for electron microscopy. The placental barrier has numerous thin areas which appear particularly suitable for diffusional exchange of lipid insoluble materials. The ferritin particles on the electronmicrographs were counted in the bloods adjacent to these areas and in the tissue spaces (10 photographs/animal > 30,000 X) and counts were divided by volume and Avagadro's number to yield concentrations. Concentrations recorded from non-injected control placentas were subtracted; counts by three observers were consistent. Concentration gradients were similar in experiments of various durations implying a steady state. Concentrations from fetal blood, basement membrane, cyto-syntiotrophoblast space and the maternal blood show that 93.8% of the concentration difference occurs across the endothelium confronting the fetal blood, whereas the middle layer (cytotrophoblast) and the layer confronting the maternal blood (syncytiotrophoblast) account for 5.6% and 0.6% each. For ferritin, the fetal endothelium appears to be the main diffusional barrier.

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DEVELOPING STUDENT CONFIDENCE IN THE USE OF COMPUTER TERMINALS C. S. Tidball. Department of Physiology, George Washington University Medical Center, Washington, DC 20037.

Recent advances in the interactive use of computers permit local telephone call access to remote computational facilities for such services as computer assisted education, computer managed instruction, bibliographic citation retrieval, patient simulation, dosage advising, and access to automated clinical consultants. In order to increase the likelihood that physicians and scientists will utilize these services after graduation, we encourage use of computer terminals during the first year of medical or graduate study. The initial exposure consists of a lecture which explains the capabilities available, describes the several terminals which will be used, and orients the students to the standardized, one-sheet, program description form. All students are then required to interact with a computer assisted education sequence called TERMLEARN. This program presents the rudiments of working with a variety of computer terminals to access remote computational facilities and gives experience in different levels of interaction such as those required when utilizing the Lister Hill Biomedical Communication Network. Use of MEDLINE, the computerized bibliographic citation retrieval service of the National Library of Medicine, is encouraged and instruction in the techniques required is provided by MEDLEARN, an orientation program designed for this purpose. Our experience indicates favorable student and faculty reaction to incorporating these new learning experiences into the first year curriculum.

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INCREASE IN AXONAL PROTEIN SYNTHESIZING ACTIVITY OF RABBIT HYPOGLOSSAL AXONS FOLLOWING NERVE TRANSECTION. G. S. Tobias* and E. Koenig. Dept. Physiol.,State Univ. N.Y. at Buffalo,Buffalo,N.Y.

In recent years evidence for local axonal protein synthesis has appeared. There is the possibility that this local synthesizing activity is concerned with normal protein turnover of the axolemma. Experiments were undertaken to ascertain whether axonal protein synthesizing activity would be enhanced under conditions in which *de novo* membrane formation would be anticipated (*i.e.*, axon regeneration). One hypoglossal nerve was transected in adult, male rabbits (2-4 kg) during barbiturate anesthesia; the contralateral nerve was left intact. Animals were allowed to survive for varying intervals up to 96 hours. At a given time interval both transected and intact nerves were removed and were incubated simultaneously with ^{3}H-leucine. Following incubation samples of myelin-free axons were dissected free-hand from 2-3 mm nerve segments and analyzed for total protein and corresponding radioactivity by microanalytical methods. Results for time intervals examined indicate that within 24 hours there is a significant increase in total protein, very likely stemming from a proximo-distal downflow of unlabeled, axoplasmic material, and in specific radioactivity of axonal protein from the proximal stump region of transected nerves over that from the intact nerves. The increase in specific radioactivity of proteins restricted to the terminal stump region--dilution by transported unlabeled, axoplasmic constituents notwithstanding--indicates that there is an increase in the rate of local protein synthesis at early times following axon transection. (Supported in part by NINDS Grant NS-04656 and NIH, NIGMS, Training Grant 5 T01 GM00341.)

METABOLITE LEVEL, REDOX STATE, AND PHOSPHORYLATION STATE OF FREEZE-CLAMPED LIVERS FROM RATS TREATED WITH DEXTRO- AND LEVO-THYROXINE. R. B. Tobin, M. A. Mehlman and R. L. Veech*. Omaha VA Hospital, Depts. of Med. and Biochem., Univ. of Nebr. College of Medicine, Omaha, Nebr. 68105; Division of Toxicology, Bureau of Foods, FDA, Washington, D.C. 20204; and St. Elizabeths Hospital, NIMH, Washington, D.C. 20032.

The comparative effects of dextro-thyroxine (D-T_4) and levo-thyroxine (L-T_4) on liver metabolites from rats treated with these agents was studied. Four groups of 160 gm Sprague Dawley strain rats were utilized: controls, and animals receiving 100 μg L-T_4/kg, 100 μg D-T_4/kg, and 1000 μg D-T_4/kg, daily for 10 days injected s.c. Following cervical dislocation, livers were excised and freeze-clamped rapidly. All thyroxine treated animals showed similar increases in malate and citrate content. The L-T_4 and high dose D-T_4 groups had increased ammonia and inorganic phosphate and decreased ATP. L-T_4 increased ADP and D-T_4 decreased ADP content. The NAD+/NADH ratio of the cytoplasm was increased and the effect with D-T_4 was greater than with L-T_4. The mitochondrial NAD^+/NADH was also increased most significantly by high dose D-T_4. The $NADP^+$/NADPH of the cytoplasm calculated from isocitric dehydrogenase reactants was decreased by both D- and L-isomers. The phosphorylation potential [ATP]/[ADP] x [Pi] was decreased significantly only by L-T_4. The responses of the metabolites to the administration of D- and L-isomers of T_4 were variable and in some cases qualitatively different.
Supported by VA and Baxter Laboratories.

PROSTAGLANDIN $F_{2\alpha}$ ($PGF_{2\alpha}$) EFFECTS ON PREGNENOLONE-3β-HYDROXY-STEROID DEHYDROGENASE (P-ONE-3β-HSD) ACTIVITY IN THE OVARY OF THE IMMATURE LABORATORY RAT. Farol N. Tomson,* Barbara A. Kasprow,* Fred Buddingh,* Leslie A. Emmert,* and Joseph Thomas Velardo (intr. by J. R. Davis). RILAMSAT, Veterans Administration Hospital, Hines, Illinois and Department of Anatomy, Loyola University, Stritch School of Medicine, Maywood, Illinois.

A series of experiments was undertaken to observe the effects of $PGF_{2\alpha}$ on progesterone biosynthesis in the ovary as revealed histochemically by the localization of P-one-3β-HSD (Wattenberg, 1958). 2 of 3 major groups of thirty 22 day old female albino rats (controls and two experimental groups) were given subcutaneous injections of 75 μg of $PGF_{2\alpha}$ or five milligrams of a prostaglandin antagonist (aspirin) twice daily. Sub-groups of ten rats in each major treatment category were necropsied, and the ovaries frozen, at 27, 33 or 37 days of age. All rats were housed in plastic cages (five animals per cage) on ground corncob bedding and fed Purina Rat Chow and water ad libitum. Average semi-quantitative estimates of P-one-3β-HSD activity in ovarian sections revealed a statistically significant ($P < 0.05$) increase in enzyme activity at day 27 in the $PGF_{2\alpha}$ group. Premature sexual maturation was observed as witnessed by early vaginal canalization, i.e. 90% of $PGF_{2\alpha}$ females had open vaginae by day 33 compared to 0% of the control group. It was postulated that this premature sexual maturation was exerted by the increased ovarian steroidogenesis, as demonstrated by the significantly higher levels of P-one-3β-HSD activity in the ovaries.
(Supported by Veterans Administration Hospital, Hines, Illinois and in part by U.S.P.H.Service G.R.S. Grant to Professor Velardo).

A POTENTIAL MOLECULAR CONTROL MECHANISM FOR MOBILIZATION OF MEMBRANE-BOUND Ca^{++} (ONE METHOD OF GENERATION OF DEPOLARIZATION). Clara Torda. Mt.Sinai School of Medicine and SUNY New York.

Experimental evidence has already been obtained that suggests at least two mechanisms whereby release of membrane-bound Ca^{++} may generate membrane depolarization:e.g. 1) Magleby and Stevens (1972) observed that, even in absence of passive Na^{+} transport, membrane depolarization may be generated through changes of local charges by release of membrane-bound Ca^{++}; and 2) The depolarization that results from passive Na^{+} transport is initiated by opening the Na^{+}-channels by an appropriate agent (e.g. release of membrane-bound Ca^{++} (see reviews of Hille(1971),Keynes(1972), Lecar and Nossal(1971))). Hendrickson and Reinertsen (1971) observed a quantitative relationship between dephosphorylation of triphosphoinositide (TPI) to diphosphoinositide (DPI) and release of Ca^{++}. Torda (1971, 1972) has found that one of the nicotinic receptors of ACH is the regulatory subunit of triphosphoinositide phosphomonoesterase (TPIPM). TPIPM has been isolated from the postsynaptic membrane. When ACH forms a complex with the regulatory subunit of TPIPM, this subunit ceases to inhibit the catalytic subunit, and the catalytic subunit dephosphorylates its specific substrate, TPI, to DPI with a potential latency of the onset of DPI-formation of a fraction of a millisecond.The present work represents an attempt to ascertain whether membrane depolarization generated through an ACH-dependent activation of the enzymatic activity of TPIPM may be effected through mobilization of membrane-bound Ca^{++}.Membrane potential changes were recorded through microelectrodes from the parasympathetic chain of the bullfrog.The effects of relative changes of the local concentrations of Ca^{++} and the enzymatic activity of TPIPM on the membrane potential were measured.The results support the assumption that ACH-activated TPIPM may initiate membrane depolarization by the release of a quantitatively predetermined amount of membrane-bound Ca^{++}.

ARTERIO-VENOUS LACTATE DIFFERENCE IN THE NORMAL DOG LUNG AT REST, DURING EXERCISE AND DURING ACIDOSIS. **G.E. Torres and N. Torbay K. (intr. by Y. Enson) Dept. of Physiology, Universidad Centro Occidental, Lara, Venezuela.**

While in-vitro lactic production by lung slices has been reported (JAP 32:477, 1972), its production in-vivo by the normal lung is not confirmed. To this end we studied 10 anesthetized, spontaneously breathing normal dogs. Simultaneous pulmonary (PA) and systemic arterial (SA) blood samples were analyzed for lactic acid concentration (LAC), pH, oxygen saturation (SO_2) and carbon dioxide tension (PCO_2). These measurements were made at rest, at the 7th minute of exercise, and during acidosis induced by infusion of 0.15N HCL solution. The following results were obtained:

State	Sample Site	LAC (mgm%)	pH	SO_2 (%)	PCO_2 (mm Hg)
Rest	PA	9.95	7.33	71	44
Rest	SA	5.45	7.39	92	35
Exercise	PA	23.4	7.31	58	47
Exercise	SA	18.75	7.33	89	39
Acidosis	PA	12.68	6.75	35	46
Acidosis	SA	42.7	6.95	75	21

These data indicate lactic acid consumption by the lung, at rest, which is augmented during exercise despite a small fall in pH. With severe acidosis, however, the arteriovenous lactate gradient is reversed and the lung appears to produce lactic acid. This alteration may stem from changes in pulmonary metabolic activity induced either by acidosis alone or in conjunction with hypoxia. The role of hypoxia is unclear since the low $PaCO_2$ suggests that intrapulmonary shunts rather than alveolar hypoxia were responsible for the low arterial SO_2.

INCREASED VENOUS RETURN IN HYPOXIA. R. J. Traystman*, S. M. Scharf*, J. K. Stene*, and S. Permutt. Dept. of Environmental Medicine, Johns Hopkins Univ. Sch. of Hygiene & Public Health, Baltimore, Md. 21205.

Occlusion of the descending thoracic aorta (AO) distal to the subclavian artery leads to an increase in venous return ($\dot{Q}$) by transferring blood volume from areas with a long time constant for venous drainage (splanchnic veins) to areas with a short time constant for venous drainage (cephalic-forelimb veins) (Fed Proc. 30:322, 1971). In 6 dogs prepared with a right heart bypass to control right atrial pressure, we studied the effects of AO during arterial hypoxia; i.e., arterial O_2 contents of 5-7 vol %. Hypoxia was produced by either an inhalation of 7% O_2 mixture (low pO_2 hypoxia) or 6000 ppm CO (CO hypoxia) for 10-20 min. at constant ventilation. $\dot{Q}$ was compared at zero right atrial pressure for the aorta patent with that during AO. During normoxia, AO resulted in an increase in $\dot{Q}$ from 1967 to 3304 ml/min (68%). Low pO_2 hypoxia increased $\dot{Q}$ to 2896 ml/min (47%) and AO during hypoxia further increased $\dot{Q}$ to 3549 ml/min (23%). CO hypoxia increased $\dot{Q}$ to 2064 ml/min (5%) and AO further increased $\dot{Q}$ to 3456 ml/min (67%). The observed increases in blood flow with hypoxia, but not those with AO, were abolished by pretreatment of the animals with phenoxybenzamine (5 mg/kg). Low pO_2 hypoxia apparently results in a transfer of blood volume out of splanchnic veins to a greater degree than CO hypoxia. AO during low pO_2 hypoxia, therefore, causes less redistribution of blood volume than during normoxia, and consequently, less increase in $\dot{Q}$. (Supported in part by PHS grants HL-14153, HL-10342, and HL-05453.)

THE METABOLIC EFFECTS OF TRANSCENDENTAL MEDITATION. M. Treichel, N. Clinch, and M. Cran (intr. by N. Stephens). Dept. of Physiol., Univ. of Manitoba, Winnipeg, Canada.

It is now accepted that mental states alter physiological function. The technique of Transcendental Meditation (TM) has been reported to produce a substantial decrease in oxygen consumption during short test periods (Wallace, Benson and Wilson, Am. J. Physiol. 221, 795). We have repeated these experiments using a method designed to reduce interference with the subject's respiration. Fifty-six experiments were run on 15 experienced meditators and a similar series of 36 experiments was made with 15 control subjects. In each case nasal air velocities were measured using heated thermistors, and nasal air was analysed continuously for pCO_2. Each experiment was divided into 3 sections. During the first 20 minutes both groups were instructed to read; during the second period of 20 minutes meditators meditated while the control group sat comfortably and relaxed with closed eyes; during the final 20 minutes both groups were instructed to read. Mean minute volume ($\dot{V}$), minute CO_2 production ($\dot{V}_{CO_2}$), as well as respiratory frequency were computed for each experimental section. Meditation was associated with decreases of $1.6 \pm .2$ liters/min and 71 ± 8 ml/min in $\dot{V}$ and $\dot{V}_{CO_2}$ respectively (means and S.E. of the means), with no significant change in respiratory frequency. These changes are in the same order of size but slightly larger than those previously reported. However the tests with non-meditating subjects unexpectedly produced similar results ($\Delta\dot{V}$ $1.3 \pm .2$ liters/min; $\Delta\dot{V}_{CO_2}$ 45 ± 10 ml/min). We conclude that under the conditions of our experiments, the decrease in metabolic rate achieved by our meditating subjects was not necessarily related to the practice of the technique. Supported by Univ. of Manitoba Research Board.

TUBULAR EXCRETION OF CHOLINE BY THE PERFUSED RAT KIDNEY: EFFECT OF HEMICHOLINIUM-3 (HC-3). Trimble, M.E., M. Acara*, and B. Rennick. V.A., Syracuse, N.Y. and Dept. Pharmacol., SUNY, Buffalo, N.Y.

The organic cation choline was excreted by active renal tubular transport in chicken and dog in vivo during exogenous loading. It was not possible to inhibit tubular transport of choline in the unanesthetized chicken with HC-3, due to the toxic effects. The mechanism of action of HC-3 to prevent acetylcholine synthesis in nerves has been attributed to prevention of entry of choline into cells. Use of Bowman's isolated perfused rat kidney permitted study of tubular transport of choline and the effects of HC-3 without systemic toxicity. ^{14}C-choline and ^{14}C-betaine were measured by Reineckate precipitation in the perfusate and urine sampled at 10 min intervals for 70 minutes. Perfusion with 1.42 mM ^{14}C-choline resulted in an initial U/P ^{14}C-choline/inulin ratio of 6.36 ± 0.28 S.E., indicating tubular secretion of choline. This ratio fell as ^{14}C-choline concentration in the recirculating perfusate decreased with time due to excretion in the urine, renal metabolism to betaine and accumulation in the kidney. Addition of HC-3 at 0.07, 0.13 and 0.27 mM inhibited the tubular secretion of choline, reduced the proportion of betaine appearing in the perfusate, and reduced the amount of label accumulated in the kidney. In summary: 1) choline was actively transported by the renal tubule in the perfused rat kidney, 2) choline was metabolized to betaine, 3) HC-3 inhibited both of these processes, and 4) the effect of HC-3 to prevent tubular transport of choline may be analogous to its action on the neuron. Supported by USPHS grants AM-14401, HL-14092, AM-10420, FTF-7-UB-72, V.A.

VIDEOMETRIC DETERMINATION OF WALL DYNAMICS IN A WORKING ISOLATED CANINE LEFT VENTRICLE. K. Tsuiki*, E. L. Ritman*, D. E. Donald, R. E. Sturm*, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota.

A metabolically supported canine heart with the free right atrial and ventricular walls resected was placed at the intersection of two orthogonal x-ray beams and used to pump 10% renovist in Ringer's/dextran solution through an artificial circulation. The coronary circulation was perfused separately with arterial blood from a donor dog. This technique permitted clear definition of the ventricular wall over the full extent of both biplane roentgen silhouettes. Wall thickness was estimated as the distance between endocardium and epicardial silhouettes at twenty points, 0.5 cm apart, around each silhouette perimeter for each 60/second video image of the cardiac cycle. The data were obtained at various heart rates, left atrial and aortic pressures. At end-diastole, the silhouette wall thickness at the apex was about half as thick as that at the base, the absolute thickness depending on the aspect of view selected. Increased end-diastolic volume resulted in uniform thinning at the base and the apex, whereas systolic ejection resulted in more relative thickening at the apex than at the base. The rate of thickening increased with increased end-diastolic volume and decreased with elevated aortic diastolic pressure. (Supported in part by NIH grants HL3532, HL4664, HL06143, and RR-7; NASA NGR 24-003-001; and AHA CI 10.)

ALTERATIONS IN RAT TESTICULAR, HYPOTHALAMIC, PINEAL, AND PITUITARY MONOAMINE OXIDASE (MAO) ACTIVITY AFTER PINEALECTOMY, MELATONIN ADMINISTRATION, AND CHANGES IN PHOTOPERIOD. R. L. Urry* and LeGrande C. Ellis. Utah State University, Logan, Utah.

Rat MAO activity was measured radiometrically by using 5-HT-^{14}C as the substrate. Testicular MAO activity was increased after injections (1 mg or 2 mg) of melatonin for 12 days, and after additions of melatonin in vitro at concentrations of 10^{-5}M through 10^{-7}M. Changes in photoperiod failed to alter testicular MAO on a per mg of tissue basis, but pinealectomy increased the activity. This increase was attributed to a possible increase in FSH synthesis and release.

Rat hypothalamic MAO activity was not affected by changes in photoperiod, but was inhibited in vitro with additions of melatonin at concentrations through 10^{-5}M. Pinealectomy increased hypothalamic MAO. Additions of melatonin in vitro decreased bovine pineal MAO activity at a concentration of 10^{-4}M and rat pineal MAO at concentrations through 10^{-7}M. Pineal MAO activity was not altered by changes in photoperiod. Rat pituitary MAO activity was increased by constant light and pinealectomy, but was decreased by constant darkness and by additions of melatonin in vitro in concentrations through 10^{-6}M. The data suggest that MAO represents a target enzyme for melatonin, and that as such may explain previously observed increases in brain serotonin noted after melatonin injections. This may also be one mechanism by which melatonin acts to inhibit the synthesis and/or release of LH and FSH from the pituitary. It may also partially explain how melatonin and the pineal influence gonadal development and associated reproductive processes.

EFFECT OF SINUSOIDAL STRETCHING OF THE SINOATRIAL NODE ON NODAL RHYTHM. J. Ushiyama and C. McC. Brooks. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

The isolated perfused s.a. nodal region of the rabbit heart was subject to sinusoidal stretch at various frequencies. Electrodes applied to the surface of atrial tissues adjacent to the node recorded the firing rhythm. A Grass polygraph was used to record the rhythm of stretch, electrical activity of the node, a tachogram of firing rate. These recordings and the effects of varying rates of stretch were also registered on magnetic tape for computer analysis. It was found that the s.a. nodal rhythm was affected by the stretch frequency. Not only did the stretch increase the rate of firing but the sinus rhythm tended to lock into that of the applied oscillation. As a result of this "lock-in" the cycle lengths became more uniform and the time of firing coincided with the stretch rather than the relaxation phase of the stretch oscillator. Since the rate of pacemaker activity tends to adapt to the imposed type of oscillation and it is known that stretching the nodal tissue causes some degree of depolarization; it is concluded that the various potentially autonomous pacemaker cells constituting the node have the ability to synchronize with each other. This synchronization within the s.a. node might be accomplished by electrotonic coupling between pacemaker cells. Supported by a grant from the New York Heart Association #B01 HIK1600.

RELATIONSHIP BETWEEN ARTERIAL BLOOD PRESSURE CHANGES (ΔP_A) AND AIRWAY PRESSURE CHANGES (ΔP_W) DURING THE SIMULATED VALSALVA MANEUVER (VM) IN THE DOG. M.E. Valentinuzzi and L.E. Baker*. Physiology Department, Baylor College of Medicine, Houston, Texas. (Grant HL-13114).

Simultaneous records of ECG, aortic pressure and airway pressure were taken from thirteen anesthetized mongrel dogs (Innovar, 1cc/6kg + Nembutal, 10mg/kg). The VM was simulated by positive pressure inflation of the lungs to known volumes held for 10 sec. (± 1 sec.). The arterial blood pressure (BP) fell rapidly at an early stage of the VM, stabilized at a reduced level with decreased pulse amplitude (accompanied by marked increase in heart rate) and, after an occasional overshoot upon cessation of the VM, returned to its initial value. These events were followed by reflex slowing of the heart. The difference ($-\Delta P_A$) between the mean arterial BP before the VM and the stabilized mean BP during the VM, and the difference ($+\Delta P_A$) between the peak arterial pressure amplitudes at the release of inflation, were statistically analyzed for each animal as functions of ΔP_W(linear regression, $Y=A + BX$, Standard Error of Estimate (SEE) and CORR). Average values from the first eleven dogs were: $\overline{A}$=6.06, $\overline{B}$=1.75, $\overline{SEE}$=4.47, $\overline{CORR}$=.913, for $-\Delta P_A$, and $\overline{A}$=15.37, $\overline{B}$=2.11, $\overline{SEE}$=6.51, $\overline{CORR}$=.862, for $+\Delta P_A$. Data from the last two dogs (not included in the analysis) were employed to assess the predictions obtained by using the above values in the linear equations. On the average, the errors between the predicted and the measured values were -7% (SD=10, N=15) for $-\Delta P_A$ and -5% (SD=13, N=16) for $+\Delta P_A$. In conclusion: (1) The decrease in mean BP at the "on" of the VM was approximately linearly related to the increase in airway pressure. (2) The increase in peak to peak BP at the "off" of the VM was also approximately linearly related to the decrease in airway pressure. (3) In both cases, there was a magnification factor reflected in a regression coefficient larger than 1.

EFFECTS OF DRUGS ON INTESTINAL WATER SECRETION FOLLOWING CHOLERA TOXIN IN GUINEA PIGS AND RABBITS. E. Valiulis* and J.F. Long - Schering Corp., Bloomfield, N.J. 07003

Diphenoxylate, morphine and indomethacin were given orally or I.P., 30 min before injecting crude cholera toxin into isolated ileal loops in guinea pigs (G.P.) and rabbits. Single loops were prepared in the G.P. ileum while multiple loops (4) were prepared in the rabbit ileum. Four hrs after toxin, the loops were removed and volume measured. Intestinal tissue was weighed and vol/gm wet wt was calculated. Studies were also performed on the spontaneous secretion observed in G.P. Spontaneous and cholera-induced secretions in G.P. were 2.24 ml/gm and 4.90ml/gm, respectively. In the rabbit, cholera-induced secretion was 5.47ml/gm; they had no spontaneous secretion. Several doses of each of the above compounds were given. The max effective dose of diphenoxylate in the spontaneous secretion of the G.P. was 5mg/kg P.O. resulting in 80% inhibition. The dose of 10mg/kg P.O. diphenoxylate provided max inhibition (55%) of cholera-induced secretion. Morphine, 8 mg/kg P.O. inhibited spontaneous and cholera-induced secretion by 60% and 40%, respectively. Indomethacin, 2.5mg/kg, P.O., produced 20% inhibition in each G.P. procedure. In the rabbit, diphenoxylate and morphine each at 10mg/kg I.P. inhibited cholera-induced secretion by 46% and 48%, respectively. Indomethacin, 2.5mg/kg I.P. produced 20% inhibition. These experiments suggest a possible mechanism for the antidiarrheal effect of diphenoxylate and morphine is inhibition of intestinal water secretion.

AEROBIC AND GLYCOLYTIC DETERMINANTS OF BASAL TENSION AND REACTIVITY TO DRUGS IN ISOLATED CUTANEOUS, MESENTERIC AND PULMONARY VEINS OF THE DOG. Paul M. Vanhoutte (intr. by John T. Shepherd). Mayo Foundation, Rochester, Minnesota.

A comparison has been made of the responses of different veins of the dog to anoxia, under resting conditions and when constricted by norepinephrine (NE), acetylcholine (ACh) and KCl; the importance of the availability of glucose has also been assessed. Changes in isometric tension of helical strips of saphenous and pulmonary veins, and of longitudinal strips of mesenteric veins were recorded. In control solution anoxia (PO_2 < 1 mm Hg for 10 to 15 minutes) did not affect basal tension in saphenous and pulmonary veins; in the mesenteric strips it decreased the strength of the spontaneous contractions. Anoxia depressed the contractions caused by NE and KCl; this effect was most pronounced in the mesenteric, and least in the saphenous vein. Anoxia depressed reactions of the mesenteric and pulmonary veins to ACh, but augmented those of the saphenous vein. In glucose-free solution all contractions were markedly depressed during anoxia. After 30 minutes incubation in glucose-free solution the effects of anoxia on basal tension did not differ from control. If the incubation was prolonged over 60 minutes a direct contraction occurred in the three types of veins with anoxia; on repeated exposure the amplitude of these contractions decreased in the saphenous strips, but increased in the other veins. These data suggest that in venous smooth muscle, particularly in the saphenous vein, anaerobic glycolysis can sustain most of the energy requirements, but that only limited amounts of intracellular energy-rich compounds are available. In the saphenous vein, acetylcholine activates preferentially the anaerobic metabolism. In the absence of glucose anoxia interferes with mechanisms responsible for maintaining the resting state.

INOTROPIC AND PERIPHERAL VASCULAR ADJUSTMENTS TO HEMORRHAGE IN CONSCIOUS DOGS. Stephen F. Vatner. Depts. Med., Harvard Med. Sch. and Peter Bent Brigham Hospital, Boston, MA 02115.

It is widely accepted that hemorrhage induces substantial increases in myocardial contractility and vascular resistance, especially in the renal bed. The responses to mild (14±2 ml/kg) and moderate (26±3 ml/kg) hemorrhage were examined in 15 healthy conscious dogs after recovery from instrumentation with arterial pressure (P) catheters and miniature P gauges in the left ventricle (LV) for LVP, dP/dt and dP/dt/P, ultrasonic LV endocardial diameter (D) gauges for LVD and dD/dt, i.e., velocity and Doppler flow probes on the coronary, mesenteric, renal and iliac arteries. The maximal increases in dP/dt (+13±2%) and dP/dt/P (+21±3%) occurred with mild hemorrhage. Moderate hemorrhage decreased mean arterial pressure (-23±2 mmHg), LV end diastolic diameter, dP/dt and velocity, while dP/dt/P returned to control and heart rate rose from 74±3 to 164±6 beats/min. Marked increases in resistance occurred in the mesenteric (from .33±.02 to .59±.06 mm Hg/ml/min), iliac (from .88±.05 to 1.72±.11 mm Hg/ml/min) and coronary (from 2.65±.14 to 3.33±.21 mm Hg/ml/min) beds. Surprisingly, renal flow was maintained and renal resistance fell (from .58±.03 to .40±.02 mm Hg/ml/min). In dogs anesthetized with pentobarbital Na, 30 mg/kg, moderate hemorrhage resulted in intense renal constriction. Renal dilation with hemorrhage in conscious dogs was not prevented with α or β adrenergic, cholinergic or histaminergic blockades but was blocked with indomethacin, 4 mg/kg, which prevents prostaglandin synthesis. Thus, 2 compensatory mechanisms considered to be fundamental in the cardiovascular response to hemorrhage, i.e., 1.) increased myocardial contractility and 2.) renal vasoconstriction were found to be of little importance in conscious dogs. In fact, renal dilation occurs with hemorrhage, which appears to be mediated by prostaglandin release.

THE THREE-ELECTRODE METHOD OF VOLTAGE CLAMP IN CARDIAC MUSCLE:A FEASIBILITY STUDY.J.Vereecke*,M.Lieberman,T.Sawanobori*,E.A.Johnson,and W. New*.Dept. Physiology,Duke University Medical Center,Durham,N.C.27710.

Application of the three-electrode method of voltage clamp of Adrian, Chandler, Hodgkin requires that the preparation of cardiac muscle behave as a one-dimensional cable and that it have a definable end.We have grown a synthetic strand of cardiac muscle having a naturally occurring definable end(Purdy et al,J.Cell Biol.55:563,1972).Experiments show that the logarithm of the steady-state electrotonic potentials and the time to half-maximum are a linear function of the distance from the site of injection of current. A comparison of the mean values of the capacitance of the preparation as determined from the time course of the foot of the action potential and the propagation velocity of the electrotonic potential shows that none of the membrane capacitance appears to be in series with a resistance.The strand can thus be described as a one-dimensional cable.Mean values of the cable parameters(λ=1.2mm;R_m=35kΩcm^2;R_i=223Ωcm; C_m=1.36$\mu F \cdot cm^{-2}$)compare very well with the values obtained from adult myocardium and those recently revised for Purkinje fibers.

Voltage clamp studies were designed to be an iterative process in which the results from experiments performed on the synthetic strand would be compared with identical experiments on a theoretical model of the strand;differences in behavior being used to force modifications in the model.As a start to this iterative process and as a test of the membrane model,we have performed experiments similar to those described by Giebisch and Weidmann in which the repolarization phase of the action potential is delayed by holding the membrane potential constant at the plateau level for several hundred msec. The results of these experiments and those of the cable analysis show that the three-electrode method of voltage clamp can be applied to the synthetic strand.

Supported by NIH grant HL12157 and the American Heart Association.

THE EFFECT OF TREATMENT WITH WHOLE BEE VENOM ON DAILY CAGE ACTIVITY AND PLASMA CORTISOL LEVELS IN THE ARTHRITIC DOG. J. A. Vick*, R. B. Brooks*, G. B. Warren*, and C. C. Hassett. Biomedical Laboratory, Edgewood Arsenal, MD.

A series of 24 mixed breed dogs were used to study the physiological effects of whole bee venom on canine arthritic-like conditions. Sixteen were randomly selected normal dogs and eight were suspect arthritic animals confirmed by X-ray and special physical examination. The control dogs were divided into Groups I and II and the arthritic Groups III and IV. Groups I and III received injections of sterile saline while Groups II and IV were given 1 mg whole bee venom S.Q. on day 30, 37, 50 and 60. Plasma cortisol levels were measured weekly and cage activity recorded daily using a K and R Pedometer. Following bee venom injection plasma cortisol levels increased in both Groups II and IV from a control of 5 μg/100 ml to 15 μg/100 ml 15 days after therapy. During this period of time the four arthritic dogs in Group IV increased daily cage activity from 4 miles/day to 10 miles/day. Groups I, II and III showed no increase or decrease in cage activity. No injections were given between day 60 and day 90. At 90, 97, 110 and 120 days, Groups I and III were given bee venom and Groups II and IV sterile saline. As before bee venom increased plasma cortisol levels in both venom treated Groups and the daily cage activity in Group III. At 120 days all injections were discontinued. Plasma cortisol levels returned to normal within 30 days, yet daily cage activity in both Groups III and IV remained significantly above control (8 to 11 miles/day). Results indicate that whole bee venom stimulates the production of cortisol and the daily cage activity in dogs exhibiting arthritic-like conditions. No significant side effects were noted in any of the dogs treated with bee venom.

ANTICHOLINESTERASE INDUCED ALTERATION IN THE FIRING PATTERN OF MEDULLARY RESPIRATORY NEURONS OF THE CAT. J.D. von Bredow, N. Adams and E. Bay (Intr. by: F.N. Craig) Biomedical Laboratories, Edgewood Arsenal, Md. 21010

The lipid soluble anticholinesterase compound, Soman, has an effect on the central as well as the peripheral respiratory mechanisms. Extracellular recordings of cells in the medullary respiratory center was accomplished in decerebrated, unanesthetized, paralyzed cats. Electrical activity of the phrenic nerve was monitored to identify cells firing in phase with the phrenic nerve as inspiratory and those firing out of phase as expiratory. Upon the i.v. administration of 60 micrograms/kg of Soman a shift occurs in the firing pattern of the cell from the inspiratory phase to the expiratory phase. The fact that this is a change in the firing pattern of the same cell rather than a shift in the recording from one cell to another cell is indicated by amplitude and by wave form analysis. Although this shift in phase pattern has been shown by other researchers to occur during the electrical stimulation of specific areas within the pons it has never been reported to occur as a result of the administration of an anticholinesterase compound.

CONDITIONS FOR REDUCTION OF PULMONARY GAS TRANSFER BY VENTILATION/PERFUSION INEQUALITY. P.D. Wagner*, J.W. Evans*, and J.B. West. Depts. of Mathematics and Medicine, University of California San Diego, La Jolla, California 92037.

It is commonly held that although ventilation/perfusion ($\dot{V}_A/\dot{Q}$) inequality interferes with pulmonary O_2 exchange, CO_2 transfer is not affected. We have therefore explored formally the characteristics of a gas which determine how its pulmonary exchange is altered by parallel $\dot{V}_A/\dot{Q}$ inequality. If its elimination is to be reduced by $\dot{V}_A/\dot{Q}$ inequality, mixed alveolar partial pressure in the inhomogeneous lung must be less than that in the homogeneous lung with the same total blood flow and ventilation. This will be the case if and only if the relation between alveolar partial pressure (P_A) and the ratio of blood flow to ventilation ($\dot{Q}/\dot{V}_A$) is strictly concave, implying that the second derivative $d^2P_A/d(\dot{Q}/\dot{V}_A)^2$ is everywhere negative. This in turn is equivalent to the requirement that the plot of the inverse of blood gas content against partial pressure be strictly convex. A similar analysis for gas uptake shows that $\dot{V}_A/\dot{Q}$ inequality reduces pulmonary gas uptake if and only if the plot of blood gas content against the reciprocal of partial pressure is strictly convex. Considering each gas individually, these graphs were drawn for inert gases (linear dissociation curves) and for O_2, CO_2, and CO. For inert gases, both uptake and elimination are always reduced by $\dot{V}_A/\dot{Q}$ inequality. For O_2, CO_2 and CO, uptake of each and elimination of CO_2 are also always reduced by $\dot{V}_A/\dot{Q}$ inequality. However, it is possible for steady-state elimination of O_2 and CO to be enhanced by $\dot{V}_A/\dot{Q}$ inequality, but only if venous P_{O_2} and PCO exceed the unphysiological values of 800 and 51 mm Hg respectively. Thus under physiological steady-state conditions, $\dot{V}_A/\dot{Q}$ inequality always reduces both the uptake and elimination of all known gases. (Supported by PHS Grant HE-13687-03 and NSF Grant GP 20863.

INFLUENCE OF REPRODUCTIVE HORMONES ON RESTING AND EXERCISE METABOLISM IN WOMEN. D. Wakat (intr. by R.E. Johnson). Human Environmental Research Unit, Univ. of Illinois, Urbana. 61801

Few extended metabolic studies have been completed with women as subjects. Thus little is known about metabolic changes with the menstrual cycle, even though estrogen and progesterone are known to influence specific metabolites. In this study, 3 adult, premenopausal women were studied daily through two complete menstrual cycles. During both cycles, resting values were obtained for respiratory gases, urinary N, hematocrit, and plasma levels of estradiol and progesterone. During the second cycle, the subjects also exercised daily on a bicycle ergometer for 30 minutes at 360 kgm/min. Respiratory gases and urinary N were again measured. The metabolic mixture was calculated for both conditions. The data were treated statistically to determine whether significant differences in metabolism existed between the luteal, menstrual and follicular phases and also to identify any relationships between metabolism and the reproductive hormones. At rest, differences were found in CHO and Fat utilization and in the respiratory quotient (RQ). No differences in caloric expenditure were observed. Estrogen was positively related to fat utilization, while progesterone did not influence resting metabolism. During exercise, differences between phases were observed for O_2 consumption, RQ, CHO, Fat, and caloric expenditure. Progesterone was positively related to fat and inversely related to carbohydrate utilization. Estrogen was inversely related to RQ. Cyclic differences in metabolism were thus present, and were not necessarily the same at rest as during exercise. Significant relationships were also seen between the hormones and specific measures of metabolism.

ELECTRON MICROSCOPE STUDY OF FIBRIL ASSEMBLAGE AND TRIAD DEVELOPMENT IN SKELETAL MUSCLE FIBERS OF THE FETAL MONKEY AND HUMAN. Sheppard M. Walker, Glenna J. Currier*, Juanita W. Yuen* and Diana D. Sarkar*. Univ. of Louisville School of Med., Louisville, Ky.

The structural relation of the sarcoplasmic reticulum (SR) to fibril formation and triad growth has been observed in muscle fibers from 8 to 22-week monkey and 8 to 28-week human fetuses. Exact cross-sections at all levels of the sarcomere and exact longitudinal sections of the fibril were examined. The fibril, in the earliest stages of development observed, is surrounded by a network of SR tubules and the Z lines of the fibrils are encircled by SR tubules continuous with the network. The encircling SR is separated from the Z line by a 100 Å space traversed by electron-opaque strands. This structural relation between SR and Z lines is found at all stages of fibril growth. When tubules of the SR network and the T system tubules become apposed, bridges form between the membranes of SR and T and thereafter unique structures form within the apposed SR and the apposed SR expands laterally. Between the 8th and 20th week of fetal development the orientation of the triads changes from predominantly longitudinal to predominantly transverse. The longitudinal triads are distributed throughout the sarcomere while the transverse triads are found at the AI junction only. It is concluded that: 1. SR formation precedes fibril formation. 2. Z line growth and fibril assemblage progress concurrently. 3. SR encircling the Z lines plays a role in development of the Z lines. 4. Formed bridges between SR and T impart a growth stimulus for development of structures within apposed SR. 5. Completion of transverse orientation of triads and completion of fibril assemblage occur simultaneously. This work was aided by NIH grants 5 R01 NS07930-05 and 1 R01 NS10257-01.

LEFT VENTRICULAR RESPONSES TO INSTANTANEOUS CHANGES IN AORTIC INPUT IMPEDANCE. William E. Walker*, Wilmer W. Nichols and William R. Milnor. The Johns Hopkins School of Medicine, Baltimore, Maryland.

To test the hypothesis that left ventricular work is independent of aortic impedance if contractile element (CE) work as well as external work be taken into account, 12 experiments were performed in 6 anesthetized, open-chest dogs. Aortic blood flow was measured by a perivascular electromagnetic flow probe, aortic and left ventricular pressures by catheter-tip micromanometers, and ejection fraction by thermodilution. Aortic impedance was raised by instantaneous partial occlusion of the descending aorta in diastole by a balloon cuff; data from the subsequent heart beat were compared with the control beat immediately preceding occlusion. Characteristic impedance (mean of impedance moduli between 2 and 12 Hz) in controls averaged 236 (SEM ±18) and rose to 404 (±42) dyne sec cm^{-5} with occlusion, while input resistance rose from 5348 (±928) to 8442 (±1313) dyne sec cm^{-5}. Stroke volume fell from 10.3 (±.84) to 7.9 (±.83) ml and ejection fraction fell from .30 (±.01) to .22 (±.01). Duration of the cardiac cycle, and of its isovolumic, ejection, and diastolic periods did not change. Contractile element velocity (V_{CE}) was calculated as sum of total wall velocity (V_T) and series elastic element velocity (V_{SE}), where V_{SE} = (dF · circumference)/(30 F.dt), F being tangential wall force. Peak V_{CE} during ejection fell from 16.8 (±.5) to 14.5 (±.8) cm/sec. A consistent alteration in the CE force-velocity relationship was observed during the ejection period in the beat after occlusion. CE work did not change significantly (control average 249 ±20, and occlusion 252 ±24 millijoules), nor did total external work (integrated product of V_T and F, 207 ±16 to 193 ±19 millijoules). These results are consistent with the hypothesis that the total mechanical work (internal + external) of the ventricle is independent of afterload represented by aortic impedance.

PHOSPHOLIPID FATTY ACID (PLFA) SYNTHESIS BY ISOLATED PERFUSED RAT LUNG. M. C. Wang* and H. C. Meng, Vanderbilt University Medical School, Nashville, Tennessee.

PLFA synthesis from ^{14}C-1-acetate (A) -1-laurate (L), -1-palmitate (P), -1-stearate (S), -1-oleate (O) and -U-glucose (G) was studied in an isolated rat lung perfusion system at 37° for 1 hr. The perfusion fluid was a Krebs-Ringer bicarbonate buffer (pH 7.4) containing 1.3 μmoles/ml ^{14}C substrate, 2.5% albumin and 100 mg% G. The lung readily incorporated 6.5, 2.9, 13.9, 7.1, 6.8 and 0.6% of the initial ^{14}C radioactivity of A, L, P, S, O and G, respectively, into PLFA. More than 80% of PLFA-^{14}C was in palmitic acid (16:0) when A and G were used as substrates, while 37, 61, 80 and 94% of PLFA-^{14}C from L, S, O and P, respecitvely, were recovered as original forms of FA used. 13-42% of the newly synthesized PLFA from L, S and O was palmitic and 10% of PLFA from S was in oleic acid. Phospholipase A hydrolysis showed that the ^{14}C radioactivity from substrates P and S was evenly distributed between 1 and 2 positions of PL. There was more ^{14}C-radioactivity at the 2 position (60-70%) when A, L, O and G were used. The newly formed lauric, palmitic and oleic acids were esterified mostly at the 2 position, and stearic acid at the 1 position of PL. It is concluded that: 1. the lung actively synthesizes FA, especially palmitic acid; it also esterifies exogenous FA directly for PL synthesis. 2. the high esterification of palmitic acid at the 2 position suggests the formation of dipalmityl lecithin. 3. the position of PLFA is determined by chain length, unsaturation and compartmentation of FA.

DECREASED BLEEDING AND PROTHROMBIN TIMES IN CHLOROQUINE-TREATED FEMALE RATS. W.F.Ward*, F.I.Lipschutz* and E.W.Hahn. Franklin and Marshall College, Lancaster, Pa. and Memorial Sloan-Kettering Cancer Center, New York, New York.

Chloroquine phosphate, (CHL) a widely used antimalarial agent, has never been reported to accelerate blood clotting in uninfected animals. We have observed such an effect. Female Sprague-Dawley rats (200-250g) were given a single injection (IP) of 40 mg/kg of (CHL) in 0.1 ml of saline. At 24 h and 96 h after injection, bleeding, (BT) and prothrombin times, (PT) and methemoglobin, (MHg) fibrinogen, (Fbr) and plasma calcium (PCa) concentrations were determined. The BT of CHL-treated animals after 24 h was 189 ± 26 sec, significantly ($p \leq 0.001$) shorter than the control value of 378 ± 27 sec. By 96 h, however, the BT of the CHL- treated and control groups, (319 ± 38 vs. 371 ± 27 sec), were not significantly different. PT was also significantly ($p \leq 0.01$) less in CHL-treated rats by 24 h (47 ± 3 vs. 74 ± 9 sec), but unlike BT the PT remained significantly depressed at 96 h after CHL treatment (50 ± 9 vs. 71 ± 6 sec). CHL treatment significatnly ($p \leq 0.01$) elevated MHg concentration from a control level of 2.0 ± 0.3 percent to 5.2 ± 1.1 percent after 24 h, but by 96 h, the MHg concentrations in CHL-treated and control groups, were not different. No significant differences in Fbr or PCa concentrations were found in the CHL-treated groups at 24 or 96 h. Concl: CHL induced reversible changes in blood clotting mechanisms in female rats. Fbr and PCa levels were not altered.

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MEMBRANE POTENTIAL CHANGES IN NEURONS IN THE VENTRAL LEAF OF NUCLEUS RETICULARIS THALAMI ASSOCIATED WITH DIFFERENT FORMS OF EEG SYNCHRONIZATION. M. Waszak (intr. by J. Schlag). VA-Hospital and Dept. Neurosurg., SUNY, Upstate Med. Center, Syracuse, N. Y. 13210.

Spontaneously occurring cortical EEG spindles and 'recruiting responses' elicited by repetitive low-frequency stimulation in thalamic intralaminar nuclei are accompanied by different alterations in membrane potential in neurons in the ventrobasal complex and ventrolateral nucleus of the thalamus. Since cells in n. reticularis thalami project to units in these and other thalamic nuclei,their behavior during these two forms of EEG synchronization was compared. In locally anesthetized encephale isole cats repetitive intralaminar stimulation elicited two modes of response in neurons in the ventral leaf of n. reticularis. One group of units responded exclusively with depolarizing potentials of up to 18mV and 90msec which were enhanced 15-80% during intracellular injection of weak hyperpolarizing currents. In the second group the depolarizations were smaller and shorter (8-15mV and 40-60msec) and were effected little or not at all by current injection. They were followed by hyperpolarizing potentials of longer duration and equal or greater amplitude which were reduced during the passage of hyperpolarizing current in some cells but remained uninfluenced in others. Cortical EEG synchronization occurring spontaneously or 'tripped' by a single thalamic shock, in contrast, was paralleled by a hyperpolarizing shift in membrane potential of up to 10mV in these neurons which was sustained throughout the entire spindle duration. These data support the view that recruiting responses and spontaneously developing EEG spindles are generated by different subcortical mechanisms. (Supported by NIH General Research Support Grant 5402 and by VA General Research Service).

ELECTROPHYSIOLOGIC EFFECTS OF McN 2840-46, A NEW ANTIARRHYTHMIC AGENT. Yoshio Watanabe, Barbara Klein*, Kemalettin Buyukozturk* and Leonard S. Dreifus. Fujita Gakuen Univ. Sch. of Med., Toyoake, Japan, and Hahnemann Med. Col. and Hosp., Philadelphia, Pa.

Electrophysiologic effects of McN 2840-46 (MN) were studied in isolated, perfused rabbit hearts and canine Purkinje-ventricular muscle preparations, with the use of microelectrode techniques. At a concentration of 50 mg/L, MN significantly prolonged the action potential duration (APd) and decreased the maximal rate of depolarization (MRD) in ventricular fibers, without affecting the action potential amplitude (APa) and membrane resting potential (MRP). No significant alterations of ventricular action potentials were observed at a concentration of 10 mg/L. In contrast, MN at 10 mg/L significantly prolonged the APd and decreased the MRD in atrial fibers. When an initial perfusion with 20 mg/L of MN was followed by lowering of potassium concentration from 4.5 to 1.5 mM, in the presence of the same concentration of this agent, MN-induced changes in ventricular APd and MRD were reversed toward the control level, and the APa and MRP tended to increase. Elevation of potassium to 7.5 mM exaggerated the effects of MN. The atrioventricular (A-V) conduction time was significantly prolonged by MN, at 10 and 50 mg/L. This prolongation of A-V interval resulted predominantly from an increase in the intraatrial and His-Purkinje conduction times, while the intranodal conduction was little affected. In spontaneously beating rabbit hearts, MN decreased the rate of sinus nodal impulse formation, whereas epinephrine-induced automaticity in canine Purkinje fibers was suppressed by MN. It is concluded that (1) the antiarrhythmic action of MN can be attributed to its membrane effects similar to those of quinidine, and (2) the atrial and the A-V nodal tissues appear more sensitive to MN than the ventricular fibers.

L-DOPA EFFECTS ON LH AND PROLACTIN IN YOUNG AND AGED FEMALE RATS. B. Watkins*, J. Euker*, J. Meites and G. Riegle. Dept. of Physiology, Mich. State University, East Lansing, MI. 48823.

The effects of L-Dopa were measured in young (4 mo) proestrus, estrus and second day diestrus, and in aged (23 mo) constant estrus and constant diestrus female Long-Evans rats. The hormones were measured by RIA in serial blood samples taken before treatment and 15, 60 and 120 min after single ip injection of saline, 3 mg L-Dopa or 30 mg L-Dopa. The 3 mg L-Dopa injection increased serum LH concentration in young estrus and diestrus groups. The 30 mg treatment increased serum LH levels in all groups except the aged constant diestrus group. The responsiveness of aged females to L-Dopa was less than that of the young group. Although the magnitude of the increase in serum LH was similar in young estrus and aged constant estrus groups, the aged group did not respond to the 3 mg treatment, the 30 mg response was delayed; serum LH was not increased by L-Dopa in the aged constant diestrus group. The 30 mg L-Dopa treatment resulted in near maximal prolactin suppression at all sampling intervals in young and aged groups. The aged groups were generally less responsive to the 3 mg injection than the young rats. Prolactin levels in the aged groups decreased 15 min after L-Dopa injection but were similar to pre-injection and control group levels at the 60 and 120 min sampling intervals while those of young rats receiving 3 mg remained depressed. These data support the concept of decreased hypothalamic-pituitary control system sensitivity in the aged animal. (Supported in part by NSF grant GB 8687 and NIH grant AM07484.)

CAPILLARY DENSITIES AND LUMINAL DIAMETERS IN MIXED SKELETAL MUSCLE DURING REACTIVE HYPEREMIA. Clinton Webb* and Hurley Myers. Physiology Dept. and School of Med, Southern Illinois University, Carbondale, Ill.

The relationship between skeletal muscle blood flow and the metabolic activity of the various muscle fibers has been used to partially explain the differential flow patterns found during exercise hyperemia. Few investigators, however, have considered the importance of this relationship in reactive hyperemia. Using fluorescein dye as a peripheral vascular marker, we have found that the increase in flow to mixed skeletal muscle fibers following arterial occlusion occurs in response to an increase in the number and size of active capillaries supplying white fibers. Twenty rats were separated into 4 groups, anesthetized and the jugular v. cannulated. The gracilis of each hind limb was exposed and the left femoral a. occluded for 2, 6, 8, or 10 min. Fifteen sec after flow was returned, a 6% soln of Na fluorescein was injected via the jugular cannula. Eight sec postinjection, the gracilis of each limb was frozen in situ. The frozen muscles were excised, sectioned, freeze-dried and then mounted under benzene for microscopic examination. Capillary densities and lumen diameters were measured from photomicrographs by profile projection. In the hyperemic muscle, the number of active capillaries was increased by about 50% of that of the control (contralateral muscle). The mean lumen diameter of capillaries in the hyperemic muscle was found to be almost twice that of the control. The number and size of open capillaries in the hyperemic muscle was not dependent on the duration of occlusion. Histochemical studies have shown that the increase in capillary number and size is localized in areas of muscle containing mostly white fibers. These data support the hypothesis of P. Johnson (AJP 223:517, 1972) that capillaries associated with primarily white fibers have a lower control rate, thus a much greater hyperemic response after occlusion.

PERIODIC BREATHING DURING SLEEP. Paul Webb, Webb Associates, Yellow Springs, Ohio.

During a study of the metabolism of sleep, we observed that a surprising number of our subjects had bouts of periodic breathing--that is, alternating periods of apnea and deep breathing, a condition which clinically is termed Cheyne-Stokes respiration, and is associated with subcortical brain damage and with circulatory failure. None of the 20 men studied were sick. Their ages were from 19 to 63, with a nearly even distribution across that range. None of the 9 men between 19 and 45 showed periodic breathing, while 9 of 11 men between 46 and 63 showed it. Periodic breathing occurred during Stage II sleep, as determined polygraphically, not in Stages III and IV nor during REM sleep. The cycles of periodic breathing were usually from 1/2 minute to 1-1/2 minutes in length; one particular apnea lasted 89 seconds. Bouts of periodic breathing ran from 4 or 5 minutes to 2 hours in duration. Oxygen consumption rate and carbon dioxide production rate varied with the breathing pattern, and RER tended to be high throughout the night. End-tidal pCO_2, as measured with a fast response CO_2 analyzer, neither rose nor fell during the periodic breathing.

EFFECTS OF WHOLE BLOOD TRANSFUSION ON FORELIMB WEIGHT, BLOOD FLOWS, ARTERIAL AND VENOUS PRESSURES, AND SEGMENTAL VASCULAR RESISTANCES (SVR) IN DOGS PREVIOUSLY INJECTED WITH ENDOTOXIN. W.J. Weidner*, R.L. Kline*, F.J. Haddy, and G.J. Grega. Department of Physiology, Michigan State University, East Lansing, Michigan 48823.

The aim of this study was to determine if transfusion leads to excessive fluid filtration and a disproportionate rise in extravascular fluid volume (EFV) in dogs previously injected with endotoxin relative to that seen in saline controls. Male mongrel dogs were anesthetized with sodium pentobarbital and injected with either purified E. coli endotoxin (5mg/Kg,i.v.) or saline, and after 2 hours were transfused with 1000 ml of cross-matched whole blood over a period of 25 min. There was no change in the forelimb parameters in the saline dogs prior to transfusion. Following transfusion forelimb weight increased markedly relative to control (≈22g in 2 hrs). The weight gain was associated with significant increases in right atrial pressure, aortic pressure, small vein pressures, hematocrit and with no change in SVR. Hence, this weight gain may be attributed, in part, to a rise in EFV subsequent to a rise in P_c. In the endotoxin dogs forelimb weight, pressures, and blood flows decreased and SVR increased as previously reported (A.J.P. vol. 221, p. 1229, 1971). Following transfusion forelimb weight increased ≈10g but failed to return to pre-endotoxin levels. This initial transient weight gain appeared to be largely due to an increase in vascular volume subsequent to a fall in SVR. These data provide no evidence for a greater rise in EFV following transfusion in endotoxin dogs than in saline dogs. Additionally, these data also fail to support the hypothesis that transfusion may be ineffectual in shock states because it leads to excessive fluid filtration largely into skin and skeletal muscle and consequently progressive plasma volume loss.

EFFECTS OF BREATHING O_2-ENRICHED GAS MIXTURES ON METABOLIC RATE DURING EXERCISE. Hugh G. Welch, John P. Mullin*, and G. Dennis Wilson*. Depts. of Physical Education and Zoology, University of Tennessee, Knoxville, Tennessee, 37916.

The administration of O_2-enriched gases has been suggested as a means of enhancing exercise tolerance both in normal subjects and in patients suffering from certain cardiovascular and respiratory disorders. To determine whether this apparent improvement is the result of an increased O_2 supply and utilization, we measured metabolic rates in 6 men breathing 20-80% O_2 during treadmill exercise over a wide range of work intensities and in an *in situ* muscle preparation in the dog, in which the muscle was stimulated to contract at various rates while the animal breathed room air or 100% O_2. During severe exercise in man, O_2 uptake ($\dot{V}O_2$) was 20% higher when breathing 80% O_2 than when breathing air. This was accompanied by a 30-35% decrease in pulmonary ventilation ($\dot{V}E$) and a slight decrease in CO_2 output ($\dot{V}CO_2$). In submaximal work, $\dot{V}O_2$ was still elevated when O_2-enriched gas mixtures were breathed, in this case by as much as 30%. Neither $\dot{V}E$ nor $\dot{V}CO_2$ changed significantly. In the *in situ* muscle preparation, neither $\dot{V}O_2$ nor $\dot{V}CO_2$ changed during maximal contractions, whether the animal breathed air or O_2, and the isometric tension exerted by the muscle was unaffected by the gas mixture used despite increases in arterial O_2 content of $>$ 10% during O_2 breathing. Since the performance of the muscle preparation is unaffected by O_2-enriched gases and since increased metabolic rates in man should be accompanied by an increased $\dot{V}CO_2$, is it possible that the apparent increase in $\dot{V}O_2$ is due to something other than an increased mitochondrial O_2 utilization?

Supported by grants from the East Tennessee Heart Association and the Faculty Research Fund of the University of Tennessee.

THE IN VIVO AND IN VITRO BINDING OF ENDRIN, ALDRIN AND DDT TO LIVER AND BRAIN PARTICULATE FRACTIONS OF INSECTICIDE-RESISTANT AND SUSCEPTIBLE MOSQUITOFISH (GAMBUSIA AFFINIS). Marion R. Wells* and James D. Yarbrough. Department of Zoology, Mississippi State University.

Susceptible mosquitofish from State College, Mississippi and resistant mosquitofish from the Mississippi Delta were assayed for endrin, aldrin and DDT binding to particulate fractions of livers and brains following in vivo and in vitro treatment. Livers and brains were homogenized and particulate fractions separated by differential centrifugation. Mitochondria from livers and brains as well as myelin were treated directly with pesticide to determine binding. Pellets resulting from differential centrifugation were identified by electron microscopy.

The in vivo studies based on protein indicate a significant difference between susceptible and resistant fish brains in the uptake of endrin, aldrin and DDT and point to a membrane barrier. The in vivo studies also indicate a more effective blood-brain barrier (two fold) in resistant fish to endrin, aldrin and DDT. There was a difference in total distribution of endrin and DDT within the brains, specifically within the cell membranes and mitochondria. It appears that the cell membranes of resistant fish retain endrin and DDT, thus reducing the amount entering the cell. The opposite effect is seen in the mitochondrial membrane as the pesticide was prevented from entering rather than being retained. A different pattern was noted for aldrin, in which there is an apparent reduction in the conversion of aldrin to dieldrin in resistant fish.

Relatively pure myelin fractions showed less binding of pesticide in all resistant myelin fractions. This indicates a structural difference in myelin in resistant fish.

FOREARM BLOOD FLOW DURING THERMAL TRANSIENTS PRODUCED BY LEG EXERCISE. C. B. Wenger,* M. F. Roberts,* J. A. J. Stolwijk, and E. R. Nadel. John B. Pierce Fndn. Lab. and Yale Univ. School of Medicine, New Haven, Ct. 06519.

Increased skin blood flow is important in dissipating the increased heat produced during exercise. Internal body temperature and skin temperatures both can affect skin blood flow, but their interaction is not well understood. Recent work from our laboratory indicates that at a given finger temperature, finger blood flow may be describes by a model consisting of a linear combination of esophageal temperature (T_{es}) and mean skin temperature ($\bar{T}_s$). Since the control of forearm blood flow differs from that of the finger in that vasodilation in the finger results solely from release of vasoconstrictor tone, we therefore studied changes in forearm blood flow during exercise as related to changes in T_{es} at different levels of $\bar{T}_s$. Subjects exercised for 30 min on a bicycle ergometer at 30, 50, and 70% $\dot{V}_{O_2max}$ at air temperatures of 15, 25, and 35°C, and vapor pressures of less than 18 torr. T_{es} was measured with a thermocouple in the esophagus at the level of the heart, and $\bar{T}_s$ computed from an area-and sensitivity-weighted mean of 8 skin sites. Forearm blood flow was measured by electrocapacitance plethysmography, and forearm skin temperature was clamped by a controlled-temperature air stream. A single model seems to predict forearm blood flow adequately both during transients in T_{es} and at steady-state. This model consists of a linear combination of T_{es} and $\bar{T}_s$, in which T_{es} is weighted several times as heavily as $\bar{T}_s$. The model thus agrees in form with our model for finger blood flow, and also with the model of central drive for sweating.

TRANSIENT VENTILATORY RESPONSES TO HYPOXIA AND HYPERCAPNIA IN MAN FOLLOWING BILATERAL CAROTID BODY RESECTION. Brian J. Whipp, Karlman Wasserman and Sankar Koyal*, Harbor Gen. Hosp., UCLA School of Med., Torrance, Calif.

Ventilatory control by peripheral chemoreceptors may be studied by adding stimulatory gases to the inspired air and noting the changes which occur before the stimulus reaches brain-stem chemoreceptors. We performed such tests in 6 normal subjects, born and resident at sea level, and 5 subjects who had previously undergone bilateral body resection (CBR), at other insitutions, for bronchial asthma. These subjects were asymptomatic when studied and had normal barostatic reflexes. Following a control period on room air, each subject breathed: a) 12% O_2 for 2 min. followed by 100% O_2 for 1 min., and b) (1 hr. later) rebreathed a gas initially containing 8% CO_2 in 92% O_2 for 3-4 mins. Normal subjects increased $\dot{V}_E$ during hypoxia and demonstrated decrements of $\dot{V}_E$ within the first few breaths of subsequent O_2 breathing. In contrast, $\dot{V}_E$ did not increase in CBR subjects during hypoxia but paradoxically increased following the transition from hypoxia to hyperoxia. We ascribe this increase to the CO_2 stimulus resulting from the Haldane effect. Following CO_2 breathing, the normal subjects had a rapid undershoot of P_ACO_2 which returned to control values within 2 mins. CBR subjects had a much smaller but more prolonged undershoot of P_ACO_2. We conclude that in man: a) the aortic bodies do not appear to be functional hypoxic ventilatory chemoreceptors, and b) there are highly sensitive and rapid CO_2 chemoreceptors other than the carotid bodies.

A NEW METHOD FOR EVALUATING RESPIRATORY CENTRE OUTPUT. W.A. Whitelaw* and J. Milic-Emili. McGill University, Montreal, Canada.

Ventilation, and more recently, respiratory work, have been used as measures of the output of the respiratory centres, but it is well known the output may be modified by vagal reflexes. In the present study we have used instead the pressure generated by the inspiratory muscles against a closed airway. In anesthetized cats the airway was occluded at FRC during spontaneous breathing of room air, of 100% O_2, of mixtures of CO_2 in oxygen, and during rebreathing. Observations were made on the negative pressure generated in the first inspiratory effort after the occlusion. During occlusion, the inspiratory effort is nearly isometric, and there is little change in lung volume to excite pulmonary stretch receptors so that the measured output is essentially unaffected by volume-related vagal reflexes. In fact the pressure generated is similar to that generated after bilateral cervical vagal section or cold block. Although the amplitude of the occlusion pressure changes with changing chemical drive, the shape of the pressure-time curve remains virtually invariant, implying that the pressure at any fixed time after the onset of inspiration is as valid a measure of respiratory centre output as is the peak pressure. This may allow the use of this technique in conscious man, where the pressure at 250 msec. after the onset of inspiration, before cortical reflex effects could occur, would be a useful measure of respiratory centre output.

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CHARACTERISTICS OF KCl CONTRACTURE IN CAT MYOCARDIUM. Jay R. Wiggins* and Arthur L. Bassett. College of Physicians and Surgeons, Columbia University, New York, New York 10032.

Contractures evoked by 140 mM KCl in isotonic Tyrode's solution were studied in cat atrial and ventricular trabeculae. At 29°, peak contracture force (P_c) and rate of force development (dp/dt) were dependent on solution flow rate. Maximum P_c was observed with linear flow rates of 1.8 - 3.1 cm/sec. Variation in P_c and dp/dt between muscles was marked, but contractures in any one muscle were reproducible. P_c was correlated inversely with muscle cross-sectional area and for thin muscles ($\sim$ 0.2 mm diameter) approached 4 g/mm^2. Contractures in atrium and ventricle differed. Atrial contractures were more reproducible, developed force more slowly, and showed less decay of contracture force with time. Temperature affected contracture characteristics. At 36°, P_c was greater than at colder temperatures (20-32°C). It has been reported that beta-receptor blockade increases P_c in cat ventricle (Morad and Rolett, J. Physiol. 224:537, 1972). Propranolol (10^{-6} to 10^{-5}M) had little effect on ventricular preparations at 36° but increased P_c to some extent at 20°. Atrial contractures were not affected by propranolol. (Supported by GM 00438 and NHLI PPG 12738).

ABSENCE OF A DIRECT EFFECT OF PLASMA CALCIUM ON FRACTIONAL PHOSPHATE CLEARANCE IN THE DOG. Randall B. Wilkening* and Franklyn G. Knox, Dept. of Physiology, Mayo Clinic, Rochester, Minnesota 55901

A direct effect of increased plasma calcium (P_{Ca}) to decrease fractional phosphate clearance (F_{PO_4}) in the dog has been reported(AJP,205: 1025,1963). However, the intrarenal $CaCl_2$ in those studies significantly decreased GFR, leaving uncertain the tubule effect. In the present studies, to avoid decreases in GFR, $CaCl_2$ was infused intravenously. Following control measurements (C), $CaCl_2$ (1 gm% in isotonic saline) was infused at .7 ml/min. Control dogs were similarly treated except that isotonic saline replaced $CaCl_2$. To control parathormone (PTH), all dogs were parathyroidectomized; Group I received bovine PTH (.005 units/kg/min throughout the experiment) while Group II received no PTH.

	GROUP I				GROUP II			
	Control		Calcium		Control		Calcium	
n dogs	(6)		(6)		(7)		(7)	
	C	NaCl	C	$CaCl_2$	C	NaCl	C	$CaCl_2$
P_{Ca} (mg%)	9.3 ± .1	9.0 .1	9.8 .1	11.8 .3	7.7 .2	7.4 .3	7.9 .2	10.5 .3
F_{PO_4} (%)	14.3 ± 4.1	16.5 4.0	15.4 3.7	19.0 3.6	6.4 3.5	6.5 3.7	6.1 2.1	7.4 3.2

The changes in the Ca infused dogs were statistically compared with the changes in the controls. P_{Ca} increased significantly in Group I (+2.3 ± .3) and Group II (+2.8 ± .1). F_{PO_4} did not change significantly in Group I (+1.5 ± 2.4) or Group II (+1.3 ± 1.9). GFR was not significantly changed in any group. We conclude that acute increases in P_{Ca}, either in the presence or absence of PTH, have no direct effect on net tubular reabsorption of phosphate in dogs.

EFFECT OF COLD ON K INFLUX IN CULTURED CELLS ORIGINATING FROM HIBERNATING AND NON-HIBERNATING ANIMALS. J.S. Willis, R.F. Foster, C.L. Behrends,* and M.J. Weber.* Depts. Physiol. and Microbiol. Univ. Ill. Urbana.

Active cation transport has been demonstrated to be relatively cold resistant in tissues of hibernating mammals and may offer a sensitively graded test of whether such species-related cold resistance persists in cell cultures. Three cell types were used for this purpose: chicken fibroblasts (CF; secondaries), monkey kidney cells (BSC) and hamster (a hibernator) kidney cells (BHK-21). When plates of monolayer cultures were transferred to a cold chamber without changing their growth medium (DME), the fall in temperature from 37 C to 5 C required about 45 min. After 2 hr. in the cold the ouabain sensitive ^{42}K influx into BHK was more than half that at 37 C, whereas in CF and BSC it was one-twelfth and one-thirtieth that at 37 C, respectively. Between 45 and 75 min. in the cold the ouabain-sensitive K influx into BHK was actually as high as or higher than at 37 C, whereas in CF and BSC it was minimal at 45 min. When the growth medium was replaced by fresh chilled minimal medium and the cells equilibrated for two hours the effect of cold on K influx was the same in CF and BSC as in the growth medium, but in BHK this procedure resulted in a 12-fold reduction due to cooling. In BHK the initial K influx after changing the medium was as high as at 37 C but it fell within 30 min. to the minimal value. In BHK changing the medium before cooling resulted in an immediate drop in influx as the cells were cooled. The results suggest that ouabain sensitive K influx in BHK is inhibited by cooling less than in other cells but that this low sensitivity depends in part upon a factor in the medium.

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INFLUENCE OF IN VITRO INCUBATION TEMPERATURE ON RAT TESTICULAR CHOLESTEROL SIDE-CHAIN CLEAVAGE ENZYME ACTIVITY. James R. Wisner, Jr.* and W. R. Gomes, Animal Reproduction Teaching and Research Center, The Ohio State University, Columbus, 43210.

Although androgens are necessary for maintenance of spermatogenesis and elevated temperatures are detrimental to sperm production, little is known regarding the effects of heat on testicular steroidogenesis. Accordingly, the effects of in vitro incubation temperature on rat testicular cholesterol side-chain cleavage enzyme activity were investigated. Adult male rats were sacrificed by cervical dislocation and testicular mitochondria prepared in 0.25M sucrose buffered to pH 7.4 with 0.02M Tris. Incubation medium (total volume 2.0 ml.) consisted of 4.7×10^5 dpm 26-^{14}C-cholesterol, 2 mg TPNH, 10umoles $CaCl_2$, 120 umoles KCl, 2 moles NaCN and mitochondrial suspension, in 0.25M sucrose buffered to pH 7.4 for each incubation temperature with 0.02M Tris. Incubations were conducted at 29°C, 33°C (rat scrotal temperature), 37°C (rat body temperature) and 41°C for 3 hours in air in Dubnoff metabolic incubators (120 oscillations/minute). Enzyme activity was assessed by measurement of 14C- isocaproic acid. Incubations conducted at 33°C revealed maximal cholesterol side-chain cleavage enzyme activity (mean specific activity expressed as dpm ^{14}C- isocaproate/mg mitochondrial protein/3 hours ± S.E.=2316 ± 366, 2894 ± 170, 1800 ± 155, and 427 ± 30 for 29°C, 33°C, 37°C and 41°C temperatures, respectively). These results emphasize the need for caution in selection of in vitro incubation temperature when assessing testicular steroidogenic capabilities. The data also suggest that an early biochemical event in cryptorchid testes or in testes subjected to ambient temperatures exceeding the thermoregulatory capacities of the scrotum and pampiniform plexus may involve reduction in cholesterol side-chain cleavage enzyme activity.

RADIOTRACER (^{113m}In) DETERMINATION OF PULMONARY BLOOD VOLUME AS PART OF PERICARDIAL SCANNING. Joseph T. Witek,* Richard P. Spencer. Section of Nuclear Medicine, Yale University School of Medicine, New Haven Connecticut 06510

Blood pool scanning, by means of a radiotracer retained in the vascular tree, is a recognized procedure for detecting pericardial effusion (and is often referred to as pericardial scanning). The apparent oligemia of the lungs in patients with such effusions, prompted our study of the pulmonary blood volume. Using a high photon yield radionuclide (^{113m}In), experimental animals or patients were positioned with their backs to a gamma ray camera, and with a detector probe over the precordium. Approximately 4 mCi of $^{113m}InCl_3$ was injected intravenously (it binds to transferrin). Data points were taken at intervals of 0.5 sec. From a blood sample at 5 minutes, the blood volume was determined. This value, plus the precordial curve, allowed calculation of the cardiac output. With the assumption that there is no major shunting (all the right sided cardiac output going to the lungs), the pulmonary blood volume was calculated from $V = T \cdot F$, where T is the mean transit time, and F is the flow (the cardiac output). Donato has discussed the use of this concept (Semin. Nuc. Med. 3:111, 1973). In some individuals with pericardial effusion, there is compromise of the lungs, with a reduction in the estimated pulmonary blood volume. At the other extreme, one patient in failure had an apparently elevated pulmonary blood volume. Since pericardial scanning is widely carried out, much patient data is potentially available. The conventional scan should likely be coupled with kinetic studies, in order to estimate the pulmonary blood volume.

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RESPIRATORY ADAPTATIONS TO DIVING IN THE NILE MONITOR LIZARD, VARANUS NILOTICUS. Stephen C. Wood and Kjell Johansen. Department of Zoophysiology, Aarhus University, Aarhus, Denmark.

The objectives of this study included direct in vivo measurements of circulating blood gases, pH, heart rate, and blood pressure during voluntary dives of unrestrained Nile monitor lizards. A Radiometer flow-through cuvette was employed for continuous recording of arterial P_{O_2}, P_{CO_2} and pH. The morphological properties of the blood revealed no particular adaptations for diving. Mean values were: hematocrit= 24 %; hemoglobin concentration = 7.1 g %; oxygen capacity = 9.3 vol %; red cell dimensions = 22 x 12 μ; red cell count = 0.67 million/μl. The respiratory properties of the blood, studied in vitro and in vivo, show distinct adaptations to habitual diving. Oxygen affinity of blood is low (P_{50} = 42.4 at pH 7.45, 25°) and the dissociation curves is markedly sigmoid (n = 3.1). These features, coupled with a Bohr factor ($\Delta \log P_{50} / \Delta pH$) of -0.48, ensure increased utilization of oxygen while maintaining relatively high tissue P_{O_2}. Arterial pH decreases during diving from about 7.5 to 7.1 due to combined respiratory and metabolic acidosis. High plasma bicarbonate (30 mM/l at P_{CO_2} = 25 mmHg) and a buffering capacity of $\Delta HCO_3^- / \Delta pH$ = 18.9 mM/l increase the tolerance to this acidosis and prolong diving time. The in vivo oxygen dissociation curve shows a 90 % depletion of arterial oxygen content during typical dives. Diving elicited a rapidly developing bradycardia with maximum of 85 % reduction in heart rate. The temperature sensitivity of HbO_2 binding was very low (ΔH = - 3 kCal). This would minimize the HbO_2 affinity increase accompanying the decrease in body temperature likely to occur in lizards going from sun basking to submergence in water. Supported by a grant from the Danish Natural Science Research Council. Present address of SCW: Biology Department, Southern Illinois University, Edwardsville, Illinois 62025.

INTEGRATED EMG AND OXYGEN UPTAKE DURING POSITIVE AND NEGATIVE WORK. Joseph J. Woods* and Brenda Bigland-Ritchie. Quinnipiac College, Hamden, Conn.

A variable speed motor driven bicycle ergometer suitable for both positive (concentric) and negative (excentric) work exercise was used in these experiments. Integrated EMG's from the vastus lateralis muscles and steady state rates of oxygen uptake were measured simultaneously at set work rates established by varying the load while maintaining a constant pedal velocity (50rpm). The relationship between each of the two variables and load was found to be linear, with a mean linear correlation coefficient of 0.98. Integrated EMG records thus provide a means of measuring the amount of muscle fiber activity involved in graded dynamic contractions. The ratio of the integrated EMG slopes for positive to negative work was 1.87 $\pm$ 0.99, while the same ratio for the oxygen uptake slopes was 6.47 $\pm$ 0.77. The discrepancy between the ratio shows that not only fewer muscle fibers required to maintain the same load during negative work exercise, but also that there is a substantial reduction in the extra oxygen taken up by each contracting fiber. This conclusion is supported by results from the literature on both heat production and force of contraction of isolated muscles that shorten or are stretched during contraction. Supported by USPH Grant #09960.

EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE BREATHING(CPAPB) ON PULMONARY FLUID FILTRATION AND CONTENT IN SHEEP. W.C.Woolverton*,K.L. Brigham* and N.C.Staub. Dept.Physiology and Cardiovascular Research Institute, Univ.Calif.,San Francisco,CA 94122

In 10 unanesthetized sheep we studied the effect of 3hr. of CPAPB (mean 10cmH20) on fluid filtration rate by measuring steady state lung lymph flow(Qlym) and postmortem extravascular lung water(Qwl) relative to dry lung weight(dQl) under baseline conditions and after elevating for 4hrs. pulmonary microvascular pressure(Pmv;0 reference level at bottom of lung). We assumed perimicrovascular hydrostatic pressure(Ppmv) equal to mean airway pressure(Paw), measured plasma and lymph oncotic pressures(π pl and π lym), and calculated fluid filtration coefficient (Kf)(see table). As previously shown(Erdmann, Fed.Proc.31:308,abs,1972) elevating Pmv did not change Kf whereas addition of CPAPB to normal or to pulmonary hypertensive sheep increased Kf significantly. Under baseline conditions CPAPB did not measurably increase lung water content, but significantly increased it in sheep with elevated Pmv compared to a separate series of 19 sheep without CPAPB but with similar levels of pulmonary hypertension. The mechanisms for these changes are unclear but probably reside in an underestimated Pmv, overestimated Ppmv, increased resistance to Qlym, increased permeability or a combination of these factors.(supported in part by HL-14201(SCOR)).

	Pmv cmH20	Paw cmH20	π pl cmH20	π lym cmH20	Qlym ml/hr	Qwl/dQl gm/gm	Kf ml/cmH20xhr
baseline	18.3	0	23.6	14.0	9.6		1.11
+CPAPB	25.4	10	23.1	13.4	9.2	375/93	1.61
baseline	18.6	0	22.7	14.3	8.6		.84
inc.Pmv	32.6	0	23.5	10.0	18.2		.96
+CPAPB	39.1	10	23.7	10.3	16.1	376/80.8	2.07

ADRENERGIC MECHANISMS IN THE HEPATIC CIRCULATION OF BABOONS. Creighton B. Wright*, David G. Reynolds* and Kenneth G. Swan. Walter Reed Army Institute of Research, Washington, D. C.

The effects of adrenergic stimulation and blockade upon hepatic arterial blood flow (HBF) were measured in anesthetized baboons to determine whether beta adrenergic receptor sites could be demonstrated and whether autoregulatory escape from vasoconstriction occurs in this circulation. HBF was measured electromagnetically; aortic (AP) and vena caval (VP) pressures were recorded. During control, mean HBF was 194 $\pm$ 19 (S.E.) ml/min. Intraarterial injections of either norepinephrine (NE), epinephrine (E) or phenylephrine (PE), in logarithmically increasing doses of 10^{-3} - 10^{0} µg (base)/kg, caused dose dependent decreases in HBF. At the highest dose NE and E each reduced HBF by 136 $\pm$ 15 ml/min ($p < .001$) and increased AP by 11 $\pm$ 1 mm Hg. PE was less of a vasoconstrictor than NE and E. All vasoconstrictor effects were significantly attenuated by alpha adrenergic blockade (phenoxybenzamine, 1.5 mg/kg, I.V.) but were not potentiated by beta adrenergic blockade (propranolol, 0.5 mg/kg, I.V.). In the same doses isoproterenol (ISO) was a vasodilator and at 10^{-1} µg/kg increased flow 49 $\pm$ 13 ml/min ($p < .001$). Higher doses did not increase the vasodilator response. These effects were attenuated by beta adrenergic blockade and unchanged by alpha adrenergic blockade. Infusions (0.025 µg/kg-min) of NE and E but not PE caused sustained vasoconstriction during a 10 minute infusion. These effects were attenuated by alpha adrenergic blockade. ISO (0.250 µg/kg-min) caused a sustained increase in HBF and this effect was attenuated with beta adrenergic blockade. These observations indicate the presence of beta receptors in the hepatic arterial circulation of the baboon. The absence of autoregulatory escape may be related to comparatively fewer beta receptors in this circulation than in other circulations or other species.

PHRENIC NERVE ACTIVITY IN THE EXTERIORIZED FETAL LAMB. I. Wyszogrodski, R.L. Williams & H.W. Taeusch, Jr. (intr. by M.E. Avery). Dept. of Physiology and McGill University-Montreal Children's Hospital Research Institute, Montreal, Canada.

Two types of respiratory activity (1-3 gasps/min. and irregular inspiratory movements of 1-4/sec.) have been described in both acute and chronic fetal lamb preparations by measuring tracheal pressure changes (J. Physiol. 220: 119, 1972). These observations have been extended by recording phrenic nerve activity together with tracheal pressure in four exteriorized fetal lambs of 120-135 days gestation. During spinal anesthesia to the ewe, the fetus was exteriorized, maintained at 39$\pm$1°C and the head enclosed in a saline filled glove. The electrical activity of small strands of the cervical phrenic nerve (dissected from either the intact nerve or central end of the cut trunk) was recorded with insulated bipolar silver electrodes immersed in a pool of paraffin. Two types of spontaneous neural activity were found. The first consisted of high frequency multi-unit bursts (mean duration 820 msec; range 450 to 2500 msec) that preceded a gasp. Individual units within these bursts reached peak discharge frequencies as high as 40 impulses/sec. The second type of neural activity consisted of single-unit, low frequency (1-14 impulses/sec), irregular background discharges lasting up to several seconds without changes in tracheal pressure. Occasionally, higher frequency bursts of single-unit activity were detected that were also unassociated with any tracheal pressure changes. Our data indicate that high frequency synchronized bursting activity occurs in the phrenic nerve which is the neural correlate of a fetal gasp. In addition, background discharges can be detected which reflect central nervous activity in the absence of tracheal pressure changes.

RESPIRATORY CYCLE OPTIMIZATION IN CO_2 INHALATION AND EXERCISE. S.M. Yamashiro*, T.N. Lauritsen*, F.S. Grodins, and J.A. Daubenspeck*. Biomedical Engineering, University of Southern California, Los Angeles, California.

By considering FRC, airflow pattern, inspiratory duration, and frequency as controlled variables contributing to the minimization of work during hyperpnea, cycle characteristics are predicted which are consistent with experimental data taken during CO_2 inhalation and exercise. Of particular interest is the prediction of a fixed relationship between inspiratory and total breath duration which is determined by static lung and chest-wall pressure-volume characteristics alone. Also, predicted respiratory frequency is a function of the static p-v curve and total respiratory resistance. In order to test the prediction formulae, the static p-v curve and total respiratory resistance were measured in all subjects (3). Breath-by-breath values of frequency and the ratio of inspired and total breath duration were computed in the steady-state at 2 levels of CO_2 inhalation (3 and 5%) and exercise (MRR = 3 and 6). In general, the data support the prediction formulae during hyperpnea but not at rest. All major observations dealing with the respiratory cycle during hyperpnea are consistent with the work minimization hypothesis. (Supported in part by USPHS, Grants GM 16437 and GM 52936.)

CARBONIC ANHYDRASE ACTIVITY IN SEPARATED MORPHOLOGIC CELL TYPES OF TURTLE URINARY BLADDER. Monroe J. Yoder* and Walter N. Scott, Dept. of Biology, New York University, and Department of Ophthalmology, Mount Sinai School of Medicine of CUNY, New York, New York.

The urinary bladder of the turtle, Pseudemys scripta, actively transports sodium and chloride and acidifies the urine. The mucosal epithelium consists of at least three morphologic cell types. We have separated the different cell types from the mucosal epithelium in an attempt to study their biochemical properties, properties that may be related to the transport functions of the different cell types. Mucosal epithelial cells were removed from urinary bladders by incubation in Ca^{2+}-free EDTA-Ringers. The isolated cells were layered over a discontinuous Ficoll gradient and centrifuged at 27,000 rpm for 45 min. Four bands of material were recovered; two bands contained viable mucosal cells. Chemical assay showed significant differences in the aminoglycan content of membrane fractions prepared from the bands of isolated cells. Electron microscopy showed one band (#2) contained predominently mitochondria-rich cells, and a more dense band (#3) contained granular cells. Cytochrome oxidase activity in band #2 was 180% of that in band #3, supporting the EM data. Carbonic anhydrase activity in the cells of band #2 (mitochondria-rich) was 250% that of the cells of band #3(granular). Our data indicate that it is possible to separate for biochemical studies the different cell types of the mucosal epithelium. The results indicate that carbonic anhydrase activity is significantly higher in the mitochondria-rich population of mucosal cells. This enzyme activity may be related to the Diamox-sensitive transport functions (chloride and bicarbonate) of the turtle bladder.

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CORONARY OCCLUSION DEMONSTRATION. Lloyd R. Yonce and David Raney* University of North Carolina Medical School, Chapel Hill, N.C.

We have prepared a television demonstration showing some of the effects of occluding a coronary artery of a dog. The student level may vary from paramedical undergraduates to medical students and graduate students, depending on the competence of the instructor. The program is organized to be used either as a self-instructional program or as a teaching package. The first segment of TV tape introduces the methods of recording arterial blood pressure, ventricular pressure, and electrocardiograms (Lead II and a wick electrode directly on the ventricle). A questionnaire on the control valves, including ectopic beats, allows the student to determine if he knows the first segment before proceeding to the second. The second segment shows the coronary occlusion with resulting color and contractibility changes in the infarcted area. The sequence ends with ventricular fibrillation and recovery following the use of defibrillating electrodes. A second questionnaire stresses important records from this sequence. The primary emphasis of this video tape demonstration is to involve the student during the presentation. Student response has indicated the objectives of the program have been accomplished.

VASCULAR RESPONSE IN SKELETAL MUSCLE TO HYPOXIA. L. R. Yonce and Enoch Wei*. University of North Carolina, Chapel Hill, N.C.

Hypoxemia in dogs, produced by breathing either 10 or 5% oxygen, causes a hypertension which reaches a peak value in 2 -5 minutes and declines to a stable level near the control value within 30 minutes. The vascular response to hypoxemia in the innervated gracilis muscle of dogs is an increased resistance which reaches a maximum in approxmately 3 min, then stabilizes within 30 min at a level below the maximum but above the control value. After the muscle is denervated, hypoxemia produces a decreased vascular resistance which reaches a minimum value within 3 minutes and then returns toward the control value within 30 minutes. If the arterial blood pressure is maintained at a constant level during the hypoxemia in the denervated muscle, the decreased resistance to hypoxemia is maintained and is inversely proportional to the arterial oxygen content. Pressure-flow curves, obtained during the hypoxemia indicate there is an "autoregulatory" type of response which is not present if the arterial blood pressure is prevented from changing. These experiments indicate the response to hypoxemia in skeletal muscle is a complex interaction between neurogenic, chemical and mechanical control mechanisms. The experimental procedures attempt to separate the components of the response due to each of the three control mechanisms. (Supported by NHLI-03757)

INCREASED GLUCOSE UPTAKE BY RAT LUNG WITH ONSET OF EDEMA S.L.Young & J.H. Knelson (intr. by T.B.Barnett) Environ. Protect. Agency, Chapel Hill, NC

We used an isolated perfused rat lung preparation (O'Neil & Tierney, Fed. Proc. 30:619,1971) to study the effect of spontaneous and NO_2 induced edema on lung glucose metabolism. The perfusate was Kreb's phosphate buffer, pH 7.40, plus 5 grams of bovine serum albumin, 4 mM glucose and 0.2 ml of washed packed red cells per 100 ml. The lungs were ventilated with 95% O_2 5% CO_2. Radiolabeled substrates were 1-^{14}C, 6-^{14}C, and U-^{14}C glucose. All lungs were ventilated and perfused for a control period of 45 min; 15 were ventilated and perfused for an additional 45 min with no change in the gas phase and 13 were exposed to edemagenic doses of NO_2 (20-40PPM) during the second 45 min perfusion period. At the end of 90 min, 8 of the unexposed lungs had a normal lung weight to DNA content ratio. Spontaneously in 7 lungs, and in all NO_2 exposed lungs, patchy visible edema developed after 30 min of the second perfusion period.

	TIME	CONTROL(n=8)	SPONT.EDEMA(n=7)	NO_2EDEMA(n=13)
GLUCOSE UPTAKE	0-45	0.46(.22)	0.50(.08)	0.54(.16)
mg/mgDNA-hr	45-90	0.54(.11)	0.85(.15)	0.84(.13)
		n.s.	p<.001	p<.001
LACTATE RELEASE	0-45	0.25(.08)	0.36(.09)	0.37(.14)
mg/mgDNA-hr	45-90	0.32(.04)	0.57(.11)	0.44(.15)
		n.s.	p<.01	n.s.

There was no correlation between the increase in glucose uptake and the degree of edema as measured by lung weight to DNA content ratios. There were no significant changes noted for post edema $^{14}CO_2$ production from any of the labeled glucose. We conclude that spontaneous and NO_2 induced edema 1) markedly increases glucose uptake 2) has a smaller and variable effect on lactate release 3) has no measurable effect on pentose pathway activity or glucose utilization by the tricarboxylic acid cycle in the isolated perfused rat lung.

COMPARTMENTAL BLOOD FLOW DISTRIBUTION IN CANINE JEJUNUM WITH FOOD OR 50 % GLUCOSE IN THE LUMEN. Y.M. Yu*, L.C. Yu* and C.C. Chou. Departments of Physiology and Medicine, Mich. State Univ., E. Lansing, Mich.

We have previously shown that luminal placement of food or 50% glucose in the canine jejunum increased local venous outflow. In the present study, we used radioactive microspheres (RM) to determine the distribution of capillary blood flow in the mucosa (MU), submucosa (SM) and muscle (MS) layers of the jejunum of fasted anesthetized (pentobarbital) dogs (N=10). Four adjacent segments of the jejunum were exposed, one lumen was left empty while the other 3 segments received 10 ml of one of the following solutions: isotonic nonabsorbable polyethylene glycol (PEG), digested dog food or 50% glucose. After 20 min., two types of RM (15 $\pm$ 5 μ, Ce-141 and Sr-85) were injected into the left ventricle 5 min. apart. Five minutes later the heart was arrested (intra-cardiac KCl), the segments were removed, separated into MU, SM and MS and their weights and radioactivities measured. The radioactivities per unit weight and distributions of RM in MU, SM and MS of the empty segment were similar to those of the segment containing PEG. Average distributions of RM in MU, SM and MS were 68.2, 5.1 and 26.7% of the total radioactivity of the jejunal wall respectively. On a weight basis, the segment containing food or 50% glucose had significantly greater radioactivities in the wall (food +47.5%, glucose +126.2%) and the MU (food +60.5%, glucose +176.7%) than did the control (empty or PEG). The radioactivity in SM or MS, however, did not change in a regular pattern. The results with Ce or Sr were the same. It is concluded that food or 50% glucose in the lumen increased total capillary blood flow of the jejunum and that the increased flow was mainly in the mucosal layer. (Supported by NIH Grant HL 15231).

BURSTING PATTERNS OF SPONTANEOUSLY ACTIVE NEURONS IN THE SENSORIMOTOR CORTEX. Irwin D. Zimmerman and Norman R. Kreisman*. The Med. Coll. of Pa., Phila. Pa. 19129 and Tulane U. Sch. Med., New Orleans, La. 70112.

Squirrel monkeys were anesthesized with alpha-chloralose, and immobilized with flaxedil. Unilateral craniotomy was performed and the sensory and motor cortex exposed. Recordings from single units were taken from the exposed areas by means of KCl filled microelectrodes, monitored on an oscilloscope and stored on magnetic tape for analysis. The data so obtained was computer processed and examined for it's burst activity; a burst being defined as any group of action potentials separated from one another by less than 10 msec. A plot of the percentage of occurrence of burst intervals resulted in a trimodal distribution for both the pre- and post-central neurons. These consisted of a first mode which contained neurons having less than 8% of their intervals below 10 msec. (post-centrally) and less than 18% of their intervals below 10 msec. (pre-centrally); a second mode containing those units whose burst discharge made up between 8 and 28% of the total intervals post-centrally and between 18 and 44% pre-centrally; and a third mode composed of units whose short intervals were at least 28% (post-centrally) and 44% (pre-centrally) of the total. An examination of the burst structure in terms of the mean interval within a burst, the mean spike per burst, the mean burst length and the mean time between bursts verified the slight dominance of burst activity in the pre-central cortex implicit in the percentage of occurrence distribution described above.